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**Abstract Book**

**June 13-16, 2023**

**LATEBREAKER**

## Health Disparities

**Social inequities in TB mortality risk in California: a decomposition approach to examine race and ethnicity, nativity, and impact of homelessness** Sara McElroy\* Sara McElroy Lisa Pascopella Pennan Barry

More than 80% of people with tuberculosis (TB) in California (CA), were born outside the U.S. Race and ethnicity are also associated with TB risk and mortality in CA, with higher TB incidence and mortality among persons of Asian, Black, or Hispanic race and ethnicity, compared to White. Racial, ethnic, and nativity inequities may be tied to social determinants of health (SDOH), e.g., experiencing homelessness. We estimated mortality risk during TB treatment and: 1) inequities between intersectional groups of race, ethnicity, and nativity; 2) the specific impact of homelessness by intersectional group, using three-way causal mediation analysis. We decomposed the effect of mortality attributed to homelessness and intersectional group into direct (PDE), indirect (PIE), and interaction effects (INTmed). Estimates are for adults in CA with active TB during 1993-2021 (n=74,671), adjusting for HIV, age, and sex. Among persons who died with TB (n=6,035), US-born (USB) Whites had the highest proportion of deaths after starting treatment (n=820, (13.8%)).

Proportions of homelessness varied across intersectional groups (from 1%, non-US-born (NUSB) Asian to 27%, USB Black), and differentially contributed to death with TB for each group (PIE). Compared to USB Whites, after controlling for the effect of homelessness, USB Blacks had a positive risk difference (RD=0.15(0.02-0.27)) and all NUSB intersectional groups had a negative RD; suggesting that TB mortality risk is greatest for USB Blacks (PDE). Mediated interaction effects were identified for NUSB Asian (RD= -0.65, (-1.2- -0.15)) and NUSB Hispanic (RD= -0.53, (-0.76- -0.29)) compared to USB White persons with TB, which indicates that these groups had lower TB mortality risk, that varied depending on the proportion of persons experiencing homelessness. Findings suggest that the experience of homelessness increases the risk of death with TB, even when controlling for unmeasured SDOH associated with race, ethnicity, and nativity.

**LATEBREAKER**

## Health Disparities

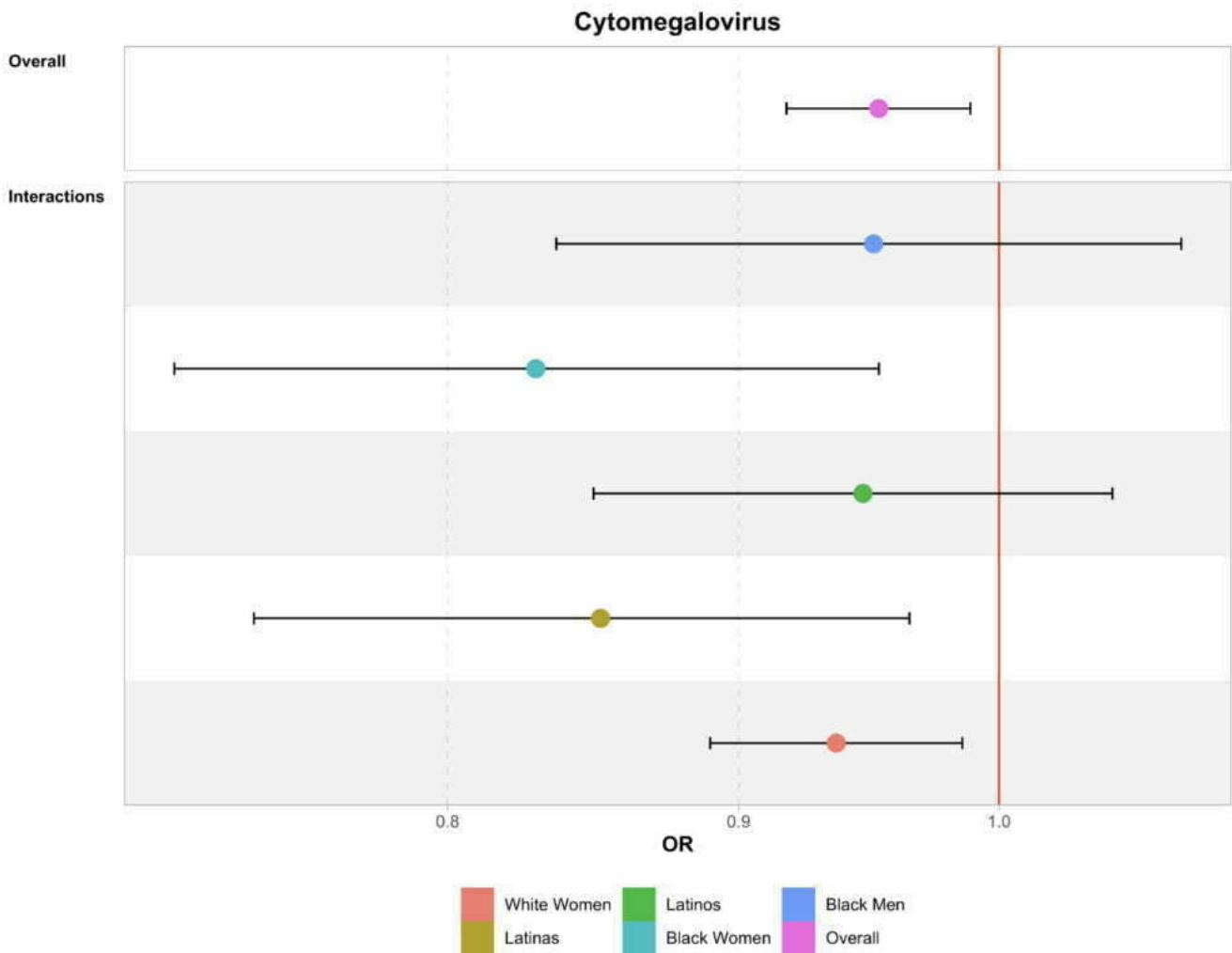
**The relationship between education and Cytomegalovirus infection varies by sociodemographic subgroup** Sokhna A. Gaye\* Sokhna A. Gaye Lucia Pacca Grace Noppert Anusha M. Vable

Previous research supports an inverse relationship between education and Cytomegalovirus (CMV) infection - indicating an association between early-life socioeconomic factors and chronic infection. However, it is unclear if this relationship varies by sociodemographic subgroup. Using the Health and Retirement Study (HRS) data, we investigated the association between education and CMV infection across gender and racial/ethnic subgroups.

Our sample included respondents interviewed in the 2016 HRS Venous Blood Study (N = 7,233). Education was operationalized as years of schooling, centered at 12. CMV infection was defined by dichotomizing CMV Immunoglobulin G (IgG) as CMV seropositive (CMV IgG  $\geq$  0.5 U/mL) and CMV seronegative (CMV IgG < 0.5 U/mL). We used logistic regressions to estimate the overall association of education with CMV, and included race-by-gender interaction terms to evaluate effect modification. We adjusted for age (centered at 60), parental education, and immigration status in all models.

In our sample (mean age 68 years, 58% women), mean education was 13 years of schooling and CMV infection prevalence was 71.3%. Overall, education was associated with lower likelihood of CMV infection (OR = 0.95, 95% CI: 0.92, 0.99). Compared to White men, each additional year of education was associated with lower odds of CMV infection for all women. The differential association was largest for Black women (OR = 0.83, 95% CI: 0.72, 0.95), followed by Latinas (OR = 0.85, 95%CI: 0.74, 0.96), and White women (OR = 0.89, 95%CI: 0.87, 0.92). There was no evidence of a differential relationship between education and CVM infection for Black and Latino men compared to White men.

We found evidence of an overall protective relationship between education and CMV infection, and evidence of differential relationships by sociodemographic subgroups such that Black, Latina, and White women benefit more from each year of education than White men.



**Figure** - The plot shows odds ratios of associations between education and CMV in our interaction model. The top panel shows the main effect of education on CMV infection for White men (the reference group); the bottom panel shows the interaction terms with education for each race-by-gender subgroup. The model adjusted for age (centered at 60), parental education, and immigration status.



**LATEBREAKER**

## Health Disparities

**Adolescent Student Bullying Victimization: Differences across Presidential Administrations**

Paul Villafuerte\* Paul Villafuerte Elizabeth Kelvin

**BACKGROUND:** Student bullying is increasingly recognized as a public health problem. Recent political shifts in the United States (US) have led to concerns that political leadership may impact bullying behavior.

**OBJECTIVE:** We assessed the association of presidential administration (Trump versus Obama) on bullying among US high school students overall and if the association was modified by race/ethnicity or sex .

**METHODS:** We used 2009-2019 national Youth Risk Behavior Survey (YRBS) data. Crude and multivariable logistic regression models were run to assess the association of the Trump administration (year 2017-2019) (versus the 2009-2016 Obama administration) with being bullied in the past year (in-person or cyber) and tested Interaction among presidential administration, sex, and race/ethnicity.

**RESULTS:** Overall, 23.9% of US high school students reported having been bullied in the past year, but there was no difference by presidential administration (aOR=1.02, p=0.698). There was significant interaction between presidential administration and race/ethnicity for Black (interaction p=0.029) and Hispanic (interaction p=0.004). In the stratified models, among Black students there was a significantly higher odds of being bullied (OR = 1.22, p < 0.001) while among Hispanics there was a significantly lower odds of being bullied (OR = 0.81, p = 0.010) during the Trump administration compared to the Obama administration.

**CONCLUSION:** National political trends, as represented by presidential administration, were associated with changes in bullying in high school that was experienced differently by racial/ethnic identity. Further research is needed to assess these associations under additional presidential administrations and to explore what was going on in the country during those administrations that impacted child behavior to inform the development of effective anti-bullying programs.

**LATEBREAKER**

## Health Disparities

**Race and Risk of Breast-Cancer Related Lymphedema in the United States 2004-2017** Janit Leonard\* Janit Leonard Chris Agala Kristalyn Gallagher Yemi Ogunleye

**Introduction:**

**Breast Cancer-related lymphedema (BCRL) is a progressive condition caused by impairment of lymphatic drainage resulting in accumulation of excess tissue fluid in the extremity and inflammatory changes. This study aimed to identify risk factors for and temporal trends of the incidence of BCRL in a population-based cancer registry.**

**Methods:**

**We used SEER-Medicare data for 2004-2017 to identify female breast cancer cases who had breast surgery and developed BCRL during follow-up time, based on ICD-9 and ICD-10 procedure and diagnosis codes. We performed a univariate analysis of risk of BCRL, assessed crude risks and relative risks for patient characteristics and BCRL diagnosis using generalized linear models and Cox proportional-hazards model to determine risk over time of developing lymphedema after breast surgery.**

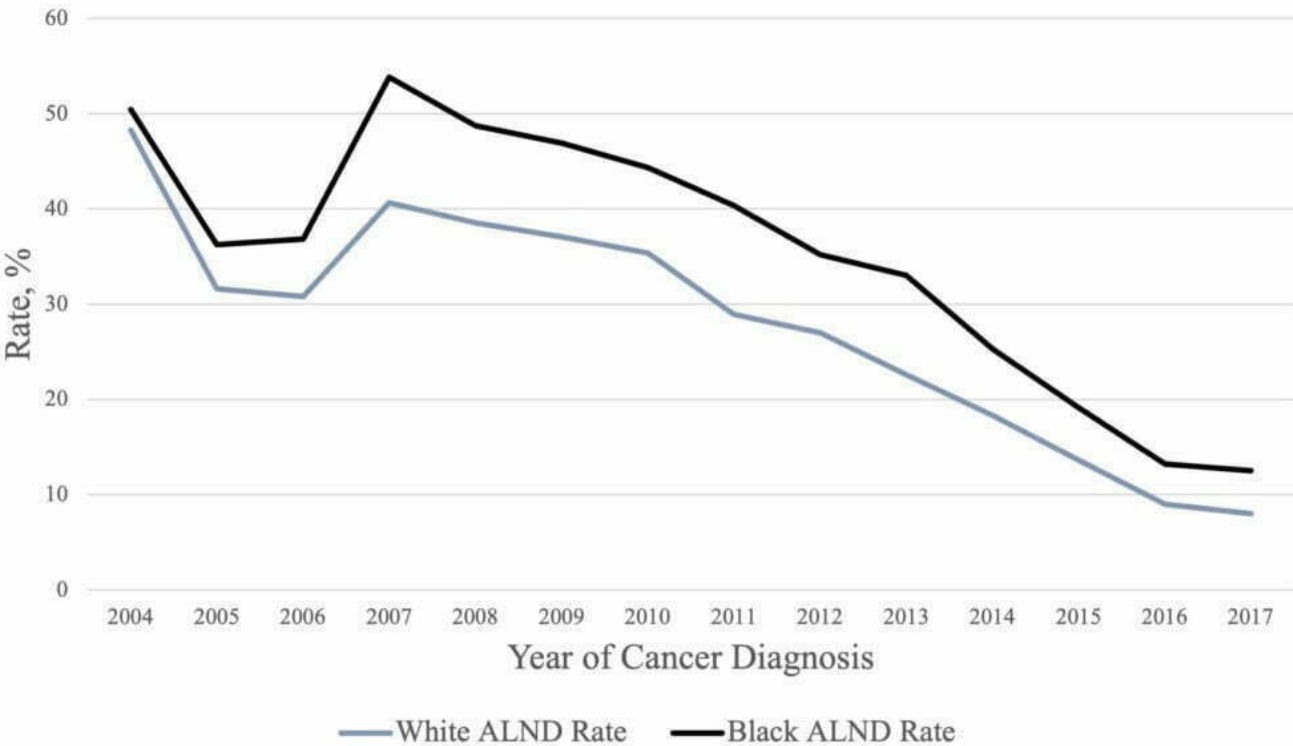
**Results:**

**A total of 187,608 female cases who had undergone breast cancer surgery were identified. Of these, 165540 (88.43%) were white, 12903 (6.89%) were black, and 8764 (4.69%) were unknown or other race. Rates of ALND ( $p<0.0001$ ) and lymphedema ( $p<0.0001$ ) decreased for all races over the study period. A total of 13571 patients (7.23%) developed BCRL. Black patients had a higher rate of ALND than white patients ( $p<0.0001$ ). Black race was associated with increased risk of lymphedema diagnosis (HR 1.153 (1.067, 1.245) in a multivariate analysis.**

**Conclusion:**

**Further research is needed to evaluate if the increased risk in black patients is due to biology of disease, variations in treatment, or other unmeasured risk factors for BCRL. Early diagnosis and treatment programs targeting these patients may help reduce the burden and severity of BCRL.**

Rates of Axillary Lymph Node Dissection (ALND) by Race, 2004-2017



**Estimating the long-term effects of lifestyle interventions for cancer survivors using target trial emulation and dynamic treatment strategies** Emma E. McGee\* Emma E. McGee Miguel A. Hernán Edward Giovannucci Lorelei A. Mucci Walter C. Willett Yu-Han Chiu Barbra A. Dickerman A. Heather Eliassen

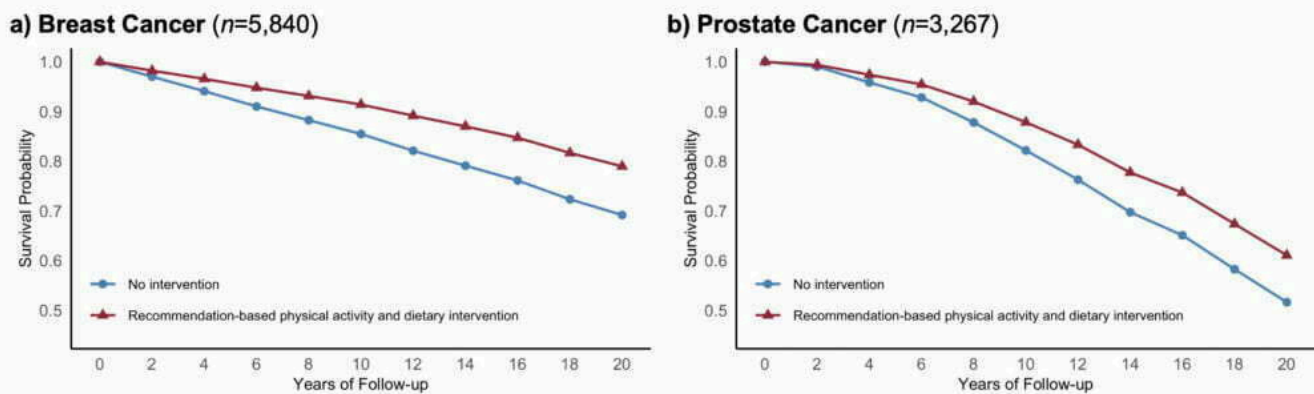
Approximately 40% of the US population is expected to be diagnosed with cancer during their lifetime. As the number of cancer survivors increases, it is imperative to identify effective lifestyle interventions for these individuals. However, randomized trials of interventions with long-term outcomes are not always practical. Observational data may therefore be needed to emulate a target trial.

Using data from 3 prospective US cohorts, we emulated a target trial of a recommendation-based, dynamic intervention which required adhering to current recommendations for physical activity and dietary intake of fruits, vegetables, whole grains, legumes, processed foods, red meat, processed meat, and sugar-sweetened beverages. Eligible individuals were diagnosed with nonmetastatic breast or prostate cancer and were free of conditions that could preclude following the recommendations at baseline. We used the parametric g-formula to estimate 20-year risks of all-cause mortality. We conducted sensitivity analyses to address potential biases, including modifying the dynamic intervention to assess potential confounding by disease severity.

Among 9,107 eligible adults diagnosed with breast or prostate cancer, 1,791 deaths occurred. The estimated 20-year mortality risk for adults with breast cancer was 21.0% under the recommendation-based intervention vs. 30.8% under no intervention (RD: -9.8%, 95% CI [-12.4%, -7.4%]; RR: 0.68, 95% CI [0.60, 0.76]). For prostate cancer, the 20-year mortality risk was 39.6% under the recommendation-based intervention vs. 48.6% under no intervention (RD: -9.1%, 95% CI [-12.6%, -5.3%]; RR: 0.81, 95% CI [0.73, 0.89]). Results were robust to sensitivity analyses.

Adults diagnosed with breast or prostate cancer may experience meaningful reductions in 20-year mortality under a sustained physical activity and dietary intervention. Our approach may inform the design of future studies evaluating the effectiveness of lifestyle interventions for cancer survivors.

**Figure 1.** Estimated survival for adults diagnosed with breast or prostate cancer under a recommendation-based physical activity and dietary intervention vs. under no intervention, Health Professionals Follow-up Study (1990 – 2018), Nurses' Health Study (1990 – 2014), and Nurses' Health Study II (1997 – 2019).<sup>1</sup>



<sup>1</sup>The recommendation-based intervention required sustained adherence to the following recommendations: (i) engage in  $\geq 1.25$  hours/week vigorous or  $\geq 2.5$  hours/week moderate physical activity, (ii) eat  $\geq 5$  servings/day fruits and vegetables, (iii) eat  $\geq 3$  servings/day whole grains and legumes, (iv) eat  $\leq 1$  serving/day processed foods, (v) eat  $\leq 3$  servings/week red meat, (vi) eat  $< 1$  serving/week processed meat, and (vii) do not consume sugar-sweetened beverages. Survival estimates were obtained from the parametric g-formula with the following covariates: age, cancer stage, primary cancer treatment modality, tumor estrogen receptor status (breast cancer), menopausal status prior to diagnosis (breast cancer), postmenopausal hormone replacement therapy use prior to diagnosis (breast cancer), Gleason grade (prostate cancer), PSA level at diagnosis (prostate cancer), smoking history, alcohol consumption, body mass index, diabetes, hypertension, hypercholesterolemia, parental history of myocardial infarction before age 60, conditions that may preclude following the recommendations (metastasis [prostate cancer], myocardial infarction, stroke, congestive heart failure, amyotrophic lateral sclerosis, or functional impairment), total energy intake, physical activity, and dietary intake of fruits and vegetables, whole grains and legumes, processed foods, red meat, processed meat, and sugar-sweetened beverages.

**Selection bias as an explanation for the observed protective association of childhood adiposity with breast cancer** C Mary Schooling\* C Mary Schooling Kezhen Fie Jie Zhao

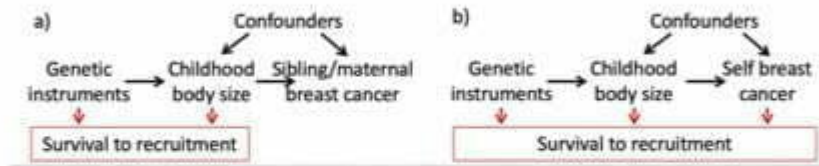
**Background:** Recalled childhood adiposity is inversely associated with breast cancer observationally, including in Mendelian randomization (MR) studies, questioning the role of childhood adiposity. Breast cancer studies recruited in adulthood only include survivors of childhood adiposity and breast cancer. We assessed recalled childhood adiposity on participant reported sibling and maternal breast cancer to ensure ascertainment of non-survivors using MR.

**Methods:** We obtained independent strong genetic predictors of recalled childhood adiposity (comparative body size at 10 years (thinner, about average, plumper)) for women and their associations with participant reported own, sibling and maternal breast cancer from UK Biobank genome wide association studies (GWAS). We obtained MR inverse variance weighting estimates.

**Results:** Childhood adiposity in women was inversely associated with own breast cancer (odds ratio (OR) 0.66, 95% confidence interval (CI) 0.52 to 0.84 for plumper compared with thinner)) but was unrelated to participant reported sibling (OR 0.85, 95% CI 0.60 to 1.20) or maternal breast cancer (OR 0.84, 95% CI 0.67 to 1.05 respectively) for the same comparison.

**Conclusions:** Weaker inverse associations of recalled childhood adiposity with breast cancer with more comprehensive ascertainment of cases before recruitment suggests the inverse association of recalled childhood adiposity with breast cancer is due to selection bias arising from preferential selection of survivors. Greater consideration of left truncation in public health relevant causal inferences is warranted.

Directed acyclic graph showing that a Mendelian randomization study of childhood adiposity on self breast cancer recruited in middle to older age is biased by selection on genetic endowment and surviving breast cancer (Figure 1b) but a study of participant reported sibling or maternal breast cancer is likely less biased because it does not select on surviving breast cancer to recruitment (Figure 1a). A box indicates selection on an attribute.



**The impact of adiposity across the life course on ovarian cancer risk** Jennifer Ritonja\*  
Jennifer Ritonja Sreenath Madathil Belinda Nicolau Kevin L'Espérance Vikko Ho Michal  
Abrahamowicz Anita Koushik

Adiposity is hypothesized to promote ovarian cancer development given its influence on hormones. The majority of past studies have measured adiposity during middle to late adulthood and have reported a possible weak positive association. Among a few studies examining early adulthood adiposity, most showed a positive association, suggesting that exposures at distinct life periods may impact risk differently. A life course approach to epidemiology provides a formal framework to link exposures over life to later health events. Using this approach, we sought to identify if ovarian cancer risk is influenced by adiposity during certain critical or sensitive life periods or accumulated over life. A population-based case-control study was conducted in Montreal, QC, Canada in 2011-16. Participants reported their tallest attained height and body weight for each decade of life from age 20 to study participation, which were used to calculate body mass index (BMI). We used a Bayesian relevant life course exposure model to estimate the relative impact of BMI on ovarian cancer risk for three different life periods: early adulthood (age 20), childbearing years (age 30), and menopause (age 50). In preliminary results among the 363 cases and 702 controls aged 50 years or older, the adjusted OR for the lifetime effect of BMI (per 5 kg/m<sup>2</sup> increase) on ovarian cancer risk was 1.14 (95% credible interval [CrI]: 0.93-1.39). In comparing different life periods, BMI in early adulthood was identified as a potential sensitive period (OR: 1.06, 95% CrI: 0.96-1.22). ORs for invasive cancer were stronger for both the lifetime effect (OR: 1.23, CrI: 0.97-1.55) and for early adulthood (OR: 1.10, CrI: 0.99-1.36). Other life period definitions (e.g., ages 20, 40, 50) also suggest a sensitive period in early adulthood. These preliminary results suggest that higher adiposity during adulthood is associated with a higher ovarian cancer risk, and early adulthood may be a sensitive period.



**Estimating the effect of pre-diagnosis physical activity on survival after breast cancer: bias, bias and more bias** Frances Albers\* Frances Albers Ziyu Wang Brigid M. Lynch Sabrina E. Wang Dallas R. English

**Background:** Pre-diagnosis physical activity is reported to improve survival for women with breast cancer. However, studies of pre-diagnosis exposures and cancer survival are affected by several biases, made clear when applying a target trial framework. We investigated the impact of selection bias, immortal time bias, confounding and adjustment for mediators in a systematic review and meta-analysis of the effect of pre-diagnosis physical activity on survival after breast cancer.

**Methods:** Medline, Embase and Emcare were searched from inception to November 2021 for studies examining pre-diagnosis physical activity and overall or breast cancer-specific survival after breast cancer. Random-effects meta-analysis was used to estimate pooled HRs and 95% CIs comparing highest versus lowest pre-diagnosis physical activity levels. Subgroup meta-analyses were used to compare HRs of studies with and without different biases. ROBINS-E was used to assess risk of bias.

**Results:** We included 19 studies. Women with highest versus lowest pre-diagnosis physical activity had higher breast cancer-specific survival across most analyses. However, uncertainty exists because overall risk of bias was serious. Protective effects were attenuated in studies that adjusted for mediators (HR = 0.95, 95% CI: 0.86 to 1.04) compared to those that did not (HR = 0.67, 95% CI: 0.54 to 0.83). Studies with immortal time bias indicated a protective effect (HR = 0.78, 95% CI: 0.67 to 0.91) whereas those without suggested no effect (HR = 0.94; 95% CI: 0.76 to 1.16). Insufficient studies were available to investigate selection bias and confounding.

**Conclusion:** Biases can substantially change effect estimates. Due to the misalignment of treatment assignment (before diagnosis), eligibility (at diagnosis), and start of follow-up (before, at or after diagnosis), bias is inevitable. It is not possible to correctly estimate the effects of pre-diagnosis exposures on cancer survival with current epidemiological methods.

**Sequence analysis in life course epidemiology of cancer: conceptualization and application**

Bernadette van der Linden\* Bernadette van der Linden Rainer Gabriel Stefan Sieber Matthias Studer Arnaud Chiolero Stéphane Cullati

**GOAL** The article presents sequence analysis and its potential for life course epidemiology of cancer

**PRINCIPLE** The life course perspective is a growingly popular approach in epidemiology and public health to study the interaction between individual lives, social changes, and health. It stresses the importance to understand outcomes, such as health, within their unfolding trajectories, which raises methodological challenges. One major challenge is to characterize the individuals' life course trajectories of employment and family, which are embedded in a societal context. Instead of focusing on the occurrence of specific events or at certain time points, the life courses of individuals are treated as a whole. Relying on data mining techniques, the method provides a typology of recurrent trajectories observed in the sample. The main concepts of life course epidemiology including duration, timing, ordering, cumulative dis/advantage, and critical periods can be considered.

**CASE STUDY** As an illustration, using data for 9,543 women from the Survey of Health, Ageing, and Retirement in Europe followed-up over 16 years, we assessed how employment trajectories predict cancer. Using sequence and clustering analyses, we identified eight employment trajectories from 16 to 65 years old: 1) mainly full-time, 2) mainly domestic/family work, 3) mainly full-time employment to domestic/family work, 4) mainly self-employed, 5) various employment to part-time, 6) domestic/family work to full-time employment, 7) mainly unemployed, and 8) other/missing (Figure). The typology of trajectory was used as a covariate in a Cox regression model predicting cancer risk. The results showed that the mainly domestic/family work trajectory was associated with the lowest risk of developing cancer.

**IMPLICATION** Sequence analysis is an insightful method to consider the whole life course of individuals. The typology of trajectories can be used to explore associations with cancer or other health outcomes.

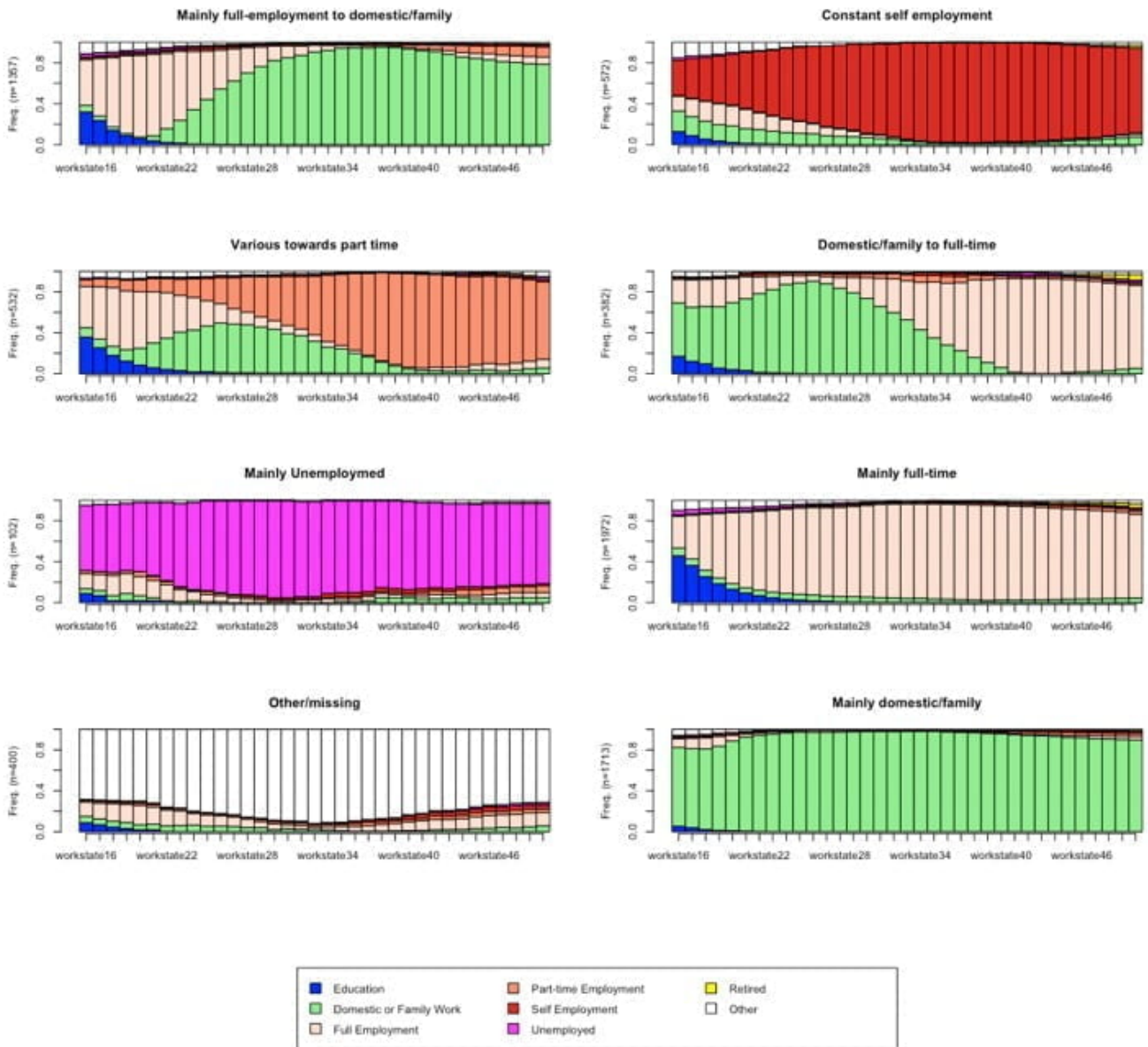


Figure: Sequence density plots for the identified employment trajectories. The bars represent the proportion of respondents in each of the employment types at a specific age.

**Adult lifetime predicted vitamin D exposure and the risk of ovarian cancer** Jennifer Ritonja\*  
Jennifer Ritonja Coraline Danieli Magnoudewa Priscille Pana Michael Palmer Kevin L'Espérance  
Vikki Ho Michal Abrahamowicz Anita Koushik

Vitamin D has received wide scientific interest in cancer prevention. Studies of serum 25-hydroxyvitamin D [25(OH)D], a biomarker of total vitamin D exposure, have suggested an inverse association with ovarian cancer risk, though not consistently. However, 25(OH)D was generally only measured in late adulthood, which may not capture the etiologically relevant period. While serum 25(OH)D is the best available biomarker of total vitamin D, a cost-efficient alternative is to use models that predict serum 25(OH)D from lifestyle and personal attributes. In a population-based case-control study in Montreal, Canada (490 cases, 896 controls), we investigated predicted 25(OH)D over the adult lifetime in relation to ovarian cancer risk. Predicted 25(OH)D scores were computed for each year of life from age 20 to two years prior to study participation using previously validated prediction models. Unconditional logistic regression models were used to estimate adjusted odds ratios and 95% confidence intervals for average lifetime 25(OH)D and ovarian cancer risk. In addition, a flexible weighted cumulative exposure model was used to account for the impact of timing of past 25(OH)D exposure. For each 20 nmol/L increase in average lifetime 25(OH)D, a 27% lower ovarian cancer risk was observed (OR: 0.73, 95% CI: 0.55-0.96). In the weighted cumulative exposure model, the inverse association was strongest 5-15 years (OR: 0.86 per 20 nmol/L increase, 95% CI: 0.73-0.98) and 45-60 years (OR: 0.89, 95% CI: 0.83-1.00) prior to study participation. Recent exposure (<5 years) was not associated with risk. In bias sensitivity analyses that assessed the potential for selection bias using inverse-probability weighting and the influence of error in our predicted 25(OH)D scores using SIMEX methodology, the results did not change appreciably. These results support that higher 25(OH)D is associated with a reduced ovarian cancer risk, and the impact may be more important in earlier life periods.

## Environment/Climate Change

**The effect of heat waves on preterm and early-term birth in three western U.S states** Amy Finch\* Amy Fitch Mengjiao Huang Matthew Strickland Andrew Newman Joshua L. Warren Howard Chang

**Background:** Heat wave frequency and intensity is increasing and this trend is more pronounced in urban areas.

**Methods:** We examined the relationship between heat waves and preterm (<37 weeks) and early-term (37-38 weeks) birth in California, Nevada, and Oregon using two approaches. First, Daymet-based temperatures were linked to births in the 8 largest metropolitan statistical areas. Second, a novel urban heat island-focused dataset was linked to births by zip code. Daily mean temperatures in each location (MSA and zip code) were used to identify heat waves from 1993 to 2017. Heat waves were defined in three ways during the 4-day exposure window preceding birth: 1) number of days over 97.5<sup>th</sup> percentile threshold, 2) number of consecutive days over the threshold, and 3) heat wave intensity (average degrees above the threshold). Live, singleton preterm or early-term births were identified from state vital records. We conducted case-crossover (conditional logistic regression) and time-series (Poisson regression accounting for overdispersion) analyses, pooling across locations using a random effects meta-analysis.

**Results:** Across the three states there were 14,685,648 total births, 1,279,298 preterm births and 3,614,744 early term births from 1993 to 2017. MSA results showed modestly elevated rates of early-term birth for heat waves occurring in the 4 days preceding birth. Pooled RRs (95% CIs) for 2-, 3-, and 4-consecutive days above the 97.5<sup>th</sup> percentile mean temperature were 1.009 (1.000, 1.017), 1.011 (0.999, 1.023), and 1.017 (0.998, 1.036), respectively. However, in the pooled MSA analysis, there was no evidence of an association between heat waves and preterm birth: 2-consecutive day RR = 1.007 (0.983, 1.031), 3-day = 0.995 (0.971, 1.019), and 4-day = 1.000 (0.966, 1.035). MSA results are being compared to zip code-based results in ongoing analyses.

**Conclusion:** We observed a stronger signal for the acute effect of heat waves on early-term birth than for preterm birth.

**Drought in Western United States displaces and amplifies coccidioidomycosis, an emerging fungal disease: a longitudinal surveillance study** Jennifer Head\* Jennifer Head Gail

Sondermeyer-Cooksey Alexandra K Heaney Alexander T Yu Isabel Jones Abinash Bhattachan Simon K Campo Robert Wagner Whitney Mgbara Sophie Phillips Nicole Keeney John Taylor Ellen Eisen Dennis P Lettenmaier Alan Hubbard Gregory S Okin Duc J Vugia Seema Jain Justin V Remais

**Background**

Drought is an understudied driver of infectious disease dynamics. Amidst the ongoing southwestern North American megadrought, California is experiencing the driest multi-decadal period since 800CE, exacerbated by temperature. We examined the influence of drought on coccidioidomycosis, an emerging infectious disease in the southwestern U.S.

**Methods**

We analyzed California census tract-level surveillance data from 2000–2020 using generalized additive models and distributed monthly lags on precipitation and temperature. We then developed an ensemble prediction algorithm of incident cases per census tract to estimate the counterfactual incidence that would have occurred in the absence of drought.

**Results**

An estimated excess of 1,467 and 2,649 drought-attributable cases were observed in California in the two years following the 2007-2009 and 2012-2015 droughts, respectively, more than offsetting declines experienced during drought. An interquartile range (IQR) increase in summer temperatures was associated with 2.02 (95% CI: 1.84, 2.22) times higher incidence in the following fall, and a one IQR increase in precipitation in the winter was associated with 1.45 (95% CI: 1.36, 1.55) times higher incidence in the fall. The effect of winter precipitation was 36% (95% CI: 25, 48%) stronger when preceded by two dry, rather than average, winters. Incidence in arid counties was most sensitive to precipitation fluctuations, while incidence in wetter counties was most sensitive to temperature.

**Interpretation**

In California, multiyear cycles of dry conditions followed by a wet winter amplifies transmission, especially in historically wetter areas. With anticipated increasing frequency of drought in southwestern U.S., continued expansion of coccidioidomycosis, along with more intense seasons, may be expected.

## Environment/Climate Change

**Is short-term exposure to heat associated with anxiety and depression? A case-crossover analysis** Anne M Weaver\* Anne Weaver Christine L Gray Erik Slawsky Joshua Moyer Cavin Ward-Caviness

**Background:** Health impacts of heat are increasingly important due to climate change. Anxiety and depression are common and understudied mental health conditions, which may be associated with heat exposure. We examined associations between short-term (5-day) mean apparent temperature and health visits for anxiety or depression in North Carolina in a case-crossover analysis of electronic health records.

**Methods:** We identified 2256 adults with anxiety or depression in a random sample of electronic health records from University of North Carolina Healthcare System patients 2004-2018. We examined 5-day mean apparent temperature (incorporating temperature and humidity) at the ZIP code level for patients during 9177 visits with a diagnosis of anxiety or depression compared to control time points 14 and 28 days before and after each visit. We used conditional logistic regression models adjusted for personal (age, sex, race, health insurance status), environmental (season, annual PM<sub>2.5</sub> concentration, climate division) and neighborhood (median household income, percent Bachelor degree or more, percent urban) factors. We conducted analyses overall and stratified by diagnosis, sex, and season.

**Results:** Median age of patients was 46 years, 70% were female, and 75% were White. Mean 5-day apparent temperature was 18.5°C (SD 10.4). We did not observe an association between 5-day mean apparent temperature and anxiety or depression overall (OR 1.00, 95% CI 1.00-1.00). However, we observed positive associations between temperature and anxiety or depression during summer months (OR 1.09, 95% CI 1.07-1.11) and inverse associations in winter (OR 0.96, 95% CI 0.95-0.98).

**Conclusions:** We did not observe associations between apparent temperature and anxiety or depression overall, but we observed season-specific associations. In hotter months, increased apparent temperature may be detrimental to mental health; in colder months, increased apparent temperature may be beneficial to mental health.

**Wildfire-related PM<sub>2.5</sub> and mortality in California** Robbie M. Parks\* Robbie Parks Tarik Benmarhnia Joan A. Casey M. Maria Glymour Marianthi-Anna Kioumourtzoglou Mathew V. Kiang

### Background and aim

Wildfires and resulting smoke are critical public health concerns, particularly in California, the most populous US State. Previous studies have comprehensively demonstrated that elevations in overall fine particulate matter (PM<sub>2.5</sub>) pollution increase population mortality. The impact of wildfire-related PM<sub>2.5</sub> may differ, however, due to potentially different composition. As wildfires increase in both intensity and frequency, comprehensive assessment of the association between wildfire-related PM<sub>2.5</sub> and all-cause and cause-specific mortality across multiple years of study is needed.

### Methods

We used daily mortality data provided by the California Department of Public Health and a comprehensive well-validated record of wildfire-related PM<sub>2.5</sub> concentrations from an ensemble-based statistical approach at the daily census tract level in California over 4 years (2016–2019). We implemented a time-stratified case-crossover design with distributed lag non-linear terms (0-6 days) to estimate associations between daily census tract-level wildfire-related PM<sub>2.5</sub> and death rates in California, accounting for daily temperature with a similar distributed lag non-linear structure. We also examined how the association varied by cause of death, sex and age group.

### Results

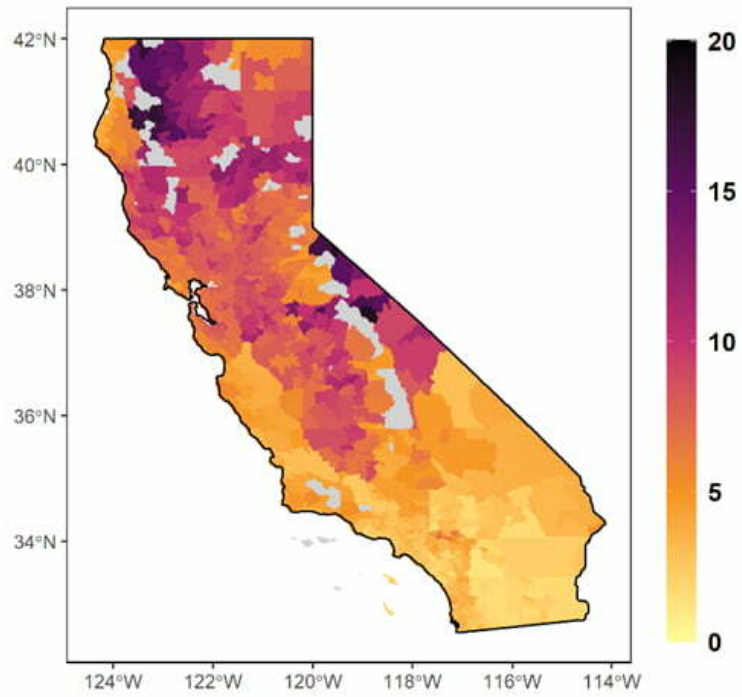
For wildfire days, wildfire-related PM<sub>2.5</sub> concentrations had an overall mean of 1.4 µg/m<sup>3</sup>, standard deviation of 5.7 µg/m<sup>3</sup>, and a maximal value of 203.2 µg/m<sup>3</sup>. There were 1,069,078 million deaths in California during 2016–2019. In preliminary results, for all-cause deaths, a 10 µg/m<sup>3</sup> increase in wildfire-related PM<sub>2.5</sub> across 0-6 lag days was associated with a cumulative 7.8% (95%CI:-0.7%,16.3%) increase in death rates for females aged 65 years or older, with an 8.7% (95%CI:-0.3%,17.7%) increase for males aged 65 years or older.

### Conclusions

Our findings demonstrate the potential deadly threat of wildfire smoke PM<sub>2.5</sub> to public health, and the need for targeted interventions and additional preparedness for wildfire-related PM<sub>2.5</sub>, especially in the immediate days following elevated concentrations.



**Mean Wildfire PM<sub>2.5</sub> ( $\mu\text{g m}^{-3}$ )  
(2006-2020)**



## Environment/Climate Change

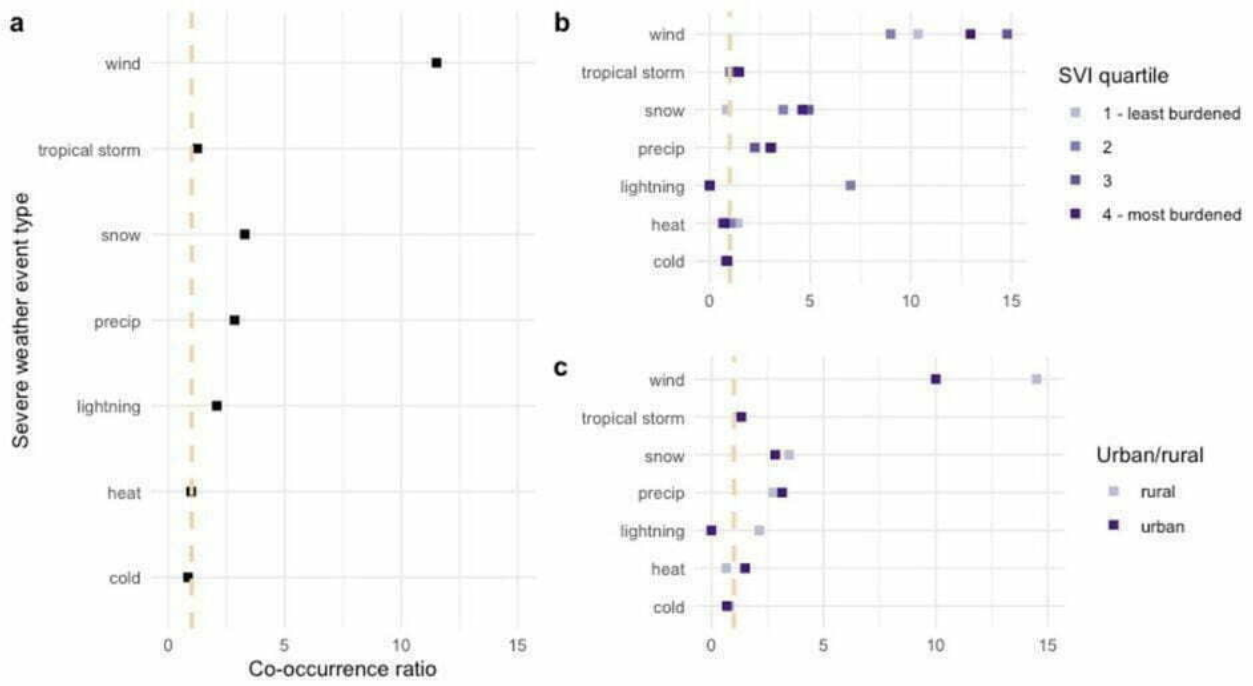
**The powerful and the power outages: a climate justice-focused assessment of severe weather-driven power outages in New York State, 2017-2020** Nina M. Flores\* Nina M. Flores Alexander J. Northrop Vivian Do Leo Y. Jiang Robbie M. Parks Diana Hernández Joan A. Casey

**Background:** As a result of discriminatory practices, marginalized communities often live in regions disproportionately impacted by flooding, extreme heat, and other severe weather events. As climate change increases such events which damage the electrical grid, power outages may present new challenges for climate justice. Here, we use granular New York State (NYS) data to characterize the impact of severe weather events on power outages, while considering neighborhood vulnerability.

**Methods:** We obtained the hourly number of customers without power in electrical power operating localities (POL; n=1865) throughout NYS from 2017-2020. We spatially aggregated hourly temperature, precipitation, wind speed, lightning strike, and snowfall data to POLs. We linked outages to severe weather (windspeed  $\geq 30$ kts, temperature  $\leq 20^\circ\text{F}$ , temperature  $\geq 90^\circ\text{F}$ , daily accumulated precipitation  $\geq 1$ inch, daily accumulated snowfall  $\geq 1$  inch, presence of tropical storm), and calculated the ratio of outages occurring with severe events. To investigate power outage-related climate injustices, we repeat the analyses stratified by (a) urbanicity (rural, urban) and (b) quartiles of the CDC Social Vulnerability Index (SVI).

**Results:** We found severe weather events contributed to 17.5% of outages across NYS with severe wind, snow, and precipitation contributing to the most outages. We observed heterogeneity in co-occurring ratios by SVI quartile and urban/rural status; we identified higher co-occurrence ratios for wind, snow, and precipitation for rural POLs and POLs with greater social vulnerability (Figure 1).

**Conclusion:** Rural regions and regions with higher social vulnerability were more likely to face wind-, snow-, and precipitation- driven outages; grid improvements should be prioritized in such regions for more equitable grid reliability in a changing climate.



**Figure 1.** The co-occurrence ratio of severe weather events and power outages presented (a) overall and stratified by (b) SVI quartile and (c) urban/rural status.

## Environment/Climate Change

**Shedding light on environmental justice and power outages in New York State** Vivian Do\*

Vivian Do Alexander J. Northrop Nina M. Flores Diana Hernández Joan A. Casey

Background: Power outages are becoming more common and severe, but outage exposure may occur differentially across communities. Health consequences associated with outages include temperature-related illnesses, injuries, and cardiovascular/respiratory hospitalizations. Housing policies and discriminatory practices may have resulted in disparate infrastructure improvements, increasing the likelihood and severity of outages. We conducted an environmental justice analysis of outages in New York State (NYS).

Methods: With hourly 2017-2020 NYS Department of Public Service data, we created a census tract-level metric, outage duration. We considered outage duration as the hours of an outage event, and we defined a tract to be exposed to an outage when the hourly percentage of customers without power exceeded the 90th percentile of all customers without power across tracts by the following strata: New York City (NYC), other urban areas, and rural areas. For each of these categories, we generated quartiles of the Centers for Disease Control Environmental Justice Index (EJI), which ranks tracts using environmental, social, and health metrics and ranges from 0 (least burden) to 1 (greatest burden). We ran negative-binomial regression models to assess the association of EJI quartiles and average outage duration stratified by NYC, other urban areas, and rural areas.

Results: Outages lasted an average of 17.1 hours in NYC, 5.4 hours in other urban areas, and 6.4 hours in rural areas. Compared to outages in the least vulnerable tracts (EJI Q1), outages in the most vulnerable tracts (EJI Q4) were 40% longer (95% CI: 10%, 80%) in NYC and 20% longer (95% CI: 10%, 30%) in other urban areas. We observed no association in rural tracts.

Conclusions: In NYC and other NYS urban areas, higher EJI was associated with longer outages. Future energy policies should focus on allocating resources equitably to reduce disparities in outage exposure.

**Genetic proxies for antihypertensive drugs and mental disorders: Mendelian randomization study in European and East Asian populations** Bohan Fan\* Bohan Fan Jie Zhao

**Background:** Mental disorders are among the top causes of disease burden worldwide. Previous evidence regarding the repurposing opportunities of antihypertensives for mental disorders treatment is conflicting and cannot establish causation.

**Methods:** We used Mendelian randomization (MR) to assess the effects of angiotensin-converting-enzyme inhibitors (ACEIs), beta-blockers (BBs), and calcium channel blockers (CCBs) on risk of bipolar disorder (BD), major depression disorder (MDD), and schizophrenia (SCZ). We used published genetic variants in antihypertensive drugs target genes and correspond to systolic blood pressure (SBP) in Europeans and East Asians, and applied them to genome-wide summary statistics of BD (cases= 41,917; controls= 37,1549 in Europeans), MDD (cases=170,756; controls= 329,443 in Europeans and cases= 15,771; controls= 178,777 in East Asians), and SCZ (cases=53,386; controls= 77,258 in Europeans, and cases= 22,778; controls= 35,362 in East Asians) from the Psychiatric Genomics Consortium. MR estimates were generated using inverse variance weighting or MR-Egger if directional pleiotropy exists, along with the weighted median, weighted mode, and Mendelian Randomization Pleiotropy RESidual Sum and Outlier (MR-PRESSO) methods, where possible. We also performed gene-specific analysis as sensitivity analysis and utilized various methods to address potential horizontal pleiotropy for CCBs.

**Results:** After multiple-testing corrections, genetically-proxied ACE inhibition was associated with a lower risk of MDD in East Asians (odds ratio (OR) per 10 mmHg lower in SBP 0.65, 95% confidence interval (CI) 0.48 to 0.89), but an increased risk of SCZ in East Asians (OR per 10 mmHg lower in SBP 6.3, 95% CI 1.9 to 20.93) and Europeans (OR per 10 mmHg lower in SBP 4.42, 95% CI 2.38 to 8.23). Genetically-proxied BBs were not associated with any mental disorders in both populations. We did not find protective effects of genetically-proxied CCBs on mental disorders, taken together results from different analytic methods and sensitivity analyses.

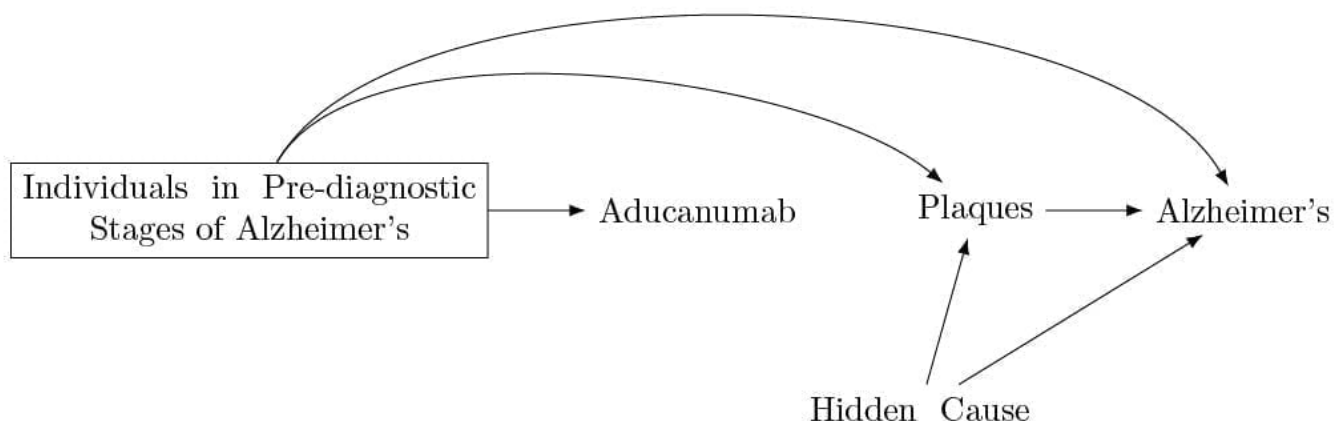
**Conclusions:** Antihypertensive drugs may have differential effects on risk of mental disorders. Our study found no evidence of a protective role of ACEIs or CCBs on mental disorders but potential harm. Their long-term use among hypertensive patients with, or with high susceptibility to, psychiatric illness needs careful evaluation.

**Surrogate Outcomes in the Causal Framework— Are we looking in the wrong place for Alzheimer’s Disease prevention?** Sarah Rothbard\* Sarah Rothbard Eleanor J Murray

In many clinical trials, the pharmacological intervention is assessed using on a surrogate outcome—that is, a biomarker proxy for which there is evidence of a statistical association between the biomarker and the true outcome of interest. Often, this biomarker is also used as an early diagnostic indicator of the disease, and their use in trials can be cost-effective and accelerate the drug development timeline. However, when we consider surrogate outcomes from a causal inference perspective, it becomes clear that the practice is ultimately flawed—at least for biomarker-based surrogate outcomes. Since surrogates cannot themselves be directly manipulated, prior research linking the surrogate with the true outcome of interest is likely to suffer from a lack of causal consistency, uncontrolled confounding, and limited transportability between research settings.

As an example, consider the novel human monoclonal antibody treatment for Alzheimer disease, aducanumab. This treatment has been widely criticized for a lack of clear efficacy, and for the limited population group in which efficacy was assessed. However, the problems with aducanumab may go far beyond this single drug. In fact, other human monoclonal antibodies, including solanezumab and bapineuzumab, have also failed to provide conclusive evidence of efficacy in preventing Alzheimer’s disease progression. These antibody-based treatments have all be developed and tested under the hypothesis that, by selectively targeting amyloid beta plaques in the brain, they can halt the progression of plaque development and thereby prevent Alzheimer’s disease-related dementia. However, the causal effect of plaques on Alzheimer’s cannot be easily tested and other causal relationships cannot be ruled out.

Here, we describe from first-principles how the inherent limitations of estimating the causal effect of a biomarker on the true outcome can result in the selection of incorrect surrogate outcomes, using aducanumab as a case study.



**Association between the use of centrally-acting and non-centrally-acting angiotensin converting enzyme inhibitors and the risk of incident dementia and Alzheimer's disease**

Celine Chui\* Edmund Cheung Celine Chui Min Fan

Ageing is a major risk factor for hypertension and dementia, with hypertension also increasing dementia risk in the mid to late-life. Alzheimer's disease (AD) is a common cause of dementia, characterized by amyloid-beta plaques in the brain. The expression of angiotensin converting enzyme (ACE) is thought to degrade amyloid-beta, while ACE inhibitors (ACEIs), an antihypertensive drug class, may reduce ACE expression and affect the risk of dementia and AD. ACEIs that enter the brain (centrally-acting) and those that do not (non-centrally-acting) may affect this differently. This study aims to compare the incidence of dementia and AD between centrally-acting and non-centrally-acting ACEI use.

This is a population-based cohort study using electronic health data from the Hong Kong Hospital Authority. The target population were those aged 40 years or older, who were new users of ACEIs from 2004-2019. Individuals required two consecutive prescriptions of the same type of ACEI and were followed up from initiation until the earliest of outcome, death or last observation. The outcomes were all-cause dementia and AD. Cox proportional hazards models adjusted with covariates were used to generate hazard ratios (HRs).

The study included 90,159 new users of ACEIs, with 82,131 (91%) centrally-acting and 8028 (9%) non-centrally-acting users. The mean age was 61 and 62 years at initiation, respectively, with a median follow-up of 9 years. Compared to non-centrally-acting users, centrally-acting users had no difference in the risk of all-cause dementia (HR: 0.94, 95% CI: 0.86-1.02) and a decreased risk of AD (HR: 0.76, 95% CI: 0.59-0.98).

This study showed that initiation of centrally-acting ACEIs reduced the risk of AD compared to non-centrally-acting ACEIs but there was no difference in the risk of all-cause dementia. Studies in other countries are needed to support these findings.

This study is supported by the Hong Kong Research Grants Council General Research Fund, No. 17113720.

**The role of grace periods in comparative effectiveness studies of different medications**

Kerollos Wanis\* Kerollos Wanis Aaron Sarvet Lan Wen Jason Block Sheryl Rifas-Shiman James Robins Jessica Young

Researchers are often interested in estimating the effect of sustained use of a pharmacological treatment on a health outcome. However, adherence to strict treatment protocols can be challenging for patients in practice and, when non-adherence is expected, estimates of the effect of sustained use may not be useful for decision making. As an alternative, more relaxed treatment protocols which allow for periods of time off treatment (i.e. grace periods) have been considered in pragmatic randomized trials and observational studies. We clarify the interpretation, identification, and estimation of treatment strategies which include grace periods. We contrast natural grace period strategies which allow individuals the flexibility to take treatment as they would naturally do, with stochastic grace period strategies in which the investigator specifies the distribution of treatment utilization. We estimate the effect of initiation of a thiazide diuretic or an angiotensin-converting enzyme inhibitor (ACEI) in hypertensive patients under various strategies which include grace periods, implementing an estimator that permits the use of flexible machine learning algorithms for confounding adjustment. We estimated that the 3-year risk of adverse cardiovascular and cerebrovascular outcomes under a strategy which initiates an ACEI and includes a 3-month natural grace period was 9.0% compared with 7.2% for a strategy which initiates a thiazide diuretic and includes a 3-month natural grace period (risk difference: 1.8 percentage points, 95% CI: 1.0, 2.6). The estimated 3-year risk difference ranged from 1.2 to 2.2 percentage points for stochastic grace period strategies which varied the investigator-specified proportion of adherence during a 3-month grace period. For all grace period strategies, we estimated that the risk was higher under treatment with ACEIs, and that this difference was larger under grace period strategies which impose lower drug utilization.



**Opioid use after hip fracture and one-year risk of subsequent fracture: a self-controlled case series analysis** Meghan Cupp\* Meghan Cupp Kaleen N Hayes Sarah D Berry Melissa R Riester Francesca L Beaudoin Richa Joshi Andrew R Zullo

### Background

Hip fractures in older adults cause severe pain that often necessitates opioid use. However, opioids may cause falls and subsequent fracture. Studies of opioids and subsequent fractures are often limited by unmeasured confounding between opioid-treated and untreated persons. To overcome this limitation, we used a self-controlled case series design to investigate rates of subsequent fracture during periods of opioid use.

### Methods

Our study included Medicare beneficiaries aged >66 years who utilized opioids after an incident hip fracture (2012-2018) and had a subsequent fracture within one-year. Follow-up began on the day of discharge from the hospitalization or post-acute care (PAC) stay after the incident hip fracture and continued until the first subsequent fracture. We categorized each day during follow-up as exposed (opioids on-hand) versus unexposed (no opioids) using Part D claims (*Figure 1*). Age-adjusted incidence rate ratios (IRR) and 95% confidence limits (CLs) for subsequent fracture in the exposed periods compared with unexposed were calculated by Poisson regression. Subgroup analyses were conducted by sex, PAC setting, and opioid type.

### Results

Of 100,236 persons prescribed opioids, 2,478 (2.5%) experienced a subsequent fracture. The overall incidence rate of subsequent fracture was 5.78 per 1,000 person-days (PDs). The rate of subsequent fracture was greater in exposed (6.86 [95%CLs 6.43, 7.33] per 1000 PDs) versus unexposed periods (5.27 [95%CLs 5.01, 5.53] per 1000 PDs); age-adjusted IRR=1.31 (95%CLs 1.22, 1.41). Risk was attenuated for individuals in inpatient rehabilitation facilities (IRR 0.98 [95%CLs 0.75, 1.14]) and enhanced for those using tramadol exclusively (IRR 1.64 [95%CLs 1.40, 1.93]).

### Conclusion

Opioid use after hip fracture may increase the risk of subsequent fracture. Since opioids are often necessary to treat pain in older adults, patients and their clinicians must take precautions to avoid falls during periods of opioid use.

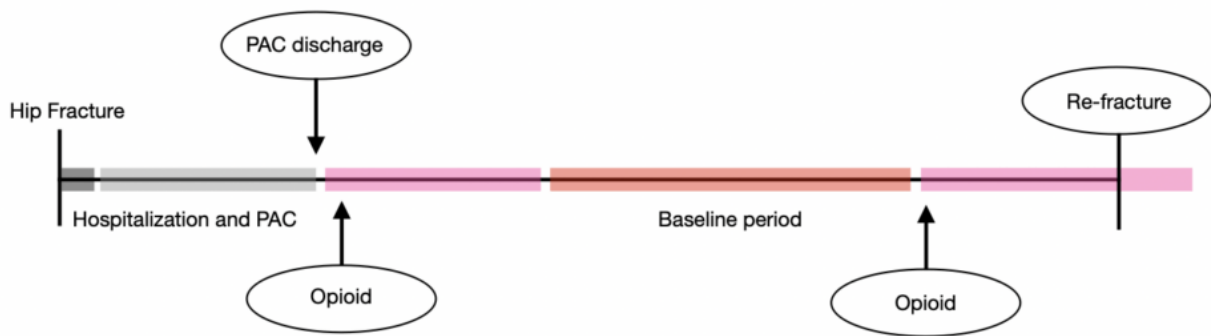


Figure 1 – Diagram showing exposed (pink) and unexposed (red) intervals for a hypothetical beneficiary, with extension of exposure interval past refracture date to preserve intended interval. Hospitalization and time spent in PAC are shown in grey as these are intervals where we are unable to ascertain the exposure of opioid use and have been excluded from analysis.

**Association of physician characteristics and their competency on prescribing of non-steroidal anti-inflammatory drugs (NSAIDs) among patients with congestive heart failure**

Fiona Chan\* Fiona Chan David W. Bates Erica E.M. Moodie John R. Boulet Robyn Tamblyn

Acute exacerbations of congestive heart failure (CHF) are a leading cause of hospitalization annually. NSAIDs are commonly used to treat pain, such as from arthritis, but are potentially inappropriate medications (PIM) for CHF patients due to increased risk of exacerbations. Physician age and sex frequently predict PIM use. While qualitative studies have attributed this to deficiencies in communication ability and clinical knowledge, these relationships have not been investigated. Our study aims to disentangle the mechanism underlying the association between physician age, sex, their competencies, and incident NSAID prescribing to CHF patients with arthritis. We obtained competency assessment scores for the cohort of International Medical Graduates (IMGs) who completed their certification exam in 1998-2004. Linking them to US Medicare patients they encountered in 2014-2015 with CHF and osteo-/rheumatoid arthritis, we analyzed these patients' outpatient and prescription records from all physicians. We identified 10,441 IMGs who performed an evaluation & management visit on 287,454 patients. In these, 1487 (14.2%) IMGs prescribed NSAIDs to 2438 (0.9%) patients within 30 days of the visit. In our bivariable GEE logistic regression models, physician age was a significant predictor of NSAID prescribing (OR per 10-year increase: 1.19 [95%CI 1.14-1.25]), but not sex. Higher clinical competency and communication scores were associated with decreased odds of NSAID use, but the effects were attenuated after adjusting for physician and patient factors. Older (OR per 10-year: 1.08 [95%CI 1.03-1.13]) and male (OR 1.15 [95%CI 1.01-1.30]) IMGs had increased odds of NSAID use in multivariable analyses. As 1.7% of patients received an NSAID from another physician after visiting a study IMG, our next step is to define the types of prior relationship between IMGs and patients. We hypothesize that the relationship type modifies the effects of physician age and sex on NSAID prescribing.

**The Big Four: Target Trial, Target Population, Target Estimand, and Target Validity - A New Paradigm for Making Causal Inferences From Observational Data** Haidong Lu\* Haidong Lu Fan Li Gregg Gonsalves

While randomized controlled trials (RCTs) are important in evaluating causal relationships, many causal questions cannot be answered through RCTs due to ethical, financial or feasibility concerns. Consequently, a great deal of causal knowledge must rely on non-randomized studies (i.e., observational data). Therefore, it is essential to develop a solid methodological framework to improve the quality of observational epidemiology, rather than circumscribing causal claims as the sole province of RCTs. In this education piece, we provide a multi-part conceptual framework for evaluating observation data in the generation of more accurate and useful causal knowledge, defining four targets for consideration - the target trial, target population, target estimand, and target validity. First, "target trial" emulation is a powerful and well-known framework for design and analyses in observational epidemiology. The key idea is that one should investigate questions using observational data as if they were the subject of a hypothetical randomized trial ("target trial"), and then to mimic the trial and its protocols as closely as possible. However, while target trial emulation can help minimize bias related to internal validity, it alone is insufficient to establish more generalizable knowledge, as external validity is still a concern due to the restricted eligibility criteria of many trials. To enhance external validity in observational epidemiology, one must also specify the "target population" that inference is to be made about and the "target estimand" that is the target effect measure to be estimated in a target population. By employing this paradigm, one can establish and maximize a joint measure of both internal and external validity, called "target validity" and hence yield more valuable effect estimates for decision making and planning purposes. We will use the example of treatment for opioid use disorder using electronic health records from the Veterans Affairs to illustrate the utility of this "four targets" paradigm for guiding causal inference from observational data.

**Generalizability of causal effects: a potential outcomes perspective** Daniel Westreich\* Daniel Westreich Alex Breskin

In recent years, epidemiology and allied sciences have given increased attention to the external validity of study results. One subject which has repeatedly arisen in both discussions and the published literature is the issue of effect measure scale. In particular, two questions have been addressed: first, whether the risk ratio (in particular) is typically generalizable from a study sample to a target population without further adjustment or weighting to ensure exchangeability, a condition we here refer to as “naïve generalizability.” And second and more broadly, whether a risk ratio is more likely to exhibit naive generalizability than a risk difference. To date most of the discussion of these points has remained somewhat inconclusive. Here, we attempt to shed additional light on the question of the generalizability of the risk difference and risk ratio, using the perspective of potential outcomes and causal response types (Doomed, Immune, Harmed, Protected).

We discuss how to calculate the causal risk difference and risk ratio from a  $2 \times 2$  table of potential outcomes, and then propose conditions in terms of the causal types in which the risk difference is generalizable, but not the risk ratio; and those in which the risk ratio is generalizable but not the risk difference. We relate those conditions to possible scenarios about how a study sample for a hypothetical trial relates to the target population of interest, thus enabling greater intuition into the conditions under which we might expect an effect estimate to generalize.

**The application of simulation to quantifying bias: a framework for epidemiologists** Jennifer Dunne\* Jennifer Dunne Gizachew A Tessema Gavin Pereira

Due to the observational nature of epidemiological studies, they are prone to various types of bias (information, selection, confounding). In particular, reproductive and perinatal epidemiological studies are subject to unique methodological challenges due to unobservable events from pre-conception to birth and the clustering of outcomes across successive pregnancies or multiple births. Therefore, to strengthen the validity of associations drawn from observational studies, it is important for researchers to be able to identify, evaluate and, quantify potential sources of bias.

Commonly used to test statistical methods, *simulation studies* are under-used in epidemiology, yet have the potential to quantify the influence of bias on exposure-outcome associations. Simulations studies involve computational methods to create data by pseudo-random sampling. They are ideal to quantify bias as the process of generating data allows greater control of the biased parameters of interest. Current simulation studies in reproductive and perinatal epidemiology lack uniformity in their design, analysis, and reporting. Lack of guidance in the application of simulation to quantify the influence of bias has hampered researchers and peer reviewers.

This paper proposes a viable framework for the application of simulation studies to quantify the magnitude and direction of biases in reproductive and perinatal epidemiological studies. Using examples, the framework aims to demonstrate and highlight the value of applying simulation methods to quantify selection, information, and bias resulting from the influence of unmeasured confounding. We will illustrate how tools for the design, implementation, and analysis of simulation studies can be applied to quantify bias in epidemiology. Finally, this framework underlines the importance of quantifying bias to remove the uncertainty of exposure-outcome associations in reproductive and perinatal epidemiology.

**Evaluating missingness assumptions for items in a frailty index** Louisa Smith\* Louisa Smith

When data is missing not-at-random (MNAR), sensitivity analysis can be used to assess robustness to plausible missing-data mechanisms. By comparing results across different sensitivity parameters, it is possible to investigate the extent to which conclusions would be affected by violations of the missing at random (MAR) assumption. When multiple variables are missing, as is often the case when items are drawn from multiple surveys or addressing sensitive topics, sensitivity parameters can be hard to specify, and the dimensionality of the parameter space makes results more difficult to interpret. In this work, we address sensitivity analysis for missing data in the context of a survey-based frailty index, a commonly used measure of health status that takes into account multiple factors, including chronic conditions, physical function, and social support. Using data on over 200,000 US adults over 50 from the NIH's All of Us program, we find that more than 90% are missing data on one or more frailty-related conditions; item-specific missingness ranged from 3% to 69%. After eliciting plausible values for sensitivity parameters from geriatricians, we assess trade-offs in assumptions and their effects on conclusions about frailty distributions. Under reasonable assumptions for the sensitivity parameters and models for the missing values, we find that conclusions about frailty distributions are similar to those under simpler MAR assumptions.

**The M-value: A simple sensitivity analysis for bias due to missing data in treatment effect estimates** Maya Mathur\* Maya Mathur

Complete-case analyses can be biased if missing data are not missing completely at random. We propose simple sensitivity analyses that apply to complete-case estimates of treatment effects; these analyses use only simple summary data and obviate specifying the mechanism of missingness and making distributional assumptions. Bias arises when: (1) treatment effects differ between retained and non-retained participants; or (2) among non-retained participants, the estimate is biased because conditioning on retention has induced a backdoor path. We thus bound the overall treatment effect on the difference scale by specifying: (1) the unobserved treatment effect among non-retained participants; (2) the strengths of association that unobserved variables have with the exposure and with the outcome among retained participants (“induced confounding associations”). Working with the former sensitivity parameter subsumes certain existing methods of worst-case imputation, while also accommodating less conservative assumptions (e.g., that the treatment is not detrimental even among non-retained participants). As an analog to the E-value for confounding, we propose the M-value, which represents, for a specified treatment effect among non-retained participants, the strength of induced confounding associations required to reduce the treatment effect to the null or to any other value. These methods could help characterize the robustness of complete-case analyses to potential bias due to missing data.



**Perspectives on harm in personalized medicine** Aaron Sarvet\* Aaron Sarvet Mats Stensrud

Explicit causal inference thinking and methodology is increasingly embedded in modern health care systems. However, there remains substantial ambiguity about the translation of seemingly basic bioethical concepts into the terms of this methodology. We focus on one such concept: “harm”, and its relation to the Hippocratic principle. We articulate competing approaches, and review their practical and philosophical differences in terms of epidemiological data analysis, as well as medical and public health decision-making. We also provide novel methodological results on the fusion of experimental and non-experimental data for personalised medicine. Broad awareness of these approaches will aid a diverse set of stakeholders — from epidemiologists, to clinicians, to policy-makers — in the successful translation of data into public good.

**Examining the contribution of socioeconomic disadvantage to racial and ethnic disparities in low-risk cesarean birth in California** Shalmali Bane\* Shalmali Bane Suzan Carmichael Mahasin Mujahid Elliott Main

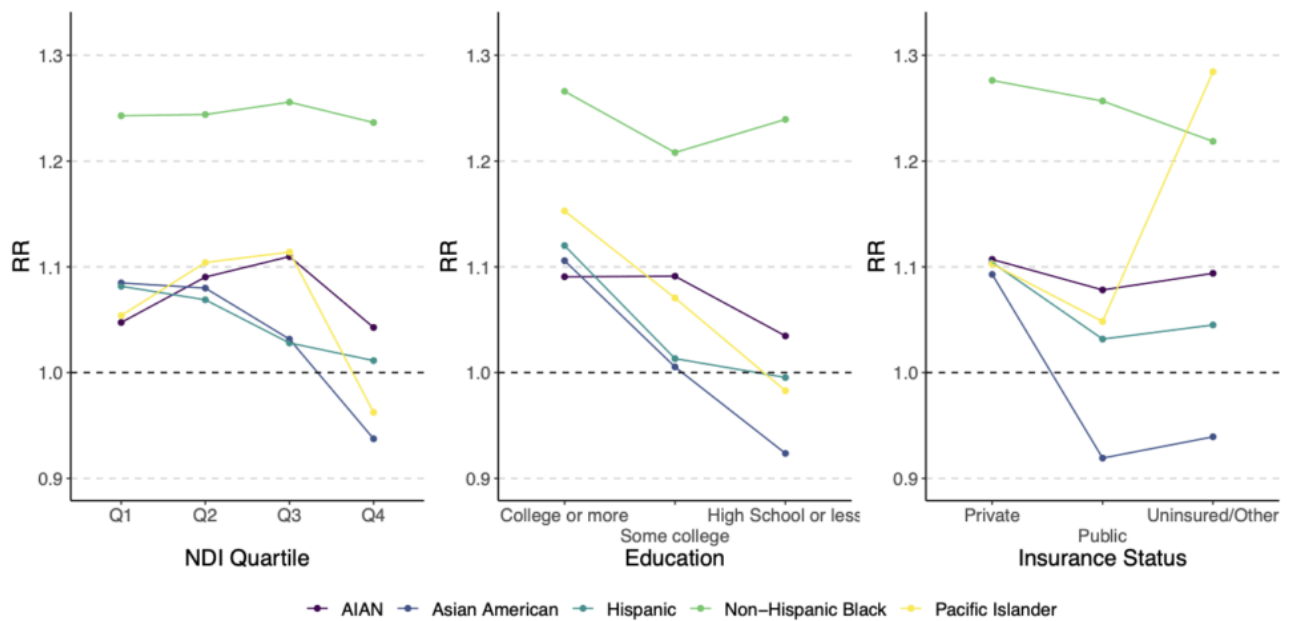
In the US, there is substantial variability in the rate of cesarean birth by social factors, such as race/ethnicity and socioeconomic disadvantage. The joint contribution of these factors, especially in a multi-level context, for low-risk cesarean birth has not been examined.

Using a dataset of live birth and fetal death certificates linked with maternal hospitalization data (2007-18), we examined the contribution of multi-level socioeconomic disadvantage (neighborhood deprivation index at the census tract level, maternal education, and insurance) to racial/ethnic disparities in low-risk cesarean (defined as nulliparous, term, singleton, vertex (NTSV)) births. We used Poisson regression models clustered by tract and sequentially adjusted for maternal characteristics, with interaction terms for race/ethnicity and measures of socioeconomic disadvantage.

Among 1,815,933 NTSV births, 26.6% were cesarean. Adjusted RR increased with increasing NDI (e.g., 1.06 95% CI 1.05-1.08 for most deprived vs. least deprived quartile), lower education (e.g., 1.12, 95% CI 1.11-1.13 for high-school education or less vs. college educated), and public insurance (1.11, 95% CI 1.11-1.12 vs. private insurance). When assessing interaction, Black individuals had an elevated RR, relative to White individuals, across all NDI quartiles. Higher education and public insurance status were associated with increased RR for NTSV cesarean for all racial/ethnic groups, relative to White. The most advantaged White individuals had the lowest RR while the least advantaged Black individuals had the greatest RR for cesarean birth.

Our findings suggest that the racial/ethnic disparity in low-risk cesarean is highest among privately insured and more educated individuals, relative to White individuals; Black individuals had a consistently elevated risk of low-risk cesarean regardless of NDI, while the risk for Asian and Hispanic individuals decreased with increasing NDI.

**Figure.** Association between measures of socio-economic disadvantage and risk of NTSV cesarean birth for Black, Asian, and Hispanic individuals, relative to White individuals: California 2007-2018 (N = 1,815,933)



All models include terms for race/ethnicity, NDI, insurance, education, age, pre-pregnancy body mass index, pregestational diabetes status, pregestational hypertension status, as well as account for clustering by census tract. Additionally, for a given exposure, the model includes an interaction term for that exposure and race/ethnicity (e.g., NDI\*race/ethnicity for the NDI model)

Abbreviations: AIAN American Indian/ Alaska Native, NDI Neighborhood Deprivation Index, NTSV nulliparous singleton, term, vertex, RR risk ratio

**A Deterministic Selection Bias Analysis of the Etiologic Association Between Periconceptional Folic Acid Supplementation and Spina Bifida in Offspring Due to Differential Participation in the National Birth Defects Prevention Study** Julie M. Petersen\*

Julie Petersen Andrew Olshan Jacob Kahrs Mollie Wood Nedghie Adrien Samantha Parker Gary Shaw Amy Herring Meredith Howley Paul Romitti Maria D. Politis

**Background:** A previous National Birth Defects Prevention Study (NBDPS) investigation reported an OR of 1.0 (95% CI 0.7, 1.2) for the association between spina bifida and periconceptional folic acid supplementation. This observation was unexpected given the wealth of research, including randomized trials, finding that folic acid supplementation can reduce spina bifida risk by 40-60%.

**Methods:** We conducted a deterministic multidimensional bias analysis in the NBDPS to investigate if there are plausible scenarios of differential participation that could explain the observed null association. We assumed the true OR was at least 0.7 given prior studies and based estimates for the prevalence of folic acid supplementation in the underlying source population from US-based reports of periconceptional folic acid use (20-40%). We also searched the literature and employed causal diagrams to consider if there are theoretical factors that could drive the differences in participation by case-control and exposure status and result in structural selection bias via collider stratification.

**Results:** If folic acid supplementation was overrepresented, relative to the US source population, in both the participating cases and controls, but more so among the cases, selection bias would be substantial enough to shift the OR from 0.7 (hypothesized truth) to 1.0 (observed). This scenario seemed plausible given that the literature supported common factors related to participation and folic acid use. Specifically, both participation and folic acid use tend to be higher among individuals who identify as Non-Hispanic White, planned the pregnancy, and/or have higher educational attainment (Figure).

**Comment:** Our investigation supported that differential participation is a plausible explanation for why a null finding between folic acid and spina bifida was observed in the NBDPS. However, other potential explanations, such as recall bias, are possible and warrant further investigation.

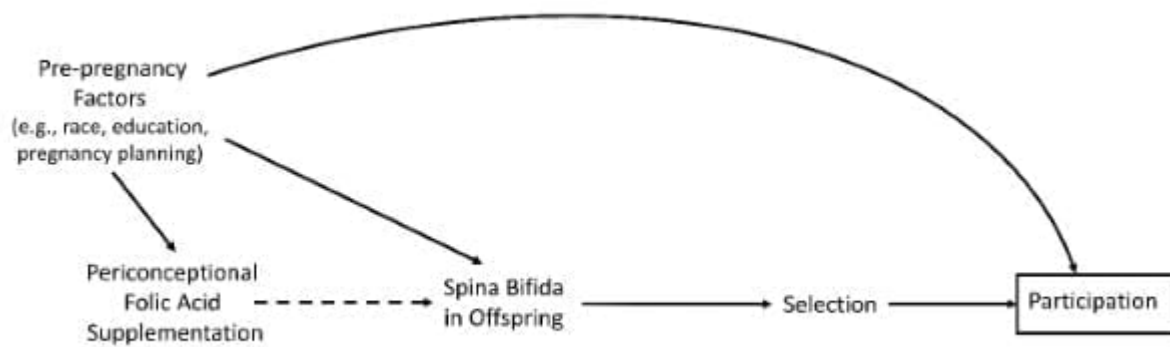


Figure. In this simplified directed acyclic graph (causal diagram), we describe a potential mechanism that could have led to selection bias of the association between periconceptional folic acid supplementation and spina bifida in offspring in the National Birth Defects Prevention Study (NBPDS). The selection node indicates random selection to be approached to participate in the study, whereas the participation node indicates individuals that ultimately participated. The box around participation indicates conditioning on participation. The dashed line indicates a modified causal relationship between periconceptional folic acid supplementation and spina bifida in offspring due to conditioning on participation (a collider). We assumed here that it is a modified (as opposed to non-) causal relationship, since there is a wealth of research, including randomized trials, supporting that folic acid prevents neural tube defects, including spina bifida.

## COVID-19 Pandemic

**Pregnancy, fetal, and newborn outcomes following a first booster dose of COVID-19 vaccine during pregnancy**

Annette K Regan\* Annette K Regan Sheryll Dimanlig-Cruz Eszter Török Jay S Kaufman Robert W Platt Siri E Håberg Christopher A Gravel Jeffrey C Kwong Gillian D Alton Tavleen Dhinsa Prakesh S Shah Kumanan Wilson Ann E Sprague Darine El-Chaâr Sarah A Buchan Sarah E Wilson Sandra I Dunn Shannon E MacDonald Jon Barrett Nannette Okun Liam Bruce Mark C Walker Deshayne B Fell

**Objective:** To assess risk of adverse pregnancy, fetal, and newborn outcomes following a 3rd dose (first booster) of COVID-19 vaccine during pregnancy (vs. no 3rd dose during pregnancy) among individuals who had already completed their primary COVID-19 vaccine series (two doses of mRNA vaccine).

**Methods:** We used provincial databases in Ontario, Canada to identify all live and stillbirths  $\geq 20$  weeks' gestation (birth registry) linked to the COVID-19 vaccine database. Individuals expected to give birth from Dec 20, 2021 (start of 3rd dose eligibility for everyone  $\geq 18$  years) to Aug 31, 2022, who had completed their primary series before pregnancy and became eligible for a 3rd dose before the end of pregnancy ( $\geq 6$  months since dose 2) were included. We estimated hazard ratios (HR) and 95% confidence intervals (CI) for study outcomes, treating dose 3 as a time-varying exposure and adjusting for confounding using inverse probability weighting.

**Results:** Among 32,693 births, 56.6% were to individuals who received a 3rd COVID-19 dose during pregnancy. Compared with eligible individuals who did not receive a 3rd dose during pregnancy, there were no increased risks of placental abruption (adjusted HR [aHR]: 0.89, 95%CI: 0.74-1.08), chorioamnionitis (aHR: 0.67, 95%CI: 0.50-0.90), postpartum hemorrhage (aHR: 1.00, 95%CI: 0.88-1.14), cesarean delivery (aHR: 0.90, 95%CI: 0.87-0.94), stillbirth (aHR: 0.57, 95%CI: 0.41-0.81), preterm birth (aHR: 0.93, 95%CI: 0.86-1.01), NICU admission (aHR: 0.96, 95%CI: 0.89-1.02), 5-minute Apgar score  $< 7$  (aHR: 0.96, 95%CI: 0.81-1.13), or small-for-gestational-age infant (aHR: 0.86, 95%CI: 0.79-0.93) associated with receiving a 3rd COVID-19 dose during pregnancy.

**Conclusion:** Receipt of a 3rd COVID-19 dose during pregnancy was not associated with an increased risk of adverse pregnancy, fetal, or newborn outcomes. These findings can help inform evidence-based decision-making about the risks and benefits of COVID-19 booster doses during pregnancy.

**Screening to generate hypotheses of potential causes of congenital heart defects using high-dimensional insurance claims data** Jeremy Brown\* Jeremy Brown Sonia Hernández-Díaz**Background**

The etiology of congenital heart defects, the most common birth defect, is poorly understood. Some genetic conditions, maternal diseases (e.g., diabetes) and medications have been linked with heart defects. Genome-wide association studies have successfully identified genetic determinants, but similar efforts to identify novel non-genetic causes have been hampered by small samples and examination of few potential causes.

**Methods**

We selected a cohort of pregnancies ending in live birth between 2011 and 2020 within a healthcare administrative database in the US. Congenital heart defects were identified with a validated claims-based algorithm. Indicator variables for any medication dispensation within the first trimester were created for the 500 most commonly dispensed medications. Mid p-values for the association between each medication and congenital heart defects were calculated using Fisher's exact test. The false discovery rate was controlled at level 0.05 using the Benjamini-Hochberg procedure. Relative risks (RR) were calculated to reflect the strength of the associations.

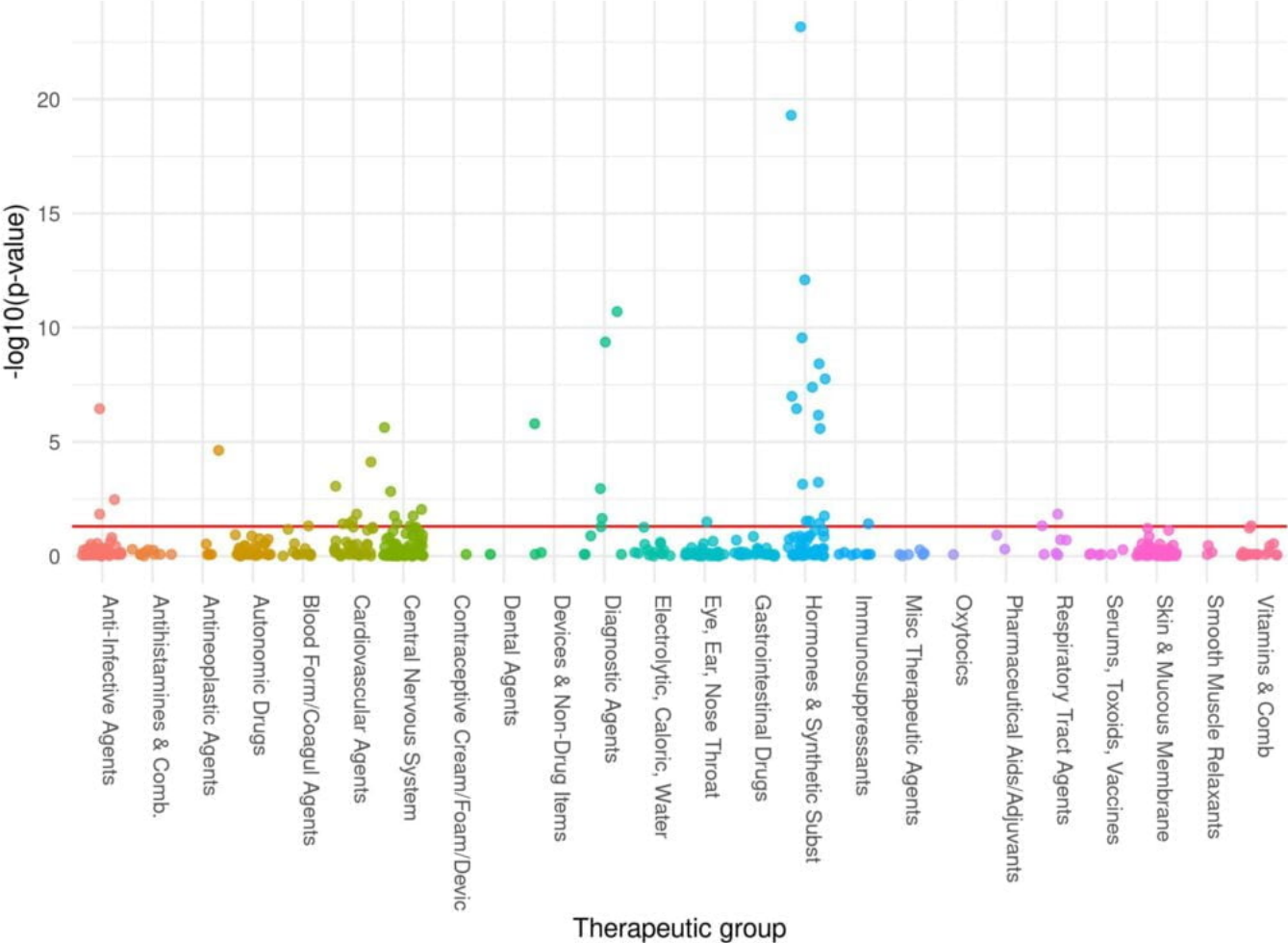
**Results**

We identified 721,506 pregnancies and 9,084 congenital heart defects. There were 45 variables that reached statistical significance of which 19 had relative risks above 2. Of these 45, 15 were related to diabetes management (12 with  $RR > 2$ ). Other frequently represented therapeutic classes were female hormones (n=5), benzodiazepines (n=3), antihypertensives (n=3), prednisolone and derivatives (n=2), and immunosuppressants (n=2).

**Discussion**

Findings corroborate the previously established association with maternal diabetes. Female hormones, benzodiazepines, hypertension, and systemic lupus erythematosus (an indication for immunosuppressants) have all been previously associated with increased risk of congenital heart defects as well, but warrant further formal evaluation. Screening healthcare data may help us identify potential causes of birth defects by generating hypotheses.

Figure 1: P-values for the associations between each medication and congenital heart defects





**A Safety Comparison of Continuing Versus Discontinuing Triptans for Acute Migraine Treatment in the First Trimester of Pregnancy Following Pre-pregnancy Triptan Use** Jacob Kahrs\* Jacob Kahrs Lauren Kucirka Mollie E. Wood

The primary medications prescribed for the acute treatment of migraines outside of pregnancy are triptans. Safety data on triptans in pregnancy is limited but prior studies are relatively reassuring: prenatal triptan use is not associated with many common pregnancy safety outcomes, such as preterm birth or major congenital malformations. Even so, many pregnant migraineurs discontinue triptans out of concern for fetal safety. This study expands on prior literature by examining associations between first trimester triptan use and several pregnancy outcomes.

Using United States commercial insurance claims data from 2004-2015, we identified a cohort of pregnant people who had an International Classification of Diseases, Ninth Revision, Clinical Modification migraine diagnosis code at an inpatient, outpatient or emergency department visit in the 90 days prior to the last menstrual period and filled a prescription for a triptan in the same window. Participants who had a first trimester triptan fill (continuers) were compared to participants who did not have a 1<sup>st</sup> trimester triptan fill (discontinuers) using generalized linear models. We used inverse probability of treatment weights to account for differences in baseline characteristics including comorbidities, medication use, demographics, healthcare utilization and proxies of disease severity.

Of the 6,081 pregnancies included in this analysis, 1,639 filled a triptan prescription in the first trimester. Triptan continuers had a decreased risk of preterm birth (risk ratio [RR] 0.79, 95% CI 0.66, 0.94) and similar risks of small for gestational age (RR 1.09, 95% CI 0.55, 2.19) and preeclampsia (1.03, 95% CI 0.76, 1.40). We observed increased risks of placental abruption (RR 1.87, 95% CI 0.63, 5.51) and placenta previa (RR 2.03, 95% CI 0.64, 6.47) associated with triptan continuation, albeit with very wide confidence intervals.

These results may be reassuring for pregnant migraineurs who need to continue using triptans.

## Environment/Climate Change

**Associations of birth outcomes and air pollution at different time windows of pregnancy and neighborhood greenery** Wei-Lun Tsai\* Wei-Lun Tsai Thomas J Luben Kristen M Rappazzo

Many studies suggest that environmental exposures, including air pollution, are associated with adverse birth outcomes. A growing body of research reports that neighborhood greenery is associated with reduced odds of adverse birth outcomes. We examine the associations between  $PM_{2.5}$ ,  $NO_2$ , and  $O_3$  and preterm birth (PTB, gestational age < 37 weeks) and the potential mediation by tree canopy, a measure of neighborhood greenery. Outcome data were obtained from the North Carolina (NC) Department of Health and Human Services for the years 2003-2015 and limited to live, singleton births (N= 1315316). Daily air pollution concentrations at the Census tract level were obtained from hybrid ensemble models, averaged over each trimester and entire pregnancy, and assigned to participants based on residential address at date of birth. Tree canopy within 250m of each residence was calculated using 30m U.S. Forest Service Percent Tree Canopy Cover in 2011. We used logistic regression models to estimate the effects of air pollution on the odds of PTB with adjustment for confounders and then potential mediation effects by tree canopy. Analyses were also stratified to examine whether disparities in air pollution and greenery exist by race/ethnicity. Exposures to air pollution during the entire pregnancy had the strongest effects on PTB, with the highest magnitude association observed for  $PM_{2.5}$  (aOR: 1.024 [95% CIs: 1.021, 1.027]), a modest positive association observed for  $NO_2$ , and a near-null association with  $O_3$ . In addition, exposures at the third trimester tended to have greater associations with PTB compared to either of the first two trimesters. Tree canopy was associated with reduced odds of PTB (0.995 [0.992, 0.999]), and there was no evidence of mediation of air pollution effects. Associations of air pollution and greenery varied by race/ethnicity. Findings from this study suggest that environmental exposures during pregnancy are generally important for birth outcomes.

**Opioid-Related Polysubstance Overdose Emergency Department Visits in Texas, 2016-2021**

Vanora Davila\* Vanora Davila Elena

Overdoses involving opioids are a major cause of mortality in the United States. This complex issue is further complicated by polysubstance use with both stimulants and other substances. We aim to assess the association of factors such as race/ethnicity, age, and co-occurring mental health conditions with opioid-related polysubstance overdose emergency department visits. We analyzed opioid-related polysubstance emergency department visits in Texas using data from the 2016-2021 Texas Hospital Inpatient and Outpatient Public Use Data Files. We restricted analyses to non-fatal visits with a combination of revenue codes and International Classification of Diseases (ICD-10-CM) codes for acute poisoning by opioids among Texas residents. Using multinomial logistic regression, we identified factors associated with three categories of polysubstance overdose visits (opioids only, opioids and non-stimulant substances, and opioids and stimulants with or without other substances). From 2016-2021, there were 9,580 non-fatal opioid-related polysubstance overdose emergency department visits in Texas. Among these, 9% involved opioids only, 60% involved opioids and non-stimulants, and 31% involved opioids and stimulants. Compared to Non-Hispanic Whites, Hispanics (OR: 1.52, 95% CI: 1.25-1.85), Non-Hispanic Blacks (OR: 1.82, 95% CI: 1.40-2.36), and persons in other racial/ethnic categories (OR: 1.52, 95% CI: 1.10-2.10) were more likely to experience an overdose involving opioids and stimulants. People aged 18-44 were more likely than any other age group to visit the emergency department for an overdose involving opioids and stimulants. A co-occurring mental health diagnosis was associated with increased likelihood of an overdose involving opioids and non-stimulant substances (OR: 1.83, 95% CI: 1.59-2.12). Our findings suggest that polysubstance use is increasingly driving opioid overdoses across Texas, with differences by demographics for certain substance combinations.

**The effect of fentanyl on state and county-level psychostimulant and cocaine overdose death rates by race in Ohio from 2010-2019: a time series and spatio-temporal analysis**

Angela Estadt\* Angela Estadt Brian White Staci Hepler William C Miller Kathryn E Lancaster David Kline

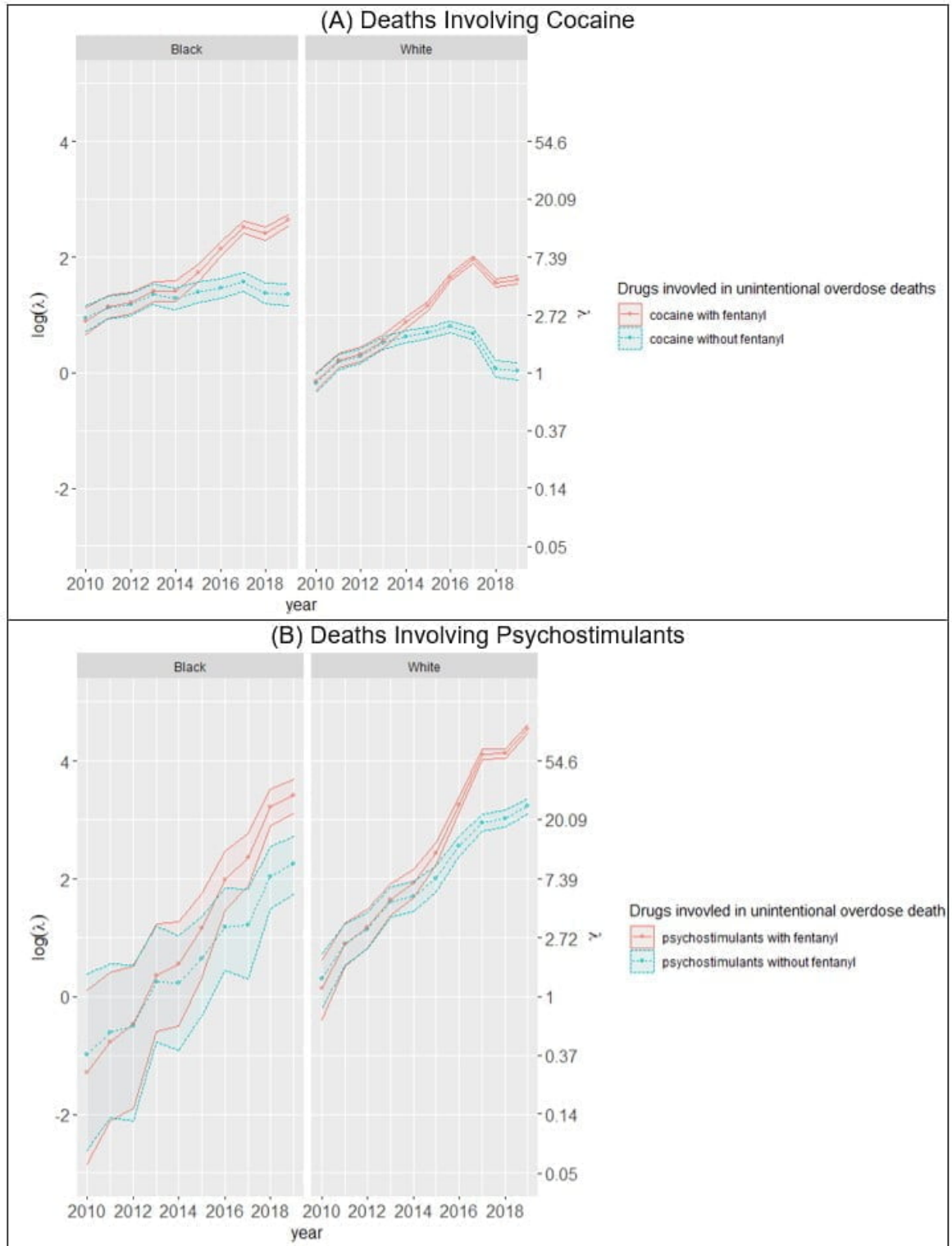
**Background:** It is unknown how fentanyl has contributed to the rise in cocaine and psychostimulant overdoses in Ohio. Our objective was to measure the impact of fentanyl on cocaine and psychostimulant overdose death rates by race in Ohio.

**Methods:** We conducted time series and spatio-temporal analyses using data from the Ohio Public Health Information Warehouse. Primary outcomes were state and county-level overdose death rates from 2010-2019 for Black and White populations. Exposure measures consisted of four drug involvement categories: 1) cocaine without fentanyl, 2) cocaine with fentanyl, 3) psychostimulants without fentanyl, and 4) psychostimulants with fentanyl. We fit a time series model of standardized mortality ratios (SMR) using a Bayesian generalized linear mixed model to estimate posterior median rate ratios (RR). We conducted a spatio-temporal analysis by modeling the SMR for each drug category at the county level to characterize county-level variation over time.

**Results:** In 2019, the greatest overdose rates were attributed to cocaine and fentanyl among Black (22.6 deaths/100,000 people) and White (8.4 deaths/100,000 people) populations. Annual mortality rate ratios were highest for psychostimulants and fentanyl among Black (aRR= 1.72; 95% CI: (1.37, 2.14)) and White (aRR= 1.64, 95% CI:(1.35, 1.90)) populations. There was little change in mortality involving cocaine without fentanyl with annual rate ratios among both White (aRR=1.04; 95% CI:(0.90,1.23)) and Black (aRR=1.05; 95% CI:(0.95, 1.16)) populations near 1. Within each drug category, change over time was similar for both racial groups. The spatial models highlighted county-level variation for all drug categories.

**Conclusions:** In 2013, the inclusion of fentanyl into the cocaine and psychostimulant drug supplies initiated a substantial rise in Ohio's overdose rates. We found differences between Black and White overdose rates from 2010-2019.

**Figure 1.** Time series model: posterior median of the  $\log(\text{SMR})$  with 95% credible intervals for cocaine, psychostimulants, and fentanyl by race in Ohio, 2010-2019



**Association between overdose prevention center implementation and neighborhood-level misdemeanor drug arrests and complaints for syringe litter in New York City: A synthetic control analysis** Bennett Allen\* Bennett Allen Brandi Moore Victoria A. Jent Brent Gibson William C. Goedel Khadija Israel Alexandra A. Collins Brandon D. L. Marshall Magdalena Cerdá

**Background:** The overdose epidemic continues unabated in the United States (US). In response, New York City (NYC) implemented the first publicly recognized overdose prevention centers (OPCs)—services where individuals can use pre-obtained substances under supervision of trained staff—on November 30, 2021. Over 200 OPCs operate in 15 countries, with prior research suggesting that OPCs are associated with reduced overdose death and improved neighborhood conditions. However, opponents of OPCs argue that such services may lead to increased illicit activity in surrounding neighborhoods. To assess this, we estimated the association between OPC implementation and misdemeanor drug arrests and public complaints of syringe litter using a synthetic control method.

**Methods:** Drug arrest and syringe litter complaint data came from NYC administrative records. To create the synthetic control, we used monthly counts of arrests and complaints and US Census measures of sociodemographic features for a 500-meter radius surrounding fixed-site syringe service programs without OPC interventions in NYC. We defined 01/01/14-11/29/21 as the pre-intervention period. The post-intervention period was measured at the monthly level (11/30/21-06/30/22). Differences between the intervention site and synthetic control were assessed with permutation tests.

**Results:** In the post-intervention period, the mean monthly count of misdemeanor drug arrests was 1.5 lower in the OPC neighborhood compared to the synthetic control (permuted  $P=0.750$ ). The mean monthly post-intervention syringe litter complaints count was 2.1 lower in the OPC neighborhood compared to the synthetic control (permuted  $P=0.875$ ).

**Conclusions:** OPC implementation did not impact neighborhood drug misdemeanor arrests or syringe litter complaints, suggesting no increase in illicit activity. Future research is needed to identify meaningful catchments areas to assess community impact of hyper-local overdose prevention interventions such as OPCs.

**Are increases in the mortality rate of opioid overdose deaths in the United States due to changes in the incidence rate or the case fatality rate?** Adam Palayew\* Adam Palayew Matthew Bonn Stephen J Mooney Kerry Keyes

Opioid overdoses have increased in the USA over the last 2 decades with over 100,000 overdoses last year. This crisis has occurred largely in 3 waves: (1) an increase in prescription opioid (PO) related deaths, (2) an increase in heroin-related deaths, and (3) an increase in fentanyl-related deaths (figure). The mortality rate (MR) has increased over each wave; however, distinct changes drove the increase in MR during each wave. Our work examines how the incidence rate (IR) and the case fatality rate (CFR), each a component of the MR, varied during the 3 waves.

In wave 1 (1999-2009), PO prescription changes drove an increase in IR, which in turn increased the MR due to greater opioid exposure in the population. During this wave, the CFR among those exposed remained stable at the relatively low level associated with medical opioid use. In wave 2 (2010-2013), restrictions in opioid prescribing reduced the IR by reducing both new prescriptions and duration of prescribing. However, these restrictions also increased the CFR due to increased transition from PO to heroin arising from a decrease in PO supply and increased heroin market expansion. Given that MR is a product of IR and CFR, the increase in the MR in wave 2 is likely explained by a greater increase in the CFR than decrease in the IR. In wave 3 (2013-2019), fentanyl saturated the drug supply, which increased the CFR, in turn increasing the MR. Notably, during wave 3 youth have been overrepresented among deaths. Recent data have shown that the IR of opioid use for youth is at a 10 year low while MR is at a historic high, thus implicating an increased CFR as the cause of increased mortality.

This evidence suggests the recent rise in opioid overdose death is driven by change in the CFR during waves 2 and 3 rather than any recent increase in IR. This points to the need for bold innovative strategies that lower the CFR related to drug use, potentially including access to a regulated supply of opioids.

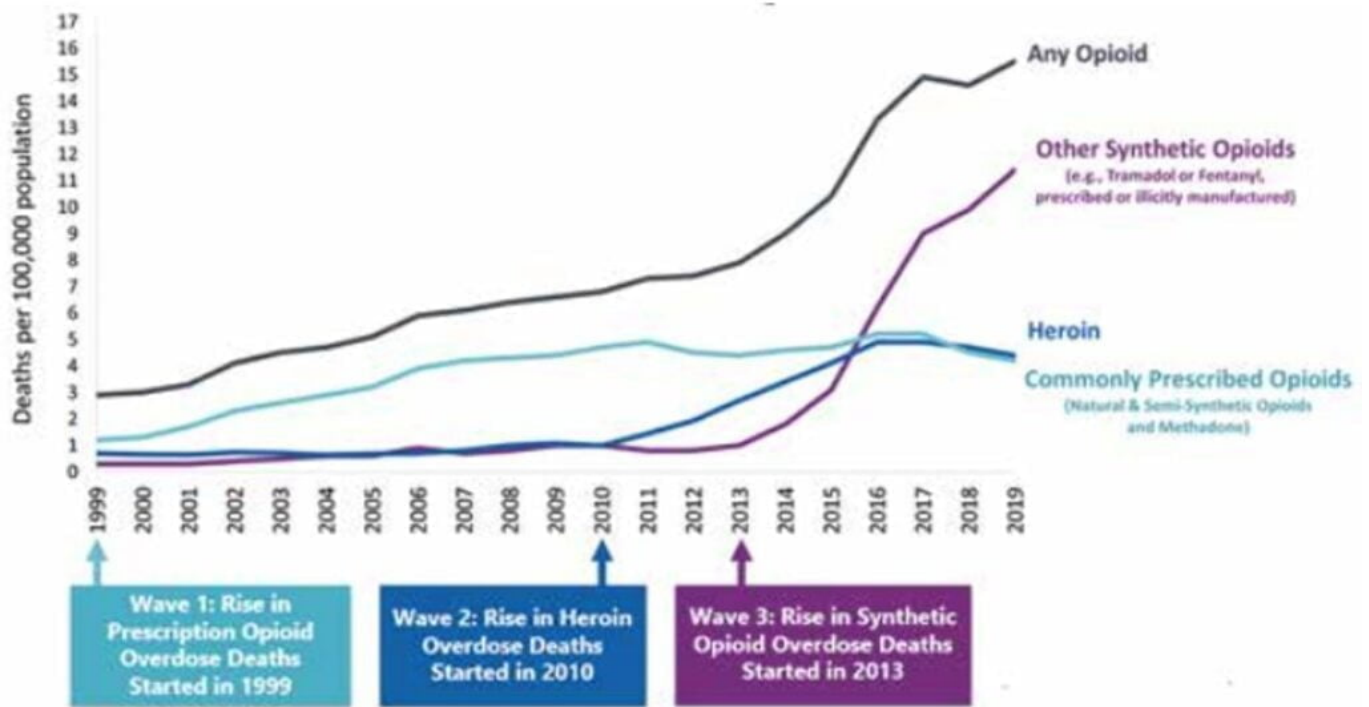


Figure. The triple wave epidemic, national vital statistics system mortality file



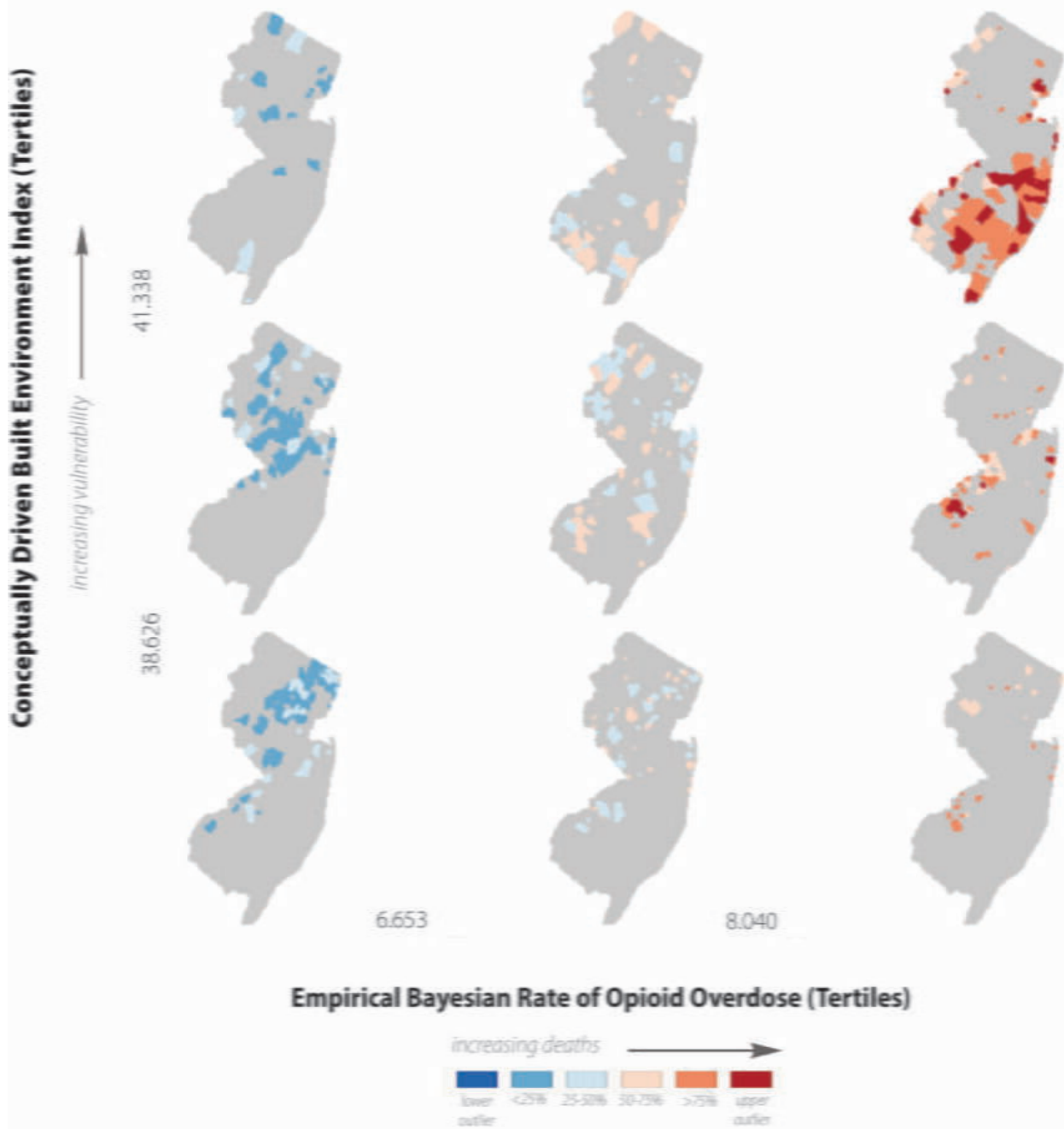
**Spatiotemporal Dynamics of Opioid Overdose Deaths & Built Environment in NJ from 2015-2018** Marynia Kolak\* Marynia Kolak Leslie Williams Danielle Ompad Barbara Tempalski

Opioid overdose deaths in New Jersey have increased over time, following country-wide trends, but with spatially heterogeneous patterns that are often associated with community contextual factors. In this study, the spatiotemporal dynamics of opioid overdose deaths and built environment factors in New Jersey are examined from 2015 to 2018. We hypothesize that advantageous built environment characteristics will be associated with fewer deaths, as they may provide more opportunities for residents and/or reduce stress loads.

We cleaned medical examiner data to establish a population cohort from 2015-2018, and geocoded place of residence for qualifying events. Crude and age-adjusted rates for opioid-related overdose events were developed in aggregate, while Empirical Bayesian (EB) rates calculated at the municipality level smoothed estimates locally using a spatial averaging approach. Statistically significant ( $p > 0.05$ ) hot spots (high overdose EB rate) and cold spots (low EB rate) were established cross-sectionally and longitudinally using Local Indicator of Spatial Autocorrelation statistics. We then analyzed the bivariate relationship of EB rate and a NJ-specific built environment index (developed previously to capture contextual risk), and generated a conditional map of these factors to uncover location-specific areas of risk.

Overdose deaths increased over the time periods studied in New Jersey, with notable expansion in geographic patterns. Associations between municipality-level opioid overdose deaths and built environment persist across time, though get stronger over time. Furthermore, areas of higher overdose rates in more advantageous built environments tend to neighbor less advantageous regions with high overdose rates, demonstrating a spatial spillover phenomenon. Incorporating a spatiotemporal perspective in understanding opioid overdose risk and built environment is crucial for future research.

## Tertile Conditional Map of Built Environment Index and EB-Smoothed Opioid Overdose Rate (4-Year Average)



**Neighborhood-level relationship between eviction and overdose death in Rhode Island**

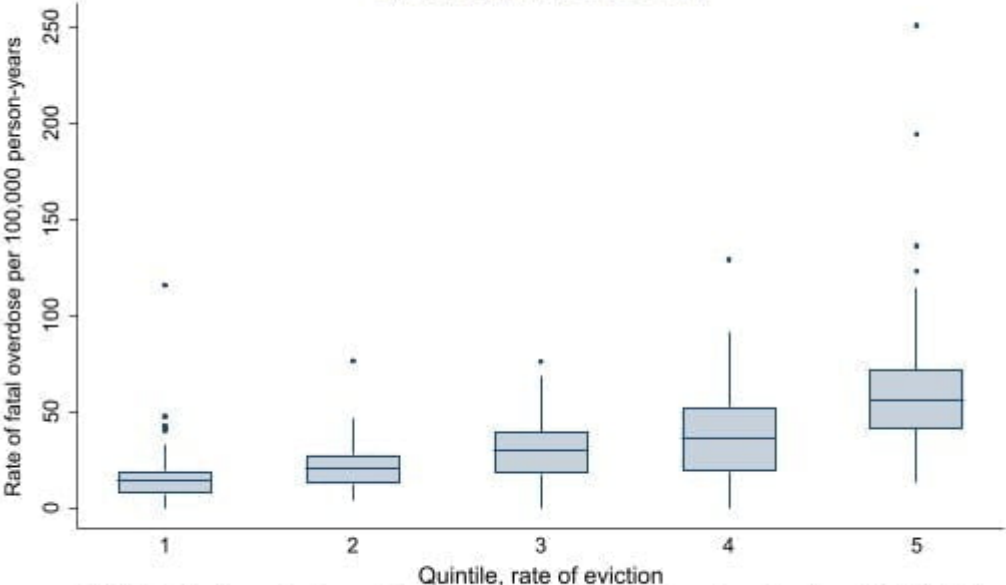
Alexandra Skinner\* Alexandra Skinner Victoria Jent William C Goedel Bennett Allen Kathryn M Leifheit Abigail R Cartus Alexandria Macmadu Yu Li Claire Pratty Elizabeth A Samuels Jennifer Ahern Magdalena Cerdá Brandon DL Marshall

Historical legacies of oppression and discriminatory contemporary policies shape the concurrent housing and overdose crises in the United States, disproportionately affecting Black, Hispanic, and American Indian/Alaska Native people who use drugs. Housing insecurity is a known risk factor for fatal overdose, yet little research has assessed the relationship between eviction and overdose at a neighborhood level. Eviction has the potential to disrupt patterns of drug procurement and consumption and to lead to increased neighborhood blight and social fragmentation – stressors that amplify overdose risk. We sought to evaluate a spatiotemporal relationship between neighborhood-level residential eviction rates and overdose mortality in Rhode Island.

We measured eviction rates using records of eviction filings in Rhode Island from 2016 through 2021, accessed via a public records request from the Rhode Island Judiciary, per the number of renter-occupied housing units reported by the American Community Survey (ACS). We obtained fatal overdose data in six-month intervals over this same time period from the State Unintentional Drug Overdose Reporting System. We aggregated these data by census tract and generated descriptive statistics to estimate a correlation between eviction and overdose deaths over time. We will model a geospatial association between rates of eviction and fatal overdose using an Integrated Nested Laplace Approximation approach, adjusted for an a priori set of ACS demographic covariates. We will further assess effect measure modification of this relationship by census tract racial/ethnic composition.

Our descriptive findings presented in the figure indicate that eviction rates were positively correlated with risk of fatal overdose ( $r=0.514$ ,  $p<0.001$ ). Coupled with our anticipated modeling results, this work provides insight into the potential role that housing policies such as eviction moratoria may play in reducing neighborhood inequalities in overdose rates.

Rate of fatal overdose by quintile of residential eviction rates,  
Rhode Island, 2016-2021



Note: Rhode Island census tracts were binned into quintiles of residential eviction rates, with the lowest quintile (Quintile 1) representing tracts with the lowest rates of eviction and the highest (Quintile 5) representing tracts with the highest rates of eviction.

**Persistent Systemic Inflammation Mediates the non-Hispanic Black vs non-Hispanic White Disparity in Cognitive Function: A Longitudinal Analysis**

Cesar Higgins Tejera\* Cesar Higgins Tejera Erin B Ware Margaret T. Hicken Matthew Zawistowski Lindsay C. Kobayashi Paris B. Adkins-Jackson Bhramar Mukherjee Kelly M. Bakulski

**Background:** Racialization is the process of grouping individuals into “races” based on phenotypic characteristics, assigning value to these groups, and disproportionately treating them. Racial health disparities may capture the differential impact of racialization, and subsequently, discrimination on these groups. In a longitudinal study of C-reactive protein (CRP), a marker of systemic inflammation, we explored trajectories of inflammation between non-Hispanic Black vs non-Hispanic White participants and tested if persistent inflammation mediated the racial disparity in cognitive function.

**Methods:** In the US Health and Retirement Study (n=4,719 adults aged >50), we used three repeated CRP and global cognitive measures at baseline (2006 or 2008), at year 4 (2010 or 2012), and year 8 (2014 or 2016). In multivariable generalized estimating equation models, we compared changes in cognitive function between non-Hispanic Black vs non-Hispanic White participants as a function of sustained elevated levels of CRP (all time points >3 vs. ≤3mg/L). We decomposed the racial disparity in cognitive function onto 1) the mediated effect due to elevated CRP, and 2) the portion attributable to the interaction between race and CRP.

**Results:** The average age at baseline was 68.8 years. Non-Hispanic Black participants (n=599) had 24% higher CRP at year 4 and 18% higher at year 8, relative to non-Hispanic White participants (n=4,120). Non-Hispanic Black participants with elevated CRP had 2.9 (95% CI: -3.2, -2.7) lower points on the global cognitive assessment than non-Hispanic White participants. In a randomized analogue model, we found that 4% (95% CI: 1%, 6%) of the racial disparity in cognitive function was mediated by sustained elevated CRP, and 14% (95%CI: 5%, 23%) attributable to the interaction between race and sustained elevated CRP.

**Conclusions:** Systemic inflammation mediates racialized disparities in cognitive function.

**Midlife Hearing, Vision, Olfactory and Motor Function Improve the Long-Term Prediction of Neurodegeneration** Natascha Merten\* Natascha Merten A Alex Pinto Carla R Schubert Richard J Chappell Corinne D Engelman Laura M Hancock Adam J Paulsen

Pathological changes in dementia often start decades before clinical symptoms making early detection of high-risk individuals important for targeted interventions. The CAIDE risk score was developed to predict dementia based on cardiovascular health. Age-related sensory (hearing, vision, olfaction) and motor changes are also associated with cognitive decline but studies on predictive values of sensory and motor function for early neurodegeneration are scarce. We aimed to assess if midlife sensory and motor function contribute to risk prediction models of present and future neurodegeneration as indicated by biomarker positivity in serum neurofilament light chain (NfL) protein levels.

This longitudinal study included 1529 (mean age 49yrs) Beaver Dam Offspring Study participants with serum NfL from baseline, 5-yr, and 10-yr follow-up. We assessed hearing, vision, olfaction, motor, and health history data, and calculated CAIDE at baseline. NfL positivity (NfL<sup>+</sup>) was defined by a value in the age-specific 97.5%ile. Logistic regressions were used to test if adding baseline sensory and motor function improves models of i) NfL<sup>+</sup> at baseline and ii) NfL<sup>+</sup> incidence over 10-years compared to risk prediction based on only the CAIDE score.

There were 69 cases of baseline NfL<sup>+</sup> and 115 of incident NfL<sup>+</sup>. The area under the receiver operating characteristics curve (AUROC) for NfL<sup>+</sup> at baseline increased from 0.53[95% CI 0.46,0.60] for CAIDE-only models to 0.63[0.56,0.71] in CAIDE-sensory-motor models( $p=0.03$ ). Adding sensory and motor function to NfL<sup>+</sup> incidence prediction improved the AUROC from 0.67[0.62,0.73] to 0.71[0.66,0.77]( $p<0.01$ ).

Midlife sensory and motor function improve risk prediction of early neurodegeneration as determined by biomarker positivity of blood-based NfL over 10 years in middle-aged to older adults. Longer follow-up is needed to determine how sensory and motor measures may contribute to long-term prediction of neurodegeneration and cognitive impairment later in life.

**Anxiety and the incidence of stroke during pregnancy in the United States** Kara Christopher\*

Kara Christopher Margarita Fedorova Jordan Scott

**Background:** Stroke during pregnancy is rare, occurring in 30 of 100,000 pregnancies, but accounting for 18% of strokes in women aged 12-35. Existing research shows that anxiety increases the lifetime risk of stroke. However, there is limited data on how anxiety impacts the development of stroke during pregnancy.

**Objective:** The aim of this project is to assess the rate of anxiety and the incidence of stroke among women during the perinatal period in the United States.

**Methods:** This study used the National Inpatient Sample (NIS) database (years 2016-2019), which is a publicly available all-payer discharge database in the United States. Women with an ICD-10 diagnosis code indicating their maternal status were included. Weighted logistic regression models were fitted, covariates in the model were age, primary payer, pre-existing hypertension, hypertensive disorders of pregnancy, gestational diabetes, and obesity status.

**Results:** Having anxiety was associated with an increased odds of stroke (aOR=1.77, 95%CI = 1.08-2.90). White women with anxiety were 91% more likely to also have a stroke (aOR=1.91, 95% CI=1.11-3.29), there were no significant findings for Black women or Latinas. Anxiety was also associated with an increased odds of having obesity (cOR=1.85, 95%CI=1.81-1.89), hypertensive disorders of pregnancy (cOR=1.61, 95%CI 1.59-1.64), and gestational diabetes (cOR=1.16, 95%CI=1.13-1.18).

**Conclusion:** Having a diagnosis of anxiety is associated with increased odds of stroke in pregnant women. Specifically, white women have higher odds of having a stroke if they have a concomitant diagnosis of anxiety. Further, among women with anxiety, they have increased odds of having other hypertensive disorders of pregnancy that could contribute to increased risk of stroke compared to women without anxiety.

**Associations of Childhood Trauma with Dementia Risk and Neuroimaging Markers in the UK Biobank Study** Ruijia Chen\* Ruijia Chen Jingxuan Wang Peter Buto Michelle Caunca Lewina Lee Natalie Slopen Laura D. Kubzansky Sarah F Ackley Maria Glymour

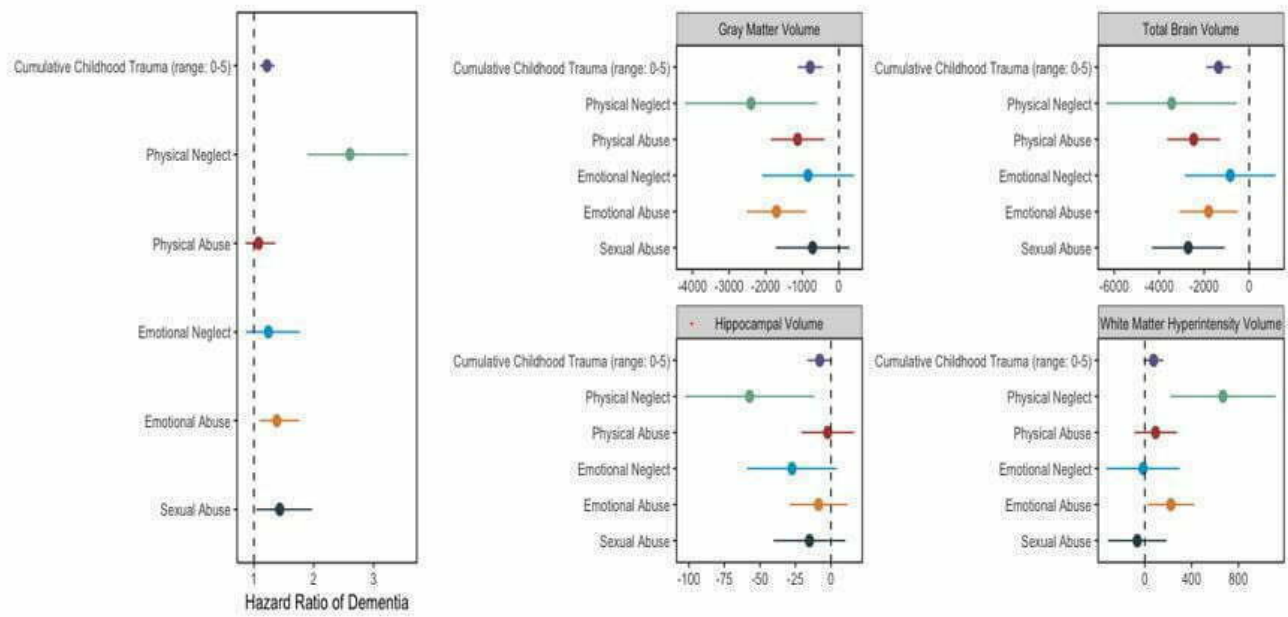
**Background:** Previous research has shown strong associations between childhood trauma and poorer cognitive function, suggesting that childhood trauma may lead to earlier dementia onset and poorer brain health. This study tested the hypothesis that childhood trauma would be associated with higher risk of dementia and poorer brain health.

**Method:** UK Biobank participants aged 40–69 years recruited between 2006–2010 completed an online Childhood Trauma Screener, which assessed physical abuse, physical neglect, emotional abuse, emotional neglect, and sexual abuse. We coded childhood trauma by counting the number of domains of abuse or neglect (range: 0 to 5). Incident dementia was ascertained for 148,060 participants with linked inpatient, primary care, and death records. Neuroimaging markers (gray matter, total brain, hippocampal, and white matter hyperintensity volumes) were available for 33,119 individuals who completed MRI scans. Cox proportional models and linear mixed-effects models examined childhood trauma in relation to incident dementia and neuroimaging markers, respectively, adjusting for age, gender, race, childhood SES proxies, and number of apolipoprotein E4 alleles. Models for neuroimaging markers were also adjusted for intracranial volume.

**Results:** Over a mean follow-up period of 12 years, 641 participants developed dementia. Cumulative childhood trauma was associated with higher dementia incidence (hazard ratio, 1.22; 95% Confidence Interval [CI], 1.10, 1.35), lower total gray matter volumes ( $\beta = -785 \text{ mm}^3$ ; 95% CI, -443, -1,127  $\text{mm}^3$ ), and lower total brain volumes ( $\beta = -1362 \text{ mm}^3$ ; 95% CI, -813, -1,911  $\text{mm}^3$ ). Across childhood trauma subtypes, physical neglect was most strongly associated with both dementia and neuroimaging outcomes.

**Conclusion:** Childhood trauma is associated with incident dementia risk and smaller gray matter and total brain volumes. Early life adversities may set up a lifetime of exposures that increase dementia risk in late life.





**Figure. Associations of Childhood Trauma with Dementia and Neuroimaging Markers in the UK Biobank Study.** Models were adjusted for age at enrollment, gender, intracranial volume, maternal smoking, number of siblings, and apolipoprotein E4 alleles. We applied inverse probability weights to account for selection into the childhood trauma survey.

**Heterogeneous associations of HbA1c with MRI measures of brain health among participants in UK Biobank** Peter T. Buto\* Peter Buto Stephen B. Asimwe Jingxuan Wang Scott C. Zimmerman Sarah Ackley Willa D. Brenowitz Melinda C. Power Anusha M. Vable Aayush Khadka M. Maria Glymour

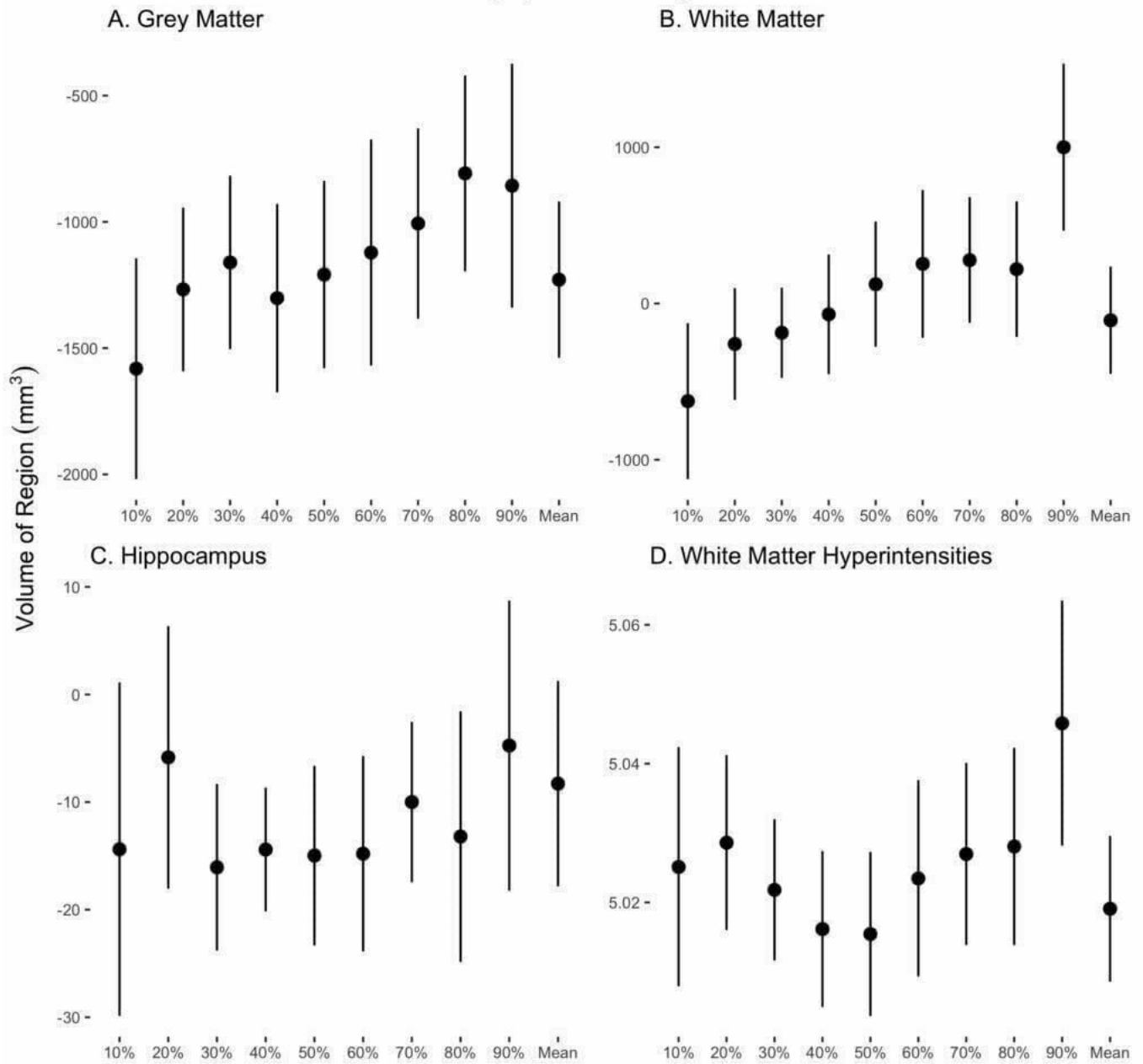
**Background:** Elevated glycated hemoglobin (HbA1c) is associated with neuroimaging markers of dementia risk. Most studies are underpowered to estimate heterogeneity in the effects of HbA1c and neuroimaging markers, which could allow identification of groups with particular vulnerability.

**Methods:** In the UK Biobank neuroimaging sample (N=42,918), we evaluated baseline HbA1c as predictors of brain MRI volumetric measures: grey matter volume (GMV); white matter volume (WMV); hippocampal volume (HV); and log-transformed white matter hyperintensity volume (WMH). Using linear regression, we evaluated whether a genetic risk score for AD (AD-GRS) or APOE4 haplotype modified the association between baseline HbA1c and brain MRI volumetric measures. We used conditional quantile regression to compare estimated effects at each decile of neuroimaging values. Analyses adjusted for age, sex, assessment center, ethnic background, education, body mass index and self-reported hypertension

**Results:** Participant mean age was 64.0 (SD=7.7) with an average HbA1c of 34.9 mmol/mol (SD=4.8). HbA1c was associated with lower mean GMV (-246 mm<sup>3</sup>, 95% CI:[-308,-183]) and higher mean WMH volume (0.4%, 95% CI:[0.2%,0.6%]). APOE4 haplotype modified the association of HbA1c only for HV; AD-GRS did not modify any association. Associations with HbA1c were greater at the lower tails of the regional brain volume distribution and smaller for at the upper tails. For example, the HbA1c was inversely associated with WMV at the 10th percentile (-125mm<sup>3</sup>, 95% CI:[-225,-25]) and positively associated at the 90th percentile (200, 95% CI: [93,307]).

**Conclusions:** Associations of HbA1c with neuroimaging measures varied across the distribution of regional brain volumes; higher levels of HbA1c especially affected those with lower regional brain volumes.

Figure 1: Adjusted associations in regional volume per 5 mmol/mol HbA1c by quantile of region



**Malnutrition and Stroke in Women of Reproductive Age** Kara Christopher\* Kara Christopher  
Xiaoyi Gao Jordan Scott

**Background:** Malnutrition in stroke patients is underrecognized and undertreated. Previous studies have shown that malnutrition before and after acute stroke results in extended hospital stays, worse functional outcomes, and higher mortality rates. Many risk factors are associated with malnutrition, including being elderly, female, having poor family or nursing care, presence of malignancy, diabetes mellitus, hypertension, and history of alcoholism. We aim to study the effect of malnutrition on the odds of stroke in women of reproductive age and the risk factors contributing to this effect.

**Methods:** We used data from the National Inpatient Sample (NIS), 2018-2019. The NIS is a nationally representative sample of hospital discharges in the US. For this study, women age 20-44 who did not have an ICD-10 code related to maternity were included. Logistic regression models were fitted and adjusted for covariates of age, type 2 diabetes, essential hypertension, dyslipidemia, and obesity status.

**Results:** Women 20-44 who had a diagnosis for malnutrition had 35% higher odds of having a stroke than women who did not were not diagnosed with malnutrition (aOR=1.35, 95%CI=1.15-1.59). When stratified by race, Black women had 68% increased odds (aOR= 1.68, 95%CI=1.24-2.27) of stroke with a diagnosis of malnutrition, and Latinas had 72% increased odds, compared to women without malnutrition. There was not a significant difference in stroke occurrence and malnutrition in white women.

**Conclusion:** In this study, we found that women of reproductive age with a diagnosis of malnutrition also had increased odds of having a stroke. It's important to address the impact malnutrition has on stroke risk since many stroke events lead to high mortality and morbidity, and early recognition of malnutrition significantly affects the outcome. Further studies are needed to investigate the disparity in malnutrition-related stroke risk among different races.

**The importance of modifiable female lifestyle characteristics to live birth: How much does lifestyle matter?** Neil Perkins\* Elizabeth DeVilbiss Una Grewal Neil Perkins

**Objective:** Identify lifestyle factors most important to live birth among women attempting to conceive and estimate their impact when modified.

**Methods:** Within a prospective preconception cohort nested within a randomized controlled trial based at 4 U.S. clinical sites, a combined *a priori* and machine learning approach was used to identify characteristics most related to live birth. The parametric g-formula were then used to emulate a target trial by estimating the causal effects of these hypothetical preconception treatment interventions on the risk of live birth, estimating absolute risk differences and 95% confidence intervals relative to no intervention (usual lifestyle). Achieving and maintaining pregnancy were also modeled to identify the drivers of changes in live birth. Multiple imputation accounted for missing data.

**Results:** Among 1228 women attempting pregnancy, reasonable improvements in psychological stress (50% reduction; 2.8%, 95% CI 0.6, 5.1 absolute increase in live birth), physical activity (attaining moderate exercise recommendations; 2.8%, 95% CI -0.5, 6.1), oleic acid (diet) (5<sup>th</sup> quintile; 2.8%, 95% CI -0.4, 6.1), and  $\beta$ -carotene (diet) (5<sup>th</sup> quintile; 3.2%, 95% CI 0.2, 6.1) were most influential in improving live birth at the population-level. A joint lifestyle intervention of all women attaining these targets preconception produced an absolute increase in live birth of 11% (95% CI 5.9, 16) at the population-level (77%, 95% CI 70, 84 vs. 66%, 95% CI 60, 71 under no intervention). This was driven by an increase in pregnancies (6.7%, 95% CI 2.9, 10), rather than a reduction in pregnancy losses (3.4%, 95% CI -0.2, 6.9).

**Conclusions:** In the absence of randomized controlled trials intervening on lifestyle factors, this study provides evidence that reducing stress levels, engaging in moderate physical activity, and increasing intake of oleic acid and  $\beta$ -carotene can improve the probability of live birth at the population-level.

**Table.** Adjusted <sup>a</sup> impact of individual and joint lifestyle interventions on population probabilities of **live birth, pregnancy, and pregnancy maintenance (no pregnancy loss)** among 1228 women attempting pregnancy for up to 6 menstrual cycles in EAGeR using g-Formula

Outcome	Intervention #	Variable	Intervention	g-form mean (%), 95% CI	Mean diff (%), 95% CI
Live birth	0	-	Nat course	66 (60, 71)	<i>Referent</i>
	1	Stress	50% ↓	69 (63, 74)	<b>2.8 (0.6, 5.1)</b>
	2	Moderate exercise	All	69 (62, 75)	2.8 (-0.5, 6.1)
	3	Vit D sufficiency	All	65 (60, 71)	-0.4 (-1.7, 0.8)
	4	Oleic acid (18:1n9c)	5 <sup>th</sup> quintile	69 (62, 75)	2.8 (-0.4, 6.1)
	5	Alpha carotene	3 <sup>rd</sup> quintile	67 (61, 72)	0.7 (-2.3, 3.7)
	6	Beta carotene	5 <sup>th</sup> quintile	<b>69 (63, 75)</b>	<b>3.2 (0.2, 6.1)</b>
	7	Zeaxanthin	5 <sup>th</sup> quintile	67 (61, 73)	1.4 (-0.6, 3.4)
	1+2+4+6	<b>Stress</b>	<b>50%</b>	<b>77 (70, 84)</b>	<b>11 (5.9, 16)</b>
		<b>Moderate exercise</b>	<b>All</b>		
	<b>Oleic acid</b>	<b>5<sup>th</sup> quintile</b>			
	<b>Beta carotene</b>	<b>5<sup>th</sup> quintile</b>			
Pregnancy	0	-	Nat course	80 (75, 84)	<i>Referent</i>
	1	Stress	50% ↓	81 (76, 86)	1.4 (-0.6, 3.4)
	2	Moderate exercise	All	81 (75, 86)	1.1 (-1.6, 3.8)
	3	Vit D sufficiency	All	79 (75, 84)	-0.3 (-1.4, 0.7)
	4	Oleic acid (18:1n9c)	5 <sup>th</sup> quintile	82 (77, 87)	2.4 (-0.2, 5.0)
	5	Alpha carotene	3 <sup>rd</sup> quintile	79 (75, 84)	-0.2 (-2.5, 2.1)
	6	Beta carotene	5 <sup>th</sup> quintile	82 (77, 87)	2.6 (-0.1, 5.2)
	7	Zeaxanthin	5 <sup>th</sup> quintile	80 (75, 85)	0.4 (-1.3, 2.0)
	1+2+4+6	<b>Stress</b>	<b>50%</b>	<b>86 (81, 92)</b>	<b>6.7 (2.9, 10)</b>
		<b>Moderate exercise</b>	<b>All</b>		
	<b>Oleic acid</b>	<b>5<sup>th</sup> quintile</b>			
	<b>Beta carotene</b>	<b>5<sup>th</sup> quintile</b>			
No loss	0	-	Nat course	85 (81, 90)	<i>Referent</i>
	1	Stress	50% ↓	87 (82, 91)	1.3 (-0.3, 2.9)
	2	Moderate exercise	All	87 (82, 92)	1.5 (-1.3, 4.3)
	3	Vit D sufficiency	All	85 (81, 90)	-0.1 (-1.0, 0.9)
	4	Oleic acid (18:1n9c)	5 <sup>th</sup> quintile	86 (81, 91)	0.2 (-1.5, 1.9)
	5	Alpha carotene	3 <sup>rd</sup> quintile	86 (82, 91)	1.0 (-1.2, 3.2)
	6	Beta carotene	5 <sup>th</sup> quintile	86 (81, 91)	0.6 (-1.5, 2.7)
	7	Zeaxanthin	5 <sup>th</sup> quintile	86 (82, 91)	0.9 (-0.5, 2.4)
	1+2+4+6	<b>Stress</b>	<b>50% ↓</b>	<b>89 (83, 94)</b>	<b>3.4 (-0.2, 6.9)</b>
		<b>Moderate exercise</b>	<b>All</b>		
	<b>Oleic acid</b>	<b>5<sup>th</sup> quintile</b>			
	<b>Beta carotene</b>	<b>5<sup>th</sup> quintile</b>			

<sup>a</sup>Outcome models adjusted for age, race, income, employment status, marital status, and education at baseline, as well as all other interventions in model

**Associations of positive childhood experiences with adaptive and maladaptive eating among college students: Findings from Research, Eating, Activity, and Community Health (REACH) pilot study** Cynthia Yoon\* Cynthia Yoon Temperance Joseph Genesis Moussa Trenton Voss Tracey Ledoux Craig Johnston

**Background:** Childhood experiences include adverse and positive childhood experiences. Although adverse childhood experiences are known factors related to maladaptive and adaptive eating behaviors, how positive childhood experiences (PCEs) are related to such eating behaviors remain unclear.

**Purpose:** To examine the relationship of PCEs with maladaptive and adaptive eating behaviors among college students.

**Methods:** Data were derived from the Research on Eating, Activity, and Community Health pilot study ( $N=827$ ; 54.5% women,  $M_{age} 20.9\pm 2.6$  yrs in 2022). PCEs (e.g., prior to age 18, did you have at least one caregiver with whom you felt safe; prior to age 18, did you have at least one good friend) were assessed with the Benevolent Childhood Experiences scale and categorized into quartiles. Six maladaptive eating behaviors (e.g., binge eating, unhealthy weight control behaviors, and chronic dieting) were assessed with the Questionnaire on Eating and Weight Patterns-Revised. Two adaptive eating behaviors (i.e., intuitive eating and mindful eating) were assessed with Intuitive Eating Scale-2 and Mindful Eating Questionnaire. Modified Poisson regressions were used to examine associations between PCEs and maladaptive eating behaviors. Linear regressions were used to examine associations between PCEs and adaptive eating behaviors.

**Results:** Compared to participants in Quartile 1 (i.e., least positive childhood experiences), Quartiles 3 and 4 each had lower risks of all maladaptive eating behaviors except for chronic dieting ( $RR=0.53-0.88$ ,  $p$  trend  $\leq .01$ ); Quartiles 2, 3, and 4 each had higher intuitive eating scores ( $\beta=1.98$ , 1.85, and 2.74, respectively,  $p$  trend  $< .01$ ); Quartile 4 had higher mindful eating score ( $\beta=0.74$ , 95% CI = 0.35, 1.13,  $p$  trend  $< .01$ ) after adjustment for age, race, and socioeconomic status.

**Conclusion:** PCEs were associated with maladaptive and adaptive eating behaviors. Future studies should explore the underlying mechanism of this relationship.

**Accelerometry-Measured Sleep, Rest-Activity Rhythms, and the Charlson Comorbidity Index in the Hispanic Community Health Study/Study of Latinos and Sueño** Alexis Garduno\*  
Alexis Garduno Linda Gallo Andrea LaCroix Linda McEvoy Loki Natarajan Humberto Parada Sanjay Patel

Sleep and circadian disturbances have been shown to adversely affect cognitive and cardiometabolic health; associations of sleep with multimorbidity are understudied. This prospective cohort study included 10,587 and 1,876 adults (men and women, age 18-74 years when enrolled) from the HCHS/SOL and the Sueño ancillary studies, respectively. We evaluated the relationship between self-reported sleep (from HCHS/SOL baseline, 2008-2011) and actigraphy assessed sleep-circadian measures (from Sueño, 2010-2013) and multimorbidity [modified Charlson Comorbidity Index (CCI), from HCHS/SOL Visit 2, 2011-2017]. We tested for statistical interactions in associations by nativity, gender, and age group ( $p < 0.05$ ). We modeled associations between sleep-circadian quartiles with CCI using a zero-inflated Poisson model, accounting for the complex sampling design with sampling weights and adjusting for sociodemographic and behavior covariates. Self-reported insomnia symptoms [Q4vs.Q1, IRR: 1.61 (95%CI:1.29-2.00), overall- $p < 0.0001$ ], excessive daytime sleepiness, and objectively assessed intra-daily variability (e.g. greater rhythm fragmentation, suggestive of increased napping and/or daytime activity) [Q4, IRR: 1.40 (95%CI:1.10-1.79), overall- $p = 0.002$ ] were associated with higher overall multimorbidity 5-6 years later. Foreign-born Latinos had significantly smaller associations between insomnia (among other sleep-circadian measures) and CCI than those born in the United States [US-born, Q4vs.Q1, IRR: 1.89 (95%CI:1.51-2.36); Foreign-born <10 years in U.S., Q4vs.Q1, IRR:1.31 (95%CI:1.09-1.57); Foreign-born 10-20 years, Q4vs.Q1, IRR: 1.39 (95%CI:1.17-1.64); Foreign-born 20+ years, IRR: 1.32 (95%CI:1.16-1.50); overall- $p = 0.002$ ]. Disrupted sleep and circadian rhythms may contribute to differences in multimorbidity; this work is consistent with prior work showing a health advantage among Latino immigrants in multimorbidity.



**Associations between tattooing and health and risk-taking behaviors in Utah** Rachel D. McCarty\* Rachel McCarty Britton Trabert Morgan M. Millar Benjamin Haaland Laurie Grieshober Mollie E. Barnard Lindsay J. Collin Jeffrey A. Gilreath Paul J. Shami Jennifer A. Doherty

**Background:** Approximately 32% of adults in the U.S. have at least one tattoo. A higher prevalence of risk-taking behaviors including smoking and recreational drug use have been observed among tattooed individuals in prior studies. We sought to quantify associations of tattooing with health and risk-taking behaviors among adults in Utah.

**Methods:** We conducted a cross-sectional study of 2020 Utah Behavioral Risk Factor Surveillance System survey respondents (n=9,353). We fit Poisson models to compute prevalence ratios (PRs) and 95% CIs regressing ever having a tattoo on health and risk-taking variables, overall and stratified by religion (Church of Jesus Christ of Latter-day Saints (LDS) vs. not LDS), separately for females and males, adjusted for age, education, and race and ethnicity.

**Results:** Having a tattoo was associated with ever smoking among females (PR=2.65, 95% CI: 2.35–2.99) and males (3.09 [2.64–3.61]), and current smoking among females (2.74 [2.10–2.77]) and males (3.30 [2.69–4.03]), compared with never smokers. These associations were strongest among LDS females (ever: 4.80 [3.59–6.42]; current: 4.69 [2.97–7.43]) and LDS males (ever: 4.80 [3.26–7.07]; current: 4.75 [2.71–8.34]). Tattooing was also associated with binge drinking (overall females: 2.17 [1.89–2.50]; LDS females: 4.79 [3.01–7.61]; overall males: 2.21 [1.91–2.57]; LDS males: 3.71 [2.43–5.67]) compared with no binge drinking, storing loaded firearms in the home (overall females: 1.72 [1.34–2.22]; overall males: 1.54 [1.16–2.06]) compared with storing firearms unloaded, and  $\geq 14$  days with poor mental health in the past 30 days (females: 1.63 [1.43–1.86]; males: 1.28 [1.06–1.55]) compared with  $< 14$  days.

**Conclusion:** We observed tattooing to be associated with smoking, binge drinking, improper firearm storage, and poorer mental health. Tattoo parlors and conventions present opportunities for public health interventions including tobacco cessation, firearm safety, and mental health resources.

**Does the smartphone-based shopping mall-walking program encourage people to walk more? A multilevel analysis of nationwide big data in Japan** Yoko Matsuoka\* Yoko Matsuoka Hiroaki Yoshida Masamichi Hanazato

### **Aim**

Shopping malls are recognized as safe for walking, and several mall-walking programs have been implemented. AEON MALL Co., Ltd., a nationwide shopping mall operator in Japan, established a mall-walking program uniquely combined with a smartphone application's lottery-based incentive system. This study was aimed at evaluating the impact of a *mall challenge* (mall-walking program) using a smartphone-based gamification system to provide incentive coupons on walking.

### **Methods**

We used nationwide big data from 223,005 male and female application users aged 18 years or higher containing daily walking steps for 25,035,159 days from November 10, 2020, to December 31, 2021. The daily participation status in the *mall challenge* and shopping mall location, as indicated by the global positioning system, were recorded. We applied multilevel mixed-effect linear regression models to estimate coefficients of participation in the *mall challenge*. We also compared the differences by region or size of the shopping mall and participants' gender and age.

### **Results**

After adjusting for gender and age, *mall challenge* participation was found to be associated with 1,211 more daily steps compared with those on the day without program enrollment. Comparison by region showed that the *mall challenges* in rural, suburban, and urban malls were associated with around 1,122, 1,402, and 1,417 more steps, respectively, compared with those on the days without participation in the *mall challenges*. Moreover, *mall challenges* in large and small malls were associated with around 1,417 and 1,048 steps more, respectively, in comparison with the steps on days without participation in the *mall challenges*. Regarding cross-level interactions, women walked 739 steps more than men, and older adults walked 216 steps more than younger participants on the day of the *mall challenge*.

### **Conclusion**

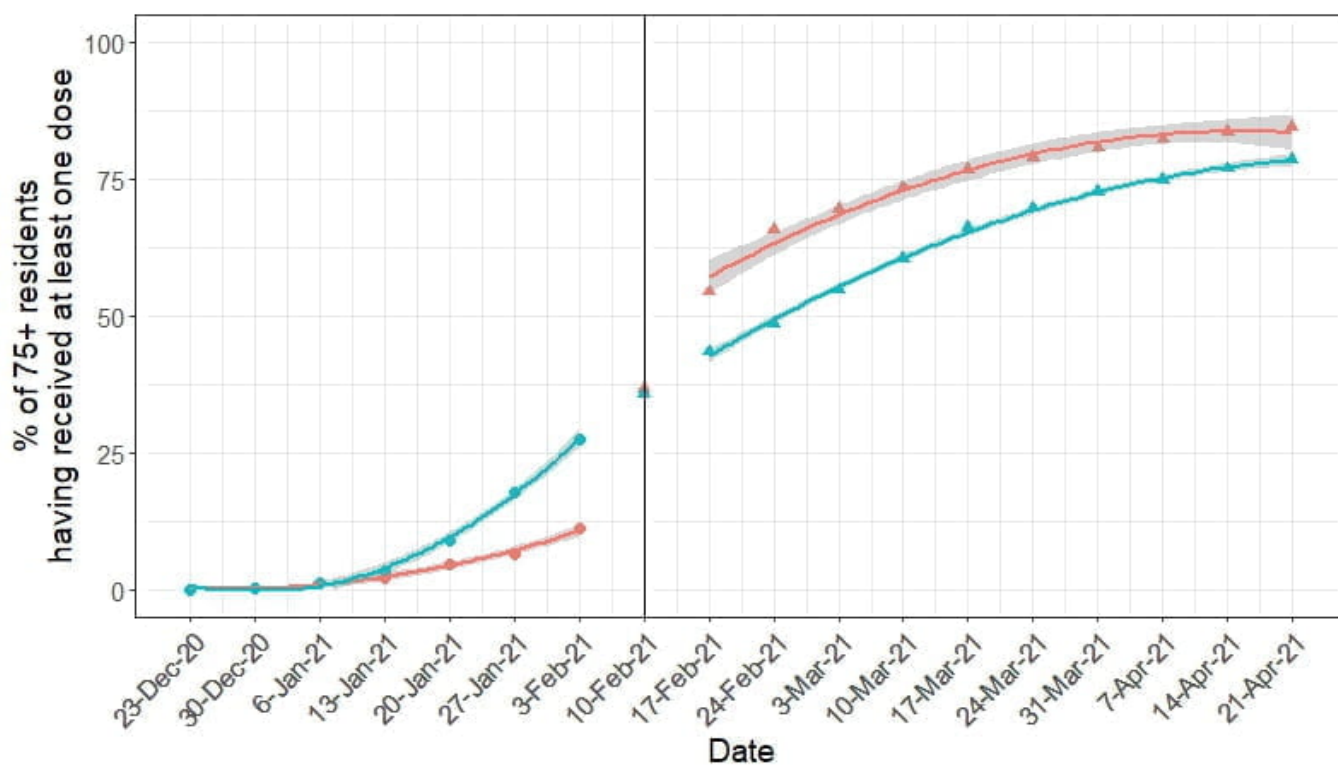
A smartphone-based mall-walking program with incentive coupons may restore the decrease in steps after the COVID-19 pandemic.

**Massachusetts companion program bolsters COVID-19 vaccine rates among seniors** Marie-Laure Charpignon\* Marie-Laure Charpignon Shagun Gupta Maimuna Shahnaz Majumder

Due to limited vaccine access and hesitancy, COVID-19 vaccination rates remained low in parts of the US until late Fall 2021. With colliding epidemics of RSV, flu, and SARS-CoV-2 in Winter 2022-2023, the retrospective evaluation of vaccine incentive policies is warranted. These are highly relevant when immediate action is needed to counteract vaccine hesitancy. Even members of the same household can have differing opinions about vaccination and prophylactic measures such as Paxlovid. Policies that leverage social and intergenerational influence can improve uptake; those not yet eligible but eager to benefit from an intervention can boost uptake among their eligible but more hesitant social contacts. The Massachusetts (MA) companion program is one example of such a policy. On February 10, 2021, the Governor's office announced that individuals who accompanied a senior citizen aged 75+ could receive their own vaccine on the same day, before younger age groups become eligible. To determine whether the program yielded a boost in COVID-19 vaccination rates among seniors, we used weekly count data from the MA Department of Public Health and characterized the percentage of state residents aged 75+ who had (1) received at least one dose or (2) been fully vaccinated, proximal to policy implementation. We performed two regression discontinuity (RD) analyses and fitted logistic growth models and generalized additive model (GAM) to each time series to account for varying supply. The program was associated with an increase of up to 35.4 points (95% CI: 29.4-41.4) in outcome (1) and of up to 22.2 points (95% CI: 15.9-28.6) in outcome (2). In contrast, the US-wide analysis (excluding MA) did not reveal any significant increases in vaccine uptake (Figure 1). In future, intervention strategies such as the MA companion program could be invaluable in scenarios where household contacts pose the greatest risk of transmission or where social ties can influence individual decision-making.

Pre- vs post-companion program launch • Pre ▲ Post

Geographical region — Massachusetts — U.S. (excluding Massachusetts)



**Targeted estimands in nutritional epidemiology: a case study on the effect of dairy consumption and cognitive function** Natalia Ortega\* Natalia Ortega Pedro Marques-Vidal Fanny Viloz Tommaso Filippini Cristian Carmeli Nicolas Rodondi Arnaud Chiolero Patricia Chocano-Bedoya

**Background:** Heterogeneity in targeted estimands and identification assumptions may lead to estimates in opposite directions in nutrition studies assessing the effect of food groups on cognition outcomes.

**Aims:** Characterize the estimands and identification assumptions in studies targeting the effect of dairy on cognition and compare them to explicitly defined estimands.

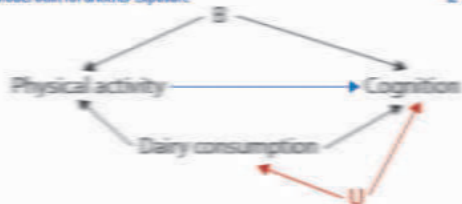
**Methods:** We examined 12 studies included in a previous systematic review. We assessed if they targeted a) total (addition of 100g dairy/d) or relative causal effects (substitution 100g/d of a food for 100g/d dairy) and the identification assumptions made. We computed total and relative effects in a population-based cohort (PsyColaus) of 1,347 adults with 5 years of follow-up. The models were adjusted for the minimal adjustment set identified via a graphical causal model by fitting general additive all-components models for 8 comprehensive cognitive function outcomes.

**Results:** The 12 studies targeted total effects. There were three main issues in the identification of their estimands: 1) adjustment for total energy without excluding the food of interest from the total, creating a collider in total energy or used the residual method recommended for computing relative effects, 2) interpretation of estimates from a model built for a different association - reported protective effects, and 3) not appropriate control for baseline cognition - reported harmful effects. In PsyCoLaus, we observed neither total nor relative clinically relevant effect (e.g., total effect for MMSE = was 0.002 (95% CI: 0.0001 to 0.003) score increase per 100g/d dairy added).

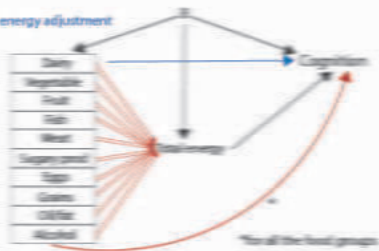
**Conclusion:** The key factors affecting the direction of the estimate were the interpretation of estimates in a model built-in for another exposure and inappropriate control for baseline cognition. Nutritional epidemiology studies should explicitly address the identification assumptions related to the targeted estimands for improved estimate interpretability.

Problems found in the dairy - cognition literature targeting Total Effects

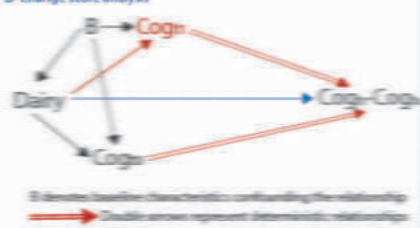
1 Model built for another exposure



2 Total energy adjustment



3 Change score analysis



PsyColaus model



References:  
 Torres et al. 2022. doi.org/10.1093/ajph/112/10  
 Torres et al. 2022. doi.org/10.1093/ajph/112/10

**Assessing agreement between the National Cancer Institute's Diet History Questionnaire II and III in a preconception cohort** Sachelly Julian-Serrano\* Sachelly Julian-Serrano Martha R. Koenig Tanran R. Wang Amelia K. Wesselink Elizabeth Lauren A. Wise Katherine L. Tucker

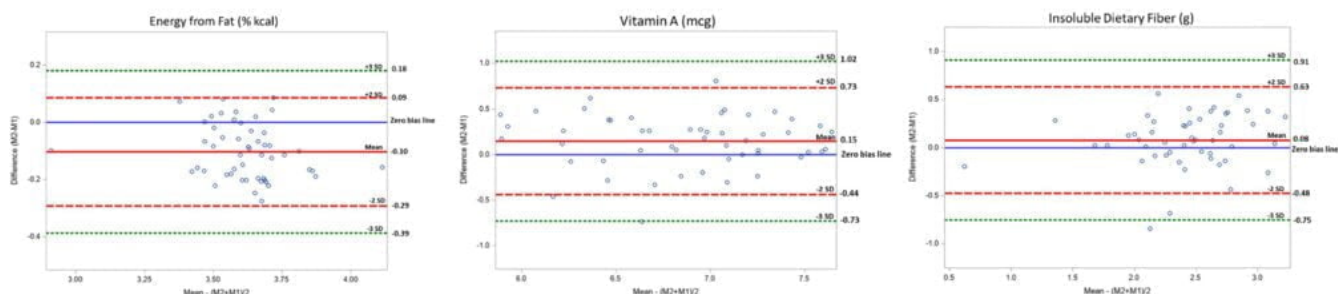
**Background:** Food frequency questionnaires require updating over calendar time due to population changes in diet, leading to potential analytical challenges in long-term prospective cohort studies. We compared the reliability and agreement between nutrients in two versions of the National Cancer Institute's web-based Diet History Questionnaire (DHQ, III vs. II) in an ongoing North American preconception study.

**Methods:** In Pregnancy Study Online (PRESTO), a North American preconception study launched in 2013, dietary data were collected with the DHQ-II (2013-2019) and updated to the DHQ-III (2020-present). For the present validation study, we invited 52 female participants aged 21-45 years to complete both the DHQ-II and DHQ-III within a 2-week period. We randomized the DHQ version order (III vs. II) with 50% probability. We compared 28 macro- and micronutrients (including percent energy) from both DHQ versions and calculated within-person reliability using intraclass correlation coefficients (ICCs). We generated Bland-Altman plots and 95% limits of agreement (LOAs) to assess agreement of log-transformed nutrients between DHQ III vs. II.

**Results:** We observed highest reliability in percent energy from carbohydrates (ICC: 0.88; 95% CI: 0.80-0.93) and cholesterol (ICC: 0.88; 95% CI: 0.80-0.93) and lowest reliability for percent energy from protein (ICC: 0.56; 95% CI: 0.34-0.72). At the group level, 25 log-transformed nutrients had LOAs wider than 2 SD suggesting "fair" agreement, whereas insoluble dietary fiber and vitamin A showed LOA wider than 3 SD suggesting "poor" agreement. Only one nutrient (percent energy from fat) showed "good" agreement, with LOA within 2 SD.

**Conclusions:** In our study, most nutrients showed fair agreement and good-to-moderate reliability. Future users should consider adjustment and calibration analysis of individual nutrients before using the DHQ-III and DHQ-II interchangeably in prospective studies.

**Bland-Altman plots of log-transformed nutrients measured by DHQ III vs. II (N=51)**



**Is BMI really that bad? Quantifying measurement error due to self-report BMI in NHANES.**

Samantha Smith\* Samantha Smith Hailey Banack

**Background:** Body mass index (BMI) is frequently criticized as a poor measure of true obesity status. Using self-report height and weight to quantify BMI status may compound issues related to measurement error. However, self-report BMI can be cost-effectively obtained in large epidemiological studies. The purpose of this research was to compare self-report and measured BMI across different demographic groups (sex, age, race/ethnicity) and to quantify the amount of bias introduced by using self-report BMI. **Methods:** Adults 40 and older who participated in NHANES waves 1999-2012 were included (N= 21,928). Means and corresponding 95% CIs were calculated for both self-report and measured height, weight, and BMI estimates. The amount of bias between self-report and measured anthropometric estimates was determined by calculating the difference between self-report and measured BMI. Sensitivity (Se), specificity (Sp), and positive and negative predictive values (PPV, NPV) were calculated for each sex, race, and age group. **Results:** Across all races/ethnicities, older women had the greatest bias result from using self-report vs. measured BMI (mean range: -0.70, -1.06). Older individuals overestimated their height more than younger individuals, regardless of race or sex. Younger women of all races/ethnicities had the greatest bias (under-estimation) between self-report vs. measured weight. The amount of bias present varied by BMI category and demographic group (sensitivity range: 0.81 to 0.99; specificity range: 0.73 to 0.95). **Conclusion:** Overall sensitivity and specificity scores were high across groups but did vary by BMI and demographic group. These results provide estimates of bias parameter values that can be used in future research to adjust self-report BMI data and generate corrected estimates using quantitative bias analysis techniques.



**Body mass index and prostate cancer screening, incidence, and mortality in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial** Lauren Hurwitz\* Lauren Hurwitz Nadine Dogbe Kathryn Hughes Barry Stella Koutros Sonja Berndt

Background: Emerging evidence suggests that obesity, as measured by body mass index (BMI), is associated with increased prostate cancer mortality. However, associations with prostate cancer incidence are inconclusive and mechanisms remain unclear. Obesity could increase risk directly or act indirectly via effects on prostate cancer screening efficacy. We examined associations between BMI and prostate cancer screening outcomes, incidence, and mortality among men undergoing prostate cancer screening as part of a randomized controlled trial.

Methods: We included men randomized to the screening arm of the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial from 1993-2001 with no history of prostate cancer and data on BMI at baseline (n=37,404). These men received annual screening with a prostate-specific antigen (PSA) blood test and digital rectal exam (DRE) for up to 6 and 4 years respectively and were followed for cancer outcomes through 2018. Associations between BMI and screening outcomes were assessed via multinomial logistic regression, and associations between BMI and prostate cancer incidence (total, early-stage, advanced-stage) and mortality were assessed via Cox proportional hazards regression.

Results: Men with higher BMI were less likely to screen positive for prostate cancer on the PSA test and/or DRE (all p-trends<0.01). Higher BMI was inversely associated with prostate cancer incidence (HR [95% CI] per 5 kg/m<sup>2</sup> BMI increase: 0.94 [0.91-0.97]), including incidence of early-stage (0.94 [0.90-0.97]) and advanced-stage (0.91 [0.82-1.02]) disease, and positively associated with prostate cancer mortality (1.21 [1.06-1.37]).

Conclusions: Within this screened population, men with higher BMI had lower risk of prostate cancer diagnosis but higher risk of dying of prostate cancer. Because higher BMI was not associated with increased risk of advanced-stage prostate cancer, the higher mortality is unlikely to be due to delayed prostate cancer detection.

**Longitudinal association of thoracic fat with all-cause and cardiovascular death: a cohort study analysis of RCT data using marginal structural models** Jonathan Weber\* Jonathan Weber  
Ruqiyya Bano Lu Chen

**Background**

Thoracic fat located outside of the pericardium is an underutilized biomarker with differing origin, location, blood supply, and composition from other well-studied epicardial fat deposits. Changes in thoracic fat and their effects on adverse outcomes have not been examined. We aimed to measure the relationship of thoracic fat volume (TFV) and long-term all-cause/CVD death using a marginal structural model (MSM).

**Methods**

We utilized data from the St. Francis Heart Study, an RCT of healthy subjects examining the effects of statin therapy on coronary artery calcium (CAC) score measured by CT and with long-term mortality. Subjects received repeat CT and clinical exams from approximately 1998-2005 and were followed for outcomes to 2018. We utilized baseline, 2-, and 4-6 year f/u CT exams to measure TFV. MSMs were constructed (Figure) using inverse prob. of treatment weights (IPTWs) and censoring weights considering time-varying lipid profile and CAC score with time-fixed baseline demo/medical history as confounders, and statin as an effect modifier. TFV was treated as continuous since cut-points have not been established. Methods to model the IPTWs included using normal homo/heterogeneous variance, truncated, or gamma distributions and quintile binning. IPTWs were applied to pooled logistic regression models with robust variance whose ORs estimate the average HR over the f/u period.

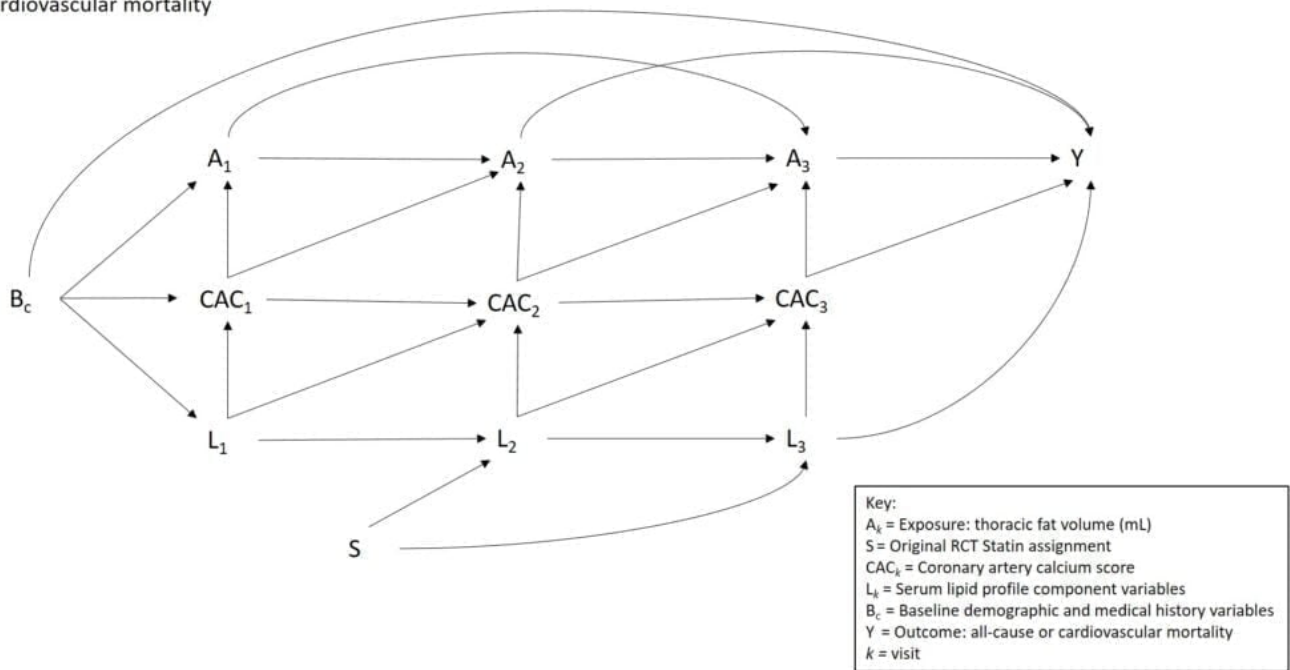
**Results**

There were 943 subjects included (26% female, age  $59 \pm 6$ , 92% white). Statin was found to have no effect modification and was treated as a confounder. After  $17 \pm 3$  years 171 died (51 from CVD). IPTW weights using a heterogeneous normal distribution demonstrated the best fit with pooled OR of 1.03 (95% CI 1.01-1.05) and 1.02 (95% CI 0.98-1.06) per 10 mL increase in TFV associated with all-cause/CVD death. Sensitivity testing of the positivity assumption did not alter the results.

**Conclusion**

Increased thoracic fat volume over time is associated with long-term all-cause mortality.

Figure: Directed acyclic graph demonstrating hypothesized relationship between thoracic fat and all-cause or cardiovascular mortality



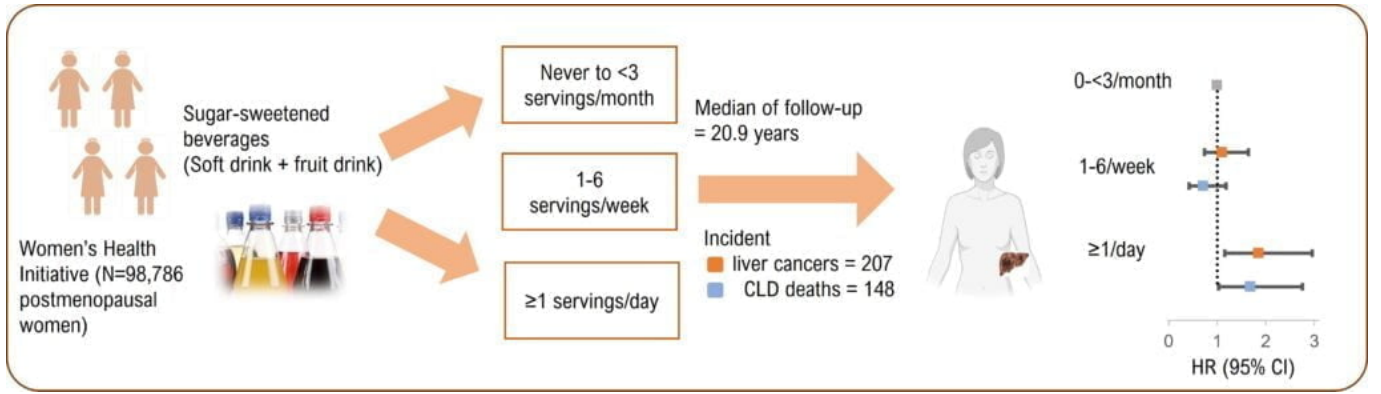
**Associations between sugar-sweetened and artificially sweetened beverage intake, liver cancer and chronic liver disease mortality** Xuehong Zhang\* Longgang Zhao Xinyuan Zhang Mace Coday David O. Garcia Xinyi Li Yasmin Mossavar-Rahmani Michelle J. Naughton Melissa Lopez-Pentecost Nazmus Saquib Aladdin H. Shadyab Michael S. Simon Linda G. Snetselaar Fred K. Tabung Deirdre K. Tobias Trang Vo Pham Katherine A. McGlynn Howard D. Sesso Edward Giovannucci JoAnn E. Manson Frank B. Hu Lesley Tinker Xuehong Zhang

**Background:** Evidence is limited on associations of sugar sweetened beverage (SSB) and artificially sweetened beverage (ASB) intake with liver cancer and non-cancer related chronic liver disease (CLD) mortality. We aimed to investigate the associations between SSB, ASB, and liver cancer and CLD mortality.

**Methods:** A total of 98,786 postmenopausal women aged 50-79 years from the Women's Health Initiative were included. SSB intake was assessed based on a food frequency questionnaire administered at baseline between 1993 and 1998 and defined as the sum of regular soft drinks and fruit drinks; ASB intake was measured at follow-up year three. We used liver cancer incidence and CLD mortality as our main outcomes. Cox proportional hazard regression models were used to estimate multivariable hazard ratios (HRs) and 95% confidence intervals (CIs) for liver cancer incidence and CLD mortality with adjustment for potential confounders including body mass index and self-reported diabetes.

**Results:** During a median 20.9 years of follow-up, 207 liver cancer cases and 148 CLD deaths were identified. Higher SSB intake ( $\geq 1$  serving/day) was associated with an 85% greater risk of liver cancer (HR, 1.85; 95% CI, 1.16 to 2.96;  $P_{\text{trend}}=0.01$ ) and 68% greater risk of CLD mortality (HR, 1.68; 95% CI, 1.03 to 2.75;  $P_{\text{trend}}=0.08$ ), compared to intake of  $<3$  servings/month. ASB intake was not associated with liver cancer (HR, 1.11; 95% CI, 0.70 to 1.77;  $P_{\text{trend}}=0.83$ ) or CLD mortality (HR, 0.95; 95% CI, 0.49 to 1.84;  $P_{\text{trend}}=0.92$ ) for the same comparison.

**Conclusions:** Our findings suggest that SSB intake may be a potential modifiable risk factor for liver cancer and CLD mortality. More studies are needed to examine these associations in diverse populations, as well as elucidate the biological mechanisms.



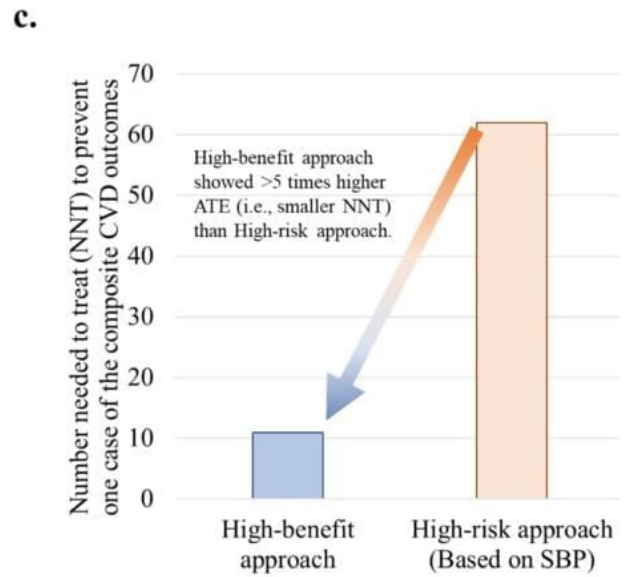
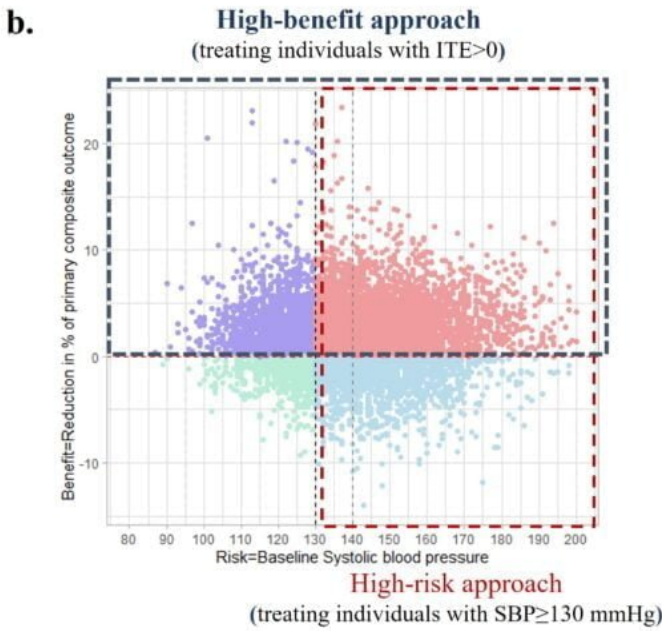
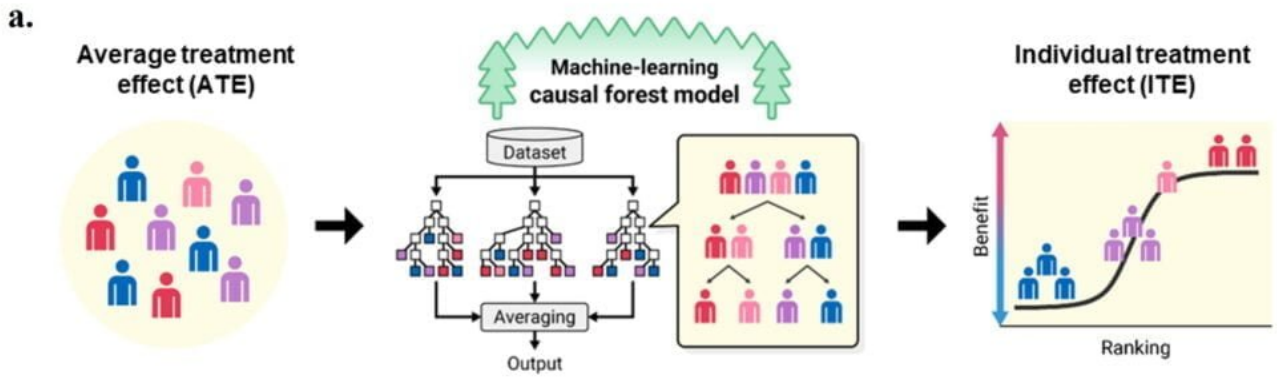
**Machine-learning based high-benefit approach versus conventional high-risk approach in blood pressure management** Kosuke Inoue\* Kosuke Inoue Susan Athey Yusuke Tsugawa

**Background:** In medicine, clinicians treat individuals under an implicit assumption that high-risk patients would benefit most from the treatment (“high-risk approach”). However, treating individuals with the highest estimated benefit using a novel machine-learning method (“high-benefit approach”) may improve population health outcomes.

**Methods:** This study included 10,672 participants who were randomized to systolic blood pressure (SBP) target of either <120mmHg (intensive treatment) or <140mmHg (standard treatment) from two randomized controlled trials (SPRINT and ACCORD-BP). We applied the machine-learning causal forest to develop a prediction model of individualized treatment effect (ITE) of intensive SBP control on the reduction in cardiovascular outcomes at 3 years. We then compared the performance of the high-benefit approach (treating individuals with  $ITE > 0$ ) versus the high-risk approach (treating individuals with  $SBP \geq 130$  mmHg). Using the transportability formula, we also estimated the effect of these approaches among 14,575 US adults from the National Health and Nutrition Examination Surveys (NHANES) 1999-2018.

**Results:** The mean (standard deviation) age was 65.5 (8.4) years, and 40.8% were female. We found that 78.9% of individuals with  $SBP \geq 130$  mmHg benefited from intensive SBP control. The high-benefit approach outperformed the high-risk approach (average treatment effect [95%CI], +9.36 [8.33-10.44] vs. +1.65 [0.36-2.84] percentage point; the difference between these two approaches, +7.71 [6.79-8.67] percentage point,  $p$ -value <0.001). The results were consistent when we transported the results to the NHANES data.

**Conclusions:** The machine-learning-based high-benefit approach outperformed the high-risk approach *with a larger treatment effect (Figure)*. These findings indicate that the high-benefit approach has the potential to maximize the effectiveness of treatment rather than the conventional high-risk approach, which needs to be validated in future research.



**A shift in data sharing paradigms: a case study on the ways in which big data and complex algorithms allow for increased data sharing while preserving privacy** Lauren Wilner\* Lauren Wilner Weipeng Zhou Amy Youngbloom Stephen J Mooney

Personal device data including that from GPS trackers and accelerometers hold considerable public health research potential. These data can be used to measure walking and explore determinants of this key cardioprotective behavior across geospatial contexts independent of interviewer, recall, and social desirability biases.

However, personal monitoring devices are expensive, so studies using these devices rarely enroll large populations. Analyses pooling monitoring data from multiple sites offer broader conclusions, but these data are personally identifying, precluding sharing the data directly. To address this gap, we developed an R package ('walkbotr') to extract patterns consistent with walking as deidentified and sharable 'walk bouts'.

A walk bout is a period of activity with accelerometer movement matching the patterns of walking with corresponding GPS measurements that confirm travel. The inputs of the walkbotr package are individual-level accelerometry and GPS data. The outputs of the model are walk bouts with corresponding times, duration, and summary statistics on the sample population, which collapse all personally identifying information. These bouts can be used to measure walking both as an outcome of a change to the built environment or as a predictor of health outcomes such as a cardioprotective behavior.

In this case study, we collapsed data from Wave 1 of the Travel Assessment and Community (TRAC) study containing 7924 days of GPS and accelerometry records from 670 participants. The result was a dataset of 4898 deidentified walk bouts that were used to assess the impact of a new transit stop on physical activity and were safely shared with other research groups investigating similar predictor-outcome relationships.

Our case study illustrates how reusable code can develop useful and non-identifying summaries of identifying data. Such code can be used to develop larger cross-site datasets to address nuanced scientific questions without privacy concerns.



**Standardization over disease risk score versus propensity score for confounding control when using random forests for model fitting** Yi Li\* Yi Li Tibor Schuster Kazuki Yoshida Robert W. Platt

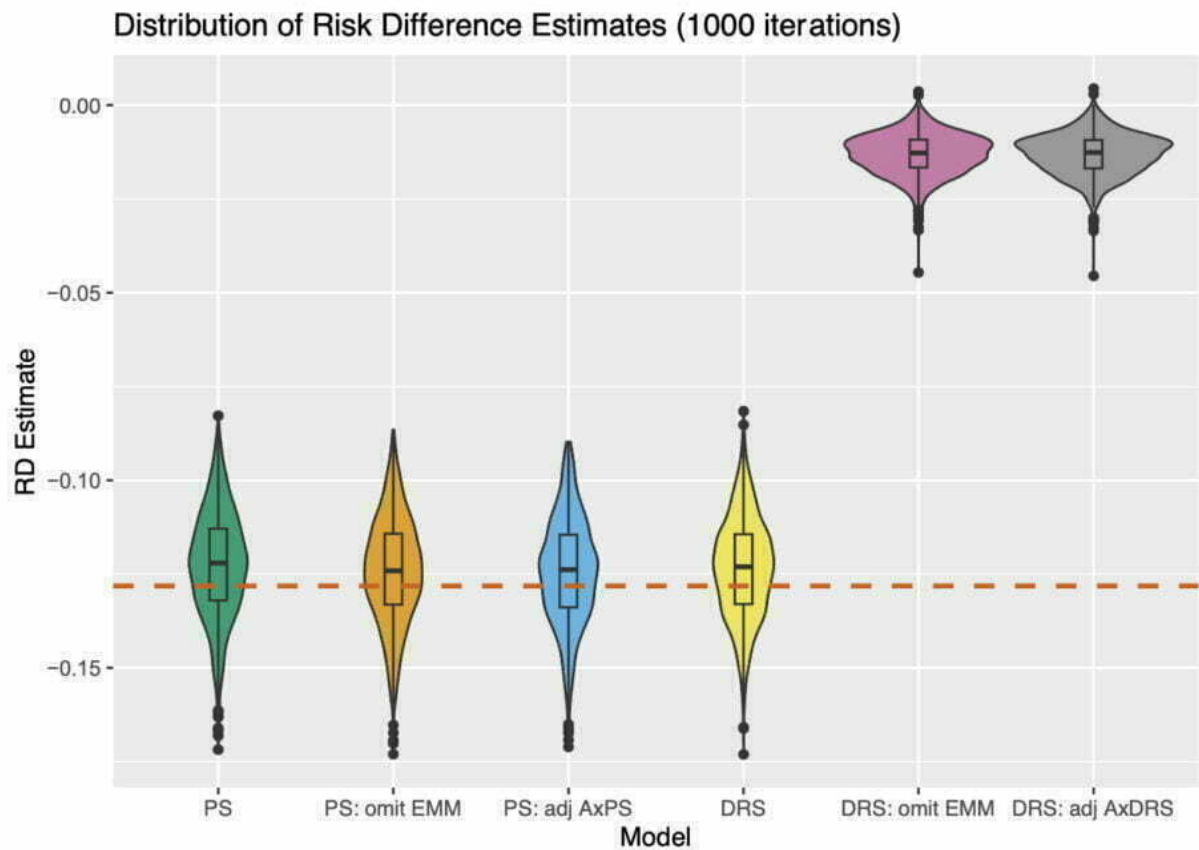
The disease risk score (DRS) is an alternative to the propensity score (PS) for confounding control. Literature has shown that DRS has comparable performance to PS in many settings. Most studies examined the performance of adjusting, stratifying or matching on PS or DRS, but very few used standardization, and few assessed the impact of misspecifying effect measure modification terms (EMMs) in the DRS model. Machine learning models have been used for PS, but not for DRS.

**Therefore, we used random forests for model fitting, and investigated the performance of standardization over PS vs. DRS when EMMs are misspecified.**

We randomly generated binary exposure (A), binary outcome (Y), measured covariates (C1-C4), and unmeasured covariate (U), for the study population. C1, C2 and U are confounders, and C3 and C4 are outcome predictors. In the data generating process, the true exposure and outcome models are complex, with polynomial and multi-way product terms. For DRS model fitting, we generated an external cohort with different model forms and parameterizations, as suggested in the literature.

Since it is impossible to know the functional form of exposure and outcome models, we fit random forests for the PS, DRS, *and* the outcome models. **We compared the performances of (1)** correctly specifying EMMs, **(2)** omitting EMMs, **(3)** adjusting for  $A \times PS$  or  $A \times DRS$  instead, in the outcome model. Risk difference estimates using PS are all nearly unbiased, with similar empirical standard error, whether EMMs are misspecified or not. For DRS method, only correctly specifying EMMs gives unbiased estimate. Either omitting EMMs or adjusting for  $A \times DRS$  gives biased estimates.

The results show that when using random forests, PS method is robust to EMMs omission, while DRS method is not. Future research may explore using these differences the potential to detect unknown EMMs using DRS through a data-driven approach by examining including which EMMs give the closest estimate to that using PS method.



True effect measure modification product terms:  $A \times C1$  and  $A \times C4$ .

**Labels:**

**PS:** correctly include  $A \times C1$  and  $A \times C4$  in the outcome model, *i.e.*,  $Y \sim A + PS + C3 + C4 + A \times C1 + A \times C4$ .

**PS: omit EMM:** omit  $A \times C1$  and  $A \times C4$ , *i.e.*,  $Y \sim A + PS + C3 + C4$ .

**PS: adj  $A \times PS$ :** omit  $A \times C1$  and  $A \times C4$ , but adjust for  $A \times PS$  instead, *i.e.*,  $Y \sim A + PS + A \times PS + C3 + C4$ .

**DRS:** correctly include  $A \times C1$  and  $A \times C4$  in the outcome model, *i.e.*,  $Y \sim A + DRS + A \times C1 + A \times C4$ .

**DRS: omit EMM:** omit  $A \times C1$  and  $A \times C4$ , *i.e.*,  $Y \sim A + DRS$ .

**DRS: adj  $A \times PS$ :** omit  $A \times C1$  and  $A \times C4$ , but adjust for  $A \times DRS$  instead, *i.e.*,  $Y \sim A + DRS + A \times DRS$ .

**Missing data methods and their impact to predictive performance equity in clinical models**

Stephanie Teeple\* Stephanie Teeple Scott Halpern Kristin Linn

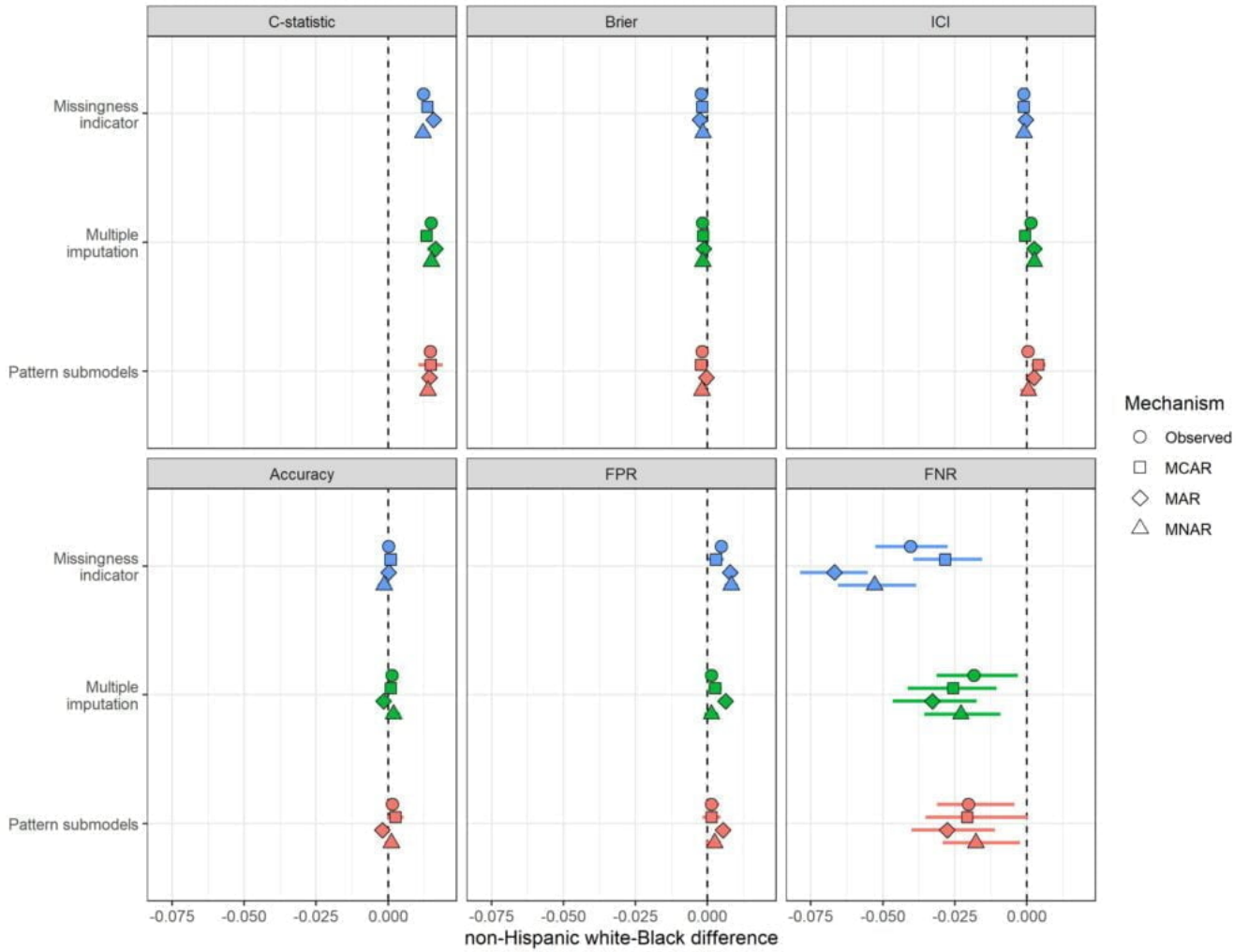
*Objective.* Missing data in electronic health record data likely varies across marginalized patient groups due to social forces (e.g., racism). We examine whether different methods for addressing missing data in clinical prediction model development differentially affects predictive performance of a mortality risk model for non-Hispanic white versus Black patients.

*Methods.* A simulation study using a cohort drawn from four hospitals within one health system, comprised of all inpatient visits between October 1 2016 through April 30 2019 where the patient was  $\geq 18$  years of age. Four data missingness mechanisms were examined: observed missingness, missing completely at random (MCAR), missing at random (MAR), and missing not at random (MNAR). Three missing data methods were implemented: missing indicators, multiple imputation, and pattern submodels.

*Results.* Across all missing data mechanisms and methods, the c-statistic was significantly higher for non-Hispanic white patients versus Black (e.g., in observed data, 0.881 vs 0.869, difference 0.012 (95% CI (0.011, 0.014))). Generally, the false negative rate was also significantly higher and the false positive rate significantly lower for Black patients (e.g., in observed data for missing indicator method, the white-Black difference in FNR -0.040 (95% CI (-0.053, -0.027))).

*Conclusion.* Different patterns of missingness exist across racialized patient groups, and choice of method to deal with missingness has implications for model predictive performance. Further exploration of missingness methods and equity of predictive performance is needed, as are interventions that target the missing data generation process directly: structural inequity in health and healthcare delivery.

Between-group differences (non-Hispanic white - Black) in predictive performance, by missingness mechanism and method



**Natural Language Processing Algorithm for Identifying Fall-Related Injuries in the Emergency Department Notes**

Lilian Maria\* Lilian Maria Godeiro Coelho Maria A. Donahue  
Wendong Ge Hunter J. Rice Sebastien Haneuse Deborah Blacker Sonia Hernandez-Diaz Sahar F.  
Zafar John Hsu Joseph P. Newhouse M. Brandon Westover Lidia M.V.R. Moura

**Introduction:** Fall-related injuries (FRIs) are a leading cause of emergency department (ED) visits among older patients. Manually identifying FRIs in Electronic Health Records (EHRs) is impractical for large cohorts. A digital tool, which finds FRIs, would help with studying predictors of and complications from FRIs. We aimed to develop an accurate Natural Language Processing (NLP) algorithm to identify FRIs in ED notes.

**Methods:** In Mass General Brigham's EHR, we found 42,302 Medicare beneficiaries 65+ years old from 2016-2019. From a stratified random sample of 2,100 patients, we abstracted 244,062 notes including 9,902 ED notes. These notes were parsed into paragraphs and scanned for 67 FRI keywords. A total of 5,000 keyword paragraphs (262 from ED notes) were labeled using Active Learning to create our "gold" dataset and 3,689 "always patterns" indicative of FRI status. These "always patterns" then generated our "silver" dataset of 93,157 paragraphs (3,602 from ED notes). An optimized BERT pretraining approach (RoBERTa) built a classifier to identify FRIs including 3 state fine-tuning stages: 1) Masked Language Modeling to learn the clinical word dependency; 2) Boolean Question-Answering (QA) with BoolQ dataset to learn general QA; 3) FRI QA with gold and silver data. We bootstrapped to construct 95% confidence intervals (CI).

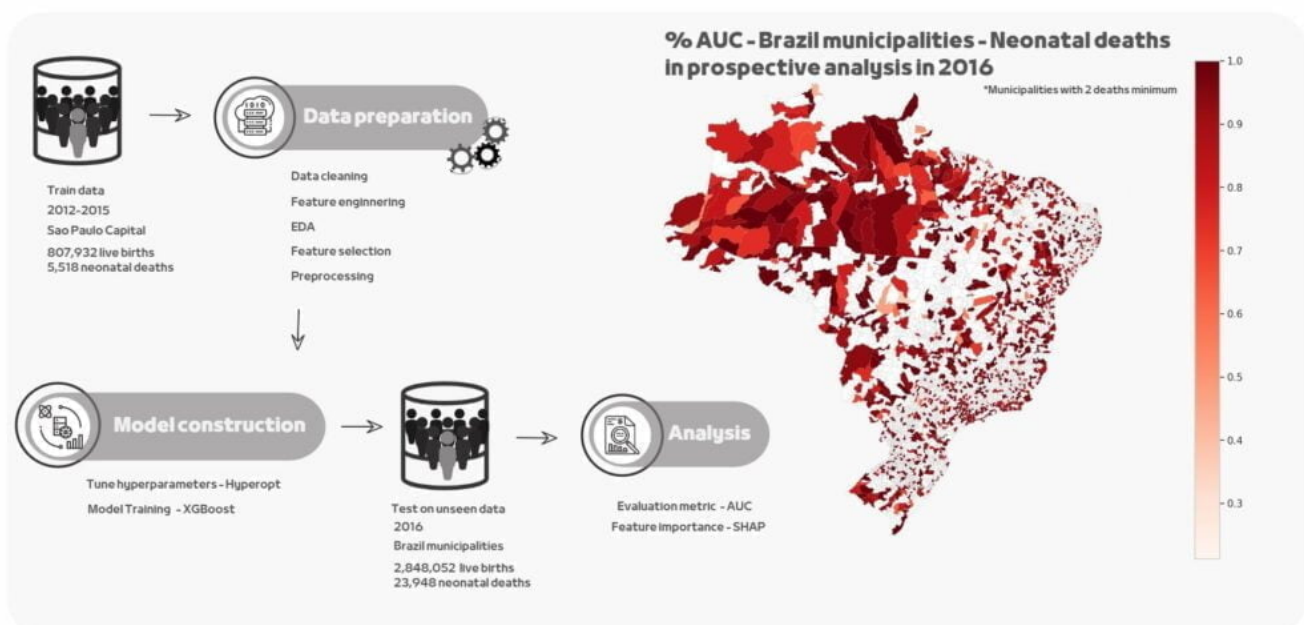
**Results:** Training and validation datasets used 94,275 non-ED paragraphs (4,738 gold and 89,537 silver). The test dataset used 262 gold ED paragraphs. For the positive category, precision was 0.91 [CI 95% 0.88-0.93], recall 0.91 [CI 95% 0.89-0.92], and the F1 score 0.91 [CI 95% 0.89-0.92]. For the negative category, the precision was 0.83 [CI 95% 0.79-0.86], recall 0.83 [CI 95% 0.81-0.86], and F1 score 0.83 [CI 95% 0.80-0.86]. The Area Under the ROC curve was 0.95 [CI 95% 0.94-0.96].

**Conclusions:** Our NLP algorithm accurately identifies older patients with FRIs from unstructured ED notes, which will be useful for large-scale EHR-based studies.

### Multicentric external validation of machine learning algorithms for neonatal mortality

**prediction** Mariane Furtado\* Mariane Furtado André Filipe de Moraes Batista Alexandre Dias Porto Chiavegatto Filho

Despite recent decreases in most countries, neonatal mortality rates remain high especially in developing regions. Predictive machine learning algorithms can bolster targeted public policies and improve preventive measures in neonatal health. We evaluated the generalization capacity of machine learning algorithms to predict neonatal deaths by testing their generalization performance in different regions of Brazil, a highly unequal country. We analyzed linkage data from Brazil's Live Birth Information System (SINASC) and the Mortality Information System (SIM) from 2012-2015 to train the algorithms with data from São Paulo, the most populous city of Brazil, which included 807.932 newborns and 5.518 neonatal deaths. The test dataset was composed of 2.848.052 live births and 23.948 neonatal deaths, from all Brazilian cities with at least two occurrences of neonatal deaths among children born in 2016. We used the XGBoost algorithm, and ten predictor variables routinely collected for live births in Brazil: place of birth, age of the mother, mother's education, mode of delivery, 1st minute Apgar score, 5th minute Apgar score, birth weight, presence of congenital anomaly, weeks of gestation, and age of the neonates. In the city of São Paulo, where the algorithm was actually trained, we found an AUROC of 0.97, which decreased only slightly for other State capitals (average of 0.96, standard deviation of 0.01), but decreased further for all other cities of Brazil (average of 0.91, standard deviation of 0.11). In conclusion, we found that although there was a decrease in the predictive performance of the algorithm, the metrics remained high even in smaller cities of a very unequal country as Brazil.



**Perinatal health and healthcare utilization during the COVID-19 pandemic: an interrupted time series analysis using the Pregnancy Risk Assessment Monitoring System** Deborah Karasek\* Deborah Karasek Daniel Collin Kaitlyn Jackson Alison Gemmill Rita Hamad

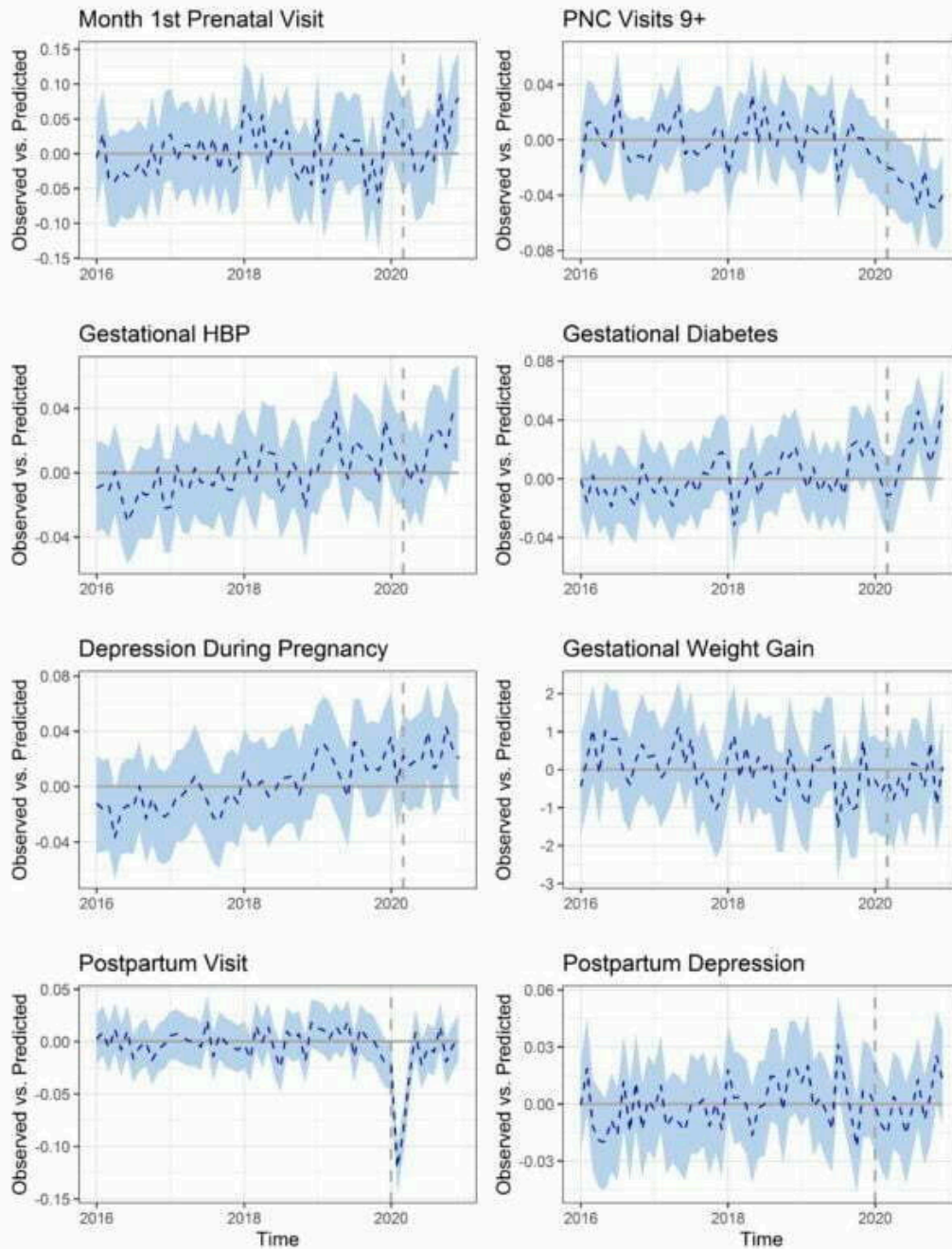
**Background:** Research evaluating the impact of the COVID-19 pandemic on perinatal health in the US has largely focused on birth outcomes. It is unclear how the pandemic affected other outcomes, including maternal health and healthcare utilization, as well as inequities.

**Methods:** Using population-based data from the Pregnancy Risk Assessment Monitoring System 2016-2020, we employed a Bayesian structural time-series approach using the *CausalImpact* R package. Prenatal and postnatal outcomes following the onset of the COVID-19 pandemic in March 2020 included prenatal care initiation and utilization, depression during pregnancy, gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy (HDP), gestational weight gain (GWG), postpartum care utilization, and postpartum depression. We specified a univariate model consisting of the outcomes without covariates. A second model included month of birth and aggregated covariates for maternal age, education, race/ethnicity, and insurer. We also examined heterogeneity by race/ethnicity and income.

**Results:** The univariate models (Fig. 2) showed evidence of reduced relative effect for prenatal care utilization (-4.3%;95% CI: -5.6, -3.1) and postpartum visit utilization (-2.8%;95%CI: -3.6, -2.0), and an increased relative effect for HDP (13.4%;95%CI: 5.1, 21.3), GDM (24.4%, 95% CI: 14.6, 34.1), and depression during pregnancy (18.7%;95%CI: 9.4, 28.0). Models did not indicate a change in prenatal care initiation, GWG, or postpartum depression. Results were similar in adjusted models. Stratified models revealed differences by race/ethnicity and income.

**Discussion:** Using a rigorous interrupted time series design, we found that stress or healthcare changes of the pandemic may have reduced prenatal and postpartum care utilization and adversely impacted maternal morbidities. As maternal health imparts enduring impacts for birthing people and infants, our result provide insight into the population health effects of the pandemic.

**Figure 2. Observed vs. Predicted Values for each Outcome**



Note: Note: Sample was drawn from 2016-2020 waves of the PRAMS. Sample was restricted to participants from states with available data in all years with live-born singleton births with a gestational age of 20-44 weeks at delivery (N=116,335). For prenatal outcomes, the post COVID-19 period corresponds to births after March 2020. For postnatal outcomes the post COVID-19 period corresponds to births after January 2020. The vertical dotted line represents the post-COVID date. The plotted dotted line represents difference between the actual and predicted values for each outcome at each time point (month of birth). Shaded blue area represents 95% CI.



## COVID-19 Pandemic

**Stressful COVID-19 experiences and the association with postpartum depression** Eliza

Kinsey\* Eliza Kinsey Stefanie Hinkle Shimrit Keddem

**Background:** The COVID-19 pandemic was a major disruptor to domestic and economic life and numerous studies have documented the adverse impact of the pandemic on mental health outcomes. We evaluated the relationship between stressful pandemic experiences during pregnancy with postpartum depression.

**Methods:** This cross-sectional, population-based study used data from 26 states (plus DC, New York City and Puerto Rico) that participated in the CDC's Pregnancy Risk Assessment Monitoring System (PRAMS) and implemented a retrospective COVID experiences survey starting in October 2020 (n=14,474 births). Survey weighted regression models were used to assess the association between stressful experiences due to COVID and the risk of postpartum depression. All models were adjusted for individual-level sociodemographic characteristics as well as for self-report of depression prior to pregnancy and gestational timing at the start of the pandemic (i.e., preconception, 0-20, 20+ weeks).

**Results:** Among the eligible 13,016 participants (weighted N=762,397), there was a high prevalence of stressful experiences due to COVID including problems paying bills (17%), loss of childcare (19%), food insecurity (13%), losing work (26%), becoming homeless (1%), and increasing intimate partner violence (2%). The prevalence of postpartum depression was 13%. Becoming homeless was most strongly associated with postpartum depression (aOR=2.1; 95% CI 1.2-3.5) while other stressors including increased intimate partner violence (aOR=1.8; 1.1-2.7), difficulty paying bills (aOR=1.4; 1.1-1.7), food insecurity (aOR=1.3; 1.0-1.7), and losing work (aOR=1.3; 1.1-1.6) were also associated with postpartum depression. Losing childcare and spending more time caring for children were not associated with postpartum depression.

**Discussion:** The COVID pandemic added additional stressors to birthing people that may have contributed to an excess number of individuals experiencing postpartum depression.

**COVID-19 and vitamin D supplement use by race/ethnicity in the Sister Study cohort** Yilda

G. Macias\* Yilda Macias Dale P. Sandler Katie M. O'Brien

**Background:** Vitamin D supplementation has several potential health benefits, possibly including a decreased risk of COVID-19 occurrence or severity. Yet, the association between vitamin D and COVID-19 remains unclear. Few studies have considered the role of race/ethnicity or disease vulnerability measures.

**Methods:** In a subset of women from the prospective Sister Study cohort who completed a special COVID-19 questionnaire (fall 2020-21; n=29,007), we evaluated the association between vitamin D supplement use since January 2020 and self-reported COVID-19 illness (confirmed or presumed positive) between January 2020 and May 2021. We used multivariable-adjusted logistic regression to estimate ORs and 95% confidence intervals (95% CI), adjusting for sociodemographic factors, health indicators, and geographic and behavioral markers of risk. We additionally considered associations between vitamin D and having had COVID-19 that was symptomatic, had severe or long-lasting symptoms, or required hospitalization.

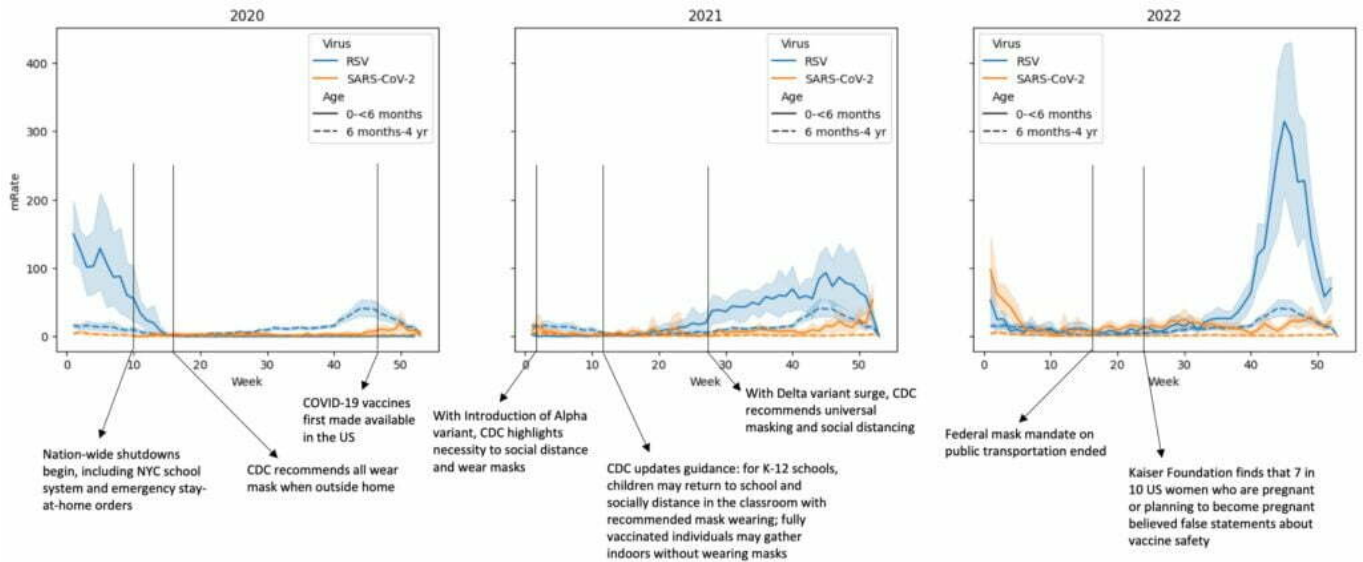
**Results:** Approximately 7% (n=2,094) of participants reported having had COVID-19 (mean age=67). Six percent (n=1,852) were symptomatic, 3% (n=911) had severe illness, and 0.5% (n=132) were hospitalized. We observed positive associations between vitamin D supplement use and all COVID-19 outcomes: any (aOR=1.14, 95 CI: 1.01-1.29), symptomatic (1.12, 0.99-1.27), severe (1.28, 1.06-1.55) or hospitalized (2.02, 1.08-3.79). The positive associations were stronger in analyses limited to Black women (aOR=1.50, 0.92-2.42 for any COVID-19; 1.42, 95% CI: 0.86-2.36 for symptomatic COVID-19).

**Conclusions:** In this large prospective cohort study, we find no evidence for a protective effect of vitamin D in COVID-19 infection and severity. Observed positive associations between vitamin D supplement use and COVID-19 health outcomes overall and among Black women may reflect biases due to residual confounding, differential recall by case status, or reverse causation.

## COVID-19 Pandemic

**The influence of COVID-19 pandemic restrictions on Respiratory Syncytial Virus in young children in the United States** Fausto Andres Bustos Carrillo\* Emily Ricotta Fausto Andres Bustos Carrillo Camille Lake

Severe acute respiratory syndrome coronavirus 2019 (SARS-CoV-2) has led to more than 650 million confirmed cases and approximately 6.7 million deaths. The US enacted pandemic restrictions on a state-by-state basis, facilitating disparate impacts on transmission, morbidity, and mortality. Critically, as state mandates for non-pharmaceutical interventions (NPIs) like masking were altered, individuals were differentially exposed to other major pathogens, including respiratory syncytial virus (RSV), a pathogen responsible for severe respiratory infections in children. Since pediatric RSV immunity is primarily facilitated through maternal transfer of neutralizing antibodies, we hypothesize that the increased incidence in children hospitalized with RSV is driven by the lack of maternal RSV exposure due to NPIs since 2020. To explore this hypothesis of “immunity debt” in US children aged 0 - 4 years, we obtained weekly hospitalization rates from the CDC’s RSV-NET and visualized incidence of RSV from 2020-2022. For comparison, we also acquired weekly SARS-CoV-2 hospitalization data from CDC’s COVID-NET. To assess the impact of COVID-19 policies on hospitalization rates, we obtained data on US state-level policies from the Oxford COVID-19 Government Response Tracker. We used multilevel linear models with a state-level random intercept to separately assess three component indices (the Government Response Index, Containment and Health Index, Stringency Index), controlling for age group and one-week-lagged incidence rates. All three indices were associated with a decrease in hospitalization rate among children 0 - 6 months old and an increase in hospitalization rate among children 6 months - 4 years old, for both RSV and SARS-CoV-2, suggesting a potential relationship between policy change and hospitalization. Ongoing work will use Bayesian and marginal structural models to analyze the data. This work was supported in part by the Division of Intramural Research, NIAID, NIH.



	RSV			SARS-CoV-2		
	Estimate	2.50%	97.50%	Estimate	2.50%	97.50%
<b>Government response index</b>						
Intercept	0.718	0.605	0.832	1.411	1.233	1.590
Index	-0.009	-0.012	-0.007	-0.014	-0.017	-0.011
Age 6mo - 4y	-0.218	-0.328	-0.109	-0.589	-0.763	-0.416
1-week lagged rate	0.828	0.813	0.844	0.407	0.379	0.435
Index*Age 6mo - 4y	0.004	0.002	0.007	0.004	0.000	0.007
<b>Containment and health index</b>						
Intercept	0.735	0.619	0.852	1.392	1.211	1.574
Index	-0.009	-0.012	-0.007	-0.014	-0.017	-0.011
Age 6mo - 4y	-0.230	-0.343	-0.118	-0.577	-0.758	-0.397
1-week lagged rate	0.828	0.812	0.843	0.411	0.383	0.439
Index*Age 6mo - 4y	0.004	0.002	0.007	0.003	-0.001	0.007
<b>Stringency index</b>						
Intercept	0.813	0.713	0.914	1.315	1.158	1.473
Index	-0.012	-0.014	-0.010	-0.013	-0.015	-0.011
Age 6mo - 4y	-0.223	-0.309	-0.137	-0.596	-0.718	-0.474
1-week lagged rate	0.799	0.783	0.816	0.384	0.356	0.412
Index*Age 6mo - 4y	0.004	0.002	0.007	0.004	0.001	0.007

Index component definitions can be obtained here: <https://github.com/OxCGRT/covid-policy->

**Household transmission dynamics from asymptomatic SARS-CoV-2-infected children: a multicenter multinational prospective controlled cohort study** Anna Funk\* Anna Funk Todd Florin Nathan Kuppermann Yaron Finkelstein Michael Baldovsky Daniel Tancredi Kristen Breslin Kelly Bergmann Michael Gardiner Chris Pruitt Deborah Liu Mark Neuman Kathy Monroe Matthew Wilkinson Lilliam Ambroggio Simon Cauchemez Richard Malley Terry Klassen Bonita Lee Daniel Payne Salah Mahmud Stephen Freedman

**Background:** Children are more likely than adults to have asymptomatic SARS-CoV-2 infection, however, it remains unclear how likely they are to transmit infections to household (HH) contacts. We sought to quantify the risk of SARS-CoV-2 transmission from asymptomatic infected children to HH contacts. **Methods:** In this prospective cohort study, we recruited asymptomatic children <18 years old who were SARS-CoV-2 nucleic acid test-positive, as well as frequency matched (age, sex) test-negative children. Participants were outpatients of 12 hospital emergency departments in Canada and the United States. Data were collected at baseline, 14 days, and 90 days. The clinical (symptomatic) and combined (test-positive or symptomatic) HH contact secondary attack rates (SAR) were calculated overall and by subgroups. **Results:** 111 test-positive and 256 SARS-CoV-2 test negative asymptomatic children were enrolled between January 2021 and April 2022; the two groups' baseline characteristics were similar. After 14 days, excluding HHs with co-primary cases, 22.0% (11/50) and 4.4% (8/182) of HHs with SARS-CoV-2 positive and negative index cases, respectively, had at least one secondary symptomatic case; RR=5.1, 95%CI: 2.2-11.9. The combined SAR among individual HH contacts of SARS-CoV-2-positive and negative index children was 14.0% (25/179, 95%CI: 9.2-19.9) and 2.0%, (13/663, 95%CI: 1.0-3.3); RR= 7.1, 95%CI: 3.7-13.6, respectively; *Table*. The HH contact combined SAR declined with increasing age of the asymptomatic SARS-CoV-2 positive index child (<5 years, 28.2%; 5 to <13 years, 20.3%; 13 to <18 years, 2.5%;  $p<0.001$ ), and differed by HH contact relationship type. **Conclusions:** One in seven HH contacts exposed to an asymptomatic SARS-CoV-2 positive child became symptomatic or test-positive within 14 days. Compared to unexposed HH, the risk of a HH contact becoming symptomatic or test-positive was approximately seven times greater in HHs with an asymptomatic SARS-CoV-2 positive child.

Table 2: Symptoms, secondary attack rates (SAR), and relative risks (RR) for contacts in households (HH) without co-primary cases

Index child's SARS-COV-2 status	All		HH contact age group					
	Positive <sup>1</sup>	Negative <sup>2</sup>	< 18 years		18 to < 50 years		50+ years	
N (% within SARS-CoV-2 status group)	179 (50 HH)	663 (182 HH)	Positive	Negative	Positive	Negative	Positive	Negative
<b>Any symptoms (clinical SAR) [95%CI]</b>	<b>19 (10.6)</b> [6.5-16.1]	<b>13 (2.0)</b> [1.0-3.3]	3 (4.8) [1.0-13.5]	1 (0.4) [0-13.5]	15 (16.1) [9.4-25.5]	10 (2.9) [1.4-5.3]	1 (4.5) [0.1-22.8]	2 (3.2) [0.4-11.0]
RR [95%CI] by HH contact age group (within SARS-CoV-2 status group)	-	-	ref	ref	3.4 [1.0-11.2]	7.1 [0.9-55.2]	0.9 [0.1-8.6]	7.8 [0.7-84.8]
RR [95%CI] SARS-CoV-2 positive vs negative (within HH contact age group)	<b>5.4</b> [2.7-10.7]	<b>ref</b>	11.9 [1.3-112.5]	ref	5.6 [2.6 - 12.1]	ref	1.4 [0.1 - 15.0]	ref
<b>Types of symptoms, n (%)</b>								
<i>Fever</i>	5 (2.8)	7 (1.1)	2 (3.2)	0	2 (2.2)	5 (1.4)	1 (4.5)	2 (3.2)
<i>Cough</i>	5 (2.8)	10 (1.5)	1 (1.6)	1 (0.4)	3 (3.3)	7 (2.0)	1 (4.5)	2 (3.2)
<i>Sore Throat</i>	9 (5.0)	6 (0.9)	0	0	8 (8.7)	4 (1.2)	1 (4.5)	2 (3.2)
<i>Runny Nose</i>	7 (3.9)	4 (0.6)	1 (1.6)	0	5 (5.4)	2 (0.6)	1 (4.5)	2 (3.2)
<i>Headache</i>	7 (3.9)	7 (1.1)	1 (1.6)	0	6 (6.5)	5 (1.4)	0	1 (1.6)
<i>Anosmia or ageusia</i>	4 (2.2)	0	0	0	4 (4.3)	0	0	0
<i>Weakness</i>	5 (2.8)	5 (0.8)	1 (1.6)	0	4 (4.3)	4 (1.2)	0	1 (1.6)
<i>Other<sup>3</sup></i>	7 (3.9)	7 (1.1)	1 (1.6)	0	6 (6.5)	5 (1.4)	0	2 (3.2)
<b>Acute respiratory illness<sup>4</sup> (%) [95%CI]</b>	<b>7 (3.9)</b> [1.6-7.9]	<b>7 (1.1)</b> [0.4-2.2]	1 (1.6) [0 - 8.7]	0 [0-1.5]	5 (5.4) [1.8-12.2]	5 (1.4) [0.5-3.3]	1 (4.5) [0.1-22.8]	2 (3.2) [0.4-11.0]
RR [95%CI] by HH contact age group (within SARS-CoV-2 status group)	-	-	ref	ref	3.4 [0.4 - 28.1]	7.1 [0.9-55.2]	2.8 [0.2 - 43.2]	0.5 [0-5.4]
RR [95%CI] SARS-CoV-2 positive vs negative (within HH contact age group)	<b>3.7</b> [1.3 - 10.4]	<b>ref</b>	Excluded	ref	3.8 [1.1 - 12.7]	ref	1.4 [0.1-15.0]	ref
<b>Any known illness<sup>5</sup> (combined SAR) [95%CI]</b>	<b>27 (14.9)</b> [10.0-21.0]	<b>13 (2.0)</b> [1.0-3.3]	6 (9.7)	1 (0.4) [0-13.5]	18 (19.6) [12.0-29.1]	10 (2.9) [1.4-5.3]	1 (4.5) [0.1-22.8]	2 (3.2) [0.4-11.0]
* test-positive and/or any symptoms								
RR [95%CI] by HH contact age group (within SARS-CoV-2 status group)	-	-	ref	ref	2.0 [0.9-4.8]	7.1 [0.9-55.2]	0.5 [0.1-3.7]	7.8 [0.7-84.8]
RR [95%CI] SARS-CoV-2 positive vs negative (within HH contact age group)	<b>7.1</b> [3.7-13.6]	<b>ref</b>	23.8 [2.9-194.1]	ref	6.8 [3.2-14.2]	ref	1.4 [0.1-15.0]	ref

Data is n(%) unless otherwise stated. <sup>1</sup>Specific age missing for 3 HH contacts <sup>2</sup>Specific age missing for 8 HH contacts <sup>3</sup>Any one or more of difficulty breathing, myalgia, chills, feeling very unwell, vomiting, diarrhea, conjunctivitis or rash <sup>4</sup>At least two of: fever or feverishness, cough, sore throat, runny nose.

## COVID-19 Pandemic

**COVID-19 and child development in a longitudinal cohort in rural Bangladesh** Helen O. Pitchik\* Helen Pitchik Lia C. H. Fernald Mahbubur Rahman Alaka Holla Laura Becerra Luna Stephen P. Luby Fahmida Tofail

**Background**

During the COVID-19 pandemic school closures in Bangladesh were some of the longest in the world, lasting 543 days. The aim of this research is to quantify the effects of the COVID-19 pandemic and associated shut-downs on child development and academic achievement among primary school-aged children in rural Bangladesh.

**Methods**

Participants are children in the 7-year follow-up of the WASH-Benefits study cohort assessed either prior to the COVID pandemic (Sept 2019-Mar 2020; "pre-covid") or following 9 (SD 1.3) months of COVID related school closures (Oct 2020-Feb 2021; "during covid"). Primary outcomes are cognitive development assessed with the Wechsler Preschool and Primary Scale of Intelligence Full Scale IQ, school achievement in reading, writing, and math, and socio-behavioral development assessed with the Strengths and Difficulties Questionnaire. For each outcome adjusted mean differences will be determined comparing the pre-covid and during covid samples using generalized linear models accounting for the block-level clustering of the original study design, and adjusting for study arm, child age, and theory-driven confounders. Analyses will be conducted both within the whole sample, and within the sample with an overlap in child age across exposure groups.

**Results**

Children assessed pre-covid were younger on average (n=2007, mean: 80.6 months, SD: 2.1) than children assessed during covid (n=1828, mean: 86.6 months, SD: 1.5). Preliminary unadjusted differences in means show higher Full Scale IQ scores for children at the pre-covid time point (pre-covid: 74.5 [95%CI: 74.1, 74.9]; during covid: 70.4 [70.1, 70.8]; unadjusted difference: 4.1 [3.6, 4.6]). Analyses are ongoing and results will include adjusted analyses for all outcomes in both the full and reduced age-overlap samples.

**Discussion**

Documenting the impact of the COVID-19 pandemic on child development is an important step to understand the implications of school closures in this setting.

**Antihypertensive deprescribing on changes in disability status in VA nursing home****residents: A target trial emulation** Xiaojuan Liu\* Xiaojuan Liu Laura A. Graham Yongmei Li  
Bocheng Jing Michelle C. Odden

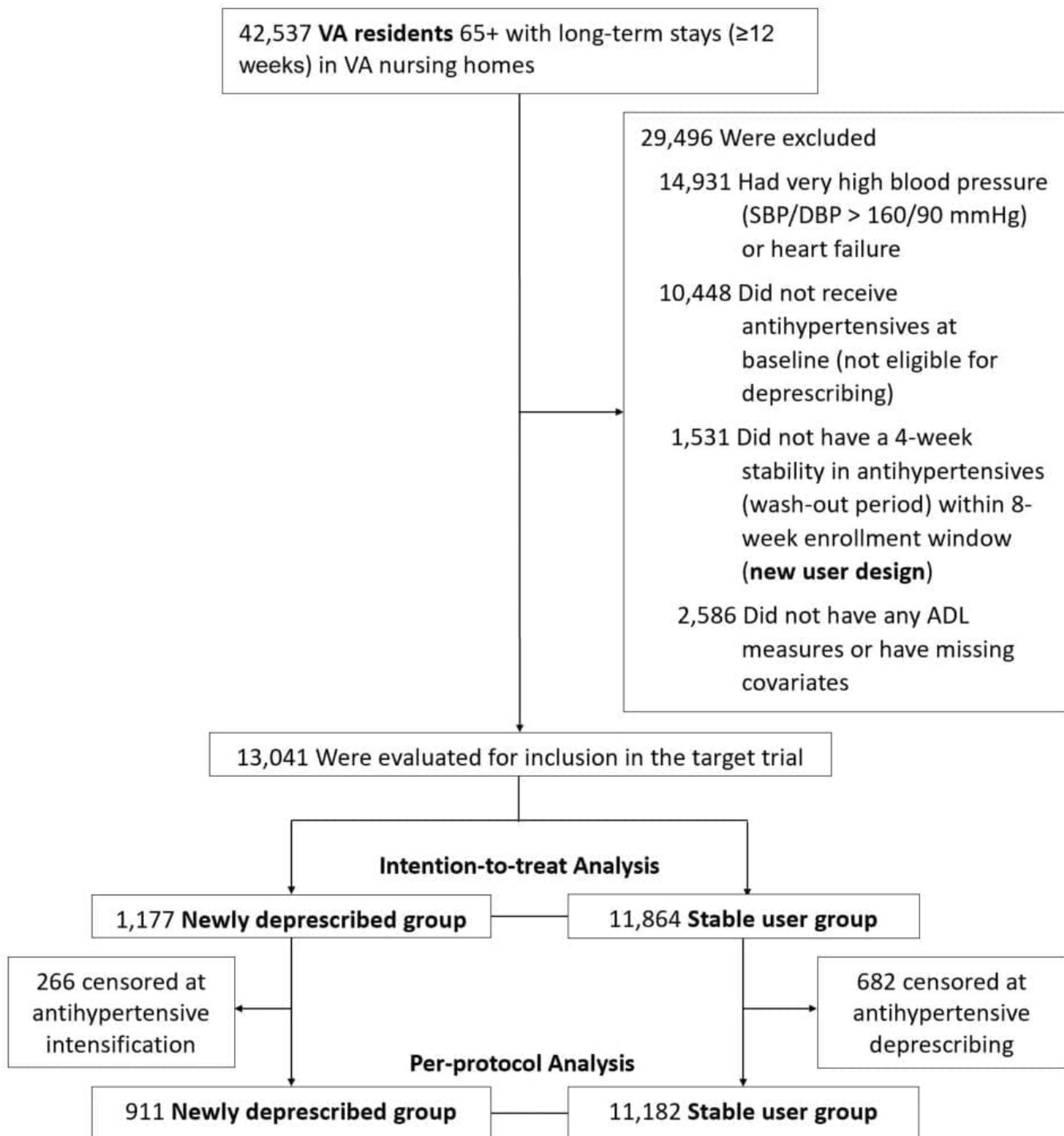
**Background** There is debate over the potential benefits or harms of intensive treatment of high blood pressure on functional status in frail older adults. Deprescribing antihypertensives is of growing interest in geriatric medicine, yet clinical trial evidence is lacking.

**Methods** We leveraged the Veterans Affairs (VA) electronic health records and emulated an antihypertensive deprescribing trial on the longitudinal change in disability, measured by activities of daily living (ADL), ranging from 0-28. Residents included were age  $\geq 65$  with long-term stays ( $\geq 12$  weeks) from 2006-2019 ( $n=42,537$ ). We excluded those not on antihypertensives and with very high blood pressure or heart failure. The eligible residents ( $n=13041$ , Figure) were divided into newly deprescribed (reduced number of antihypertensives or dose of  $\geq 30\%$ ) and stable users and followed up for 2 years or censored at death/discharge. We applied linear mixed-effects regressions to estimate intention-to-treat effects of deprescribing vs stable use. We used inverse probability of treatment weighting (IPTW) to adjust for confounders and additional inverse probability of censoring weighting to account for informative censoring at non-adherence to estimate per-protocol effects. These probabilities were estimated using the SuperLearner algorithm.

**Results** Newly deprescribed residents ( $n=1,117$ ) had a worse ADL score at baseline ( $\beta_{\text{treat}}$  [95% CI] = 1.01 [0.589, 1.431]) compared to stable users ( $n=11,864$ ). Over time, ADL scores increased (worsened) by 0.036/week ( $\beta_{\text{time}} = 0.036$  [0.034, 0.037]) while antihypertensive deprescribing attenuated this increase at 0.003/week ( $\beta_{\text{time} \times \text{treat}} = -0.003$  [-0.011, 0.005]) although this effect was imprecise. Results remained unchanged in per-protocol analysis.

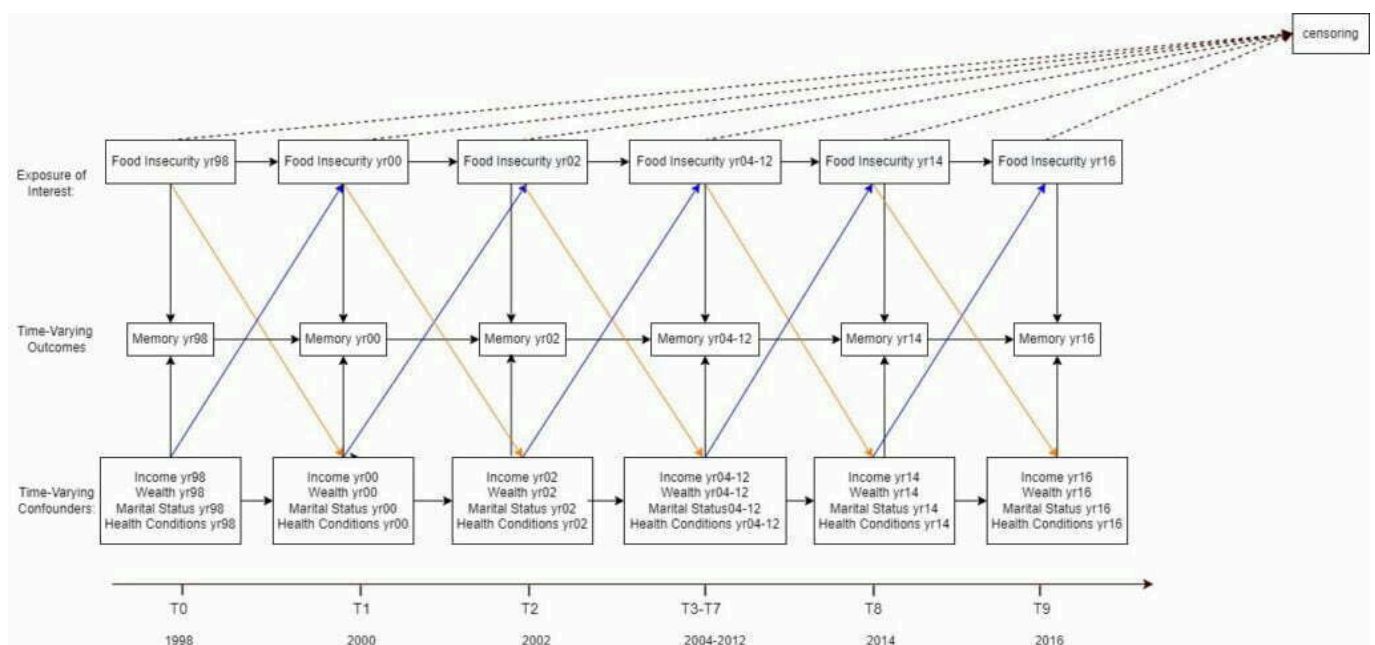
**Conclusion** Deprescribing antihypertensives appeared to have no impact on change in disability status in nursing home residents. More evidence is needed to inform the benefits and harms of deprescribing in long-term care populations.





**Food insecurity and memory function among older adult Americans: The Health and Retirement Study** Peiyi Lu\* Peiyi Lu Katrina Kezios Neal Jawadekar Samuel Swift Anusha Vable Adina Zeki Al Hazzouri

While most existing research on food insecurity and cognition is cross-sectional in nature, food insecurity status and cognition can change over the life course. Longitudinal studies using methods appropriate for time-varying confounding are needed to investigate this relationship. This study examined the longitudinal association between changes in food insecurity and changes in memory function among older Americans. We used longitudinal data (1998-2016) from 12,609 participants aged 50+ from Health and Retirement Study. In each biennial interview, respondents were asked about their food insecurity status and completed memory assessments. We used marginal structural models incorporating the inverse probability of treatment and censoring weighting to account for time-varying confounders and attrition, and we applied weighted linear mixed-effect models to estimate the effect of food insecurity on memory decline. We found that the annual rate of memory decline among food-secure respondents was -0.046 standard units (95%CI: -0.046, -0.045). Compared with this, memory decline among food-insecure respondents was significantly faster ( $\beta_{\text{time*food insecurity}} = -0.003$ , 95%CI: -0.007, -0.00005), corresponding to an annual rate of -0.049 standard units for this group, which translated to an additional 0.65 years of excess cognitive aging over 10 years for food insecure respondents. After accounting for time-varying confounding, we found food insecurity was associated with slightly faster memory decline among older Americans. Our findings highlight the potential importance of food assistance programs to slow cognitive aging among persons who experience food insecurity.



**Does schooling attained by adult children affect parents' psychosocial well-being in later life? Using Mexico's 1993 compulsory schooling law as a quasi-experiment** Sirena Gutierrez\*  
Sirena Gutierrez Renata Flores Romero Maria Glymour Jacqueline M. Torres

Emerging research suggests that higher adult child educational attainment may benefit older parents' psychosocial well-being in later life. This work may have particularly important implications in low- and middle-income countries given the comparatively large increases in educational attainment achieved by recent generations. Quasi-experimental approaches are needed to address the residual confounding expected in observational studies on this topic.

We used data from the Mexican Health and Aging Study (n=7185), a nationally representative study of adults aged  $\geq 50$  years (2012). We leveraged the exogenous variation in adult child education induced by Mexico's compulsory schooling law (CSL) passed in 1993, which raised minimum schooling from 6 to 9 years. We used two-stage least squares (2SLS) regression to identify the effects of increased schooling among oldest adult children on parents' (respondents') depressive symptoms and life satisfaction scores. Covariates included respondents' demographic and socioeconomic status characteristics and we examined heterogeneity by respondents' gender.

Participants were on average 60.2 years old and 54.9% were female. Exposure to the higher CSL was associated with 0.61 (95% CI: 0.38, 0.84) additional years of schooling. In the 2SLS analyses, each year of increased schooling among oldest adult children was associated with fewer depressive symptoms ( $\beta = -0.23$ ; 95% CI: -0.45, -0.01); findings were null for life satisfaction ( $\beta = -0.00$ ; 95% CI: -0.20, 0.20). In stratified models, the association of adult child schooling and depressive symptoms was significant among mothers ( $\beta = -0.25$ ; 95% CI: -0.49, -0.01), but not among fathers ( $\beta = -0.14$ ; 95% CI: -0.51, 0.23). There were no differences according to parent gender for life satisfaction.

Our findings suggest that increases in schooling achieved by current generations of adult children may benefit their older parents' psychosocial well-being, especially their mothers.

**Associations of long-term exposure to fine particulate matter and its components, oxides of nitrogen, ozone, and carbon monoxide with late-life amyloid burden in the Atherosclerosis Risk in Communities (ARIC) study cohort** Erin E. Bennett\* Erin Bennett Katie M. Lynch Xiaohui Xu Chelsea Liu Emma K. Stapp Eun Sug Park Qi Ying Richard L. Smith James D. Stewart Eric A. Whitsel Thomas H. Mosley Jeff D. Yanosky Dean F. Wong Duanping Liao Rebecca F. Gottesman Melinda C. Power

*Background:* Studies suggest associations between long-term ambient air pollution exposure and late-life cognitive impairment. Whether a link exists between pollutants and brain amyloid accumulation, a biomarker of Alzheimer's disease, is unclear. We assessed whether long-term air pollutant exposures (PM<sub>2.5</sub> and its components, NO<sub>2</sub>, NO<sub>x</sub>, O<sub>3</sub>, CO) are associated with late-life brain amyloid deposition in Atherosclerosis Risk in Communities (ARIC) study participants.

*Methods:* We used a chemical transport model with data fusion to estimate pollutant concentrations in arrays of 12-, 4-, and 1.33-km grid cells in ARIC study areas. We linked concentrations to geocoded participant addresses and calculated mean exposures from 2001 to 2010. We measured amyloid deposition using florbetapir amyloid positron emission tomography (PET) scans in 346 participants with normal cognition or mild cognitive impairment in 2011-2014 and defined amyloid positivity as a global cortical standardized uptake value ratio  $\geq$  the sample median of 1.2. We used logistic regression models to quantify the association between amyloid positivity and each air pollutant, adjusting for demographics and cognitive status. We explored effect measure modification by *APOE* e4 allele status and tested whether results were consistent using alternate exposure estimation methods.

*Results:* At imaging, eligible participants with full exposure and covariate data (n=312) had a mean age of 78 years, 56% were female, 43% were Black, and 26% had mild cognitive impairment. We found no evidence of associations between and long-term exposure to any pollutant and brain amyloid positivity in adjusted models. There was no evidence of effect measure modification by *APOE* e4 allele status. Results were consistent when we used alternate exposure estimation methods.

*Conclusions:* Air pollution may promote dementia through non-Alzheimer's disease pathways, though our small sample size may have limited power to detect subtle effects.

**Association of loneliness with healthcare transitions and mortality in community-dwelling older women and men** Rachel Savage\* Rachel Savage Rinku Sutradhar Jin Luo Rachel Strauss Jun Guan Paula A Rochon Andrea Gruneir Claudia Sanmartin Vivek Goel Laura C Rosella Nathan M Stall Stephanie Chamberlain Christina Yu Azmina Altaf Susan E Bronskill

**Background:** There is growing interest in understanding the impact of loneliness in older adults on health systems, yet existing studies focus on single settings of care, lacking a system-wide perspective. We evaluated whether loneliness was associated with the rate at which older adults transitioned to and between multiple healthcare settings and death and assessed potential sex differences.

**Methods:** We conducted a retrospective cohort study of community-dwelling adults aged  $\geq 65$  years in Ontario by linking representative survey data (2008/09 Canadian Community Health Survey - Healthy Aging) with health administrative data. Loneliness was measured at baseline using the Three-Item Loneliness Scale and categorized as not lonely, moderately lonely, or severely lonely. We used continuous-time multistate transition models under a Markov assumption to estimate relative rates of transition to inpatient, home care, long-term care settings, and death, over 12 years of follow-up.

**Results:** Of 2,684 participants, 635 (23.7%) were moderately lonely<sub>(ML)</sub> and 420 (15.6%) were severely lonely<sub>(SL)</sub>. Lonely participants transitioned from the community to home care at a higher rate than those who were not lonely after adjustment ( $RR_{ML}$  1.31; 95% CI 1.12-1.54, and  $RR_{SL}$  1.26; 95% CI 1.04-1.53). Severely lonely older adults transitioned from community to long-term care at a rate that was 2.5 times higher ( $RR_{SL}$  2.52; 95% CI 1.47-4.33) than those who were not lonely. Loneliness was also associated with transitions from inpatient settings, with slower transitions from this setting to the community and faster transitions to death. Female and male participants had similar transition patterns.

**Conclusion:** Lonely older adults in the community transitioned more quickly to home care and long-term care than those who were not lonely. Our findings suggest interventions for loneliness could not only benefit the health and well-being of older adults but could also improve health system sustainability.

**The Concept of Healthy Ageing Among Japanese Older Adults: Understanding the Relationship Between Functional Ability and Well-being** Marisa Nishio\* Marisa Nishio Maho Haseda Kosuke Inoue Masashige Saito AMUTHAVALLI THIYAGARAJAN, Jotheeswaran Naoki Kondo

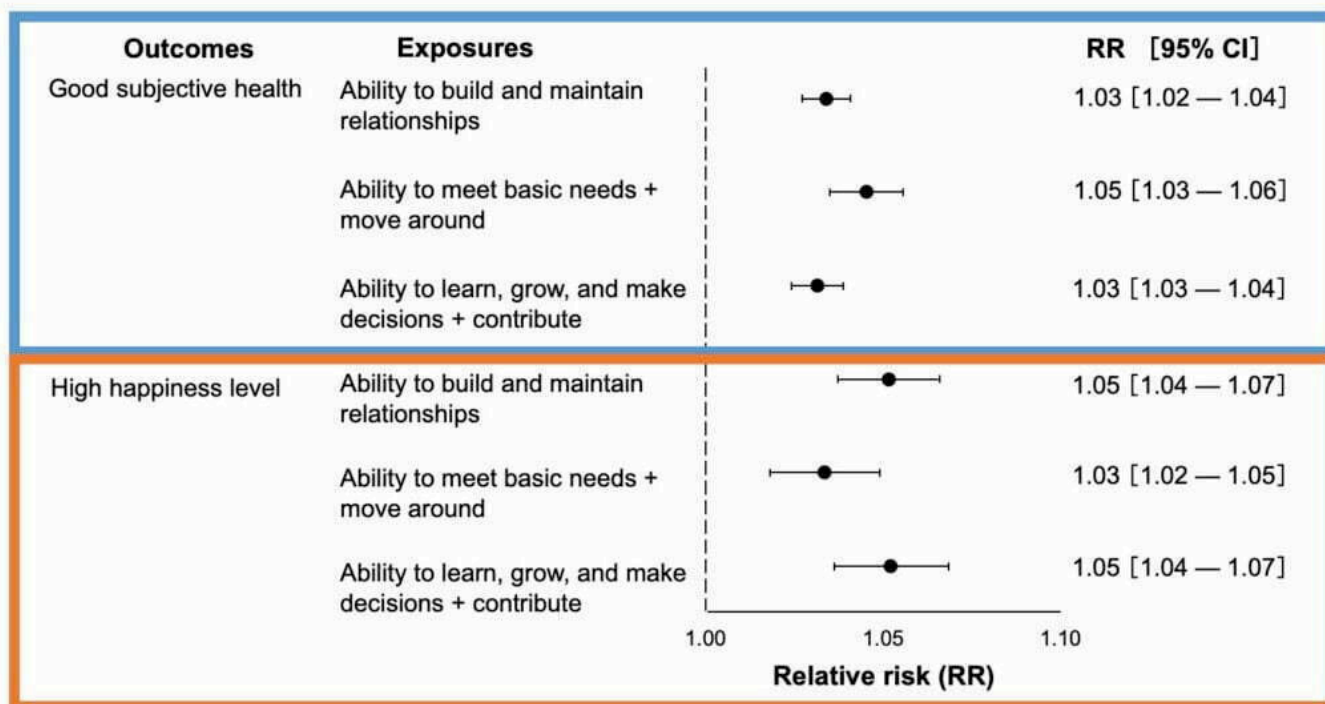
**Background:** WHO proposed healthy ageing as “the process of developing and maintaining the functional ability that enables well-being in older age”, but empirical examination of the validity of its concept is limited. We aimed to examine the predictive validity of functional ability for subsequent well-being using longitudinal data.

**Methods:** We used the panel data of 35,093 community-dwelling older adults (aged 65+) from the Japan Gerontological Evaluation Study in 2013-16-19. Missing values were imputed with a random forest approach. Each of subjective health and happiness in 2019 was measured as the aspects of well-being. Three domains of functional ability in 2016 were measured using a standardized factor score (domain #1: ability to build and maintain relationships, #2: ability to meet basic needs + move around, and #3: ability to learn, grow, and make decisions + contribute). We employed the modified Poisson regression analysis to estimate the relative risk [RR] for high happiness level and good subjective health when each domain of functional ability increased by 1 SD, adjusting for potential confounders in 2013.

**Results:** Mean age was 72.1 years, and female were 52%. 17,753 (51%) reported high happiness level and 29,836 (85%) reported good subjective health. After adjusting for the potential confounders, all three domains of functional ability were shown to predict both happiness and good subjective health three years later (good subjective health, domain #1, RR[95%CI]=1.03[1.02-1.04]; #2, RR[95%CI]=1.05[1.03-1.06]; and #3, RR[95%CI]=1.03[1.03-1.04]; happiness, domain #1, RR[95%CI]=1.05[1.04-1.07]; #2, RR[95%CI]=1.03[1.02-1.05]; and #3, RR[95%CI]=1.05[1.04-1.07]).

**Conclusion:** Using data of older adults in Japan, we found that functional ability was associated with subsequent well-being. Our findings indicate that increasing functional ability would lead to well-being among older adults, which should be the subject of future research.

### Relative risks (RR) for good subjective health and high happiness level



Note: Each model was standardized and adjusted for pre-baseline potential confounders, including gender, age, education, equivalized income, comorbidities, marital status, living status, functional ability domain of interest, and well-being of interest.

## Health Disparities

**Impacts of Racism on Youth Behavioral Health** Meredith Cahill\* Meredith Cahill Lisa Crabtree  
Paula Brown

Racism is a public health threat. Encounters with racial bias, ethnic discrimination, and hate crimes are linked to mental and emotional harm. Among youth, racism has been identified as an important determinant of health and wellbeing but remains understudied. Therefore, we examined the association between experiencing racism and behavioral health indicators—serious psychological distress, suicidal ideation, and substance use—among a cohort of Kentucky youth.

We conducted a secondary analysis of data gathered by the 2021 Kentucky Incentives for Prevention (KIP) Survey, a statewide behavioral health survey of more than 92,000 middle and high school students in Kentucky. Self-reported data on experiencing racism in the past year, 30-day serious psychological distress, past year suicidal ideation, 30-day cannabis use, and 30-day vape use were analyzed using multivariate logistic regression controlling for student grade level and race/ethnicity to compute odds ratios (ORs) and 95% confidence intervals (CIs).

Among the entire cohort of students, 7% reported experiencing racism in the past year. The prevalence of experienced racism varied by racial/ethnic group. Non-Hispanic Black students were the most likely to report experiencing racism (25%) followed by non-Hispanic Asian students (23%). Experiencing racism was associated with higher odds of reporting 30-day serious psychological distress (OR: 2.8, 95%CI: 2.6-3.0), suicidal ideation in the past year (OR: 2.8, 95%CI: 2.7-3.0), 30-day cannabis use (OR: 2.2, 95%CI: 2.0-2.5), and 30-day vape use (OR: 2.3, 95%CI: 2.1-2.4).

Experiencing racism was associated with an increase in the odds of poor behavioral health outcomes among Kentucky youth. These findings highlight the importance of recognizing racism as a determinant of adolescent health and wellbeing, call attention to the need for ongoing research into the harms of racism, and underscore the need for anti-racist, systemic change.



**The impact of changing racial composition of the UAW-GM workforce on Black-White disparities in cardiovascular disease mortality** Hilary Colbeth\* Hilary Colbeth Corinne Riddell Marilyn Thomas Ellen Eisen

**Background:** There is evidence that neighborhood racial composition affects health, but little is known about the impacts of workplace racial composition on chronic disease. Using longitudinal data on 39,693 hourly Michigan autoworkers in the United Autoworkers – General Motors (GM) cohort employed at three plants, we examined the cumulative effect of plant-level racial composition from 1950-2015 on cardiovascular disease (CVD) mortality.

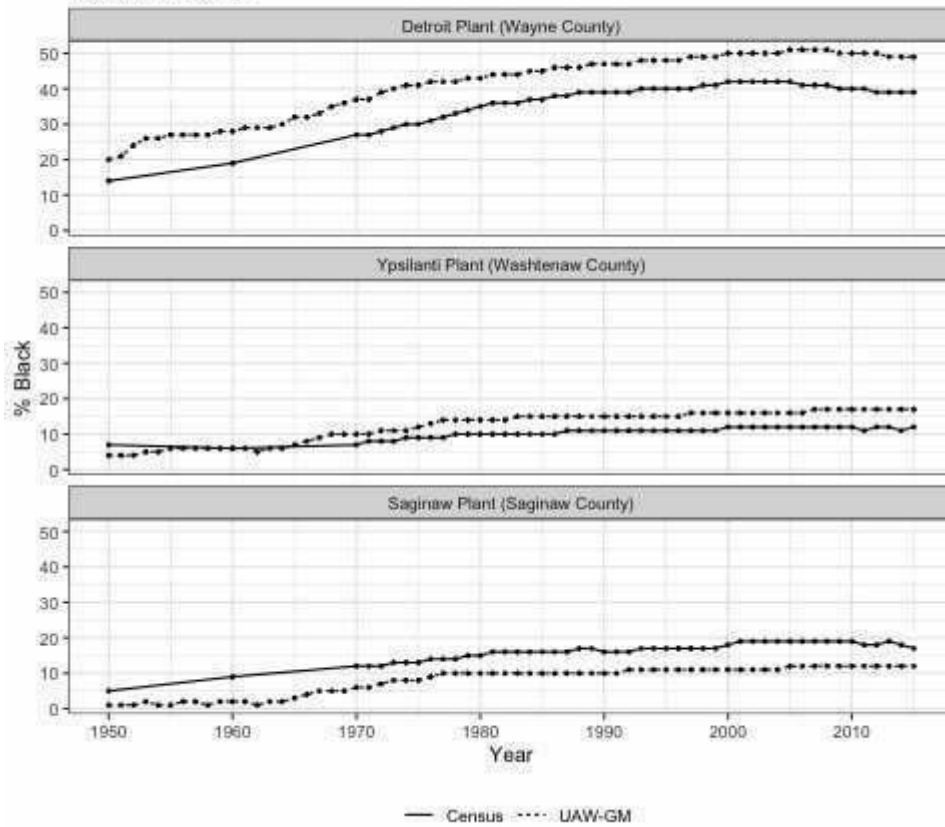
**Methods:** Our goal is to isolate the racial composition of each plant from that of the surrounding community, which would otherwise confound its effect. First, we measured the annual racial composition (% Black autoworkers) at each plant. Second, we measured the annual racial composition (% Black residents) of the surrounding county. We will estimate the effect of cumulative exposure to the time-varying difference in workplace-county racial composition on CVD mortality. Our final models will be stratified by individual-level race and fit using Cox proportional hazards.

**Results:** Among the 3,205 autoworkers who died from acute myocardial infarction (AMI) and the 1,312 from stroke, 330 (11%) and 290 (22%) were Black. Comparing Black to White workers, crude mortality rate ratios were 0.50 and 1.19 for AMI and stroke. The Detroit and Ypsilanti plants had a consistently higher percentage of Black individuals than their surrounding counties, whereas the Saginaw plant had a smaller percentage. Racial composition at baseline was highest in Detroit (20% Black) and remained so throughout follow-up.

**Conclusion:** Each plant presents a distinctive exposure scenario which will allow us to understand the long-term impacts of both workplace racial composition relative to the community and the absolute level of diversity over time. Our results will examine, by race, the impacts of exposure to the accumulated effects of workplace racial composition over time on the risk of CVD mortality.

Percent Black population in each United Autoworkers-General Motors (UAW-GM) plant and the corresponding Michigan county (1950-2015)

County population estimates retrieved from the United States Census Bureau (<https://www.census.gov>)



**Residential segregation, breast cancer mortality and the effect of a conditional cash transfer (Bolsa Família) programme: results from the 100 million Brazilian Cohort** Joanna MN Guimarães\* Joanna MN Guimarães Julia M Pescarini J Firmino de S Filho Andrea Ferreira Gervasio Santos M da Conceição C de Almeida Ligia Gabrielli Emanuelle Goes Dandara Ramos Mauricio L Barreto Estela MML Aquino

Women living in economically segregated areas are less likely to receive adequate breast cancer care and access community resources, which may heighten breast cancer mortality risk. We investigated whether the conditional cash transfer programme Bolsa Família (BFP) could mitigate the detrimental effects of living in segregated areas on breast cancer mortality.

We analysed data on 20,680,930 women from the 100 Million Brazilian cohort, linked to nationwide mortality registries (2004-2015). The association between womens' residential segregation at the municipality level (low/medium/high) and breast cancer mortality was analysed using Poisson models adjusted for age, race, education, area of residence (rural/urban), municipality's area size and population density. Effect modification by BFP receipt (yes/no) was assessed.

Breast cancer mortality rates were greater among women living in high (adjusted Mortality rate ratio=1.18, 95%CI 1.12-1.23) and medium (1.07, 1.03-1.12) vs low segregated municipalities. Women not receiving BFP had higher breast cancer mortality rates (1.12, 1.08-1.17) than BFP recipients. Among BFP recipients strata, women living in high vs low segregated municipalities had a 12% (1.12, 1.06-1.19) greater risk of dying from breast cancer; among BFP non-recipients strata, the risk of dying for women living in high vs low segregated municipalities was 23% higher (1.23, 1.14-1.33) (P for interaction=0.008). When stratifying by the time in years receiving the benefit, associations between segregation and mortality were stronger for women receiving BFP benefit for less time (<4 years: 1.10, 1.01-1.20; 4-7 y: 0.97, 0.89-1.07; 8-11 y: 1.09, 0.95-1.25) (P for interaction<0.001).

Place-based inequities in breast cancer mortality due to residential segregation might be mitigated by the BFP, possibly by improving women's familial income and access to preventive cancer care services, leading to early detection and treatment and ultimately reducing mortality.

**Census tracts aren't neighborhoods: Issues in examining the impact of historical redlining on present-day health outcomes** Maret M Maliniak\* Maret Maliniak Leah Moubadder Rebecca Nash Timothy L. Lash Michael R. Kramer Lauren E. McCullough

**Background:** Research examining the effects of historical redlining on present-day health outcomes is often complicated by the misalignment of contemporary census boundaries with the neighborhood boundaries drawn by the US Home Owners' Loan Corporation (HOLC) in the 1930s. Multiple methods exist to assign historical HOLC grades to contemporary geographies, but how well they capture redlining exposure is unknown.

**Methods:** Our analysis included 7,711 residences identified in the Multiple Listing Service database in Atlanta, Georgia (2017-2022). We evaluated classification of HOLC grade assignment (A, B, C, D, or ungraded) when assigning exposure under four different area-level methods (Centroid, Majority Land Area, Weighted Score, and Highest HOLC) compared to using complete address data (gold-standard). We examined assignment methods across three 2020 census geographies (tract, block group, and block).

**Results:** When comparing the use of census tracts to complete address data, sensitivity was highest for the Weighted Score method, which correctly identified 77% of residences in truly A-D graded neighborhoods as compared to the Majority Land Area (44%), Centroid (54%), and Highest HOLC (59%) methods. Regarding specificity, the Majority Land Area method best classified residences in truly ungraded neighborhoods (93%) as compared to the Weighted Score (65%), Centroid (81%), and Highest HOLC (54%) methods. Classification improved regardless of assignment method when using census block compared to census tract.

**Conclusions:** Misclassification of historical redlining exposure is inevitable when using census geographies rather than complete address data. This study can help researchers understand the resulting spatial misalignment and different approaches to handling it.

**Gentrification May Do More Than Displace Residents: An Ecological Analysis Examining Gentrification and HIV Diagnoses in Four US Cities** Shayla Nolen\* Shayla Nolen Chanelle J Howe Patrick S Sullivan Bridgette M Brawner Rice Katie B Biello Brandon DL Marshall

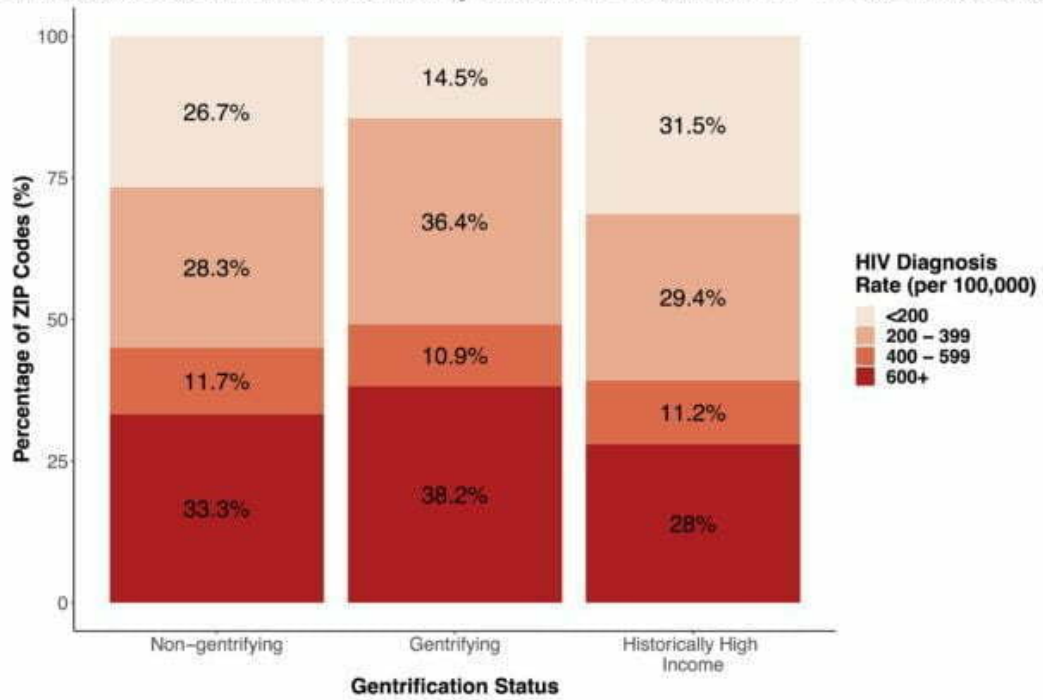
**Objectives:** This study examined the relationship between gentrification and HIV diagnosis rates in four US cities- Atlanta, Philadelphia, New York City, and San Francisco- and determined if this relationship differed by race/ethnicity.

**Methods:** The 2014 ZIP code level gentrification status was determined based on Census and American Community Survey socioeconomic characteristics and categorized into three groups: gentrifying, non-gentrifying, and historically high income. We used 2014-2018 HIV diagnosis data from AIDSvu and the Philadelphia Department of Public Health for our outcome variable. We examined the overall relationship between gentrification and HIV diagnosis rates at the ZIP code level using multivariable Tobit models, which account for data suppression in the publicly available datasets. Lastly, we stratified the model by race/ethnicity to evaluate evidence for effect measure modification.

**Results:** Of the 286 ZIP codes included in the analysis, 19.9% were gentrifying, 25.2% were non-gentrifying, and 54.9% were historically high income. In the multivariable Tobit model, we found that gentrifying ZIP codes had higher HIV diagnosis rates than non-gentrifying ZIP codes. In the race/ethnicity stratified models, there was evidence that race/ethnicity was an effect measure modifier. Specifically, there was a more prominent, positive association between gentrifying ZIP codes and high HIV diagnosis rates among African American/Black residents compared to the Hispanic and White individuals.

**Conclusion:** This study provides preliminary evidence that gentrification is a possible structural determinant of HIV risk and transmission, particularly among African American/Black people in the US. Future research should examine the relationship between gentrification and HIV transmission using other study designs (i.e., prospective and simulation modeling) and data (i.e., multi-level and individual-level GIS data), and focus on evaluating racial/ethnic inequities.

**Figure 1.** Adjusted ZIP Code Level HIV Diagnosis Rate (per 100,000) among African American/Black Residents, Stratified by Gentrification Status of ZIP Codes, 2014 (N=278)



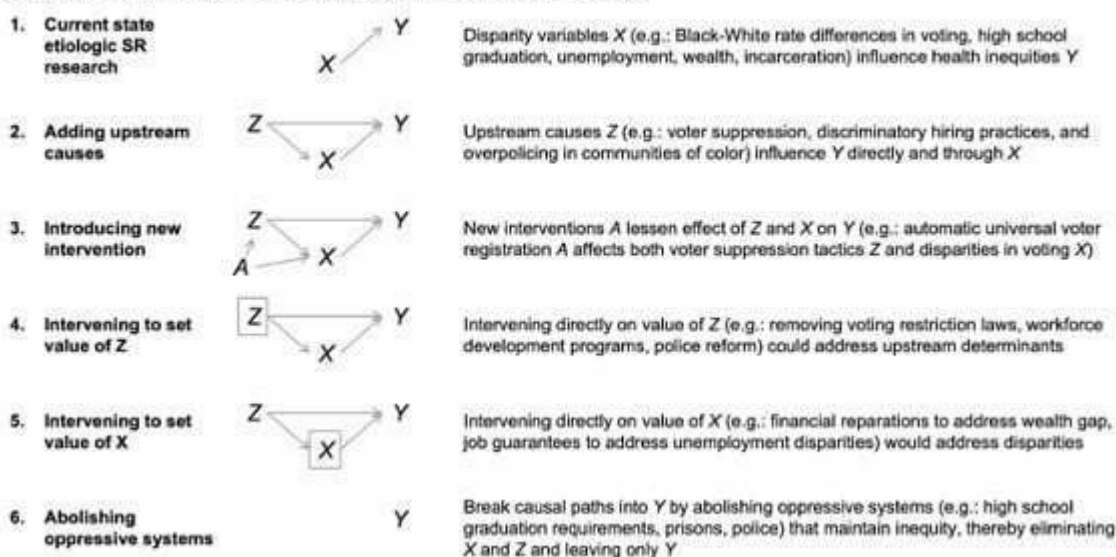
## Using DAGs to imagine dismantling structural racism: turning our gaze upstream Tracy Lam-Hine\* Tracy Lam-Hine Esther Velasquez Kevin F. Lee Tainayah Thomas David Rehkopf

Structural racism (SR, racism embedded between and across society's institutions) is increasingly accepted as a cause of US racial health inequities, but no approach to modeling SR has yet gained consensus in epidemiology. Several recent, well-received studies combine Black-White disparities in multiple ecologic variables to construct proxy index measures of SR. Such approaches are clear, replicable, and have helped produce consistent evidence linking SR and health inequities. Given these findings, we suggest that including upstream *causes* of proxy variables currently used could transform measurement and interventions to prevent SR.

Directed acyclic graphs (see figure) may help explicate. Let  $Y$  represent health, and  $X$  subsume Black-White race differences in voting, unemployment, and incarceration. But is  $X$  a true marker of SR, or just a symptom of it? Let  $Z$  precede  $X$  and  $Y$  and include modifiable policies and practices that cause disparities in  $X$ , e.g. measures of voter suppression, hiring discrimination, and overpolicing.  $H$ , historical processes shaping modern SR, likely precedes  $Z$  and  $Y$ ; figures omit  $H$  for simplicity. Current approaches only model  $X$ - $Y$ , likely underestimating SR's total treatment effect on  $Y$ .

Conceptualizing SR as both  $X$  and  $Z$  encourages consideration of both pragmatic and radical interventions. New interventions  $A$  could lessen  $X$  and  $Z$ 's effects on  $Y$  (e.g. automatic universal voter registration to reduce suppression and disparities). Changing  $Z$ 's value is likely feasible (e.g. removing voter restriction laws, funding workforce development, police reform); intervening on  $X$ 's value could be more challenging (e.g. job guarantees to eliminate unemployment gap). Most radically, abolishing oppressive systems that maintain inequity (e.g. prisons, police) would eliminate  $X$  and  $Z$  entirely, breaking SR's causal paths into  $Y$ . Though  $H$  may still influence  $Y$ , reimagining measures of SR to include  $Z$  will improve scientific rigor and our tools to dismantle SR.

**Figure:** Directed acyclic graphs showing (1) current approaches to the study of structural racism, (2) an expanded approach considering causes of observed disparity measures, and (3-6) potential interventions to address structural racism



**LATEBREAKER**

Cancer

**Assessing *Helicobacter pylori* infections among adults from the Navajo Nation** Dornell Pete\*

Dornell Pete Amanda I. Phipps Nina R. Salama Johanna W. Lampe Michael C. Wu

The Navajo Nation, the largest American Indian tribe in the Southwestern United States, is experiencing a higher incidence of stomach cancer compared to the general population in the region, possibly due to the high prevalence of *Helicobacter pylori* (*Hp*) infection, an infectious pathogen that colonizes the stomach and is a risk factor for stomach cancer. To assess the *Hp* prevalence, *cagA* virulence gene carriage, and risk factors for *Hp* infection in Navajo adults, we initiated a cross-sectional study in two geographic areas of the Navajo Nation.

In 2021 during the COVID-19 pandemic, participants were recruited using online and offline platforms (i.e., social media, study website, newspaper ads, flyers, and outreach). Demographic, health, behavioral, environmental, and diet factors were assessed from health and food frequency questionnaires, and *Hp* infection and *cagA* virulence were detected from stool samples by droplet digital PCR.

Of 99 participants, 56.6% (95% CI: 46.2-66.5) of participants were infected with *Hp* and, among *Hp*-infected participants, 78.6% (95% CI: 65.6-88.4) were infected with a *cagA*-positive *Hp* strain. Having a prior *Hp* infection was inversely associated with *Hp* infection (OR=0.05, 95% CI: 0.01-0.34), and using Navajo herbal medicine once a month was positively associated with *Hp* infection (OR=7.28, 95% CI: 1.40-61.12). No significant associations were observed with other risk factors (e.g., older age, males, lower education levels, smoking, alcohol use, and high sodium intake).

The prevalence of *Hp* infection was two times higher in study participants compared to the US population (27% seroprevalence), and the prevalence of the *cagA* gene in *Hp*-infected participants was four times higher than the US population *cagA* gene prevalence in White people (19% seroprevalence). These findings provide a greater understanding of the burden of *Hp* and *cagA*-positive infections and can inform prevention strategies to reduce *Hp* infections in the Navajo Nation.



**LATEBREAKER**

Cancer

**Presence of multi-morbidities and colorectal cancer screening utilization among breast cancer survivors** Meng-Han Tsai\* Meng-Han Tsai Grunert, Caitlyn Vo, Jacqueline B. Moore, Justin X. Guha, Avirup

**Purpose:** Our study aimed to cross-sectionally examine the association between the presence of chronic diseases and guideline-concordant colorectal cancer (CRC) screening utilization among breast cancer survivors.

**Methods:** Data from the 2016, 2018, and 2020 Behavioral Risk Factor Surveillance System were used. The primary outcome was receipt of guideline-concordant CRC screening. The exposures were chronic disease conditions, including diabetes, coronary heart disease/myocardial infarction, stroke, chronic obstructive pulmonary disease, emphysema/chronic bronchitis, arthritis, depressive disorder, or kidney diseases. Descriptive statistics and multivariable logistic regressions were applied to assess the mentioned association.

**Results:** Among 1,324 breast cancer survivors, those with multi-morbidities (88.3%) had higher CRC screening use compared to those with one (84.4%) or two (85.4%) chronic diseases (p-value<0.05). In multivariable analysis, survivors with multi-morbidities exhibited higher odds of having CRC screening (OR, 2.10; 95% CI, 1.11-3.98) compared to those with one. Among survivors with multi-morbidities, Black women (OR, 14.07; 95% CI, 5.61-35.27), those who reported frequent poor physical health (OR, 3.32; 95% CI, 1.57-7.00), and those who received a follow-up care plan (OR, 4.89; 95% CI, 1.92-12.47) were positively associated with CRC screening behaviors. Conversely, those survivors with frequent poor mental health were 67% less likely to receive CRC screening.

**Conclusions:** The presence of multi-morbidities were positively associated with guideline-concordant CRC screening among breast cancer survivors, highlighting the importance of chronic disease management considering mental and physical health status in cancer survivorship care. Use of patient navigation programs may increase adherence to screening recommendations and other follow-up care simultaneously among breast cancer survivors.

**LATEBREAKER**

Cancer

**One-carbon metabolism biomarkers and upper gastrointestinal cancer in Golestan, Iran**Maki Inoue-Choi\* Maki Inoue-Choi Neal D. Freedman Arash Etemadi Maryam Hashemian  
Gholamreza Roshandel Hossein Poustchi Sandy Dawsey Reza Malekzadeh

**Background:** High incidences of esophageal and gastric cancer are disproportionally observed in certain regions of the world including Iran, where vitamin B deficiency is common.

**Methods:** We measured vitamin B2 (riboflavin and flavin mononucleotide, FMN), B6 (pyridoxal phosphate, PLP), B12 (cobalamin), folate (para-aminobenzoylglutamate, pABG), and total homocysteine (tHcy) in stored plasma samples in matched case-control studies of esophageal squamous cell carcinomas (ESCC; 340 cases and 340 controls) and gastric cancer (GC; 353 cases and 353 controls) within the Golestan Cohort Study in Iran. We also measured methylmalonic acid (MMA) as an indicator of deficient cobalamin and 3-hydroxykyurenine (HK)-ratio, a novel functional marker of B6 insufficiency. Participants were categorized by quartiles of each biomarker in controls. We estimated ORs and 95% CIs using conditional logistic regression models adjusting for potential confounders. Linear associations were assessed per half an interquartile range as a unit.

**Results:** Low cobalamin and elevated MMA were observed in a large proportion of subjects. tHcy levels were inversely correlated with pABG ( $r=-0.136$ ,  $P<0.01$ ) and associated with higher risks of ESCC ( $OR_{Q4 \text{ vs. } Q1}=2.63$ , 95% CI=1.45-4.75) with a risk increasing by 9% per one unit increment (95% CI=1.01-1.17). There was a marginally increased risk of ESCC per unit of MMA ( $OR=1.06$ , 95% CI=0.99-1.13). Higher tHcy levels were also associated with higher risks of GC ( $OR_{Q4 \text{ vs. } Q1}=2.20$ , 95% CI=1.24-3.90) with a risk increasing by 5% per unit (95%CI=0.99-1.11). Higher HK-ratios were associated with higher risks of GC ( $OR=1.97$ , 95%CI=1.11-3.52) with an 11% risk increase per one unit increment (95%=1.00-1.23). The observed associations were mostly similar for cardia and non-cardia GC.

**Conclusions:** Higher tHcy levels were associated with higher risks of ESCC and GC. Insufficient status of vitamin B12 and B6, indicated by MMA and HK-ratio, was associated with higher risk of GC.

**LATEBREAKER**

Cancer

**Kinetics of EBV Antibody-based NPC Risk Scores in Taiwan NPC Multiplex Families** Jun Tao\* Jun Tao Wan-Lun Hsu Sheng Fu Kelly J. Yu Julia Simon Tseng-Cheng Chen Pei-Jen Lou Alisa M. Goldstein Kai Yu Allan Hildesheim Tim Waterboer Cheng-Ping Wang Zhiwei Liu

**Background**

Epstein-Barr virus (EBV) antibody testing has shown potential for the screening of nasopharyngeal carcinoma (NPC). Multiple results can be combined into risk scores, but the long-term stability of the scores is unclear. Here, we investigated the kinetics of two EBV-antibody NPC risk scores among NPC multiplex families.

**Methods**

The Taiwan NPC Multiplex Family Study with participants enrolled from 1996 to 2005 were our study population. We examined 533 NPC unaffected family members (controls) and 12 family members developing into NPC (cases) with two or three blood samples collected during follow-ups. A 2-marker ELISA score and 13-marker multiplex serology score were evaluated. To determine the stability of these scores, we calculated the intra-class correlation coefficient (ICC) by fitting a linear mixed model which accounted for the clustering effect of multiple measurements per subject and age. We also estimated the clustering of positive tests within the same individual using Fleiss's kappa statistic.

**Results**

The median follow-up duration was 20.3 years (range 16.0-24.7) and 13.5 years (range 3.1-20.7) for controls and cases, respectively. The 2-marker score showed high stability over time in serial blood samples, whereas the 13-marker score was more variable ( $p < 0.05$ ). The ICCs for the 2-marker score among controls and cases were 0.671 (95% confidence interval [CI]=0.638-0.701) and 0.811 (0.503-0.991), respectively; those for the 13-marker score among controls and cases were 0.370 (95%CI=0.322-0.412) and 0.402 (0.000-0.758), respectively. Positive tests were more likely to cluster within the same individual for the 2-marker score than the 13-marker score ( $p < 0.05$ ). The 2-marker score had a specificity of 89.7% (95%CI = 87.2-92.5%) for a single measurement and increased to 96.1% (94.3-97.7%) and 98.4% (97.1-99.4%) with one and two repeats. The 13-marker score yielded a specificity of 73.2% (95%CI = 69.2-76.9%) for a single measurement and increased to 89.2% (86.1-91.7%) and 92.5% (89.9-94.7%) with one and two repeats.

**Conclusions**

Increased specificity of EBV-antibody scores is achieved by repeated measures for NPC detection among NPC multiplex families. Further studies are warranted to validate the findings and establish reasonable time intervals for clinical follow-up.

**LATEBREAKER**

Cancer

**Trends in Colorectal Cancer Screening over the past 30 years in the U.S.: An Analysis of Data from the Behavioral Risk Factor Surveillance System** Nadine Dogbe\* Nadine Dogbe  
Lauren Hurwitz Lisa Kahle

**Background:** Given that Colorectal Cancer (CRC) is the third most common cancer and the second leading cause of cancer death in the U.S., we sought to evaluate how screening rates for CRC have changed over time in the U.S.

**Objectives:** We examined CRC screening rates in the U.S. population between 1991-2021 and evaluated differences in screening rates by gender, education, healthcare coverage, and race/ethnicity.

**Methods:** This study analyzed data from the Behavioral Risk Factor Surveillance System (BRFSS) from 1991-2021, including all years except 2017 which did not have information on CRC screening. We included participants age 50 years or older and answered questions regarding colorectal screening with colonoscopy, sigmoidoscopy, or proctoscopy. SUDAAN was used to estimate population screening rates and to compute logistical regression models evaluating differences by age, gender, race/ethnicity, education, and health care coverage, adjusting for potential confounders.

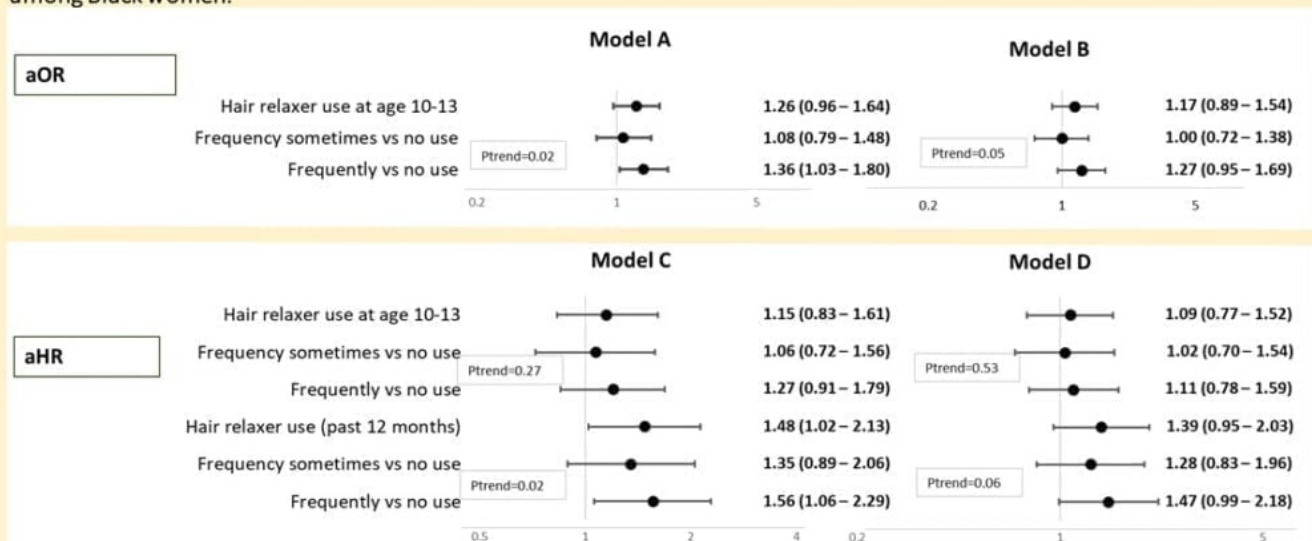
**Results:** CRC screening rates increased over time in the U.S. from 35.0% (95% CI: 32.9-37.1%) in 1991 (before CRC screening recommendations) to 75.6% (95% CI: 74.1-77.1%) in 2021. However, significant disparities between racial/ethnic groups were observed, even after controlling for education and health care coverage ( $P < 0.05$ ). Although screening rates increased over time for all populations, Hispanics and other racial/ethnic groups (American Indian or Alaska Native only, Asian only, Native Hawaiian or Other Pacific Islander only, Other) had consistently lower screening rates compared to non-Hispanic whites (OR=0.76, 95% CI: 0.72-0.79 for Hispanics, OR=0.76, 95% CI: 0.69-0.74 for others). No significant difference was observed for non-Hispanic blacks (OR=0.99, 95% CI: 0.96-1.03).

**Discussion:** Our analysis shows the increase in colorectal cancer screening in the U.S. over time. However, more public health efforts are needed to improve screening rates among historically racial/ethnic groups.

**Chemical hair straightener use in adolescence and adulthood in relation to prevalent and incident fibroids among Black/African American women** Kemi Ogunsina\* Kemi Ogunsina katie M. O'brien Alexandra J. White Che-Jung Chang Symielle Gaston Chandra L. Jackson Dale P. Sandler

**Background:** For myriad reasons, chemical hair straightener/relaxer use remains common among Black women who are, therefore, exposed to hormone disruptors and other chemicals. It is unknown whether straighteners/relaxers contribute to the increased risk for uterine fibroids in Black women. **Objective:** Examine the association of straightener/relaxer use and fibroids among Black women. **Study design:** Utilizing data from Black women in the Sister Study (2003–21), we studied associations with prevalent fibroids diagnosed before age 50 among women 50–74 years at enrollment (n=1447), and with incident fibroids among women 35–60 years with an intact uterus and no history of fibroids at enrollment (n=1252). Participants self-reported frequency of straightener/relaxer use at ages 10–13 and in the 12 months prior to enrollment, and fibroid diagnosis. In the prevalence analysis, multivariable logistic regression models estimated adjusted OR and 95% CI for the association between straightener/relaxer use at ages 10–13 years and fibroids adjusting for age at baseline and childhood socioeconomic status. In the prospective analysis, we used multivariable Cox models to estimate HRs for the association between fibroids and straightener/relaxer use at both time points, additionally adjusting for use of other hair products, including grease/pomade. **Results:** Overall, any straightener/relaxer use (aOR 1.26, 95% 0.96–1.64) and frequent use versus no use at ages 10–13 (1.36, 1.03–1.80) were associated with history of fibroids (n=691 cases). During a mean follow up of 6.5 years (maximum 16 years), use of straightener/relaxer at 10–13 years (aHR 1.15, 0.83–1.61) and just prior to enrollment (1.48, 1.02–2.13) were both associated with incident fibroids (n=236 cases). Though modestly attenuated with adjustment for grease/pomade, the associations remained (Figure). **Conclusion:** Hair straightener/relaxer use at 10–13 years and in adulthood were associated with uterine fibroids.

Figure : Adjusted odd ratios (aOR) and hazard ratios (aHR) for the association of chemical straightener/relaxer and fibroids among Black women.



Prevalence analysis (n=1447): **Model A** is adjusted for age at baseline and childhood SES factors; **Model B** is additionally adjusted for hair grease/pomade use in childhood. Incidence analysis (n=1252): **Model C** is adjusted for age at baseline, reproductive, and adult SES factors; **Model D** additionally adjusted for hair grease/pomade use in adulthood

## Environment/Climate Change

**Personal care product use and perfluoroalkyl substances in pregnant and postpartum****women and adolescents: The MIREC and HOME studies** Amber M Hall\* Amber Hall Jillian

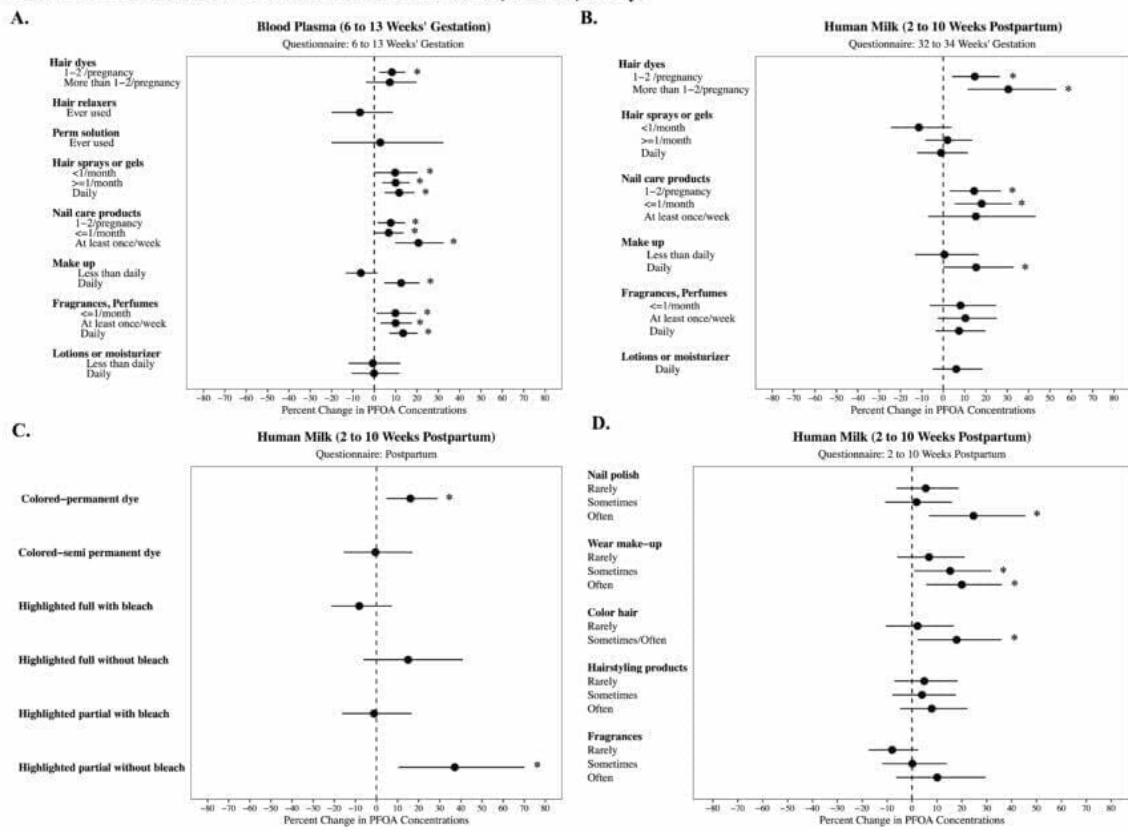
Ashley-Martin Chun Lei Liang Tye E Arbuckle Michael M Borghese Jessie P. Buckley Kim M. Cecil Aimin Chen Mandy Fisher Bruce P. Lanphear Jana Palaniyandi Dorothea FK Rawn Kimberly Yolton Joseph M Braun

**Background:** Perfluoroalkyl substances (PFAS) are ubiquitous toxic chemicals routinely detected in personal care products (PCPs). Few studies have quantified the contribution of PCP use on PFAS concentrations. This study evaluates PCP use and PFAS in maternal plasma, human milk, and adolescent serum.

**Methods:** We used data from 2 pregnancy cohorts. MIREC (2008-2011) enrolled women from 10 Canadian cities and HOME (2003-2006) enrolled women from Cincinnati Ohio. Participants reported frequency of use for 8 PCP categories in MIREC and past 24-hour use for 15 PCPs in HOME. In MIREC, we quantified PFAS in maternal plasma (6-13 weeks' gestation; N=1,940) and human milk (2-10 weeks postpartum; N=664). In HOME, we measured PFAS in adolescent serum (11-14 years; N=193). Using linear regression, we estimated percent differences in PFAS concentrations with PCP use, adjusted for sociodemographic factors.

**Results/Conclusions:** In MIREC, more nail care product, fragrance, hair dye, spray and gel, and makeup use was associated with greater maternal plasma perfluorooctane sulfonic acid (PFOA) and/or perfluorooctane sulfonic acid (PFOS) concentrations. Greater hair dye, partial highlights, nail care product, makeup, and nail polish use were associated with higher PFOS or PFOA in human milk (Figure 1: PFOA results). More hair dye, hair styling product, and makeup use was associated with greater human milk perfluorononanoic acid. Additionally, greater nail care product and polish use and full highlights without bleach were associated with higher human milk perfluorohexane sulfonic acid concentrations. No PCP-PFAS associations were observed in HOME; the lack of associations may be explained by the smaller sample size or narrower window of PCP use (past 24-hour vs. general use). Our results suggest that some PCPs contribute to maternal plasma and human milk PFAS. Future studies could examine if associations depend on country and age, timing and frequency of use, or product formulation.

**Figure 1. Associations between personal care product use and maternal plasma and human milk PFOA concentrations in the Maternal-Infant Research on Environmental Chemicals (MIREC) Study.**



Note. PFOA, perfluorooctane sulfonic acid. Reference group is 'never use' for all categories except lotions or moisturizer at 32-34 weeks' gestation, where the reference is 'not daily'. Effect estimates represent a percent change in PFOA concentrations relative to the reference group. PFAS measures below the LOD were imputed as LOD/2. Results were derived from linear regression models adjusted for maternal age, parity, education, and country of birth.

**Preconception Serum Per- and Polyfluoroalkyl Substances (PFAS) and Risk of Spontaneous Abortion in a Prospective Cohort of North Americans: Preliminary Findings**

Samantha Schildroth\* Samantha Schildroth Amelia K. Wesselink Michael D. McClean Ganesa Wegienka Elizabeth E. Hatch Lauren A. Wise

**Background:** Per- and polyfluoroalkyl substances (PFAS) are a class of endocrine-disrupting chemicals that are ubiquitous in the environment. Prior studies have linked PFAS exposure with increased risk of spontaneous abortion (SAB, pregnancy loss <20 weeks gestation), but few studies have measured PFAS before pregnancy or have captured early SAB (<8 weeks).

**Methods:** We used data from Pregnancy Study Online (n=163), a prospective cohort study of North American females aged 21-45 years (2015-2021), to assess associations between PFAS concentrations and self-reported SAB (pregnancy loss <20 weeks' gestation). We quantified five PFAS in preconception serum samples using isotope dilution tandem mass spectrometry. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CIs, adjusting for *a priori* selected confounders. We further stratified results by parity status (parous vs. nulliparous), as pregnancy is an important route of PFAS elimination.

**Results:** Median concentrations (ng/mL) for PFOS, PFOA, PFNA, PFHxS, and PFDA were 2.8, 1.3, 0.4, 0.8, and 0.2, respectively. Spearman correlations between PFAS ranged from 0.38 (PFHxS vs. PFDA) to 0.84 (PFOS vs. PFNA). Nearly 19% (N=30) of participants reported SAB during follow-up, with 50% of losses occurring <8 weeks' gestation. In adjusted models, the HR for an interquartile increase in PFNA concentrations was 1.6 (95% CI=0.6-4.4). Associations for other PFAS were generally null. Among parous participants, there was a consistent trend of increased risk of SAB with increasing concentrations for all PFAS, and associations were strongest for PFOS (HR=3.0, 95% CI=0.5-19.6) and PFNA (HR=2.4, 95% CI=0.4-15.2).

**Conclusions:** Preliminary findings indicate that preconception PFAS concentrations are associated with increased rate of SAB, particularly among parous participants, though results were imprecise. Further work includes expanding the sample size and examining the influence of PFAS mixtures on SAB.



## Study Design

**Exposure to chemicals in personal care products among women with high daily use** Caroll Co\* Caroll Co Angela Jeffers Peter P Egeghy Steven E Prince Daniel M Stout II Raquel A Silva Lillian Alston Richard Walker Helen Cunny Timothy J Buckley Andrew A Rooney Kyla W Taylor

**Background**

Endocrine disrupting chemicals (EDC) such as parabens, phthalates, and phenols are found in many personal care products (PCP). Measuring exposure to these chemicals from PCP use can be difficult due to the breadth of available products. This study evaluated behavioral data collection methods for measuring EDC exposure among high PCP users.

**Methods**

We conducted a 10-day pilot study using a convenience sample of 9 women in North Carolina who reported daily use of  $\geq 15$  consumer products. Subjects provided daily urine samples, logged daily PCP use with a digital diary, and completed questionnaires on frequency of historical and recent PCP use. We calculated Kendall's tau ( $\tau$ ) to estimate the rank correlation across data collection methods. We used nationally representative NHANES data as the referent population to compare EDC concentrations and used the Kaplan-Meier method to derive percentiles in the presence of nondetectable values.

**Results**

Of the 9 women, 4 reported using  $\geq 15$  PCPs at least 4 times within the past 10 days and at least once per week within the past 12 months. On average, participants reported a greater number of PCPs on the historical use questionnaire (mean=17.4) compared to both the daily diary (mean=13.3) and recent use questionnaire (mean=12.4). Correlations across all modes of data collection were high, ranging from  $\tau=.74$  to  $.81$ . Compared to median values of biomarkers reported in NHANES, most women in our study had a higher 10-day median concentration for both MHINCH, a phthalate-alternative metabolite, and benzophenone-3, a UV filter. Among paraben and phthalate metabolites, most study participants measured higher than the national median on DIBP but lower on MEP, MBZP, and methyl and propyl parabens.

**Conclusion**

We found high consistency in responses relating to PCP use among questionnaires and the daily diary; however, self-reported PCP use may not correlate with urinary levels of paraben and phthalate biomarkers.

**Menstrual cycle and menses length in relation to endometrium PFAS levels** Joanna M. Marroquin\* Joanna Marroquin Cherie Marfori Jenna R. Krall Vimailkumar Krishnamoorthi Kurunthachalam Kannan Anna Z. Pollack

**Background:** Menstruation has been suspected as a mode of excretion of per- and polyfluoroalkyl substances (PFAS). This study aims to determine if menses and menstrual cycle length (MCL) are associated with PFAS levels in eutopic endometrium in menstruators with and without gynecological disease.

**Methods:** The Investigating Mixtures of Pollutants and Endometriosis in Tissue Study included 423 women aged 18-44 years, from 14 clinical centers in Utah and California from 2007-2009. PFAS levels in endometrial tissue were obtained using tandem mass spectrometry. A questionnaire and one-cycle daily diary assessed MCL characteristics. Menses length was categorized as <2 days, 2-7 days, and >7 days. MCL was categorized as short (<20 days), normal (21- 35 days), and long (>35 days). Adjusted linear regression models evaluated the association of log-transformed PFAS levels with the 12-month average MCL and menses length. Models were adjusted for body mass index, age, and hormonal contraceptive use.

**Results:** Median eutopic concentrations of PFOSA (0.12ng/g), PFHxS (0.65ng/g), PFOS (6.58ng/g), PFOA (1.93ng/g), and PFNA (0.58ng/g) were obtained. Lower PFOA ( $\beta$  -0.24 CI, -0.46, -0.03), PFOSA ( $\beta$  -0.53, CI -1.09, 0.03), PFOS ( $\beta$  -0.17, CI -0.34, 0.01), and PFNA ( $\beta$  -0.44, CI -0.88, 0.001) were associated with menses >7 days compared to 2-7 days. Short MCL was associated positively with PFNA ( $\beta$  0.53 CI 0.03-1.04) compared to normal MCL (21-35 days). PFOSA, PFOS, and PFHxS were not associated with menses length. Continuous MCL was not associated with and PFAS.

**Conclusion:** Menses duration and menstrual cycle length may be a route of PFAS excretion.

**LATEBREAKER**

Social

**Neighborhood Mortgage Lending Bias and Preterm Birth among NHB and NHW births in North Carolina** Anjali D. Kumar\* Anjali Kumar Kristen Rappazzo Chantel L. Martin**Background**

Contemporary redlining, measured through mortgage lending bias, is a form of institutional racism in the United States. Contemporary redlining may impact the neighborhood social environment and resulting health outcomes, particularly at critical windows. We examined racial mortgage lending bias in relation to preterm birth, the leading cause of infant mortality, among Non-Hispanic Black (NHB) and Non-Hispanic White (NHW) births in North Carolina (NC).

**Methods**

We used 2012-2017 Home Mortgage and Disclosure Act (HMDA) data to derive a measure of racial bias in mortgage lending in Durham, Orange, and Wake counties of NC. Odds of mortgage loan denial per census tract for NHB compared to NHW homeowner applicants were estimated accounting for loan-to-income ratio and applicant sex and merged with 2013-2018 NC birth records. Preterm birth was defined as gestational age at delivery less than 37 weeks. Maternal residential addresses from birth records were geocoded and linked to odds of loan denial by census tract. Associations between racial mortgage lending bias and preterm birth were estimated with multilevel mixed models adjusting for maternal age, education level, marital status, insurance status, and parity and stratified by race.

**Results**

In a cohort of 92,818 births, prevalence of preterm birth was 12.41% for NHB births and 8.26% for NHW births. Crude odds ratios (OR) for mortgage loan bias and preterm birth differed for NHB (OR: 1.15; 95% CI: 1.08, 1.24) and NHW births (OR: 1.04; 95% CI: 0.96, 1.12). Estimates slightly attenuated for NHB (OR: 1.15; CI: 1.07, 1.24) and NHW births (OR: 1.02; CI: 0.94, 1.10) after adjusting for potential confounders.

**Conclusion**

Racial mortgage loan denial is associated with preterm birth for Non-Hispanic Black births, but may not be for Non-Hispanic White births in NC. Racial bias in mortgage lending may play a role in understanding how forms of structural racism shape health inequalities in birth outcomes and infant mortality.

**LATEBREAKER**

Social

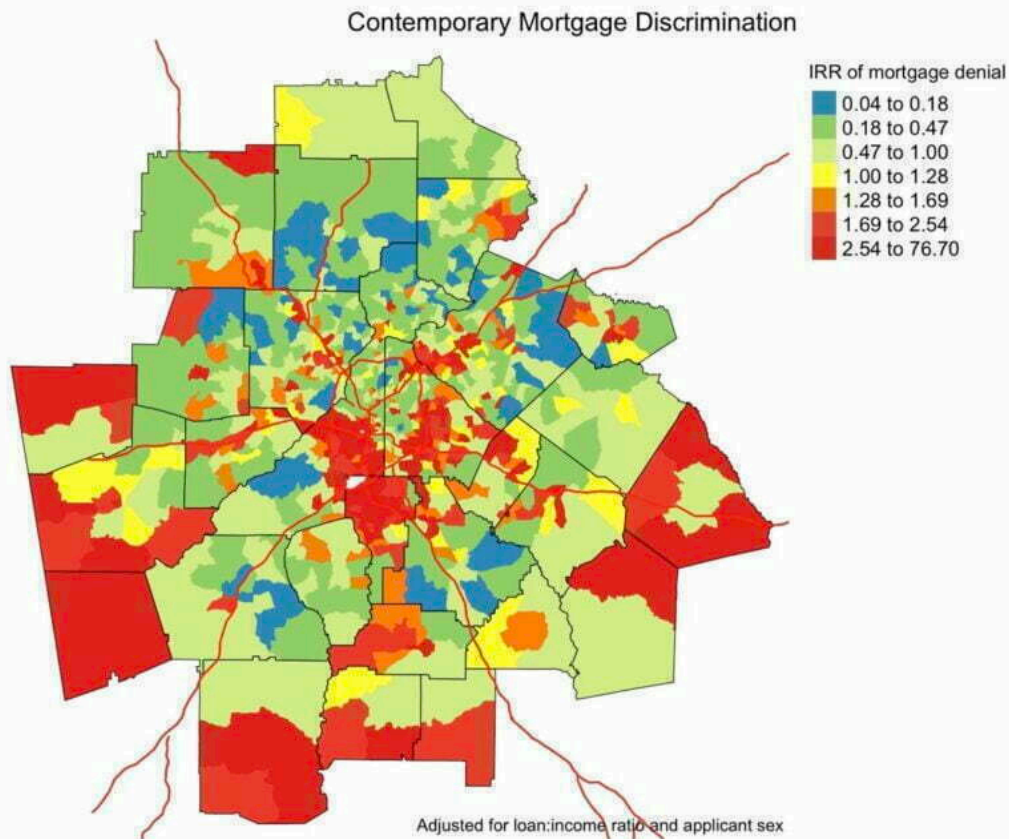
**Spatial Patterns of Mortgage Discrimination in Metropolitan Areas in the Southeastern United States** Leah Moubadder\* Leah Moubadder Maya Bliss Maret Maliniak Lauren Barber Jasmine M. Miller-Kleinhenz Jeffrey M. Switchenko Michael R. Kramer Lauren E. McCullough

Mortgage discrimination remains an upstream contributor to health disparities by altering the distribution of investment, opportunity, and economic advantage. In this study, we sought to create a method for measuring the rate of mortgage discrimination and apply it to urban areas in the Southeastern US.

In this study, we used Home Mortgage Disclosure Act data to estimate the rate of mortgage denial within 40 metropolitan statistical areas (MSAs) in the Southeastern US. We estimated the median rate ratios (RR) by census tract—relative to the of the respective MSA—using a Bayesian spatial model with conditionally autoregressive priors and integrated nested Laplace approximation for estimating the posterior distributions. This approach accommodates spatial dependencies by borrowing statistical information through spatial and non-spatial priors, which results in stable estimates in the presence of sparse data.

Areas with mortgage discrimination ( $RR > 1.0$ ) exhibited higher proportions, on average, of Black, Hispanic, and immigrant Americans, and households below the poverty line. All 40 MSAs included at least one census tract with evidence of mortgage discrimination. Approximately 17% of all census tracts showed an increased rate of mortgage discrimination relative to their respective MSA after accounting for individual-level loan-to-income ratio and sex. Finally, our analysis revealed spatial variation in the extent of discrimination within and across MSAs.

By providing a robust and transparent method for measuring mortgage discrimination, our novel approach can inform interventions to promote equitable lending practices in these areas. We will also make our code and analytic approach publicly available, allowing researchers to adapt our methods and advance the understanding of the impact of mortgage discrimination on affected communities. This will facilitate the replication and extension of our findings and encourage collaborative efforts to address this pressing issue.



**Figure 1.** Map of estimated posterior probabilities of mortgage discrimination in Metro Atlanta, Georgia (as an example), generated using a Bayesian spatial model. The map shows areas of high posterior probability (red) and low posterior probability (blue) of experiencing discrimination in mortgage lending. The results highlight the persistent disparities in access to credit and housing opportunities in urban areas.

**LATEBREAKER**

Social

**The Association Between Perceived Discrimination and Body Mass Index Among Asian Women** Sarpong Boateng\* Yvette Cozier Sarpong Boateng Hyeouk Hahm Phuong K Tran Rajesh Gururaghavendran Uyen-sa Nguyen Yvette C Cozier

Perceived racial discrimination is associated with poor health outcomes, including high body mass index (BMI) among U.S. Black and Latino populations. This association, however, has not been well established among Asian Americans. Since the start of the COVID-19 pandemic, there has been a significant surge in anti-Asian racism and hate crimes leading to increased psychosocial stress and possibly metabolic dysregulation. We explored whether perceived discrimination might be associated with BMI among Asian American women. The Epidemiology of Asian Women's Action for Resilience and Empowerment (EPI-AWARE) study is a follow-up of Asian women conducted between December 2019 and September 2022. Using an online questionnaire assessing demographic, medical, and lifestyle factors, participants were asked about experiences of racial discrimination using five self-report items measuring everyday discrimination (e.g., "how often do people act as if they are better than you?"), and six items measuring lifetime discrimination (e.g., unfair treatment due to your race "at school"). A cumulative discrimination score was created by combining the everyday and lifetime scores and dichotomizing into low (<3) vs high ( $\geq 3$ ) for analysis. Self-reported BMI was categorized as either low (<25kg/m<sup>2</sup>) or high ( $\geq 25$ kg/m<sup>2</sup>). Multivariable binomial regression was used to estimate risk ratios (RR) and 95% Confidence Intervals (CI) controlling for age, sexual orientation, nativity, history of poverty, and physical activity. In this cross-sectional analysis, a total of 153 women aged 18-59 years (median=26 years) completed study questionnaires of which 76.56% reported high racial discrimination (range: 0-9), and 22.93 % reported high BMI (range=16.5-42.1 kg/m<sup>2</sup>). Women reporting high levels of discrimination, compared to low levels, were significantly more likely to be classified in the high BMI category (RR: 4.8; 95% CI =1.2-18.9) (*P*-value: 0.013). Our data suggest that experiences of racism may impact BMI among Asian Americans. This finding may have particular relevance given the marked increase in anti-Asian racism in the U.S. initiated during the COVID-19 pandemic. Further research is needed to understand the underlying mechanism(s) contributing to this association and to identify needed resources.

**LATEBREAKER**

Social

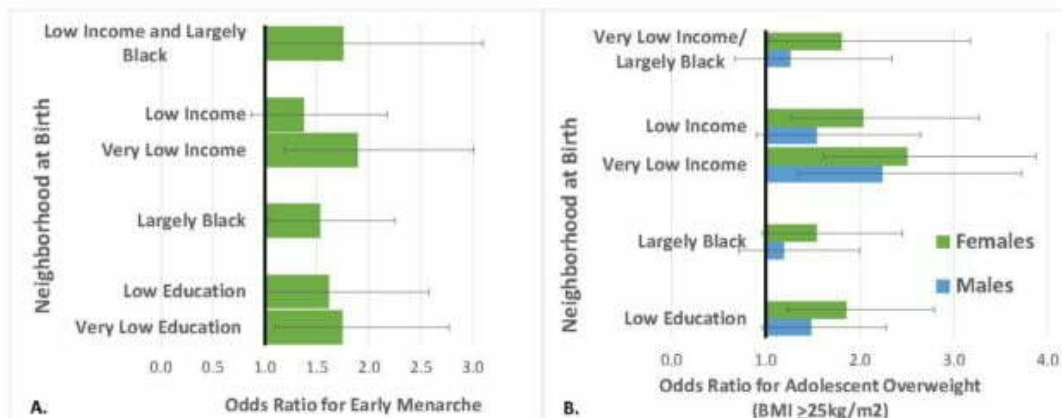
**Associations of early menarche and adolescent overweight with neighborhood indices of social polarization: evidence from the Child Health and Development Studies** Corinna Keeler\* Caitlin Murphy Piera Cirillo Nickilou Krigbaum Corinna Keeler Barbara Cohn

**Background:** Geospatial measures of “social polarization” termed Indexes of Concentration at the Extremes (ICEs) have been linked to adverse health outcomes, and represent meaningful proxies for exposure to toxic environmental stressors.

**Methods:** A subset of offspring born into The Child Health and Development Studies (CHDS) pregnancy cohort from 1959-1960 in Oakland, CA were recruited for an Adolescent study at ages 15-17 years, n=2,020. ICE measures for these participants were calculated using residence at birth to characterize neighborhood race/ethnicity, income, education and combined income and race, capturing social polarization during infancy, a critical window of development. ICE indices at birth were determined by linking tract-level 1960 census data with geocoded address at birth. Adolescent study report of age at menarche and in-person measurement of weight, height were used to assess early menarche as <12 vs. ≥12 years and to classify overweight as BMI ≥25 vs. <25 kg/m<sup>2</sup>. We used log-linear models to estimate associations of early menarche and adolescent overweight with ICE indices at birth, adjusted for individual factors and family clustering.

**Results:** Address at birth was geocoded for 87% (n=884) of Adolescent Study males (n=1,017) and 86% (n=865) of females (n=1,003). Adolescents born into neighborhoods with a high concentration of Black residents, low education, low income and combined low income and high concentration of Black residents had significantly higher risk of early menarche and being overweight at adolescence (**Figure**). Sex differences were not significant but estimates for females were higher, suggesting girls were more impacted by neighborhood stressors. Associations persisted after adjusting for individual factors.

**Conclusions:** Findings underscore the potential for indices of neighborhood social polarization to serve as proxies for early markers of morbidity and inequalities in health risk, beyond individual risk factors.



**Figure Legend: A. Odds Ratios for Early Menarche (<12 years) and Neighborhood ICE Measures.** Very low and low neighborhood education were assessed as quintiles 1 and 2 (respectively) vs quintiles 3-5 of Education ICE based on neighborhood of birth address, adjusted for mother's education (less than High School and High School vs. else) at offspring birth and adolescent overweight. Largely Black neighborhood was assessed as quartile 1 vs quartiles 2-4 of Race ICE based on neighborhood of birth address, adjusted for adolescent overweight. Very low- and low-income neighborhoods were assessed as quintile 1 and quintile 2 (respectively) vs quintiles 3-5 of Income ICE, adjusted for family income (below 1960 median income vs. else) at offspring birth and adolescent overweight. Low income and largely Black neighborhood was assessed as quartile 1 vs quartiles 2-4 of Income and Race ICE, adjusted for adolescent overweight, and for family income (below 1960 median income vs. else) at offspring birth and maternal Black race.

**B. Odds Ratios for Adolescent Overweight ( $\geq 25\text{kg/m}^2$ ) and Neighborhood ICE Measures.** Low neighborhood education was assessed as quartile 1 vs quartiles 2-4 of Education ICE based on neighborhood of birth address, adjusted for mother's education (less than High School and High School vs. else) at offspring birth. Largely Black neighborhood was assessed as quartile 1 vs quartiles 2-4 of Race ICE based on neighborhood of birth address, adjusted for mother's race (Black vs. else). Very low- and low-income neighborhoods were assessed as quintile 1 and quintile 2 (respectively) vs quintiles 3-5 of Income ICE, adjusted for family income (below 1960 median income vs. else) at offspring birth. Very low income and largely Black neighborhood was assessed as quintile 1 vs quintiles 3-5 of Income and Race ICE, adjusted for family income (below 1960 median income vs. else) at offspring birth and maternal Black race.

Indices of Concentration at the Extremes, ICE, were calculated as follows: **Education ICE:** (College - less than High School) / Education Total; **Race ICE:** (White - Black Race) / Total Population; **Income ICE:** ([Family Income > 10,000] - [Family income < 3,999]) / All Family Income; **Income and Race ICE:** ([White family Income > 10,000] - [Non-white family income < 3,999]) / All Family Income.



**LATEBREAKER**

Social

**The Health of Mexican Immigrant Families: Do Climates of Immigrant Inclusivity Shape Childhood Diet and Obesity?** Lindsay Fernandez-Rhodes\* Lindsay Fernandez-Rhodes

Children of Mexican immigrants are particularly vulnerable to obesity and this disparity places them at elevated risk of Type 2 diabetes as they age. It is estimated that as many as 1/3 Mexican children have an unauthorized immigrant parent. Despite the majority being US citizens themselves, structural xenophobia such as partnerships between local law enforcement and Immigration and Customs Enforcement, ICE, and exclusionary policies towards immigrants, may be a barrier for Mexican children to maintaining a healthy lifestyle and weight. To assess the association between these two forms of structural forces on Mexican immigrant families, we designed a two-part study by: 1) curating a 10+ year contextual dataset on publicly available Immigrant Legal Resource Center (ILRC) data on county involvement with ICE and previously-published immigration policy climate scores (IPC, comprised of state public health and welfare, education, labor and employment, driver's licenses and identification policies); and 2) merging the contextual with individual-level public and restricted (i.e., geographic and household indicators) data from continuous National Health and Nutrition Examination Survey (2009-2018). Findings from the first phase of this work reveal a strong correlation ( $\rho=0.6$ ) between county-level partnerships with ICE and the exclusion of immigrants from state policies, 2017-2019. Percent Hispanic and income inequality (index of concentration at the extremes) from the American Community Survey 5-year estimates were weakly to moderately correlated with ILRC ( $0.03 < \rho < 0.1$ ; 2017-19) and IPC scores ( $0.01 < \rho < 0.4$ ; 2009-2019). The second-phase research is underway; pending final approval, these results will be presented in a SER late-breaker session. We will present the test our hypothesis that children of Mexican immigrants living with higher structural xenophobia will have unhealthier dietary patterns and elevated adiposity (body mass index percentiles and waist circumference) using multi-level survey regressions. To our knowledge, previous studies have not investigated variation in structural xenophobia towards immigrants and obesity in a nationally-representative sample of children, which means that these results will add to the literature on immigrant xenophobia as a social determinant of health.

**Long-term educational and economic outcomes after preterm birth: Evidence from a national population-based cohort** Asma Ahmed\* Asma Ahmed Eleanor Pullenayegum Sarah D. McDonald Jason D. Pole Shahirose Premji Marc Beltempo Fabiana Bacchini Prakeshkumar S. Shah Petros Pechlivanoglou

**Background:** Preterm birth (PTB) at <37 weeks gestation affects approximately 10% of births worldwide; however, data on the socioeconomic outcomes of these children is limited and inconclusive. We aimed to examine the effect of PTB on individuals' educational attainment, income, and employment during adulthood.

**Methods:** Using linked administrative data from Statistics Canada, we created a population-based cohort of children born in Canada between 1983 and 1996 (~4 million births). We tracked these individuals until the end of 2018 (age 21-34 years) to ascertain the following at age  $\geq 18$  years: postsecondary education enrollment and attainment, annual employment income, and employment rate. We estimated mean differences and RR using generalized estimating equations (linear and log links respectively), accounting for differences in baseline characteristics (e.g., birth year, parental demographics) using exact matching and adjusting for age and period effects.

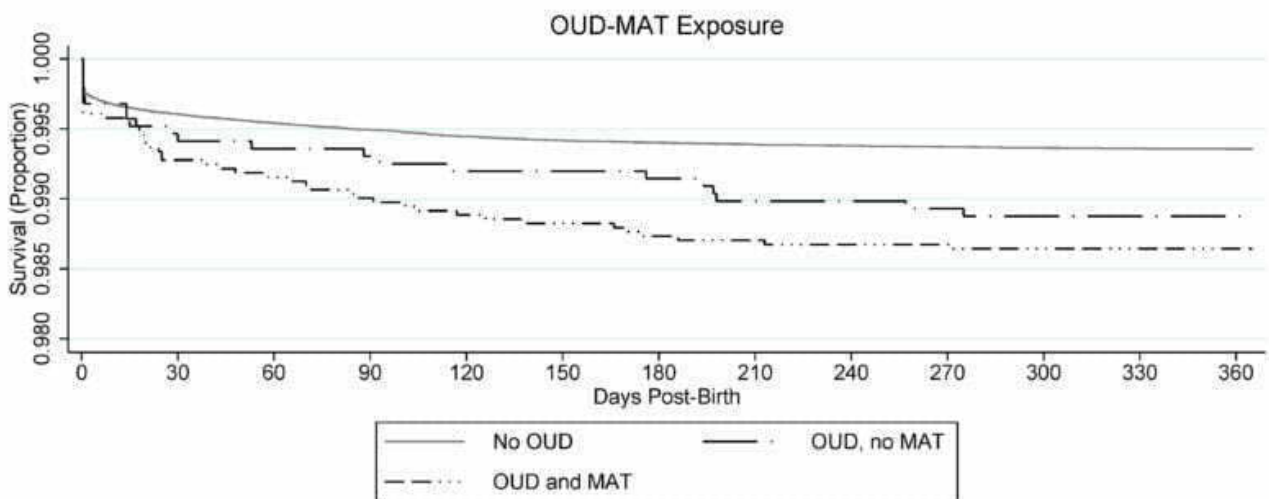
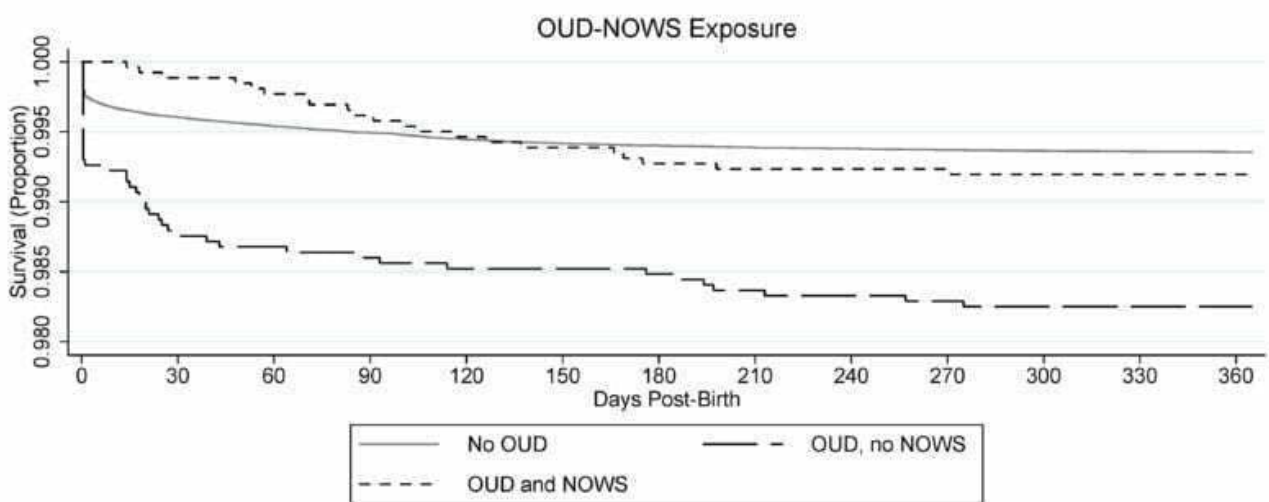
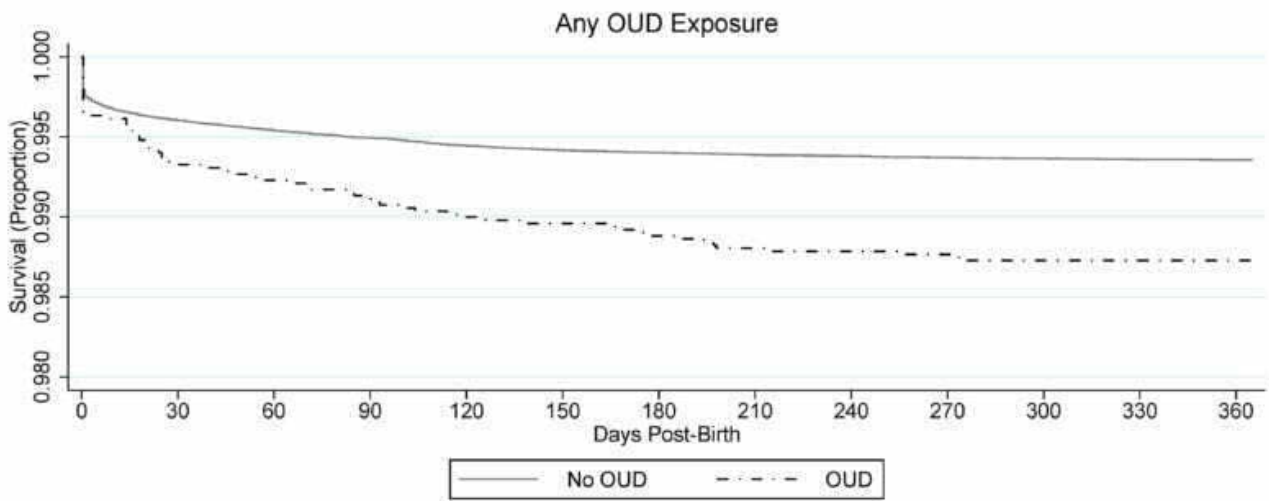
**Results:** In analyses conducted on a 10% random sample to efficiently test statistical codes and obtain preliminary results, infants born preterm were less likely to have enrolled in postsecondary education (RR 0.86 (95% CI 0.84 to 0.88)) and to graduate with a bachelor's degree or higher (RR 0.85, 95% CI 0.83 to 0.87)). They, on average, earned -2,331 CAD (95% CI: -2,656, -2,007) lower per year than those born at term and were 4% (RR 0.96, 95% CI 0.96 to 0.97)) less likely to be employed. The risks of these outcomes were inversely proportional to gestational age (GA). Estimates for those born <28 weeks were -10,356 CAD (-12,177, -8,535) per year for mean income differences and RR 0.38, 95% CI 0.31 to 0.45, for graduation with  $\geq$  bachelor's degree.

**Conclusion:** Individuals born preterm had lower educational and economic achievements in their second and third decades after birth than those born at term, and the risks were higher with decreasing GA at birth. This is the largest study to date to show long-term socioeconomic disadvantages associated with PTB.

**Maternal opioid use disorder and infant mortality in Wisconsin, 2010-2018** David Mallinson\*  
David Mallinson Hsiang-Hui Daphne Kuo Russell Kirby Lawrence Berger Deborah Ehrental

Opioid use disorder (OUD) during pregnancy has increased over the past decade. The extent to which prenatal OUD exposure affects infant mortality (death before 365 days post-birth) is uncertain. We measure the association between maternal OUD during pregnancy and infant mortality with data from a population-based cohort of linked Wisconsin birth records, death records, and Medicaid claims. We also investigate whether that association varies by neonatal opioid withdrawal syndrome (NOWS) diagnosis and by maternal medication-assisted treatment (MAT) for OUD during pregnancy. Our sample consists of Medicaid-paid live deliveries during 2010-2018 (N=235,777 births). There are three measures of OUD exposure: any OUD (no OUD; OUD), OUD-NOWS (no OUD; OUD without NOWS diagnosis; OUD with NOWS diagnosis), and OUD-MAT (no OUD; OUD without MAT; OUD with MAT).

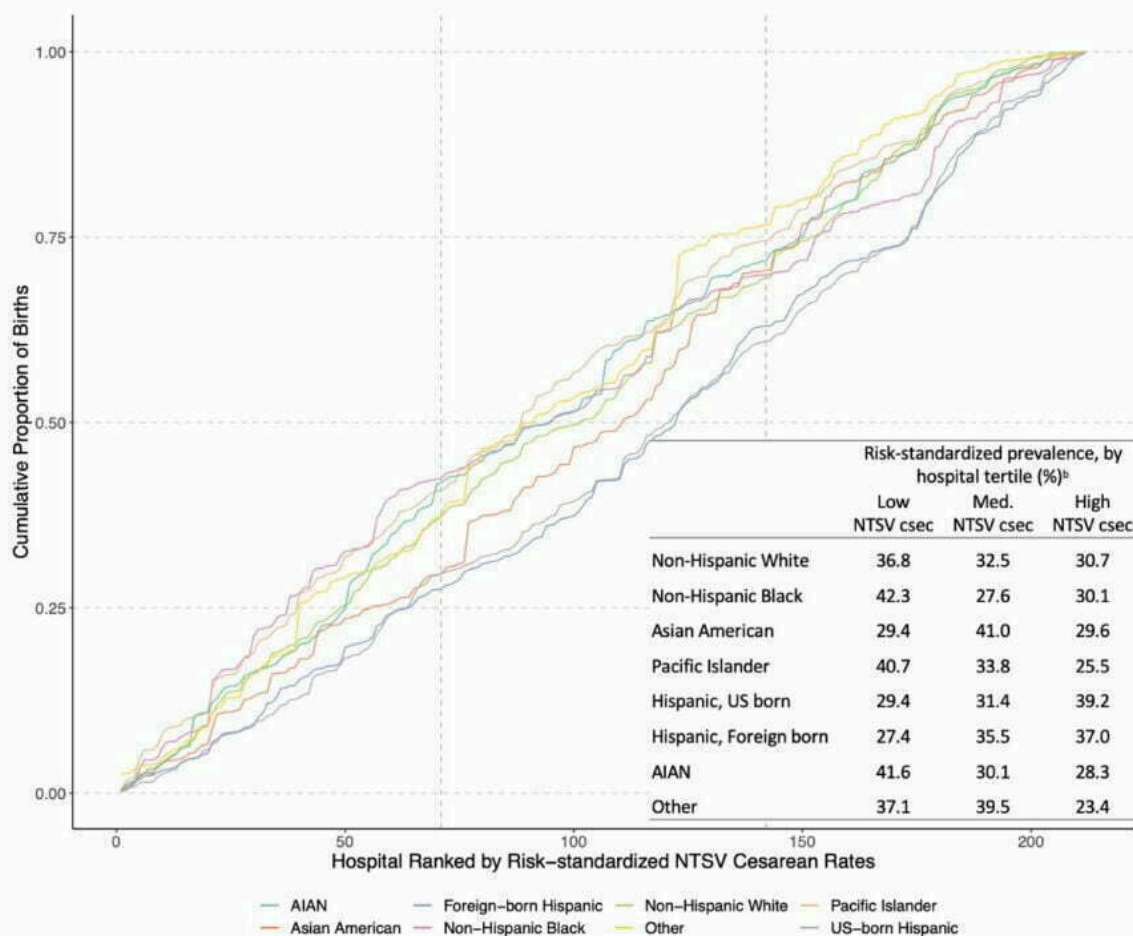
In 5,186 births (2.20%), mothers had OUD during pregnancy. Among these, 2,614 infants (1.11%) had NOWS, and 3,317 births (1.41%) had mothers who received MAT. Approximately 1.3% of OUD-exposed infants died relative to 0.6% of unexposed infants (**Figure 1**). Mortality was most common among OUD-exposed infants without a NOWS diagnosis, and roughly 40% of deaths in this group occurred within five days of birth. However, mortality was similar between unexposed infants and OUD-exposed infants with NOWS. Additionally, mortality did not notably differ among OUD-exposed infants by MAT status. Cox regressions that adjusted for maternal demographics indicated that maternal OUD was positively associated with the incidence of infant mortality (HR 2.07; 95% CI 1.60-2.68) relative to no OUD. OUD without NOWS was also associated with infant mortality (HR 2.69; 95% CI 1.98-3.67), as were OUD without MAT (HR 1.66; 95% CI 1.07-2.56) and OUD with MAT (HR 2.34; 95% CI 1.71-3.20). However, OUD with NOWS was not significantly associated with infant mortality. Findings suggest that OUD may increase the risk of infant mortality.



**Can birth hospital explain racial/ethnic differences in cesarean birth among low-risk births? An analysis of California data, 2007-2018** Shalmali Bane\* Shalmali Bane Suzan Carmichael Mahasin Mujahid Elliott Main Peiyi Kan

In the US, there is substantial variability in low-risk cesarean birth rate by hospitals and race/ethnicity. The contribution of inequitable hospital quality to disparities in low-risk cesarean births is uncertain. Using a dataset of live birth and fetal death certificates linked with maternal hospitalization data (2007-18), we examined the role of birth hospital on racial/ethnic disparities in low-risk cesarean (defined as nulliparous, term, singleton, vertex (NTSV)) births. Poisson regression models clustered by hospital were used to compare racial/ethnic differences in cesarean prevalence, adjusted for maternal and hospital characteristics. We calculated risk-standardized NTSV cesarean prevalence per hospital and used g-computation to assess how the cesarean prevalence by racial/ethnic group would change if all births occurred at the same distribution of hospitals as for White individuals. Among 1,594,277 NTSV births at 212 hospitals, 26.9% were cesarean. Adjusted RRs ranged from 1.01 for US-born Hispanic (95%CI: 0.99-1.05) to 1.28 for Black individuals (95%CI: 1.22-1.33), relative to White individuals. Higher proportions of Black (42.3%), Pacific Islander (40.7%), and AIAN (41.6%) individuals gave birth in hospitals in the lowest tertile of cesarean prevalence, higher proportions of Asian individuals gave birth in the middle tertile (41.0%), and highest proportions of Hispanic individuals (foreign-born: 37.0%, US-born: 39.2%) gave birth in the highest tertile. In the substitution analysis, NTSV cesarean prevalence would be reduced for certain groups but not others, ranging from 87 excess events (0.3% increase) among the Black population to 6,473 avoided events (5.6% decrease) among US-born Hispanic populations. Our findings suggest that rates of cesarean would be reduced in Black, Asian, and Hispanic populations if they gave birth at similar hospitals as white women. Future efforts should consider the role of within-hospital

**Figure.** Risk-standardized cumulative distribution of births by race and ethnicity among hospitals ranked by NTSV cesarean prevalence, California 2007-2018 (N = 212 hospitals)<sup>a</sup>



Abbreviations: AIAN American Indian or Alaska Native, NTSV, nulliparous, term, singleton, vertex.

<sup>a</sup> Risk standardized estimates are adjusted for the following: age, education, payer, pre-pregnancy BMI, pregestational diabetes, pregestational hypertension

<sup>b</sup> Assuming hospital cesarean section rate among NTSV births as a proxy for hospital quality, Lowest tertile (“Low” in figure) corresponds to highest quality hospitals, while the highest tertile (“High” in figure) corresponds to lowest quality hospitals

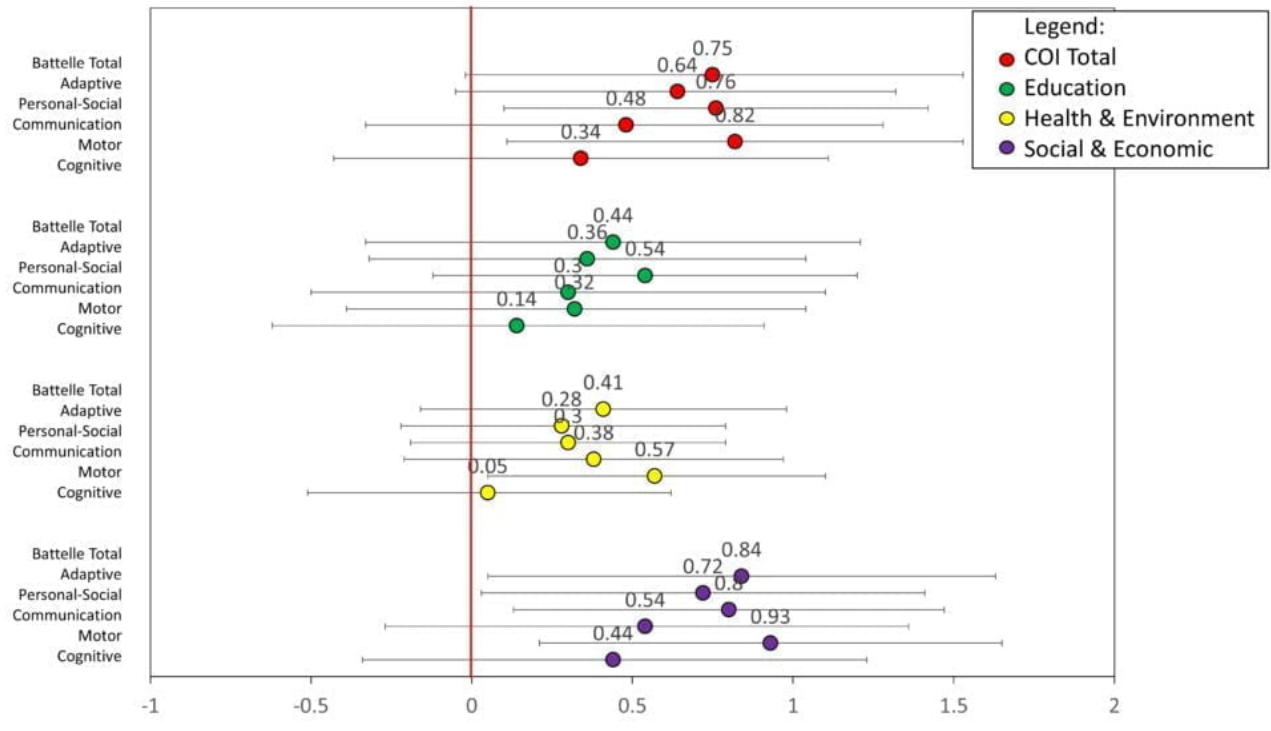
**Child Opportunity Index at birth and early development at age 4 years** Diane Putnick\* Diane Putnick Erin Bell Jordan Tyris Akhgar Ghassabian Pauline Mendola Rajeshwari Sundaram Edwina Yeung

The Child Opportunity Index (COI) is a place-based measure of 29 social determinants of health, selected and weighted relative to adult life expectancy, mental and physical health, and social mobility. The COI has demonstrated ability to predict child hospitalizations and cardiometabolic health but remains to be explored with respect to child development.

This study explored how COI at birth related to child development in 594 children from the Upstate KIDS cohort across New York state. Home addresses were extracted from birth certificates and linked to the COI 2.0 at the census tract level. The COI has three subdomains—education, health/environment, and social/economic—and was state-normed from 1-100. Children were administered the Battelle Developmental Inventory 2<sup>nd</sup> edition at 4 years by trained study personnel to assess overall, adaptive, personal-social, communication, motor, and cognitive development relative to age norms ( $M=100$ ,  $SD=15$ ).

On average, families lived in tracts with  $COI=65.80$  ( $SD=23.11$ ; range=1-100), and children scored nearly 1SD above the mean on the Battelle on average ( $M=113.50$ ,  $SD=18.47$ ; range=46-145). Unadjusted linear mixed models with identity link suggested that each 10-point increase on COI or subdomains at birth was associated with .45 to 1.79 higher scores on the Battelle (unstandardized beta (B) for total COI and total Battelle=1.67, 95% CI=0.93, 2.41). Adjusting for child and maternal factors attenuated associations (adjusted B for total COI and total Battelle=0.75, 95% CI= -0.02, 1.53), but associations for the social/economic subdomain remained (Figure 1).

The environment a child is born into may be related to their early development. This study supports the Child Opportunity Index as a measure of social determinants of some aspects of healthy child development, but this cohort was skewed toward higher COI and therefore results should be replicated in a more diverse sample.





**Associations of Neighborhood Opportunity and Vulnerability with Incident Asthma Among U.S. Children in the ECHO cohorts** Izzuddin M. Aris\* Izzuddin Aris Wei Perng Dana Dabelea Amy Padula Akram Alshawabkeh Carmen M Vélez-Vega Judy L. Aschner Carlos A. Camargo Jr. Tamara J. Sussman Anne L. Dunlop Amy J. Elliott Assiamira Ferrara Christine LM Joseph Anne Marie Singh Carrie V. Breton Tina Hartert Ferdinand Cacho Margaret R. Karagas Barry M. Lester Nichole R. Kelly Jody M. Ganiban Su H. Chu Thomas G. O'Connor Rebecca C. Fry Gwendolyn Norman Leonardo Trasande Bibiana Restrepo Diane R. Gold Peter James Emily Oken

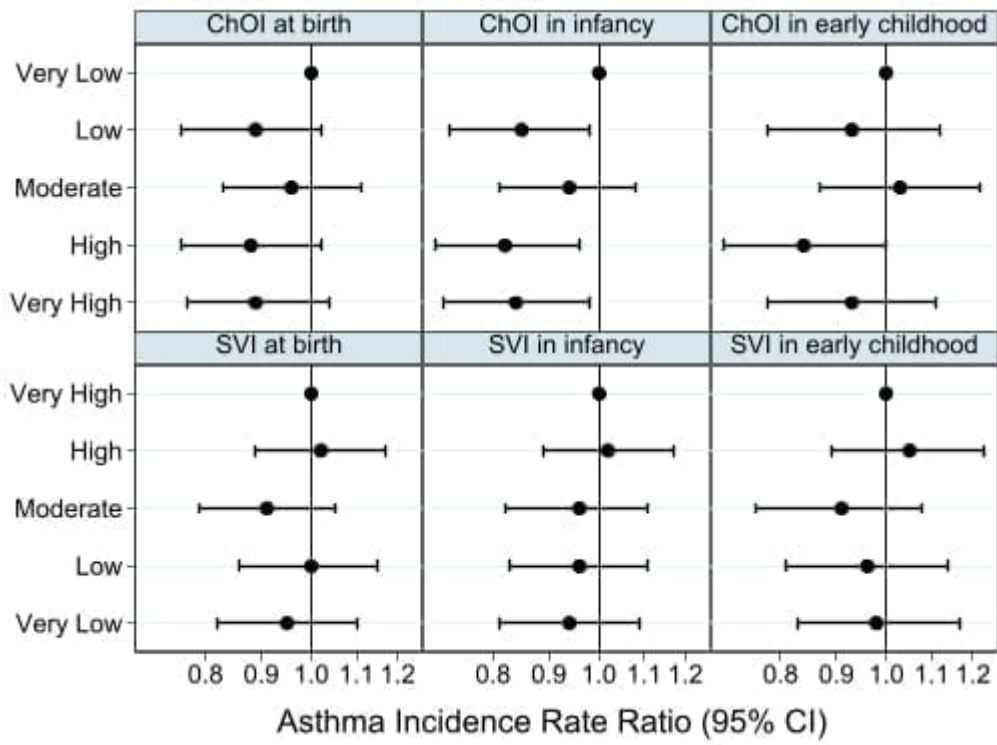
**Background:** Physical and social attributes of neighborhoods may promote or inhibit healthy child development. The extent to which these attributes play a role in the development of childhood asthma remains understudied.

**Objective:** To examine associations of neighborhood-level measures of opportunity and social vulnerability with asthma incidence rates in childhood.

**Methods:** We used residential address and parental report of physician-diagnosed asthma data obtained from 10,516 children participating in the nationwide Environmental influences on Child Health Outcomes (ECHO) program. We linked geocoded residential addresses at birth, infancy (median 1.4 years), and early childhood (median 4.7 years) to census-tract level Child Opportunity Index (ChOI) and Social Vulnerability Index (SVI). We followed children to the date of asthma diagnosis, date of last visit or loss to follow-up, or age 20 years. We used multilevel Poisson regression to estimate asthma incidence rate ratios (IRR) associated with ChOI or SVI, adjusting for family sociodemographic factors, parental asthma history, and prenatal characteristics.

**Results:** Overall, 23.4% of ECHO children lived in neighborhoods with very high ( $\geq 80^{\text{th}}$  percentile, based on nationwide distributions) ChOI or very low ( $< 20^{\text{th}}$  percentile) SVI. We identified 2,452 incident asthma cases in 105,073 child-years of follow-up; median age at asthma diagnosis was 6.6 years. Compared with very low ChOI, high ( $60^{\text{th}} - < 80^{\text{th}}$  percentile) and very high ChOI in infancy was associated with lower asthma incidence: adjusted IRR 0.82 (95% CI 0.71, 0.96) and 0.84 (95% CI 0.72, 0.98), respectively. Higher ChOI at birth and early childhood were also associated with lower asthma incidence but estimates were nonsignificant. However, SVI was not associated with asthma incidence.

**Conclusion:** Access to high levels of neighborhood opportunities in infancy, compared with very low neighborhood opportunities, are associated with lower asthma incidence in childhood.



**A mixed-methods study to define and measure community wellbeing: developing indicators for public policy and surveillance**

Adrian Foster\* Adrian Foster Camilla Michalski Apira  
Ragunathan Lief Pagalan Casey Chu Lori Diemert John F. Helliwell Diana Urajnik Ruth Speidel Tina  
Malti Dianne Fierheller Laura Fusca Ian Zenlea Scott McKean Laura C. Rosella

**Objectives:** Defining social indicators that go beyond individual-level conceptions of health and wellbeing is necessary to capture the relational nature of communities. This study characterizes community wellbeing (CWB) themes for the development of a well-defined exposure for etiological study.

**Methods:** Using sequential mixed-methods, cross-sectional surveys (N=398) followed by semi-structured focus groups (N=15) were conducted with community residents ( $\geq 18$  years) of four regionally distinct Ontario cities (Toronto, Peel, Greater Sudbury, and Thunder Bay). Survey items were derived from a theoretical framework that focused on access to and satisfaction with key themes of CWB (e.g., community services, social connection). Focus groups were performed with a sample of survey respondents that prioritized diversity (across age, race, and gender) and results were thematically analyzed using descriptive and interpretive methods to identify novel CWB themes.

**Results:** Survey respondents identified cost of living (63%), safety (56%), and housing (52%) as the three most significant aspects contributing to CWB. The plurality stated their sense of community belonging was somewhat strong (47%), with younger, racialized, and female participants being more likely to report weaker belonging. Four CWB themes were characterized in our focus groups, with each theme being composed of subcomponents: (1) community belonging, (2) services and amenities, (3) effective decision-making, and (4) opportunity. Three cross-cutting layers spanned each theme: (1) flourishing, (2) relationality, and (3) equity.

**Conclusion:** The development of a community-derived measure of CWB is necessary for social epidemiology research (i.e., surveillance) and community health. We characterized four CWB themes from pre-existing frameworks and perspectives derived from community residents. This work informs the development of an exposure measure to examine the impact of CWB on population health.

**Comparing Two-Step Approaches to Measuring Gender Identity: Ascertain Sex Assigned at Birth versus Transgender Self-Identification** Diana M. Tordoff\* Diana Tordoff Brian Minalga Nicole Lynn Perry Atlas Fernandez Bennie Gross Sara N. Glick The Seattle Trans and Non-binary Sexual Health (STARS) Advisory Board

**Background:** The two-step method for measuring gender identity is recommended by numerous research institutions and transgender advocacy organizations. Commonly, the two-step method separately asks about a person's current gender and the sex they were assigned at birth (SAAB). However, some researchers and transgender and gender diverse (TGD) people have expressed concern about asking SAAB questions, which can be harmful or perceived as invasive for some TGD people.

**Methods:** We used 2021 data collected from an online cross-sectional survey of LGBTQ+ people in Washington State and compared two different approaches for measuring gender identity via a two-step question that collected data on: (1) current gender and SAAB, and (2) current gender and transgender self-identification (via a question that asked "Are you transgender?"). The gender identity question used a select-all-that-apply format with 10 response options that explicitly included gender diverse identities (e.g., nonbinary, genderqueer). We assessed the reliability of these two approaches to identify TGD and cisgender participants based on the percent agreement and unweighted Cohen's Kappa.

**Results:** There were 2,275 participants aged 9-81 (mean 36.7 years). Response rates were high for the survey items of interest (98% to gender identity, 99.7% to SAAB, and 96% to transgender self-identification) with 192 unique combinations of responses to these three items. There was near perfect concordance between the two methods in their ability to identify TGD participants (percent agreement=99.7%, unweighted Cohen's Kappa=0.99). Overall, 63% of participants were cisgender, 35% TGD, and 2% could not be categorized.

**Conclusion:** Two-step approaches that use a SAAB versus transgender self-identification performed nearly identically in a survey of LGBTQ+ adults and adolescents. Researchers should consider acceptability of SAAB questions and its relevance to answering their specific research question when designing surveys.

**Radicalization and deradicalization into and out of white supremacy: a qualitative exploration of public health opportunities to address racism** Jessie Seiler\* Jessie Seiler Shilpa Patel Elizabeth Walker

### **Introduction**

In this age, public health work is shaped by a growing body of knowledge demonstrating that racism creates health inequities. Epidemiology is often focused on documenting the effects of racist systems and policies, but our understanding of white supremacy is limited. The fields of violence/injury prevention and social epidemiology may contribute to a deeper understanding of how and why people are radicalized into violent racism. Critical steps in building a public health approach to addressing racist violence begin with detailing risk factors for radicalization and barriers and facilitators of deradicalization, our goals for this study.

### **Methods**

After conducting semi-structured interviews with six self-identified former white supremacists, we used grounded theory to build theories of radicalization and deradicalization specific to white supremacy. Grounded theory, a qualitative method of forming theoretical models, involves iterative definition of themes rooted in responsiveness to data.

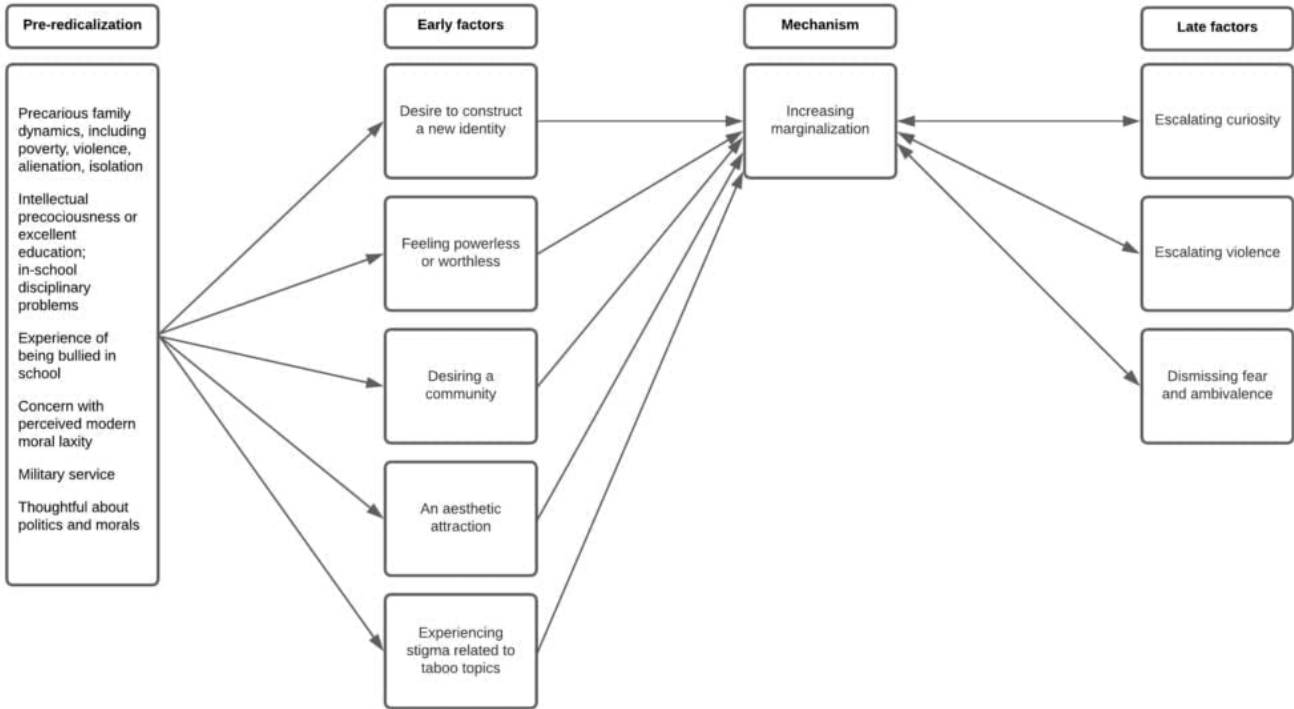
### **Results**

All participants experienced radicalization in childhood, with online behaviors being a key driver. Complete deradicalization appears to be a possible outcome even for those who have committed race-based violence. Key themes related to radicalization included the desire to construct a new identity, feeling powerless or worthless, new communities, an aesthetic attraction to symbols of white supremacy, and experiencing stigma related to wanting to discuss taboo topics (see figure). Themes related to deradicalization included support from new communities separate from white supremacist groups, newly powerful ambivalence about white supremacist beliefs, identity changes, demarginalization, reckoning with lingering racist beliefs, and healing.

### **Conclusion**

Race-based violence and racist beliefs on the individual level are changeable behaviors. Epidemiology can play a valuable role in identifying risk factors for radicalization and barriers and facilitators of deradicalization.

**Radicalization**



**Redlining and Health Research: Pitfalls and Possibilities** Elizabeth S McClure\* Elizabeth McClure

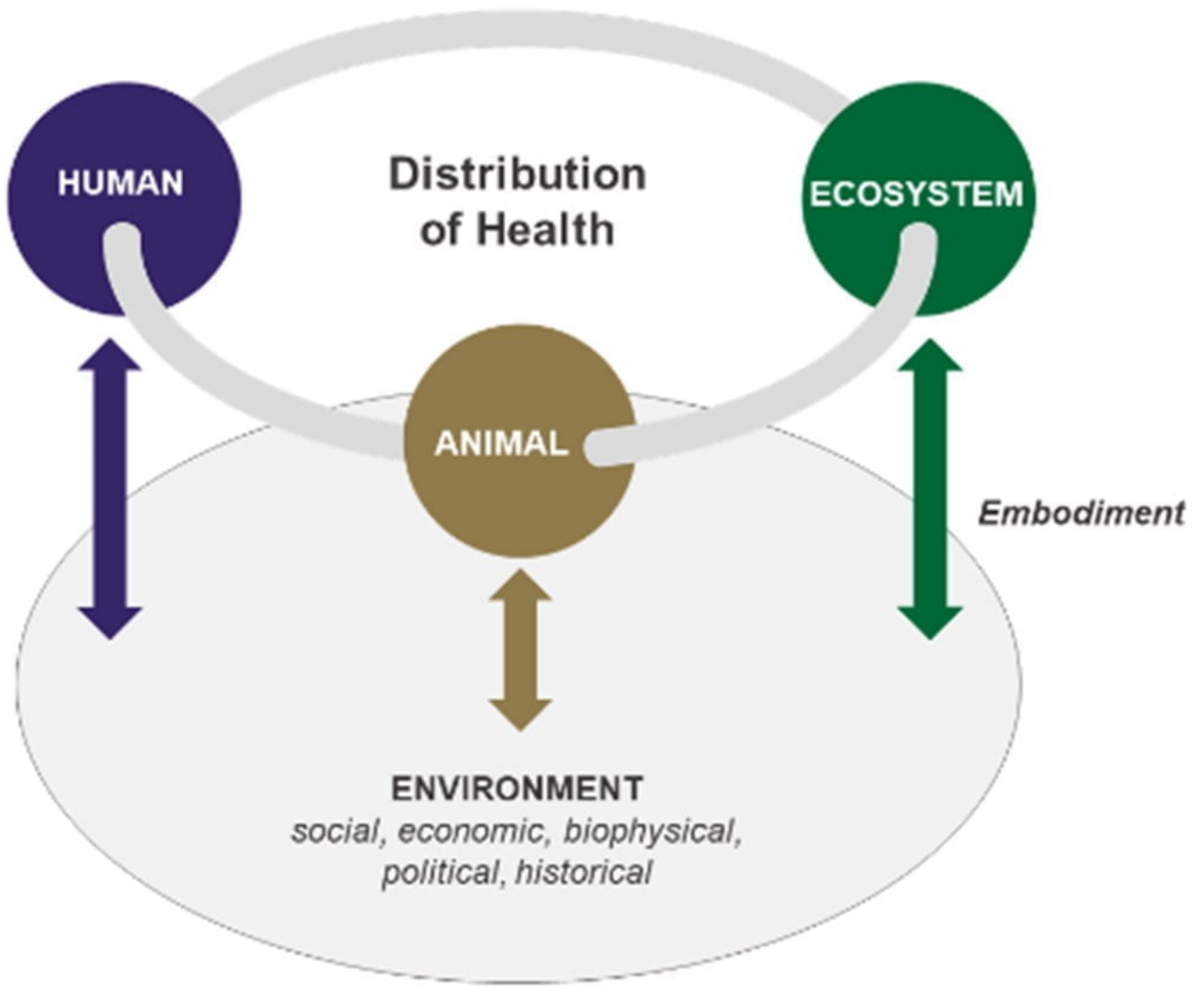
There is a rapidly growing body of epidemiology assessing impacts of redlining. It demonstrates a positive shift in public health dialogue toward understanding structural racism. However, more thoughtful and contextualized approaches are needed in this line of research. When it comes to quantifying the impacts of redlining specifically, there are several issues that are frequently oversimplified or ignored. First, racism in housing did not begin in the 1930s, nor was it created by the Home Owners Loan Corporation (HOLC), i.e. the institution that generated financial risk maps that are frequently digitized and used in health research. These lending practices were logical sequelae of the rules created by white settlers on stolen land. Second, while HOLC maps are centered in much of the contemporary research, the maps themselves are only a representation of one of many racist practices executed by institutions and supported by quotidian data. Third, epidemiology research on redlining often shoehorns a complex process into traditional regression models. When the null hypothesis is “no impact,” we imply that there is even a remote possibility that structural racism was not harmful, when we know that it was and still is. Fourth, treating redlining as the main analysis variable in research overshadows (and absolves responsibility for) the innumerable federal, state, local, and individual practices that recreate segregation and were executed between the 1930s and today. Ultimately, fetishizing redlining in health research only serves researchers benefiting from publications while inflicting the greatest disservice upon those most impacted by historical and contemporary structural racism. To make historical data like HOLC maps useful for antiracist research, we must ask different questions and design our analyses differently. Research should be more expansive, conducted in service to those most impacted by harmful practices, and centrally highlight ways to make change.

**Political One Health: a framework for more-than-human health** Julianne Meisner\* Julianne Meisner Amira Roess Peter Rabinowitz Mosbei Jeptoo Boku Bodha John Gachohi

One Health is a conceptual framework that views human, animal, and ecosystem health as interconnected. One Health is increasingly mainstreamed in international health policy in light of the COVID-19 pandemic, however outside of limited exceptions, epidemiologic research continues to ignore more-than-human dimensions of health: both their bearing on the health of humans, and the dignity of non-human beings who share our world. By the same token, the application of One Health has focused on veterinary and medical care and disease surveillance, neglecting larger contexts which govern the distribution of health.

We propose the Political One Health theoretical framework (Figure), an extension of the Political One Health model and the ecosocial theory of disease distribution, and apply it to case studies from pastoralist communities in Kenya and Ethiopia. Under this framework, the distribution of health is a collective over animals, ecosystems, and humans, with each component recognized as health bearers. These biotic and abiotic beings share a common environment which has economic, biophysical, political, historical, and social contexts, and influences health through the active, reciprocal process of embodiment. Under this framework, the social and material world created by humans, including inequity, shapes more-than-human health.





**LATEBREAKER**

## Substance Use

**Spatial Analysis of Drug Use-related Mortality in Iran** Mohammad Ebrahimi Kalan\* Fatemeh Baberi Mohammad Ebrahimi Kalan

**Background:** Drug use is a major public health issue worldwide. It causes undesirable consequences and leads to other drug-related disorders, including death. To explore the spatial distribution and the underlying factors associated with drug use-related mortality in 431 cities of Iran, we aim to analyze the spatial autocorrelation and conduct a geographically weighted regression (GWR).

**Methods:** In this ecological study, we investigated 20 variables under three categories (i.e., demographic, economic and social) with registered data in Legal Medicine Organization spanning from 2013 to 2017. The Global Moran Index (Moran's I) and the Local indicators of spatial association (LISA) were used to detect the spatial autocorrelation and analyze the local spatial correlation characteristics, respectively. A Poisson model and adaptive Gaussian kernel were modified to perform GWR. We employed the best bandwidth with the golden selection option of the GWR. In addition, the spatial characteristic was described in a thematic map.

**Results:** The overall death rate among studied cities was 196.2 per million. The highest rates were reported in the west, northwest, and southeast regions of Iran. The value of Moran's I was positive (Moran's I= 0.015, Z-score=2.44, p=0.014), indicating a spatial correlation at the country level with obvious spatial clustering. Hotspot clustering was observed mostly in the northwest. The GWR analysis demonstrated that drug use mortality was strongly positively or negatively correlated with economic variables (e.g., house renters, RR=1.36-1.66, 95% [CI]: 1.13-1.97, p<0.001, Gross Domestic Product, RR=0.58-0.94, 95% [CI]: 0.46-0.97, p<0.001), social variables (e.g., urbanization, RR= 1.45-2.06, 95% [CI]: 1.23-2.11, p<0.001) and, demographic variables (e.g., marriage ratio, RR= 1.34-2.03, 95% [CI]: 1.19-2.11, p<0.001), respectively.

**Conclusion:** Our findings showed a higher mortality rate was more pronounced in the economic and social variables. In order to avert an unnecessary loss of life in low-income countries such as Iran, it is imperative to reinforce country-specific policies that establish effective preventative measures.

**Keywords:** Drug use, Mortality Rate, Spatial Analysis, GWR

**LATEBREAKER**

## Substance Use

**Family and Peer-Related Mediators of the Relationship Between Parental Supply of Alcohol and Subsequent Alcohol-Related Harms Among Australian Adolescents** Tim Slade\* Tim Slade Philip Clare Wing See Yuen Alexandra Henderson Raimondo Bruno Louisa Degenhardt John Horwood Delyse Hutchinson Kypros Kypri Nyanda McBride Jim McCambridge Jake Najman Monika Wadolowski Richard Mattick Amy Peacock

**Purpose** Parental supply of alcohol is a relatively common practice in Australia, believed by some parents to be an effective means of teaching their children to drink responsibly. Contrary to this common belief, research suggests that parental provision of alcohol to adolescents is associated with elevated risk of subsequent alcohol use severity and problems. What remains unclear is what mechanisms connect parental supply of alcohol to later alcohol-related harms. In a critical step toward identifying prevention targets, this study used causal mediation analysis to test potentially causal mediators of the relationship between parental supply of alcohol and subsequent harms among adolescents.

**Methods** Data were drawn from waves 1-7 (ages 13 to 19) of the Australian Parental Supply of Alcohol Longitudinal Study (n=1906; 45% female). The mediating effects of family and peer factors on the association between parental supply of alcohol (i.e., giving alcohol to adolescents) and three alcohol outcomes: binge drinking, negative alcohol-related consequences, and alcohol use disorders were investigated. Family factors included parental monitoring, alcohol-specific rules, and alcohol norms and peer factors included peer supply of alcohol, peer substance use, and peer disapproval of substance use. To reduce risk of bias, analyses used targeted maximum likelihood estimation, which was estimated using machine learning.

**Results** Thirty-five percent of participants reported parents providing alcohol by age 15. Evidence was found for indirect effects of parental supply of alcohol through both family and peer factors on all outcomes. Sixty-nine percent and 63% of the effect of parental supply of alcohol on monthly binge drinking and negative alcohol-related consequences, respectively, were explained by natural indirect effects.

**Conclusions** The current investigation provided support for a causal link between parents providing alcohol to their adolescent children and subsequent alcohol-related harm by age 19. Evidence for mediation through both family factors and peer factors suggests further potential avenues for intervention to reduce the risk of harm to youth. For parents, these include boosting general parental monitoring, setting alcohol-specific rules, and addressing norms around the acceptability of alcohol use during adolescence.

**LATEBREAKER**

## Substance Use

**Alcohol Consumption and Flares of Low Back Pain: A Longitudinal Case-Crossover Study**

Adrienne D Tanus\* Adrienne Tanus Andrew Timmons Bianca Irimia Janna L Friedly Anna Korpak Clinton Daniels Carina A Staab Daniel Morelli Paul W Hodges Nathalia Costa Melissa A Day Patrick J Heagerty Mark P Jensen Pradeep Suri

**Objective:** To examine the associations between participant-reported alcohol consumption and flares of low back pain (LBP) in Veterans, assessing both 1) the number of alcohol-containing drinks in the past 24 hours, and 2) any alcohol consumption.

**Methods:** We performed a longitudinal case-crossover study of 305 Veterans (age 18-65 years) who were seen for LBP in primary care. Participants completed up to 36 scheduled surveys and additional patient-initiated surveys (triggered by the onset of new flares) over up to 1 year of follow-up. Each survey inquired about current flare status (a period of increased LBP). Each survey also inquired about alcohol consumption over the 24 hours and 2 hours prior to survey completion (if no flare was reported), or alcohol consumption over the 24 hours and 2 hours prior to flare onset (if a flare was reported). Conditional logistic regression was used to estimate the association between alcohol consumption and flares.

**Results:** After excluding 32 participants who did not have at least 1 flare and 1 non-flare period, 273 participants (mean age 47 years, 74% male) were included in the case-crossover analysis. There were 4,230 non-flare periods (914 [22%] preceded by alcohol consumption in the past 24 hours and 273 [6%] in the past 2 hours), and 1,950 flare periods (329 [17%] preceded by alcohol consumption in the past 24 hours and 89 [5%] in the past 2 hours). After adjustment for weekend/weekday, depression, sleep quality, and cigarette use, there were no significant associations between the number of drinks (OR 0.95 [95% CI 0.89, 1.02]) or any drinks (OR 0.86 [95% CI 0.69, 1.06]) in the past 24 hours and subsequent flares. Both greater number of drinks (OR 0.82 (95% CI 0.70, 0.95)) and any drinks in the past 2 hours (OR 0.49 (95% CI 0.35, 0.68)) were associated with lower odds of subsequent flare.

**Conclusion:** Alcohol consumption in the past 2 hours, but not the past 24 hours, was associated with lower odds of a subsequent LBP flare.

**LATEBREAKER**

## Substance Use

**Evolving rates of co-use of cannabis and tobacco among adolescents in the US, Chile, and Uruguay, from 2001-2021: a comparative approach of three national school-based surveys**

Nicolas Rodriguez\* Nicolas Rodriguez Constanza P. Silva Alvaro Castillo-Carniglia Ariadne Rivera-Aguirre Richard A. Miech

**Background:** Most people who use tobacco start during adolescence, and the probability of subsequent cannabis use increases during this developmental stage. Smoking is the most common mode of administration of both substances, increasing the likelihood of concurrent and future use of the other substances. These patterns, however, differ by cultural and contextual factors such as country of origin and regulation of tobacco and cannabis products. For example, cannabis use has increased in Chile and Uruguay adolescents and remained stable in the US, while tobacco use has declined in the three countries. **Methods:** We examined how cannabis and tobacco co-use in the past 30 days has evolved among adolescents from the US, Chile, and Uruguay, using methodologically comparable repeated nationally representative cross-sectional surveys in the school population from 2001 to 2021. We used the age-period-cohort-interaction (APC-I) model to estimate inter-cohort deviations from the age and period main effects and test intra-cohort variation.

**Results:** Results reveal similar patterns in the age effect in the US, Chile, and Uruguay, with a higher probability of co-use among older adolescents. After adjusting for age, adolescents in Chile and Uruguay exhibit a similar pattern of period effect, reaching its peak in the middle 2010s. By contrast, students in the US show a consistent period effect decrease. Findings reveal different inter-cohort and intra-cohort dynamics among countries. Inter-cohort effect peaks in 1994-1995 for the US and 1983-1986 for Chile. The inter-cohort effect is later for Uruguay (1996-2003), and the effect size and volatility of the cohort deviations are more accentuated than in other countries.

**Conclusions:** The results suggest different trends and effects on adolescent cannabis and tobacco co-use between the US, Chile, and Uruguay. Differences between countries may be associated with evolving cultural and regulatory factors.

**Assessing the harmonization potential of data sources on policy interventions to combat COVID-19** John Kubale\* John Kubale Megan Chenoweth James McNally

Since early 2020, numerous large-scale data-collection efforts have been undertaken to study the impact of the COVID-19 pandemic. Our objective was to examine the potential for harmonization across data sources that focused on policy interventions to combat COVID-19 given implications for potential comparability of study results. In total, we reviewed 7 distinct, publicly shared sources. While most of these sources (5 of 7) focused on state-level policies, some included data from other levels of government (e.g., counties and municipalities) and/or data from outside the U.S. These sources also varied widely in the types of policies they examined; most policies examined were related to face coverings, school or business closures, and “lockdowns.” Substantial heterogeneity was observed across specific policies captured as well as their measurement and/or operationalization. Areas where this heterogeneity presented the most challenges for harmonization included: the inclusion/exclusion of dates for policy initiation and descension, treatment of policy mandates vs. guidance in the data source, the intended target population (e.g., the unvaccinated, business types, etc.), and the presence/absence of policies restricting specific public health interventions (e.g., bans on mask mandates). While data collected throughout the pandemic has yielded invaluable insights regarding the impact of policy interventions on COVID-19 control, substantial heterogeneity in these data poses challenges for harmonization and subsequent comparison across studies. Through this review we identified areas for improvement and propose tangible best practices, such as developing common data elements (CDEs) which build consensus regarding measuring key concepts, to foster harmonization of measures in future data collection efforts. It is essential to proactively develop and incentivize such standards so that they may be ready for the next emergency.

**Calculating and validating 118th Congress metrics for the Congressional District Health Dashboard using a geospatial aggregation method** Taylor M. Lampe\* Taylor Lampe Isabel S. Nelson Alexander S. Chen Anne Yuruo Marc N. Gourevitch Lorna E. Thorpe Ben R. Spoer

Congressional districts (CDs) are policy-relevant geographies for which actionable health data are often unavailable. Federal policymakers and advocacy organizations need timely CD data to advance national policy impacting the health of their constituencies. The CD Health Dashboard ('The Dashboard') was launched in January 2023 to meet this need, utilizing a geospatial aggregation method to derive 36 metrics of health and its drivers for CDs, and harmonizing data from numerous sources otherwise unavailable for the most recent 118<sup>th</sup> congress. This abstract describes our methodologic validation results.

The Dashboard team created Census block-level population weights to measure extent of overlap between county or tract ("source geography") populations and corresponding CDs. Weights were applied to source geography estimates and summed to CD-level. To validate, we produced metric estimates for 116<sup>th</sup> Congress CDs and compared those to 116<sup>th</sup> CD estimates from ACS for three metrics: high school completion, broadband connection, and unemployment. Sensitivity analyses assessed accuracy of using different source geographies, aggregating counts vs percentages, and having varying amounts of source-level missingness.

In validation, we found derived CD estimates were comparable to estimates released by ACS when comparing means (high school completion: mean=87.45% vs. 87.84%; broadband connection: mean= 67.32 vs. 67.74; unemployment: mean=5.58% vs. 5.41%), and applying various measures of error (RMSE, MAE). Estimates were additionally robust using different source geographies and aggregating counts vs. percentages, although starting with tract estimates produced more stable estimates. Source geography missingness impacted estimate accuracy differently across metrics.

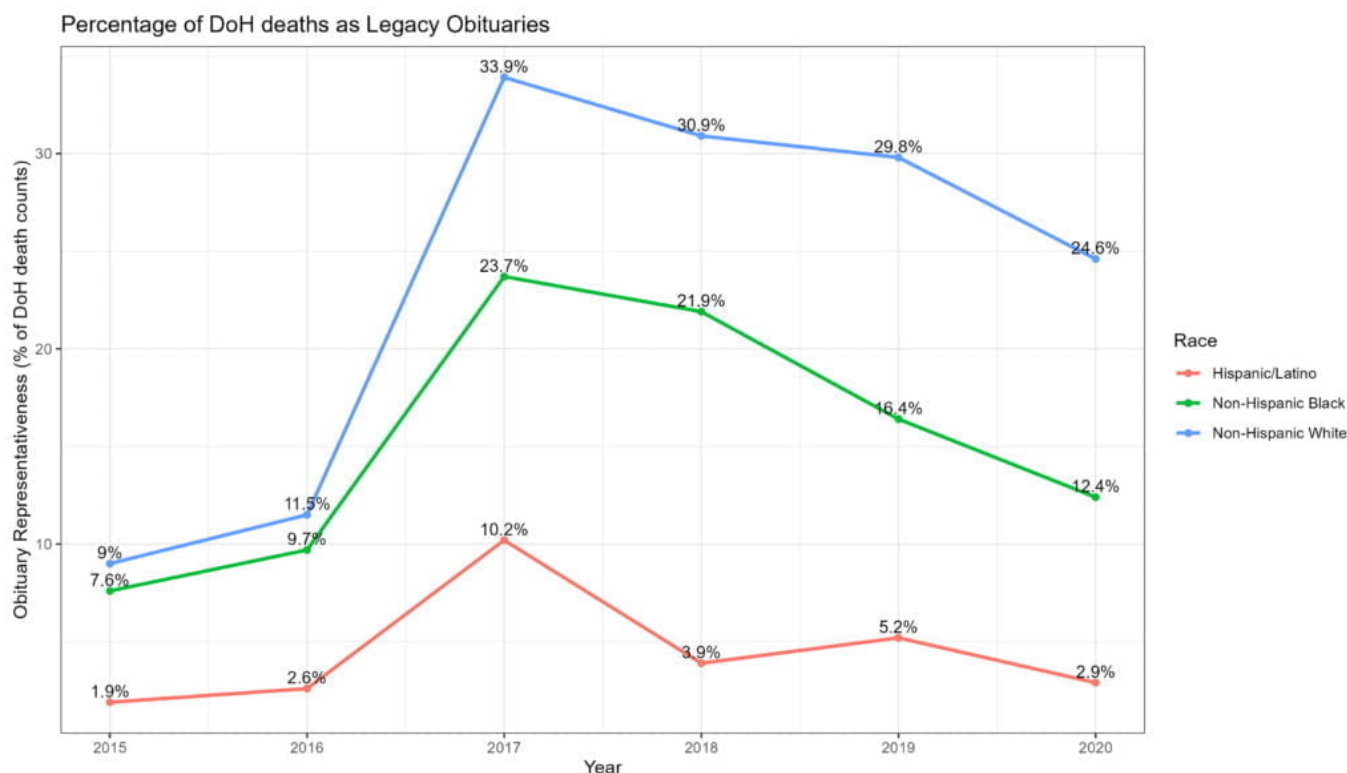
The Dashboard presents timely data for the 118<sup>th</sup> Congress. Our validation demonstrates the utilized aggregation method's accuracy and robustness to different calculation decisions across metrics.

## Big Data/Machine Learning/AI

### Evaluating the use of online obituaries for public health surveillance Jaren R. Haber\* Jaren Haber Maria L. Alva Lisa Singh Srujana S. Illa Angela Jing Rohan Mathur

This study evaluates the feasibility and accuracy of using openly available online obituary data and official death records to monitor COVID-19. We aim to understand the reliability and measurement properties of online obituaries by analyzing their representativeness across age, gender, race, and neighborhood as compared to death certificate records for DC residents who died in DC. We collect death certificates from DC Health Vital Records Division and obituaries from Legacy.com, a large obituary aggregation website, from January 2015 to December 2021. We use Python to scrape Legacy.com for obituaries in Washington, DC; extract text and photo data; and process these texts to derive the decedent's birth day, death day, gender, and race.<sup>[1]</sup> To evaluate representativeness by demographics, we compare the DC obituaries to death certificates through matching by name, date of birth, and date of death (see Figure for matching results by race). Our scraped data matches no more than a third of official death records, with White individuals being best matched and overrepresented relative to other racial groups. Our estimates scale the representativeness of online obituaries across demographic strata and neighborhoods, providing important inputs for mortality-predicting models that can correct for these biases with standard analytical tools (e.g., post-stratification weighting). Our results suggest that automated text and image mining of online obituaries could allow quick, granular predictions of mortality distributions in a cost-effective way, informing more effective policy responses by bypassing the standard two-year lag before death records are released. Our work can also provide foundation for disease monitoring should future pandemics arise, because online death records are easier and cheaper to access than administrative data.

[1] Our obituary scraping workflow is documented and openly accessible online at [https://github.com/comp-strat/scrape\\_obituaries](https://github.com/comp-strat/scrape_obituaries).



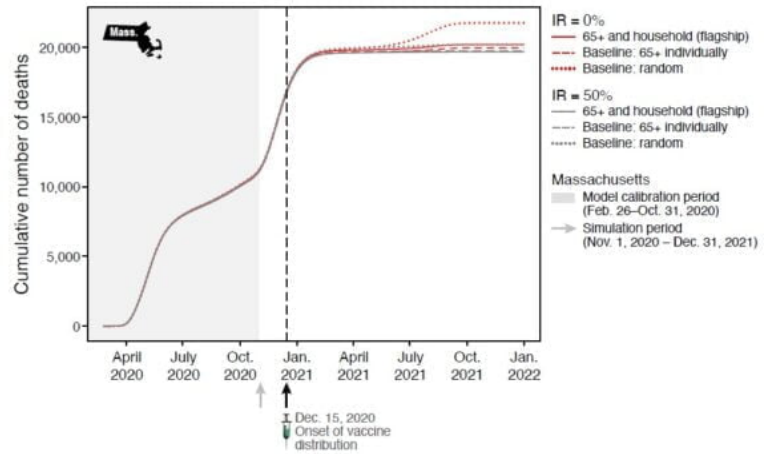
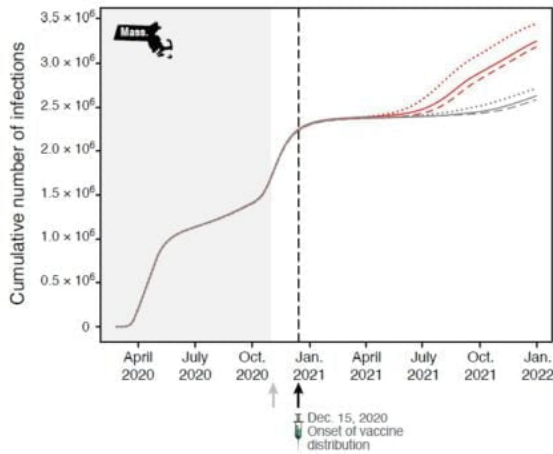
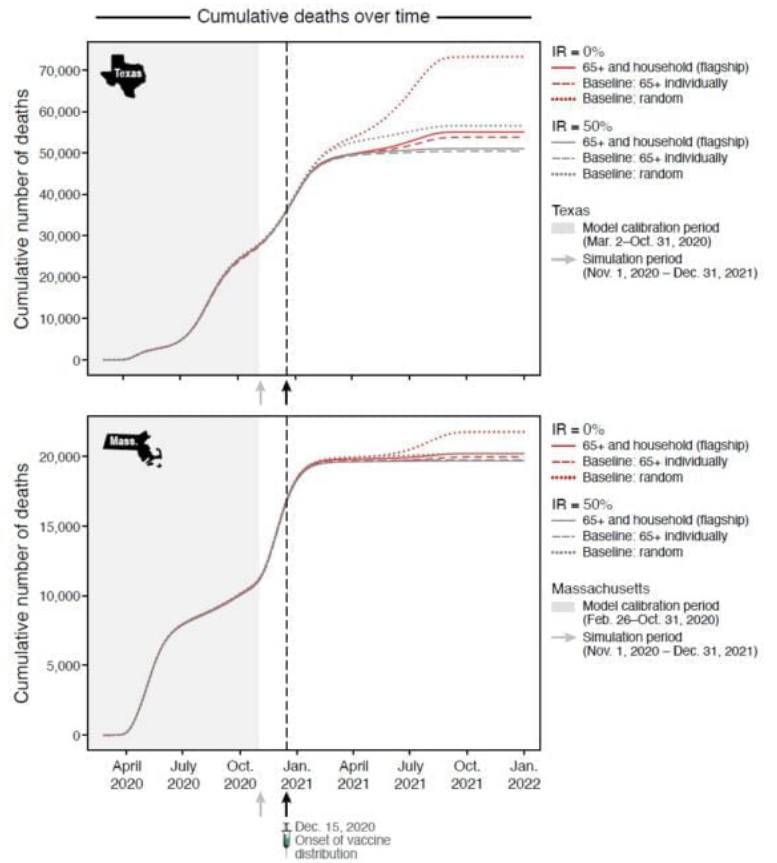
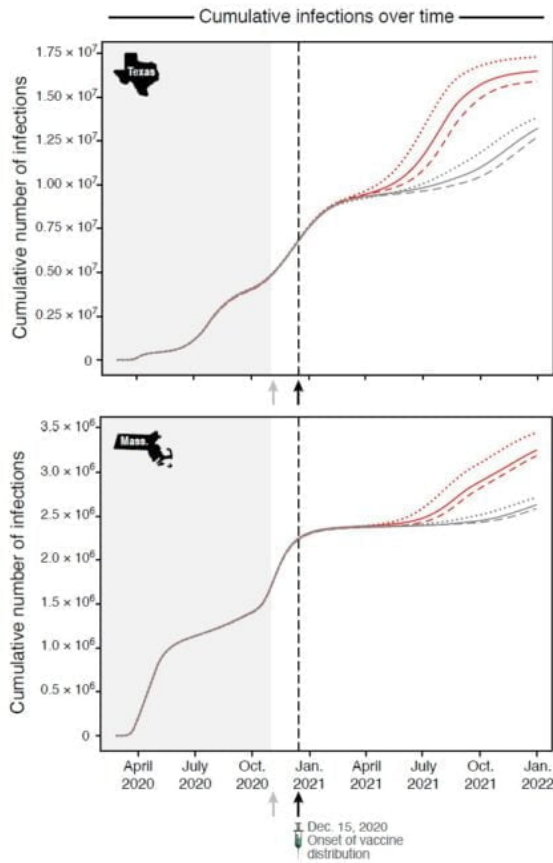


**State-level decoupling between COVID-19 morbidity-mortality and general public interest is associated with political leaning** Anika Puri\* Marie-Laure Charpignon Anika Puri Maimuna Shahnaz Majumder

During epidemics, the success of interventions are contingent upon public interest and adherence to recommended measures. Fluctuations in public interest and adherence are driven in part to the timing of announcements made by public health leaders, but also by “crisis fatigue” as an epidemic persists. As crisis fatigue increases, decoupling between public interest in the crisis and objective measures of the crisis (e.g., morbidity-mortality) also increases (e.g., interest may remain limited even as morbidity increases). In this study, we examined state-level crisis fatigue in the United States from February 1, 2020 to May 31, 2022 by quantifying the extent of decoupling between COVID-19-related morbidity-mortality (i.e., case and death counts from the CDC) and public interest in COVID-19 as ascertained via Google Search Trends (GST). Overall, we found that states with a larger share of Republican voters demonstrated a significantly increased decoupling between the intensity of public interest in COVID-19 and morbidity-mortality (cases: -0.72,  $p=1.26e-09$ ; deaths: -0.33,  $p=1.79e-02$ ). To account for confounders of this observed relationship, we are currently developing a multivariable regression model that further adjusts for local levels of social vulnerability, internet penetration, and vaccine uptake. Beyond our contributions to the literature regarding crisis fatigue during the COVID-19 pandemic, our findings have important implications for the design and calibration of epidemic models that leverage GST. The presence of decoupling between public interest and COVID-19 morbidity-mortality suggests that the information value of GST may vary over time and space, and thus, caution is warranted when leveraging this data source for epidemic models of COVID-19.

**Vaccine Distribution through Augmented Companion Programs May Improve Infectious Disease Outcomes** Marie-Laure Charpignon\* Marie-Laure Charpignon Shagun Gupta April Chen Bryan Wilder Andrew Perrault Maimuna Shahnaz Majumder

The COVID-19 pandemic demonstrated that mRNA-based therapeutics targeting specific variants have the potential to fight emerging strains during future epidemics; however, there still remain challenges with uptake, availability, and cost. To combat these issues, the state of Massachusetts implemented an augmented companion vaccination program during the COVID-19 pandemic, whereby people aged 75 or over and their household members were vaccinated first. Building upon this successful precedent, we quantify the impact of companion-like vaccine allocation mechanisms prioritizing seniors sharing a home with younger generations on projected infections and deaths. Specifically, we implement an agent-based model (ABM) incorporating household structure, using a synthetic population defined by state-specific micro-census data and temporal social distancing scores derived from GPS data and provided by Unacast. This procedure yields posterior distributions for four epidemiological parameters (e.g., the probability of infection given contact and age-specific mortality and infectiousness multipliers), as well as three mobility-related adjustment factors. In simulations based on Massachusetts and Texas, two states with distinct population structures and epidemic trajectories, the proposed vaccination program outperformed randomization and age-based prioritization, reducing infections by up to 4% and deaths by up to 7%. We are currently adapting our population sampling procedure to demographic structures in India and Bangladesh to assess the generalizability of our approach, particularly in low- and middle-income countries where multigenerational living arrangements are common. This intervention strategy could be invaluable in scenarios where household contacts pose the greatest risk of transmission (e.g., viral respiratory infections) or where social ties can influence individual decision-making (e.g., Paxlovid hesitancy).



**Persistent low job control and subsequent major depression over time: A prospective cohort study using the Australian Longitudinal Study on Male Health** Yamna Taouk\* Yamna Taouk Tania King Zoe Aitken Anthony LaMontagne

Workers' perception of control over work is a key construct in the relationship between the psychosocial work environment and health. While exposure to low job control has been prospectively linked to poor mental health including depression and anxiety, there is scant extant research examining whether persistent exposure to low job control over time has an even greater negative impact on mental health. Data from 4,762 men aged 18-55 years in the Australian Longitudinal Study on Male Health was used to explore the association between persistent low job control over time and subsequent major mental health problems. Persistent low job control measure was based on consecutive low job control exposure indication over two waves of data (waves 1 & 2). A dichotomous measure of major depression was derived from the Patient Health Questionnaire-9 in wave 3. The association between persistent low job control and subsequent major depression was assessed using logistic regression models. Controlling for sociodemographic, health and major depression at baseline, persistent exposure to low job control was significantly associated with subsequent major depression (OR 1.78, 95% CI 1.27, 2.48). The inclusion of a term representing the interaction between persistent low job control and baseline major depression did not improve overall model fit ( $p = 0.65$ ), suggesting the effect of persistent low job control on major depression was not differential for people with and without baseline depression. Additional analysis examining men exposed to persistent low job control versus those persistent high job control and subsequent major depression did not change results (OR 1.70, 95% CI 1.17, 2.49). This study addresses reverse causation and confounding strengthening the evidence regarding the causal relationship between psychosocial working conditions and mental health, underlining the important role that repeated exposure to low job control contributes to the development of major depression.

**Associations between pandemic-related policies and disordered eating risk across five countries** Amanda Raffoul\* Amanda Raffoul Ariel L. Beccia Sharon I. Kirkpatrick David Hammond S. Bryn Austin

Disordered eating affects adults globally and worsens mental and physical health. Increased prevalence of disordered eating during the COVID-19 pandemic may be partially attributable to stay-at-home orders that disproportionately impacted at-risk individuals, including women and those in low-income households. We explored relationships between stringency of pandemic policies and disordered eating across 5 countries. Data were drawn from a cross-sectional online survey of adults (Nov/Dec 2020) in Australia, Canada, Mexico, UK, and US (n=21753). Disordered eating indicators included binge eating, self-induced vomiting, and thinness preoccupation. The exposure-“stringency”, a composite measure of governments’ “lockdown style” policies from Jan 31-Oct 31, 2020-was operationalized as 1) average stringency and 2) cumulative stringency, the number of days stringency was >70 out of 100. Both scores were standardized, with higher values indicating stricter lockdowns. We fit 3-level logistic models, with individuals nested within regions nested within countries, for each indicator across all countries and within countries with regional-level data (Australia, Canada, US), adjusting for gender, age, race/ethnicity, income, and education. The current prevalence of disordered eating varied across countries, ranging from 18-44% for binge eating, 5-14% for self-induced vomiting, and 18-24% for thinness preoccupation. Across countries, average and cumulative stringency were associated with significantly elevated odds of binge eating (OR=1.29, CI 1.07-1.56; OR=1.31, CI 1.12-1.54) and cumulative stringency was associated with lower odds of vomiting (OR=0.58, CI 0.48-0.71). Within countries, there were no significant associations between regional stringency and disordered eating. The findings suggest differences in disordered eating between countries; however, the extent to which these differences were associated with pandemic-related policies remains unclear and warrants future study.

**Can data-driven methods identify unique patterns of mental health service use using healthcare administrative data in Ontario, Canada?** Christa Orchard\* Christa Orchard  
Elizabeth Lin Laura Rosella Paul Kurdyak Jessica Gronsbell Peter Smith

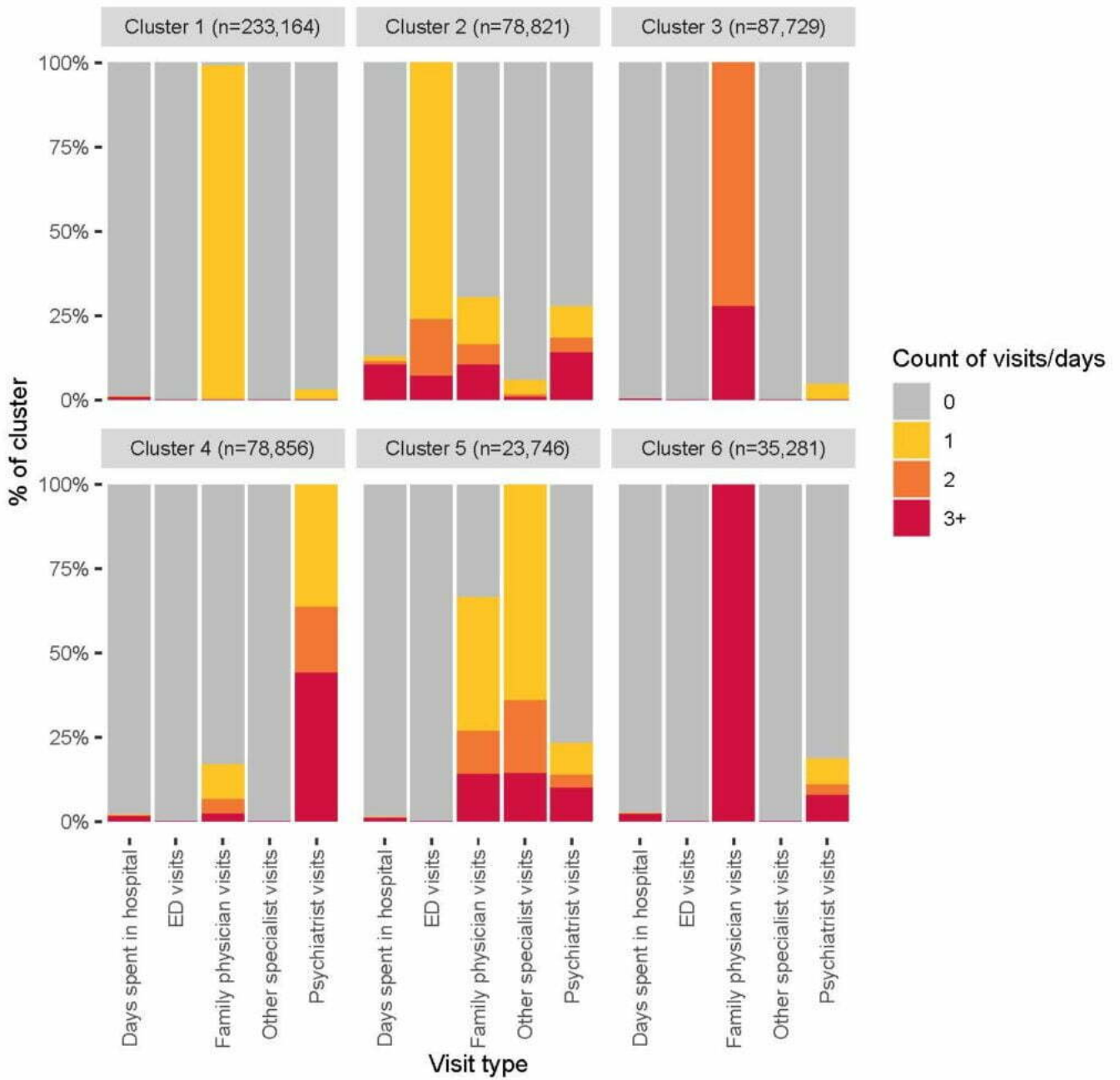
**Background:** The universal publicly funded Ontario Health Insurance Plan covers the cost of mental health services including inpatient hospital services, emergency care, and care provided by physicians, including psychiatrists. While much of our current understanding of how the mental health system is functioning relies on system-level indicators (e.g. hospital re-admission rates), advancements in data science and computer processing power provide opportunities to parse through large amounts of complex healthcare administrative data to find meaningful patterns of service use at the population level. The goal of this research is to use a data-driven approach to identify and characterise distinct 12-month patterns of mental health service use.

**Methods:** Mental health and addictions related episodes of care were identified in the administrative data holdings using existing algorithms. Among adults who accessed mental health services in Ontario in 2012, days spent as an inpatient, and count of family physician visits, psychiatrist visits, other specialist visits and emergency care visits were computed for the 12-month period after their index visit. Three unsupervised machine learning algorithms were used to identify clusters in this data; the solution that produced the highest internal cluster validity, robustness and clinical utility was selected.

**Results:** The dataset included 538,597 eligible individuals who accessed mental health or addictions related care in 2012, and a total of 1,569,247 mental healthcare episodes. The Clustering Large Applications algorithm with Bray-Curtis distance produced the solution with the best internal validity and utility, identifying 6 mental health service use patterns with distinct combinations of types of care and intensity of use (see figure).

**Conclusions:** This research demonstrated how using a multivariate data-driven clustering method can build upon our current understanding of how patients access mental healthcare in Ontario.

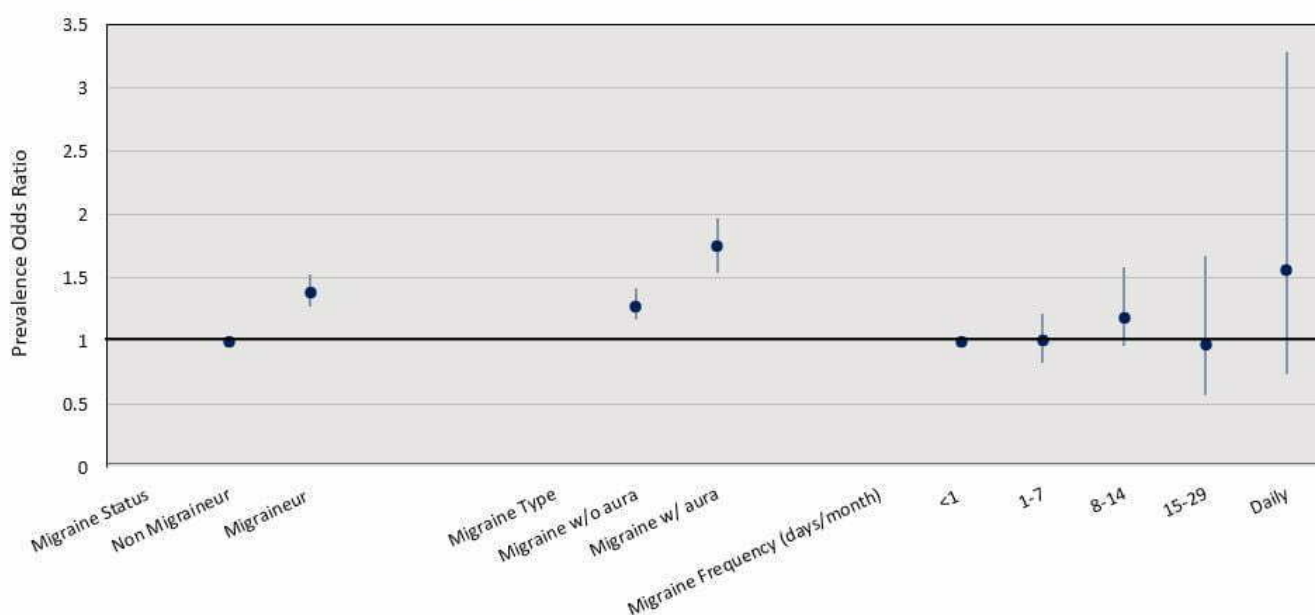
### Count of visits/days by cluster and visit type



**A cross-sectional analysis of migraine and post-traumatic stress disorder in Nurses' Health Study II** Holly Crowe\* Holly Crowe Laura Sampson Janet Rich-Edwards Kathryn Rexode Karestan Koenen

Nearly one in five women experience migraine, the highest cause of disability worldwide. Both post-traumatic stress disorder (PTSD) and migraine are two to three times more prevalent in women than men, and individuals with comorbid PTSD often experience greater migraine frequency and disability. Hormonal factors, inflammation due to stress, and nervous system hyperexcitability may partially explain this co-occurrence, but the exact mechanism is unknown. We examined the association between physician-diagnosed (ever) or recent (past two years) migraine status and lifetime PTSD using an analysis of women who responded to prior migraine questions and participated in a trauma substudy within the Nurses' Health Study II cohort (n=33,327). Participants reporting a physician-diagnosis of migraine on questionnaires in 1989, 1993, or 1995, or any migraine attacks in the past two years on questionnaires in 2009 or 2013 were considered migraineurs. We assessed lifetime PTSD on a separate 2018 questionnaire using a modified PTSD Checklist for the Diagnostic and Statistical Manual, Version 5. We used logistic regression to compute prevalence odds ratios (PORs) and 95% CIs, adjusting for demographic, lifestyle, and medical factors associated with migraine and PTSD. The overall prevalence of lifetime PTSD in this cohort was 8.6% and migraine prevalence was 36%. Migraineurs were 39% more likely to have lifetime PTSD than non-migraineurs (POR= 1.39, 95% CI: 1.27-1.53). The prevalence of PTSD was further elevated among individuals with migraine with aura (POR=1.75 95% CI: 1.54-1.97) and individuals who reported daily migraines (POR= 1.56, 95% CI: 0.74-3.28), compared to people without migraines. Our results indicate an association between migraine and PTSD that is more evident among individuals with migraine with aura.

**Migraine and PTSD in NHS II**





**Factors Associated with Utilization of In-school and Outside Therapy Services** Gisselle Soto Rivas\* Gisselle Soto Rivas

Mental health problems have increased substantially in recent years among adolescents. Supportive services, such as in-school counseling and out of school therapy, are critical to improving youth mental health, but are often underutilized. However, it is unknown whether certain populations are more likely to access mental health services.

Data were from 2,933 adolescents (aged 13-15 years) enrolled in a California cohort. At baseline (Fall 2021), participants reported sociodemographic factors, frequency of substance use, and mental health symptoms (depression, anxiety, OCD, social phobia, separation anxiety, and panic disorder). Data on use of in-school and outside therapy services were collected at follow-up (Spring 2022). Adjusted logistic regression models evaluated associations of demographics, substance use, and mental health with use of supportive services.

At follow-up, 16.0% of students reported in-school counseling, and 7.7% reported out of school therapy. Students with any mental health condition, or who reported current use of alcohol or e-cigarettes (but not cannabis) had greater odds of reporting seeing a therapist in or out of school (ORs:1.17-1.94,  $p < 0.05$ ). Asian youth had the lowest prevalence of out of school therapy attendance. Female, and sexual and gender minority youth generally had higher odds of therapy utilization. Students whose parents had a high school education or less (vs. those with an advanced degree) had lower odds of seeing a therapist outside of school; lower odds of seeing a therapist in school were observed for those who report speaking a language other than English at home.

While some students who need mental health services are receiving them, there are disparities based on parental education and language spoken at home. Findings indicate a need for interventions to increase access to mental health services inside and outside of school, particularly for youth from lower-income and non-English speaking households.

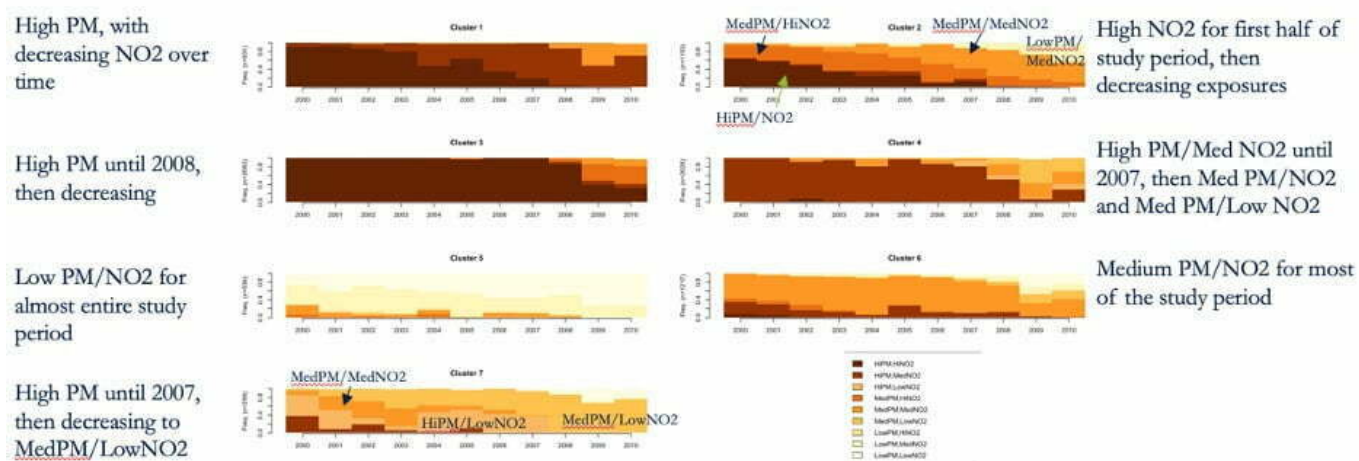
**Does type and timing of ambient air pollutant (PM<sub>2.5</sub>, NO<sub>2</sub>) exposure influence cognitive function and decline? A novel co-pollutant examination using sequence analysis** Kristina Dang\* Kristina Van Dang Maria Glymour Jennifer Weuve Mary Haan Kevin Lane Michael Brauer Isabel Allen Anusha Vable

Historic patterns of longitudinal changes in air pollution exposure may be relevant to cognitive risk in older adulthood. We characterized 10-year trajectories of PM<sub>2.5</sub> and NO<sub>2</sub> exposure using sequence analysis and evaluated their association with cognition in a US-representative sample.

The National Health and Aging Trends Study (NHATS) is a representative sample of 8,245 Medicare beneficiaries ages 65 or older at baseline in 2011, with annual cognitive assessments. We obtained annual PM<sub>2.5</sub> and NO<sub>2</sub> (trichotomized at 2010 25<sup>th</sup> and 75<sup>th</sup> percentiles [PM<sub>2.5</sub>: 7.9 g/m<sup>3</sup>, 10.8g/m<sup>3</sup>; NO<sub>2</sub>: 4.8 ppb,10.8 ppb]) from 2000-2010 at each participant's residential census tract. We characterized PM<sub>2.5</sub> and NO<sub>2</sub> air pollution trajectory similarity using sequence analysis and hierarchical clustering to group similar air pollution trajectories. Each participant's episodic memory score each year was the mean of their immediate and delayed word recall scores, standardized to NHATS 2011 scores. We used linear mixed models to estimate the association of air pollution trajectory with memory, adjusted for age, gender, education, race/ethnicity, smoking status, neighborhood SES, and census division.

We clustered the 1,208 unique 10-year air pollution trajectories into 7 exposure groups based on similarity. In general, participants occupying the higher exposure clusters had lower memory scores (e.g. high NO<sub>2</sub> and PM<sub>2.5</sub> until 2008, followed by medium level exposure by 2010 = -0.19; 95%CI: -0.29, -0.09).

Through this novel application of sequence analysis, we identified 7 distinct air pollution trajectories. A participants' historic pattern of air pollution exposure differentially predicted memory level such that, despite more recent lower exposures, higher exposures in the more distant past were associated with the greatest memory deficit. Our findings provide further support that use of more expansive air pollution exposure histories may offer more comprehensive discovery of air pollution's adverse cognitive effects in older adulthood.



## Environment/Climate Change

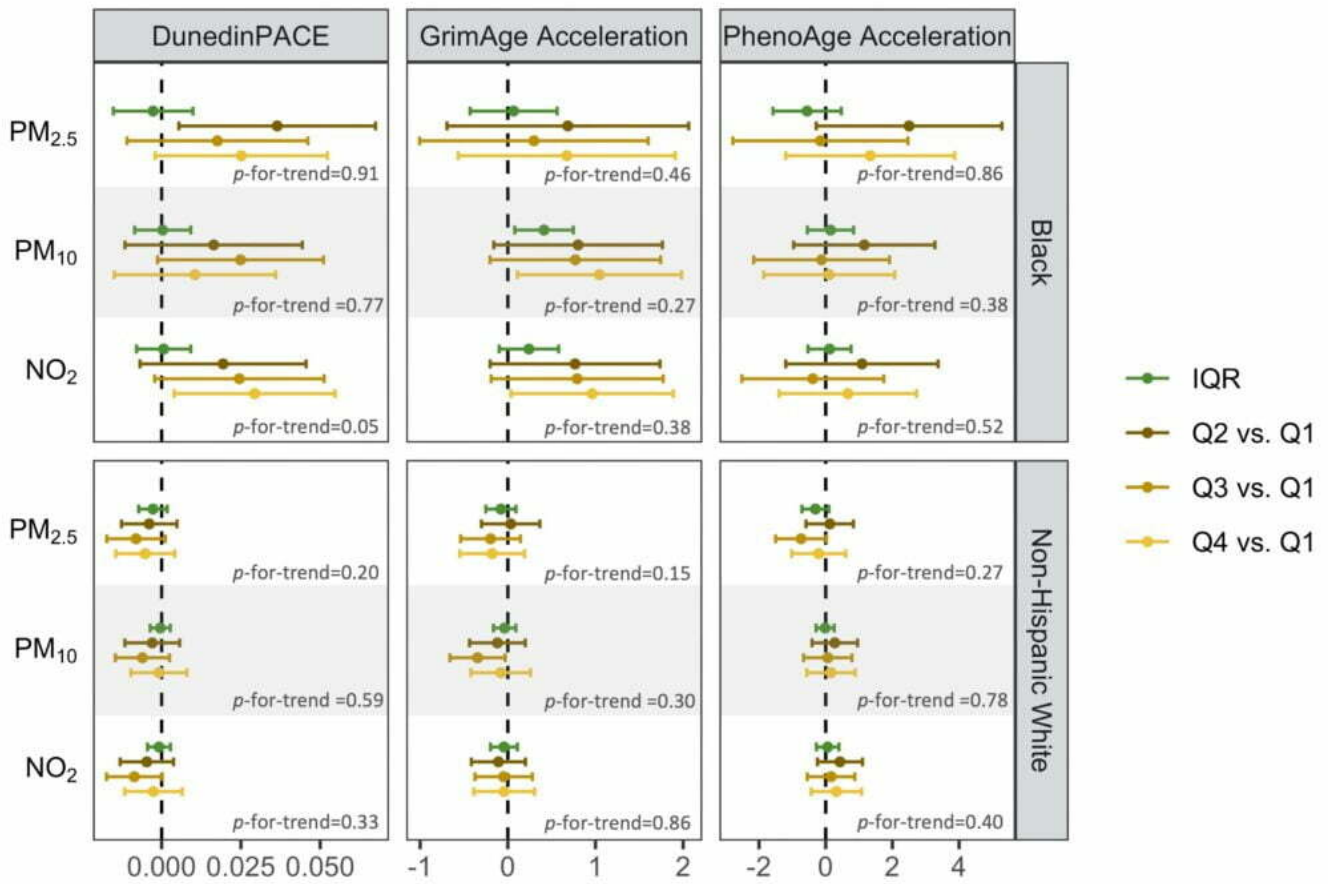
**Outdoor residential air pollution and DNA methylation-based metrics of biological age among Black and White women in the US** Sarah H. Koenigsberg\* Sarah Koenigsberg Che-Jung Chang Jennifer Ish Jacob K. Kresovich Zongli Xu Kaitlyn G. Lawrence Joel D. Kaufman Dale P. Sandler Jack A. Taylor Alexandra J. White

**Background.** DNA methylation (DNAm)-based metrics of biological age may reflect early biological changes linking air pollution to aging-related outcomes. However, there are few studies of air pollution and epigenetic age acceleration in diverse populations.

**Methods.** In a sample of self-classified Black (n=633) and non-Hispanic White (NHW; n=3,495) women from the Sister Study residing in the contiguous US, we estimated annual average outdoor residential exposure to nitrogen dioxide (NO<sub>2</sub>, 2006), particulate matter <10 μm (PM<sub>10</sub>, 2000) and <2.5 μm in diameter (PM<sub>2.5</sub>, 2006) using validated models. Blood DNAm was measured at enrollment (2003-2009) with the Illumina HumanMethylation450 or MethylationEPIC array. DNAm age acceleration was measured by GrimAgeAccel and PhenoAgeAccel, and DNAm aging rate was measured by DunedinPACE. We used multivariable linear models, adjusted for DNAm array and other confounders, with sampling weights to estimate cross-sectional associations between air pollutants and the three biological age metrics.

**Results.** Black participants had higher average exposure to all pollutants than NHW participants (e.g., mean NO<sub>2</sub> Black: 10.8 ppb vs NHW: 8.0 ppb). We observed negligible associations between air pollutants and biological aging among NHW participants. Among Black participants, we observed positive associations with GrimAgeAccel for an interquartile range increase in PM<sub>10</sub> (β=0.41, 95% CI: 0.08-0.75), and both PM<sub>10</sub> and NO<sub>2</sub> when comparing the highest to the lowest quartile (PM<sub>10</sub>: β=1.04, 95% CI: 0.11-1.98; NO<sub>2</sub>: β=0.96, 95% CI 0.04-1.89). A monotonic dose-response relationship was also observed between NO<sub>2</sub> and DunedinPACE (NO<sub>2</sub>: Q4 vs Q1: β=0.029, 95% CI: 0.004-0.055; *p*-for-trend=0.05) among Black participants.

**Conclusion.** Our findings provide some evidence that air pollution is associated with faster biological aging in a sample of Black, but not NHW, women living in the US, supporting the importance of reducing harmful exposures in this population.



**Figure 1. Effect estimates and 95% CIs for the association between air pollutants and epigenetic aging, by race and ethnicity.** Abbreviations: CI=confidence interval, IQR=interquartile range, Q1-4=quartile 1-4, NO<sub>2</sub>=nitrogen dioxide, PM<sub>2.5</sub>=particulate matter < 2.5 μm, PM<sub>10</sub>=particulate matter < 10 μm.

**Machine learning assisted discovery of synergistic interactions between environmental pesticides, phthalates, phenols, and trace elements in child neurodevelopmental outcome**

Vishal Midya\* Vishal Midya Cecilia Sara Alcala Elza Rechtman Irva Hertz-Picciotto Chris Gennings Maria Rosa Damaskini Valvi

**Background:** Literature suggests higher developmental exposure to individual or mixtures of endocrine-disrupting chemicals is associated with autism spectrum disorder (ASD). However, the effect of interaction among these environmental chemicals is understudied since most methods: (1) estimate statistical interactions that don't usually coincide with biological interactions; (2) ignore the interaction thresholds beyond which synergism or antagonism might arise; and finally, (3) cannot efficiently search for high-order interactions as chemical exposures increase. We aim to discover multi-ordered synergistic interactions between environmental chemicals that (1) are present only in a proportion of the sample whose chemical concentrations are higher than certain thresholds and (2) are associated with higher odds of ASD even after considering the effects of chemical mixtures.

**Methods:** We used a combination of Weighted Quantile Sum (WQS) regression and a machine-learning tool called signed iterative random forest (SiRF). In a cross-sectional dataset from the Childhood Autism Risks from Genetics and Environment study, we evaluated multi-ordered synergistic interactions among 62 chemicals measured in the urine samples of 479 children (30 phenols and parabens, 20 phthalates, 6 pesticides, and 6 trace elements) in association with increased odds for ASD.

**Results:** WQS-SiRF discovered two synergistic two-ordered interactions: (1) trace element cadmium and alkyl-phosphate pesticide - diethyl-phosphate (DEP), and (2) 2,4,6-trichlorophenol (TCP-246) and DEP. Among the children with urinary concentration of cadmium and DEP over the 75<sup>th</sup> percentile, the cadmium/DEP interaction was associated with increased odds of ASD, even after controlling for the WQS-mixture effect and covariates.

**Conclusion:** Using the inferential power of WQS and predictive accuracy of machine learning, WQS-SiRF algorithm discovered biologically meaningful interactions among urinary biomarkers associated with ASD.

**The Effects of Metal Mixture in the Associations Between Socioeconomic Status and Blood Pressure among Rural Bangladeshi Adults: A Four-way Decomposition Approach** Juwel

Rana\* Juwel Rana Syed E Haque Habibul Ahsan Jay S. Kaufman

**BACKGROUND AND AIM:** The socioeconomic differentials in blood pressure (BP) outcomes are well established but the mechanism of these differences remains unclear, particularly in the context of low and middle-income countries (LMICs). We, therefore, examined and quantified the role of the heavy metal mixture in the associations of socioeconomic status and BP outcomes in rural Bangladeshi adults.

**METHODS:** Our study included 5923 rural Bangladeshi adults prospectively followed for six years in the Bangladesh vitamin E and selenium Trial (BEST). Blood pressure was measured at baseline and during three biennial follow-up examinations. Blood concentrations of lead (BPb), arsenic (BAs), selenium (BSe), and urinary concentration of arsenic (UAs), including SEP (based on agricultural land ownership), years of education, and potential confounders were measured at baseline. A parametric g-formula-based four-way decomposition approach was applied with metal mixture as a mediator to decompose the total effects (TE) of SEP and education into four components: controlled direct effect (CDE), randomized analogue of reference interaction (rINTRef), randomized analogue of mediated interaction (rINTMed), randomized analogue of pure natural indirect effect (rPNIE).

**RESULTS:** Participants with higher SEP and education were less likely to be exposed to metal mixtures than their counterparts. With metal mixture as a mediator, there were both pure mediation and interaction effects of SEP and education on systolic blood pressure (SBP), diastolic blood pressure, pulse pressure, and mean arterial pressure. For example, the TE indicates that higher education at baseline increased SBP by 3.5 mmHg (95% CI: 2.2, 4.8) after six years of follow-up. The rINTRef was 1.2 mmHg (95% CI: -1.0, 3.3), and rPNIE reveals that education can reduce SBP by -0.4 mmHg (95% CI: -0.6, -0.3) at six years via intervening on metal mixture (per decile increase) only. However, higher SEP reduced SBP by -0.6 mmHg (95% CI: -1.5, 0.5) SBP, and 41% of this TE was attributable to the metal mixture only.

**CONCLUSIONS:** Our study suggests socioeconomic differentials in BP outcomes may be explained by inequalities in metal mixture exposure in rural Bangladesh.

**A unified framework for assessing interaction effects among environmental exposures in epidemiologic studies: a case study on temperature, air pollution, and kidney-related conditions in New York State** Lingzhi Chu\* Lingzhi Chu Kai Chen Zhuoran Yang Susan Crowley

Robert Dubrow

**Background:** Co-exposure to multiple non-optimal environmental conditions is ubiquitous, making evaluation of the interaction effects among exposures essential. However, there are various methods to evaluate interaction effects, making it complex to synthesize existing findings; and quantification of the magnitude of interaction (e.g., multiplicative interaction defined as the ratio of the joint relative risk over the product of the two independent relative risks) and its uncertainty is rarely performed. This study aimed to develop a unified and quantitative framework for assessing interaction effects.

**Methods:** We introduced a flexible product term among environmental exposures to models with a loglinear relative risk function. We derived general closed-form expressions for marginal associations, joint associations, multiplicative interaction effects, and their uncertainties. We conducted a case study on interaction effects between temperature and air pollution (i.e., PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub>) on morbidity risk for kidney-related conditions in New York State.

**Results:** We designed a symmetric bi-directional case-crossover study with conditional logistic regression using the moving averages at lag 0-5 days for air pollution (linear) and daytime mean outdoor wet-bulb globe temperature (WBGT; natural cubic spline). We found a significant multiplicative interaction effect (IE) between outdoor WBGT at the 99<sup>th</sup> percentile (median as the reference) and 1) PM<sub>2.5</sub> (per 5 µg/m<sup>3</sup> increase; IE = 1.052; 95% confidence interval [CI]: 1.019, 1.087) for acute kidney failure and 2) O<sub>3</sub> (per 5 ppb increase; IE = 1.022; 95% CI: 1.008, 1.036) for urolithiasis. There were no IEs for other pollutants and outcomes.

**Discussion:** Our framework unifies different functional forms of exposure variables in the interaction and harmonizes the two-way evaluation. The case study underscores co-consideration of heat and air quality when estimating health burden and designing heat/pollution alert systems.

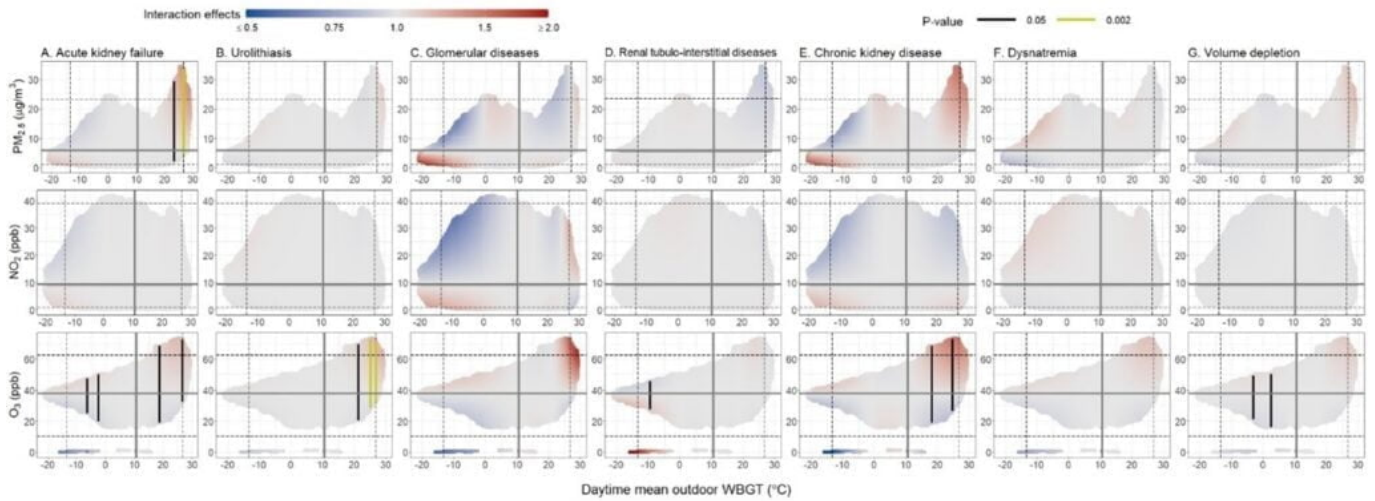


Figure 1. Multiplicative interaction effects associated with different combinations of daytime mean outdoor wet-bulb globe temperature (WBGT) and air pollution levels for PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> at lag 0-5 days, respectively, from three-pollutant models with an interaction term using natural cubic splines for daytime mean outdoor WBGT and linear functions for air pollutants, with the median pollution level (the solid horizontal gray line) and the median temperature (the solid vertical gray line) as the reference, in relation to risk for acute kidney failure (n=206,618), urolithiasis (n=519,297), glomerular diseases (n=4,023), renal tubulo-interstitial diseases (n=176,359), chronic kidney disease (n=18,748), dysnatremia (n=67,568), and volume depletion (n=217,321). All models were adjusted for daily mean dew point temperature, wind speed, and solar radiation. The two dashed vertical or horizontal lines represent the 1<sup>st</sup> and the 99<sup>th</sup> percentiles of temperature or air pollution distributions, respectively. Yellow contours for the p-value indicate the Bonferroni-corrected p-value level [i.e., 0.05/(3 pollutants × 7 diseases) ≈ 0.002].



**Prenatal exposure to toxic air contaminants and risk of cerebral palsy** Haoran, Zhuo\* Haoran  
Zhuo Zeyan, Liew

Cerebral palsy (CP) is the most common neuromotor disorder that permanently affects children's physical mobility, while the etiology remains unexplained. Increasing evidence suggests that in-utero exposure to toxic air contaminants (TACs) affects fetal neurodevelopment, we conducted a California statewide study to investigate whether prenatal exposure to TACs is associated with CP in childhood. We analyzed a case-cohort study sample of live births in California (2005-2015) with geocoded maternal residential address within the 5-mile buffer around TACs monitors. We identified 799 CP cases using the California Department of Developmental Services records and randomly selected 20% birth records as the controls (N=147,820). We selected 33 TACs (22 volatile organic compounds (VOCs) and 11 metals) with potential developmental and neurological toxicity as our primary focus. The association between pregnancy- and trimester-averaged exposures to individual TAC and CP were estimated using logistic regression. We also utilized the quantile-based g-computation method to estimate the joint effect of VOC mixtures or metals on CP. Potential confounders include maternal sociodemographic characteristics. Per interquartile-range increase of maternal pregnancy level to 8 VOCs (acetaldehyde, acetone, benzene, methyl ethyl ketone, perchloroethylene, styrene, toluene, trichloroethylene) and 6 metals (antimony, iron, lead, manganese, nickel, vanadium) were associated with 7-20% higher odds for CP in the offspring (e.g., acetone: OR=1.19, 95% CI: 1.09-1.30, antimony: OR=1.20, 95% CI: 1.01-1.25). Trimester-specific exposures suggest elevated odds in the first and second trimesters. The estimated joint effects for exposure to VOCs mixtures were 1.20 (95% CI: 1.10-1.32) and metals were 1.32 (95% CI: 1.14-1.51). This is the first study suggests prenatal exposures to ambient TACs, specifically VOCs and metals from urban traffic and industry emissions, may increase the risk for CP in children.

**Trajectories of lifetime cardiovascular risk predict pregnancy outcomes: The Bogalusa Heart Study and the Cardiovascular Risk in Young Finns Study** Nicole Cohen\* Emily Harville Juuso Hakala Suvi Rovio Kathja Pahkala Olli Raitakai Terho Lehtimäki

**Background:** Life course patterns of change in risk - trajectories - affect health.

**Objective:** To examine how trajectories of cardiovascular risk factors are associated with pregnancy and birth outcomes

**Methods:** Data from two cohort studies participating in the International Childhood Cardiovascular Consortium - The Bogalusa Heart Study (BHS) and the Cardiovascular Risk in Young Finns Study (YFS) were used. Both followed children into adulthood and measured cardiovascular risk factors, including body mass index (BMI), systolic and diastolic blood pressure (SBP/DBP), serum triglycerides, total-, LDL- and HDL-cholesterol. Latent class analysis was used to divide each cohort into distinct trajectories according to these risk factors from childhood to early adulthood and these groups were then used to predict pregnancy outcomes including low birthweight (LBW; <2500 g), preterm birth (PTB; <37 weeks' gestation), hypertensive disorders of pregnancy (HDP), and gestational diabetes mellitus (GDM).

**Results:** BMI, SBP, and HDL-cholesterol for YFS fell into more latent classes than for BHS, for which 3 classes generally seemed to be sufficient to represent the groups in the population across risk factors. In both cohorts, steeper increases in BMI were also associated with HDP and GDM. The steepest trajectory of SBP was also associated with LBW and PTB.

**Discussion:** Life course trajectories of cardiovascular risk, particularly those that represent more rapid worsening of cardiovascular health, are associated with higher risk of pregnancy complications.

**Postpartum hemorrhage and long-term maternal mortality** Holly Elser\* Holly Elser Sunni L. Mumford Katherine L. Grantz Anna Z. Pollack Pauline Mendola Jim L. Mills Edwina Yeung Cuilin Zhang Enrique F. Schisterman Stefanie Hinkle

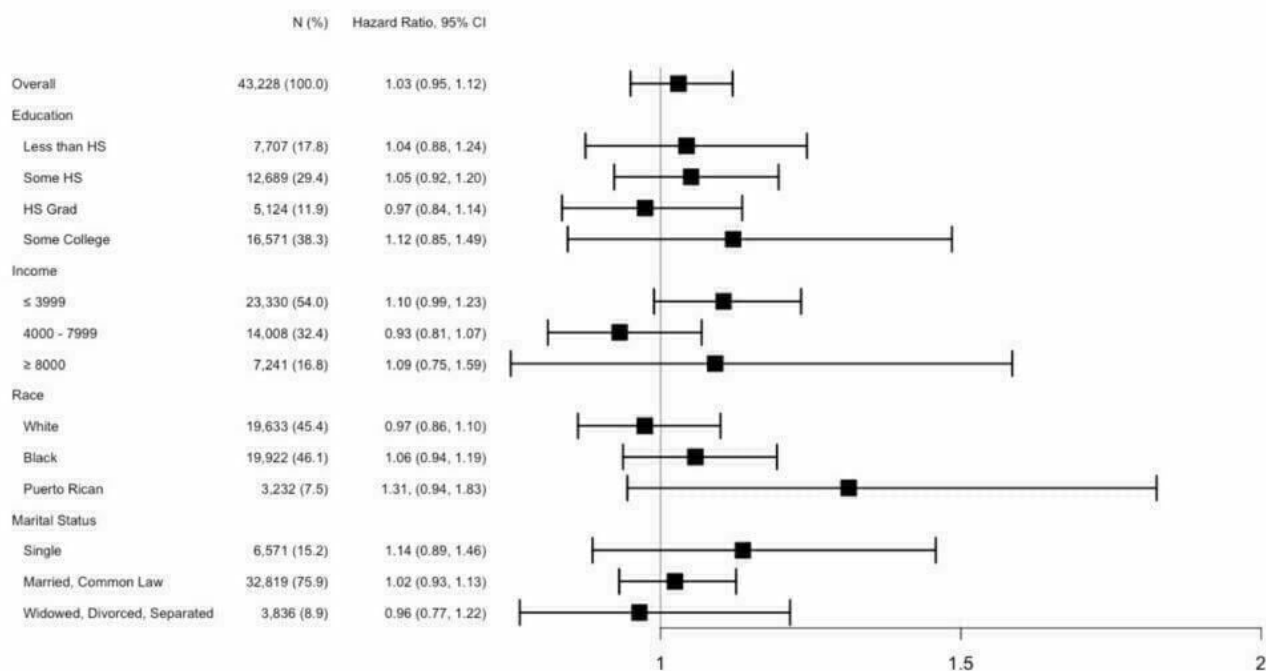
**Background:** Postpartum hemorrhage is among the leading causes of short-term maternal mortality in the United States; whether it is associated with long-term mortality risk is unclear.

**Methods:** The Collaborative Perinatal Project (CPP) Mortality Linkage Study linked maternal participants in the CPP, a prospective pregnancy cohort (1959–1965) to the National Death Index and Social Security Death Master File for vital status through 2016. Postpartum hemorrhage was defined by obstetric records. Women who died during their hospital admission were excluded from this analysis (N=8). We used Cox proportional hazards regression to examine associations between postpartum hemorrhage and long-term all-cause mortality adjusting for parity, pregnancy complications, prior chronic conditions, smoking, race/ethnicity, education, income, marital status, and study site. Because maternal mortality risk associated with postpartum hemorrhage varies across demographic subgroups, we conducted secondary analyses by race/ethnicity, education, and income.

**Results:** Of the 43,228 women included in our analysis, 45.4% were White, 46.1% were Black, and 7.5% were Puerto Rican. The majority (79.5%) completed at least some high school. There were 1,521 with postpartum hemorrhage (3.5%) and 17,025 (39.3%) who died by 2016. Post-partum hemorrhage was associated with increased all-cause mortality risk in crude models (HR=1.14, 95%CI:1.05,1.23) but not in fully adjusted models (HR=1.03, 95%CI:0.95,1.12). Although hazard ratios varied somewhat across subgroups, there was little evidence of heterogeneity (**Figure**).

**Conclusions:** While postpartum hemorrhage is associated with increased mortality risk in the postpartum period, these findings are generally reassuring that it is not associated with long-term mortality.

### Postpartum Hemorrhage and All-Cause Mortality



**Figure. Post-partum hemorrhage and all-cause mortality risk overall and by population subgroup.** We used Cox proportional hazards regression to examine associations between postpartum hemorrhage and long-term all-cause mortality adjusting for parity, pregnancy complications, prior chronic conditions, smoking, race/ethnicity, education, income, marital status, and study site. Because maternal mortality risk associated with postpartum hemorrhage may vary across demographic subgroups, we conducted secondary analyses by race/ethnicity, education, and income.

**No increased risk of cardiovascular death after preeclampsia in over 40% of women: a population based cohort study** Sage Wyatt\* Sage Wyatt Liv Grimsvedt-Kvalvik Kari Klungsøyr Truls Østbye Aditi Singh Rolv Skjærven

**Introduction:** Preeclampsia (PE) most commonly appears only in the first pregnancy among women. Previous literature estimated cardiovascular disease mortality risk to be doubled after PE. But this estimate is biased by including high risk groups, such as one-child mothers and recurrent PE.

**Aim:** To estimate the risk of cardiovascular death in women with PE by parity, preterm delivery and stillbirth

**Methods:** Using data from the Medical Birth Registry of Norway, the Norwegian Cause of Death Registry, and the Norwegian Population Registry, we identified 891,076 mothers with first pregnancies registered between 1967-2013. Our primary outcome was mothers' cardiovascular death between age 40 - 69, defined as death caused by ischemic heart disease, cerebrovascular disease, or peripheral arterial disease. The reference group was women with no preeclamptic pregnancies. Our exposure was PE in the first pregnancy among women who had no PE in later pregnancies by considering interactions with preterm and stillbirth. The association between the exposure and outcome was estimated by Cox proportional hazard model, adjusted for education, mother's age at first birth, year of birth and marital status.

**Results:** 5.2% of mothers (891,076) had term PE in their first pregnancy and 1.0% of mothers had preterm PE in their first pregnancy. 44% of mothers (30,665) with PE only had PE in the first pregnancy and no PE in later pregnancies. Among mothers with two pregnancies, mothers with a first term preeclamptic pregnancy and no PE in their second pregnancy did not exhibit an elevated risk of cardiovascular death (HR 1.0, 95%CI 0.8-1.3). The same trend was observed in mothers with 3 children after excluding mothers with stillbirths (HR 1.1, 95%CI 0.8 - 1.6).

**Conclusion:** Multiparous women with term PE only in the first pregnancy and no preeclamptic pregnancies later have no increased risk of death from cardiovascular causes.

**History of Infertility and Risk of Endometrial Cancer in the Women's Health Initiative** Holly Harris\* Holly Harris Kimberly Lind Cynthia Thompson Nazmus Saquib Aladdin Shadyab Peter Schnatz Rogelio Robles-Morales Lihong Qi Howard Strickler Denise Roe Leslie Farland

Several studies have suggested a relationship between infertility and endometrial cancer. Most studies have evaluated this relationship in premenopausal women, yet the mean age of endometrial cancer is 60 years old, after the age of menopause for most women. Further, obesity is a strong risk factor for endometrial cancer, but few studies have adequately controlled for it when examining the association with infertility. Our objective was to examine the association between history of infertility and risk of postmenopausal endometrial cancer within the Women's Health Initiative (n=86,216) after controlling for covariates, including body mass index (BMI). Infertility was self-reported, "Have you ever tried to become pregnant for more than one year without becoming pregnant." Cox proportional hazards models were used to calculate the hazard ratios (HRs) of incident endometrial cancer comparing participants who indicated they experienced infertility to parous participants without a history of infertility. Approximately 16% of participants reported a history of infertility. No statistically significant association was observed between infertility and risk of endometrial cancer overall (HR=1.11; 95% CI=0.98-1.26). While point estimates suggested an increase in risk of endometrial cancer among women with higher BMI (BMI 30+ HR=1.19; 95% CI=0.98-1.44; BMI of 25-29.9 HR=1.12; 95% CI=0.89-1.41), none of the associations were statistically significant. Our findings highlight, as observed in previous studies, that risk factors for endometrial cancer may vary by body mass index.

**Longitudinal metabolomic changes during pregnancy and ischemic placental diseases****(IPD)** Tahmineh Romero\* Tahmineh Romero Beate Ritz Sherin Devaskar Carla Janzen Kimberly Paul Qi Meng Doug Walker Irish Del Rosario

In recent years many publications are devoted to understanding and describing the metabolomic changes during pregnancy. Metabolomics are the intermediate or the product of cellular biochemistry that provide an invaluable window into understanding the maternal-fetal interface. The placenta is the primary site of maternal-fetal exchange, responsible for ensuring a healthy pregnancy. We studied the association between ischemic placental disease (IPD) and temporal changes observed in 94 known metabolites. IPD refers to preeclampsia, preterm birth, and intra-uterine growth restriction.

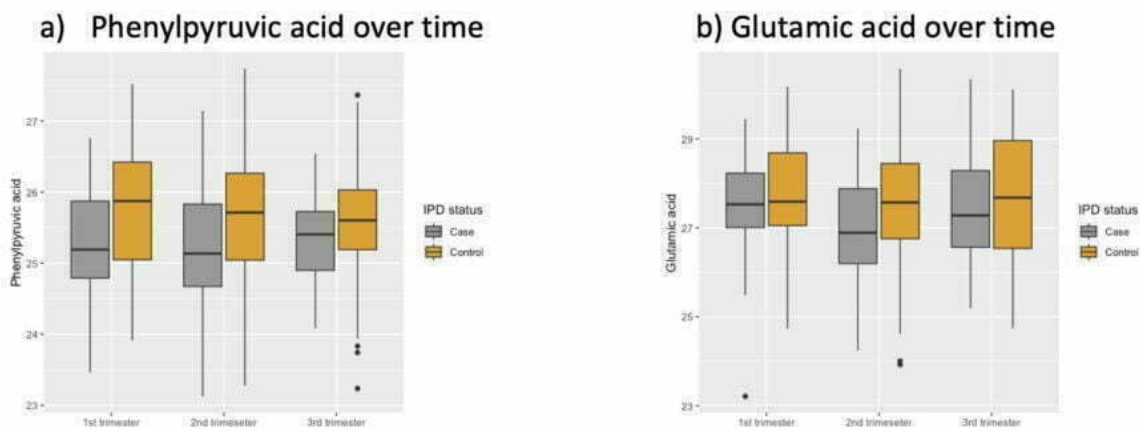
PARENTs cohort, a prospective study, recruited women early in their pregnancy from antenatal clinics at the University of California Los Angeles from 2016 to 2019. The serum samples were processed using a high-resolution metabolomics (HRM) platform employing high-resolution MS and advanced data extraction algorithm to measure up to 20,000 chemicals in biological samples (at Emory). We have followed the pipeline of untargeted metabolomics study; however, we restricted these analyses to the 94 in-house named metabolites. After excluding subjects with diabetes (n=1) and hypertension (n=16), longitudinal serum samples were available for 131 healthy pregnant women with live births. Forty-three, 173 and 111 samples were collected during first, second and third trimesters of pregnancy, respectively. Thirty-three women (25%) experienced IPD. We performed linear regression models, modeling metabolites as response variables and adjusting for gestational age (GA), IPD, pre-pregnancy BMI, fetal sex, mother's age and race as independent covariates. Eight metabolites were significantly associated with IPD, of which 4 remained statistically significant after adjusting for false discovery rate (FDR). Further investigation of these particular metabolites revealed the largest difference seen with IPD (yes/no) was during the first and second trimesters of pregnancy (GA<26 weeks) (figure 1).

We suggest that further untargeted metabolomic approaches in this racially diverse and rich dataset would help unravel a better understanding of the pathophysiology of IPD, thereby extending this knowledge in crafting modalities of care for mother and child.

Figure 1. distribution of phenylpyruvic acid and glutamic acid stratified by IPD (yes/no) over the three trimesters of pregnancy. Adjusted p-value 0.018 and 0.049, respectively.

This work was supported by the NIH-U01 HD087221 and the NIEHS CHEAR program

Figure 1. distribution of phenylpyruvic acid and glutamic acid stratified by IPD (yes/no) over trimester of pregnancy. Adjusted p-value 0.018 and 0.049, respectively.





**Exposure to PM<sub>2.5</sub> during pre-conception, pregnancy, and 1-year after parturition in relation to later cardiometabolic alterations in Mexican women** Sandra India Aldana\* Sandra India Aldana Nicolò Foppa Pedretti Damaskini Valvi Allan C. Just Iván Gutiérrez-Avila Martha María Téllez Rojo Maricruz Tolentino Ivan Pantic Andrea Baccarelli Robert O. Wright Elena Colicino

### **Background/Aim**

Pregnancy is a critical window for long-term programming of the effects of airborne particulate matter  $\leq 2.5\mu\text{m}$  (PM<sub>2.5</sub>) exposure. However, very little is known about the long-term effects for the mothers. This study aims to assess the association of potential critical windows of PM<sub>2.5</sub> exposure during and around pregnancy with later-life differences in markers for cardiometabolic health.

### **Methods**

The study population included ~300 pregnant women (mean age  $\pm$  standard deviation (SD): 29  $\pm$  5.6 years) in the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) study, a prospective Mexican cohort with cardiometabolic outcomes measured at 48, 72, and 96 months after delivery. Monthly PM<sub>2.5</sub> exposure was estimated at each participant's address using a validated satellite-based spatiotemporal model from 2 months prior to conception to 1-year after delivery. To examine potential critical windows of PM<sub>2.5</sub> exposure on cardiometabolic endpoints (body mass index (BMI), cholesterol, triglycerides, glucose, glycated hemoglobin (HbA1c), blood pressure, and waist circumference) at each follow-up visit, we used distributed lag models (DLMs) controlling for age, pre-pregnancy BMI, socio-economic status, smoking during pregnancy, marital status, parity, meteorological season, cardiometabolic medications, and alcohol intake.

### **Results**

Women were exposed to an overall average (SD) PM<sub>2.5</sub> concentration of 22.7 (1.4)  $\mu\text{g}/\text{m}^3$  and had a mean (SD) pre-pregnancy BMI of 26.7 (4.4)  $\text{kg}/\text{m}^2$ . DLMS showed that potentially adverse effects of PM<sub>2.5</sub> were higher due to mid-pregnancy exposure for most biomarkers at 48-72 months, including total cholesterol, high-density lipoprotein, and BMI. However, PM<sub>2.5</sub> effects peaked around conception exposures for glucose at 48 months. We also observed that PM<sub>2.5</sub> exposure during the 2<sup>nd</sup> and 3<sup>rd</sup> trimesters of pregnancy and post-partum was associated with higher maternal BMI from 24 to 72 months after delivery.

### **Conclusion**

In women of childbearing age, pregnancy may be a susceptible window to PM<sub>2.5</sub> exposure for altered cardiometabolic health later in life.

**The impacts of the census tract socioeconomic status on colorectal and cervical cancer screening** Mimi Ton\* Mimi Ton Andrea Burnett-Hartman Amy Hughes Christopher Li Christine Neslund-Dudas Amanda Phipps Sandi Pruitt Jasmin Tiro Trang VoPham Doug Corley Sarah Knerr Natalie Del Vecchio

#### BACKGROUND/AIMS

There is striking variation in colorectal cancer (CRC) and cervical cancer incidence globally, as well as across the US. However, there has been limited research in the US on how specific differences in features of the neighborhood environment, such as, transportation, land use, housing and/or urbanicity, may influence screening uptake and thus impact CRC and cervical cancer outcomes.

#### METHODS

The Population-based Research to Optimize the Screening Process (PROSPR) consortium uses electronic medical records and administrative databases to collect information on demographics, health care utilization, health insurance, orders, test results, and pathology results. For each patient's residential census tracts, we determined neighborhood socioeconomic status (nSES) using Yost scores (which incorporate information on poverty, education, home value, income, employment, mortgage, and rent) and urbanicity using Rural-Urban Commuting Area (RUCA) codes (which incorporate information on population density, urbanization, and daily commuting). Incident cancer screening was defined using diagnostic tests or procedures. Multivariable Poisson regression was used to calculate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for the association between census tract-level nSES and urbanicity and incidence of CRC or cervical cancer screening, adjusting for birth year, sex, and race and ethnicity.

#### RESULTS

There were n=7,260,630 and n=1,027,128 participants in the CRC and cervical cancer cohorts included in this analysis, respectively. Yost score was associated with lower cervical (lowest quintile vs. highest quintile, IRR: 1.77, 95% CI: 1.75, 1.77) and CRC screening (lowest quintile vs. highest quintile, IRR: 0.68, 95% CI: 0.68, 0.69). RUCA was associated with cervical (isolated small rural town vs. urban, IRR: 0.38, 95% CI: 0.37, 0.39) and CRC screening (isolated small rural town vs. urban, IRR: 1.39, 95% CI: 1.38, 1.39).

#### CONCLUSION

Our results suggest that there may be an association of census tract-level nSES and rurality with CRC and cervical cancer screening. It may suggest that policy makers and health systems look at reducing barriers to screening that may be the result of low SES and rural living.

**Government housing assistance and cancer screening participation among adults with low-income** Jordan Baeker Bispo\* Jordan Baeker Bispo Hyunjung Lee Zinzi Bailey Ahmedin Jemal Farhad Islami

Adults with low income experience a disproportionate burden of preventable cancer morbidity and mortality. Access to affordable housing may support cancer control by alleviating financial barriers to preventive care. We used data from the 2019 and 2021 National Health Interview Survey to examine relationships between cancer screening and receipt of government housing assistance (e.g., public housing and housing voucher programs) among low-income adults. Respondents were classified as up-to-date or not with breast cancer (BC), cervical cancer (CVC) and colorectal cancer (CRC) screening guidelines. We used multivariable logistic regression to model guideline-concordant screening as a function of participation in any government housing assistance program, overall and stratified by year, urban-rural status, and sex. Sensitivity analyses included defining alternative poverty thresholds for study inclusion and propensity-score weighting of housing assistance comparison groups. Analyses for BC, CVC and CRC screening included 2,265, 3,154 and 3,252 respondents, respectively, of whom 31%, 18% and 25% received housing assistance. Screening for BC and CRC was higher among those who received housing assistance compared to those who did not (60% vs. 51%,  $p < 0.01$  for BC; 57% vs. 44%,  $p < 0.01$  for CRC). In adjusted overall models, receiving housing assistance was associated with increased odds of BC screening, but the effect was not statistically significant (aOR=1.23, 95% CI=0.97-1.56). In stratified models, housing assistance was associated with significantly higher odds of BC screening in urban settings (aOR=1.35, 95% CI=1.06-1.72) but not rural (aOR=0.72, 95% CI=0.39-1.33). Housing assistance was not associated with CVC or CRC screening. Sensitivity analyses afforded similar conclusions. Policies that address housing affordability may reduce socioeconomic cancer disparities for women in urban areas. More research on housing policy and cancer screening in rural areas is needed.

**Disparities in timely cervical cancer screening in women with disabilities, Behavioral Risk Factor Surveillance System 2021** Franz Castro\* Franz Castro

**Introduction.** There is a paucity of data on utilization of preventive health services in women with disabilities. To better understand disparities impacting this population, we aimed to explore the association between disability and timely utilization of cervical cancer screening services.

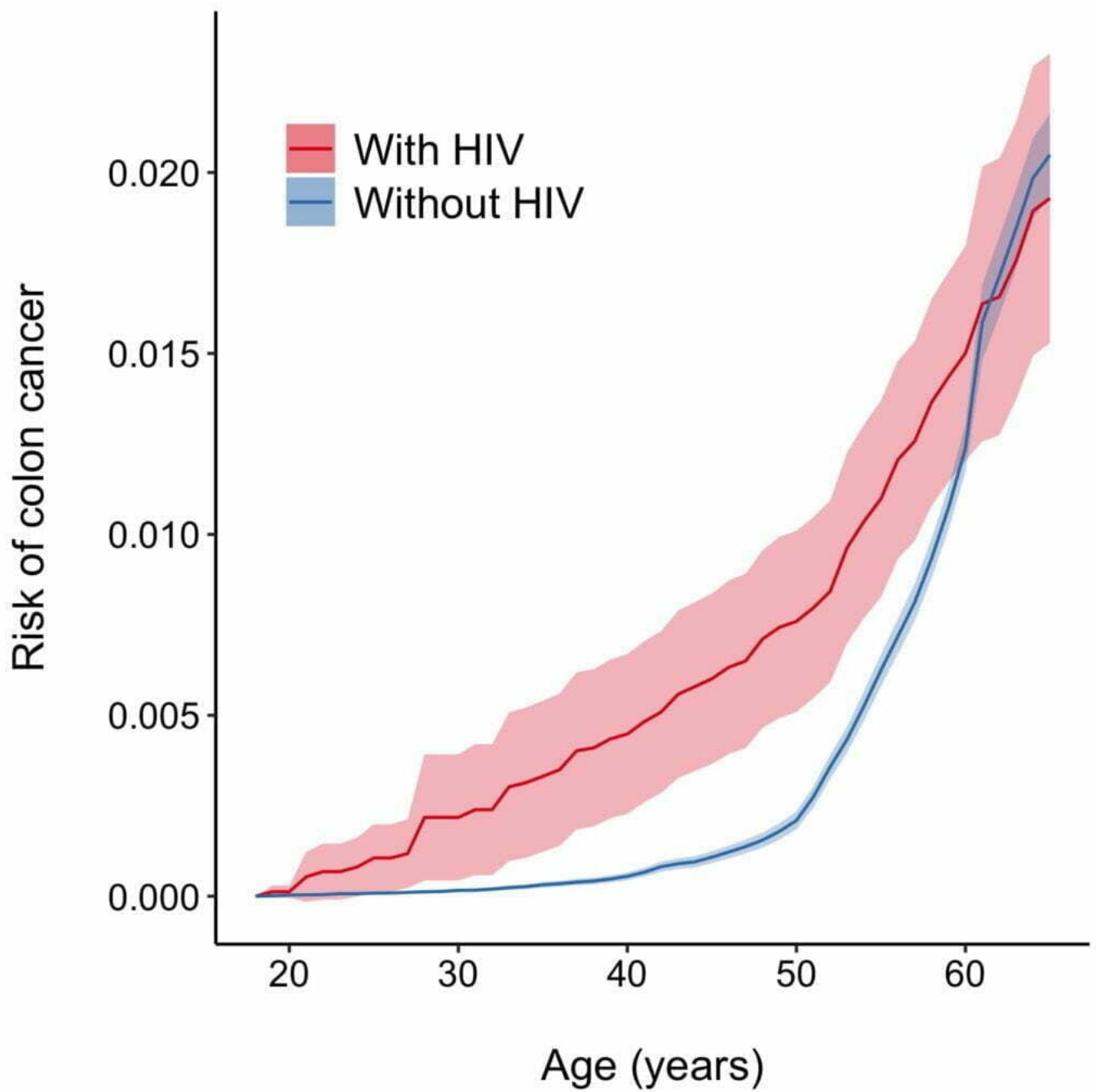
**Methods.** We analyzed cross-sectional data from the 2021 Behavioral Risk Factor Surveillance System (BRFSS), a state-based system of telephone health surveys, including U.S. women between 25 and 65 years of age ( $n = 3.4$  million, weighted). Disability was defined as reporting limitations in any of the following domains: visual, hearing, cognitive, mobility, and independent living. Timely cervical cancer screening was defined as having utilized this preventive service within the past five years. We fitted a Poisson regression model with robust standard errors, adjusting by age, race/ethnicity, educational attainment, income, region, healthcare coverage, and self-reported general health status. Results were expressed as prevalence ratios (PR) and 95% confidence intervals (CI).

**Results.** The adjusted model showed that women with disabilities had a lower prevalence of having a timely cervical cancer screening as compared to those without disabilities (PR: 0.92, 95%CI: 0.87, 0.98,  $p: 0.01$ ).

**Conclusion.** For women with disabilities, preventive health services constitute a means to social inclusion and participation in society. Policy should address the issue of universal accessibility in primary care facilities and the role of the social context as an additional barrier to cervical cancer screening.

**Adherence to colorectal cancer screening protocols and incidence of colon cancer among Medicaid beneficiaries with and without HIV, 2001-2015** Jacqueline Rudolph\* Jacqueline Rudolph Keri Calkins Bryan Lau Corinne Joshu

Cancer is an important comorbidity for people with HIV (PWH). Colon cancer incidence has been increasing among PWH. Colorectal cancer screening via colonoscopy is an important tool for cancer prevention. To assess whether the impact of colorectal cancer screening is similar among PWH and those without HIV, we sought to estimate the difference in colon cancer incidence by HIV status, controlling for differences in screening patterns. Our study sample included Medicaid beneficiaries, enrolled 2001-2015 and aged 18-64 years. We excluded beneficiaries with a history of colon cancer and those with dual enrollment in Medicare or private insurance. For computational efficiency, we sampled 10% of the eligible beneficiaries without HIV, for a total sample of 4.5 million beneficiaries (186,871 with HIV). Our exposures were HIV status at baseline and time-varying adherence to a screening protocol requiring beneficiaries have no endoscopies below age 50 and at least 1 but no more than 2 endoscopies by age 64. We estimated cumulative incidence of colon cancer from baseline, with age as the time scale, accounting for death as a competing event and censoring beneficiaries when they disenrolled from Medicaid or deviated from the screening protocol. We used inverse probability weights to control for confounders of the HIV-cancer and screening-cancer relationships and obtained 95% CIs using 500 bootstrap resamples. As shown in the Figure, PWH had higher colon cancer incidence at most ages, but the curves crossed at age 62, resulting in RDs at ages 35, 50, and 64 of 0.30% (95% CI: 0.09, 0.51), 0.55% (95% CI: 0.30, 0.80), and -0.12% (95% CI: -0.54, 0.30). These findings suggest that PWH had higher incidence of colon cancer below age 50, despite these beneficiaries having no record of an endoscopy; further work needs to investigate these cancers. Above age 50, colon cancer incidence among beneficiaries without HIV adhering to the screening protocol surpassed those with HIV.



**Survival after cervical cancer diagnosis by immigrant and screening status: a population-based retrospective cohort study in Ontario, Canada** Geetanjali D Datta\* Geetanjali D Datta Hong Lu Alexander Kopp Smanatha Lee Marie-Helene Mayrand Rachel Aisha Lofters

**Background:** Despite improvement in screening and HPV vaccination, cervical cancer is the 4<sup>th</sup> most frequent cancer among Canadian women aged 15 to 44 years. Immigrants in Ontario, Canada's most populous province, are known to have lower rates of cervical cancer screening, but potential differences in survival are unknown. **Methods:** Multiple linked health-administrative databases were used to create a census of Ontarians diagnosed with cervical cancer between April 1, 2012 and March 31, 2017 (sampling size=4301), and we examined the association of immigration-related, sociodemographic, and healthcare-related factors with 5-year survival. Cox proportional Hazards models were stratified by age (<50, ≥50) and stage [early-stage (1 and 2), late-stage (3 and 4)]. Multivariate models included age in years, neighborhood income quintile, number of Aggregated Diagnosis Group (ADG) comorbidities, number of primary care visits prior to diagnosis, and continuity of care. **Results:** Overall, 5-year mortality among immigrants was 21% and 28% among non-immigrants. In adjusted models, among those younger than 50-years of age, immigrant status was not associated with 5-year survival regardless of stage at diagnosis. However, among those 50 years and older, immigrant status was associated with an inverse relationship with mortality (e.g. late stage:  $HR_{imm} = 0.6$ , 95% CI=0.4-0.9). Never having been screened (e.g.  $HR_{early, <50yrs} = 3.2$ , 95% CI=1.2-8.0) and screening at intervals longer than recommended (e.g.  $HR_{early, <50yrs} = 2.5$ , 95% CI=1.5-4.2) were associated with increased mortality in both early- and late-stage patients across ages. Additionally, increased comorbidities were associated with increased mortality among those diagnosed with late-stage disease in both age groups. **Conclusion:** No immigrant-base inequalities in survival were observed among women after adjusting for relevant covariates. However, sub-optimal screening history and comorbidities were associated with increased mortality.

**Changes in Knowledge and Awareness for a Community-based Cancer Screening Educational Program** Shenghui Wu\* Shenghui Wu Shenghui Wu PATRICIA CHALELA

**Background:** Cervical cancer (CC), colorectal cancer (CRC), and breast cancer (BC) are diseases that can be prevented/detected through early test. Through educational programs, individuals can become better informed about these cancers and understand the importance of screening and early detection. A community-based educational program was developed to improve knowledge and awareness toward the screening of the three cancer types in a South Texas underserved population.

**Methods:** Residents living in Laredo, Texas were invited to participate in the present education program. From January 2020 to April 2021, participants were recruited using social media and flyer distributions in general community. Participants received a free live web cancer education presentation delivered by bilingual community health educators, and online pre- and post-education surveys for CC, CRC, and BC separately. Pre-post changes in knowledge for individual items were compared using McNemar's chi-squared tests.

**Results:** Overall, participants demonstrated increases in CC (n=237), CRC (n=59), and BC (n=56) screening knowledge and awareness after receiving the cancer screening education ( $P_s < 0.05$ ). After receiving the cancer screening education, 85-97% of participants had an intent to talk to a healthcare provider about CC/CRC/BC screening, 88-97% had an intent to get a CC/CRC/BC screening test in the next 12 months or at the next routine appointment, and 90-97% had an intent to talk about CC/CRC/BC with their family members or friends.

**Conclusion:** A community-based educational program can help increase knowledge and awareness about cervical, colorectal, and breast cancer screening, promote positive changes in population's knowledge and awareness about the benefits of cancer screening.



**Table 1. Knowledge and awareness on cervical cancer screening before and after screening education delivery**

	Presurvey		Postsurvey		P
	N	%	N	%	
<b>Risk factors of cervical cancer (yes vs. no)</b>					
Chances of developing cervical cancer are higher if there is a family history of cervical cancer	131	80.86	140	86.42	0.09
The human papilloma virus (HPV) is one of the major risk factors for cervical cancer	133	85.26	148	94.87	<b>0.003</b>
Smoking	100	42.19	165	69.62	<b>&lt;0.0001</b>
Long term use of oral birth control pills	80	33.76	125	52.74	<b>&lt;0.0001</b>
A diet low in fruits and vegetables	62	26.16	132	55.70	<b>&lt;0.0001</b>
Being overweight	75	31.65	135	56.96	<b>&lt;0.0001</b>
<b>Symptoms of cervical cancer (yes vs. no)</b>					
Persistent pelvic/abdominal pain	122	78.71	135	87.10	<b>0.02</b>
Unusual vaginal discharge that may contain blood	108	72.48	111	74.50	0.61
Vaginal bleeding after going through menopause	94	59.87	146	92.99	<b>&lt;0.0001</b>
<b>Prevention of cervical cancer (yes vs. no)</b>					
Using protection during sexual activity can help lower my chances of getting HPV	91	58.71	138	89.03	<b>&lt;0.0001</b>
Having an HPV infection means you will get cervical cancer (no vs. yes).	52	34.21	69	45.39	<b>0.03</b>
Cervical cancer can be prevented with regular screening	139	89.68	155	96.77	<b>0.008</b>
<b>Early detection of cervical cancer</b>					
Cervical cancer screening is recommended only for women who have symptoms (no vs. yes).	135	83.85	137	85.09	0.67
Should have a Pap test every 3 years at ages 21-29 (yes vs. no)	77	32.49	86	36.29	0.20
The Pap test together with the HPV test should be performed every 5 years starting at age 30 (yes vs. no).	103	66.03	117	75.00	<b>0.04</b>

**Table 2. Knowledge and awareness on colorectal cancer screening before and after screening education delivery**

	Presurvey		Postsurvey		P
	N	%	N	%	
<b>Risk factors of colorectal cancer</b>					
Lack of physical activity	24	40.68	29	49.15	0.31
Heavy alcohol consumption	28	47.46	29	49.15	0.84
Overweight/obesity	19	32.20	28	47.46	<b>0.02</b>
Low fiber and high-fat diet	16	27.12	30	50.85	<b>0.004</b>
Only people with family history of colon cancer will get the disease (no vs. yes)	30	93.75	31	96.88	1.00
A diet high in red meats and processed meats (lunch meat, hot dogs) increases chances of developing colorectal cancer (yes vs. no)	31	96.88	31	96.88	1.00
People younger than 50 years don't get colon cancer (no vs. yes)	31	96.88	31	96.88	1.00
<b>Symptoms of colorectal cancer (yes vs. no)</b>					
Having blood in the stool or dark stools	31	96.88	30	93.75	1.00
Having a decrease in appetite	27	84.38	28	87.50	1.00
Experiencing unintentional weight loss	27	84.38	28	87.50	1.00
Even if I have no symptoms, I may still have colorectal cancer	29	90.63	29	90.63	1.00
<b>Early detection of colorectal cancer (yes vs. no)</b>					
In general, a colonoscopy should be performed every 10 years starting at age 50	14	43.75	28	87.50	<b>0.006</b>
A stool-based test (FIT/FOBT) checks your stool (poop) for blood	26	81.25	25	78.13	0.75
It is ok to skip colorectal cancer screening if do not have any symptoms (no vs. yes)	25	78.13	30	93.75	0.18
In general, a stool (poop) test (FIT or FOBT) should be done every year starting at age 50	16	50	26	81.25	<b>0.004</b>

**Table 3. Knowledge and awareness on breast cancer screening before and after screening education delivery**

	Presurvey		Postsurvey		P
	N	%	N	%	
<b>Risk factors of breast cancer</b>					
Getting older is a risk factor for breast cancer (yes vs. no)	28	82.4	30	88.3	0.63
Smoking increases my risk of breast cancer (yes vs. no)	30	88.2	32	94.1	0.69
Drinking alcohol increases my risk of breast cancer (yes vs. no)	26	76.5	31	91.2	0.23
Breastfeeding may decrease my risk of breast cancer (yes vs. no)	29	85.3	26	76.5	0.45
Having my mother or a sister with breast cancer means I am more likely-get it (yes vs. no)	33	97.1	32	94.1	1.00
Married women are more likely-get breast cancer (no vs. yes)	31	91.2	33	97.1	0.50
<b>Symptoms of breast cancer</b>					
A lump in the breast is always breast cancer (no vs. yes)	31	91.2	31	91.2	1.00
If a lump does not hurt, it is not breast cancer (no vs. yes)	30	88.2	33	97.1	0.38
A woman can have breast cancer and not have any signs or symptoms (yes vs. no)	33	97.1	32	94.1	1.00
<b>Early detection of breast cancer</b>					
A mammogram is a blood test for breast cancer (no vs. yes)	32	94.1	34	100	
If a woman had a mammogram once, she does not need to have a mammogram done again (no vs. yes)	31	91.2	33	97.1	0.63
What age should you start getting mammograms? (choice=40 years)?	13	38.2	17	50.0	0.34
What is the best way-detect breast cancer (choice=mammography or mammogram)?	32	94.1	34	100	

**A quantitative bias analysis of tuberculosis diagnostic tests among a national sample of people living with and without HIV in South Africa** Emma Kileel\* Emma Kileel Alana T Brennan Matthew P Fox Jacob Bor Leslie Scott Helen E Jenkins Robert C Horsburgh Karen R Jacobson Kamy Chetty Koleka Milsana Wendy Stevens

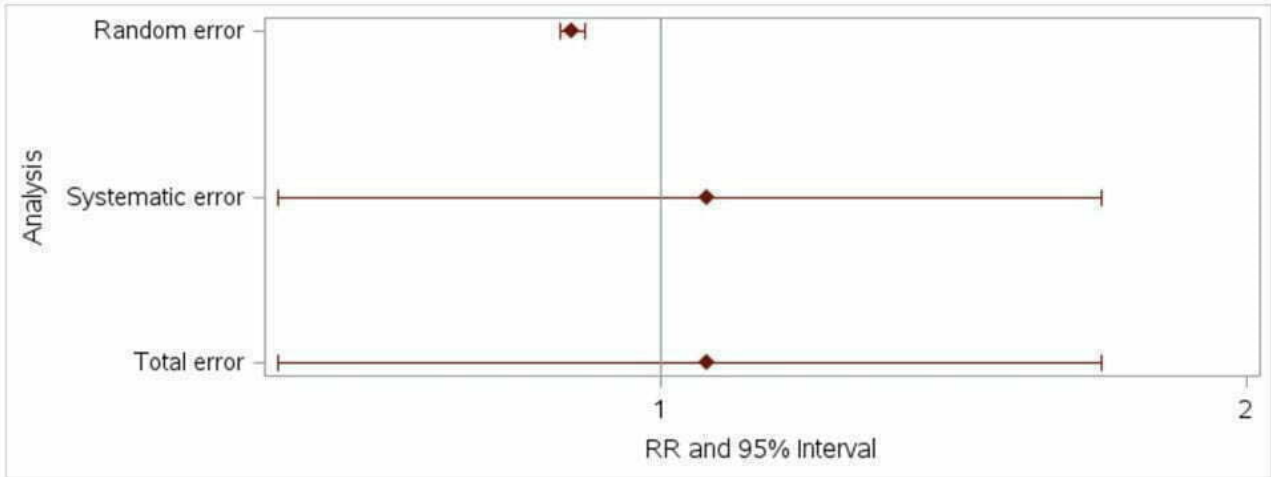
**Background:** While commonly used to diagnose tuberculosis (TB) in South Africa, sputum smear microscopy and GeneXpert (Xpert) tests have low sensitivity and may have poorer performance among people with HIV (PWH). Using data from South Africa's National Health Laboratory Service National HIV Cohort, we conducted a quantitative bias analysis adjusting for outcome misclassification to estimate the risk of TB diagnosis among adults age  $\geq 16$  years by HIV status.

**Methods:** Data from patients with a) smear+culture or b) Xpert+culture diagnostic tests between 2011-2018 were used as internal validation data (culture as gold standard) to estimate bias parameters by HIV status. Validation data were used to adjust the RR of TB diagnosis among adults with only smear or Xpert available for diagnosis. We specified beta distributions for sensitivity as: among PWH smear:  $\sim\text{beta}(1849,7494)$ , Xpert  $\sim\text{beta}(511,1485)$ ; among people without HIV (PWOH): smear  $\sim\text{beta}(4472,14196)$ , Xpert  $\sim\text{beta}(1002,2675)$ . Both tests had high specificity, therefore a uniform distribution of 0.95-0.99 was used. We ran 100,000 Monte-Carlo simulations, randomly sampling values of sensitivity and specificity from the distributions and using standard formulas to obtain an adjusted RR of TB diagnosis. Simulations accounting for random and systematic error were summarized using the median as the point estimate and the 2.5<sup>th</sup>-97.5<sup>th</sup> percentiles as the 95% simulation interval (SI).

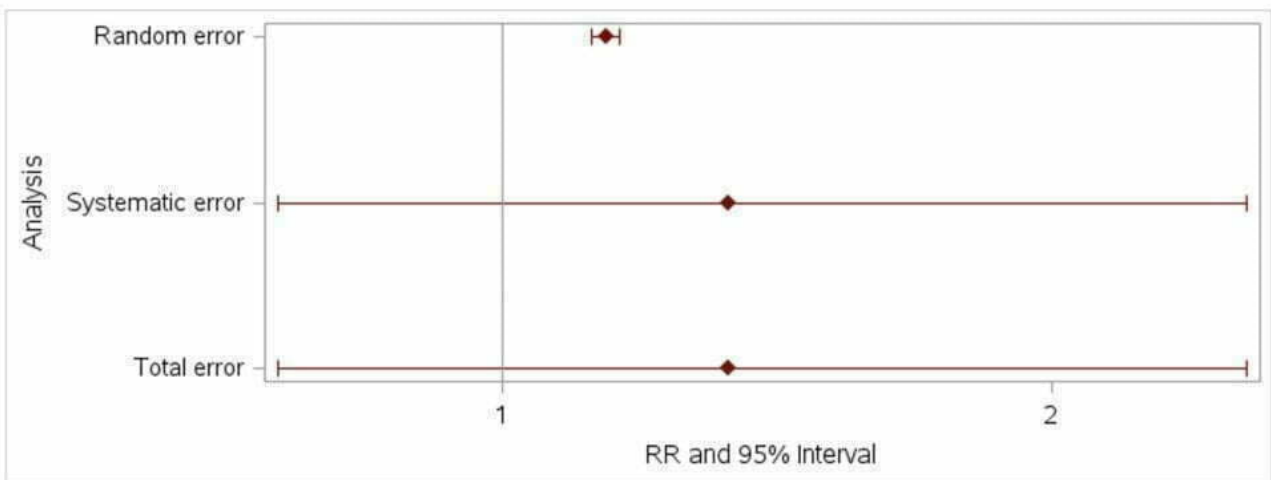
**Results:** Crude estimates showed PWH vs PWOH have a 10% decrease in risk of smear-diagnosed TB (RR: 0.90, 95% CI: 0.89-0.92) and a 13% increase in risk of Xpert-diagnosed TB (RR: 0.94, 95% CI: 0.92-0.96). Accounting for random and systematic error, the median adjusted RR using smear tests was 1.05 (95% SI: 0.64-1.69) and 1.33 (95% SI: 0.75-2.56) using Xpert tests (Figure).

**Conclusion:** PWH have higher rates of false negative smear and Xpert tests compared to PWOH, resulting in a greater risk of TB diagnosis when accounting for outcome misclassification.

### A) Smear



### B) GeneXpert



**Measuring disparities in the Hepatitis C care cascade among people who inject drugs in Ontario: a population-based retrospective cohort study** Zoë Greenwald\* Zoë Greenwald Jordan J Feld Dan Werb Peter C Austin Andrew Mendlowitz Daniel Fridman Sofia Bartlett Naveed Z Janjua Christina Greenaway Beate Sander Jeffrey C Kwong

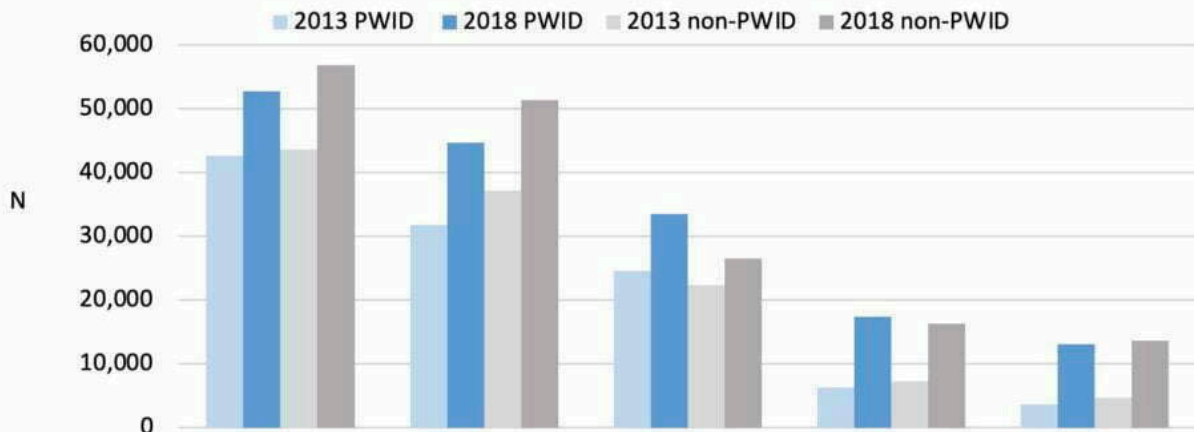
**Background:** In Canada, people who inject drugs (PWID) experience a high burden of hepatitis C virus (HCV) and disparities in care outcomes. We aim to estimate a population-level HCV care cascade among PWID in Ontario, Canada, before and after the introduction of direct-acting antiviral (DAA) HCV treatments.

**Methods:** We constructed a retrospective population-based HCV cohort by linking laboratory-documented HCV cases in Ontario from 1999-2018 to health administrative data. PWID were identified using a validated case-finding algorithm ( $\geq 1$  billing claim, emergency department visit or hospitalization for substance use). HCV care cascade stages included: HCV antibody diagnosed, HCV RNA tested, HCV RNA positive, treatment initiated, and sustained virologic response to treatment (SVR, i.e., HCV cure). HCV care cascades were compared descriptively by PWID status (any vs no indication) in the pre-DAA (up to Dec 31, 2013) and DAA eras (up to Dec 31, 2018). Deaths were censored from analyses.

**Results:** Among 109,509 Ontarians diagnosed with HCV in 2018, 48% were estimated to be PWID. PWID were younger (median 39 vs 48 years at diagnosis) and more often male (64% vs 56%) relative to non-PWID. HCV care cascade measures improved among PWID from 2013 to 2018 (**Figure 1**), including an increase in RNA testing (75% to 85% RNA tested among those HCV antibody+), doubling in treatment uptake (26% to 52% treated among those RNA+), and increase in HCV cure (58% to 75% SVR post-treatment). However, PWID experienced lower rates of RNA testing, treatment, and cure relative to non-PWID in both the pre-DAA and DAA eras.

**Conclusion:** Despite overall improvements in the HCV care cascade in Ontario in the DAA era, disparities persist for PWID relative to non-PWID. Results are preliminary and upcoming analyses will focus on addressing missing data, identifying barriers to DAA treatment uptake, and exploring the potential for harm reduction interventions to address HCV care gaps for PWID.

**Figure 1: Ontario Hepatitis C care cascade stratified among those with any vs no indication of being a person who injects drugs and in the pre-DAA era (up to Dec 31, 2013) and DAA era (up to Dec 31, 2018)**



	Diagnosed HCV Ab+	RNA tested	RNA positive	Treated	Documented SVR
2013 PWID	42,613	31,770 (75%)	24,564 (77%)	6,281 (26%)	3,644 (58%)
2018 PWID	52,697	44,687 (85%)	33,444 (75%)	17,376 (52%)	13,086 (75%)
2013 non-PWID	43,649	37,154 (85%)	22,365 (60%)	7,268 (32%)	4,709 (65%)
2018 non-PWID	56,812	51,384 (90%)	26,529 (52%)	16,260 (61%)	13,645 (84%)

**Figure legend**

Percentages represent the proportion of individuals progressing from the prior cascade stage.

*Abbreviations:* PWID: people who inject drugs; HCV Hepatitis C virus; Ab+: antibody positive; SVR: sustained virologic response

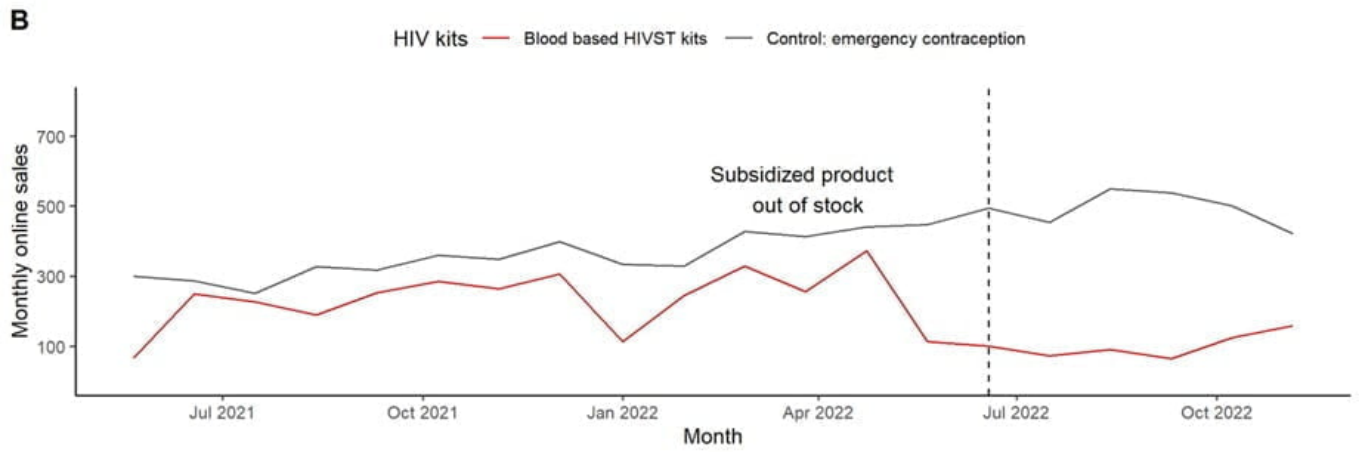
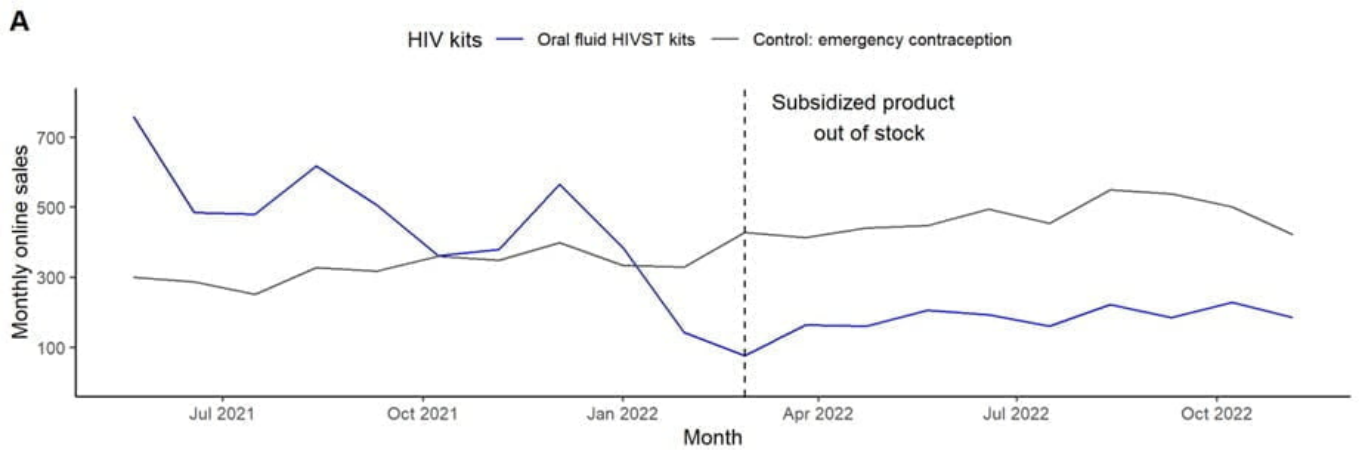
**Removal of a subsidy for HIV self-testing kits reduces online kit sales in Kenya** Carlos Culquichicon\* Carlos Culquichicon Obinna I. Ekwunife Maeve Rafferty Paulami Naik Nicky Nyamasyo Tony Wood Daniel Were Kenneth Ngure Melissa Mugambi Annie Haakenstand Katrina F. Ortblad

**Background:** HIV self-testing (HIVST) can enable individuals to learn their HIV status confidentially without fear of stigma, which may result in an earlier linkage to prevention or treatment interventions. To help increase HIVST access, international donors and nongovernmental organizations partnered to subsidize HIVST kits in 50 low-income countries. In Kenya, this subsidy started in 2019 and ended in 2021. To understand the impact of this subsidy removal on online HIVST kit sales in Kenya, we used controlled interrupted time series (cITS) methods, a quasi-experimental approach.

**Methods:** For our analysis, we used monthly sales data from MYDAWA, the first licensed fully online pharmacy in Kenya. During the subsidy period, both oral-fluid (OF) and blood-based (BB) HIVST kits were available via MYDAWA at 250 KES (~\$2.30 USD) per kit. On March 3, 2022, MYDAWA ran out of subsidized OF HIVST kits and the price for these kits rose to 470 KES (~\$4.30 USD); on May 25, 2022, the price of BB HIVST kits rose to 760 KES (~\$6.90 USD) for the same reason. We conducted a cITS analysis to understand the impact of the subsidy removal on online OF and BB HIVST kit sales via MYDAWA, using sales of an emergency contraceptive product as a control.

**Results:** From May 2021 to November 2022, we had 20 monthly time units of online sales data for HIVST kits and related products. For OF HIVST kits, we had 12 time units in the pre-subsidy and 8 time units in the post-subsidy period; for BB HIVST kits, we had 15 time units in the pre-subsidy and 5 time units in the post-subsidy period. When the subsidy was removed for OF HIVST kits, this reduced online monthly sales by 1.5-fold, with 357 fewer kits (95% CI 207-507) sold monthly compared to the control, **Fig. 1**. When the subsidy was removed for BB HIVST kit sales, this reduced monthly online sales by 27-fold, with 226 fewer kits (95% CI 83-369) sold monthly compared to the control.

**Conclusions:** Removal of a subsidy for HIVST kits significantly decreased the online sale of both OF and BB HIVST kits in Kenya, resulting in potential missed opportunities for early HIV detection and linkage to prevention and treatment services. This evidence suggests that subsidies are effective at increasing the demand for HIVST and should be considered to increase HIV testing in Kenya and similar settings.



**Initiation of dolutegravir versus efavirenz for first-line art on viral suppression and retention: a regression discontinuity design** Amy Zheng\* Amy Zheng Alana T. Brennan Matthew P. Fox Jacob Bor Willem DF Venter Mhairi Maskew

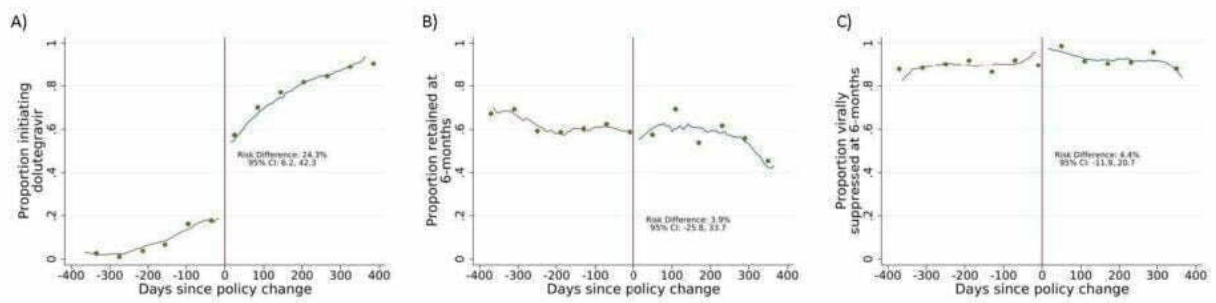
**Background:** In 2019, South Africa's Antiretroviral Therapy (ART) Treatment Guidelines replaced efavirenz with dolutegravir in first-line ART. We assessed the impact of this national guideline change on viral suppression and retention in the Themba Lethu Clinical Cohort, Johannesburg, South Africa.

**Methods:** We applied a regression discontinuity design in a prospective cohort study of 1908 adults living with HIV initiating first-line ART within 12 months ( $\pm 12$  months) of the guideline change. The unbiased mean square error-optimal bandwidth was used. We compared outcomes in individuals presenting just before and after the guideline changes using local linear regression and estimated intention-to-treat effects on initiation of a dolutegravir- vs efavirenz-based regimen. Primary outcomes were retention in care and viral load suppression (defined as viral load  $\leq 1000$  copies/mL) at 6 months ( $\pm 3$  months). Participants were considered retained if they had a visit within 3 months of the 6-month end-point.

**Results:** The 2019 guideline change led to an increase in uptake of dolutegravir; we noted a 24.3 percentage point increase in the proportion initiating dolutegravir (95% Confidence Interval (CI): 6.2-42.3; Figure 1). We saw a small increase in viral suppression (Risk Difference (RD): 4.4 percentage points; 95% CI: -11.9, 20.7) and in retention (RD: 3.9 percentage points; 95% CI: -25.8-33.7) at 6 months at with initiation of dolutegravir, though findings were imprecise (Figure 1).

**Conclusion:** Our estimates suggest early uptake of the revised treatment guidelines after implementation. For those initiating dolutegravir, retention in care and viral suppression at 6-months after ART initiation appears equal, if not better, compared to those on efavirenz. Our results are consistent with previous research supporting the use of dolutegravir as the preferred antiretroviral drug of choice in first-line ART in low- and middle-income settings.

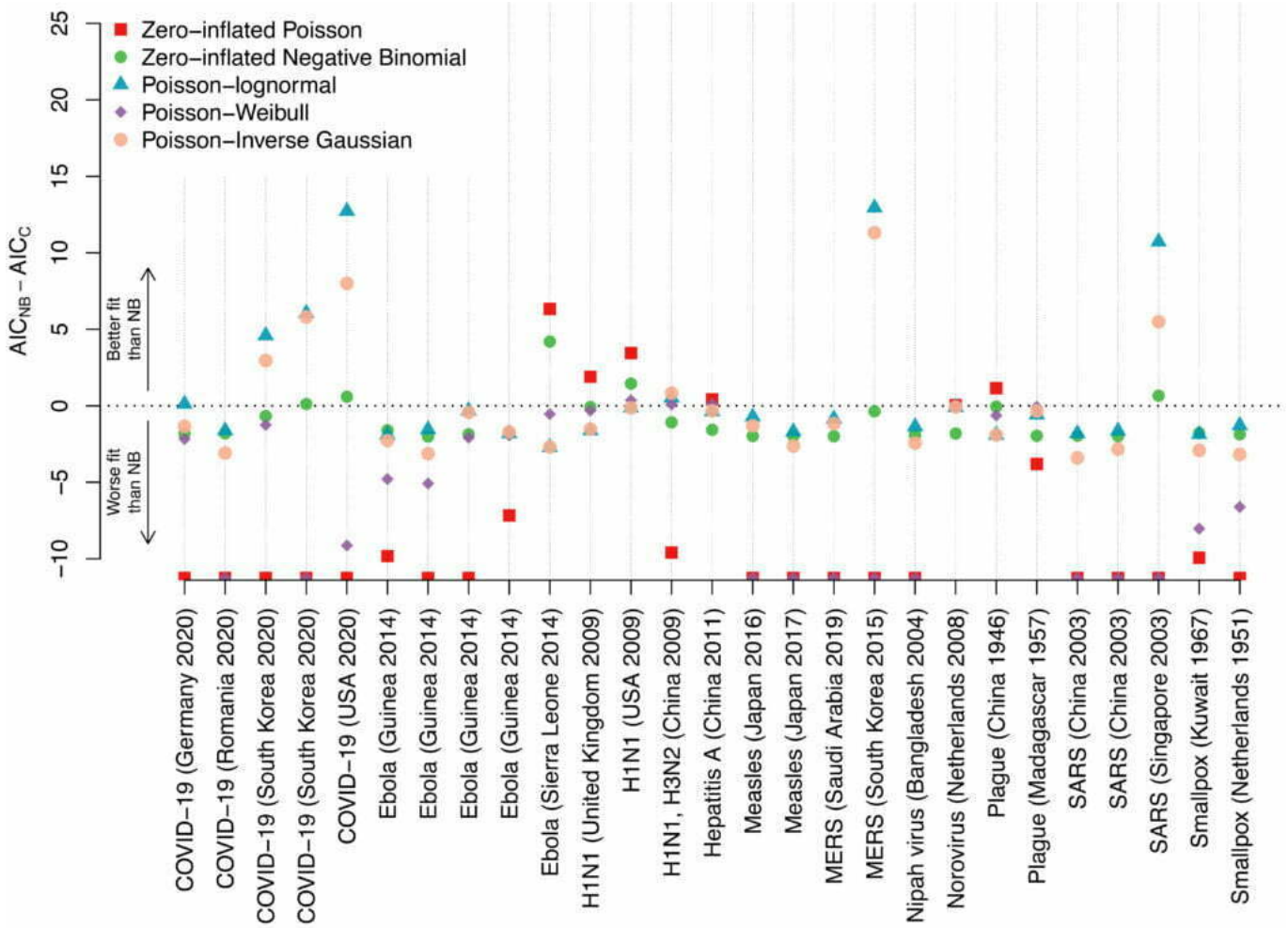




**Figure 1.** A) Probability of receiving dolutegravir as first-line ART among treatment-naïve clients receiving care at Themba Lethu Clinic, South Africa (N = 1908, Risk Difference (RD): 24.3%, 95% Confidence Interval (CI): 6.2, 42.3). The red line represents the trend on either side of the threshold. The unbiased MSERD (h) bandwidth of 115 was used. B) Proportion of clients who are lost to follow-up/dead at 6-months based on Definition 1 (RD: 3.9% 95% CI: -25.8, 21.7) C) Proportion of clients virally suppressed (Viral Load < 1000 copies/mL) at 6-months (RD: 4.4% 95% CI: -11.9, 20.7).

**Characterizing and comparing individual-level heterogeneity in transmission of infectious disease outbreaks** Jonathan P. Smith\* Jonathan Smith Charlene Jamie Miciano John M. Drake  
Juliana Taube Paige Miller Andrew N. Hill Sourya Shrestha

The shape and trajectory of an infectious disease outbreak varies widely between pathogens and populations. Thus, the accurate characterization of transmission dynamics is a fundamental aspect of public health programs seeking to optimize outbreak response. Prior work has shown that transmission of infectious pathogens feature substantial individual-level heterogeneity (“superspreading”). This phenomenon is generally characterized using a negative binomial distribution. However, it is unclear that this specific distributional assumption best captures the heterogeneity observed in transmission. Unfortunately, little epidemiologic work has quantitatively compared the NB to other distributions. We used individual-level data across various pathogens and populations obtained from a systematically collected database of infectious disease outbreaks (OutbreakTrees) with at least 25 total cases and more than one generation of spread. We compare the NB distribution to the following epidemiologically relevant distributions: zero-inflated Poisson (ZIP), zero-inflated NB (ZINB), Poisson-lognormal (PLN), Poisson-Weibull (PWB), and Poisson-Inverse Gaussian (PIG). Using a maximum likelihood framework, we fit outbreak data to candidate distributions and assessed model superiority using Akaike Information Criterion (AIC). We compared model fit with (1) the observed data and (2) when accounting for missing cases (via joint likelihood). A total of 27 outbreaks fit inclusion criteria. When modeling observed data, the NB was superior in 14/27 (52%) studies, followed by the PLN (6/27, 22%), ZIP (6/27, 22%), and PIG (1/27, 4%) (Figure 1). Results were similar when accounting for imperfect observation: 14/27 (52%) NB, 5/27 (19%) PLN, 4/27 (15%) ZIP, 4/27 (15%) PIG. These results suggest alternative distributions may be important to consider for programs seeking to characterize the trajectory of potential outbreaks and evaluate proposed prevention measures.



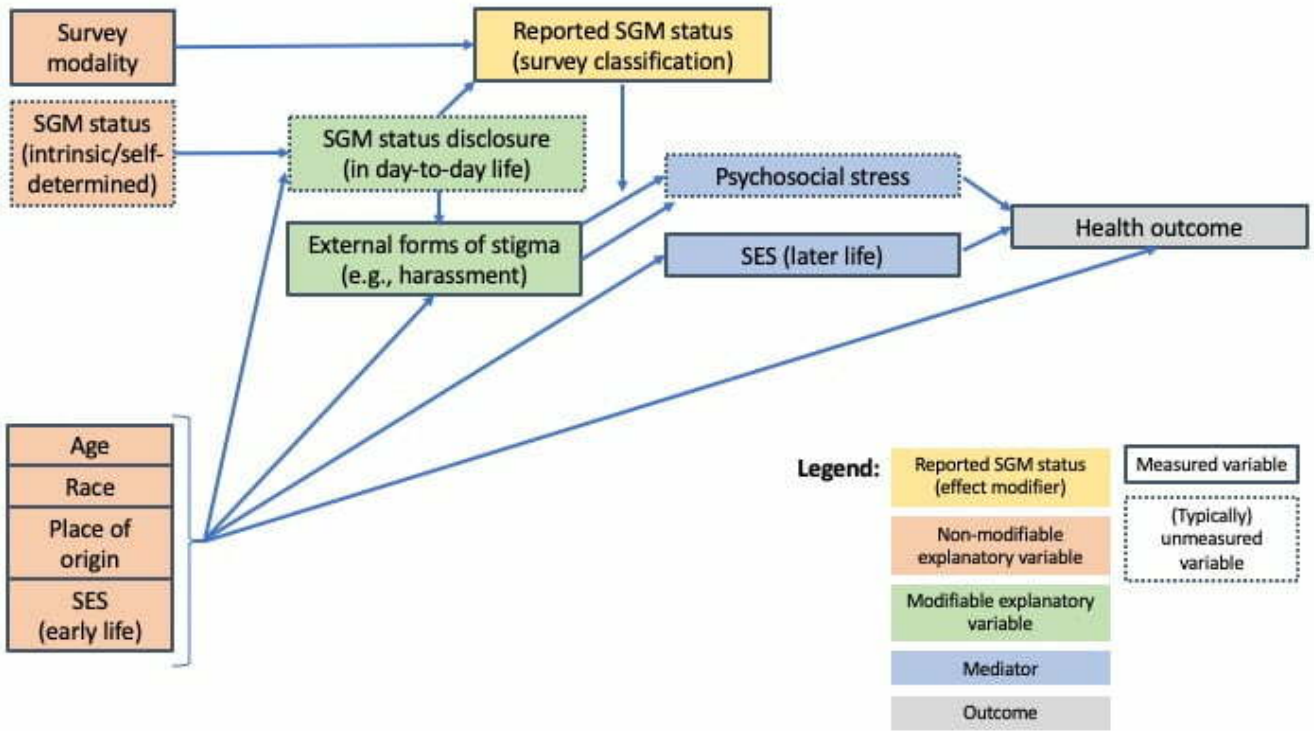
**Figure: Comparison of model fit across candidate distributions (observed data).** Model fit was evaluated using Akaike Information Criterion (AIC). Points resting on the x-axis have a difference in AIC below -10. NB, negative binomial distribution;  $AIC_{NB}$ , AIC of the negative binomial distribution;  $AIC_C$ , AIC of the candidate distribution; SARS, Severe Acute Respiratory Syndrome; MERS, Middle East Respiratory Syndrome; COVID-19, Coronavirus disease; Plague, pneumonic plague; USA, United States of America.

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

Social epidemiologists have debated how to apply directed acyclic graphs (DAGs) when studying non-modifiable variables like gender/sex and race. Similar quandaries are relevant but remain unaddressed in sexual and gender minority (SGM) epidemiological research. SGM status is intrinsic and self-determined. By contrast, proximate constructs like SGM status disclosure and experiences of minority stress are malleable and implicated in causal mechanisms investigated in SGM disparity research.

In this talk, we draw on recent empirical examples of SGM health research to consider ways in which SGM epidemiologists are employing DAGs as tools to strengthen causal inference. Integrating these examples, we then propose three solutions that SGM researchers can use when constructing DAGs or conceptual diagrams (**Figure**):

- Reported SGM status can be conceived as an imperfect proxy for day-to-day disclosure of SGM status, thereby susceptible to a form of information bias, determined by characteristics such as age, race, place of origin, and early life socioeconomic status (SES). This is notably influenced by modality of data collection, whereby SGM community surveys and self-completed questionnaires are less prone to information bias than general population or interviewer-collected surveys.
- External forms of stigma (e.g., harassment) can be conceived as ‘exposure’ variables of interest, given that these are modifiable through policies and campaigns to diminish structural or environmental stigma. SGM status (always imperfectly measured and unknowable to the researcher) is an antecedent component cause of this exposure but not a sufficient cause—in the same way racism (rather than race) is a fundamental cause of race-based health disparities.
- The effect of non-specific stigma on health may be modified by SGM status, given literature demonstrating that SGM identity (esp. bisexual, gay/lesbian) may potentiate the negative effects of stigma on health, which vary among SGM subgroups.



**Impact of availability of college education on later-life blood pressure distribution: An instrumental variable analysis of a natural experiment** Amanda Irish\* Amanda Irish Jillian Hebert Rita Hamad Fei Jiang Maria Glymour Anusha Vable

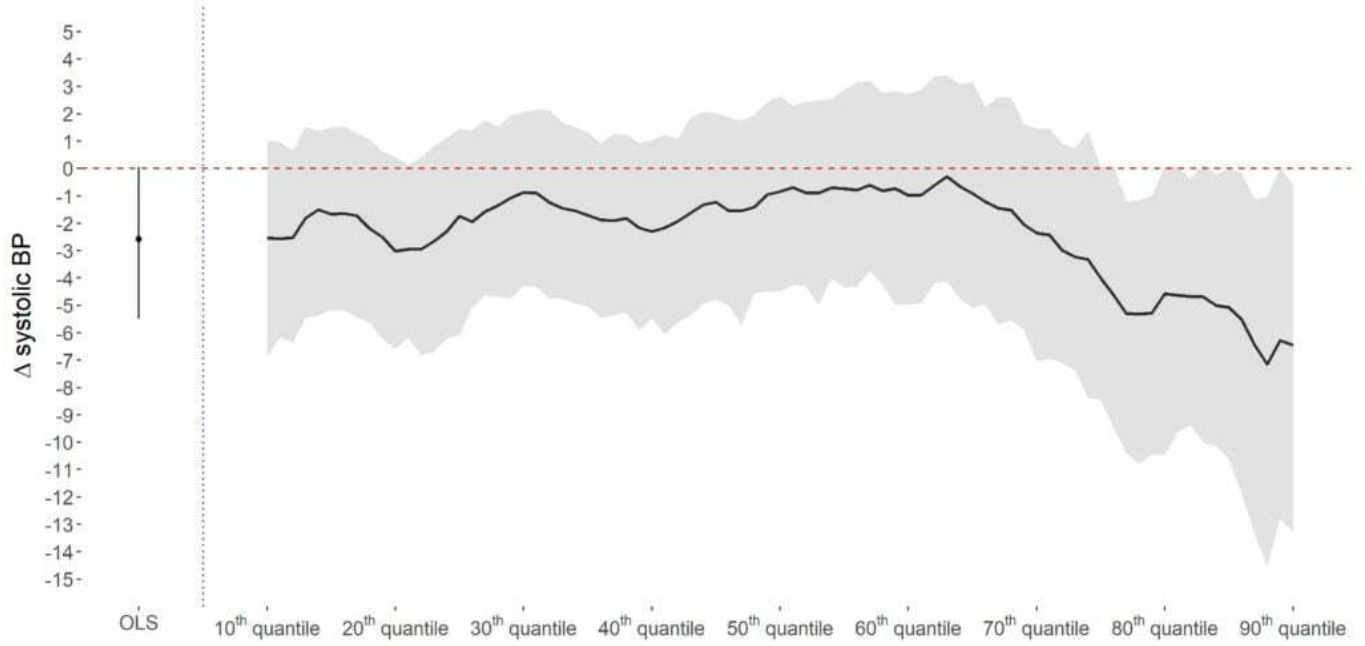
**Introduction.** More schooling predicts lower blood pressure in later life, but work thus far has focused on how education affects mean blood pressure rather than its distribution. Education may not affect blood pressure uniformly along its distribution, and because cardiovascular risk increases non-linearly with blood pressure, larger effects at higher blood pressure values would have larger public health effects. We leveraged a natural experiment, geographic variation in availability of postsecondary education in the US, to evaluate how education impacts later-life blood pressure at the 10th-90th quantiles of systolic and diastolic blood pressure (SBP, DBP).

**Methods.** Using U.S. Health and Retirement Study data (N = 6,224), we instrumented years of education with the number of 2- and 4-year colleges per county per year (when the respondent was about 18 years old) from 1940 to 1982. Outcomes were measured SBP and DBP (in millimeters of mercury, mmHg). Second stage models included ordinary least squares (OLS) and quantile regressions adjusted for individual- and state-level covariates.

**Results.** We confirmed that college availability was associated with educational attainment in the 1st stage of IV models (F-statistic 17.5). More education caused lower but imprecisely estimated mean blood pressure (SBP: -2.58 [95% CI: -5.49, 0.06]; DBP: -1.35 [95% CI: -3.28, 0.35]). Using unconditional quantile regressions, we found little relationship between education and SBP across most outcome quantiles; but a strong, protective relationship at higher quantiles (see figure). For DBP, the mean estimate was a reasonable approximation of effect estimates at all quantiles across the distribution.

**Conclusion.** More years of education resulted in lower SBP overall, with greater decreases at higher quantiles of the distribution. This suggests that interventions to increase availability to higher education could disproportionately benefit those at the highest risk for cardiovascular disease.

### Comparing results from mean models with results from estimator for quantiles of the marginal outcome distribution



**Measuring long-term disinvestment to understand firearm violence in Philadelphia, PA**

Jonathan Jay\* Jonathan Jay Manish Patel Kristal Xie Mudia Uzzi Maggi Price Sandro Galea

**Purpose:** Disinvestment from racially segregated areas has shaped the built environment of U.S. cities. Most disinvestment measures are based on acute physical disorder. However, long-term disinvestment influences the distribution of key assets (*e.g.*, tree canopy) and hazards (*e.g.*, abandoned properties). We developed a long-term, racialized disinvestment measure that encodes the association between present-day built environment and historical redlining. Validation included testing the measure as a predictor of firearm violence.

**Methods:** We joined 1937 Homeowners Loan Corporation (HOLC) redlining grades to a 500x500m grid in Philadelphia, PA. Units of analysis were grid squares in areas with HOLC grades (N = 5,436). For each square, we obtained an aerial image captured in 2019, then used deep learning to extract 256 image features, akin to latent variables. We used ridge models to regress HOLC grades on image features, predicting each 20% of locations based on the other 80%. Predicted HOLC grades served as long-term disinvestment scores.

To assess validity, we visually inspected imagery for relevant features. We tested correlation with actual HOLC grades and related variables, *i.e.*, census data on population density and racialized economic segregation and counts of trees, vacant properties, and off-premises alcohol outlets. Firearm outcomes were 2015-2021 counts of fatal or non-fatal shootings, which we analyzed with quasi-Poisson regressions.

**Results:** On visual inspection, predicted "A" scores showed high tree canopy; "D" scores showed high density of streets and buildings. Scores were correlated with actual HOLC grades ( $r = 0.61$ ,  $p < 0.001$ ) and all other related measures at  $p < 0.001$ , with magnitudes ranging from 0.18 to 0.40.

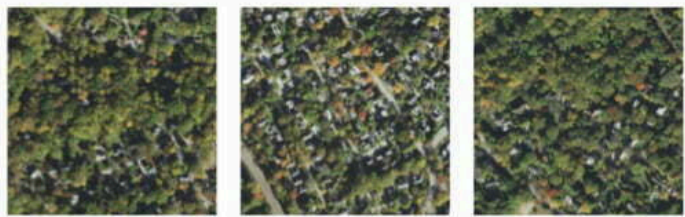
Scores predicted differences in shootings across all model specifications. In a bivariate model, a "D" score was associated with 47.4 times increased risk (95% CI [18.3, 185.0],  $p < 0.001$ ), compared to an "A" score. In a fully adjusted spatial model, we still found a strong association (IRR = 2.3, 95% CI [1.3, 4.1],  $p = 0.004$ ).

**Implications:** We showed that imagery, redlining data, and machine learning can be used to measure long-term disinvestment associated with historical racial segregation. This measure can help explain patterns in present-day firearm violence.



**Figure.** Sample study imagery and long-term disinvestment scores, reported as predicted HOLC grade.

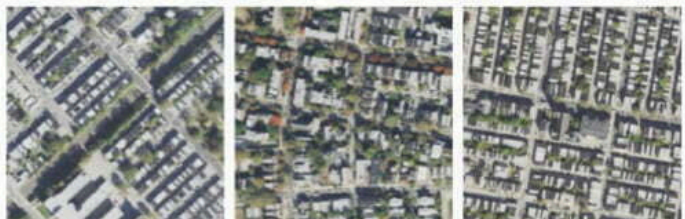
Predicted HOLC grade: **A**



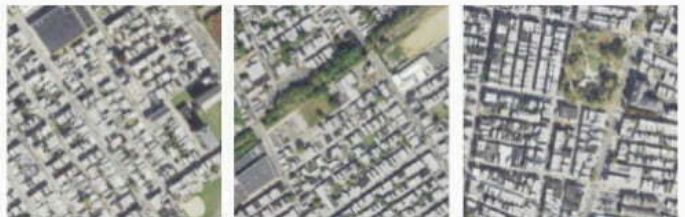
Predicted HOLC grade: **B**



Predicted HOLC grade: **C**



Predicted HOLC grade: **D**



*Notes.* "A" represented most favorable grade ("best"). "D" represented most unfavorable grade ("definitely declining," *i.e.* redlined).

**Confirmatory factor analysis to operationalize county-level structural racism exposure over the lifecourse** Joëlle Atere-Roberts\* Joëlle Atere-Roberts Taylor Hargrove Allison Aiello Chantel Martin

**Background:** Measurement and operationalization of structural racism (SR) are challenging given the complex and multifaceted societal domains involved. Furthermore, life course perspectives challenge us to examine SR as a dynamic exposure that can impact population health over time. Needed, then, are examinations of manifestations of SR across multiple societal domains over the life course.

**Methods:** Using longitudinal data on Black and White respondents in the National Longitudinal Study of Adolescent to Adult Health (n=10,404), we conducted confirmatory factor analysis (CFA) to specify a two-factor confirmatory factor model of 6 indicators of county-level SR during adolescence and young adulthood. Goodness-of-fit model statistics were evaluated for the final models using root mean square error of approximation (RMSEA), comparative fit index (CFI), and Standardized Root Mean Squared Residual (SRMR).

**Results:** The final model identified two strongly correlated latent constructs: “adolescent SR” and “young adulthood SR” (Figure 1). Five of the six indicators of the latent constructs reflecting SR were statistically significant at  $p < 0.001$  and the 5-item measurement model fit appropriately (RMSEA= 0.01, CFI=0.97, SRMR=0.05) The final model included factor scores for Black-White unemployment ratio, Black-White median household income ratio, Black-White Bachelor’s degree ratio, racial segregation, and racial & economic segregation.

**Discussion:** The development of theory-informed measures of SR is necessary to provide evidence of its harm to population health. These results represent the preliminary research necessary to derive such measures and make connections to health. We will expand on this study by examining associations between the latent constructs of adolescent and young adulthood SR and cardiometabolic health. Ultimately, this research can help advance population health research and guide health equity intervention efforts.



Figure 1. Standardized model coefficients and standard errors from confirmatory factor analysis for measurement of adolescent and young adulthood structural racism; n=10,404 National Longitudinal Study of Adolescent to Adult Health

## Policing/Incarceration

**Mass Probation: Effects of sentencing severity on mental health for Black and White****individuals** Katherine LeMasters\* Katherine LeMasters Rachael K. Ross Jessie K. Edwards Hedwig Lee Whitney R. Robinson Lauren Brinkley-Rubinstein Paul Delamater Brian Pence

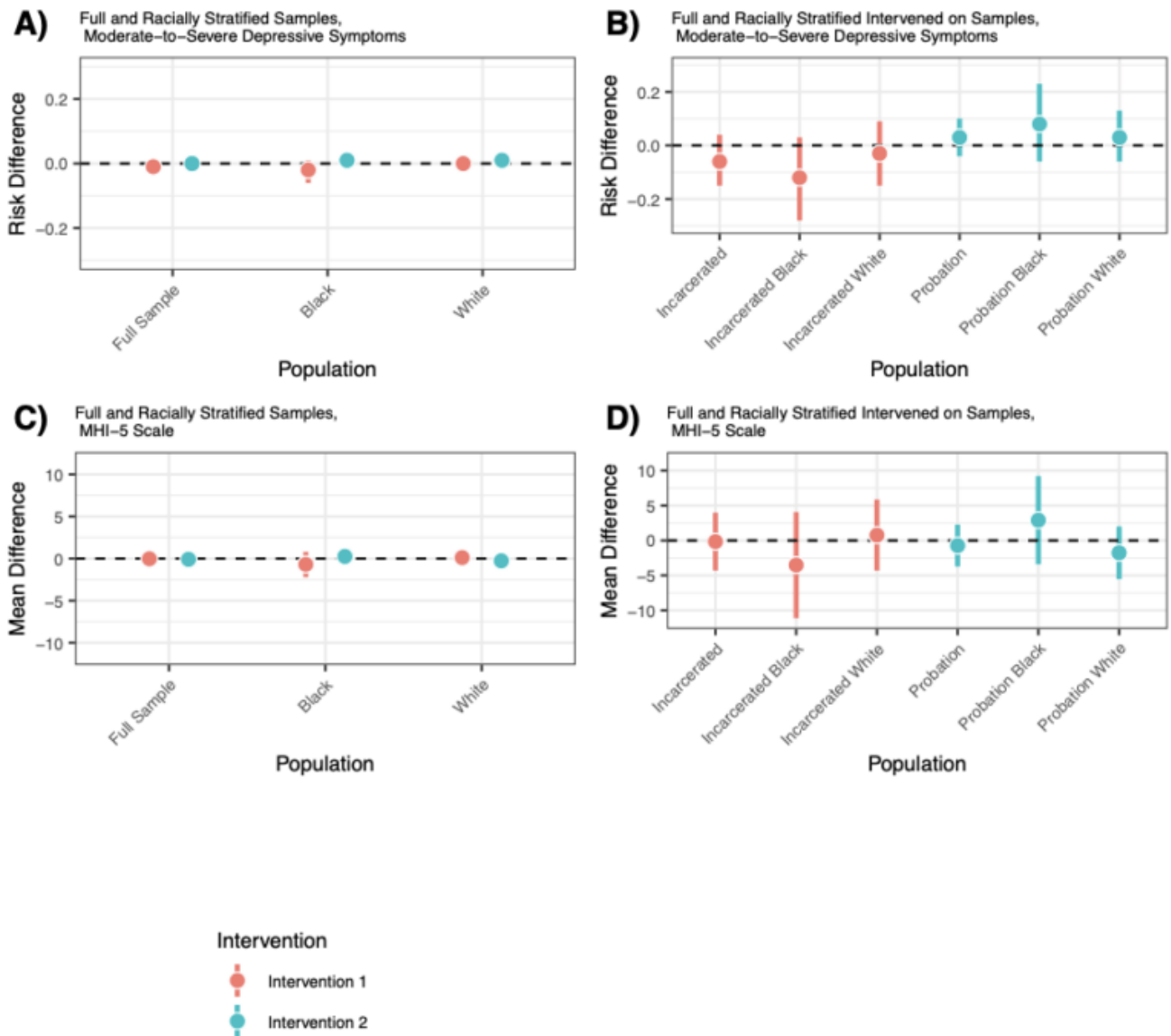
Incarceration negatively impacts mental health. Probation, a form of community supervision, has been lauded as an alternative. Yet, the effect of probation on mental health is unclear. Our objective was to estimate the impact on mental health of reducing sentencing severity at the first adult criminal-legal encounter.

We used the National Longitudinal Survey on Youth 1997, a nationally representative dataset of youth followed into their mid-thirties. Restricting to those with an adult encounter (arrest, charge alone/no sentence, probation, incarceration), we used parametric g-computation to estimate the difference in mental health at age 30 (Mental Health Inventory-5) if (1) everyone who received incarceration for their first encounter had received probation and (2) everyone who received probation had received no sentence.

Among 1,886 individuals with adult encounters, 19% were Black and 65% were White. Median age at first encounter was 20. Under hypothetical interventions to reduce sentencing, we did not see better mental health at the population level (Intervention 1, incarceration to probation: RD: -0.01; CI: -0.03, 0.01; Intervention 2, probation to no sentence: RD: 0.00; CI: 0.00, 0.01). When estimating the impact among those whose sentence was reduced under intervention, we saw the strongest potential signals for Black individuals: reduced mental health symptoms among those receiving Intervention 1 (RD: -0.12; 95% CI: -0.28, 0.03) and worsened symptoms for those receiving Intervention 2 (RD: 0.08; 95% CI: -0.06, 0.23) (**Figure 1**).

Among those with criminal-legal encounters, hypothetical interventions to reduce sentencing did not improve mental health overall; there may be slight benefits to receiving probation versus incarceration and to receiving probation versus no sentence for Black individuals. As incremental sentencing reductions did not improve mental health, we should consider preventing individuals' first criminal-legal encounter to see stronger effects.

**Figure 1:** Hypothetical Intervention Effects for Changing First Adult Criminal Legal Encounter Level on Risk of Poor Mental Health by Age 30, Those Experiencing Adult Criminal Legal Encounters (N=1,886), NLSY97<sup>a,b,c,d</sup>



<sup>a</sup> Weighted to account for sampling design

<sup>b</sup> Results standardized by race, sex at birth, parental education, juvenile criminal-legal encounter, education, employment, marital status, child, health, drug use, reported crime, stressful life event, region, county percent Black, county poverty rate, county unemployment rate, county mental health shortage, county rurality, county incarceration rate, county violent crime rate

<sup>c</sup> Vertical line at null value of 0

<sup>d</sup> Intervention 1: if everyone who received incarceration had instead received probation; Intervention 2: if everyone who received probation had instead received no sentence (a charge or conviction alone)

**Impact of Medicaid Expansion on Homicide, Opioid Overdose, and Suicide Death Rates among Formerly Incarcerated Persons in Rhode Island from 2009-2018** Pasangi S. Perera\*

Pasangi Perera Vanessa E. Miller Kate Vinita Fitch Monica E. Swilley-Martinez David L. Rosen Lauren Brinkley-Rubinstein Brian W. Pence Brandon Marshall Andrew L. Kavee Shabbar I. Ranapurwala

**Background:** Medicaid expansion, implemented in 2014 by various states within the United States (US) increased health care access for vulnerable populations including formerly incarcerated persons (FIPs) who experience high post-release mortality. We assessed the effect of Medicaid expansion on post-release deaths from all causes, and separately for deaths due to opioid overdose, suicide, and homicide among FIPs in Rhode Island (RI), which expanded Medicaid, compared to North Carolina (NC), which did not expand Medicaid.

**Methods/ Approach:** Individual prison release data for FIPs ages 18 and over from 2009-2018 were linked to RI and NC death records. Deaths for opioid overdose, homicide, and suicide were coded using ICD-10 codes. We conducted controlled interrupted time series using autoregressive integrated moving average models for 274,132 FIP releases to measure the effect of Medicaid expansion on quarterly all-cause mortality and opioid overdose death rates, and yearly homicide and suicide death rates between RI and NC.

**Results:** Compared to no expansion in NC, all-cause mortality among FIPs in RI declined 67.3/10,000 person-years (10K PY) (95% CI: -148.1,13.5) in the quarter immediately after Medicaid expansion, and further declined [ 16.3/10K PY (-23.4,-9.4)] each quarter thereafter until 2018. Opioid overdose death rates declined immediately by -62.3 (-121.4,-3.14) and thereafter by -12.3 (-17.5,-7.2); suicide death rates declined immediately by -14.7 (-37.6,8.2) and thereafter by -2.7 (-10.6,5.1); and homicide death rates did not change immediately, but declined thereafter by -12.6 (-18.2,-6.1).

**Conclusions:** This study detected immediate and sustained decreases in all-cause mortality, death by opioid overdose, and suicide, and sustained decreases in homicides among RI FIPs relative to NC FIPs. These findings demonstrate the benefit of Medicaid expansion to reduce post-release mortality among FIPs.

**State-Level Firearm Laws and Firearm Homicide in United States Cities: Heterogenous Associations by City-Level Characteristics** Ben Spoer\* Byoungjun Kim Lorna Thorpe Ben R. Spoer Andrea Titus Julian Santaella-Tenorio Magdalena Cerdá Marc N. Gourevitch Ellicott C. Matthay

**Background:** Little is known about the associations of state-level firearm laws with city-level firearm homicide rates or how associations vary depending on the type of laws and city characteristics. We examined the associations of 5 categories of state-level firearm laws related to buyers, dealers, domestic violence, gun type/trafficking, and possession with city-level firearm homicide, including differential associations by city socioeconomic contextual factors. We focused on contextual factors for which links with firearm homicide are well-established: poverty, unemployment, vacant housing, and income inequality.

**Methods:** We analyzed hierarchical panel data on 78 cities nested within 33 states from 2010 to 2020. Using linear regression, we modeled the log-transformed firearm homicide rate as a function of the firearm law categories, city and year fixed effects, and time-varying city-level potential confounders. We considered effect measure modification by four city-level socioeconomic contextual factors with established links to firearm homicide: poverty, unemployment, vacant housing units, and income inequality.

**Results:** A one standard deviation increase in state gun type/trafficking, possession, and dealer provisions were associated with 27% (95% CI: -0.39, -0.13), 18% (-0.29, -0.06), and 15% (-0.27, -0.02) lower city firearm homicide rates, respectively. Associations were smaller in magnitude in cities with higher unemployment and larger in cities with high income inequality.

**Conclusions:** State adoption of a greater number of gun type/trafficking, possession, and dealer provisions was associated with lower city-level rates of firearm homicide, but provisions related to buyers and domestic violence were not. Firearm laws may have differential effects on firearm homicides based on socioeconomic contextual factors. Understanding these differences may help inform allocation of prevention resources, particularly in cities where state firearm laws may be less effective.

**Short- and Long-Term Associations Between City-Level Government Spending and Youth Violence Perpetration** Veronica Pear\* Veronica Pear Julia Lund Tiffani Johnson Katherine Keyes  
Garen Wintemute Shani Buggs

Sustained, meaningful reductions in violence require addressing its root causes, which are themselves shaped by structural and sociohistorical forces. This study examined city-level government spending on public goods and services as a potentially modifiable structural determinant of youth violence in the US.

This was a time series study of 113 cities in 38 states, 1999-2017. We used standardized city-level spending data from the Lincoln Institute of Land Policy to account for differences in how overlaying governmental units allocate fiscal responsibilities. City spending was measured annually per capita and categorized by domain into policing, education, health, public welfare, parks & recreation, and housing & community development. Youth violence was measured as the annual count of arrests for aggravated assault or homicide among people aged 10-24, as measured in the Uniform Crime Reporting data. We examined short- and long-term associations (with lags of 0-10 years) for each spending category using unconstrained distributed lag Poisson models with city fixed effects, adjusting for year and the other (lagged) spending categories.

Within cities, mean per capita spending ranged from \$167 on parks & recreation to \$1,952 on education. Modest reductions in youth violence were associated with each \$25 increase in past 1-year spending on housing & community development (RR: 0.98, 95% CI: 0.96, 0.99) and parks & recreation (RR: 0.98, 95% CI: 0.96, 0.99) as well as past 10-year spending on education (RR: 0.993, 95% CI: 0.987, 0.999). Spending on parks & recreation and education were also cumulatively associated with reduced violence over 10 years (parks, RR: 0.91, 95% CI: 0.86, 0.97; education, RR: 0.98, 95% CI: 0.97, 0.99). Spending on policing, health, and welfare was not associated with youth violence.

City investment in parks & recreation, education, and housing & community development may yield both short- and long-term reductions in youth violence perpetration.



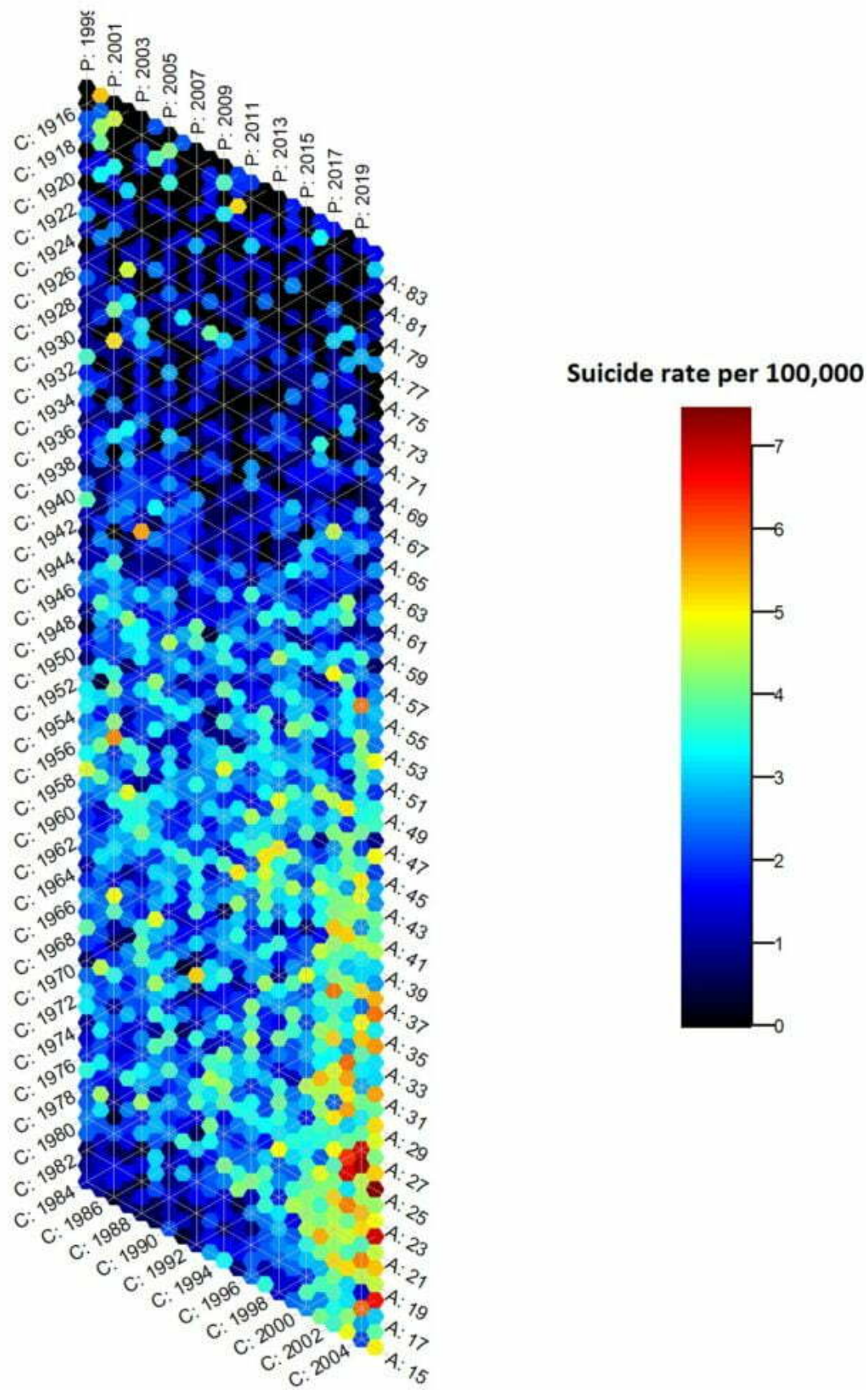
**Cannabis Use and Homicide Victimization: Case-Control Analysis Using Data Fusion and Machine Learning Techniques and Multiple National Data Systems** Guohua Li\* Guohua Li  
Hun Lee Stanford Chihuri Qixuan Chen

With more states legalizing cannabis use, the prevalence of cannabis detected in homicide victims has doubled in the past decade. Toxicological testing results indicate that about one-third of homicide victims were positive for cannabis. Although cannabis use has been causally linked to violence, the association between cannabis use and homicide victimization has not been rigorously assessed through analytical epidemiologic studies. We performed a case-control analysis using data fusion and machine learning techniques and three national data systems: the National Violent Death Reporting System (NVDRS), the National Roadside Survey of Alcohol and Drug Use by Drivers (NRS), and the National Survey on Drug Use and Health (NSDUH). Cases were homicide victims aged 16 years and older selected from the NVDRS and controls were participants aged 16 years and older in the NRS and the NSDUH. Weighted multivariable logistic regression models revealed that marijuana use was associated with over 3-fold increased odds of homicide victimization [adjusted odds ratio (OR) 3.49, 95% confidence interval (CI) 2.70 — 4.52] if NRS participants were used as controls; OR 3.66, 95% CI 2.77 — 4.55 if NSDUH participants were used as controls]. Alcohol use and demographic characteristics (Black race, male sex, 21-34 years of age, and less than high school education) were also associated with significantly increased odds of homicide victimization. Results of this study demonstrate that data fusion and machine learning techniques could be used to harness the power of existing national data systems for addressing questions of public health importance and that cannabis use is a major risk factor for homicide victimization.

**Epidemiology of suicide among Black women 15-84 in the U.S., 1999-2020** Victoria Joseph\*

Victoria Joseph Katherine Keyes Gonzalo Martinez-Ales

**Objectives:** Recent increases in suicide disproportionately affected Black women; our objective was to clarify the epidemiology of suicide among Black girls and women, by estimating age-period-cohort effects on suicide rates among decedents coded as female aged 15-84 in the U.S., including trends by state and census region from 1999-2020. **Methods:** Deaths coded as X60-X84, Y87.0 according to ICD-10 were included based on vital records. Analyses included individuals classified as Black or African American and female aged 15-84. Suicide rates by age, period, and cohort were visualized using hexagonal maps, and estimated using modified Poisson regression to address identifiability. Suicide rates by U.S. state and census region were also assessed. **Results:** In total across all years, our analysis included 9,271 suicide deaths. From 1999 to 2020, suicide rates among Black females increased from 2.1 to 3.4 per 100,000. Rate increases were concentrated among those aged 15-24, increasing from 1.9 to 4.9 per 100,000. Results indicated the presence of all three effects: (i) a clear age effect, with higher rates at younger ages and lower rates at older ages, regardless of cohort and time, (ii) compared with 2010, the period effect in suicide was 1.5 times higher in 2020, and (iii) a cohort effect, with suicide rates concentrated among females born after 2002. Across regions, rates were highest among 15-24- and 25-34-year-olds with highest rates in the West of the U.S. (4.4 to 4.8 per 100,000). **Conclusion:** Findings indicate strong age, period, and cohort effects: suicide is increasing rapidly among Black females - with particularly concerning trends among the youngest Black females born in most recent birth cohorts. In addition, there is state and regional variation with high rates concentrated in the West, pointing to the need for regionally targeted prevention efforts. Future research should consider trends among different ethnicities and gender identities.



**Look both ways before you case-crossover: examining the impact of control selection in car crash epidemiology** Adam Palayew\* Adam Palayew Stephen J Mooney James A Hanley Sam Harper

Background: The case-crossover design is commonly used to study traffic crash risks associated with specific holidays. In this design, incidence of an outcome on a day of concern (the exposure day) and is compared with incidence on two comparison days: typically one 7 days before and one seven days after. In principle, this design controls by design for both day of the week and seasonality. However, it relies on the assumption that the control days represent the incidence that would have been observed had the exposure day not been a holiday, and not all days are created equal. Notably, the Christmas holiday (December 25<sup>th</sup>) is always exactly one week before the New Year's holiday (January 1). We examined sensitivity of estimates of the change in risk on Christmas to the selection of control dates.

Methods: We analyzed data in the Fatality Analysis Reporting System dataset from 1974-2019 applying a -7/+7 day case-crossover design to estimate change in incidence due to the Christmas holiday. We then calculated a parallel estimate and standard error using two extra control days that were -14/+14 from Christmas. Finally, we used a negative binomial regression controlling for day of the week (a known confounder).

Results: Using the -7/+7 comparison days, Christmas Day had an RR of 0.83 95%CI(0.70,0.93). When applying the 2 extra comparison days of -14/+14 the point estimate was modestly attenuated 0.85 95%CI(0.74,0.98). Finally, when comparing the day of concern to all other (same day of week) of that year we found that Christmas had an RR of 1.15 95%CI(1.01,1.33) (Figure).

Conclusion: The -7/+7 point estimate is sensitive to changing the control period. It should be kept in mind that, when temporality is a non-negligible factor, control selection should take this into account with different approaches required for specific questions. It is important to remember to look both ways (and not just nearby) before you case crossover.

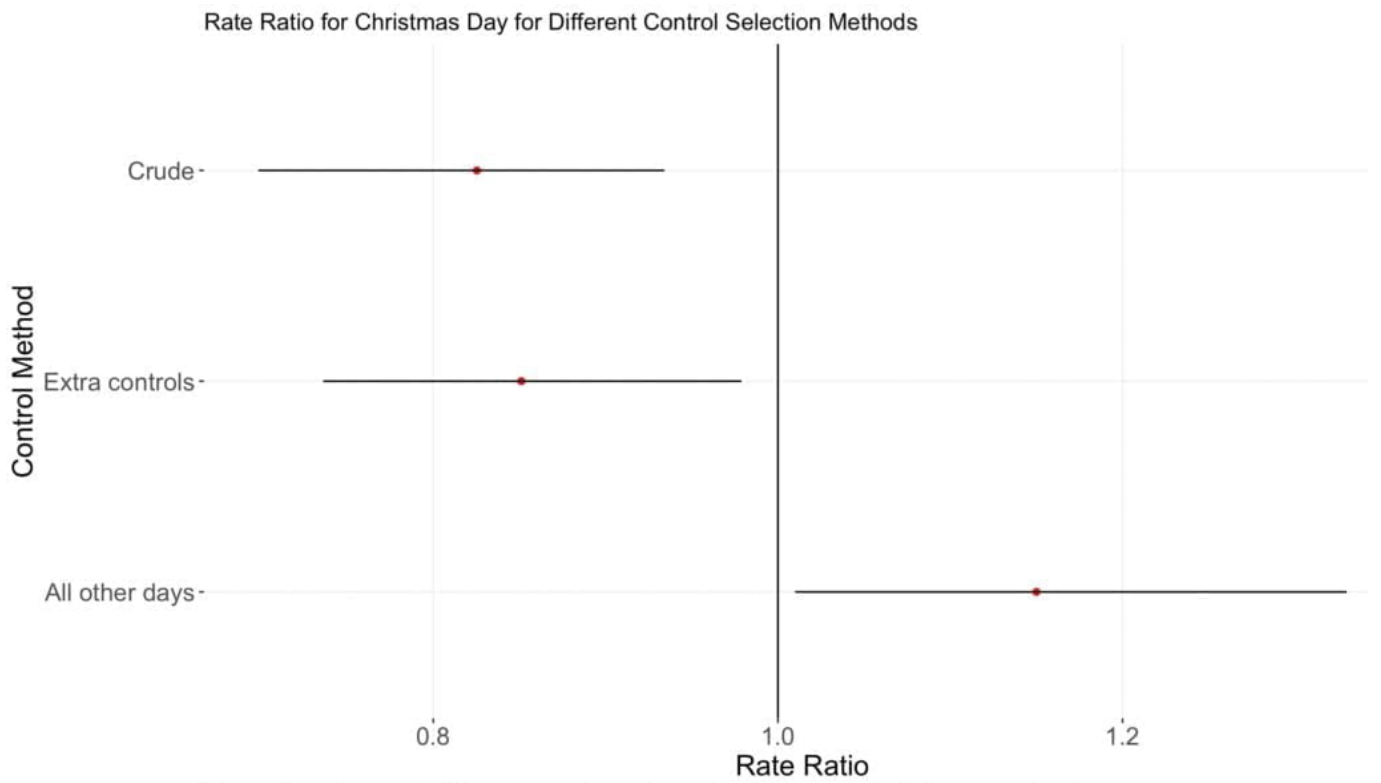


Figure: The rate ratio for different scenarios to determine whether or not Christmas is a day of concern. Point estimates are rate ratios from Negative Binomial regression with 95%CI calculated using robust standard errors.

**Accounting for recent injuries in the relationship between physical activity and injury risk: checking for time-dependent confounding using the parametric g-formula** Chinchin Wang\*  
Chinchin Wang Russell J. Steele Jay S. Kaufman Niels Wedderkopp Ian Shrier

**Background:** Sudden large increases in physical activity are believed to increase injury risk, which may affect subsequent activity. Improper adjustment for these relationships may create bias when assessing the causal effect of activity on injury.

**Objective:** Examine the effect of increasing activity on injury risk and assess the importance of controlling for recent injury as a time-varying covariate using the parametric g-formula.

**Methods:** We used weekly data from 1670 schoolchildren collected over 5.5 years. Our outcome was current injury, defined as new symptoms of pain in the current week. We applied generalized linear mixed models to model the risk of current injury as a function of current activity, adjusted for average activity over the previous 4 weeks, sex, age and school. We controlled for recent injury, defined as any new or recurring pain symptoms in the previous 4 weeks, by: 1) regression adjustment, where recent injury was included in the model; and 2) parametric g-formula, where recent injury was predicted as a function of previous activity and covariates, and current injury was modelled as a function of current and previous activity, predicted value of recent injury and covariates. We calculated injury risk ratios comparing populations where everyone tripled or doubled their activity relative to their previous activity, with one where activity remained unchanged relative to previous activity. We estimated 95% CIs by bootstrap.

**Results:** Using the g-formula, a tripling of activity was associated with an injury RR of 1.75 (95% CI: 1.71, 1.80) relative to no change in activity, while a doubling of activity was associated with an injury RR of 1.32 (1.29, 1.36). Results did not differ using standard regression adjustment.

**Conclusion:** Large increases in physical activity are associated with increased risk of new injury, regardless of whether one had a recent injury. Results did not differ whether recent injury was treated as affected by previous activity or not.

**Delayed high school start times impact depression symptoms: heterogeneous effects in a natural experiment** Ekaterina Sadikova\* Ekaterina Sadikova Rachel Widome Elise Robinson Izzuddin M. Aris Henning Tiemeier

### Background

Initiatives to delay high school start times prolong weekday sleep. However, it is not clear if longer sleep alleviates depression symptoms and if the impact is homogeneous across adolescents.

### Methods

Leveraging a natural experiment design, we examined the effect of a start time delay policy on the Kandel-Davies depression symptom scores in 2134 high school students (mean age  $15.15 \pm 0.35$  years) from the Minneapolis metro area. Using the policy as an instrument, we estimated the impact of a sustained gain in weekday sleep on depressed mood. We used SuperLearner prediction and hierarchical *tmle* to detect if the policy's effect is heterogeneous and to evaluate if optimizing the delay's implementation to subgroups that benefit most results in lower depression symptoms relative to random or universal implementation.

### Results

The delay policy reduced overall depression symptoms at 1 year (-1.98 points, 95%CI [-3.43,-0.53]) but not 2 years (-0.12 points, 95%CI [-0.27,0.03]) of follow-up. A sustained 1-hour gain in weekday sleep decreased overall depression symptoms by 1.18, 95%CI [-1.19,-1.16] points over 2 years. Motivation and sleep-related symptoms were most strongly affected. The impact of the delay was heterogeneous for low mood, hopelessness, and worry symptoms, with an expected reduction of 1.26 points, 95%CI [-1.93,-0.59] under optimal vs random delay implementation. Allowance for longer weekday morning sleep was particularly efficacious for older students with higher BMI and greater daily screen use, but optimization did not yield benefit relative to universal implementation (-0.13 points, 95%CI [-0.79,0.53]).

### Conclusion

High school start time delay is likely to universally decrease motivation and sleep-related symptoms of depression in adolescents. Students who benefit most with respect to low mood, hopelessness, and worry are older, heavier, and spend more time on screens.

**Effectiveness of mHealth consultation services for preventing postpartum depressive symptoms: a randomized controlled trial** Yuki Arakawa\* Yuki Arakawa Maho Haseda Kosuke Inoue Daisuke Nishioka Shiho Kino Daisuke Nishi Hideki Hashimoto Naoki Kondo

**Background:** Although many conventional healthcare services to prevent postpartum depression are provided face-to-face, physical and psychosocial barriers exist. These barriers may be overcome by using mobile health services—mHealth. Therefore, we examined the effectiveness of mHealth consultation services in preventing postpartum depressive symptoms in Yokohama, Japan, where universal free face-to-face perinatal care is available.

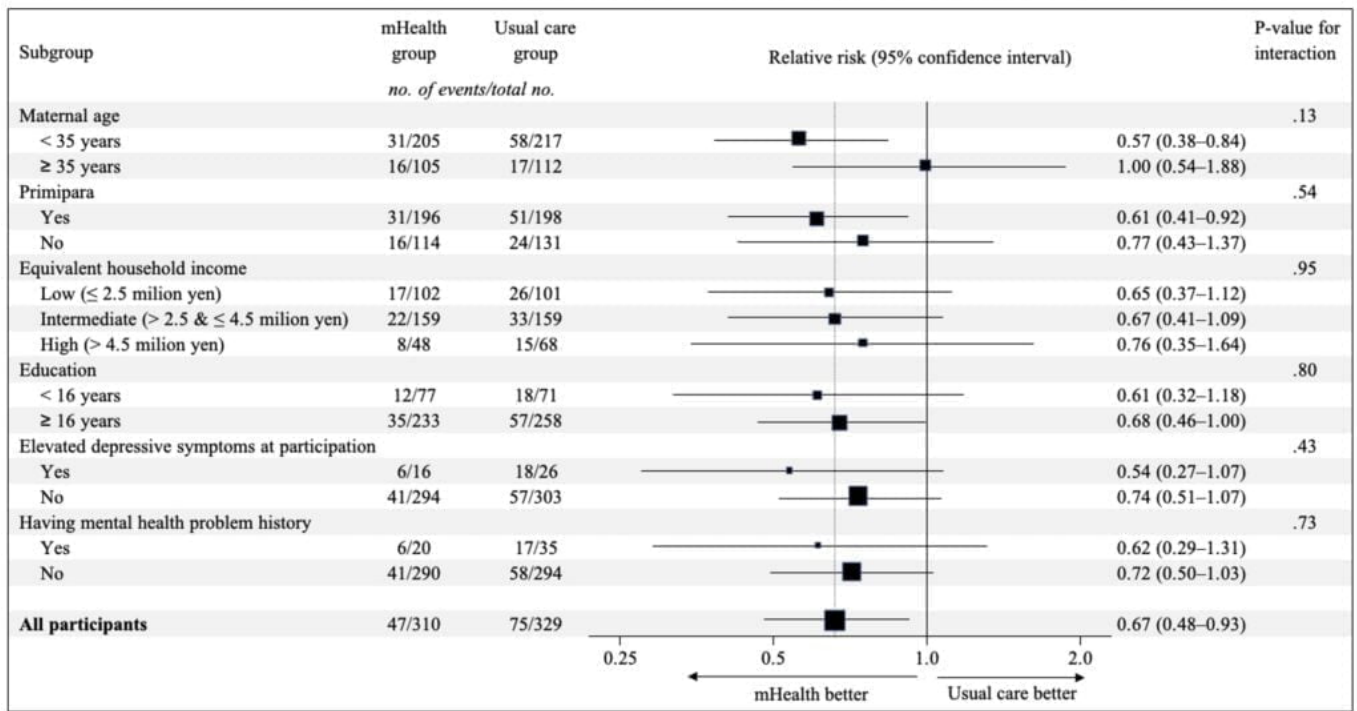
**Methods:** We conducted a randomized controlled trial to compare the mHealth group, where perinatal women could consult with gynecologists/obstetricians, pediatricians, and midwives, with the usual care group. The primary outcome was the risk of elevated postpartum depressive symptoms (Edinburgh Postnatal Depression Scale score  $\geq 9$ ). Secondary outcomes were self-efficacy, loneliness, and perceived barriers to healthcare access. All outcomes were collected using a self-reported online questionnaire three months post-delivery. Modified Poisson regression models were employed to estimate the treatment effect among the overall study sample and subgroups defined by demographic characteristics.

**Findings:** Of the 734 women, 365 and 369 were assigned to the mHealth and usual care group, respectively. Most ( $n = 639$ ) women completed all questionnaires. Compared to the usual care group, women in the mHealth group had a lower risk of elevated postpartum depressive symptoms three months post-delivery (47/310 [15.2%] vs. 75/329 [22.8%], risk ratio: 0.67 [95% confidence interval: 0.48-0.93]). Furthermore, women in the mHealth group displayed higher self-efficacy, less loneliness, and lower perceived barriers to healthcare access. The association was found regardless of the women's socioeconomic status, such as income and education level.

**Conclusions:** Removing physical and psychological barriers to healthcare through mHealth can be a valuable strategy for reducing postpartum depression in real-world settings.



**Figure:** Subgroup analysis: Relative risks of the incidence of elevated postpartum depressive symptoms (EPDS  $\geq 9$ ) per participants characteristics.



**Using the evidence-informed directed acyclic graph to investigate the association between diet and mental health outcomes in youth** Julia Dabravolskaj\* Julia Dabravolskaj Karen A. Patte Shelby Yamamoto Scott T. Leatherdale Paul J. Veugelers Katerina Maximova

**Background:** Dietary intake has been proposed as a potential intervention target to promote mental health in youth. Yet, methodological concerns in studies on the diet-mental health relationship in youth include indiscriminate and inconsistent adjustment for covariates, which may introduce or amplify biases (overadjustment and collider biases).

**Methods:** Guided by the Evidence Synthesis for Constructing Directed Acyclic Graphs (ESC-DAG) approach, we created an evidence-based DAG to identify the minimally sufficient adjustment set (MSAS): mental health at baseline, socio-economic status, age, eating behaviours, lifestyle behaviours, and social support. Linear mixed-effects models were used to estimate the effect of dietary intake (servings of vegetables & fruit) at baseline on depressive and anxiety symptoms (CESD-R-10 and GAD-7 scores, respectively) at 1-year follow-up in a sample of 13,887 Canadian high school students from the longitudinal COMPASS study. Sensitivity analyses included the use of a positive exposure control (self-concept, or conscious beliefs about self) and adding covariates that were not included in the MSAS to assess if effect estimates remain robust.

**Results:** Once adjusted for the MSAS, prospective associations between vegetables & fruit and depressive ( $\beta=0.03$ , 95%CI: -0.02, 0.07) and anxiety ( $\beta=0.03$ , 95%CI: -0.01, 0.07) symptoms disappeared, with adjustment for mental health at baseline yielding the biggest reduction in Akaike's information criterion and effect estimates. In contrast, prospective associations between self-concept at baseline and depressive ( $\beta=0.19$ , 95%CI 0.17, 0.22) and anxiety ( $\beta=0.12$ , 95%CI 0.10, 0.15) symptoms remained strong. Adjusting for additional covariates did not affect effect estimates.

**Conclusion:** We found no evidence of a prospective association between vegetables & fruit consumption and mental health in youth. Analyses underline the importance of constructing an evidence-based DAG to inform regression analyses.

**Ascertaining the validity of suicide classifications from death certificate data by industry/occupation: A validation study** Nate Wright\* Nate Wright Marizen Ramirez

Suicide is a leading cause of death in the United States. Misclassification, however, plagues suicide data, but few evaluations of suicide classifications have been done. We conducted a validation study to examine the misclassification of suicides identified from death certificates in Minnesota overall and by occupation and industry.

The target population was comprised of unnatural deaths (i.e., homicide, suicide, unintentional, or undetermined intent), among working age adults (i.e., 16-64 years). Deaths occurring from 2017 through 2020, with the decedents' usual occupation listed on the death certificate, were included in this study. The data sources were Minnesota death certificates, along with Minnesota deaths from the National Violent Death Reporting System and the State Unintentional Drug Overdose Reporting System. A validation study was conducted in which suicides reported from death certificates were compared with a proxy gold-standard measure: the Self-Directed Violence Classification System. This was chosen as the gold-standard because the definitions represent agreed upon standards for suicide surveillance. Estimates for sensitivity, specificity, and predictive values were then calculated.

Across the study period, 7774 deaths met the inclusion criteria, with one-third ( $N = 2260$ ) selected for abstraction. Preliminary results from review of 25% of cases (546 deaths) show limited evidence of suicide misclassification. Only eight cases were identified as misclassified suicides; drug overdose was the most common cause of death among this group. However, unknown or missing injury circumstance data were prevalent ( $\geq 50\%$ ), thus making suicide classification difficult.

This research shows how suicide misclassification can be understood. The extent to which suicide statistics are used mandates that efforts be made to improve the validity of suicide data. By applying methods that correct for misclassification, we can better document disparities in suicide.

**Heterogeneity across outcomes reported in randomized controlled trials for older adults with major depressive disorder: findings from a systematic survey** Myanca Rodrigues\*

Myanca Rodrigues Zuhayr Syed Pegah Ghiassi Alexander Dufort Nitika Sanger Stephanie Sanger Balpreet Panesar Alessia D'Elia Sameer Parpia Zainab Samaan Lehana Thabane

**Background:**

Heterogeneity in the use of outcomes across clinical trials creates challenges for the interpretation of results regarding intervention effectiveness. Core outcome sets (COS), a minimum set of outcomes that must be reported in trials, have been proposed as a viable solution to address inconsistency in the selection of outcomes. We conducted a methodological review to synthesize the definitions and measurement of outcomes reported in trials for older adults with depression, which represents the first step towards the development of a COS.

**Methods:**

We searched four databases to identify trials assessing any intervention for major depressive disorder among older adults published between 2011 and 2021. We grouped reported outcomes thematically and mapped them onto core outcome areas (physiological/clinical, life impact, resource use, adverse events, and death), and used descriptive analysis to summarize outcome heterogeneity.

**Results:**

There were 434 total outcomes reported by 49 included trials, which were measured using 135 different outcome measurement instruments and grouped into 100 unique outcome terms. Most outcome terms mapped to the physiological/clinical core area (47%), followed by life impact (42%). Over half of all terms (52%) were reported by only a single study. The majority of trials (n=31/49) reported a single, discernable primary outcome. The most commonly reported outcome, "depressive symptom severity" was assessed by 40 studies using 16 different outcome measurement instruments.

**Conclusions:**

There is substantial heterogeneity in the outcomes and outcome measurement instruments used in geriatric depression trials. A standard set of outcomes and accompanying measurement tools is necessary to facilitate comparison and synthesis of trial findings.



**Population-level metrics in racial disparities research: a Multiracial health equity****simulation study** Tracy Lam-Hine\* Tracy Lam-Hine Amani Allen Patrick Bradshaw Corinne A. Riddell

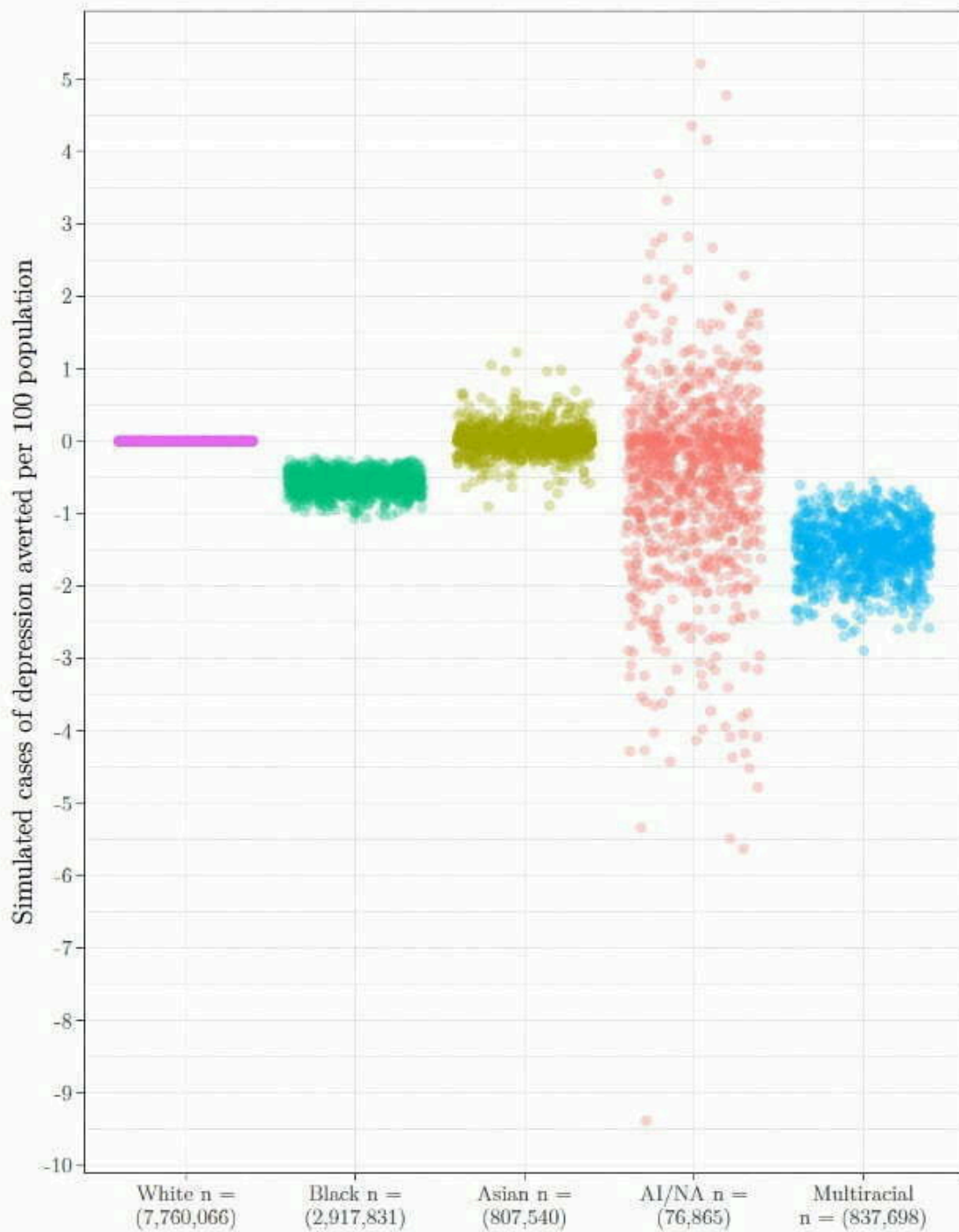
**Background:** Multiracial people report the highest mean Adverse Childhood Experiences (ACEs) score of any racial group and have high risk of several negative physical and psychobehavioral outcomes, including depression. Though absolute ACEs are highest among Multiracial people, studies have not found the association between ACEs and depression to be stronger in this group. Interaction and attributable fraction analyses are useful for identifying priority subgroups and evaluating interventions, but stochastic intervention methods combine benefits from both approaches by simulating population-level parameters that incorporate uncertainty in exposure distributions.

**Methods:** We analyzed data from Waves 1 (1995-97) through 4 (2008-09) of the National Longitudinal Study of Adolescent to Adult Health (Add Health), a nationally-representative longitudinal study of 20,745 adolescents followed into adulthood. We modeled the association between ACEs and depression, and then simulated a stochastic intervention over 1,000 resampled datasets to quantify the race-specific RDs in depression if all racial groups had the same ACEs exposure distribution as Whites.

**Results:** Simulated RDs (see figure) were largest for the Multiracial group, (median = -1.470 cases per 100 averted, 95% UI: -2.330, -0.803). The model predicted smaller risk reductions per 100 for Black (-0.568, 95% UI: -0.896, -0.318) and AI/NA (-0.258, 95% UI: -3.450, 1.660) participants, and a risk increase for Asians (0.002, 95% UI: -0.361, 0.481). Uncertainty intervals around AI/NA and Asian group estimates included the null.

**Conclusion:** Multiracial participants likely stand to benefit more than any other racial group in absolute reduction in cases of depression from a health equity intervention to reduce ACEs. Stochastic intervention simulations offer substantial benefits compared to traditional racial disparities research methods, and should be used more frequently in health disparities research and practice.

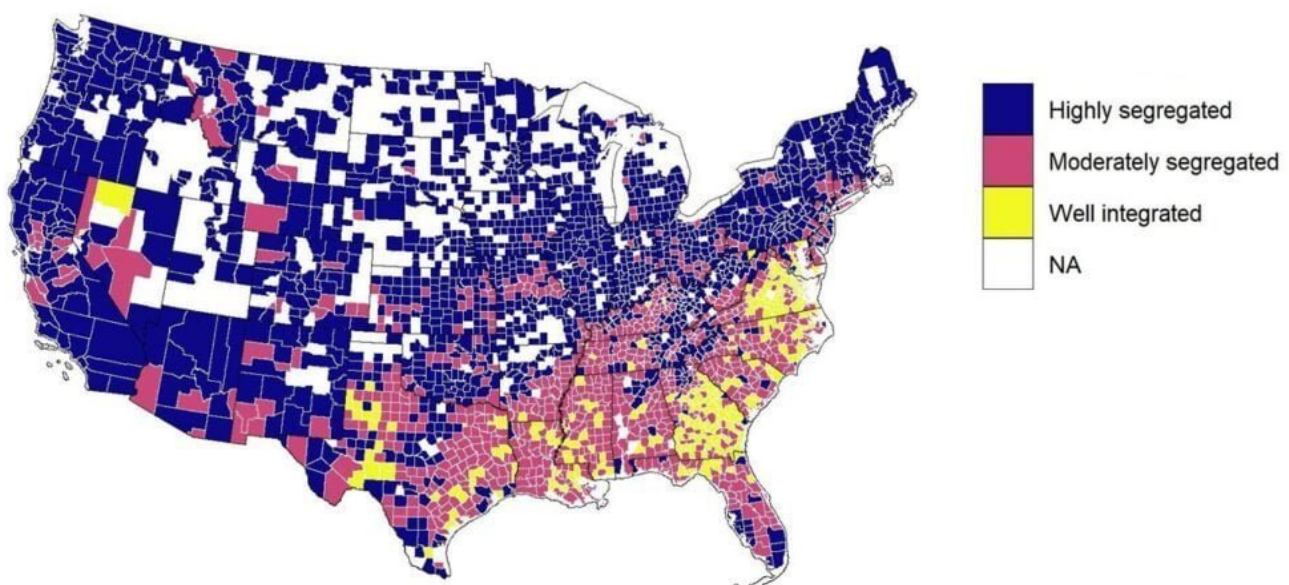
**Figure:** Simulated number of cases of depression averted per 100 population, results and subgroup sample sizes calculated from 1,000 resampled datasets



**Methodological challenges of emulating a target trial assessing the effect of early-life racialized residential segregation on later-life cognitive health** Taylor Mobley\* Taylor Mobley L. Paloma Rojas-Saunero Joan A. Casey Elizabeth Rose Mayeda

Racialized residential segregation in the United States (US) is a product of structural racism. Segregated neighborhoods present unequal environmental hazards and fewer social resources, contributing to health disparities. We discuss methodological challenges of emulating a target trial assessing the effect of early-life segregation on later-life cognitive health in a nationally-representative cohort. Measurement is one key challenge. We used the dissimilarity index (DI), which measures differences in the distribution of two groups (e.g., privileged vs minoritized) across geographical subunits within a larger area and ranges from 0 (no segregation) to 1 (highly segregated). We used complete count 1940 census enumeration district (ED) data to calculate white vs Black DI at the county-level. Constructing this exposure presented several challenges: (1) EDs (representing the area covered by a single census taker) are the only geographic units approximating neighborhoods that existed across the US in 1940, but they are inconsistent in population and geographic size; (2) DI is inflated with small minoritized group populations, and it does not conceptually address geographic areas with no minoritized group residents; (3) the DI distribution unexpectedly suggested the southern US was fairly well integrated in 1940 (Figure). Defining conceptually meaningful interventions of the DI as a proxy for segregation is essential for meaningful research in this area. Approaches might include shifting each county's DI by a constant (e.g., subtracting 0.1) or setting a cut-point to mimic a "well integrated" scenario. Emulation of such a trial also requires conceptualization of policy-level confounders and individual-level covariates that influence attrition and survival. Social theory, the target trial framework, and causal methods can guide study design decisions that answer a well-defined question around segregation under explicit assumptions, critical steps to promote health equity.

Figure. 1940 US county-level dissimilarity index distribution<sup>1</sup>



<sup>1</sup>Highly segregated county DI range: 0.6-1.0; Moderately segregated county DI range: 0.3-0.6; Well integrated county DI range: 0-0.3



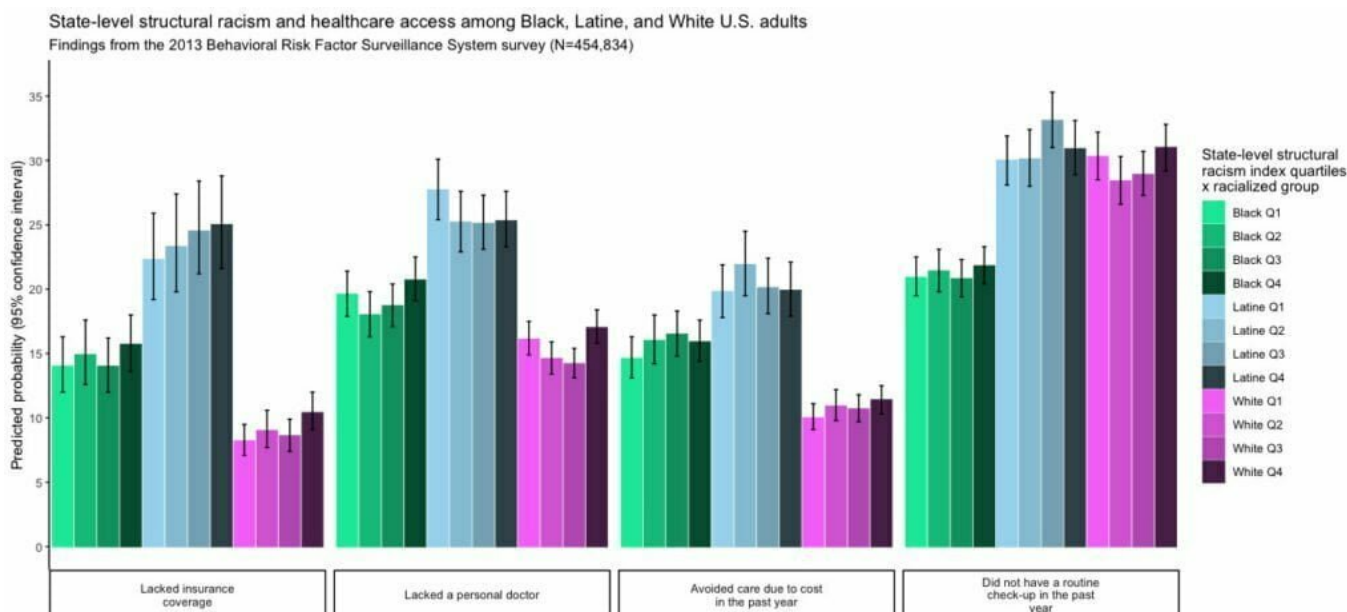
**State-level structural racism and healthcare access among Black, Latine, and White US adults** Dougie Zubizarreta\* Dougie Zubizarreta Jarvis T. Chen Jaquelyn L. Jahn Ariel L. Beccia S. Bryn Austin Madina Agénor

**Background:** Racialized healthcare inequities in the US are marked and persistent, yet root causes remain understudied. We examined joint associations of state-level structural racism and race/ethnicity with healthcare access among Black, Latine, and White US adults.

**Methods:** We created a state-level structural racism legal index (SRLI) using 2013 data from the Structural Racism-Related State Law Database on relevant policies (e.g., stand-your-ground and minimum wage laws) and analyzed inequities in the prevalence of 4 healthcare access indicators from the 2013 Behavioral Risk Factor Surveillance System (N=454834). To estimate prevalence ratios by quartiles of SRLI (Q1=less structural racism, Q4=more structural racism) and racialized group, we fit survey-weighted multilevel Poisson models adjusted for individual- and state-level covariates.

**Results:** Overall, we found substantial healthcare access inequities across racialized groups within SRLI quartiles, and few significant inequities within racialized groups across SRLI quartiles (see Figure for predicted probabilities of each outcome by racialized group and SRLI quartile). Latine adults in Q4 states were 140% more likely to lack insurance coverage; 75% more likely to have avoided care due to cost in the past year; and 49% more likely to lack a personal doctor than White adults in Q4 states. Black adults in Q4 states were 40% more likely to have avoided care due to cost in the past year and 30% less likely to not have had a routine check-up in the past year than White adults in Q4 states. Black adults in Q4 states were up to 12% more likely than those in Q1 states to lack healthcare access across the indicators examined, though findings were non-significant.

**Conclusions:** Findings underscore the need to address structural racism in laws and political environments to improve healthcare access and eliminate racialized inequities. Future work with more recent data should identify mechanisms to inform policy interventions.

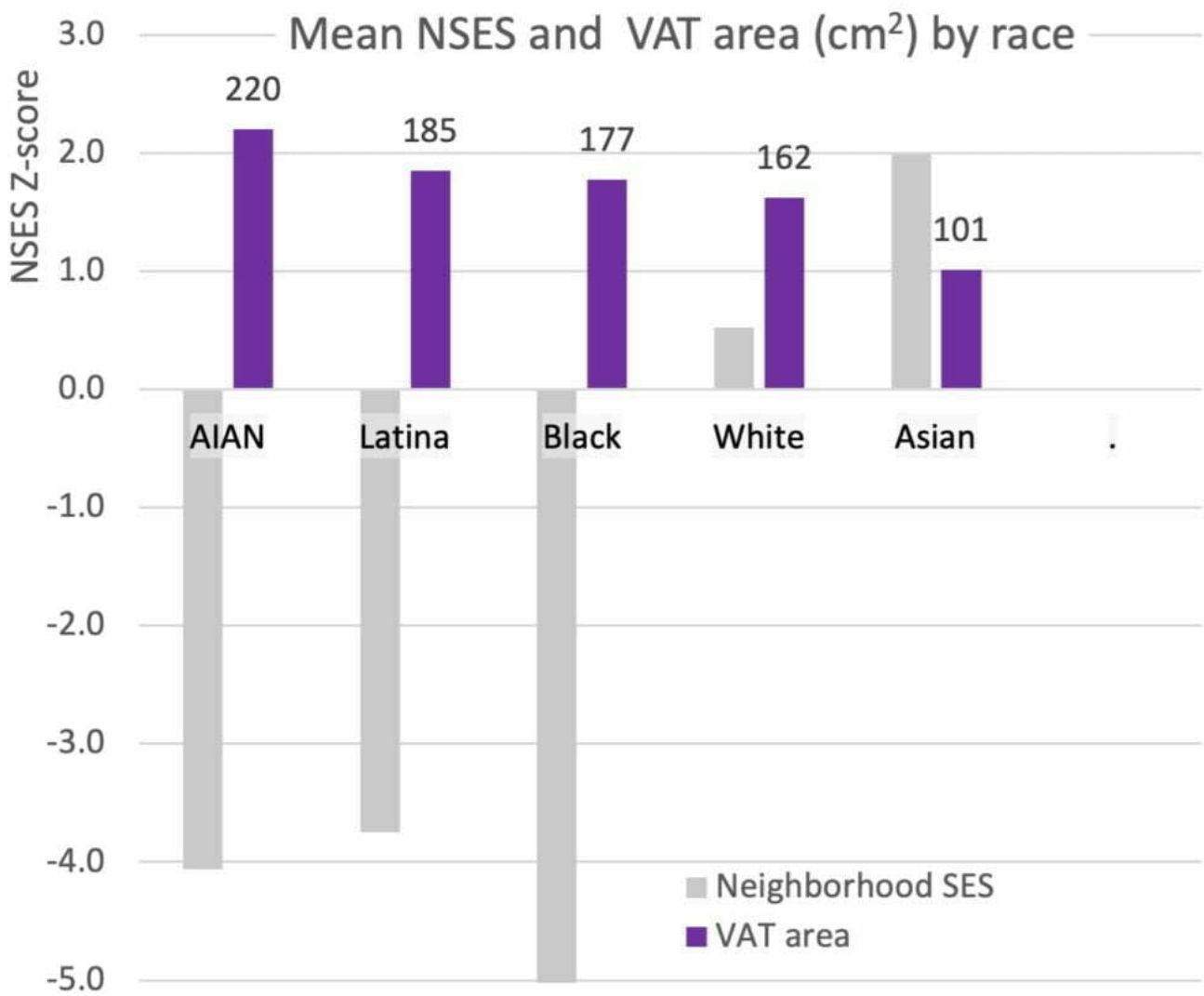


**Racial and ethnic disparities in neighborhood socioeconomic characteristics and associations with visceral adipose tissue patterning** Shawna Follis\* Shawna Follis Jeremy Shropshire David Rehkopf Eric A. Whitsel Marcia Stefanick Andrew Odegaard

**Introduction:** Visceral adipose tissue (VAT) accumulation is hypothesized to have a more significant role in the pathophysiology of cardiometabolic diseases than subcutaneous adipose tissue (SAT). Previous research suggests structural racism is associated with racial disparities in obesity through myriad social, material, and biological exposures. One pathway in the embodiment of structural racism may be the chronic stress response, which is associated with larger increases in VAT relative to SAT. To understand the role of structural racism in VAT accumulation, we investigated racial disparities in the association between baseline neighborhood socioeconomic status (NSES) and increases in VAT accumulation over 6 years.

**Methods:** We measured abdominal VAT and SAT area (cm<sup>2</sup>) at years 0, 3, and 6 using dual-energy X-ray absorptiometry in a subsample (n=11,020) of the Women's Health Initiative (age 50-79). We obtained geocoded, participant address-specific, tract-level NSES Z-scores from the US Census. We evaluated racial and ethnic disparities in the exposure and outcome using analysis of variance. We evaluated associations between NSES with VAT and VAT/SAT ratio over 6 years using mixed effects regression models. We tested whether the effect of NSES on VAT varies over time using an interaction term between NSES and year.

**Findings:** Mean NSES and VAT area differed by race and ethnicity. American Indian and Alaska Native (AIAN), Black, and Latina participants were significantly ( $P<0.01$ ) more likely than White or Asian participants to live in neighborhoods with NSES Z-scores below the population mean (Z-score=0; Figure 1). Congruently, AIAN, Latina, and Black women had the highest VAT: 220 cm<sup>2</sup>, 185 cm<sup>2</sup>, and 177 cm<sup>2</sup>. Findings support the hypothesis that associations between NSES and VAT differ by race and ethnicity. Results from mixed effects models are expected to provide longitudinal evidence that structural racism is associated with increases in VAT accumulation.



**Applying the emulation of a target trial approach to identify neighborhood level****intervention strategies on the risk of preeclampsia** Kharlya Carpio\* Kharlya Carpio Jennifer Adibi Ethan Blum Sonja Swanson Xu Xin Dara Mendez James Roberts

**Background:** Longstanding racial disparities in the risk of preeclampsia are a result of upstream social and environmental inequities which can be intervened on. One approach to assess and prioritize areas for intervention is to simulate target trials using observational methods. The g-formula can be used to estimate the expected change in a given outcome under a hypothetical intervention. **Objective:** To specify an intervention on four neighborhood-level risk factors, and to estimate the counterfactual risk of preeclampsia under those interventions and within two levels of race. **Methods:** We estimated the relative and absolute risk reduction under hypothetical risk reduction strategies for unemployment, crime, poverty, and greenery in 1337 women who delivered at a large metropolitan hospital in Pittsburgh, PA (2007-2014). Women were randomly selected on a 1:3 case-to-control ratio yielding 336 preeclampsia cases. All women reported their race as Black or White which was an indicator for lived experience. We examined whether the racial disparity in preeclampsia risk changed under different intervention scenarios. These included setting a neighborhood-level risk factor to a specific value, shifting distributions for all women and then for Black women only, and limiting risk factor levels to a specific cutoff value. **Results:** The estimated risk of preeclampsia under no intervention was 5.1% greater in Black women than in White women. For greenery, when the greenery score was increased for all women, the risk decreased by 25.8% in Black women and 21.1% in White women. When the greenery score was increased for Black women only, the risk decreased by 8.6%. The most impactful intervention was to reduce the neighborhood unemployment rate to below 130 households with an unemployed person. In a subset of subjects, we have information on placental hormone levels which will be analyzed as putative indicators of neighborhood environmental effects on the risk of preeclampsia, to support inferences. **Discussion:** These methods allow for the re-analysis of historic cohort data to move beyond describing disparities in the risk of preeclampsia to identifying and outlining intervention strategy.

**The magnitude and potential influence of pre-baseline survival bias on cognitive impairment prevalence: Findings from the HAALSI cohort in rural South Africa** Molly Rosenberg\* Molly Rosenberg Erika Beidelman Xiwei Chen Kathleen Kahn Chodziwadziwa Kabudulac Lindsay Kobayashi

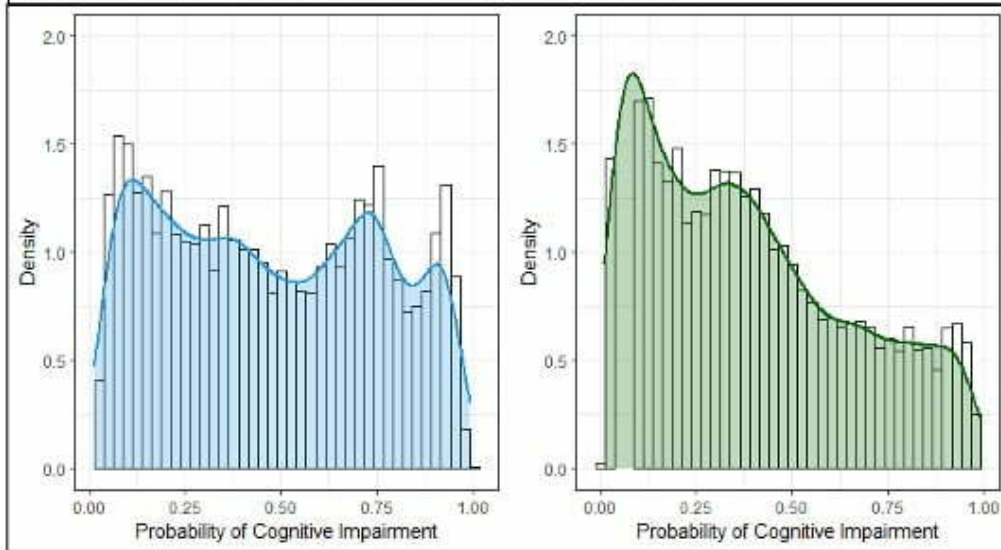
**Background:** All cohorts are conditioned on pre-baseline survival. If potential participants who die prior to study enrollment have different covariate structures than those who survive, there are concerns for the validity of the inference we can draw from the cohort of survivors. The threat of this bias grows in aging cohorts because of the strong relationship between age and mortality.

**Methods:** To explore the potential impact of pre-baseline survival bias on cognitive impairment, we used data from the HAALSI Cohort of older adults in rural South Africa (n=5059 in 2014) and a 'Ghost Cohort' of people who would have been eligible for HAALSI but died before they had the opportunity to enroll (n=9363, 2000-2014), using complete historic data on the source population from the Agincourt Health and socio-Demographic Surveillance System (AHDSS). We simulated the prevalence of cognitive impairment in a resampled cohort under different assumptions about the prevalence of cognitive impairment in the Ghost Cohort. We constructed a Random Forest Classification model to predict cognitive impairment in the Ghost Cohort and compared it to observed HAALSI estimates.

**Results:** The simulated prevalence of cognitive impairment in the counterfactual cohort in which everyone survived was sensitive to different assumptions about prevalence in the Ghost Cohort, with extreme bounds estimates ranging from 4.7% (95% CI 4.2-5.4%) to 46.8% (95% CI: 45.5-48.2%). Applying the predictive model to the Ghost Cohort revealed higher predicted probability of cognitive impairment (22.5%) relative to the HAALSI Cohort (8.2%, Fig 1).

**Conclusions:** Researchers should consider pre-baseline mortality as a potential source of study bias, especially when the magnitude of pre-baseline deaths is large. This process could bias prevalence/incidence estimates, as observed here, but could also lead to biased effect estimates in the likely event of unmeasured confounding between exposure and pre-baseline mortality.

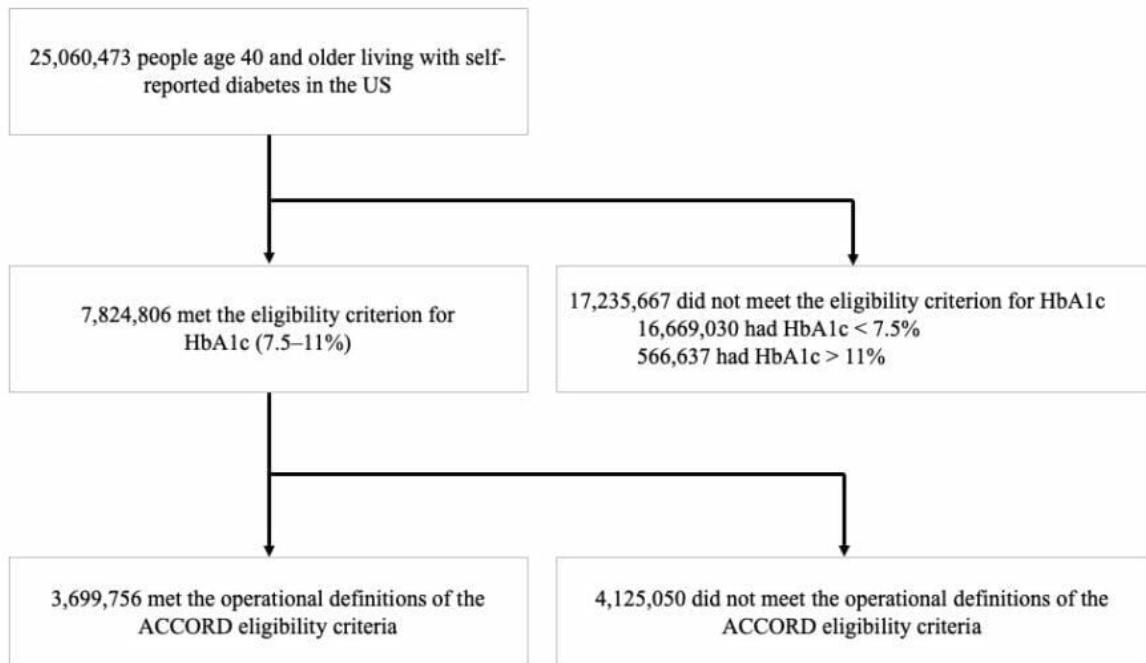
**Figure 1.** Distribution of predicted probability of cognitive impairment in the Ghost Cohort (left) vs. the HAALSI Cohort (right) from a Random Forest Classification model using 13 socio-demographic characteristics (AUC=0.793)



**Representativeness of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial Participants among Middle-aged and Older Adults Living with Diabetes in the US** Ryo Ikesu\* Ryo Ikesu Scott C. Zimmerman Peter Buto Melinda C. Power M. Maria Glymour Elizabeth Rose Mayeda

**Background:** Randomized controlled trial (RCT) participants are typically highly selected, often causing large differences between RCT participants and target populations for whom the trials would guide clinical care. This is a key rationale for using observational data for emulated trials, but we do not know how widespread and severe these differences are, and whether they are essential trial design features. The landmark Action to Control Cardiovascular Risk in Diabetes (ACCORD) Trial aimed to evaluate effects of intensive glycemic control on cardiovascular events among people with type 2 diabetes at high cardiovascular risk. ACCORD was discontinued due to higher all-cause mortality in the intensive glycemic control arm. We evaluated the extent to which ACCORD participants represent US middle-aged and older adults with diabetes. **Methods:** Using the nationally-representative National Health and Nutrition Examination Survey (NHANES) 2017-2018 with sampling weights for people age 40+ with self-reported diabetes, we calculated the percentage of middle-aged and older adults with diabetes who met ACCORD eligibility criteria and evaluated which criteria were essential. **Results:** Based on analysis of 769 NHANES participants (representing 25,060,473 US population) age 40+ with diabetes (median age, 65), only 14.8% of US adults with diabetes met ACCORD eligibility criteria that could be evaluated in NHANES. The most restrictive eligibility criterion was HbA1c 7.5-11%: 31.2% met this criterion. Among those who met HbA1c eligibility, 47.3% met additional eligibility criteria. **Discussion:** ACCORD eligibility criteria only includes a fraction of middle-aged and older adults with diabetes in the US and only half of those who would be candidates for intensive glycemic control based on HbA1c. Our findings highlight the need for careful consideration of RCT eligibility criteria. Trial findings may need to be augmented with observational analyses to draw inferences for broad populations.

Figure. Overview of the weighted number of NHANES participants who met the eligibility criteria of the ACCORD trial





## Study Design

**California State Study of People Experiencing Homelessness: Novel methods to construct a representative sample for surveying California's unhoused population** Paul Wesson\* Ryan

Assaf Paul Wesson Dave Graham-Squire Eve Perry Ryan D Assaf Meghan Morris Angelica DeGaetano Kara Young Ponder Margot Kushel

Homelessness is a critical public health issue associated with high rates of morbidity and mortality. Challenges in quantifying and characterizing people experiencing homelessness (PEH) leads to knowledge gaps, particularly for unsheltered people. Existing literature on homelessness draws on small, non-representative samples often from service providers, populations with comorbidities, or areas where sheltered homelessness is disproportionately high. California is home to nearly a third of PEH in the US and over half of the unsheltered population. We designed a rigorous sampling strategy to generate a state-representative sample of PEH to investigate the antecedents of homelessness, understand health status, and inform policy solutions.

The multistage sampling design incorporated randomization at three levels: county, venue, and individual. Stratifying the state into eight geographic regions, we randomly sampled counties by region until we identified the combination of eight counties that best reflected statewide demographics. Within each county, we sampled venues to match the expected proportion of sheltered and unsheltered residents, using benchmarks from the latest point-in-time counts (PIT). Within venues, interviewers followed randomization protocols to sample individuals. Sample weights accounted for nonresponse; we post-stratified to PIT benchmarks. In parallel, we used respondent-driven sampling to reach pre-identified groups through social networks who may otherwise be under-sampled. Our community-engaged multistage sampling design yielded 3000 quantitative surveys and 300 qualitative interviews. Sample demographics closely match the distribution found in the PIT with the added strength that multi-level randomization facilitates statistical inference.

This is the first study of PEH to randomly sample and draw inference on a large population that did not depend on service utilization. Our methods may inform future efforts to understand this population.

**Inclusion of asymptomatic individuals in test-negative design studies estimating COVID-19 vaccine effectiveness: a simulation study.** Edgar Ortiz-Brizuela\* Edgar Ortiz-Brizuela Cong Jiang Denis Talbot Mabel Carabali Mireille Schnitzer

The post-licensure evaluation of COVID-19 vaccine effectiveness (VE) has provided critical insight into questions not addressed by randomized clinical trials. Among the observational studies used for this purpose, the test-negative design (TND) has gained increasing popularity, in part due to its relatively simple implementation. In the TND, the study sample is usually prospectively selected from symptomatic individuals who are tested for the disease targeted by the vaccine. Then, *VE against illness related to the targeted pathogen* is estimated by comparing patients with positive and negative test results via logistic regression. Under the assumption that healthcare-seeking behavior (HSB) is binary in nature (i.e., present vs. absent), the TND is said to control for confounding by this factor since only those individuals seeking medical care are included. However, to estimate *VE against infection*, some studies modify the TND such that the only eligibility criterion is the availability of a test result; that is, the presence of symptoms is not required to be selected into the study. Nevertheless, the validity and interpretability of these studies are likely influenced by many factors, including the reasons for testing, the amount and accessibility of diagnostic resources, and the possibility of differential HSB between cases and non-cases. Although several studies have examined the validity of the TND in its usual format, none have formally evaluated potential sources of confounding and collider/selection bias when sampling occurs without regard to a clinical definition. This study aims to demonstrate potential sources of bias in the TND for VE against infection by using DAGs-based simulated scenarios, which represent the evolving role of COVID-19 diagnostic testing in response to the pandemic.

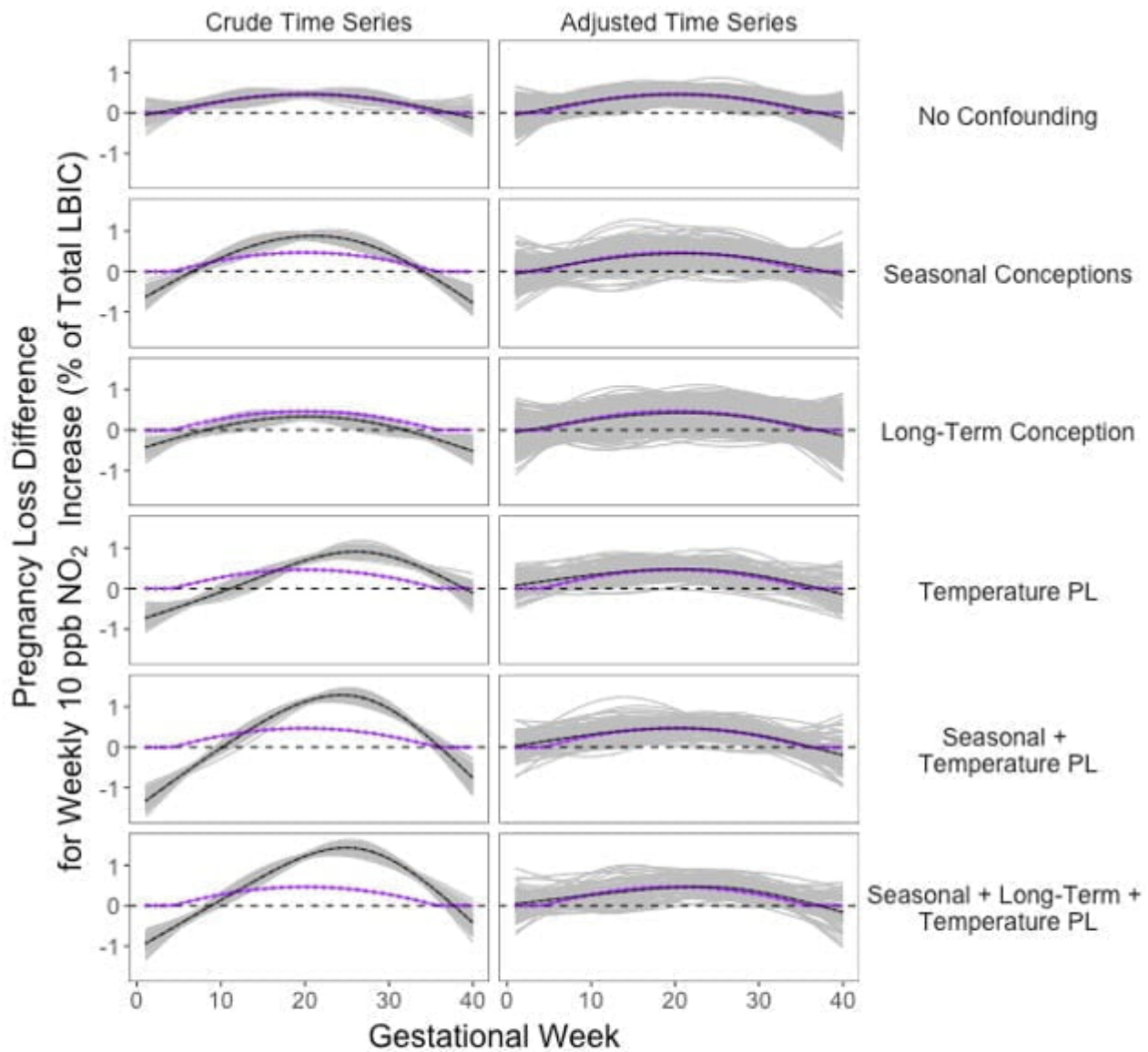
**Inferring effects of time-varying prenatal exposures on pregnancy loss from live-birth-identified conceptions: A simulation study** Michael Leung\* Michael Leung Sebastian T Rowland Brent A Coull Ander Wilson Marc G Weisskopf Marianthi-Anna Kioumourtzoglou

**Background:** Identifying the determinants of pregnancy loss is a critical public health concern. However, it is difficult to enumerate the outcome, and so past studies have been limited to medically-identified losses or small, highly selected cohorts. Instead, we show through a simulation study of the effect of nitrogen dioxide (NO<sub>2</sub>) on pregnancy loss that researchers can use records of live births and gestational ages to identify live-birth-identified conceptions (LBICs) —the difference between the total number of conceptions and those lost for a given time window— to infer effects about pregnancy loss.

**Methods:** We simulated ten years of conceptions, pregnancies, losses, and births under several confounding patterns (no confounding, seasonal conceptions, temperature-influenced loss, long-term conception trends, and the previous three combined), and two NO<sub>2</sub> effect forms (no effect and moderate effect). We used a time-series design and fit quasi-Poisson distributed lag model adjusted for season, year, and temperature. We considered two approaches to estimate the week-specific and 40-week cumulative effects of NO<sub>2</sub> on pregnancy loss: 1) direct interpretation of estimated regression coefficients from the quasi-Poisson model and 2) g-computation to estimate the corresponding additive effects.

**Results:** Across all scenarios, our models, on average, correctly identified the critical window with appropriate coverage (range: 90% to 100%) and low percent bias (range: -0.51% to 1.5%). For example, under a moderate NO<sub>2</sub> effect and combined confounding structure, the average bias and coverage for the additive cumulative association was 1.1% (standard deviation: 6.28%) and 96%, respectively.

**Conclusions:** We demonstrated through simulations that our method relying on LBICs (typically available in administrative datasets) offers a viable approach to infer effects on pregnancy loss under realistic confounding scenarios.



**Figure 1.** Simulation results showing the time-varying association between  $\text{NO}_2$  and pregnancy loss (PL) across all gestational weeks under several confounding structures (no confounding, seasonal conceptions, long-term conception, temperature-induced PL, seasonal + temperature-induced PL, and all combined) and confounding adjustment methods (crude time series: unadjusted; adjusted time series: adjusted for year, temperature and seasonality using a pair of harmonics). Grey lines show the lag-response relationships from each iteration of the simulation, black solid lines indicate the average across all simulation (500 replicates), the black dashed line indicates the null hypothesis of no effect across all weeks, and the purple dotted line indicates the true simulated effect.

## Study Design

**Investigating the causal effect of cohort participation on mortality in an aging rural South African population: A longitudinal analysis of the HAALSI cohort** Erika Beidelman\* Erika

Beidelman Christina Ludema Ryan G. Wagner Kathleen Kahn Lindsay Kobayashi Chodziwadziwa Kabudula Molly Rosenberg

*Background:* Cohort participation may be considered an exposure that alters the health trajectories and mortality of participants. These 'research participation effects' are rarely studied due to a lack of data on source populations but may be an important source of bias in effect estimation. We linked data from a rural, aging South African cohort to mortality data from an annual census of the underlying source population to estimate the causal impact of cohort participation on mortality.

*Methods:* We used data from the Agincourt Health and Socio-demographic Surveillance System to characterize mortality trajectories for 96.4% of the source population underpinning the 'Health and Aging in Africa: A Longitudinal Study of an INDEPTH community' (HAALSI) cohort from study inception (July 2014) to March 2022. We categorized the population into three groups: cohort participants (n=5055), sampled non-participants (n=986), and the background population (n=6369). To assess the causal effect of cohort participation on mortality, we fit a Cox Marginal Structural Model using Inverse Probability Weights of treatment, non-enrollment, and censoring, comparing participants to all non-participants, stratified by sex.

*Results:* No causal effect of cohort participation on the hazard of death for females was observed (HR=0.94, 95% CI: 0.81-1.08). For males, cohort participation significantly decreased the hazard of death by 40% (HR=0.60, 95% CI: 0.48-0.74).

*Conclusions:* Participation in a cohort study of older adults in rural South Africa significantly decreased mortality among men, a group with traditionally low healthcare engagement. Our findings indicate that research participation effects need to be considered as potential sources of bias when interpreting results from cohort studies. These results also point to the potential to leverage community-based health screening interventions to promote healthy aging in groups with low healthcare engagement.

*Table 2.* Results of the Marginal Structural Cox Proportional Hazards Model for the causal effect of cohort participation on the hazard of death, stratified by sex (restricted to ages <80 years)

	<b>Unweighted HR (95% CI)</b>	<b>Stabilized IPW HR (95% CI)</b>
<i>Females</i>	<b>1.18 (1.04, 1.36)</b>	0.94 (0.81, 1.08)
<i>Males</i>	<b>1.25 (1.06, 1.47)</b>	<b>0.60 (0.48, 0.74)</b>

Notes. IPW = Inverse Probability Weight and is the product of the Inverse Probability of Censoring Weight, Inverse Probability of Non-Enrollment Weight, and the Inverse Probability of Treatment Weight; Reference group = All untreated individuals (non-participants and background population)

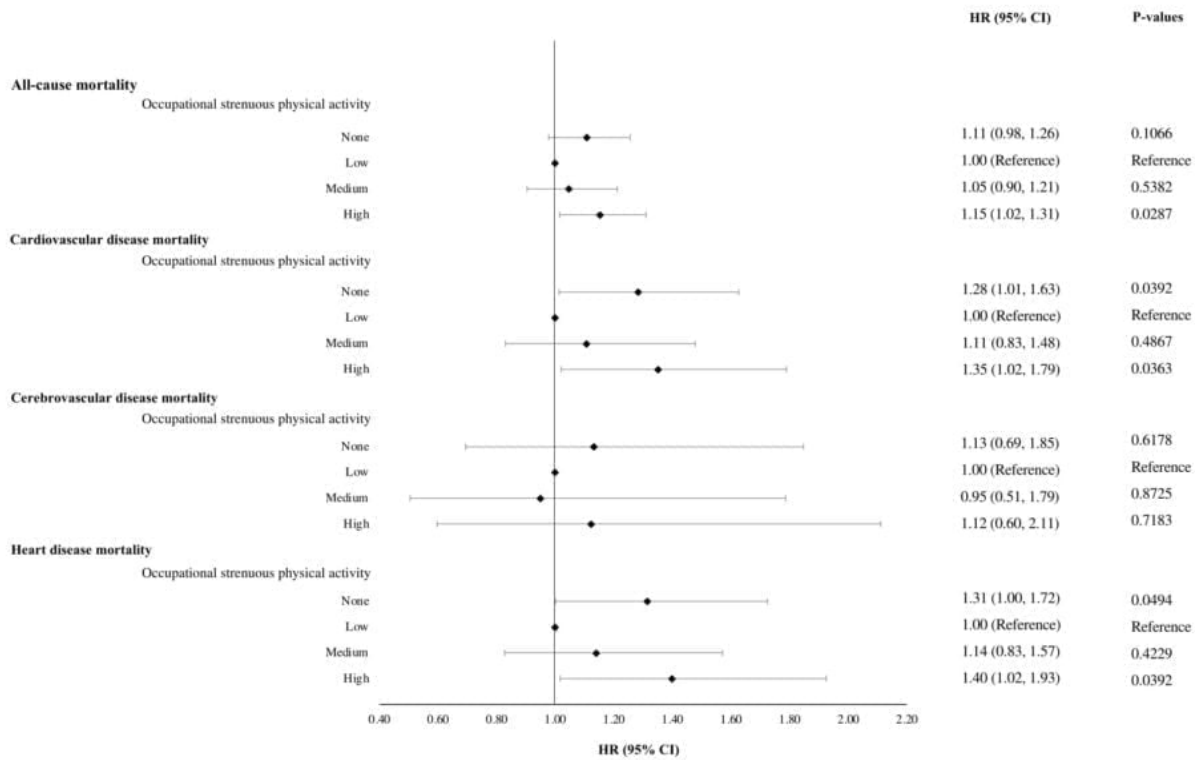
**Associations of occupational physical activity with all-cause and cardiovascular disease mortality among workers in the United States, 1988-2019** Tong Xia\* Tong Xia Liwei Chen Jian Li

**Introduction:** The newly observed “physical activity paradox” [i.e., leisure time physical activity is beneficial but occupational physical activity (OPA) may be harmful to health] has attracted attention, however, evidence from the United States (U.S.) is still sparse. This study aimed to examine prospective associations of OPA with mortality using a large representative sample of U.S. adult workers.

**Methods:** The study included 24,897 workers ( $\geq 18$  years) who participated in the 1988 U.S. National Health Interview Survey (NHIS). OPA in terms of time spent on workplace strenuous physical activity was assessed at baseline by a questionnaire and classified into 4 groups [i.e., none (0 minute/week), and low, medium, and high based on the distribution of non-zero time of OPA]. Information on all-cause and cardiovascular disease (CVD, total and separated by cerebrovascular and heart disease) mortality was collected through 31 December 2019 with a linkage to the National Death Index. Multivariable Cox proportional hazard models with sampling weights were performed to evaluate associations of OPA with mortality, adjusting for age, sex, race, marital status, education, annual household income, occupation type, and pre-existing cardiometabolic disorders at baseline.

**Results:** Across four OPA groups, the adjusted hazard ratios (95% confidence intervals) of the none, low, medium, and high groups were 1.11 (0.98-1.26), 1.00 (reference), 1.05 (0.90-1.21), and 1.15 (1.02-1.31) for all-cause mortality; 1.28 (1.01-1.63), 1.00 (reference), 1.11 (0.83-1.48), and 1.35 (1.02-1.79) for CVD mortality; 1.13 (0.69-1.85), 1.00 (reference), 0.95 (0.51-1.79), and 1.12 (0.60-2.11) for cerebrovascular disease mortality; and 1.31 (1.00-1.72), 1.00 (reference), 1.14 (0.83-1.57), and 1.40 (1.02-1.93) for heart disease mortality.

**Conclusions:** We found U-shaped associations of OPA with all-cause and CVD mortality among U.S. workers. Further studies are needed to explore the role of OPA to improve health.



**Figure 1.** Prospective associations of occupational physical activity with all-cause and cardiovascular disease (total and separated by cerebrovascular and heart disease) mortality, 1988-2019.

The multivariable Cox proportional hazard regression models were used. Hazard ratio (HR), 95% confidence interval (CI) and P-values were reported. Sampling weights were applied. Adjusted for age, sex, race, marital status, education, annual household income, occupation type, and pre-existing cardiometabolic disorders. Occupational physical activity in terms of time spent on workplace strenuous physical activity was classified as none (0 minute/week) and other three groups by tertile distribution without considering none [low (>0 and ≤110 minutes/week, reference group), medium (>110 and ≤325 minutes/week), and high (>325 minutes/week)].



**Differential associations between education and cardiovascular risk by gender and race/ethnicity**

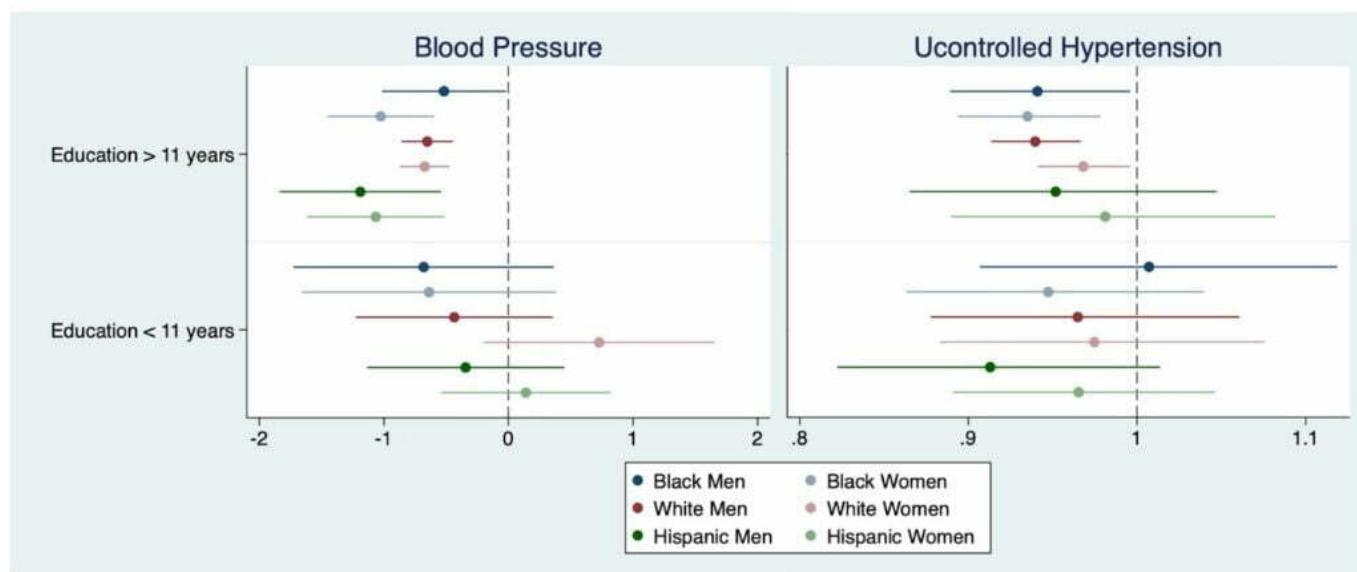
Lucia Pacca\* Lucia Pacca Amanda M. Irish Catherine Duarte Alicia R. Riley Anusha M. Vable

Previous research suggests higher education is inversely associated with hypertension (HTN), a strong risk factor for cardiovascular disease (CVD). However, little work has examined whether the protective association of education on CVD risk differs by gender and race/ethnicity. We investigate the association between education and CVD risk across gender and racial/ethnic groups.

We used longitudinal data (2006-2018) from the U.S. Health Retirement Study (HRS) (N = 23,142). Education was operationalized as a spline with a discontinuous knot at 11 years. CVD risk outcomes were (1) measured systolic blood pressure (SBP) and (2) uncontrolled HTN (blood pressure  $\geq$  140/90 mmHg after HTN diagnosis). We used generalized estimating equations to estimate the relationship between education and CVD risk in the overall sample and added interaction terms to evaluate differential returns by race/ethnicity and gender. All models adjusted for birth year, birthplace, parents' education and survey year.

In our sample (mean age 67.7 years), mean SBP was 129.5 (sd=20.2), and prevalence of uncontrolled HTN was 37.2%. Before 11 years, CVD risk did not appreciably vary with increasing education. After 11 years of education, however, each additional year was associated with lower SBP (b = -0.05 mmHg; 95% CI: -0.07, -0.04) and lower likelihood of uncontrolled HTN (OR= 0.95, 95% CI: 0.93, 0.96). Compared to White men, each additional year of education after 11 years was associated with larger SBP benefits for: White women, Black women, Hispanic women, Hispanic men (e.g. Hispanic women\*education interaction: b= -0.73, 95% CI: -1.31, -0.16)

Results suggest a protective association between education and CVD risk overall, and that structurally minoritized groups generally benefit more from each year of education than White men, consistent with prior work. However, Black men do not enjoy the same cardiovascular returns to education as other structurally minoritized groups.



**Figure** - Associations between years of education and cardiovascular risk (systolic blood pressure and uncontrolled hypertension) by gender and race/ethnicity. The graph shows beta coefficients for SBP and Odds Ratios for uncontrolled HTN. All point estimates are adjusted for birth year, birthplace, maternal and paternal education and year of BP measurement (2006-2018).

**Perceived job discrimination and hypertension risk among US women: Findings from the Sister Study** Matthew M. Coates\* Matthew Coates Onyebuchi A. Arah Timothy A. Matthews Dale P. Sandler Chandra L. Jackson Jian Li

Hypertension is a leading risk factor for cardiovascular disease in the United States. Socially patterned stressors, such as discrimination, have been linked to hypertension. We used prospective cohort data from the Sister Study (enrollment: 2003-2009) to estimate hypertension risk in relation to job discrimination based on race, gender, age, sexual orientation, and health status. Perceived job discrimination in the past five years was assessed in 2008-2012 during the first study follow-up. Incident hypertension was defined in those without hypertension at first follow-up by self-reported doctor-diagnosed hypertension at the date of diagnosis. Among 18,385 ever-employed eligible participants aged 37 to 78 years, 9.5% of White and 24.7% of Black participants reported at least one of five types of job discrimination in the past five years. In a Cox proportional hazards model adjusting for baseline sociodemographics, behavioral factors, health conditions, non-job-related discrimination, and the other four types of job discrimination, HR for hypertension ranged from 0.91 [0.59-1.38] to 1.15 [0.91-1.46] for job discrimination related to sexual orientation and health status, respectively. Report of at least one type of job discrimination compared to none was associated with an 11% (HR=1.11 [95% CI: 1.00-1.24]) higher hypertension risk with no strong evidence of heterogeneity across race, age, education, or income. Evidence of a dose-response relationship between more types of job discrimination reported and hypertension risk emerged when excluding those with high measured blood pressure or antihypertensive use at baseline or restricting to years with consistent hypertension diagnosis guidelines. In conclusion, perceived job discrimination was associated with a higher risk of hypertension in this cohort. If the link is causal, interventions to address job discrimination may have health and workplace equity benefits, particularly for those most at risk of discrimination.

**Cardiovascular Diseases, Risk Factors, and Health Care Use: Associations with A Summarizing Measure of Social Determinants of Health** Guixiang Zhao\* Guixiang Zhao  
Machell Town Jing Fang

**Introduction:** Cardiovascular disease (CVD) remains the leading cause of death worldwide. This study assessed the associations of CVD and related risk factors and healthcare use with a summarizing measure of social determinants of health (SDOH) among US adults.

**Methods:** The 2017 Behavioral Risk Factor Surveillance System collected SDOH data in 16 states. A computed SDOH score summarizing individual social risk measures including housing insecurity (1 item), food insecurity (2), financial insecurity (1), unsafe neighborhood (1), healthcare cost barrier (1), and loss of employment (1) was categorized as 0, 1, 2, 3, and  $\geq 4$ . Adjusted prevalence ratios (APRs) were computed by conducting log-linear regression analyses with control for demographic characteristics.

**Results:** Of 102,641 adults aged  $\geq 18$ y, percentages of adults with SDOH scores of 0, 1, 2, 3, or  $\geq 4$  were 45.0%, 27.0%, 11.0%, 7.4%, and 9.6%, respectively. After adjustment for demographics, comparing with participants scoring of 0, adults with 1 to  $\geq 4$  SDOH scores had significantly increasing prevalences for heart disease (APR ranging 1.29-2.80), stroke (1.45-2.94), hypertension (1.11-1.47), hypercholesterolemia (1.09-1.44), diabetes (1.34-2.04), obesity (1.20-1.45), current smoking (1.25-2.67), unmet physical activity recommendations (1.09-1.17), and physical inactivity (1.20-1.45) (all  $P < 0.05$ ). Prevalences for taking anti-hypertensive medication (among adults with hypertension) or having cholesterol or hemoglobin A1C checked within the previous year (among adults with hypercholesterolemia or diabetes, respectively) were significantly lower among those with higher SDOH scores.

**Conclusions:** SDOH scores are a useful predictor for CVD risks among US adults. CVD prevention programs and interventions may target individuals with increasing social risks.

**Exposure to artificial light-at-night and cardiometabolic health: an urban perspective from the Catalan GCAT cohort study**

Anna Palomar-Cros\* Anna Palomar-Cros Salva Bará Alejandro Sánchez Antonia Valentín Marta Cirach Gemma Castaño-Vinyals Kyriaki Papantoniou Ana Espinosa Beatriz Cortés Anna Carreras Natàlia Blay Dora Romaguera Manolis Kogevinas Barbara N Harding

**Background**

Experimental evidence indicates that exposure to artificial light-at-night (ALAN) may lead to metabolic disturbances through circadian misalignment.

**Objective**

To investigate whether exposure to residential ALAN is associated with an increased risk of cardiometabolic diseases.

**Methods**

We used data from 9,752 participants (59% women) in the Genomes for Life (GCAT) cohort study in Barcelona. Residential ALAN was assessed from nighttime images taken by the International Space Station with a 30m resolution. We estimated visual and blue light (relevant for circadian regulation), in lux. We examined associations between ALAN and prevalent general and abdominal obesity, hypertension, and diabetes. We prospectively assessed incident cardiometabolic diseases ascertained through electronic health records. We adjusted our main models for individual demographic characteristics and further adjusted for urban exposures.

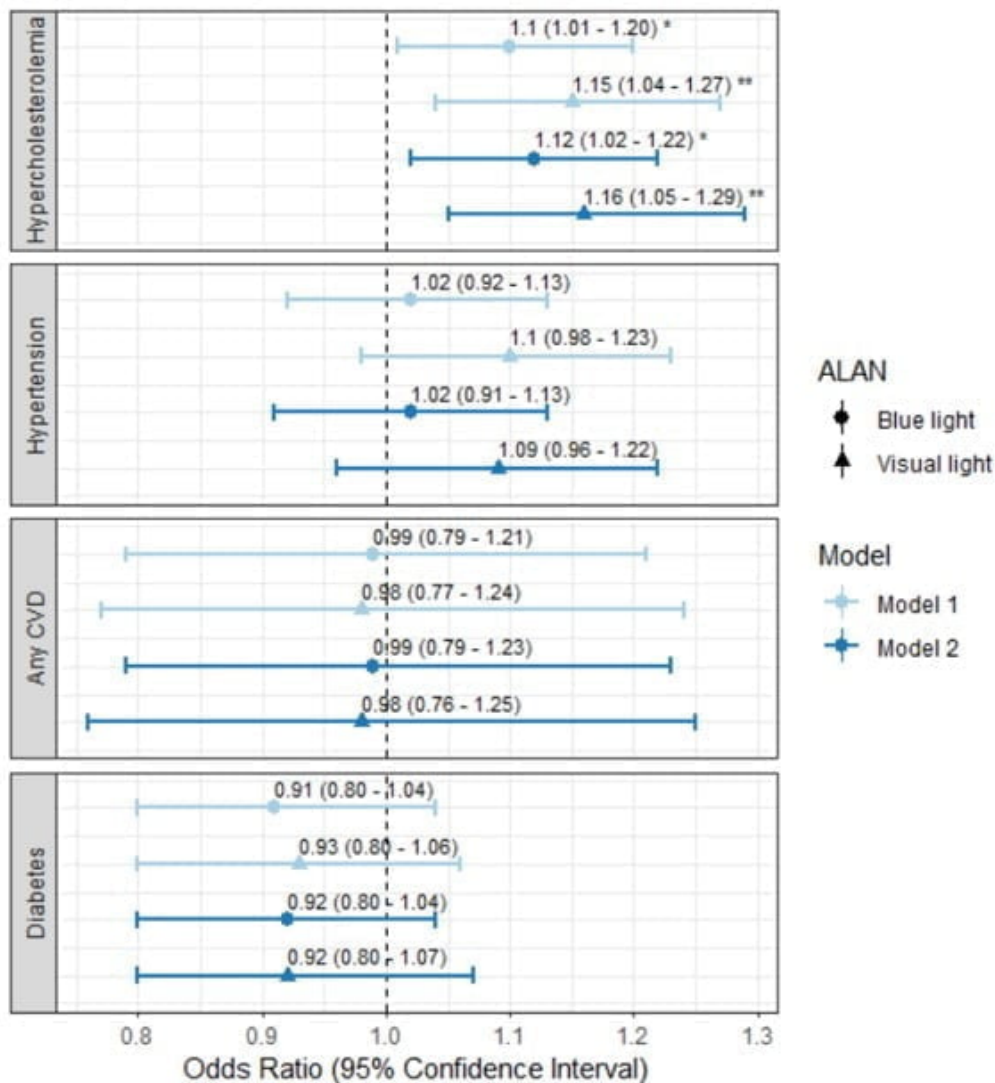
**Results**

We found an association between visual and blue light and prevalent hypertension, OR = 1.09 (1.01-1.16) and 1.08 (1.01-1.14) per interquartile range increase (0.59 lux and 0.16 lux, respectively). Visual, but not blue, light was linked with prevalent general obesity, OR = 1.06 (1.00 - 1.12), nevertheless, this association was unstable after considering other factors such as socioeconomic status or sleep. In prospective analyses (figure), visual and blue light were associated with incidence of hypercholesterolemia OR = 1.15 (1.04-1.27) and OR = 1.10 (1.01-1.20). We did not observe an association between ALAN and other incident cardiometabolic outcomes.

**Discussion**

The present study suggests an association between visual and blue ALAN and prevalent hypertension and risk of hypercholesterolemia, key risk factors in the development of cardiometabolic diseases. Results should be interpreted carefully since satellite-based ALAN assessment, even in high resolution, estimates residential exposure but not the total individual exposure.

**Figure.** Forest plot of prospective associations between ALAN indicators and incident cardiometabolic diseases in 9,752 participants from the GCAT cohort.

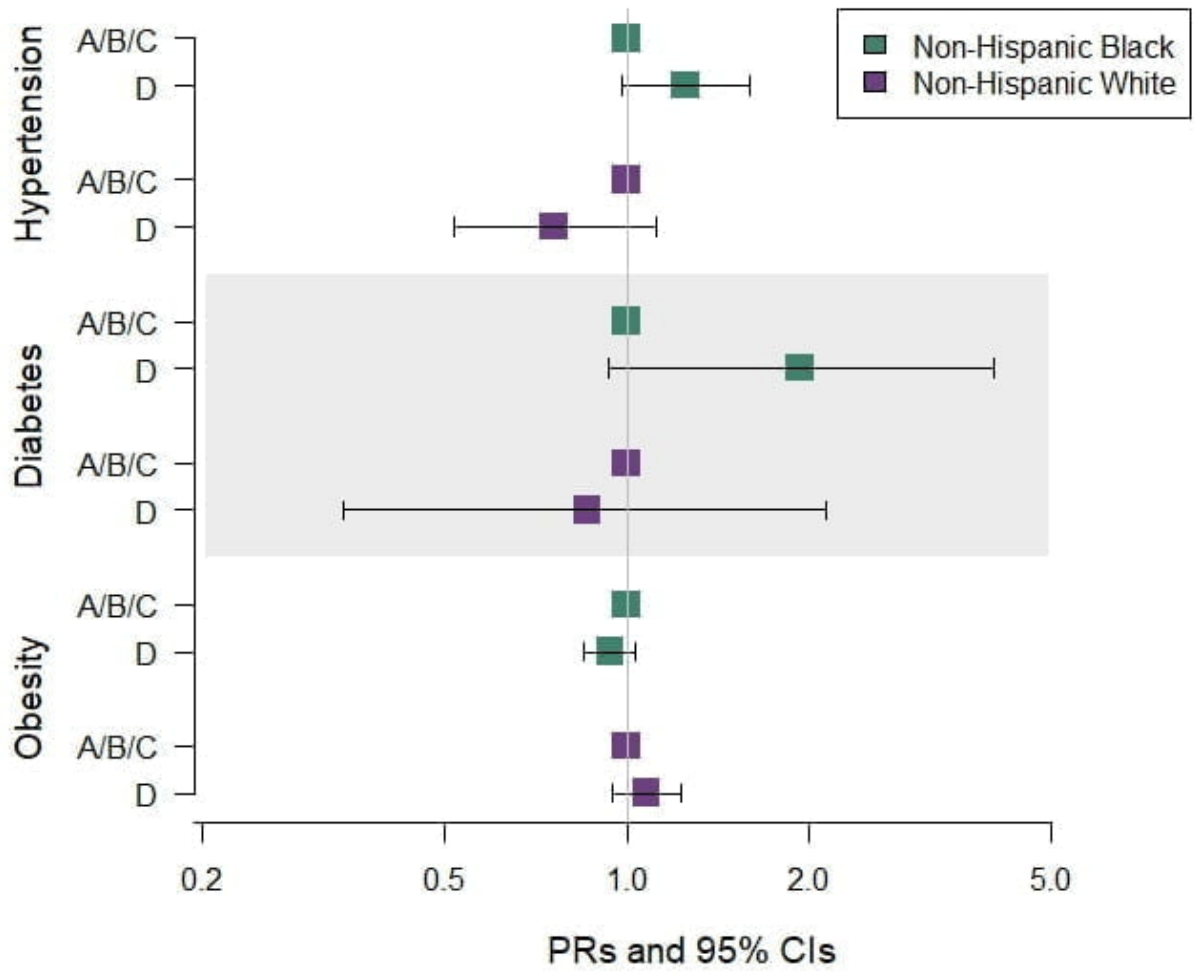


Model 1 = Adjusted for age, gender, educational level (less than primary education, primary education, secondary education and university), adherence to Mediterranean diet assessed through MEDAS (low, medium, high), tobacco consumption (never, past smoker, current smoker), daily alcohol consumption (none, past drinker, low, moderate, high, very high) and physical activity (inactive, moderately inactive, moderately active, active). Model 2 = Adjusted as model 1 and ndvi, pm2.5, population density and nightly road noise. Logistic regression model per interquartile range increase (IQR). IQR for visual light = 0.59 and IQR for blue light = 0.16. Incident cases / total sample across cardiometabolic diseases differ because of exclusion of prevalent diseases in each case: Hypercholesterolemia (735 / 8,569), Hypertension (522 / 8,891), Any CVD (121 / 9,727), Diabetes (370 / 9,617).

**Historic redlining and prevalent diabetes, hypertension, and body mass index in GuLF****Study participants** Marina R. Sweeney\* Marina Sweeney Kaitlyn G. Lawrence Kate Christenbury W. Braxton Jackson II Emily J. Werder Lawrence S. Engel Dale P. Sandler

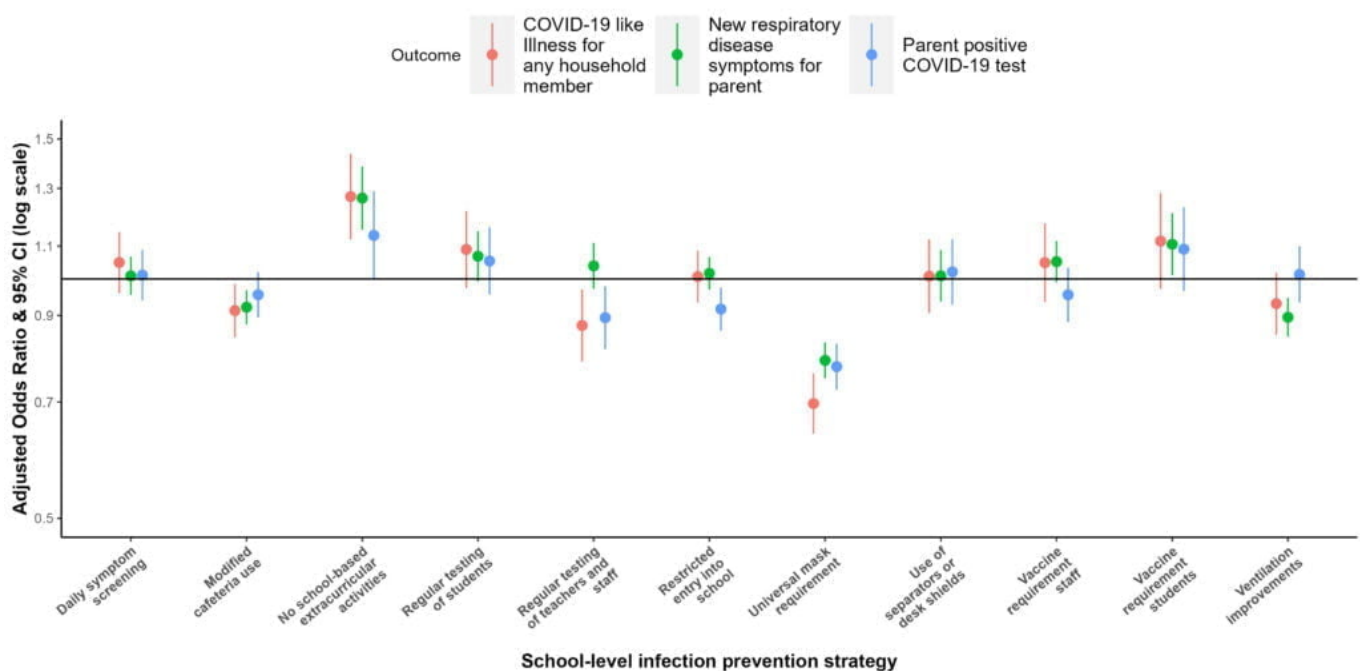
**Background:** Historic residential segregation due to “redlining” has been linked with cardiovascular disease (CVD) related outcomes, but studies have been limited. **Aim:** Evaluate cross-sectional associations between historic redlining and CVD risk factors among Gulf Long-Term Follow-Up Study participants living in cities with redlining data. **Methods:** At enrollment, participants reported height, weight, physician-diagnosed hypertension and diabetes, and residential address. The Home Owners’ Loan Corporation (HOLC) assigned neighborhood grades (based largely on the proportion of Black residents) to 239 cities in the 1930s to facilitate federal mortgage lending. We linked HOLC grades, which range from A (“best”) to D (“hazardous,” indicated on maps in red, hence “redlining”), to participant addresses (n=1,537) at the census tract level. Modified Poisson regression was used to determine PRs and 95% CIs for overall and race-stratified associations between HOLC grade and categorical BMI, diabetes, and hypertension. Models were adjusted for demographic, lifestyle, and socioeconomic factors. **Results:** Non-Hispanic (NH) Black participants were more likely to live in grade D (66%) and less likely to live in grade A or B neighborhoods (5%) than NH White participants (25% and 28%, respectively). Overall, living in a grade D neighborhood was positively associated with diabetes (PR=1.94, 95% CI: 0.80-4.70) compared to grades A/B (combined due to small numbers). HOLC grades were not associated with BMI or hypertension in the total sample. Among NH Black participants, estimates were elevated for diabetes (D vs. A/B/C: PR=1.93, 95% CI: 0.93-4.02) and hypertension (D vs. A/B/C: PR=1.25, 95% CI: 0.98-1.59); there were no associations among NH White participants. **Conclusion:** Historical redlining may have persistent impacts on a community’s health. More research is needed to evaluate the influence of redlining on current racial CVD health disparities.

### HOLC Neighborhood Grades and the Prevalence of Hypertension, Diabetes, and Obesity Stratified by Race



**School-based infection prevention strategies and household COVID-19 and respiratory disease related outcomes** Sanjana Pampati\* Sanjana Pampati Elizabeth A. Stuart Lance A. Waller Benjamin Lopman Jodie L. Guest Justin Lessler Kirsten E. Wiens Jeb Jones

In addition to being settings of education, schools play an integral role in the community but can also contribute to the spread of infectious diseases, including COVID-19 and other respiratory diseases. We analyzed data from January-June 2022 from the COVID-19 Trends and Impact Survey (2,654,636 surveys completed), a large, daily, cross-sectional survey. We examined associations between 11 school-based infection prevention strategies (e.g., ventilation improvements) and 3 household outcomes: positive COVID-19 test for parent, any new respiratory disease symptoms for parent (e.g., cough, fever, sore throat), and COVID-19 like illness for any household member. Analyses were restricted to responses from parents with a child <18 years old who was attending school in-person (n=228,624). Multivariable, quasibinomial regression models accounting for complex survey design were fit, adjusting for child-, household-, and county-level confounders (e.g., occupation, county-level COVID-19 case rate). Ventilation improvements at their child's school were associated with 10% (AOR = 0.90, 95% CI: 0.85, 0.95) lower odds of new respiratory symptoms for parents. Universal mask requirements were associated with 22% (AOR = 0.78, 95% CI: 0.73, 0.83), 21% (AOR = 0.79, 95% CI: 0.75, 0.83), and 30% (AOR = 0.70, 95% CI: 0.64, 0.76) lower odds of a positive COVID-19 test for parents, new respiratory symptoms for parents, and COVID-19 like illness for any household member, respectively. Restricted entry into school, regular testing of teachers and staff, modified cafeteria use (e.g., eating outdoors) were also associated with lower odds of specific household outcomes. Several school-based strategies had null or mixed relationships with household outcomes (e.g., daily symptom screening). Effective prevention strategies in schools are critical to support safe, in-person learning and reduce the spread of infectious diseases, particularly in periods of high community transmission.





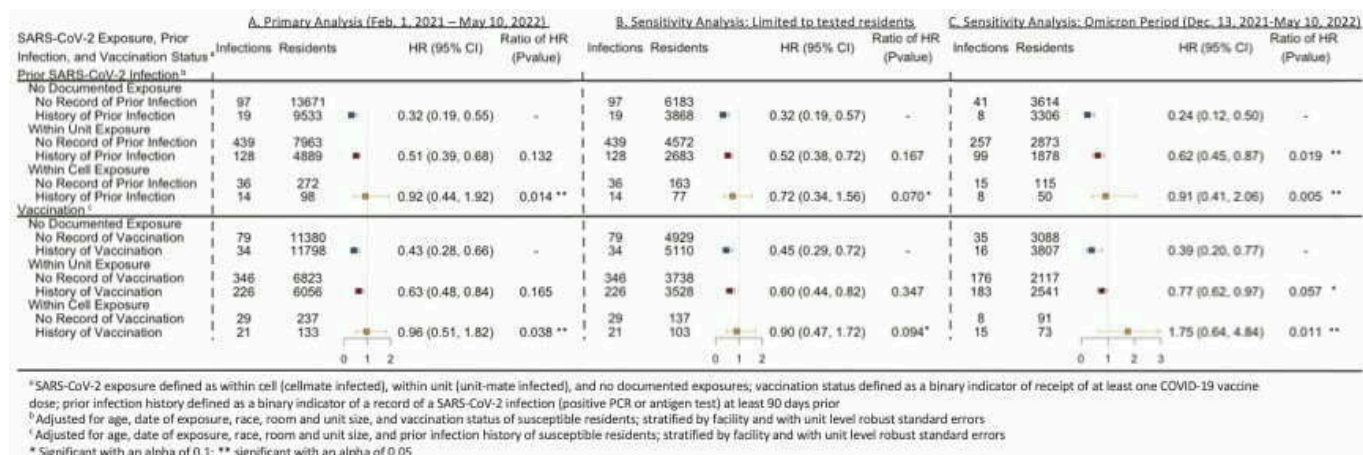
**Evidence for Leaky Protection Associated with Vaccination and Prior Infection in a Correctional Facility Population** Margaret L Lind\* Margaret Lind Murilo Dorion Byron S Kennedy Robert P Richeson Amy J Houde Mary Lansing Sarah Lapidus Russell Thomas Matt DT Hitchings Jason Andrews Derek AT Cummings Albert I Ko

Background: It remains unknown if COVID-19 vaccination and prior infection provide leaky or all-or-nothing protection against SARS-CoV-2. Leveraging the controlled social structure of correctional facilities (CFs), we examined the effect of vaccination and prior infection on the susceptibility of people with close, prolonged exposure (within cell), moderate exposure (within unit), and no known exposures.

Methods: We conducted a rolling matched cohort analysis of people who resided in Connecticut CF cells between February 2, 2021, and May 10, 2022. Residents with cell, unit or no documented exposures were matched on facility and date and followed for 14 days. We examined the effect of vaccination and prior infection on SARS-CoV-2 infection risk using Cox Proportional Hazards models. Sensitivity analyses evaluated the effect of potential testing bias and variant.

Results: We identified 370 residents with cell, 12,852 with unit and 23,204 with no documented exposures. Vaccination and prior infection reduced the susceptibility of residents with no documented exposures (HR: 0.43 [CI: 0.28-0.66]; and 0.32 [CI: 0.19-0.55]; respectively) and unit exposures (HR: 0.63 [CI: 0.48-0.84]; and 0.51 [CI: 0.39-0.68]; respectively) but not with residents with cell exposures (HR: 0.96 [CI: 0.51-1.82]; and 0.92 [CI: 0.44-1.92]; respectively; Figure.A). Vaccination and prior infection were associated with significantly less protection for residents with cell than no documented exposures (Pvalue: 0.038; and 0.014, respectively). The findings held after restricting to residents tested during follow-up and the Omicron period (Figure.B/C).

Discussion: COVID-19 vaccination and prior infection reduced the susceptibility of people with limited exposures but not with prolonged, close exposures. These findings suggest that protection may be exposure dependent (leaky) and may have broad implications for prevention (e.g. need for layered interventions) and modeling future SARS-CoV-2 transmission.



**Characterizing responsiveness to the COVID-19 pandemic in the United States and Canada using mobility data** Jean-Paul R. Soucy\* Jean-Paul R. Soucy David N. Fisman Derek R. MacFadden Kevin A. Brown

**Background:** Mobile phone-derived human mobility data are a proxy for disease transmission risk and have proven useful during the COVID-19 pandemic for forecasting cases and evaluating interventions. We propose a novel metric using mobility data to characterize how different jurisdictions responded to rising case rates.

**Methods:** We examined weekly reported COVID-19 incidence and retail and recreation mobility from Google Community Mobility Reports for 50 U.S. states and nine Canadian provinces from December 2020 to November 2021. For each jurisdiction, we calculated the responsiveness of mobility to COVID-19 incidence when cases were rising. Responsiveness across countries was summarized using subgroup meta-analysis. We also calculated the correlation between the responsiveness metric and the reported COVID-19 death rate during the study period.

**Findings:** Responsiveness in Canadian provinces ( $\beta = -1.45$ ; 95% CI: -2.45, -0.44) was approximately five times greater than in U.S. states ( $\beta = -0.30$ ; 95% CI: -0.38, -0.21). Greater responsiveness was moderately correlated with a lower reported COVID-19 death rate during the study period (Spearman's  $\rho = 0.51$ ), whereas average mobility was only weakly correlated with the COVID-19 death rate (Spearman's  $\rho = 0.20$ ).

**Interpretation:** Our study used a novel mobility-derived metric to reveal a near-universal phenomenon of reductions in mobility subsequent to rising COVID-19 incidence across 59 states and provinces of the U.S. and Canada, while also highlighting the different public health approaches taken by the two countries.

**Circulation and evidence of sarscov2 transmission from humans to dogs, cats, rodents in the city of Guayaquil.** Alberto Orlando\* Alberto Orlando Joselyn Calderón Ariana León Naomi Mora Miguel Ángel García

The recent pandemic caused by SARS-CoV-2 virus, has highlighted the need for multidisciplinary approaches to address zoonotic diseases. To date, there have been many reports of SARS-CoV-2 in domestic and wild animals, yet the transmission mechanisms remain uncertain. In this study, we aimed to investigate the presence of SARS-CoV-2 in dogs, cats and synanthropic rodents in areas with reported human cases of COVID-19 during 2021. Oropharyngeal and rectal swabs were collected from dogs and cats 10 days after the human patient's diagnosis. In addition, a questionnaire was applied to the owners of the animals to determine the human-pet interaction. Wild rodents were captured using traps, and organs were collected for analysis. RNA was extracted from all samples, and SARS-CoV-2 was detected using RT-qPCR. We collected samples from 78 domestic dogs, 25 domestic cats, and 234 wild rodents. The positivity rate was 21.8% for dogs, 16% for cats, and 6% for rodents. The presence of the virus was confirmed by sequencing the complete genome in samples from positive domestic dogs. A logistic regression analysis of risk factors was performed, and results showed that sharing food with the owner had an odds ratio of 12.79 (95% CI 1.80-90.82,  $p=0.011$ ). This study highlights the potential of domestic animals and wild animals as reservoirs of SARS-CoV-2, and the need for multidisciplinary approaches to understand the transmission mechanisms of zoonotic diseases. The findings of this study also emphasize the need for ongoing surveillance and research to identify potential zoonotic sources of future outbreaks, particularly in Latin America, where large populations of roaming dogs and cats persist and where social conditions in these countries are ideal for the presence of rodents.

**Far-right-wing voting and COVID-19 vaccine hesitancy** Insa Backhaus\* Insa Backhaus Hanno Hoven Ichiro Kawachi

**Background:** As of January 11<sup>th</sup>, almost one-fourth of the European population has not been vaccinated against COVID-19 and vaccine hesitancy is a growing public health problem. Over the past months, especially far-right parties have expressed skepticism toward the safety of the COVID-19 vaccine. Consequently, people associating with far-right parties may be more hesitant to get vaccinated. We aim to investigate the association between far-right-wing voting and COVID-19 vaccine hesitancy and to explore if the association varies by individual-level and country-level factors. **Methods:** We use cross-sectional data of 28,057 individuals from 19 countries who participated in the European Social Survey between 2020 and 2022 and apply a series of multi-level regression models. We also test for interactions between far-right-wing voting with individual-level (e.g., gender, institutional trust and social participation) and country-level factors (e.g., income inequality, COVID-19-stringency and excess mortality). **Results:** Far-right-wing voters were 2.7 times more likely to hesitate to get vaccinated against COVID-19 than mainstream voters (Prevalence Ratio: 2.69, 95% Confidence Interval: 1.46-4.94). Even after considering institutional trust and social participation, the association remains robust (Adjusted Prevalence Ratio: 2.39, 95% Confidence Interval: 1.30-4.41). Apart from gender, no other individual- or country-level factor seems to modify the association substantially. **Conclusions:** We conclude that far-right-wing voting is associated with COVID-19 vaccine hesitancy, independently from trust and social participation and that the association is similar among European countries, regardless of how hard the pandemic has hit them, how stringent the public health measures were and how great the income inequality was. The reason why far-right voters demonstrate a higher level of vaccine hesitancy remains puzzling. This must be further investigated and closely monitored.

**Elevated mortality among women with perinatal depression: a nationwide register-based study in Sweden** Donghao Lu\* Donghao Lu Naela Hagatulah Emma Bränn Anna Sara Oberg Unnur Anna Valdimarsdóttir Qing Shen

**Purpose:** Women experiencing postpartum psychiatric disorders overall have been found at risk for premature death. The risk related to perinatal depression (PND), occurring during pregnancy or after childbirth, is unclear, and the role of familial factors has not been addressed. We therefore examined whether women with PND are at elevated risk of premature death compared to unaffected women and their full sisters.

**Methods:** We conducted a nationwide population-based matched cohort study of 86 551 women receiving a first-ever diagnosis of PND during 2001-2017 in Sweden and 1:10 unaffected women (N=865 510) matched on age and calendar year at delivery using incidence density sampling. We also compared risk within 279 586 full sisters to address familial confounding. PND was identified through a clinical diagnosis of depression or dispensation of anti-depressants during pregnancy (antepartum) or up to one year after delivery (postpartum). We used multivariable Cox regression to estimate HRs of mortality comparing women with PND to unaffected women/sisters.

**Results:** During up to 18 years of follow-up, 522 deaths (0.82 per 1 000 person-years) were observed among women with PND diagnosed at a mean age of 31.0 years. Compared to unaffected women, women with PND had an elevated risk of death (adjusted HR 2.11, 95% CI 1.86- 2.40). The risk elevation was greater for postpartum (HR 2.71, 95% CI 2.26-3.26) than for antepartum depression (HR 1.62, 95% CI 1.34-1.94). An attenuated, yet significant, association was noted for PND in the sibling comparison (HR 1.49, 95% CI 1.18-1.88). The association was most pronounced within the first year after PND and for suicide.

**Conclusion:** Our findings suggest that even when accounting for familial factors, women with PND are at risk for premature death, particularly during the first year after diagnosis and due to suicide. Affected women, their families, and health professionals should be aware of these severe health hazards following PND.

**A prospective study of hypertensive disorders in pregnancy and subjective cognitive decline**

Alexandra Purdue-Smithe\* Alexandra Purdue-Smithe Janet W. Rich-Edwards Deborah L. Blacker  
Kathryn M. Rexrode

Subjective cognitive decline (SCD), defined as self-reported deterioration in cognitive function, is increasingly recognized as an early risk state for dementia. Emerging research suggests that hypertensive disorders in pregnancy (HDP) may be associated with greater risk of dementia in women during late life, but whether HDP are associated with SCD during midlife is unknown. We prospectively examined associations of self-reported HDP with SCD among 49,038 parous participants of the Nurses' Health Study II with data on lifetime pregnancy history and SCD, and no history of pre-pregnancy cardiovascular disease, type II diabetes, or chronic hypertension. SCD was assessed in 2017 (at median age 63 years) via participants' responses to 7 questions, which were summed to a total SCD score (0-7) and then categorized as good (0; 57%), moderate (1-2; 31%), and poor ( $\geq 3$ ; 12%). Multinomial regression models were used to estimate OR (95% CI) for moderate and poor compared to good SCD score. After adjusting for age, income, and pre-pregnancy BMI and other health and behavioral factors, HDP in a first pregnancy (9%) was associated with greater odds of a poor SCD score (OR=1.15; 95% CI=1.05-1.26), but not a moderate SCD score (OR=1.03; 95% CI=0.96-1.11), compared to those with normotensive first pregnancies. Preeclampsia was slightly more strongly associated with a poor SCD score (adjusted OR=1.16; 95% CI=1.04-1.30) than gestational hypertension (adjusted OR=1.12; 95% CI=0.96-1.32). In stratified analyses, HDP in a first pregnancy was more strongly associated with a poor SCD score in older than in younger women (SCD assessment at  $>63$  years OR=1.23; 95% CI=1.05-1.43 vs.  $\leq 63$  years OR=1.10; 95% CI=0.98-1.24). Our results suggest that HDP is a risk factor for SCD in midlife, which may reflect early neuropathological changes related to dementia. Women with a history of HDP may benefit from enhanced monitoring for cognitive change during midlife and dementia risk factor management.

**Adverse pregnancy outcomes and risk of type 2 diabetes in the Women's Health Initiative**

Kexin Zhu\* Kexin Zhu Jean Wactawski-Wende Pauline Mendola Nisha I. Parikh Michael J. LaMonte Vanessa M. Barnabei Rachael Hageman Blair JoAnn E. Manson Simin Liu Meng Wang Robert A. Wild Aladdin H. Shadyab Linda Van Horn Erin S. LeBlanc Rachel Sinkey Peter F. Schnatz Nazmus Saquib Lina Mu

**Background:** Although gestational diabetes (GDM) and delivering high birth weight infants are known to predict a higher risk of future type 2 diabetes (T2D), the associations of other adverse pregnancy outcomes (APOs) with T2D are not well established. We aimed to examine the associations between different types of APOs and incident T2D among postmenopausal women.

**Methods:** The Women's Health Initiative, a nationwide cohort of postmenopausal women, collected self-reported history of APOs including GDM, hypertensive disorders of pregnancy (HDP), preterm birth (PTB), and delivering low [ $<2,500$ g, LBW] or high birth weight [ $>4,500$ g, HBW] infants. Participants self-reported incident T2D treated with medication annually from baseline (1993-1998) through March 2021. We used logistic regression to examine the associations of any and individual APO with T2D. Stratified analyses were conducted to assess effect modification by body mass index (BMI), race and ethnicity, education, parity, breastfeeding, and age at first birth.

**Results:** This analysis included 49,717 women without T2D at enrollment who had at least one pregnancy and responded to the questionnaire about APOs. After adjusting for BMI, demographic, lifestyle, and reproductive factors, GDM (OR 2.26, 95% CI 1.94-2.63), HBW (OR 1.30, 95% CI 1.18-1.44), and HDP (OR 1.18, 95% CI 1.08-1.30) were independently associated with higher odds of T2D, respectively, while PTB and LBW were not associated with T2D risk. A history of more than two APOs was associated with higher odds of T2D (OR 1.55, 95% CI 1.28-1.88). We further observed higher odds of T2D (OR 3.69, 95% CI 2.38-5.70) among women with a history of both GDM and HDP. We did not observe significant effect modifications.

**Conclusion:** Postmenopausal women with a history of GDM, delivering HBW-infants, or HDP are at risk for future T2D. In addition, those with two or more conditions had an augmented risk and might be prioritized for screening and prevention efforts for T2D.

**Pregnancy history at age 40 as a marker of cardiovascular risk** Liv Grimstvedt Kvalvik\* Liv Grimstvedt Kvalvik Rolv Skjærven Gerhard Sulo Aditi Singh Quaker Harmon Allen J. Wilcox

**Background:** Individual pregnancy complications (such as preeclampsia, small birth weight and preterm delivery) have been linked to increased maternal risk of cardiovascular disease. We assessed how well a woman's total pregnancy history at age 40 predicts her risk of dying from atherosclerotic cardiovascular disease (ASCVD).

**Methods:** In this population-based, prospective study we used data from the Medical Birth Registry of Norway, the national cause-of-death registry, the national education database and the population registry in the period 1967-2020. We identified 854,442 women born after 1944 or registered with a pregnancy in 1967 or later, and surviving to age 40. Our main outcome was the hazard ratio of ASCVD mortality up to age 69 for 40-year-old women, as predicted by exposure categories of combined parity (0, 1, 2, 3, or 4 recorded pregnancies) and number of complicated pregnancies (preterm delivery <35 gestational weeks, preeclampsia, placental abruption, perinatal death and term or near-term births <2700grams). Women with three pregnancies and no complications had lowest ASCVD risk and served as the reference group. Estimates were adjusted for women's birth year.

**Results:** Among women reaching age 40, risk of ASCVD before age 69 increased with greater number of complicated pregnancies in a strong dose-response fashion, reaching 24-fold risk (95% confidence interval 11-54) for women with four complicated pregnancies. Based on pregnancy history alone, 19% of women at age 40 (including nulliparous women) had ASCVD mortality increased 2.5 to 5-fold.

**Conclusions:** Pregnancy history at age 40 is highly predictive of ASCVD mortality over the next thirty years. Pregnancy history at age 40 could be useful as a routine clinical screen to identify at-risk women young enough to benefit from intervention, and perhaps even before clinical markers of CVD risk have fully emerged.



**Infertility and Risk of Postmenopausal Breast Cancer in the Women's Health Initiative**

Leslie V. Farland\* Leslie V. Farland Kimberly Lind Cynthia A. Thomson Nazmus Saquib Aladdin H. Shadyab Peter F. Schnatz Rogelio Robles-Morales Lihong Qi Howard Strickler Denise J. Roe Holly R. Harris

Although infertility (i.e., failure to conceive after  $\geq 12$  months of trying) is strongly correlated with established breast cancer risk factors (e.g., nulliparity, number of pregnancies, and age at first pregnancy), its association with breast cancer is inconclusive. Previous studies are primarily small clinic-based or registry studies with short follow-up, predominately focusing on premenopausal breast cancer. The objective of this study was to assess the relationship between infertility and postmenopausal breast cancer risk among participants in the Women's Health Initiative (analytic sample=144,244; >25 years of follow-up). At study entry, participants were asked about their pregnancy history, infertility history, and perceived cause of infertility. Incident breast cancers were self-reported with adjudication by trained physicians reviewing medical records. Cox proportional hazards models were used to estimate risk of incident postmenopausal breast cancer for women with infertility (overall and specific infertility diagnoses) compared to parous women with no infertility. The contribution of mediating factors was calculated. We observed a modest association between infertility (n=23,406) and risk of postmenopausal breast cancer (HR=1.07; 95% CI: 1.02-1.13). The association was largely mediated by age at first pregnancy (natural indirect effect: 46.4% mediated, CI:12.2%-84.3%). We did not observe associations with separate infertility diagnoses except for male factor infertility (HR: 1.21, 95% CI: 1.07-1.38). The association with male factor infertility was primarily observed among participants with an older age at first birth (>30 years HR: 1.50, 95% CI: 1.14-1.97;  $\leq 30$  years HR: 1.15, 95% CI: 0.95-1.40; p-value test for interaction:0.12). These findings suggest that infertility may be associated with future risk of breast cancer due to age at first pregnancy and highlight the importance of incorporating reproductive history across the life course into breast cancer analyses.

**Estimating the association of daytime racial and economic microsegregation with hypertensive disorders of pregnancy in metro Atlanta using mobile phone location data**

Katherine Campbell\* Katherine Campbell Meredith Dixon Courtney Victor Michael Kramer

Hypertensive disorders of pregnancy (HDPs) contribute to maternal/fetal morbidity and mortality, disproportionately affecting marginalized groups. Disparities in disease burden are associated with concentrated racial and income inequality defined by the place of residence, but may also be associated with daytime population mixing and mobility of the population. We estimate the association of daytime racial and income segregation with HDPs among women who gave birth in metro Atlanta and the interaction with maternal insurance status, and race/ethnicity.

Data for live births in 2018 and 2019 were abstracted from vital records to determine HDP diagnosis and maternal residence by census tract ( $n = 98,906$ ). Anonymized mobile phone location data were used to estimate median household income density in each census tract and racial/ethnic density, as a function of where devices moved during daytime hours. Mobility data was not linked to individual health records. Mixing of devices in each census tract by race and income was estimated by the Index of Concentration at Extremes (ICE). Logistic regression models were used to estimate odds of HDPs in census tracts with micro-segregation and income inequality during the daytime, compared to no concentration. 8.9% of births occurred among women with a diagnosed HDP, with a higher rate for Black women compared to White women (9.9% versus 7.9%). Higher daytime micro-segregation was associated with greater odds of HDPs compared to no concentration (OR = 1.20; 95% CI=1.14, 1.27). Higher daytime income inequality was also associated with higher odds of HDPs (OR = 1.23, 95% CI = 1.16, 1.30). Interaction by race showed concentrated affluence was more protective for White women compared to Black women, with no evidence for modification by insurance status or maternal education. Understanding social mixing during the daytime by describing the undercurrents of population mobility in neighborhoods may inform disparities in maternal health.

**Covariate Adjustment in LGBTQ+ Health Disparities Research: Aligning Methods with Assumptions** Colleen Reynolds\* Colleen Reynolds Jarvis T. Chen Brittany M. Charlton

In 2016, the NIH designated LGBTQ+ individuals (i.e., lesbian, gay, bisexual, transgender, queer, and all sexual and gender minorities) as a health disparities population. The growing interest in studying the health of LGBTQ+ populations merits revisiting the methodological approaches researchers employ. We elucidate how researchers can identify appropriate adjustment sets for both descriptive and causal questions using directed acyclic graphs (DAGs). To illustrate these points, we simulated a simplified example using pregnancy loss as the outcome (Figure 1), wherein we generate 1,000 datasets with a sample size of 10,000 individuals.

We first argue that in descriptive research, adjustment should be minimal as there are implicit value judgments in adjusting for nuisance variables. Using the example of sexual orientation-related disparities in pregnancy loss, we demonstrate how such adjustment can obscure the magnitude of disparities. Second, we motivate why covariates that are commonly used in LGBTQ+ health disparities research (e.g., health insurance status) are mediators, not confounders, and how adjusting for these variables in causal research can induce bias by blocking part of the indirect effect of exposure on the outcome (DAG A).

Next, we illustrate the complexity of mediation analyses with social exposures due to mediator-outcome confounding induced by exposure (node Z on DAG B), and compare potential approaches, such as inverse probability weighting (IPW) and randomized intervention analogues. Finally, we demonstrate how incorporating heterosexism (i.e., stigma and discrimination) as an unobserved node in our DAG can guide decision-making on appropriate adjustment sets (DAG C). For example, by eliminating the effects of sexual orientation (i.e., through method of conception) on pregnancy loss using IPW, sexual orientation can be used as a proxy for the discriminatory effects of heterosexism.

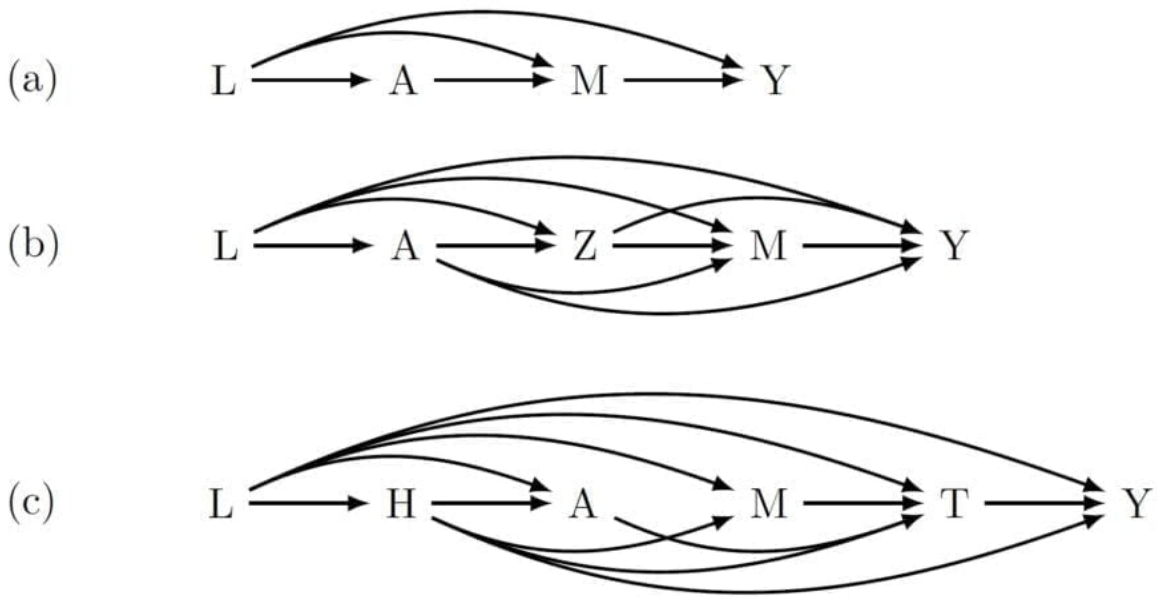


Figure 1. Directed Acyclic Graphs for a simplified illustrative example. Where L: birth cohort, A: sexual orientation, M: health insurance, Z: adult socioeconomic status, Y: pregnancy loss, H: heterosexism [unmeasured], T: method of conception.

**Variable Selection for Transporting to External Target Populations** Michael Webster-Clark\*  
Michael Webster-Clark Rachael Ross Alex Keil Robert Platt

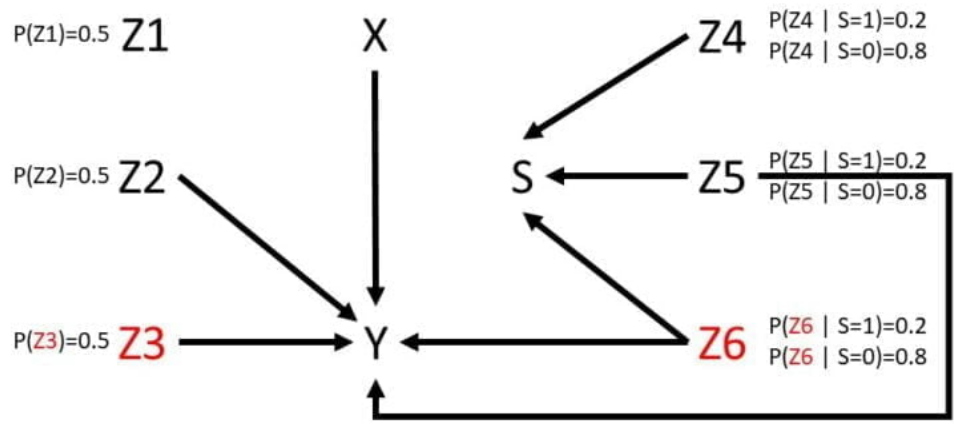
External validity is crucial for epidemiologic research. External validity bias can be reduced by weighting and modeling to account for differences in effect measure modifier (EMM) distributions between trial and target populations. For internal validity, control of non-confounding variables can improve variance. For external validity, however, it is unclear how control of non-EMM variables impacts variance.

We assessed how including various types of variables when transporting estimates using inverse odds weights (IOW) affected variance of the transported risk difference (RD).

We simulated 1000 replicates of a 10000-person randomized trial ( $S=1$ ) of a binary treatment  $X$  and binary outcome  $Y$  and a 10000-person target population ( $S=0$ ). 6 binary, independent covariates  $Z1-Z6$  were simulated in both (**Figure 1**), with EMMs in red.  $Z1$  was distributed identically in both populations and had no direct effect on  $Y$ ;  $Z2$  was distributed identically, caused  $Y$ , and was not an EMM;  $Z3$  was distributed identically, caused  $Y$ , and was an EMM; and  $Z4-Z6$  differed between the trial and target but were otherwise identical to  $Z1-Z3$  regarding associations with  $Y$  and EMM. We standardized  $Z6$  (a minimally sufficient set for external validity) and assessed the impact of including other covariates in the sampling model on empirical standard errors (ESE).

The true RD in the trial was 0.17 and the true RD in the target was 0.23. All models with  $Z6$  were unbiased. The ESE when adjusting only for  $Z6$  was 0.0174. ESEs did not change when including  $Z1$ ,  $Z2$ , or  $Z3$ . Including  $Z4$  (ESE: 0.0313) or  $Z5$  (ESE: 0.0317) substantially increased ESEs. Similar trends were observed when transporting with outcome models.

Variables that differ between study and target populations that are not EMM increase variance when included in statistical models, regardless of their outcome association. Adjusting for all outcome-related variables when transporting treatment effect estimates can reduce precision.



$$P(Y = 1) = 0.1 + 0.1 * X + 0.1 * Z2 + 0.1 * Z3 + 0.1 * Z5 + 0.1 * Z6 + 0.1 * X * Z3 + 0.1 * X * Z6$$

**A simulation study to evaluate a method to adjust summary level data for both confounding and misclassification** Tyler Richter\* Tyler Richter Richard MacLehose Tim Lash Thomas Ahern Lindsay Collin Allison Domingues

**Background:** Uncontrolled confounding and misclassification are well-known threats to validity. Published studies adjust for confounders, but concern may remain about bias due to misclassification. If authors report the crude  $2 \times 2$  table, an external analyst can adjust for the misclassification, but the result will be biased due to confounding. Some use an *ad hoc* procedure to adjust for both misclassification and confounding: First, compute an estimate for bias due to confounding by comparing the difference (ratio for multiplicative measures) between the crude effect estimate and confounding-adjusted effect estimate. Next, adjust for misclassification in the  $2 \times 2$  table using validation data. Last, address confounding bias by adding (or multiplying) the estimated bias due to confounding to the misclassification-adjusted estimate. **Objectives:** Evaluate the performance of this *ad hoc* procedure using a simulation study to compare the estimated bias, coverage probability, and mean squared error between 1) the confounding-adjusted estimates that ignore misclassification, 2) the misclassification-adjusted estimates that ignore confounding 3) the *ad hoc* procedure to adjust for both biases. **Methods:** We conducted a simulation study to generate datasets that have both confounding and misclassification. We implemented the 3 adjustment approaches in each dataset. The extent of confounding and misclassification were varied across simulations. We evaluated the performance of the methods for each set of parameters using 10,000 iterations. **Results:** On average, the *ad hoc* procedure performed better than other approaches. It had lower bias, lower mean squared error, and better coverage for the RD, RR, and OR. However, the *ad hoc* procedure is biased in many scenarios. **Conclusion:** If validation data are available, this process can provide estimates accounting for both confounding and misclassification using only summary-level data and published estimates of adjusted effects.

**Non-parametric sensitivity analysis for causal mediation analysis** Qinyun Lin\* Qinyun Lin  
Kenneth A. Frank

Causal mediation inference relies on assumptions such as the sequential ignorability. It is important to conduct a sensitivity analysis to evaluate whether a potential violation of such assumptions may easily change a conclusion. We propose a non-parametric approach based on a potential outcomes framework that extends the Robustness of an Inference to Replacement (RIR) approach and links to the Fragility Index. RIR expresses the robustness of inference as the amount of data that must be replaced to change the conclusion. Such approach has been applied widely in linear regression models across different fields. For dichotomous outcomes, RIR quantifies how many treatment cases with positive outcomes would have to be replaced with hypothetical patients who did not receive a treatment to change an inference. The RIR addresses known limitations of the Fragility Index by accounting for the observed rates of outcomes. In the causal mediation context, we extend the RIR based upon the fundamental definitions of key estimands within the counterfactual framework (e.g., natural indirect effect, controlled direct effect). Our approach provides a comprehensive framework to quantify potential bias due to different types of confounders, including those that confound different pathways (e.g., the exposure-mediator path, and/or the mediator-outcome path in the treatment group). Importantly, the method is built upon a non-parametric framework that does not require any assumptions such as linearity or no exposure-mediator interactions. At the same time, the approach can be easily applied to applications that employ linear regression models estimating mediation effects. As inherent in the general RIR approach, the mediation RIR can be used for varying thresholds for inference as well, including clinical importance. We illustrate the approach using a perinatal epidemiology example where twinning mediates the relationship between fertility treatment and adverse outcomes like preterm birth.



**Identifying individuals causing positivity violations as missing exclusion criteria: a decision trees-based algorithm** Arthur Chatton\* Arthur Chatton Gabriel Danelian Johann Foucher Maxime Léger Florent Le Borgne

Classical approaches to handle positivity (a.k.a. common support) violations change the characteristics of the sample and therefore shift the targeted population and the estimand, compromising the external validity of the results. Furthermore, the existing approaches for diagnosing such violations do not easily allow the identification of problematic individuals.

We propose an algorithm based on regression trees to identify such subgroups: the Po(sitivity) Regression Trees algorithm (PoRT). PoRT looks for combinations of predictors, where the exposed and unexposed samples are highly imbalanced, and the subgroup's size is sufficiently high. First, PoRT learns a succession of regression trees across different combinations of predictors. Second, it identifies imbalanced subgroups using two user-defined hyperparameters: the minimum size of the subgroup, and the maximum probability of being (un)exposed in the subgroup.

We applied PoRT by reanalyzing four recently published studies. We identified the two structural positivity violations reported by the authors. Additionally, we identified ten subgroups with a suspicion of violation, including seven likely structural according to domain experts.

We believe that this algorithm has far-reaching implications across epidemiological, economic, and political sciences by facilitating the definition of the target population. Finally, extensions to the PoRT algorithm for longitudinal settings and mediation analyses will be discussed.

**Methodological considerations in target trial emulation using cohort studies: estimating the effect of antihypertensive medication initiation on incident dementia in ARIC, CHS, and HRS** Erin E. Bennett\* Erin Bennett Jingkai Wei Chelsea Liu Emma K. Stapp Kan Z. Gianattasio Scott C. Zimmerman Sarah F. Ackley Michael E. Griswold Annette L. Fitzpatrick Rebecca F. Gottesman Lenore J. Launer B. Gwen Windham Deborah A. Levine Alison E. Fohner Jamie Robins M. Maria Glymour Melinda C. Power

*Background:* Observational studies link high midlife blood pressure (BP) to increased dementia risk, though most randomized controlled trials (RCTs) have not demonstrated a benefit to dementia risk through antihypertensive medication. We aimed to emulate a target trial of antihypertensive medication initiation on dementia risk to understand whether observational data could replicate findings from published RCTs.

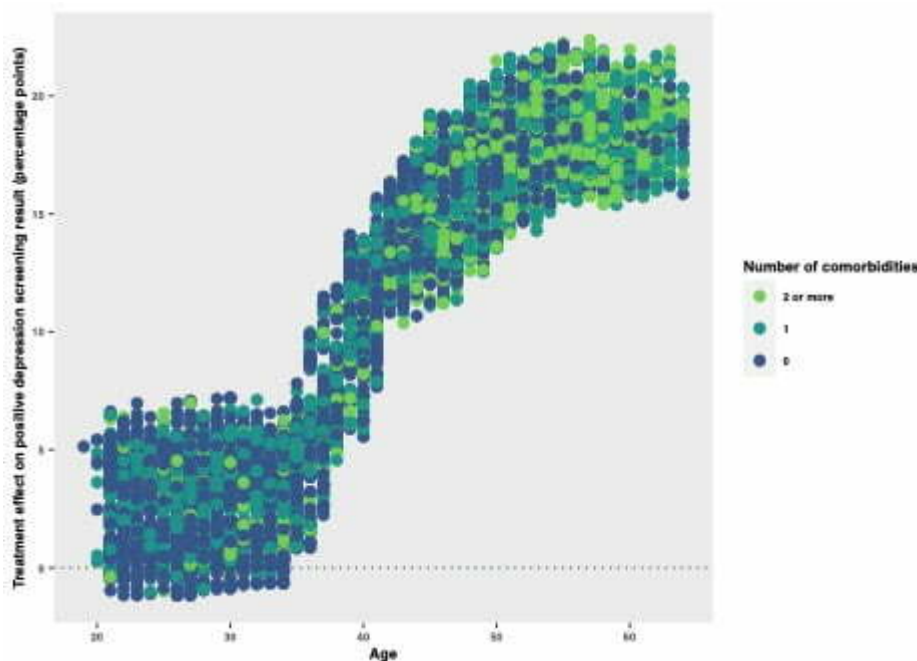
*Methods:* We estimated the effect of initiating antihypertensive medication use on incident dementia and coronary heart disease (CHD), a positive control outcome. Atherosclerosis Risk in Communities (ARIC) study, Cardiovascular Health Study (CHS), and Health and Retirement Study (HRS) participants who met eligibility criteria similar to those in extant trials (e.g., unmedicated systolic BP  $\geq 140$  mmHg) and had propensity scores for initiating antihypertensive medications common to both new users and never users were eligible for inclusion. We analyzed each cohort separately using adjusted Cox models.

*Results:* Few participants (ARIC,  $n=636$ ,  $\sim 4\%$ ; CHS  $n=638$ ,  $\sim 19\%$ ; HRS  $n=1,124$ ,  $\sim 4\%$ ) met eligibility criteria. Associations between antihypertensive medication initiation and incident dementia were inconsistent (HRs ranged from 0.36 - 1.63) and were not statistically significant. Positive control outcome analyses consistently and unexpectedly suggested antihypertensive medication initiation was associated with greater risk of CHD (e.g., ARIC HR=2.13, 95% CI: 0.72, 6.34).

*Conclusions:* While target trial emulation improves conceptual alignment of observational analyses with RCTs, these efforts are limited by the challenges of observational data. Few observational study participants meet RCT eligibility criteria, and exchangeability may be difficult to achieve based on measured covariates. Use of formalized processes for evaluating exchangeability (e.g., positive control outcomes) will strengthen confidence in target trial emulation efforts.

**Machine Learning Detects Heterogeneous Effects of Medicaid on Depression: Oregon Health Insurance Experiment** Ryunosuke Goto\* Ryunosuke Goto Kosuke Inoue Itsuki Osawa Katherine Baicker Scott L. Fleming Yusuke Tsugawa

Expanding health insurance coverage is a policy priority, but the cost can be high and evidence on health benefits is mixed. The *ex ante* characterization of subpopulations who are likely to benefit most from health insurance coverage could allow programs to be both more effective and financially sustainable. We aimed to identify subpopulations that experienced greater improvements in depression from Medicaid coverage using baseline characteristics and to assess the potential effectiveness of targeting expansions to those with high predicted benefit using machine learning. We analyzed data on 10,068 individuals who responded to in-person surveys in the Oregon Health Insurance Experiment, a randomized controlled trial of the effects of Medicaid coverage. We estimated the individual treatment effect (ITE) of Medicaid coverage on screening positive for depression (defined as a Patient Health Questionnaire-8 score  $\geq 10$ ) using the machine learning causal forest model. We found that the effects of Medicaid coverage on depression were heterogeneous; individuals with high estimated ITEs were older and had more physical or mental health conditions at baseline (**Figure**). We then assessed the policy of expanding Medicaid coverage only to individuals with high predicted benefit versus expanding coverage to all eligible individuals in the study sample. Covering individuals with high estimated ITEs achieved greater risk reduction in depression (21.5 vs. 8.8 percentage points; adjusted difference [95% CI], +12.7 [+4.6 to +20.8];  $P=0.003$ ) and lower annual healthcare spending per case of depression prevented (\$16,627 vs. \$36,048; adjusted difference [95% CI], -\$18,598 [-\$156,953, -\$3,120];  $P=0.04$ ) than covering all eligible individuals. By prioritizing Medicaid coverage based on individuals' predicted benefit, policymakers may be able to improve the mental health of low-income individuals more effectively and efficiently.



**Spatially Quantifying the Downstream Impact of Structural Interventions: Role of Minority Depository Institutions in Improving Mortgage Lending Disparities and Community Health**

Ariana Mora\* Ariana Mora Snigdha Peddireddy Michael Kramer

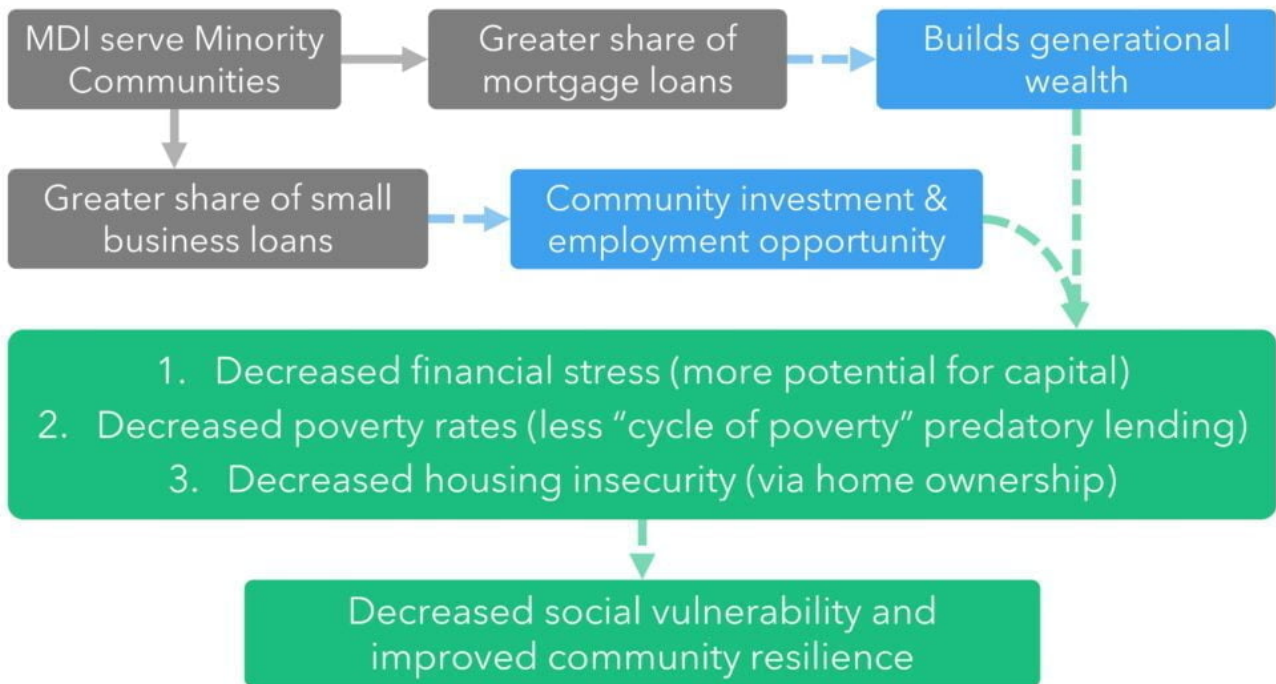
Background: Minority Depository Institutions (MDI) serve minoritized communities historically disadvantaged by traditional banks. Quantifying the influence of structural factors, like MDI, on health outcomes is difficult. We utilize spatial spillover models to quantify the impact of MDI as a structural intervention for lending inequity on downstream community health.

Methods: We deconstructed the proposed causal pathway for MDI into expected proximate outcomes (mortgage approval) and theoretical downstream outcomes (Social Vulnerability Index (SVI)) (figure). **Proximate model:** "Banking effect area" of an MDI was determined via comparing different spatial spillover neighbor definitions. We chose the best-fitting (lowest AIC) spatial Durbin spillover model (K-Nearest Neighbor, k=15) for quantifying MDI presence on nearby 2019 mortgage approval rates, controlling for tract-level confounders (minority %, debt-to-income ratio, population density, median income). **Downstream model:** Utilizing above model specification and spillover area (k=15), we assessed impact of MDI presence on time-lagged tract SVI in 2020. Durbin model impacts and valid variance estimates computed via MCMC (R=1000). Analysis restricted to Southeastern U.S. metropolitan tracts due to computational constraints.

Results: **Proximate:** the indirect impact of MDI on mortgage approval was 0.09 (CI: 0.03, 0.15), indicating significantly higher approval rates in the 15 tracts surrounding an MDI. **Downstream:** significantly lower social vulnerability in tracts surrounding MDI (indirect impact: -1.5; CI: -2.9, -0.2) and overall (surrounding tracts + MDI tract) (total impact: -1.7; CI: -3.3, -0.3).

Conclusions: After adjusting for tract-level confounders, MDI have a positive financial and social impact that extends beyond the tracts in which they reside and have a broader positive community effect. This analysis demonstrates a stepwise approach to quantify downstream community impacts of structural interventions.

**Minority Depository Institutions Theory of Social Change:** Relationships represented by solid arrows were reported by FDIC in 2019<sup>1</sup> and are the basis of the proximate outcome model. Dashed arrows reflect theoretical community effects as the basis for the downstream outcome model.



<sup>1</sup>Federal Deposit Insurance Corporation. Minority Depository Institutions: Structure, Performance, and Social Impact. 2019.

**Racial and Ethnic Inequities in Home- and Community-Based Services Waivers for People with Intellectual/Developmental Disabilities: A Nationwide Analysis** Adele Levine\* Eric Rubenstein Adele Levine Na Wang Amy Michals Megan Cole

7.4 million people in the US have intellectual and development disabilities (IDD) and experience health inequities compared to peers. Inequities are compounded for minoritized people with IDD. Medicaid Home and Community Based Service (HCBS) waivers are policies designed to improve service access and community integration for disabled people. Yet, waiver enrollment is capped and inequities in receipt have not been studied. Therefore, we analyzed nationwide Medicaid claims of enrollees with IDD to characterize HCBS waiver program use and to estimate the association between race/ethnicity and use.

Using 2016-2019 Medicaid data, we examined continuously enrolled adults with IDD identified via ICD-10 diagnosis codes (n= 950,702).

We examined associations between race/ethnicity and waiver receipt using binomial regression adjusted for age, IDD type, sex, and region. We ran models for any- and three specific waivers: 1915(b), 1915(c), section 1115. In sensitivity analysis we excluded 21 states with poor quality race data.

83% of enrollees with IDD used  $\geq 1$  waiver during the period. Black non-Hispanic (OR=0.91, CI 0.90-0.93) and white Hispanic (OR=0.68, 95% CI 0.67-0.70) enrollees were less likely to use any waiver program compared to non-Hispanic white enrollees. Every racial/ethnic group was less likely to use 1915(c) waivers compared to non-Hispanic white enrollees. Black enrollees regardless of ethnicity were more likely to use 1915(b) waivers and every racial/ethnic group was more likely to use 1115 waivers compared to non-Hispanic white enrollees. Results were robust to sensitivity analysis.

Medicaid waiver programs enable access to HCBS for many enrollees with IDD. We found racial and ethnic disparities in the use of HCBS waiver programs, suggesting inequities in enrollees' choice of providers, eligible services, and benefit generosity. Our study underscores the need to facilitate equitable access to HCBS for people with IDD on waitlists for waiver programs.

Table 1. Odds ratios of Home- and Community-Based Services waiver program use among adult Medicaid enrollees with intellectual and developmental disabilities continuously enrolled from 2016-2019, comparing by racial/ethnic group (n=950,702)

Racial/ethnic group	Any waiver program OR (95% CI) (n=784,341)	1915(c) waiver OR (95% CI) (n=481,654)	1915(b) OR (95% CI) (n=296,619)	1115 waiver OR (95% CI) (n= 253,707)
Non-Hispanic Black N=165,931	0.91 (0.90, 0.93)	0.88 (0.87, 0.89)	1.09 (1.08, 1.11)	1.45 (1.43, 1.47)
Hispanic Black N=6866	0.96 (0.90, 1.02)	0.77 (0.73, 0.81)	1.65 (1.54, 1.77)	1.96 (1.85, 2.07)
Non-Hispanic Non-white or Black N= 98,669	0.99 (0.97, 1.01)	0.83 (0.82, 0.84)	1.01 (0.99, 1.03)	2.07 (2.04, 2.11)
Hispanic non-white or Black N=85,946	1.21 (1.18, 1.24)	0.86 (0.85, 0.88)	2.07 (2.03, 2.11)	2.70 (2.65, 2.75)
Hispanic white N=35,511	0.68 (0.67, 0.70)	0.97 (0.95, 0.99)	0.49 (0.47, 0.50)	1.56 (1.52, 1.60)
Non-Hispanic white N=585,194	REF	REF	REF	REF

## **Heterogeneous Effects of Medicaid Expansions on County-Level Uninsurance Rates: An Application of Structural Nested Mean Models Fit Under Parallel Trends Assumptions**

Meghana Shamsunder\* Meghana Shamsunder Zachary Shahn Mustafa Hussein

### Background

Effects of ACA state Medicaid expansions have been widely studied with Difference-in-Differences (DiD) methods under parallel trends assumptions. However, recent DiD methods are unable to model heterogeneity in expansion effects by time-varying covariates and magnitude of expansion. Recent work has shown that Structural Nested Mean Models (SNMMs) are identified under DiD-type parallel trends assumptions, which enables modeling time-varying heterogeneity of Medicaid expansion effects.

### Methods

A SNMM is a model for the conditional effect of treatment at time  $t$  on outcomes at times  $k > t$  given covariate history among units treated at  $t$ . We specified a SNMM in which Medicaid expansion effects on county-level uninsurance rate varied with year of expansion, time since expansion, population, and Medicaid eligibility thresholds prior to expansion. Using county-level data, we estimated the SNMM parameters via doubly robust g-estimation under a conditional parallel trends assumption.

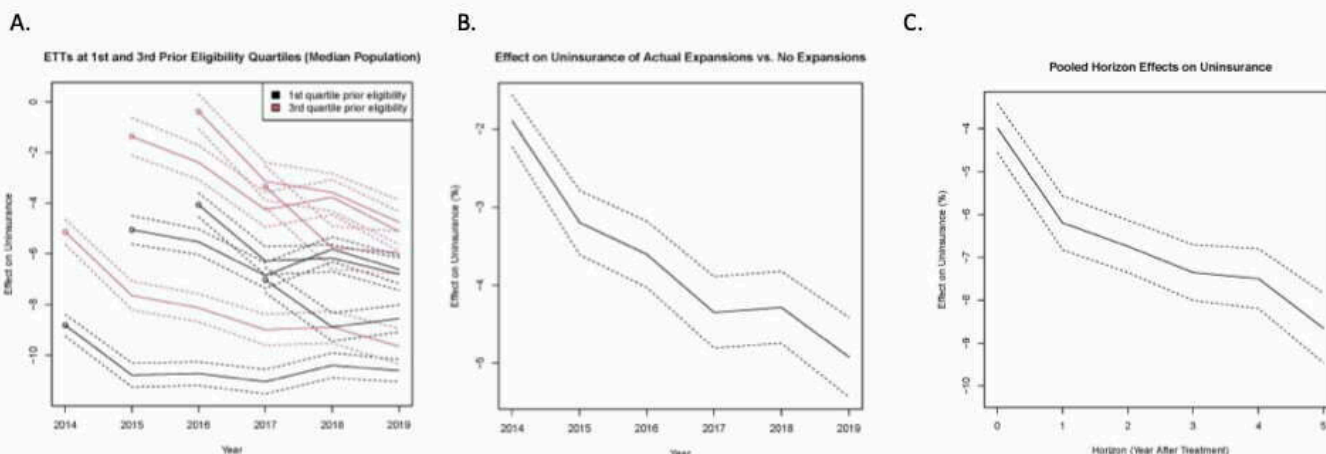
### Results

Among adults <138% of the federal poverty line, Medicaid expansion reduced county uninsurance rates *more* in less populous counties and counties with less generous pre-expansion eligibility. For example, the average effect of expansion in 2014 on uninsurance in 2017 in counties with bottom-decile population and mean prior eligibility thresholds would be -11.0 percentage points (pp) [-11.6pp,-10.5pp], and the average effect in similar counties with top-decile population would be -9.3pp [-9.9pp,-8.7pp]. Fig 1 depicts variation in effects over prior eligibility thresholds and time for counties with median population.

### Conclusion

Our results were qualitatively unsurprising—expanding benefits from a lower baseline should have a larger impact, and it was already thought that expansion effects were larger in sparsely populated areas. However, quantitatively modeling this effect heterogeneity is informative and highlights substantive advantages of DiD-SNMMs for health policy research.

## Effects of Medicaid Expansion on County-Level Uninsurance Rate (Estimated by a Structural Nested Mean Model Fit Under a Parallel Trends Assumption)



**A:** Effect heterogeneity of Medicaid expansion on county-level uninsurance rate by prior Medicaid eligibility threshold quartile and time. In counties with more stringent/less generous eligibility requirements (black lines), Medicaid expansion led to greater reductions in uninsurance rate compared to more generous counties (red lines). Each line represents expected ongoing effects of an expansion at the year the line originates in counties with pre-expansion generosity level corresponding to the color of the line. Black lines (effects of expansions in low generosity counties) are lower and thus indicate greater uninsurance reduction effects than red lines (effects of expansions in high generosity counties) originating in the same year. The graph also shows how estimated effects vary by year of expansion and years since expansion. **B:** In each calendar year, the effect of all prior expansions on total population level uninsurance rate compared to the estimated counterfactual uninsurance rate had there been no expansions. **C:** The average (county population weighted) effects of Medicaid expansion on uninsurance rates in expansion state counties by years since expansion, averaged over expansions that occurred in different years. The effects of expansions grow over time since expansion.



**The Interaction of Smoke-free Workplace and Hospitality Laws and Cigarette Taxation****Among Youth** Catherine Vander Woude\* Catherine Vander Woude Yanmei Xie Megan E. Patrick  
Nancy Fleischer

Many studies have demonstrated that taxation and smoke-free laws can reduce smoking behaviors among youth, but few have examined how these policies interact while doing so. Using a nationally representative probability sample of 8<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup> graders from the 2001-2021 Monitoring the Future study, we investigated the interaction of taxation and smoke-free policies on smoking participation, initiation, and intention, and examined differences by sex, race/ethnicity, parental education, and college plans. We estimated the average marginal effects (AMEs) using modified Poisson regression with a sandwich variance estimator, stratifying by grade. Among 12<sup>th</sup> graders, the relationship between taxation and lower smoking participation was more pronounced in populations covered by either hospitality or workplace smoke-free laws versus not covered (Workplace: AME = -0.009, 95% CI = -0.016, -0.002; Hospitality: AME = -0.010, 95% CI = -0.018, -0.003). These policies did not interact to affect any outcome among 8<sup>th</sup> or 10<sup>th</sup> graders, nor smoking initiation or intention among 12<sup>th</sup> graders. We also examined three-way interactions between taxation, smoke-free policies, and sociodemographic subgroups. Among 8<sup>th</sup> graders whose parents had some college education, taxation was more strongly associated with a lower probability of initiating daily smoking when they were covered by hospitality smoke-free laws versus not covered, compared to 8<sup>th</sup> graders whose parents had less education. In contrast, among 8<sup>th</sup> graders with a highest parental education level of college or more, taxation was more strongly associated with a lower probability of daily smoking initiation when they were not covered by hospitality smoke-free laws versus covered. There were no other subgroup differences after adjusting for multiple comparisons. Future research is needed to further characterize the interactions of tobacco control policies on smoking behaviors, including differences across populations.

**The effect of returning to normal: Evaluating politically-motivated social policy decisions on health** Matthew Lavalley\* Matthew Lavalley Isaacson Michel Caitlin O'Connor Nadia N. Abuelezam

**Background:** Understanding how social programs shape social determinants of health (SDOH) is a national priority. We analyzed politically motivated changes to Nebraska's Supplemental Nutrition Assistance Program (SNAP) policy during the COVID-19 pandemic to understand the linkage between social policy and public health.

**Methods:** We used synthetic control methods to estimate the causal effect of Nebraska's decision to reject emergency allotments (August-December, 2020) on mental health and hospital capacity indicators. Data was acquired from the Census Bureau's Household Pulse Survey and the Center for Disease Control and Prevention. A counterfactual for Nebraska was created by weighting data from the rest of the United States. We used a data-driven process to weigh the relative importance of each variable (household size, race, gender, age, income, educational attainment, and outcomes during the pre-intervention period) to create a counterfactual that closely matched Nebraska in the pre-intervention period (March-July, 2020).

**Results:** After Nebraska rejected additional funding for SNAP recipients, we saw an 8.3% increase in inability to stop worrying, a 14% increase in inpatient beds filled and a 92% increase in inpatient beds filled by COVID-19 patients. These results were confounded by the pandemic, which worsened as 2020 progressed. Our synthetic counterfactual captured these changes; we estimated the causal effect of Nebraska's policy change on these same outcomes: an 8.2% increase in inability to stop worrying ( $p < 0.05$ ), a 5.2% increase in inpatient beds filled ( $p < 0.05$ ), and a 4.7% increase inpatient beds filled by COVID-19 patients ( $p < 0.05$ ).

**Discussion:** SNAP policy changes in Nebraska during the early days of the COVID-19 pandemic increased the prevalence of mental health conditions and the amount of public health capacity consumed. Politically motivated policy changes directly impact SDOH and should be studied more closely when data is available.

**Feminine care products and incidence of hormone-related cancers: A quantitative bias****analysis** Katie O'Brien\* Katie O'Brien Kemi Ogunsina Jessie K Edwards Clarice R. Weinberg Aimee A. D'Aloisio Nicolas Wentzensen Dale P. Sandler

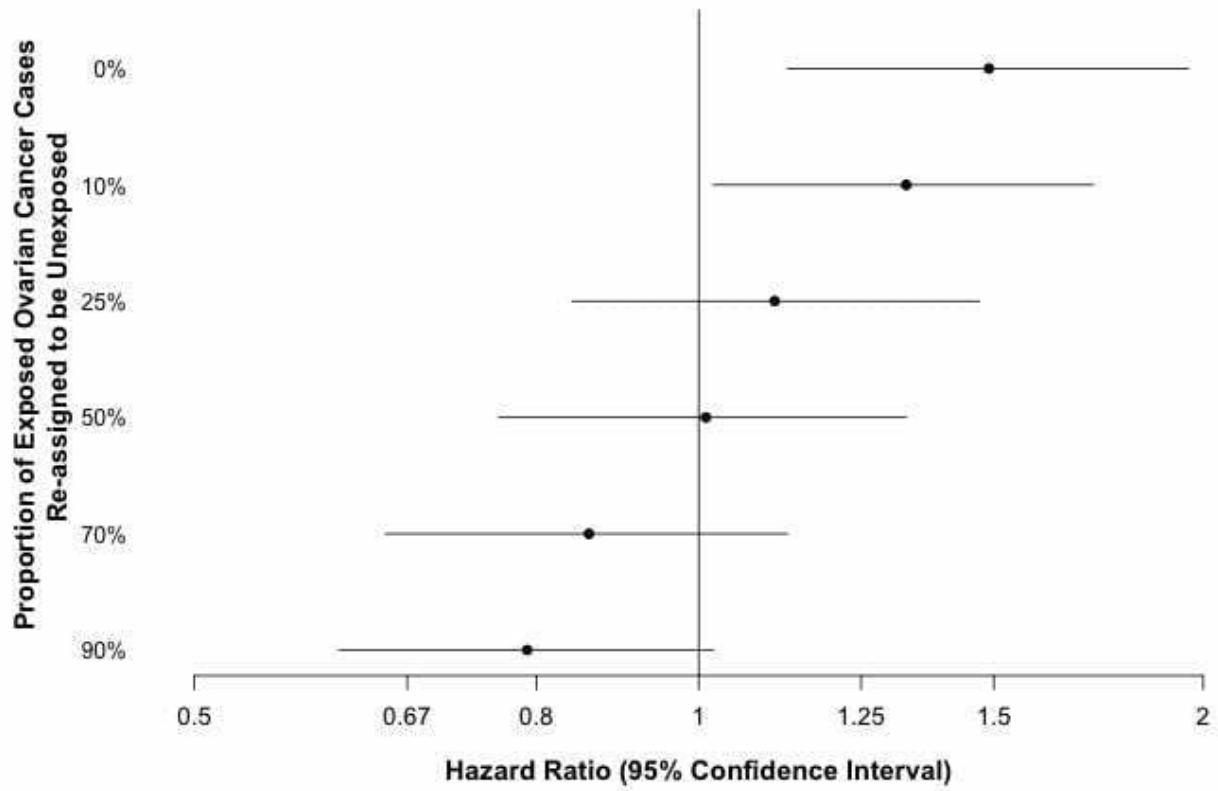
**Background** Feminine care products may contain substances with the potential to increase users' risks of developing certain gynecologic or hormone-related cancers. The relationship between genital talc use and ovarian cancer has been particularly well-studied, but concerns about recall bias and exposure misclassification have precluded firm conclusions.

**Methods** Data on genital talc use and douching were collected at enrollment (2003-09) and on a follow-up questionnaire (2017-19) in the US-based Sister Study cohort (n=50,196 eligible women). To evaluate the influence of recall bias and missing data on risk estimates, we conducted quantitative bias analyses using varied approaches to re-classify or multiply impute data. We analyzed each version of the data using Cox proportional hazards models to estimate HRs for 3 cancers (breast, ovarian, uterine) and myocardial infarction, which served as a negative control.

**Results** Depending on our assumptions, between 41-64% of participants ever used douche and 35-56% ever used genital talc. In a multiple imputation model designed to correct for inconsistencies, having ever used genital talc prior to enrollment was positively associated with ovarian cancer incidence (HR=1.49, 95% CI: 1.13-1.96). Recall bias would alter the strength and direction of the association (Figure), yet scenarios assuming that 10% (HR=1.33, 1.02-1.72) or 25% (HR=1.11, 0.84-1.47) of cases misreported being genital talc users still yielded HRs consistent with a positive effect. Other than a possible relationship between genital talc use and breast cancer (HR=0.92, 0.86-0.99), neither douching nor genital talc use were associated with other hormone-related cancers or myocardial infarction.

**Conclusions** This analysis provides some evidence in support of a positive association between genital talc use and ovarian cancer incidence, though quantitative bias analyses demonstrate how differential exposure recall by case status could upwardly bias effect estimates.

### Potential Impact of Recall Bias on the Association between Genital Talc Use and Ovarian Cancer



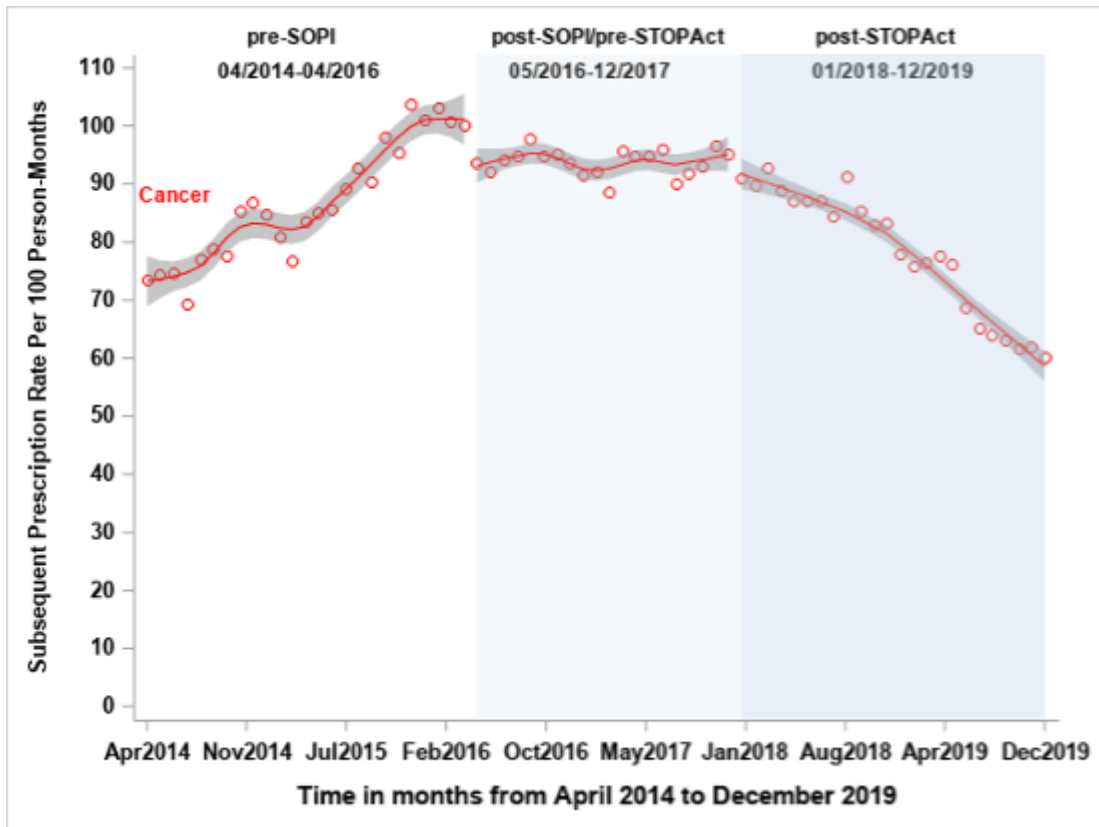
**The unintended consequences of opioid prescribing policy for cancer patients using interrupted time series, 2014-2019** Theo G. Beltran\* Theo Beltran Brian W. Pence Naoko Fulcher Stephen W. Marshall Maryalice Nocera Courtney N. Maierhofer Bethany L. DiPrete Nabarun Dasgupta Li-Tzy Wu David A. Edwards Timothy S. Carey Paul Chelminski Juan Hincapie-Castillo Scott K. Proescholdbell Joacy G. Mathias Whitney R. Robinson Shabbar I. Ranapurwala

**Background:** While many states have imposed policies to reduce opioid prescribing to combat opioid-related morbidity and mortality, there is an urgent need to understand the unintended consequences of these policies. We examine changes in opioid prescribing among cancer pain patients receiving opioid prescriptions (Rx) in North Carolina (NC) due to two state-wide policies.

**Methods:** We conducted controlled and single series interrupted time series analyses using electronic health records from two large integrated healthcare systems, including all cancer pain patients >11 years of age from April 2014 to December 2019. The two policies were the NC safe opioid prescribing investigative initiative (SOPI) implemented in May 2016 and a state law mandating limits to days' supply of initial opioid Rx for acute and post-surgical pain (STOP act) implemented in January 2018. Outcomes included: 1) Proportion and rates of patients receiving an index and subsequent opioid Rx and 2) days' supply and morphine milligrams equivalent for dispensed index and subsequent Rx.

**Results:** Of the 26,919 cancer patients treated within two North Carolina healthcare systems between April 2014 and December 2019, 64.06% received an index opioid Rx for cancer pain control. No changes in index opioid proportion or Rx rates were observed after the two policies. However, there were sustained declines in subsequent opioid Rx rates after both, SOPI [-15.8% per year (95%CI: -19.3, -12.4)] and STOP act [-11.9% per year (-15.4, -8.4)]. After both policies, black Americans experienced a larger sustained decline in subsequent opioid Rx rate compared to white Americans.

**Conclusions and Relevance:** While SOPI and the STOP act meant to impact opioid Rx for surgery and injury, we saw a large decline among subsequent opioid prescriptions for cancer patients, an unintended consequence of these policies. Racial disparities in policy effects may point to implicit and explicit bias in pain management practices.



**Association of OncotypeDx Testing with Race and Treatment** Sarah Van Alsten\* Sarah Van Alsten Matthew Dunn Sanah Vohra Xiaohua Gao Ebonee Butler Joannie Ivory Lisa Carey Melissa Troester

**Background:** The OncotypeDx assay is recommended for certain estrogen receptor positive, human epidermal growth factor receptor 2-negative breast cancer (ER+/HER2-) stage I-II breast cancer patients. Women with low scores are generally treated without chemotherapy, but not all eligible women receive testing. The objectives of this analysis were to determine whether nontesting contributes to overtreatment, and to assess variations in testing by race and geography.

**Methods:** We extracted OncotypeDx testing results for 1,117 women in the Carolina Breast Cancer Study with ER+/HER2-, node negative, Stage I-II tumors. For women who received testing, we took scores directly from the pathology record; scores in nontested women were derived from measured RNA expression. We estimated prevalence differences (PDs) and 95% CIs of sociodemographic characteristics and chemotherapy receipt between tested and nontested women, adjusting models for pathologic tumor grade. We assessed county and census tract level variation in testing by calculating the proportion of eligible women in each geographic area who received OncotypeDx, both overall and by race.

**Results:** 55% of women in this cohort (N=643) were not tested. Nontesting was more common for Black than white women (PD=9%, 95% CI=3%-14%) and those with lower socioeconomic status versus higher (PD=7%, 95% CI=1%-13%). Among those with low scores (<18), nontested women had an 11% higher prevalence of chemotherapy receipt than tested women (95% CI=6% -17%). Although nontesting was more prevalent in rural areas, urban areas showed greater inequities in testing with potentially eligible Black urban women having 20-40% lower prevalences of OncotypeDx testing than white urban women.

**Implications:** Underutilization and limited access to Oncotype Dx assay may contribute to overtreatment of some women based on race and geographic location, which can affect patient's health and quality of life without survival benefit.

**A population-based study of birth defects in offspring of adolescent and young adult women with a history of cancer** Caitlin Murphy\* Caitlin Murphy Andrea Betts Philip Lupo Aubree Shay Barbara Cohn Marlyn Allicock Sandi Pruitt

**Background:** To estimate prevalence of birth defects in offspring of adolescent and young adult (AYA) women with a history of cancer.

**Methods:** We identified women diagnosed with cancer at age 15-39 years from January 1, 1999 to December 31, 2015 using population-based data from the Texas Cancer Registry. We linked these data to: 1) live birth certificates through December 31, 2016 to identify the first singleton delivery after diagnosis; and 2) Texas Birth Defects Registry to identify birth defects diagnosed in offspring through age 12 months. We estimated prevalence of any birth defect using British Pediatric Association Classification of Diseases codes, as well as 10 specific types of anomalies. To compare prevalence to the general population, we randomly selected singleton deliveries to women without cancer during the same period, matched 3:1 by maternal age, race and ethnicity, and year of delivery.

**Results:** There were 6,789 singleton deliveries to AYA women after diagnosis. AYA women were commonly diagnosed with thyroid (29.1%) and breast (10.8%) cancer and lymphoma (12.6%); 8.9% were non-Hispanic Black and 30.0% were Hispanic. Mean time from diagnosis to delivery was 4.0 years (SD=2.7). Compared to offspring of women without cancer (n=20,367), prevalence of any birth defect was higher in offspring of AYA women (PR 1.17, 95% CI 1.05, 1.31), as well as prevalence of the following types of anomalies: central nervous (PR 1.43, 95% CI 1.02, 2.00), genitourinary (PR 1.34, 95% CI 1.09, 1.67), heart and circulatory (PR 1.11, 95% CI 0.95, 1.37), musculoskeletal (PR 1.19, 95% CI 0.99, 1.43), and eye or ear (PR 1.30, 95% CI 0.99, 1.70). Prevalence of clefts, respiratory, gastrointestinal, skin, hair, or nails, and chromosomal anomalies was similar between the two groups.

**Conclusions:** Prevalence of birth defects was higher in offspring of AYA women compared to offspring of women without cancer. Additional work is needed to identify mechanisms contributing to these findings.



**LATEBREAKER**

## Health Disparities

**Racial/ethnic disparities in case presentation and outcomes of care among US-born individuals diagnosed with tuberculosis, 2003-2019** Mathilda Regan\* Mathilda Regan Yunfei Li Nicole A Swartwood Terrika Barham Garrett R Beeler Asay Ted Cohen Andrew N Hill C Robert Horsburgh, Jr Awal Khan Suzanne M Marks Ranell Myles Joshua A Salomon Julie L Self Nicolas A Menzies

**Background** Persistent racial/ethnic disparities exist in tuberculosis (TB) incidence in the United States, but less is known about disparities in TB diagnosis and treatment outcomes.

**Methods:** We extracted data from the US National TB Surveillance System on US-born TB patients during 2003-2019. To estimate the association between race/ethnicity and TB diagnosis and treatment outcomes, we fit log-binomial regression models adjusting for calendar year, sex, age category, and regional division. We quantified racial/ethnic disparities as adjusted relative risks (aRRs) using non-Hispanic White persons as the referent group, and estimated time trends for each outcome to evaluate whether disparities were closing or widening. We also calculated the Index of Disparity (ID) as a summary measure which quantifies the dispersion in a given outcome across all racial/ethnic groups, relative to the population mean. To calculate the ID, we used predicted probabilities from our regression models to estimate the mean value of each study outcome (e.g., dead at diagnosis) for each racial/ethnic group when standardized to the distribution of covariates in the overall study population. We used a Monte Carlo approach to propagate the uncertainty in analytic outcomes.

**Findings:** There were 72,809 US-born individuals diagnosed with TB disease during 2003-2019. We observed an overall higher risk of any adverse outcome (defined as dead at diagnosis, treatment discontinuation prior to completion, or died during treatment) for non-Hispanic Black persons (aRR 1.27, 95% CI 1.12-1.32), Hispanic persons (1.20, 1.14-1.27), and American Indian/Alaska Native persons (1.24, 1.12-1.37), relative to non-Hispanic White persons. The Index of Disparity for this summary outcome did not significantly change ( $P < .05$ ) over the study period.

**Interpretation:** Targeted initiatives are needed to reduce diagnostic delays and improve treatment outcomes for US-born racial/ethnic minority persons with TB in the United States.

**LATEBREAKER**

Environment/Climate Change

**Prenatal residential proximity to oil and gas wells and depression among urban Latina pregnant women in Los Angeles, CA** Elizabeth Kamai\* Elizabeth Kamai Roxana Khalili Rima Habre Shohreh Farzan Theresa M. Bastain Carrie Breton Jill Johnston

Growing evidence links proximity to oil and gas production with adverse health outcomes, but there is sparse data on how this exposure affects women's health. We investigated the impacts of living near oil and gas wells on antenatal depression in an urban pregnancy cohort.

We included women who enrolled in the Maternal And Developmental Risks from Environmental and Social Stressors (MADRES) study - an ongoing, prospective pregnancy cohort of predominantly low-income Latina women in Los Angeles - in 2016-2021 and completed the Center for Epidemiologic Studies Depression Scale (CES-D) 1-3 times during pregnancy. Those with at least one score  $\geq 16$  were classified as having probable antenatal depression. Locations and monthly production data (barrels of oil equivalents [BOE]) of oil and gas wells were spatially linked to residential addresses. We summed the total number of active wells and BOEs produced at distances of  $\leq 1$  and  $\leq 5$  kilometers (km) from women's residences in the three months prior to conception and excluded women living  $> 10$  km from an active well. We used generalized linear models to estimate risk of antenatal depression associated with the number of wells and volume of BOEs produced, modeled both continuously and categorically.

Of 694 women, 194 (24%) had probable depression. 557 (80%) lived  $\leq 5$  km from a well (median: 18 wells, 42,000 BOEs); 58 (8%) lived  $\leq 1$  km from a well (median: 6 wells, 6,300 BOEs). In adjusted models, women  $\leq 1$  km from an active well during the preconception period had a 14.8% increased risk of depression (95% CI 2.4%, 27.3%). Each additional well  $\leq 1$  km was associated with a 1.9% increased risk of depression (95% CI 0.3%, 3.4%). The risk of depression among women in the highest quartile of wells  $\leq 5$  km was 11.5% higher (95% CI 0.3%, 22.6%) than that of the lowest quartile.

To our knowledge, this is the first study to evaluate associations between proximity to oil and gas production and depression during pregnancy in an urban cohort.

**LATEBREAKER**

Environment/Climate Change

**Exposure to endocrine disruptors and adverse child health measures in teenagers born extremely preterm** Amaree\* Amaree Gardner Ali Oran Lauren A. Eaves Michael O'Shea Rebecca C. Fry

Infants who are born extremely prematurely (<28 weeks) are at increased risk for health challenges such as impaired neurodevelopment. Exposure to endocrine disrupting chemicals during critical periods of development, such as adolescence, may increase the risk of adverse health outcomes like metabolic syndrome. Those born premature may be particularly vulnerable but are understudied as a population in relation to chemical exposures at multiple key development windows. This study leverages the Extremely Low Gestational Age Newborn Cohort (ELGAN) cohort, a multi-site, ongoing prospective cohort of children born <28 weeks' gestation between 2002-2004. We evaluated the association between 15 known endocrine disruptors (toxic metals, phthalates, and bisphenols) assessed in the urine of ELGANs at age 15 years and the positive child health index (PCHI), a quantification of positive health summarizing 11 adverse health conditions. PCHI was binarized as those with scores of 100%, (i.e. no adverse conditions, termed "good health"), and scores below 100%, (i.e. those with at least one adverse condition, termed "poor health"). Logistic regression was used to analyze exposures in binary form (above vs below median) and as tertiles. When analyzed as binary exposures, those with high bisphenol A (BPA) exposure had 2.14 times the odds of having a poor health compared to those with low exposures [OR=0.68 CI 95%=0.55,0.84]. Compared to teens in the lowest tertile, teens in the highest tertile of BPA and monobenzyl phthalate (MBzP) had 3.86 and 2.55 times the odds of poor health, respectively (BPA: OR=3.86 CI 95%=1.81,8.26) (MBzP: OR=2.55 CI 95%=1.23-5.29). Our results thus far show that higher exposures of BPA and MBzP are associated with poor health. Further analysis will generate adjusted and mixtures assessment. Understanding the resiliency of preterm children in the face of exposure to environmental chemicals can help in efforts to improve the health of these children.

**LATEBREAKER**

Environment/Climate Change

**Climate change-related exposures and risk of hospitalization among children aged 0-17 in New York State, 2005-2019: Preliminary analyses from the Understanding Pediatric Susceptibility Across Temperature and Environment in New York (UPStATE NY) Study** Lisa Frueh\* Lisa Frueh Rachit Sharma Ellen J. Kinnee Allan C. Just Perry E. Sheffield Jane E. Clougherty

UPStATE NY aims to identify community assets that shape relationships between climate change-related exposures and pediatric health in NY State. Here, we link 2005-2019 NY pediatric hospitalization data from the Statewide Planning and Research Cooperative System (SPARCS) with residential block-group level estimates for minimum temperature ( $T_{\min}$ ) and fine particulate matter ( $PM_{2.5}$ ) on admission day and 6 lag days using conditional logistic regression in a time-stratified case-crossover design.

Among children aged 0-17, excluding newborns ( $N = 1,906,971$ ), a  $10 \mu\text{g}/\text{m}^3$  increase in  $PM_{2.5}$  conferred an increased risk of hospitalization year-round, [1.22% excess case-day risk (95% CI: 0.87, 1.57)] adjusted for case-day  $T_{\min}$ . Associations were stronger among younger children (0-4y), males, urban areas, and in warmer months. Case-day  $PM_{2.5}$  was most strongly associated with risk of hospitalization for injury [3.53% (95% CI: 2.32, 4.75)], non-infectious respiratory disease [3.24% (95% CI: 2.18, 4.31)], and respiratory infections [2.21% (95% CI: 1.22, 3.20)].

A  $10^\circ\text{F}$  increase in case-day  $T_{\min}$  conferred an increased cool-season risk of hospitalization [2.46% (95% CI: 2.18, 2.73)] and decreased warm-season risk [-2.02% (95% CI: -2.45, -1.59)] adjusted for case-day  $PM_{2.5}$ . Only warm-season associations were stronger among younger children (0-13y), males, and urban areas. Associations were strongest for respiratory and psychiatric outcomes. Injury and infections/parasitic diseases were positively associated year-round, with stronger warm-season associations [injury: 3.58% (95% CI: 2.12, 5.06), infections: 4.05% (95% CI: 2.00, 6.14)].

These results suggest that younger children in urban areas are particularly vulnerable to temperature and  $PM_{2.5}$ . Future analyses will include ozone exposure, emergency department visit outcomes, and community-identified assets and stressors as potential effect modifiers. Finally, we will estimate future pediatric health impacts using climate projections.

**LATEBREAKER**

Environment/Climate Change

**Does air conditioning modify the temperature-mortality association in Southern California? A study at the census-tract level using a novel measure of air conditioning use**

Jaime Reyes Sanchez\* Jaime Reyes Sanchez Mostafijur Rahman Sandrah P. Eckel Sam Silva McKenna Peplinski Kelly Sanders Rob McConnell Erika Garcia

**Introduction:** Growing evidence from city- or county-level studies suggests that air conditioning (AC) prevalence modifies the heat-mortality association. But data on actual AC use at a finer geographic scale is scarce. By using a novel measure of AC use penetration (ACUP, proportion of households using AC) at the census tract (CT) level in Southern California, we evaluated whether ACUP modifies the CT-specific effect of heat on mortality.

**Methods:** We performed a two-stage study. In the first stage, we used a time-stratified case-crossover design and conditional logistic regression to estimate the CT-specific effect of daily maximum temperature on all-cause mortality from 2014 through 2019. These effect estimates were then used in the second stage and regressed against CT-specific ACUP (deciles), which were estimated from household-level smart meter electricity data between 2015 and 2016. In the second stage, we used linear regression marginal structural models with inverse probability weighting to adjust for confounders at the CT level (income, temperature, percent elderly, percent working outdoors, percent area not covered by trees). Analyses were stratified by climate zone.

**Results:** We analyzed 2,203 CTs encompassing five different climate zones, from coast to desert. We observed a statically significant and negative association between AC use penetration and CT-specific heat-mortality effect estimates only for climate zone 14 (desert): compared with the lowest decile of AC use penetration, each higher decile of AC use penetration was associated with a decrease in the heat-mortality effect (in the logit scale) between 0.19 and 0.29 ( $p < 0.01$  for all 9 contrasts, with no evidence of a trend). Associations between ACUP and heat-mortality effects were less consistent in other climate zones.

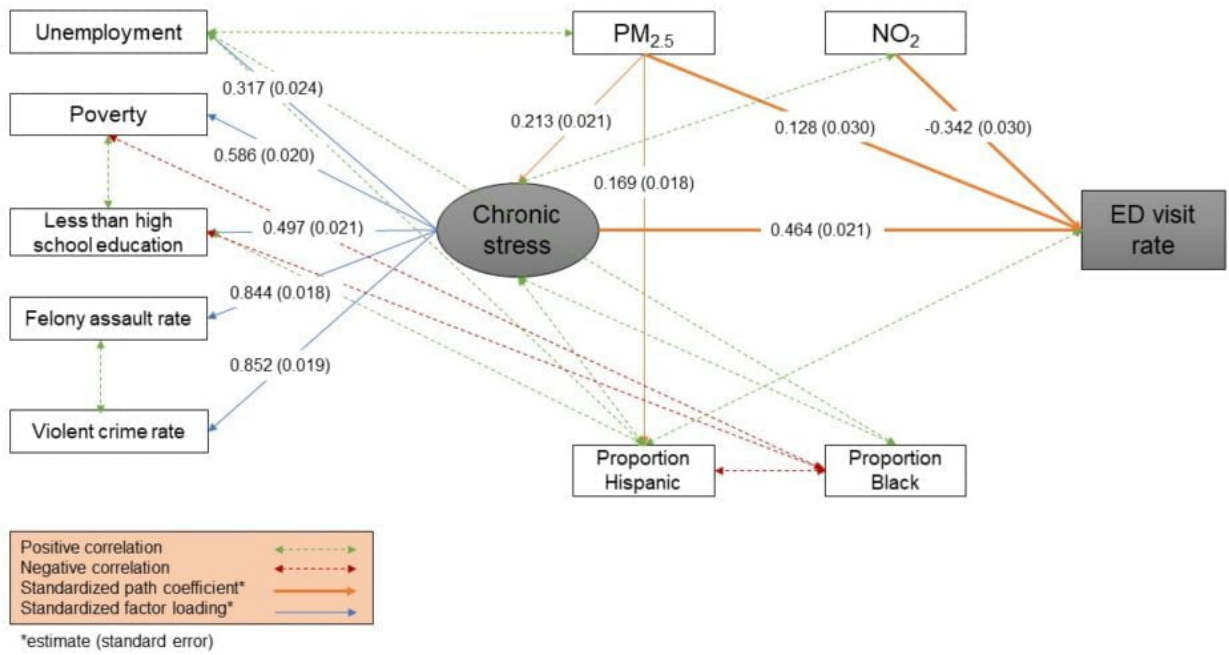
**Conclusions:** Using CT-level data on AC use, we found that higher AC use in desert communities of Southern California reduces the effect of heat on mortality.

**LATEBREAKER**

Environment/Climate Change

**Air pollution, temperature, and social stressors in pediatric seizures and epilepsy: A Structural Equation Modeling approach** Rachit Sharma\* Rachit Sharma David Gefen Perry E. Sheffield Jane E. Clougherty

Air pollution, temperature, and social stressors are linked to multiple neurological disorders, but research on seizures and epilepsy is scarce. Using covariance-based structural equation modeling (CBSEM), we examined the effects of multiple pollutants, temperature, and social stressors on seizures and epilepsy among children (0-4 years) in New York City. Data on seizure and epilepsy cases (n = 28,385), presented at NYC emergency departments from 2005 to 2011 were obtained from New York Statewide Planning and Research Cooperative System. Age-standardized annual ED visit rates were assigned to each census tract. Tract-level annual average concentrations of PM<sub>2.5</sub>, NO<sub>2</sub>, SO<sub>2</sub>, O<sub>3</sub>, and minimum temperature (Tmin) were assigned using NYC Community Air Survey spatial data and U.S. EPA and NOAA temporal data. Point-level NYPD crime data were aggregated to create tract-level annual average rates. Tract-level ACS 2007-11 estimates of percent poverty, percent not graduated from high school, percent unemployed, median household income, and percent population Hispanic and Black were assigned. 'Chronic stress' reflected by crime and ACS indicators was modeled as a latent construct in exploratory and confirmatory factor analyses. Pollutants, temperature, and 'chronic stress' were then fitted in a CBSEM as potential predictors of ED visit rates under maximum likelihood estimation. PM<sub>2.5</sub> was positively associated with ED visit rates [path coefficient = 0.128 (95% CI: 0.069, 0.186)], NO<sub>2</sub> was negatively associated [-0.342 (-0.402, -0.283)], and SO<sub>2</sub>, O<sub>3</sub>, and Tmin effects were statistically insignificant. Positive association was also observed with 'chronic stress' [0.464 (0.423, 0.505)], with violent crime and felony assault rates explaining the most variability [factor loadings= 0.852 and 0.844, respectively]. Also, PM<sub>2.5</sub> was positively associated with 'chronic stress', and percent population Hispanic. Chronic stress and PM<sub>2.5</sub> may be associated with pediatric seizure and epilepsy risk.



**A Warning About Using Predicted Values to Estimate Descriptive Parameters** Rachael K. Ross\* Rachael Ross Alexander P. Keil Stephen R. Cole Jessie K. Edwards Jeffrey S.A. Stringer

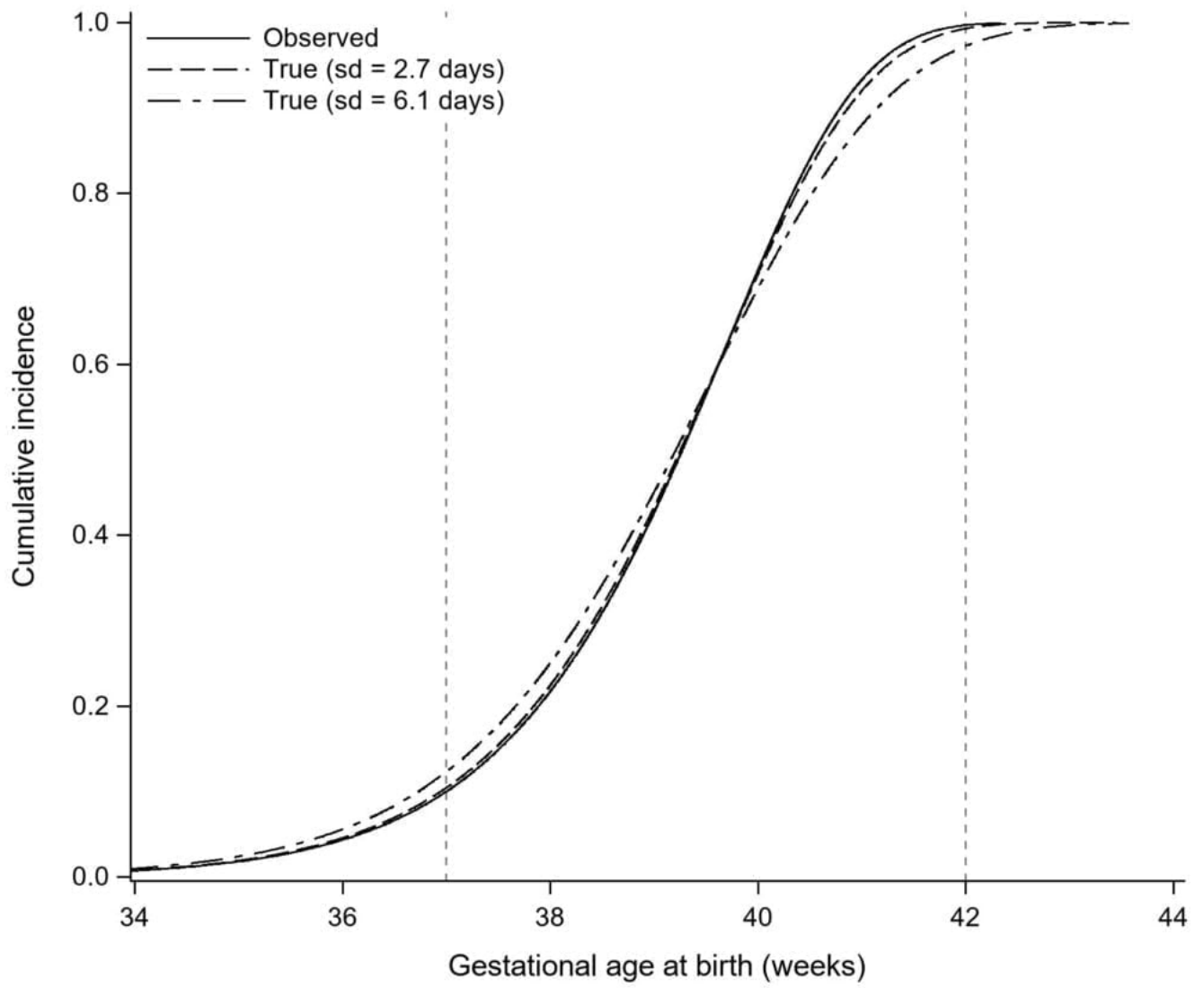
A common descriptive parameter is the proportion of the population with a value of some variable  $Y$  below or above a threshold (cumulative distribution function [CDF]). Sometimes we are not able to measure  $Y$ , but instead rely on  $V$ , a prediction of  $Y$  obtained from a model conditional on covariates.

For example, consider the distribution of gestational age at birth. Common descriptive parameters are the proportion pre- or post-term (CDF and 1-CDF at 37 and 42 weeks, respectively). Gestational age is generally not measured but is calculated from a model that predicts gestational age, given fetal size measurements. All fetuses the same size obtain the same predicted age ( $V$ ), even though the true age ( $Y$ ) varies. Motivated by this example, we conducted a simulation with empirically-based parameters to assess bias in the CDF when we use  $V$  instead of  $Y$ . We simulated  $V$  to mimic the observed distribution in the US (10% preterm, 0.3% post term). We simulated  $Y$  under two plausible values for the standard deviation (sd) of the distribution of  $Y$ , given fetal size, 2.7 and 6.1 days. The Figure plots the CDFs. The proportions pre- and post-term estimated using  $V$  were too small; the true proportions were 12.3% and 2.7%, respectively (when  $sd=6.1$  days). Although we focus on the CDF, other nonlinear functions of  $V$  may also be biased.

If  $Y$  is unavailable, we can use multiple imputation to reduce bias from using  $V$ . We illustrate this approach to estimate the proportions pre- and post-term in an example using real data. We multiply impute  $Y$  as draws from a normal distribution with mean  $V$ .

In general, caution is warranted when using predicted values in place of measurements in epidemiology. We often cannot naively replace an unmeasured variable with predicted values to estimate our quantities of interest. Our results suggest that studies in which predictions are routinely used may benefit from collecting and using data on the variability that is hidden by predictions.





**Comparison of the performance of nested case-control and case-crossover study designs for assessing adverse outcomes of concomitant drug use: a simulation study** Alvi Rahman\*  
Alvi Rahman Janie Coulombe Robert W. Platt Christel Renoux

**Introduction:** Nested case-control studies provide a pragmatic approach to analyze a well-defined cohort assessing the risk of adverse outcomes associated with concomitant drug use. Case-crossover studies offer inherent adjustment for time-invariant confounding, while carrying strong and possibly infeasible assumptions. To inform appropriate selection of study design, we compared the robustness of these designs to the violation of their assumptions.

**Methods:** We generated 1,000 cohorts of 50,000 patients exposed to an object drug (oral anticoagulants) and a precipitant drug (selective serotonin reuptake inhibitors). Daily probability of the outcome, major bleeding, was generated as a function of the two exposures. The estimand, the OR of the outcome associated with concomitant use of both drugs, compared with object drug use only, had a true value of 1.35. We conducted nested case-control and case-crossover analyses in all cohorts. In the base case simulation, no design assumptions were violated. In four alternative scenarios, we introduced the following: residual time-invariant confounding, time-varying confounding, time trend in precipitant use, and non-transient precipitant exposure.

**Results:** In the base case scenario, estimates from both analyses had minimal bias. However, estimates from the case-crossover analysis were substantially biased in scenarios with time-varying confounding (OR 2.00) and time-trend in exposure (OR 0.92), while remaining relatively unbiased in the nested case-control analysis. With a non-transient exposure, only the case-crossover analyses led to some bias (OR 1.48). Finally, residual time-invariant confounding caused bias in nested case-control (OR 1.46) but not in case-crossover analyses.

**Conclusion:** Nested case-control analyses appear more robust than case-crossover in most scenarios, though strong residual confounding leads to some bias. Nonetheless, greater bias may result from time-varying confounding in case-crossover analyses.

**Correlated confounders in a mixtures analysis context** Hanna Jardel\* Hanna Jardel Alison K. Krajewski Kristen M. Rappazzo Alex Keil

**Background:** Environmental exposures, like air pollutants, are often correlated with each other, and may also be correlated with factors that require analytic control, like social determinants of health, that may act as confounders. Performance of methods for analysis of correlated exposures, or exposure mixtures, with correlated confounders is poorly understood. We characterized performance of two mixtures analysis methods, weighted quantile sums (WQS) and quantile g-computation (QGC), in the context of correlated confounders.

**Methods:** We simulated data emulating preterm birth and 8 ambient pollutants (benzene, cadmium, lead, toluene, xylenes, phenols, ethylbenzene, hexane) based on the empirical correlation matrix from the 2011 National Air Toxics Assessment for North Carolina. We also simulated correlated years of education and annual income. Simulated log-odds ratios of pollutants on preterm birth were all either null or positive. We fit crude (pollutant), partially adjusted (+ education), and fully adjusted (+ education + income) WQS and QGC models. We compared true values to observed estimates across 500 simulations of  $N=5000$  to estimate mean absolute error (MAE) and mean squared error (MSE).

**Results:** Simulated pollutants ranged from highly correlated (xylenes:ethylbenzene  $r = 0.99$ ) to uncorrelated (phenol:cadmium  $r = 0.02$ ). Income was moderately correlated with education ( $r = 0.45$ ) and was weakly correlated with phenol ( $r = -0.11$ ). QGC quantile estimates consistently showed lower MSE than WQS on a per-model basis (crude QGC MSE: 0.0059 vs. crude WQS MSE: 0.0085). WQS showed lower MAE than QGC in adjusted and semi-adjusted models (adjusted QGC MAE: 0.0611 vs. adjusted WQS MSE: 0.0286) but not in crude models (crude QGC MAE: 0.0595 vs. crude WQS MSE: 0.0800).

**Conclusion:** QGC MAE was less variable with adjustment than WQS, indicating that, with adjustment, QGC produces less biased, but more variable, mixture estimates than does WQS.

**Leveraging external data to account for outcome misclassification** Rachael K Ross\* Rachael Ross Stephen R. Cole Jessie K. Edwards Paul N. Zivich Daniel Westreich Julie L. Daniels Joan T. Price Jeffrey S.A. Stringer

Measurement error is a threat to validity. Many error-correction approaches use validation data internal to the study sample, which may be unavailable. Alternatively, external data may be available, however, to use such data, we need to address systematic differences between these data and the study sample (i.e., our target).

Here we consider g-computation estimators of the sample average causal effect that leverage external validation data to account for outcome misclassification.

To account for measurement error, we propose using external validation data to estimate misclassification probabilities (i.e., sensitivity and specificity). As the validation data are external, the misclassification probabilities need to be transported from the validation to the study sample. If there are variables related to misclassification that differ in distribution between the validation and study sample, the misclassification probabilities are not generally transportable. We introduce two ways to account for these variables in order to make misclassification probabilities transportable: 1) stratify the misclassification probabilities or 2) weight the validation to match the study sample distribution before calculating the misclassification probabilities. Once the misclassification probabilities are transportable, we obtain stratified outcome risks (accounting for misclassification) and then standardize to the study sample distribution to estimate the marginal risk.

We assessed performance of the two approaches in simulation. Naïve analysis ignoring the need to transport was biased. Both approaches for transport were valid when assumptions were met; stratifying was more precise than weighting. We also implemented these approaches in an applied example using real data.

Measurement error should not be ignored; it can be addressed using external validation data via transportability methods.

**Association Between Subjective Cognitive Decline and Objective Rate of Cognitive Decline in a Racially and Ethnically Diverse Cohort of Older Adults**

Natalie Gradwohl\* Natalie Gradwohl Joseph Fong Taylor Mobley Ruijia Chen Rachel Whitmer Paola Gilsanz Sarah Farias Nancy Chen Elizabeth Rose Mayeda

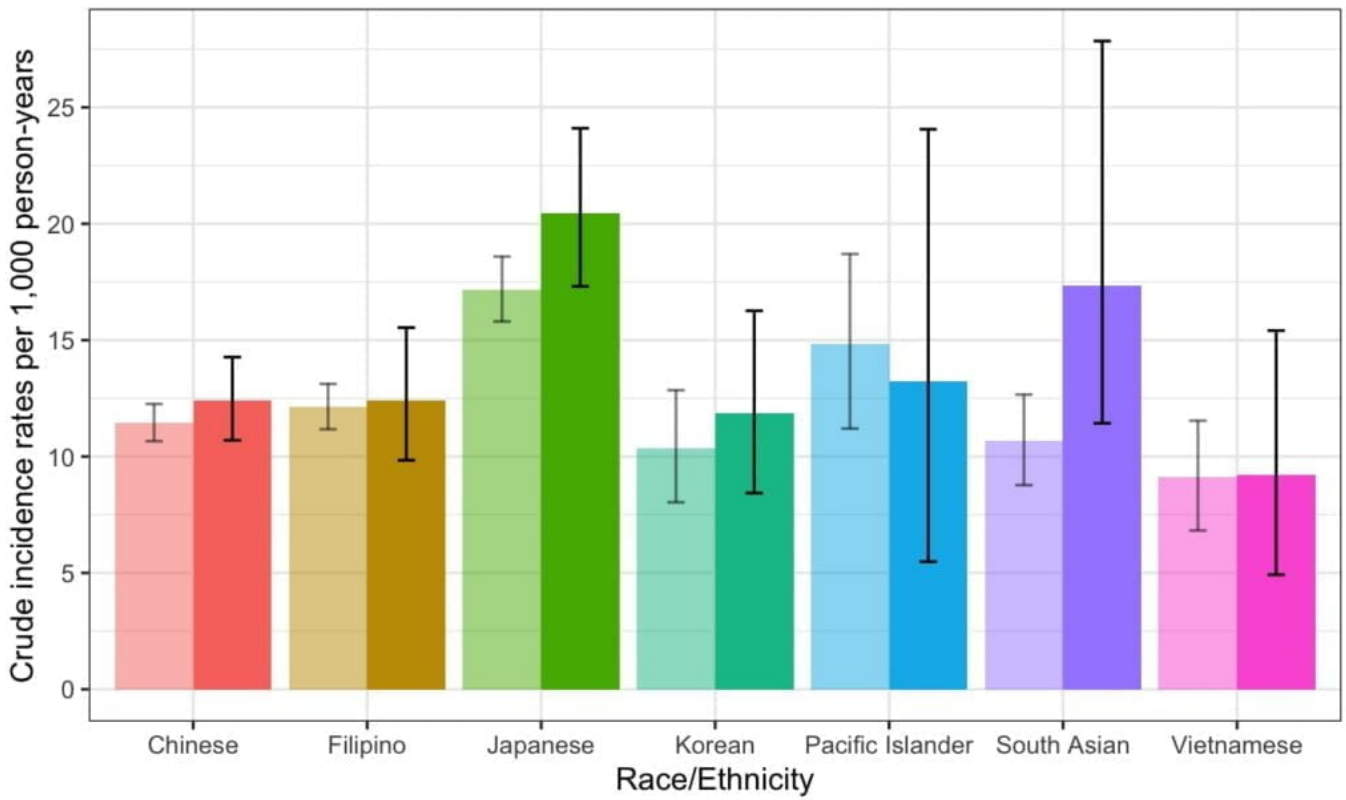
**Background:** Subjective cognitive decline (SCD) may be a low-burden indicator of future objective cognitive decline and dementia risk. However, the robustness of this measure depends on consistent performance across sociodemographic groups. **Methods:** We evaluated the association between SCD and subsequent objective cognitive decline over an average follow-up of 2.5 years among Kaiser Healthy Aging and Diverse Life Experiences participants (n=1615). SCD was measured using log transformed scores from the 12-item Everyday Cognition (ECog) scale. Executive function and verbal memory were assessed using the Spanish and English Neuropsychological Assessment Scales. We used linear mixed models to evaluate the association between log(ECog scores) and annual rate of decline in executive function and verbal memory using time on study as the time scale. We assessed baseline age, sex/gender, race/ethnicity, and years of formal education (continuous) as potential modifiers; we included two-way interactions between each covariate and time and three-way interactions between each covariate, time, and log(ECog score). **Results:** Log(ECog scores) ranged from 0-1.24. Average rate of cognitive decline was faster for those with greater SCD (higher log(ECog scores)), although estimates were imprecise. For example, the mean difference in annual rate of decline in verbal memory scores was 0.04 (95% CI: -0.02 to 0.11) standardized units faster per 1 unit higher log(ECog) score. Associations between SCD and objective cognitive decline did not vary by age, sex, race/ethnicity, or educational attainment. **Conclusions:** SCD predicted future objective cognitive decline over a relatively short follow-up time in a racially/ethnically diverse cohort of older adults; results were similar across sociodemographic groups. These findings suggest that SCD could be a tool to predict dementia risk among diverse older adults.

**Estimating dementia incidence in older Asian Americans and Pacific Islanders in California: an application of inverse selection weights** Eleanor Hayes-Larson\* Eleanor Hayes-Larson Yixuan Zhou Yingyan Wu Marissa J Seamans Paola Gilsanz Rachel A Whitmer Elizabeth Rose

Data from electronic health records (EHR) shows heterogeneity in dementia incidence rates across racial and ethnic groups including Asian Americans and Pacific Islanders (AAPI), but there are no population-representative estimates of dementia incidence rates among AAPI. We used inverse odds of selection weights (IOSW) to estimate ethnicity-specific population-representative dementia incidence rates in AAPI ethnic groups. We harmonized and pooled sociodemographic and health data from a large cohort of dementia-free AAPI Kaiser Permanente Northern California (KPNC) members age 60+ at baseline and AAPI 60+ in the California Health Interview Survey (CHIS, 2005-2009), a population-representative dataset. IOSW were defined as the inverse of an individual's conditional odds of KPNC participation (from logistic regression), multiplied by unconditional odds of KPNC participation. Time to dementia diagnosis was obtained from KPNC EHR. Incidence rates (total cases/total person-time) were calculated with and without applying IOSW. All analyses were conducted stratified by ethnicity (n=6415 Chinese, n=5020 Filipino, n=3314 Japanese, n=675 Korean, n=426 PI, n=1061 South Asian, and n=604 Vietnamese in KPNC cohort). Factors affecting selection into KPNC differed by ethnicity, as did impact of weighting on estimated dementia incidence rates. Weighted estimates of dementia incidence were similar to (Chinese, Filipino, Vietnamese) or higher than (Japanese, Korean, and South Asian) unweighted estimates. Estimated dementia incidence in Pacific Islanders after weighting was slightly lower, with wide confidence intervals. Conditional exchangeability on age was a key driver of results. Our work is the first to estimate population-representative dementia incidence rates among AAPI. It is also one of few studies to apply transportability tools to observational data, and highlights areas in need of further methodological development.

Figure: Dementia incidence rates per 1,000 person-years by race/ethnicity in the Kaiser Permanente Northern California sample.

Light bars represent unweighted results, and dark bars represent weighted results.



**Racial/Ethnic Disparities in the Association between Depression and Cognitive Health**

Marcia P. Jimenez\* Marcia P. Jimenez Emma L. Gause Eleanor Hayes-Larson Emily P. Morris  
Franchesca Arias Alicia Riley Evan Fletcher Jennifer Manly Maria Glymour

Depression is associated with late-life cognitive decline and dementia risk. Researchers have reported racial/ethnic disparities in depression and later life cognitive health. However, research on the association between depression and cognition by race/ethnicity is limited.

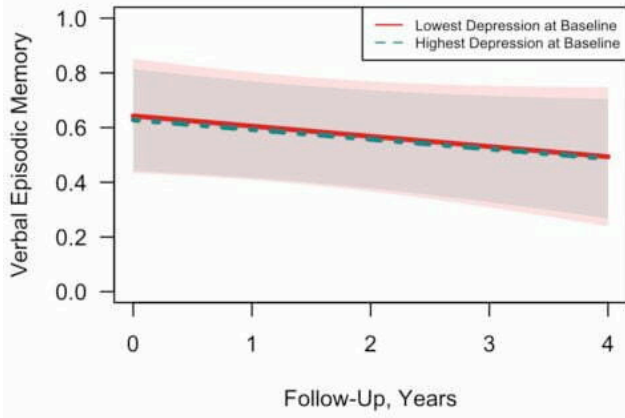
Among Asian, Black, LatinX, and White participants in the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE, age 65+) and the Study of Healthy Aging in African Americans (STAR, age 50+), we examined whether baseline depressive symptoms (assessed with the NIH toolbox) were associated with cognition, cognitive decline (N=2398), and MRI assessments of white matter hyperintensities (WMH; N=416) - a marker of brain aging. Participants underwent up to three repeated measures of cognition over four years using the Spanish and English Neuropsychological Assessment Scales (SENAS), including verbal episodic memory (VEM). WMH was measured once during follow-up. Linear multilevel models were used to examine baseline depressive symptoms and cognitive level and decline over follow up. Linear regression was used to assess the association of depressive symptoms and log-transformed WMH. Analyses were stratified by race/ethnicity and adjusted for age, sex, education, income, and marital status.

Results suggest differences in depression and cognitive health by race (interaction for WMH:  $p < 0.001$ ; VEM:  $p = 0.04$ ). In stratified models, among Black participants, higher depressive symptoms were not associated with baseline VEM level but were associated with faster decline in VEM [-0.025 (95%CI: -0.048, -0.002)], and more WMH [15% (7%, 24%)]. For LatinX participants, higher depressive symptoms were associated with lower VEM score at baseline [-0.15 (-0.26, -0.04)], and more WMH [19% (3%, 38%)] but not with cognitive decline in VEM. No other significant associations were observed.

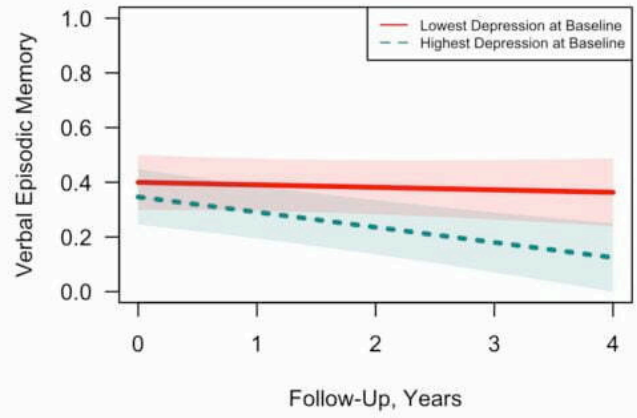
In a diverse sample of older adults, greater depressive symptoms were associated with cognitive health in certain race/ethnic groups.



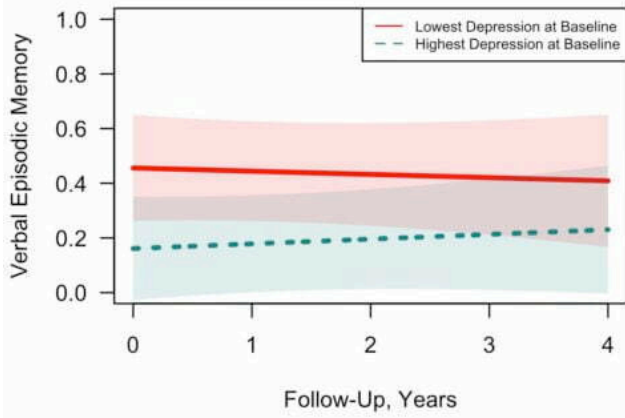
**Asian**



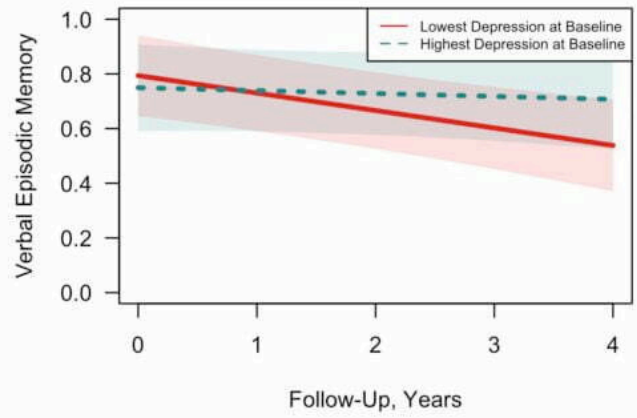
**Black**



**LatinX**



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## Aging

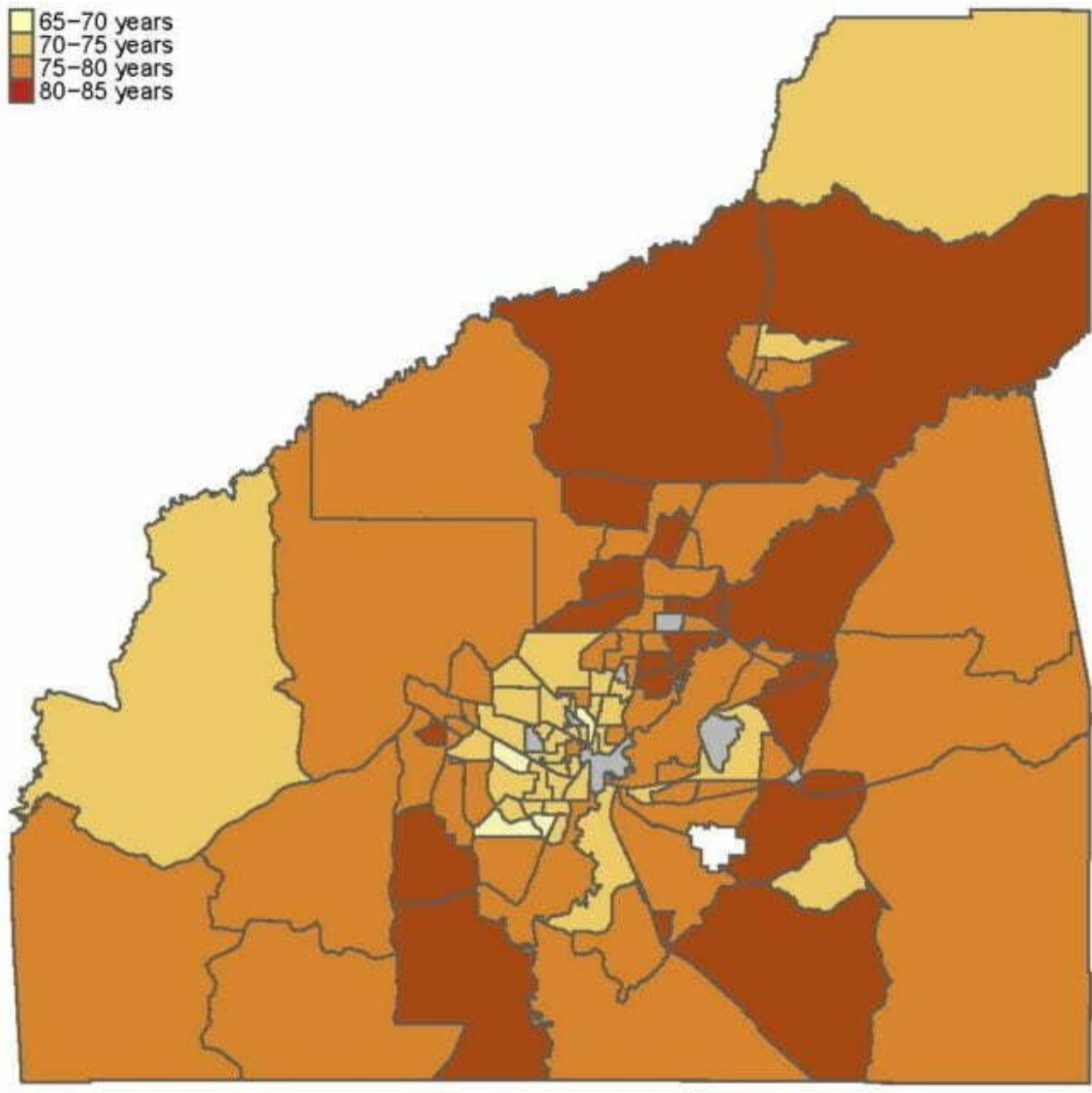
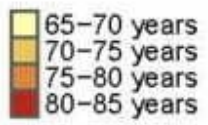
**Neighborhood Factors and Survival to Old Age: The Jackson Heart Study** Michelle C. Odden\*  
Michelle Odden Yongmei Li Roland J. Thorpe, Jr. Annabel Tan Kendra Sims Jourdan Ratcliff Hoda  
Abdel Magid Mario Sims

**Background:** Although there is growing interest in the role of the environment on aging, especially in minoritized populations, few studies have evaluated survival to old age.

**Methods:** Our study included 913 African American participants in the Jackson Heart Study (JHS) who resided in the tri-county area of the Jackson, MS metropolitan area and were 65-80 years at baseline. Participants were followed from 2000 through 2019 for the outcome of survival to 85 years old. We evaluated each of the following census tract-level measures of the social/physical environment as exposures: socioeconomic status, cohesion, violence, disorder, healthy food stores, residential land use, and walkability. We assessed mediation by physical activity, stress, and chronic conditions. As a complementary ecologic analysis, we used census-tract data to examine whether the proportion of homeownership or proportion living with others was associated with a greater life expectancy.

**Results:** A total of 501 (55%) participants survived to age 85 years or older. Higher social cohesion and greater residential land use were modestly associated with survival to old age (risk difference = 25%, 95% CI: 0-49%; and 4%, 95% CI: 1-7%, respectively). These neighborhood effects were modestly mediated through leisure time physical activity; additionally, social cohesion was mediated through home and yard activity. In our ecologic analysis, life expectancy estimates varied from 67.8 to 85 years by census tract in the tri-county area (Hinds, Rankin, Madison) of the Jackson, MS metropolitan area. **(Figure)** A greater percentage of homeowners and a greater proportion of people living in partnered families were associated with higher census-tract level life expectancy.

**Conclusion:** African American older adults living in residential neighborhoods or with high social cohesion were more likely to survive to old age.



**The South African Old Age Pension expansion impact on blood pressure of older rural men: Findings from the HAALSI study** Haeyoon Chang\* Haeyoon Chang Lindsay Kobayashi Janet Jock Molly Rosenberg Chihua Li Thomas Gaziano Lynda Lisabeth

The South African Old Age Pension (OAP) gradually lowered men's age eligibility from 65 to 60 (2008 to 2010), creating exogenous variation in pension income based on birth year. We used a quasi-experimental design to examine the impact of additional years of OAP expansion eligibility on systolic and diastolic blood pressures (BP) among older men in rural South Africa. We compared the BP of men  $\geq 60$  by OAP expansion eligibility using the population-representative "Health and Aging in Africa: A Longitudinal Study of an IN-DEPTH Community in Rural South Africa" (HAALSI; 2014/15, n=1,247). We used intention-to-treat analysis to categorize birth cohorts of men eligible for zero years (controls aged 65 at OAP expansion) to five years of additional pension income based on age. Next, we used multivariable linear prediction models based on the control group to estimate predicted BPs for men exposed to OAP expansion eligibility. Finally, we estimated the difference between observed and predicted BPs for men in each expansion cohort, representing the change in BPs attributable to the OAP expansion. While those cohorts exposed had lower mean BPs than the controls, the differences were not statistically significant ( $p=0.413$  for systolic and  $p=0.380$  for diastolic BP). For example, the mean difference in observed versus predicted systolic BP for those who received five additional years of OAP eligibility was  $-2.86$  mmHg (95% CI:  $-8.63, 2.91$ ) on a population level. Furthermore, I performed a negative control analysis with women to address a potential birth cohort effect. The fact that women's results differed from men's demonstrated that previously observed OAP expansion impact on BPs among men was not due to a birth cohort effect. Over the relatively short time period studied, the OAP expansion did not contribute to a meaningful reduction in BPs among older men in rural South Africa. However, future research should examine the health impacts of expanded pensions over longer periods.

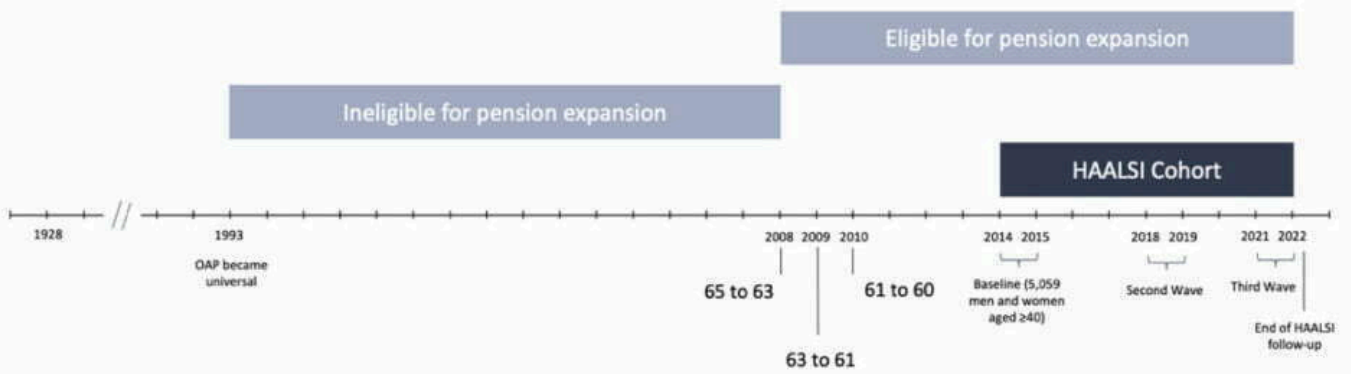


Figure 1. The timeline of the South African Old Age Pension and HAALSI study survey in rural Agincourt Mpumalanga province, South Africa.

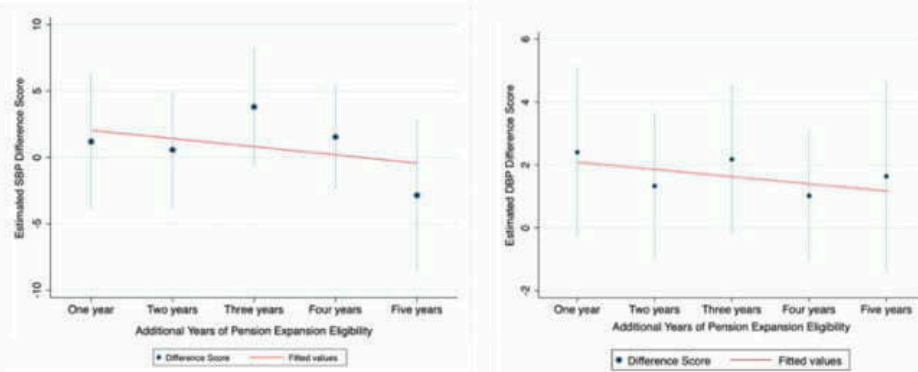


Figure 2. Estimated Difference Score in Systolic Blood Pressure (SBP; left) and Diastolic Blood Pressure (DBP; right) between each of the five expansion cohorts in additional years of OAP expansion eligibility among older men ( $p=0.413$  and  $p=0.380$ , SBP and DBP respectively), Health and Aging in Africa: A Longitudinal Study of an IN-DEPTH Community in South Africa (HAALSI), Agincourt sub-district, Mpumalanga province, South Africa, 2014/15. OAP=Old Age Pension

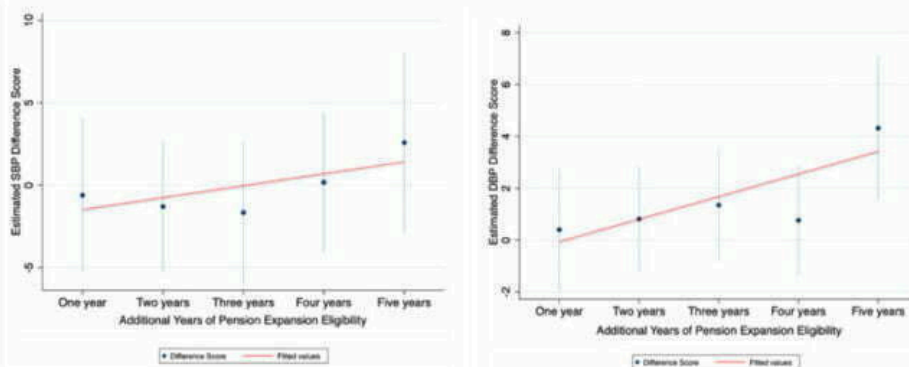


Figure 3. Negative control analysis, estimated Difference Score in Systolic Blood Pressure (SBP; left) and Diastolic Blood Pressure (DBP; right) between each of the five expansion cohorts in additional years of OAP expansion eligibility among women ( $p=0.155$  and  $p=0.126$ , SBP and DBP respectively), Health and Aging in Africa: A Longitudinal Study of an IN-DEPTH Community in South Africa (HAALSI), Agincourt sub-district, Mpumalanga province, South Africa, 2014/15. OAP=Old Age Pension

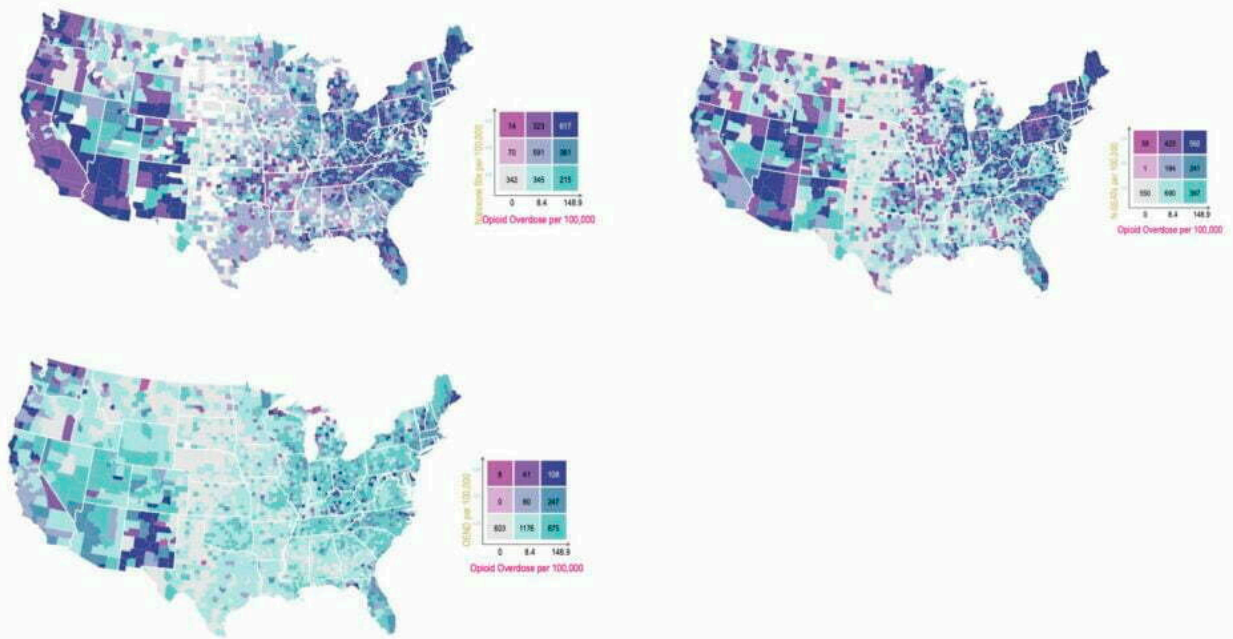
**Geographic variability and county-level associations of access to naloxone across three sources** Spruha Joshi\* Spruha Joshi Victoria Jent Corey Davis Magdalena Cerda

More people died from overdose in the United States (US) in the past year than any year in recorded history. Naloxone is an opioid antagonist that rapidly reverses opioid overdose. Making it widely available is a leading strategy to reduce opioid-related harms. This study describes the current availability and distribution of naloxone in the US and its relationship to local opioid-related overdose mortality. Naloxone availability was measured across three distribution venues: community-based programs, pharmacies, and opioid use disorder treatment centers.

Data on community-based distribution programs was obtained from Harm Reduction Coalition and North America Syringe Exchange Network as of May 2022. Pharmacy naloxone fills were obtained from the 2019-IQVIA Longitudinal Prescription Data. Treatment centers providing naloxone were obtained from the 2019-National Survey of Substance Abuse Treatment Services. Naloxone availability was geocoded to the county level and generalized estimating equations were used to test whether county-level characteristics were associated with naloxone availability. Of all 3,142 US counties, 484 (15.4%) had community-based distribution facilities, 1,501 (47.8%) had treatment centers that provided naloxone, and 2,240 (68.7%) had at least one pharmacy naloxone fill.

Opioid dispensing at the county level was associated with the availability of naloxone across all three sources. Counties with higher rates of fatal opioid overdose were not more likely to have naloxone available. Counties with a greater proportion voting Republican were less likely to have naloxone available through community-based distribution programs and treatment centers. These findings demonstrate that most US counties lack access to naloxone through community-based naloxone distribution facilities and treatment centers. In particular, there is a lack of access to naloxone in counties with higher opioid overdose mortality, where the need is the highest.

Figure 1. The relationship between naloxone availability across three sources and opioid overdose mortality rates per 100,000 across the United States



**Comparative effectiveness of buprenorphine/naloxone versus methadone for treatment of opioid use disorder: emulating target trials with population-level data** Jeong Eun Min\*

Fahmida Homayra Jeong Eun Min Megan Kurz Bohdan Nosyk

**Background:** Previous studies on the comparative effectiveness of buprenorphine and methadone featured challenges that limit their applicability to clinical practice. Our objective was to determine the comparative effectiveness of buprenorphine/naloxone versus methadone, both overall and within key populations, using population-level data and both intention-to-treat and per-protocol study designs.

**Design, setting, and participants:** 44,446 recipients of buprenorphine/naloxone and methadone treatment for OUD, 18 years or older, with no history of cancer or palliative care, and not pregnant at initiation in British Columbia, Canada, from January 1, 2010 to March 17, 2020.

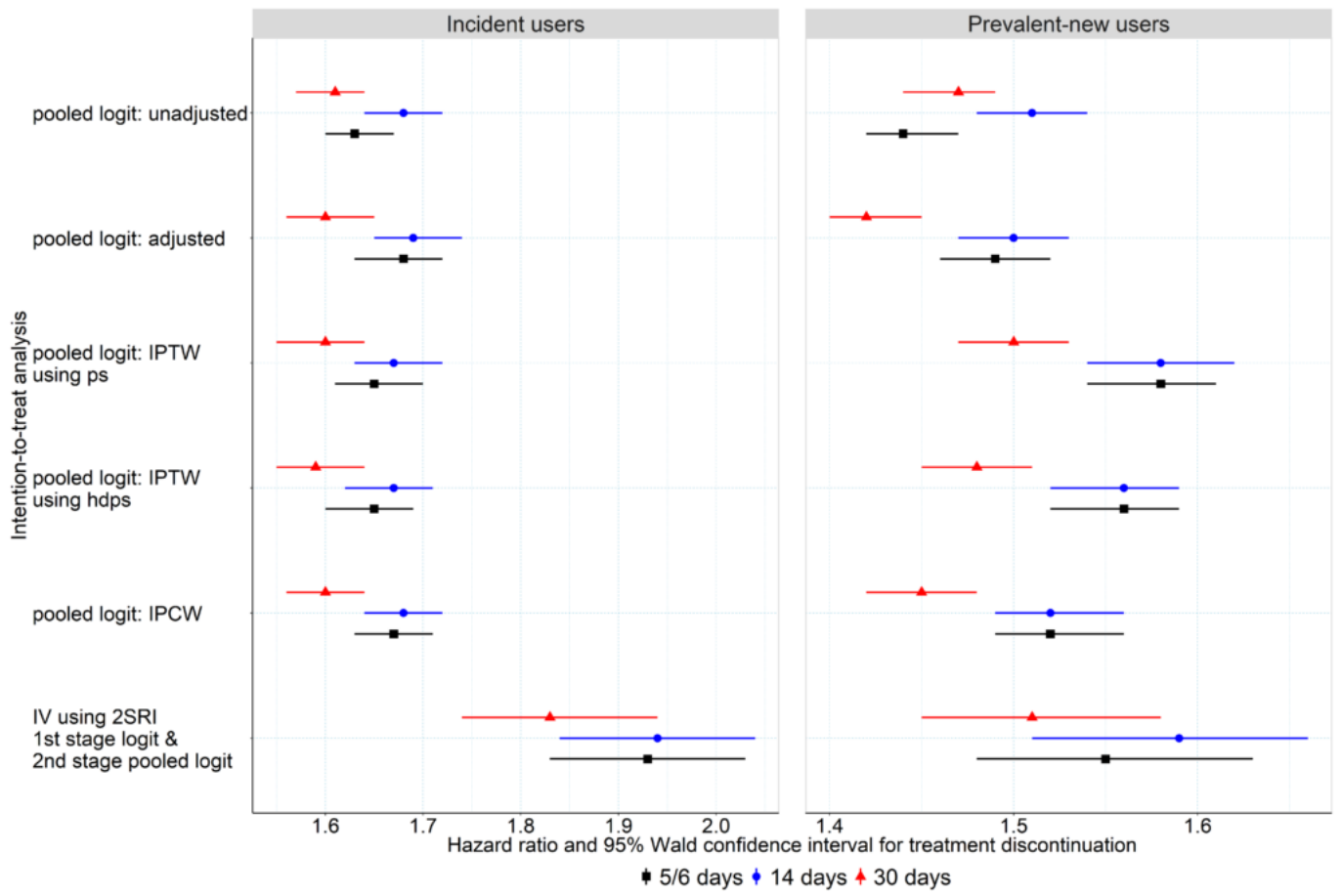
**Exposures:** Receipt of buprenorphine/naloxone, methadone among incident users and prevalent new users.

**Main Outcomes and Measures:** Hazard ratios (HRs) with 95% Wald confidence intervals were estimated for treatment discontinuation using pooled-logistic regression models for the intention-to-treat analysis, and generalized estimating equation (GEE) model and marginal structural models (MSM) for per-protocol analyses.

**Results:** After controlling for baseline covariates, the hazard ratio for treatment discontinuation for buprenorphine/naloxone versus methadone obtained using intention-to-treat analysis was 1.49 (95% Wald CI; 1.46, 1.52). After controlling for time-dependent covariates using per-protocol analysis, the HR decreased to 1.40 (1.36, 1.45) obtained by GEE, and 1.38 (1.35, 1.42) obtained by MSM.

**Conclusions and Relevance:** Assessing the comparative effectiveness of buprenorphine-naloxone versus methadone through both intent-to-treat and per-protocol perspectives addresses the potential confounding by indication at and time-varying confounding, thus providing pragmatic real-world clinical evidence to inform the clinicians and policy makers.

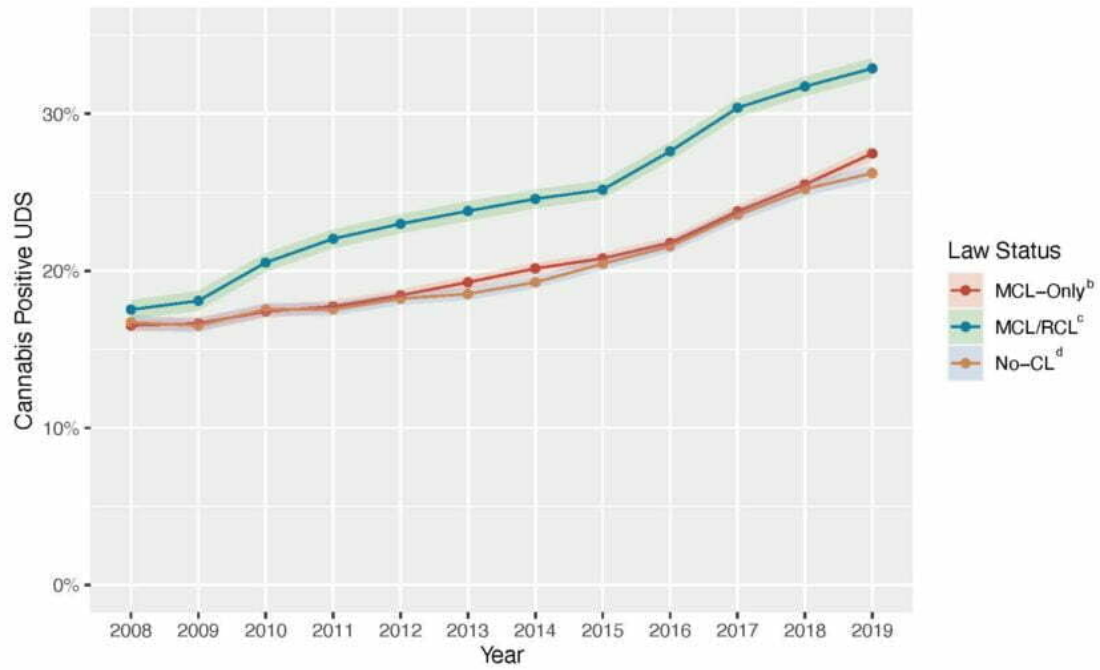




**State cannabis legalization and changes in cannabis use as determined by biologic testing in emergency department patients in the U.S. Veterans Health Administration, 2008 to 2019** Deborah Hasin\* David Fink Hillary Samples Andrew Saxon Carol Malte Melanie Wall

National studies investigating the effect of medical cannabis laws (MCL) and recreational cannabis laws (RCL) have largely relied on self-reported survey measures or cannabis use disorder (CUD) diagnoses in patient populations, which may not accurately capture changes in use due to underreporting of symptoms in survey responses and concealing symptoms in patient populations. Few studies have addressed the role of cannabis legalization using biological measures of use. We aim to quantify the role of MCL and RCL enactment on changes in cannabis positive urine drug screens (UDS) among Veterans Health Administration (VHA) emergency department (ED) patients, 2008-2019. Participants were veteran patients, age 18-75 years, with <sup>31</sup> VHA ED visit with a UDS collected within each calendar year (n=79,484 to 120,936). Difference-in-differences (DiD) analyses were used to estimate MCL and RCL effects, with state and year fixed effects, time-varying cannabis law status, state-level sociodemographic covariates, and patient age-group, sex, race and ethnicity. From 2008 to 2019, cannabis positive UDS increased from 7.39% to 14.92% among all patients, 16.7% to 26.2% in states with no cannabis law (no-CL), 16.5% to 27.5% in MCL-enacted states, and 17.5% to 32.9% in RCL-enacting states. DiD results indicated that overall, enacting RCL led to a 15.4% absolute increase in cannabis positive UDS, i.e., that 13.8% of the total increase in cannabis positive UDS in RCL-enacting states could be attributed to RCL. Increases in MCL-enacting states were comparable with contemporaneous changes in no-CL states. In VHA ED patients, RCL enactment contributed to higher cannabis use, as measured by UDS, but not in MCL-enacting states. Results indicate that survey measures and patient diagnoses may underestimate the true change in cannabis use or that effects of legalization on CUD diagnoses may require longer follow up times for some patients to go from use to disorder.

**Figure 1.** Trends in cannabis positive urine drug screens (UDS)<sup>a</sup> from 2008 to 2019, aggregated within the three groups of states defined by their status at the end of 2019



MCL=medical cannabis law; RCL=recreational cannabis law

<sup>a</sup>Staggered-adoption difference-in-differences (DiD) regression model, adjusted for age, sex, race/ethnicity, and state-level covariates (yearly estimates of median household income, % unemployed, % below the poverty threshold, % male, % non-Hispanic white, % non-Hispanic Black, % Hispanic, and % 18 years of age or over). <sup>b</sup>22 states and DC made a change from no-CL to MCL-only during the period from 2005-2019. <sup>c</sup>11 states and DC made a change from MCL-only to RCL/MCL during the period. Note, 3 of these states and DC made both changes between 2005-2019 (i.e., from no-CL to MCL-only and then later to RCL/MCL), hence contributing information to both effects. <sup>d</sup>There were 20 states (3 with MCL-only and 17 with no-CL in 2019) that made no law changes between 2005-2019; in the DID model, they contribute to background secular trends.

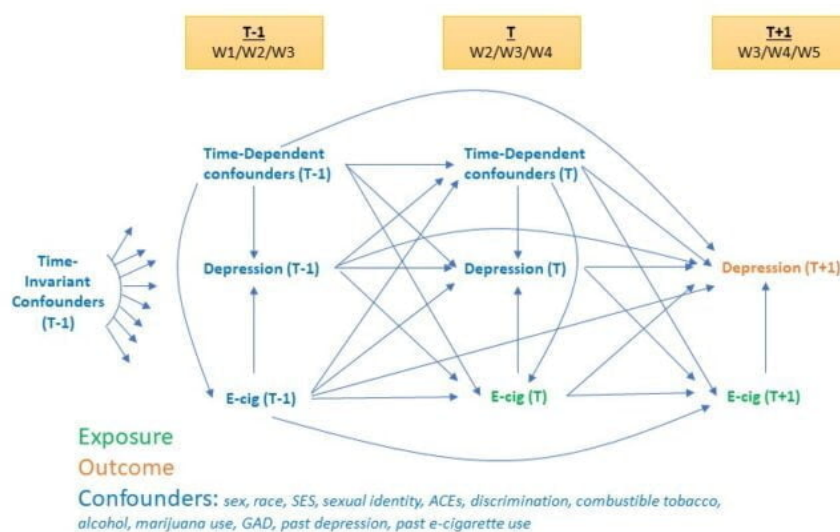
## Substance Use

**The Association between in utero Cannabis Exposure and Neonatal Outcomes in a Large Integrated Healthcare Delivery System** Lyndsay Avalos\* Lyndsay Avalos Sara R. Adams Stacey E. Alexeeff Nina R. Oberman Monique Does Deborah Ansley Amy Conway Nancy Goler Alisa Padon Lynn Silver Kelly C. Young-Wolff

Despite the increasing prevalence of prenatal cannabis use, research evaluating the association between *in utero* cannabis exposure and adverse neonatal outcomes has been largely inconclusive. This study evaluated associations between *in utero* cannabis exposure and adverse neonatal outcomes. We conducted a population-based retrospective birth cohort study of children born (January 1, 2011-July 31, 2020) to pregnant Kaiser Permanente Northern California members universally screened for cannabis use via self-report and/or urine toxicology. Data were ascertained from electronic health records. A directed acyclic graph (DAG) informed the study design and analytic model. Multivariable logistic regression was conducted. *In utero* cannabis exposure was defined as any use (yes versus no; primary) and frequency of use (among those with self-report data; secondary). Of the 364,915 infants, 6.2% (n=22,626) were exposed to cannabis *in utero*. *In utero* cannabis exposure was associated with greater odds of low birthweight (aOR:1.19, 95%CI: 1.12, 1.27), SGA birth (aOR:1.23, 95%CI: 1.17, 1.29), preterm birth (aOR:1.06, 95%CI: 1.01, 1.13), and NICU admission (aOR:1.06, 95%CI: 1.01, 1.11), with a trend noted for early preterm birth (aOR:1.11, 95%CI: 1.00, 1.24) and respiratory support (aOR:1.07, 95%CI: 0.97, 1.18), after adjustment for exposure to other *in utero* substances and additional potential confounders. A dose-response relationship emerged for associations with low birth weight and SGA birth. Sensitivity analyses excluding individuals with other substance use during pregnancy produced similar results. *In utero* cannabis exposure was associated with an increased likelihood of adverse neonatal outcomes. Care for individuals considering pregnancy and pregnant individuals should include education about the adverse neonatal health effects associated with prenatal cannabis use, and cannabis policy on labeling, marketing and public education should address neonatal risks.

**Vaping Transitions and Depression Symptoms among Young Adults: A Marginal Structural Model Analysis** Alyssa F. Harlow\* Alyssa Harlow Andrew C. Stokes Dae-Hee Han Adam M. Leventhal Jessica Barrington-Trimis

Studies on vaping and depression symptoms have not adequately examined longitudinal vaping transitions or accounted for time-dependent confounding. Using data from a prospective cohort of young adults from California (2018-2022), we estimated repeated measures marginal structural models to examine the association of four e-cigarette transitions between time  $t$  and  $t+1$  (persistent use, cessation, persistent non-use, initiation) with depression symptoms at  $t+1$ , simultaneously across three time-intervals (i.e., W2-W3; W3-W4; W4-W5). E-cigarette use was defined as past 30-day use, and depression was a continuous score measured with the Center for Epidemiologic Studies Depression Scale. Repeated measures linear regression models used stabilized inverse probability of treatment weights to adjust for baseline and time-dependent confounders, including prior depression symptoms, prior e-cigarette use, sex, race, financial status, sexual identity, adverse childhood experiences, discrimination, anxiety, combustible tobacco, alcohol, and cannabis use. Among  $n=5,113$  observations (1,948 participants, mean baseline age in each interval=19.5, 20.5, 21.5 years), 9.6% reported persistent e-cigarette use at both time points, 5.6% reported cessation (i.e., use at  $t$  and no use at  $t+1$ ), 77.8% reported no e-cigarette use at both time-points, and 7.0% initiated e-cigarettes (i.e., no use at  $t$  and use at  $t+1$ ). Young adults who quit vaping between waves reported reduced depression symptoms (versus persistent use; *mean diff*=-1.7, *95%CI*:-3.0 to -0.32). Compared to persistent non-use, estimates for initiation indicated a small but imprecise increase in depression symptoms (*mean diff*=0.51, *95%CI*:-0.55 to 1.6), and persistent use was positively associated with depression symptoms (versus persistent non-use; *mean diff*=1.7, *95%CI*: 0.67-2.6). Young adults who quit vaping may experience mental health benefits. E-cigarette use may worsen mental health for young adults who vape continuously over time.



**Figure.** Directed acyclic graph (DAG) for the association of e-cigarette transitions between T and T+1 and depression symptoms at T+1. Stabilized inverse probability weighting removes the arrows going into E-cig (T+1) and final weighted outcome models are additionally adjusted for confounders, depression, and e-cigarette use at T-1.

**LATEBREAKER**

## COVID-19 Pandemic

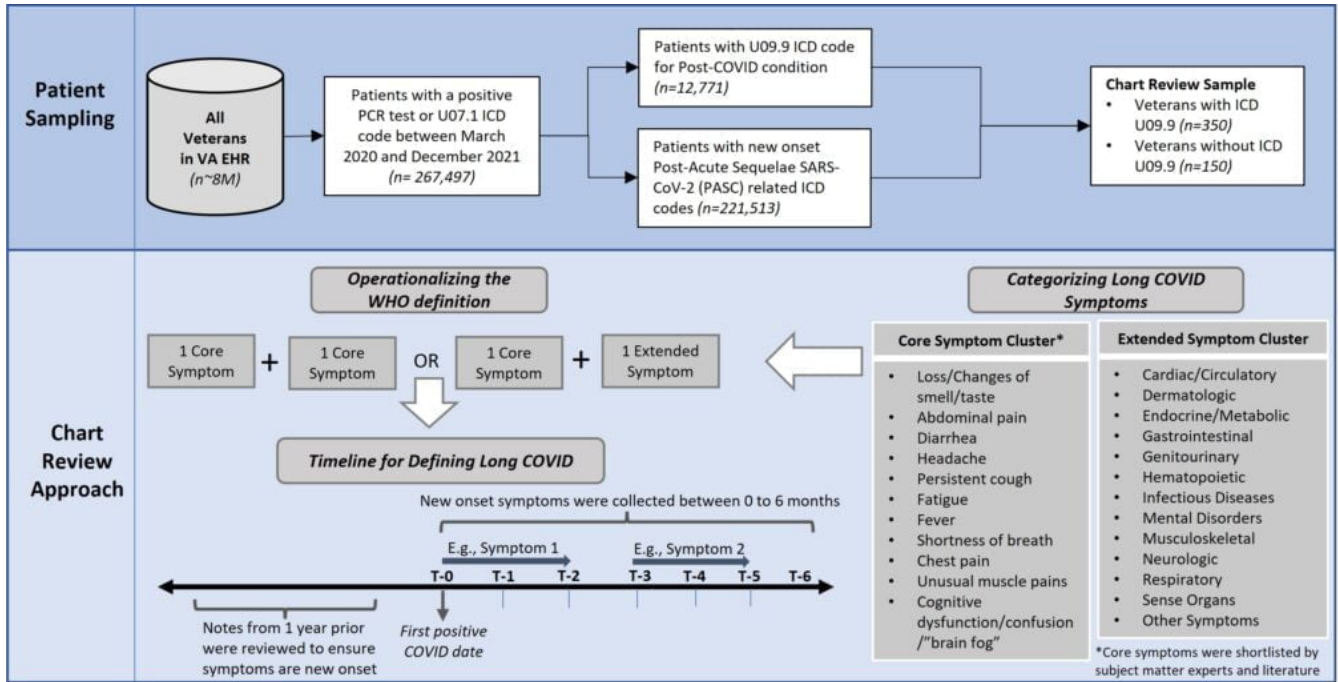
**Characterizing Long-COVID and Understanding the Utilization of Post COVID-19 Condition ICD code U09.9 in the Veterans Health Administration** Monika Maripuri\* Monika Maripuri Jacqueline P Honerlaw Chuan Hong Yuk-Lam Ho Andrew T Dey Vidisha Tanukonda Vidul Ayakulangara Panickan Xuan Wang Harrison G Zhang Malarkodi Jebathilagam Samayamuthu Brendin R Beaulieu-Jones Katherine P Liao Zongqi Xia Sumitra Muralidhar Gabriel A Brat Tianxi Cai Kelly Cho

**Background:** Long COVID characterized as post-acute sequelae of SARS-CoV-2 (PASC) has no universal clinical case definition. Recent efforts have focused on defining and understanding long COVID. Researchers using electronic health records (EHR) frequently rely on International Classification of Diseases (ICD)-10 code U09.9, introduced in October 2021, to identify patients with long COVID. However, the accuracy of this code is unclear. This study aimed to evaluate the accuracy of the U09.9 code in the US Department of Veterans Affairs (VA) healthcare system by conducting a chart review of the long COVID phenotype per the World Health Organization (WHO) definition.

**Methods:** A sample of 500 COVID positive Veterans i) with a U09.9 code and ii) without a U09.9 code but with PASC related ICD codes, were used. To operationalize the WHO definition, we grouped symptoms into a “core” cluster of 11 commonly reported symptoms among long COVID patients and an extended cluster, that captured all other symptoms. (Figure) Patients having at least 2 symptoms persisting for  $\geq 60$  days that were new onset after COVID infection, and with at least one symptom in the core cluster, were labeled as having long COVID.

**Results:** The prevalence of long COVID in the sample was 23%. Among patients with the U09.9 code, 30% had long COVID based on the operationalized WHO definition, and among the patients without the code, 7% had long COVID. The positive predictive value (PPV) of the U09.9 code in this cohort was 0.30 and the sensitivity was 0.91.

**Discussion:** Our results showed that the U09.9 code should be used with caution to identify long COVID. This code was found to be highly sensitive but given the low prevalence of long COVID in this cohort, the PPV was poor. Our findings also suggest the importance of EHR system specific validation of the U09.9 code. Further development of a more refined and reproducible long COVID phenotype algorithm is underway.



**LATEBREAKER**

## COVID-19 Pandemic

**COVID-19 Vaccine Reduces Long COVID Incidence Among Infection-Naive Adults in the U.S.: a Target Trial Emulation in a Community-Based Cohort** Yanhan Shen\* Yanhan Shen McKaylee M Robertson Avantika Srivastava Sarah G. Kulkarni Chloe Mirzayi Rebecca Zimba Christian Grov Denis Nash

**Background:** Overall, 7.3% of U.S. adults had long COVID as of July 2022. We aimed to assess the impact of COVID-19 vaccination on long COVID incidence among infection-naive adults.

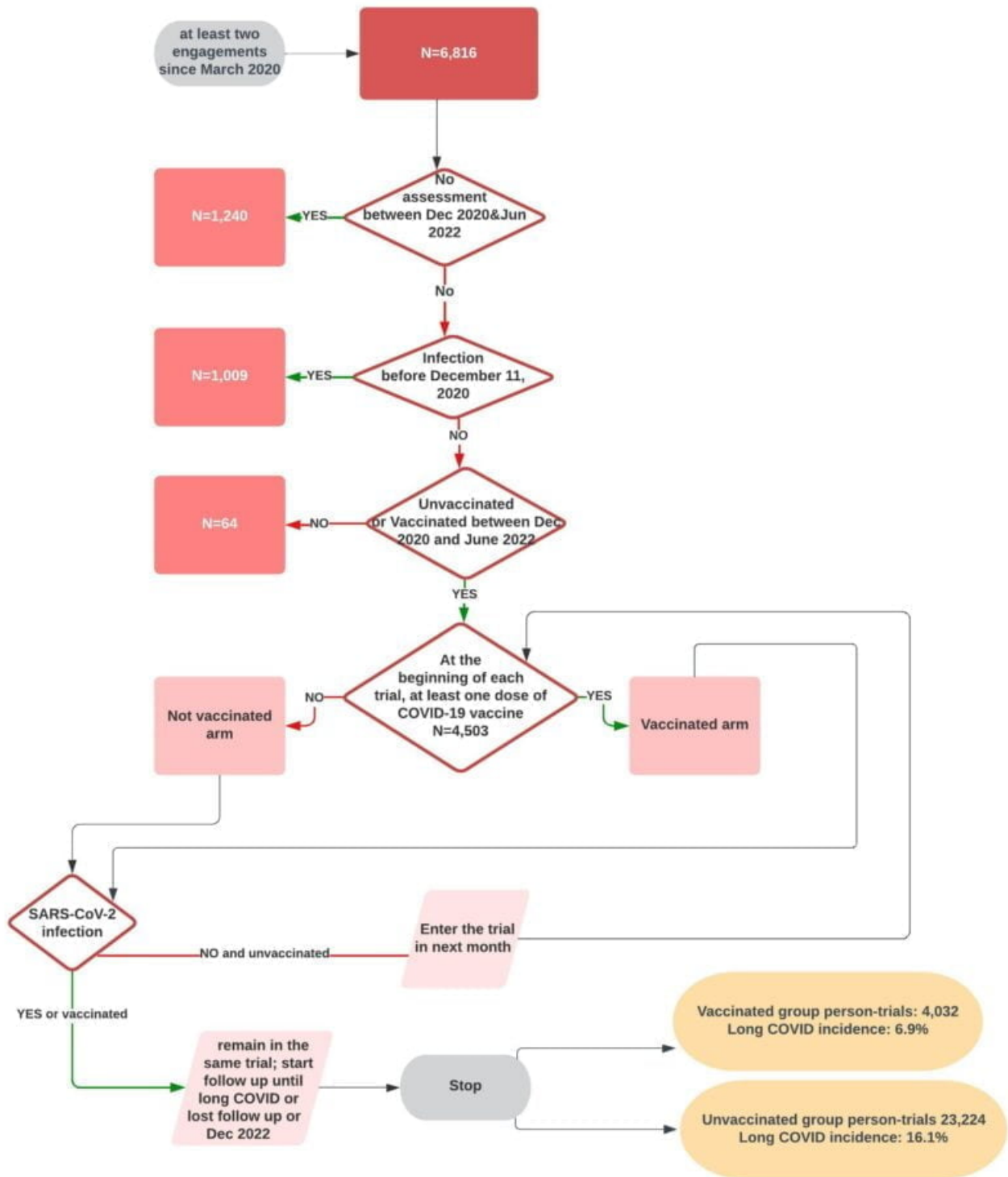
**Methods:** Using data from the CHASING COVID Cohort study, a prospective longitudinal national community-based cohort, we emulated the design protocol and intention-to-treat (ITT) analysis of a randomized controlled trial with a minimum of 6 months of follow-up after trial entry. We operationalized a sequence of monthly observational 'target trials' from December 2020 to June 2022 in which SARS-CoV-2 infection naive participants were classified as either vaccinated with at least one dose of COVID-19 vaccine or unvaccinated. Participants were allowed to enter a subsequent trial if they remained unvaccinated and uninfected; those who became vaccinated or infected during a trial remained in that trial for the duration of follow-up. We defined long COVID in alignment with the World Health Organization definition, which includes persistent symptoms of fatigue, shortness of breath or trouble concentrating >3 months from acute infection that lasted >2 months. Inverse probability of treatment and censoring weights (IPTW and IPCW) were estimated by age, gender, education, income, obesity, asthma, diabetes, and COVID-19 susceptibility index, an indicator of increased SARS-CoV-2 infection risk or severity. The ITT OR was estimated, adjusting for calendar time and applying IPTW and IPCW.

**Results:** There were 4,503 unique eligible SARS-CoV-2 naive participants and 27,256 emulated person-trials, including 4,032 vaccinated person-trials and 23,224 unvaccinated person-trials. Participants who completed at least one dose of primary COVID-19 vaccine before they were infected had a lower risk of incident long COVID (risk: 6.9% vs. 16.1%, aOR: 0.40 [95% CI: 0.32 - 0.51]) than those participants who did not.

**Conclusions:** Staying up-to-date on COVID-19 vaccination may have the added benefit of preventing long COVID.



Figure: Flowchart of selection of the 4,503 eligible SARS-CoV-2 naïve participants from the CHASING COVID cohort study, the process of meeting eligibility criteria and time zero, and trial arm assignment in each sequential target trial, December 2020-June 2022



**LATEBREAKER**

## COVID-19 Pandemic

**Comparative Effectiveness of Alternative Intervals between First and Second Doses of the mRNA COVID-19 Vaccines: a trial emulation approach**

Kayoko Shioda\* Kayoko Shioda  
Alexander Breskin Pravara Harati Allison Chamberlain Benjamin A Lopman Elizabeth Rogawski  
McQuade

**Background:** mRNA COVID-19 vaccines require two primary doses. The optimal timing of second dose administration with respect to vaccine effectiveness of the primary series has not been thoroughly evaluated and has implications for vaccine strategies.

**Methods:** We employed a trial emulation approach (clone-censor weight analysis) to assess whether the effectiveness of mRNA COVID-19 vaccines (Pfizer-BioNTech and Moderna) against SARS-CoV-2 infection differed by varying intervals between the first and second doses of the primary series among the general population. We estimated the risk of SARS-CoV-2 infection after the first dose administration under the scenario where the total study population had followed each of the following protocols defined by interdose interval: recommended by the Food and Drug Administration (FDA) (17-25 days for Pfizer-BioNTech; 24-32 days for Moderna), late-but-allowable (26-42 days for Pfizer-BioNTech; 33-49 days for Moderna), and late ( $\geq 43$  days for Pfizer-BioNTech;  $\geq 50$  days for Moderna). Our study population included individuals who received  $\geq 1$  dose of mRNA COVID-19 vaccines in Georgia, USA, between December 13, 2020 and March 16, 2022.

**Results:** In the short-term, the cumulative risk of SARS-CoV-2 infection was lowest under the FDA-recommended protocol (risk ratio (RR) on Day 50 after the first dose administration compared to the FDA-recommended protocol: 1.08 [95% confidence interval 1.07-1.10] under the late-but-allowable and 1.14 [1.12-1.16] under the late protocol). Longer-term, the late-but-allowable protocol resulted in the lowest risk (RR on Day 120: 0.83 [0.82-0.84] for the late-but-allowable and 1.10 [1.08-1.12] for the late protocol). The late protocol consistently yielded the highest risk among all protocols.

**Discussion:** Delaying the timing of the second dose administration by approximately one week may provide stronger long-term protection against SARS-CoV-2 infection, but a longer delay would increase the risk of infection.

**LATEBREAKER**

## COVID-19 Pandemic

**Social and structural inequalities in COVID-19-related mortality over time: a population-based study of 11 million adults in Ontario, Canada** Linwei Wang\* Linwei Wang Sarah Swayze Andrew Calzavara Beate Sander Hind Sbihi Sean P. Harrigan Jeffrey C. Kwong Sharmistha Mishra

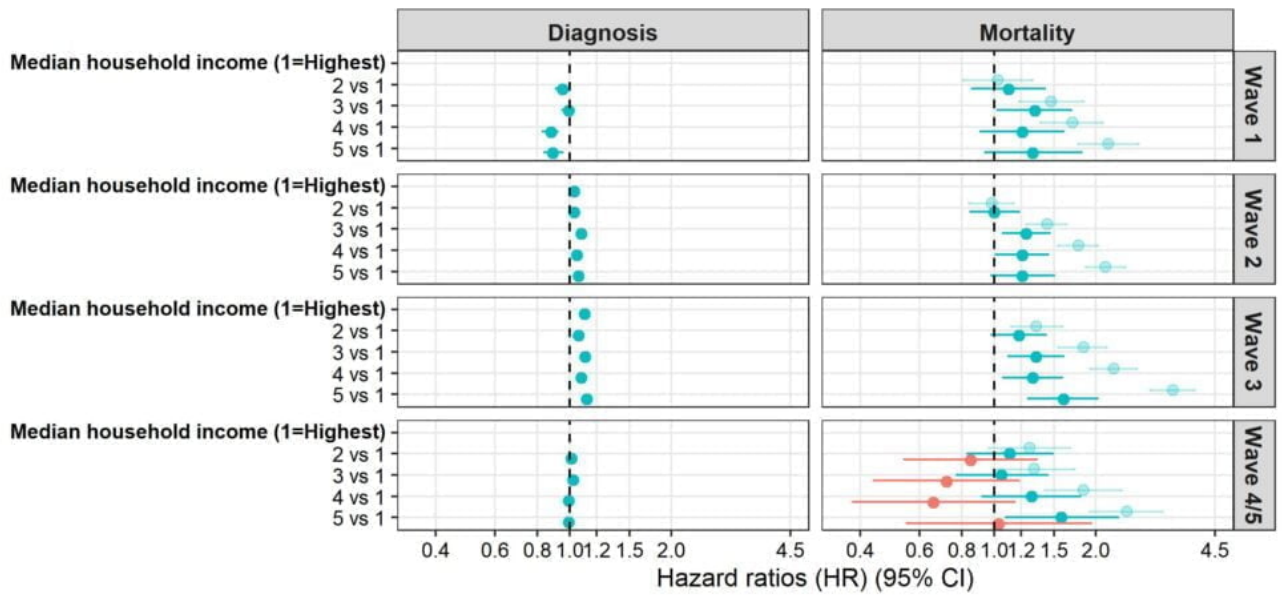
**Background:** Social and structural inequalities in COVID-19 outcomes were evident in early pandemic waves, but less is known about these patterns over time.

**Methods:** We followed residents of Ontario, Canada aged  $\geq 18$  years from Mar 1, 2020 to Dec 31, 2021. We examined two social determinants of health (SDOH) using 2016 Census data: area-level median household income and proportion of racially minoritised groups. We examined associations between each SDOH and COVID-19-related mortality (death within [-7,30] of diagnosis) using cause-specific hazard models, stratified by wave (1: Mar 1-Aug 31, 2020; 2: Sep 1, 2020-Feb 28, 2021; 3 [Alpha dominant]: Mar 1-Jul 31, 2021; 4-5 [Delta and Omicron dominant]: Aug 1-Dec 31, 2021) and vaccination status.

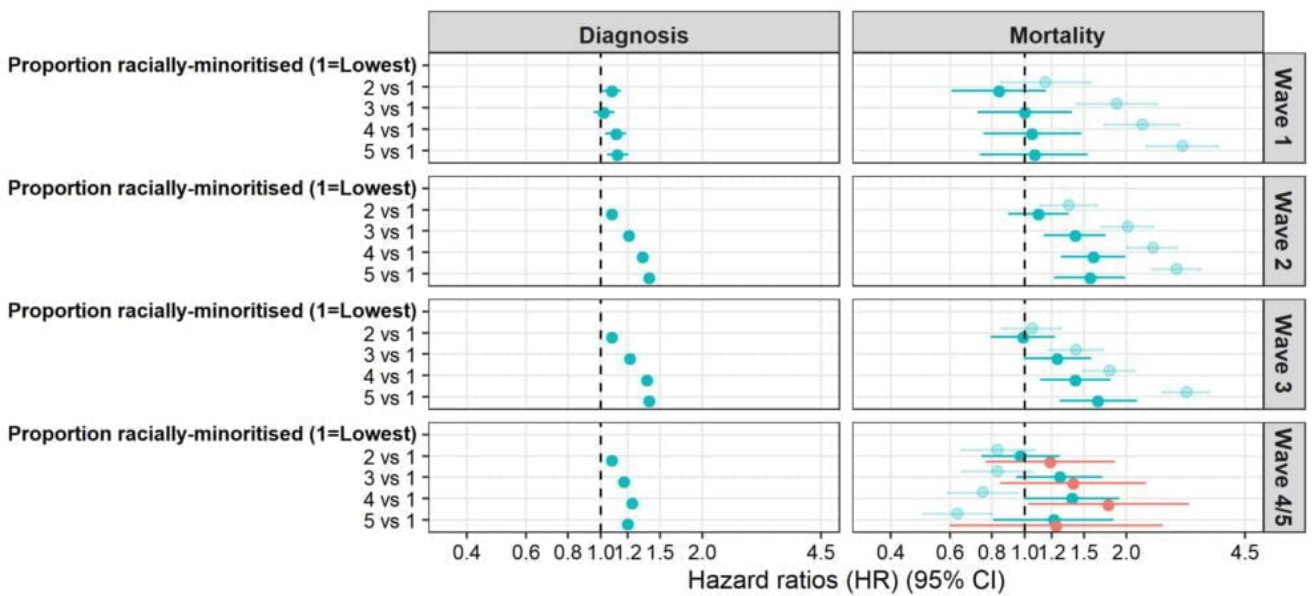
**Results:** Of 11,470,880 individuals, we observed 7,645 (0.07%) COVID-19-related deaths. After accounting for individual-level demographics, baseline health, and other area-level SDOH, lower income and higher proportion racially minoritised were associated with increased hazards of COVID-19-related death across waves (**Figure 1**), with a slight reduction in magnitude in wave 4-5. In wave 4-5, compared to the highest income quintile, the lowest was associated with 1.58 times hazard of COVID-19-related death (95%CI: 1.08-2.33), despite similar hazards of diagnosis (**Figure 1A**). Although the crude pattern of deaths by proportion racially minoritised was reversed in wave 4-5 compared to earlier waves, the reversal did not persist after adjustment (**Figure 1B**). Among vaccinated, income was not associated with COVID-19-related mortality; while higher proportion racially minoritised was associated with elevated hazards of mortality despite vaccination (**Figure 1**).

**Conclusions:** Social and structural inequalities in COVID-19-related mortality persisted over time. Next steps include examining roles of vaccination and virus of concern as a mediator and effect modifier in explaining patterns of inequalities using causal mediation analyses.

**A**



**B**



Vaccination ● Fully vaccinated ● Entire cohort    Model ● Adjusted ● Unadjusted

**LATEBREAKER**

## COVID-19 Pandemic

**Characterizing the socio-spatial distribution of excess mortality in Michigan during the COVID-19 pandemic** Kelly Broen\* Kelly Broen Jon Zelner Krzysztof Sakrejda

Data and analytic challenges associated with measuring the burden of infection and mortality from COVID-19 have been central challenges to effective disease surveillance and resource allocation since the beginning of the pandemic. To assess the scale of the gap between official estimates of SARS-CoV-2 mortality and the true burden of mortality from COVID-19 in Michigan during the period from March 2020 through June 2022, we used fine-scale spatiotemporal information on cause-specific mortality to characterize spatial and sociodemographic variation in excess mortality attributable to respiratory infection. We assess mortality trends across six distinct phases of the COVID-19 pandemic which are defined by variation in lockdown stringency, vaccination coverage, availability of effective antivirals, and viral shifts in infectiousness and case-fatality. We estimated area-specific excess mortality using a hierarchical Bayesian Poisson regression model including sociodemographic covariates at the census tract level. We found that the rate of excess mortality from respiratory infection was greatest during the first phase of the pandemic (March-May 2020), when there were an average of 5.9 excess deaths per expected death (95% CI: 3.0 - 8.7), and lowest during the second phase of the pandemic, (June-August 2020), when there was an average of 4.6 excess deaths per expected death (95% CI: 1.8 - 7.5). Mortality from respiratory infections remains elevated throughout the sixth analyzed pandemic phase (December 2021 - June 2022; 4.6 excess deaths per expected, 95% CI: 2.0 - 7.3). These results demonstrate that the COVID-19 pandemic continues to produce large increases in excess mortality from respiratory infection above the pre-pandemic baseline, and that these deaths are only partially captured by official data.

**Income inequality and sleep in Canadian adolescents: a multilevel path analysis** Priya Patel\*

Priya Patel Roman Pabayo

**Background:** Sleep deprivation is a substantial public health concern with 30% of Canadian adolescents not getting the recommended amount of sleep. According to the Social Determinants of Health Framework, characteristics of the social environment may play a role in sleep deprivation. One such characteristic is income inequality, the gap between rich and poor within a society. No prior study has examined the role of income inequality in teen sleep. Considering the increasing prevalence of sleep deprivation among teens and income inequality, describing the association between income inequality and sleep duration is of paramount importance.

**Objective:** The aim of the current study is to determine if depression and social cohesion act as mediators between income inequality and sleep duration.

**Methods:** Using cross-sectional data of 74,501 secondary school students from wave 7 (year 2018-2019) of the Cohort on Obesity, Marijuana use, Physical activity, Alcohol use, Smoking, and Sedentary behaviour (COMPASS) study, a multilevel path analysis was conducted. Income inequality (Gini coefficient) was measured at the census division level and sleep duration, depression, and social cohesion were measured at the individual level.

**Results:** A full mediation effect of depression was found wherein greater income inequality predicted greater depression scores which in turn, predicted lower sleep duration ( $\beta=-2.62$ ,  $p=0.04$ , 95% CI=-5.15 to -0.10) (Figure 1). No direct effect of income inequality on sleep duration was found. The model had strong fit statistics (TLI=1.00, CFI=1.00, RMSEA=0.01).

**Conclusion:** Our study findings provide further rationale for public health policy to focus on reducing the income gap between society members. Interventions that reduce income inequality may prevent depression and improve sleep in teens. Furthermore, public health interventions aimed at improving sleep behaviour should be targeted towards teens living in neighbourhoods with higher income inequality.

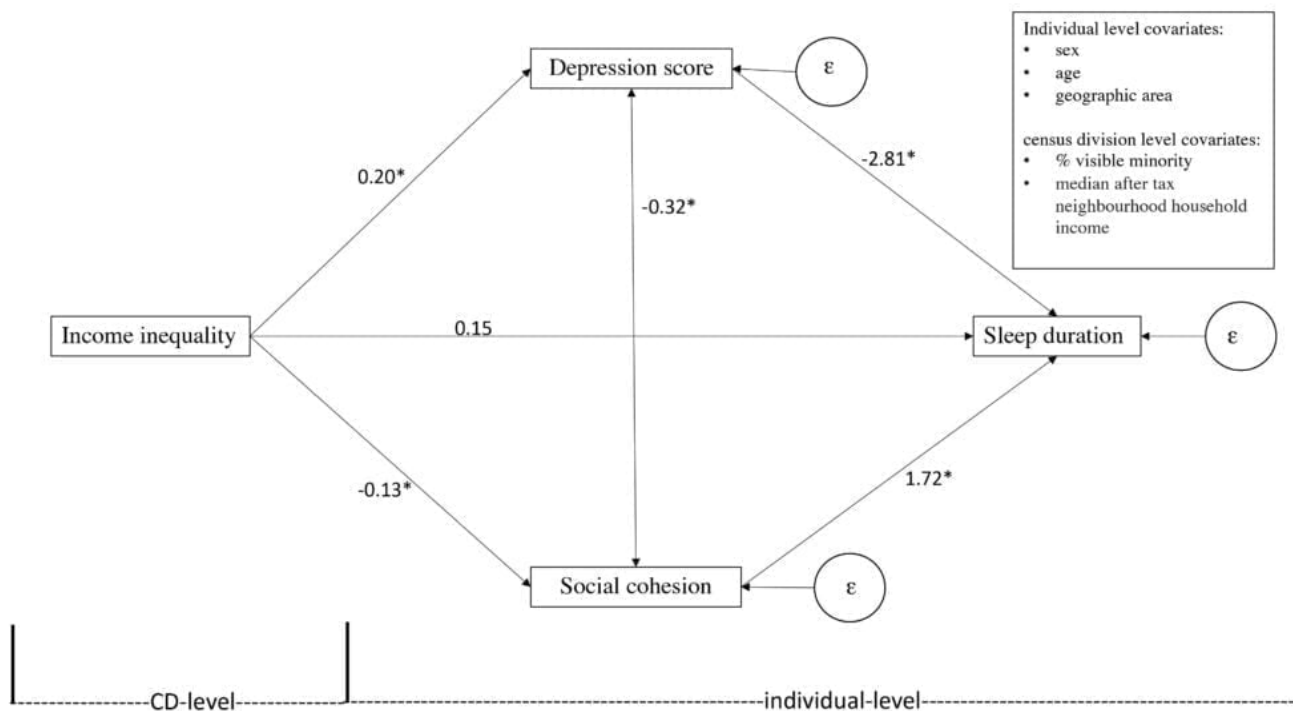


Figure 1. Multilevel path model with unstandardized coefficients of direct and indirect paths. \*p<0.001

**The association between the spouse's working hours and self-rated health in Japan, based on the nationwide survey** Yuka Suzuki\* Yuka Suzuki Kaori Honjo

It is widely known that one's working hours affect own physical and psychological health. Furthermore, possibilities that spouse's working hours negatively affect own health have been suggested. Japan has higher proportion of long-hour workers compared to other countries, thus, the public health impact from long working hours may large if the association between the spouse's working hours and own health is identified. Therefore, we aim to examine the association between the spouse's working hours and own poor self-rated health (SRH).

We analyzed the nationwide, self-administrated questionnaire data of the 2019 Comprehensive Survey of Living Conditions for 131,783 people (55,389 men, 76,394 women) those who were aged 20-64, currently married, and living with their spouse who had a job. We excluded people whose SRH data and the spouse's working hour data were missing. We divided people into 3 groups based on their spouse's working hour; 1) 0-39 hours (part-time work), 2) 40-49 hours (full-time work), and 3) 50 hours or more (long-hour work). Poor SRH was defined if the person answered his/her current health status as "not so good" or "not good." The ORs for poor SRH according to the spouse's working hours were calculated by multivariable logistic regression.

Among men, no statistically significant association between the spouse's working hours and men's poor SRH was observed. On the other hand, among women, the ORs (95% CI) for poor SRH were 1.09 (1.02-1.17) for the part-time work group, and 1.09 (1.03-1.14) for the long-hour work group, compared to the full-time work group, thus women whose spouse worked part-time or long hours had a significantly higher proportion of people having poor SRH.

We examined the association between the spouse's working hours and own poor SRH, and identified the existence of the sex difference in the association. This suggests the importance to address people's working hours as a family health issue, not only as a personal health issue.



**Leading Causes of Death in Korean Americans in the United States and Koreans in South Korea (2005-2020)** Gina Kim\* Gina Kim George Hung Sanah Vohra Shozen Dan Armaan Jamal Eunjung Lee Jiseun Lim Robert Huang Malathi Srinivasan

**Background**

Korean Americans are the fifth largest Asian American subgroup in the United States (US). However, data on mortality patterns specific to Korean Americans (KA), particularly among foreign-born and US-born KAs in comparison to native Koreans in South Korea (SK), have been scarce.

**Methods**

The 2005-2020 mortality records provided by the US National Center for Health Statistics and Statistics Korea were analyzed to study the leading causes of deaths among KA and native Koreans (in SK), respectively. Age-adjusted mortality rates (AMR) for each cause by sex and nativity were calculated to examine mortality trends and difference between KA and SK during this time period.

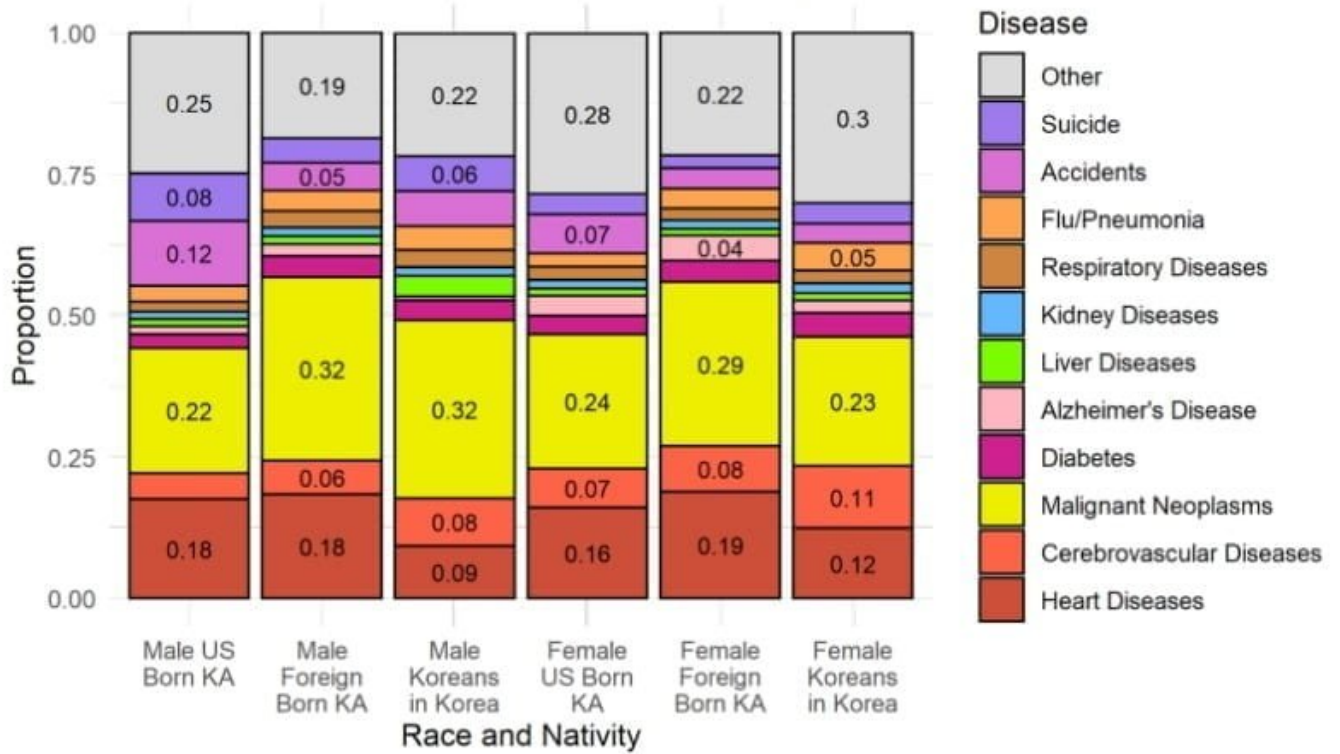
**Results**

The top two leading causes of deaths for male and female US-born KA, foreign-born KA, and Koreans (in SK) were malignant neoplasms (22%/24% in US-born KA; 32%/ 30% in foreign-born KA; 32%/23% in Koreans in SK) followed by heart diseases (18%/16%; 18%/19%; 9%/12%). When adjusting for age, the top three leading causes of death in all three populations overlapped: malignant neoplasms (male/female AMR per 100,000: 192/146; 119/78; 247/103), heart diseases (151/89; 75/57; 86/63), and cerebrovascular diseases (40/39; 24/23; 79/53). For each of the 11 leading causes of death overall, males had higher AMRs than females in all three populations and foreign-born KAs had remarkably lower AMR than SK. However, this reduction in mortality was modest or not observed among US-born KAs. It is notable that US-born KA had higher AMRs for heart diseases and Alzheimer's disease compared to foreign-born KA and SK.

**Conclusions**

Our analyses of mortality data by sex, nativity, and residency indicate that foreign-born KAs experience similar leading causes of death to SK at a lower AMR; however, US-born KA experience diverging mortality rates. Further research is warranted to understand acculturation and environmental factors that underlie the observed mortality differences and to develop preventive strategies.

# Leading Causes of Death by Proportion



## Health Disparities

**Does my Children's Education Reduce my Risk of Dementia?** Erika Meza\* Erika Meza Karla Renata Flores Romero Isabel Elaine Allen Hector Gonzalez Maria Glymour Jacqueline Torres

Prior work suggests resource transfers from adult-children to their parents may benefit parents' late-life health. Few studies have assessed such upward resource transmission effects on cognitive aging, and no studies have examined this among Latinos.

For White and Hispanic US Health and Retirement Study participants (1998-2018, N=22681), we examined associations of their adult-children's education with parental incident cognitive impairment. Age-eligible cognitively healthy respondents (i.e. no Cognitive Impairment Not Demented [CIND] or probable dementia) at baseline were assessed biannually. Adult-children's education was measured using the highest years of schooling for all adult-children (25 years and older) of a parental respondent. Impaired cognition (CIND or probable dementia) was classified using the Langa-Weir 27-point scale. We used Proportional Hazard Models to evaluate the associations between adult-child's education and incident impaired cognition adjusted for parental age, sex, education, birthplace, number of children, and included an interaction to evaluate effect modification by parent's race and ethnicity.

The sample was 14% Hispanic and 46% male. The mean education of the most educated adult child was 15.1 (sd: 1.94) years among White and 14.1 (sd: 2.3) years among Hispanic participants, and 35% of our sample was classified with impaired cognition during follow-up. A one-year increase in adult child education was associated with 3% lower (HR: 0.97; 95% CI: 0.95, 0.98) incidence of impaired cognition among White older adults and a 6% lower (HR: 0.94; 95% CI: 0.91, 0.96) among Latino older adults (interaction p-value: 0.004).

Higher adult children's education was associated with lower parental incidence of impaired cognition, for both White and Hispanic older adults, with larger benefits for Hispanic parents. Future work should examine potential mechanisms underlying this association and assess for differences across Latino ethnic subgroups.

**Mediating pathways of neighborhood violence on adverse pregnancy outcomes in California**

Caitlin Chan\* Caitlin Chan Shelley Jung Dana Goin Kara Rudolph Kristen Marchi William Dow Paula Braveman Mahasin Mujahid Mark van der Laan Jennifer Ahern

Neighborhood violence may contribute to adverse pregnancy and perinatal health outcomes. The contribution of mediating pathways, such as coping behaviors and medical conditions, is not well understood which limits understanding of the mechanisms underlying health disparities in historically minoritized populations exposed to neighborhood violence.

We examined mediating pathways from acute changes in neighborhood violence to adverse perinatal outcomes, restricting analyses to within-neighborhood comparisons to control for time-constant neighborhood factors by design.

We combined California neighborhood violence data with hospital records of singleton live births from 2007-2011. We estimated the excess risk of infant mortality, neonatal mortality, preterm birth, gestational diabetes mellitus (GDM), and preeclampsia among birthing individuals exposed to acute increases in neighborhood violence. We estimated risk differences with targeted maximum likelihood estimation, adjusting for individual- (age, race, parity, education, insurance, conception year and season) and time-varying neighborhood- (temperature, precipitation, unemployment) level potential confounders. Substance use and maternal infection during pregnancy were analyzed as mediators.

Acute increases in neighborhood violence were associated with elevated risk of GDM (2.2/1000 RD 95% CI (1.4/1000, 3.1/1000)), preeclampsia (2.4/1000 RD 95% CI (1.6/1000, 3.1/1000)), and preterm birth (0.9/1000 RD 95% CI (0.0/1000, 1.7/1000)). Both maternal infection and substance use mediated effects on all outcomes. Across all outcomes, maternal infection had a larger mediating role than substance use. For example, 21% and 16% of the effect of acute violence on preterm birth was mediated by maternal infection and substance use, respectively. Future analyses will consider additional mediators and estimate mediation effects by racial/ethnic group.

**A novel weighting approach to addressing healthy worker survivor bias** Alexander Keil\*

Alexander Keil Yi Li Kaitlin Kelly-Reif

Radon gas is a major source of ionizing radiation exposures in humans. Human carcinogenicity of radon has been established, in part, in studies of exposed workers such as uranium miners. Impact estimates from occupational studies are subject to healthy worker survivor bias, which has been proposed to result in substantial underestimates of radon's health effects. However, existing analytic methods for addressing bias due to healthy worker survivor bias are sensitive to model misspecification.

We describe a new approach for estimating health effects of occupational exposures that addresses healthy worker survivor bias while reducing modeling assumptions. This approach treats occupational standards as a dynamic treatment regime and utilizes inverse probability weights. We use this approach to estimate impacts of hypothetical occupational standards on lung cancer mortality using data from 4124 miners from the Colorado Plateau Uranium Miners' cohort followed through 2005.

The estimated cumulative lung cancer mortality risk at age 80 was 14.9% (95% confidence interval [CI] = 13.7%, 16.1%). Under a hypothetical intervention to limit exposure to 20 working levels, we estimated a risk reduction (at age 80) of 2.7% (95%CI = 1.7%, 3.6%). Estimates at lower exposure levels were larger but subject to greater uncertainty than previous analyses in this cohort using modeling-based estimators.

Our approach offers computational simplicity and reduced reliance on modeling assumptions relative to other approaches to healthy worker survivor bias. Use within this highly exposed cohort also highlighted challenges with using our approach to estimate effects at low exposure levels: model-based extrapolation with the parametric g-formula can be used to reduce uncertainty under stronger assumptions. The proposed approach provides a simple approach to addressing healthy worker survivor bias that provides promise for reducing modeling assumptions in studies of occupational exposures.

**Machine learning and natural language processing in occupational classification using Korea Working Condition Survey** Jin-Ha Yoon\* Jin-Ha Yoon Myeong-Hun Lim Byungyoon Yun

The importance of data including occupational information and disease have emphasized to reveal occupational risk factors. Traditionally, Job (occupational) classification were done manually, but recently the automatic process using by machine learning are suggested. We aim to develop an algorithm which converts sentences of natural language related to occupational classification to standardized categories.

We used an 80 thousand data set which included natural sentence responses to job related questionnaires in the Korea Working Condition Survey 5th, 6th. The questionnaire is “where, what, how do you do your job?”, and the response are natural sentences such as “I make and sell food in a small restaurant downtown”. The responded sentences were categorized into 123 job classifications by trained researchers.

The grammar is checked and the sentences are modified by google API. The train and test set are split into 7:3 proportions. The ANN models were trained on 70 percent of data with cross validation, and the balanced accuracy was 0.92 in the test data set. For the most common 15 job classification, the balanced accuracy is 0.98 in the test data set.

This study presented the application which changed natural language into occupational classification by using machine learning. We hope our current program supports occupational epidemiology research where automatic occupational classification was needed.

**Comparison of work-related injuries and illnesses in New York City transit workers from before and during the COVID-19 pandemic: preliminary findings** Michael Cziner\* Michael Cziner Robyn Gershon Alexis Merdjanoff Devan Hawkins Jonathan Rosen

**Background:** The COVID-19 pandemic led to unprecedented challenges for critical infrastructure workers. In New York City (NYC), transit workers reportedly also experienced increased workplace violence. We compared work-related incidents (injuries and non-COVID-19 illnesses) in NYC transit workers before and during the pandemic.

**Methods:** The Transport Workers Union, Local 100 provided work-related injury/illness data from 2018 to 2021 that had been collected by the Metropolitan Transportation Authority. After excluding all reported cases of COVID-19, the remaining incidents were categorized by type. Two time periods: pre-pandemic (January 1, 2018 to February 29, 2020) and peri-pandemic (March 1, 2020 to December 31, 2021) were compared using Poisson regression.

**Results:** A total of 4,686 work-related incidents among NYC transit workers were reported in the pre-pandemic period. After excluding reported COVID-19 infections, 4,075 incidents were reported in the peri-pandemic period. Despite similar total reports, the frequency of certain incident types changed significantly between the two periods. Compared to the pre-pandemic period, physical assaults and mental health problems *increased* by 45% and 27%, respectively (both  $p < 0.001$ ) during the peri-pandemic period. Certain physical labor-related incidents, such as overexertion ( $p = 0.01$ ), abrasions ( $p < 0.001$ ), and chemical contact ( $p < 0.001$ ), *decreased* during the peri-pandemic period compared to the prior period.

**Conclusion:** Significant differences were noted in reported injury types between the pre-pandemic and peri-pandemic periods, with physical assaults much more common in the peri-pandemic period. The results indicate that critical infrastructure workers may be at increased risk of physical assault and adverse mental health incidents during pandemics in addition to the health risks associated with pandemics. Pandemic planning should include interventions that address these other workplace risks.

**Tobacco use patterns and mental health of construction workers during the COVID-19**

**pandemic** Yetunde Olubusayo Tagurum\* Yetunde Tagurum Olusanya Joshua Oluwole Yue Pan  
Kenneth D Ward Taghrid Asfar

**Introduction:** Over one-third of US construction workers use tobacco products and disparities exist across different types of products used. There is emerging evidence that the coronavirus disease (COVID-19) pandemic resulted in increased prevalence of the use of tobacco products and mental illnesses. This study aims to examine and compare tobacco use and mental illness patterns between construction workers and the general population during the pandemic.

**Methods:** We conducted a secondary analysis of **cross-sectional data from the 2020 and 2021** National Health Interview Surveys (NHIS) among construction workers (n = 2406) and the general population (n = 58644). Descriptive analyses of these subpopulations were reported and differences between them were assessed using student's t-test and Chi-square as appropriate. We performed logistic regression analyses to compare tobacco use and the prevalence of mental illnesses between construction workers and the general population.

**Results: Results:** Current tobacco use prevalence was higher among construction workers than the general population (5.21% v 4.06%;  $p < 0.001$ ), but the prevalence of anxiety (12.91% v 4.78%;  $p < 0.001$ ) and depression (10.81% v 3.38%;  $p < 0.001$ ) disorders were however higher in the general population. Compared to the general population, the rate of COVID-19 vaccination was lower (50.4% v 72.74%;  $p < 0.001$ ), and the prevalence of COVID-19 diagnosis was higher among construction workers (23.2% v 18.48%;  $p = 0.023$ ). Among construction workers, non-Hispanic Blacks (aOR:0.12; 95% CI:0.03 - 0.60), those with a college education (aOR:0.53; 95% CI:0.29 - 0.98), and current cigarette smokers (aOR:0.34; 95% CI:0.18 - 0.66) were less likely to be diagnosed with COVID-19. Among construction workers, those older (aOR:1.04; 95% CI:1.03 - 1.06), with a college education (aOR:2.60; 95% CI:1.58 - 4.30), and health insurance coverage (aOR:2.77; 95% CI:1.80 - 4.25) were more likely to be vaccinated against COVID-19 while those born in the US (aOR:0.42; 95% CI:0.24 - 0.73) and current cigarette smokers (aOR:0.60; 95% CI:0.38 - 0.94), were less likely to be vaccinated.

**Conclusions:** More enlightenment on COVID-19 vaccination is needed among construction workers to improve vaccination uptake among them.



## Occupational

**COVID-19 vaccination uptake among adults with asthma, by occupation** Katelynn E. Dodd\*  
Katelynn Dodd Bethany Barone Gibbs Christopher Martin Jacek M. Mazurek Caroline P. Groth

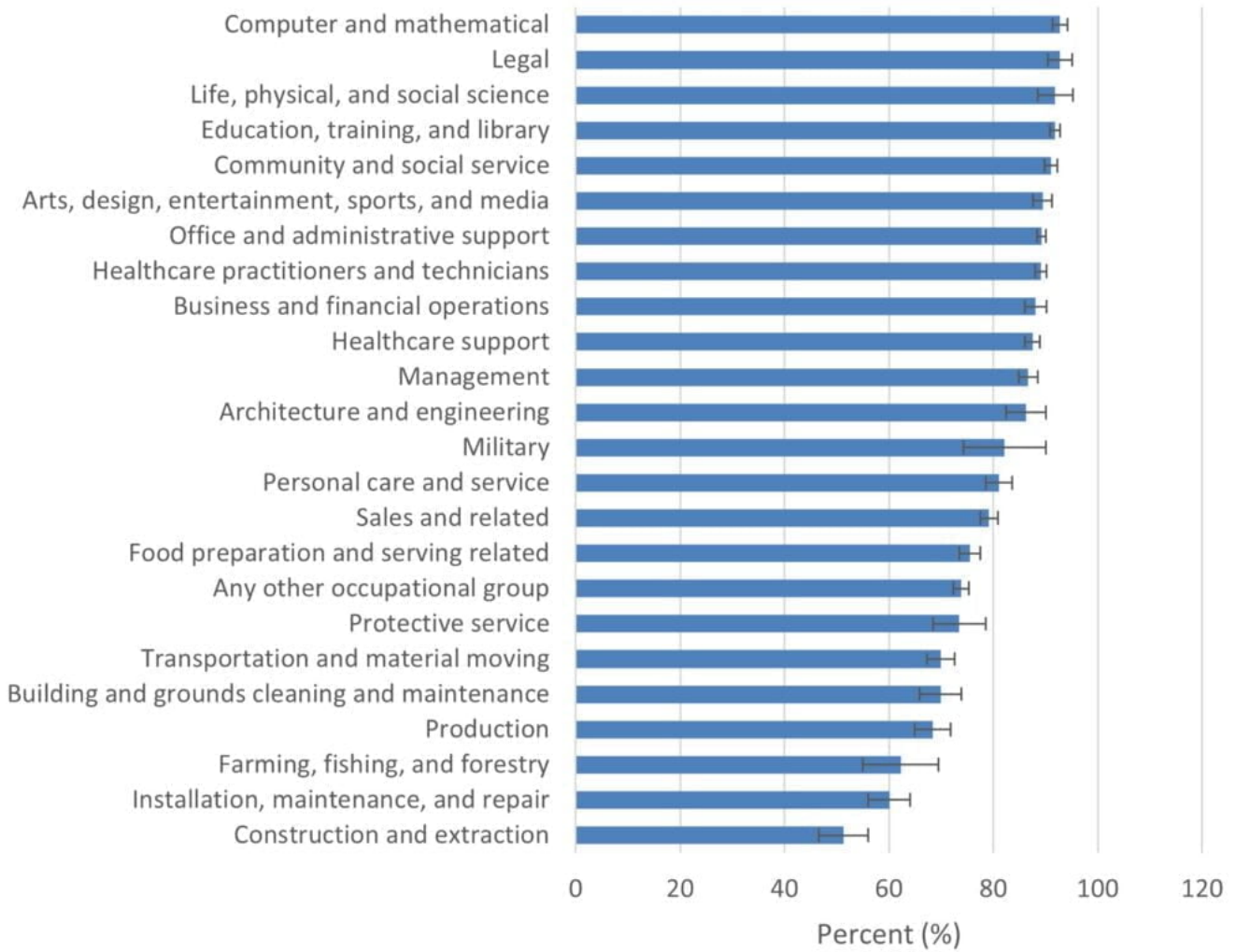
**Background:** The CDC recommends that adults with asthma remain up to date on their COVID-19 vaccinations, including after recovering from a COVID-19 infection and receiving a booster when eligible. COVID-19 vaccines are safe and effective in preventing COVID-19-related illnesses, hospitalizations, and deaths.

**Methods:** To evaluate COVID-19 vaccine uptake among adults with asthma by occupation, Facebook/Delphi Group COVID-19 Trends and Impact Survey (Delphi US CTIS) data were analyzed from U.S. adults aged  $\geq 18$  years who responded during October–December 2021. Persons with asthma were those who reported ever being told by a doctor, nurse, or other health professional that they had asthma. Information on occupation was examined among survey respondents who were employed for pay in the 4 weeks prior to the survey. Proportions (and 95% confidence intervals) were weighted to the U.S. general population.

**Results:** An estimated 14.2% of adults employed in the 4 weeks prior to the survey had asthma. Among these adults with asthma, 80.5% (95% CI=80.0–80.9%) reported having received at least one dose of a COVID-19 vaccine, compared to 78.9% (95% CI=78.7–79.1%) among those without asthma. Among those with asthma, COVID-19 vaccination was greatest among females (85.7% [95% CI=85.3–86.2%]), those aged 65–74 years (91.6% [95% CI=90.6–92.5%]), college graduates (89.4% [95% CI=88.9–89.9%]), and nonsmokers (84.8% [95% CI=84.4–85.3%]). By occupation, COVID-19 vaccination ranged from 51.3% (95% CI=46.6–56.0%) among construction and extraction occupations to 92.8% (95% CI=91.4–94.2%) among computer and mathematical occupations.

**Conclusions:** Vaccine uptake remains below the World Health Organization target of 70% among some working adults with asthma. Certain occupations, such as construction and extraction, installation, maintenance, and repair, and farming, fishing, and forestry, might benefit from targeted interventions to enhance vaccine uptake among these workers.

## COVID-19 Vaccine Uptake Among Adults with Asthma, by Occupation



## Occupational

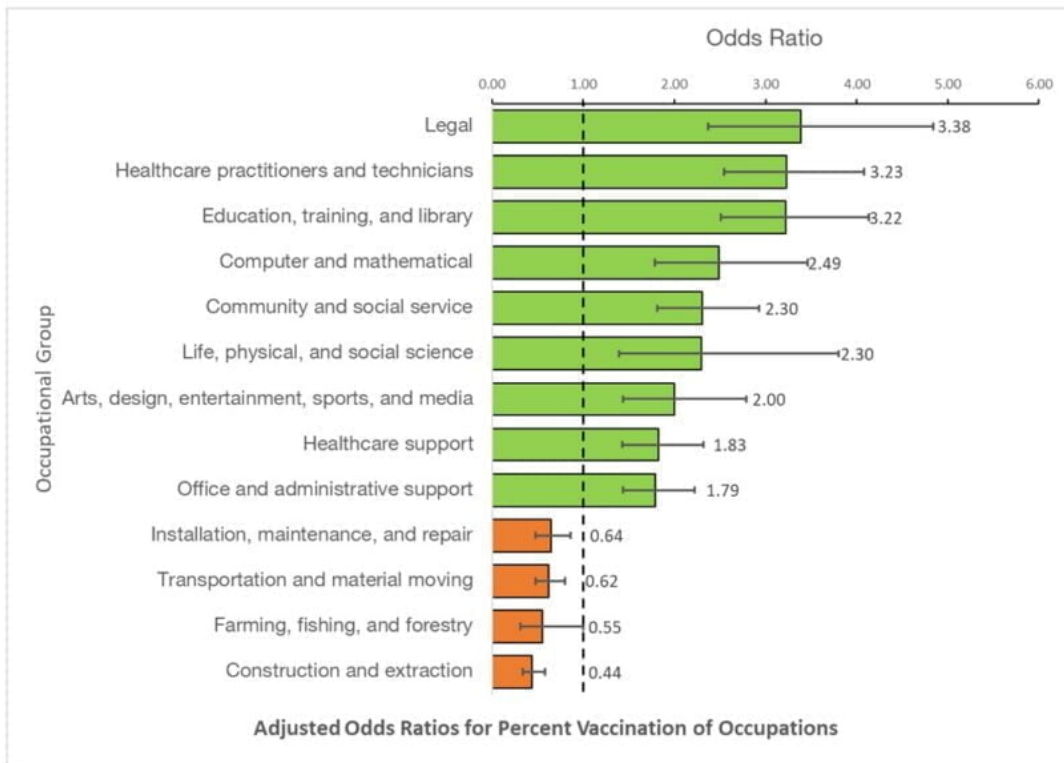
**Differences in Vaccination Percentage by Occupation among West Virginia Workers: Findings from the Facebook/Delphi Group COVID-19 Trends and Impacts Survey** Matthew J. Myers\* Matthew Myers Garret Guthrie Jean M. Cox-Ganser Paul K. Henneberger Caroline P. Groth

**Background:** By December 2022, West Virginia (WV) adults had the 9<sup>th</sup> lowest percentage (77.4%) with at least one COVID-19 vaccination among states. Little is known about vaccine uptake by occupation in WV.

**Methods:** Facebook/Delphi Group COVID-19 Trends and Impacts Survey data were analyzed for WV adults aged  $\geq 18$  years who answered the question "Have you had a COVID-19 vaccination?" and were employed for pay within the prior 4 weeks. Self-reported occupations were classified by the 2018 Standard Occupational Classification (SOC) system. Percentages were weighted to the US general population. Vaccination status was modeled with multivariable logistic regression, yielding odds ratios (ORs) for major SOCs adjusted for potential confounders: gender, age, race/ethnicity, working from home, and pre-existing medical conditions.

**Results:** The 33,717 WV workers surveyed from January 2021 to June 2022 were half females and half 18-44 years old, and most were non-Hispanic white (88.4%) and worked outside the home (84.4%). Overall, 69.1% were vaccinated. The occupation reference category was "Personal care and service" (65.2% vaccinated). The 4 major SOCs with lower odds of vaccination were "Installation, maintenance, and repair" (51.2%, OR 0.64, 95%CI 0.48-0.80); "Transportation and material moving" (52.2%, OR 0.62, 95%CI 0.48-0.86); "Farming, fishing, and forestry" (46.7%, OR 0.55, 95%CI 0.31-1.00); and "Construction and extraction" (41.8%, OR 0.44, 95%CI 0.34-0.58). Nine major SOC groups had elevated odds of vaccination, including the 3 highest with ORs  $> 3.0$ , "Legal" (86.3%, OR 3.38, 95%CI 2.37-4.84), "Healthcare practitioners and technicians" (85.3%, OR 3.23, 95%CI 2.55-4.08), and "Education, training, and library" (85.9%, OR 3.22, 95%CI 2.51-4.13).

**Conclusions:** Low vaccine uptake was observed in multiple occupations within WV. Information on vaccine uptake by occupation can aid targeting public health interventions for COVID-19 or other future infectious disease epidemics.



**LATEBREAKER**

Aging

**Increased Depression, Anxiety, and Stress Survey (DASS) scores are associated with increased epigenetic age acceleration in a prospective study** Andrey Egorov\* Andrey Egorov Shannon Griffin Wei Guo Edward Hudgens Timothy J. Wade

**Background.** Epigenetic age acceleration (EAA), a measure of biological aging based on DNA methylation, is known to be affected by environmental and social factors, and to be predictive of systemic morbidity and mortality. This epidemiologic study assessed temporal changes in EAA in relation to temporal changes in perceived stress, anxiety, and depression.

**Methods.** DNA methylation was measured in 279 blood samples (3 per person at 4-month intervals) from 97 adults (mean age 58 years, range 31–85 years) using Illumina EPIC microarrays. Epigenetic age values were estimated using formulas developed by Hannum et al. (2013) and Li et al. (2018), and EAA values were calculated as residuals from regressing them on chronological age. Two EAA slopes for each person were derived from linear regression of EAA values on time. Depression, Anxiety, and Stress Survey (DASS) questionnaires were administered at baseline and end of follow-up. Results were scored for each component using the standard DASS methodology.

**Results.** Temporal changes in depression, anxiety, and stress scores were positively associated with both Li's and Hannum's EAA slopes in all linear regression models but these effects were not statistically significant. Stronger evidence of associations was observed when combining Li's and Hannum's EAA slopes into a single ordinal outcome variable with three categories: (1) both slopes negative (N=19); (2) slopes in different directions (N=43); and (3) both slopes positive (N=35). Ordinal logistic models with non-proportional odds adjusted for baseline EAA values showed that ten-point increases in depression, anxiety, stress, and total DASS scores were associated with 4.4 (95% confidence limits 1.3; 15), 2.1 (0.7; 6.6), 2.8 (1.1; 7.3), and 1.9 (1.2; 3.2) odds ratios of having two positive slopes vs. two negative slopes.

**Conclusion.** This study linked, for the first time, temporal increases in stress, anxiety, and depression levels with epigenetic aging.

**LATEBREAKER**

Aging

**Childhood self-reported socioeconomic status modifies the genetic risk of Alzheimer's on mid- and late-life cognitive decline in a population-based study** Yuexuan Xu\* Yuexuan Xu  
Corinne Engelman

**Background:** Childhood socioeconomic status (c-SES) and genetic risk of Alzheimer's disease (AD) contribute to an individual's risk of developing AD in later life. A better understanding of the interactions between these risk factors can help design policy interventions to eliminate AD disparities at the earliest possible stage in life. In this study, we investigated whether global and domain-specific c-SES index modified the effect of genetic predisposition to AD on mid-to-late life cognitive decline.

**Methods:** We evaluated longitudinal associations of cognitive aging with validated global and domain-specific c-SES index, including childhood financial, human, and social capital domains. In the Health and Retirement Study, we separately tested interactions between the global and domain-specific c-SES index and a non-*APOE* polygenic risk score (PRS) and *APOE*. We fitted all analyses using a linear mixed effects model and adjusted for within-individual and within-family correlation. Inverse probability weighting is used to adjust for selection mortality in the genetic sample.

**Results:** Self-reported overall and domain-specific c-SES index can significantly modify the age-related effect of non-*APOE* PRS on longitudinal global cognition, particularly among *APOE*  $\epsilon 4$  carriers. After FDR correction, model parameters predicted that statistically significant PRS-related differences in simple slopes between people with high (1 SD+ from population mean) and low (1 SD- from population mean) global and domain-specific c-SES index started showing after people reached age  $\sim 77$ , with individuals who have low c-SES bearing greater detrimental effect from the currently known combined effect of non-*APOE* common variants as they age, and greatest among people who are also *APOE*  $\epsilon 4$  carriers.

**Conclusion:** Self-reported childhood SES can modify the association between non-*APOE* PRS and longitudinal cognition decline.

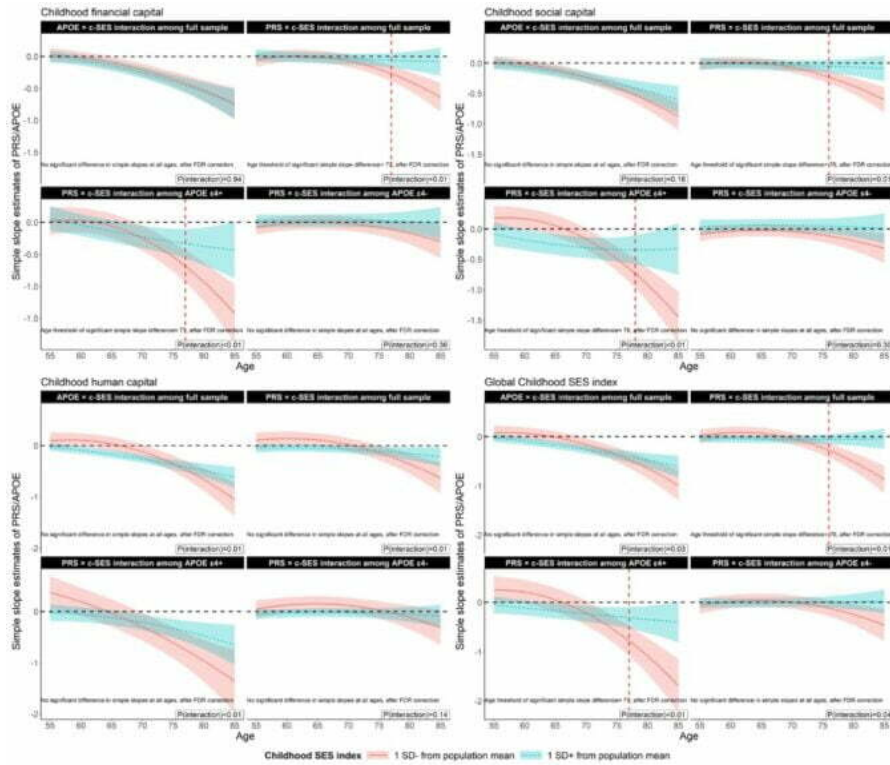


Figure 1. Plot of the simple slope estimates of PRS/APOE for individuals with high (1 SD+ from population mean) or low (1 SD- from the population mean) global or domain-specific childhood SES (c-SES) index from age 50 to 85 on global cognition score. In addition to the global c-SES, domain-specific c-SES include the childhood financial capital index, childhood social capital index, and childhood human capital index. Details about the construction of these c-SES indexes have been described in Vable et al. (2017). All c-SES indexes have been standardized with a mean of 0 and standard deviation of 1, with a higher number reflecting higher SES in childhood. The red line represents the longitudinal trajectory of simple slope estimates of PRS/APOE among individuals whose c-SES is one standard deviation below the population mean, while the blue line represents simple slope estimates of PRS/APOE among individuals whose c-SES is one standard deviation above the population mean. The PRS is constructed by including genome-wide significant SNPs identified by the most recent diagnosed case-control Alzheimer's disease genome-wide association studies meta-analyses. We have used continuous APOE score in the full sample analysis to ease post hoc simple analyses. All APOE and PRS predictors have been standardized with a mean of 0 and a standard deviation of 1. Bands represent 95% confidence intervals. The red dashed vertical reference line represents the earliest threshold of statistically significant difference in simple slope estimates of PRS/APOE between individuals with high or low c-SES after FDR correction. The simple slope estimates are calculated using package "emmeans" in R and were based on the results obtained using the linear mixed effect model and adjusted for within-individual/family correlation. In addition to PRS/APOE, age (quadratic), childhood SES, and their interactions, additional covariates include gender, education years, practice effect, cohort, stroke, birthplace, and the first five principal components. Age is centered at year 65, and education is centered at the mean. Considering the previously discovered APOE  $\epsilon 4 \times$  PRS  $\times$  polynomial age interaction, we studied APOE  $\epsilon 4 \times$  c-SES  $\times$  polynomial age interaction in the full sample and sample stratified by APOE  $\epsilon 4$  carrier status. P-value within each panel represents the significance of the joint effects of interactions with polynomial terms, which is tested by likelihood ratio tests and is calculated as the ratio between the log-likelihood of the nested model (model without three-way interaction terms) to the full model (model with polynomial age $\times$ PRS/APOE $\times$ c-SES terms).

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Kuriko, Brian W., Benjamin Genter-Billy, Rebecca Sims, Joshua C. Bis, Vincent Damico, Adam C. Ng, Anne Ballard et al. "Genetic meta-analysis of diagnosed Alzheimer's disease identifies new risk loci and implicates A $\beta$ , immunity and lipid processing." *Nature genetics* 11, no. 3 (2011): 414-426.

## **Identifying Multimorbidity Patterns Using Network Analysis** Yeonjae Kim\* Yeonjae Kim Bomi Park

### **Objectives**

Chronic disease multimorbidity is a major concern in public health because of rapid population ages. In this study, we aimed to explore disease networks to find multimorbidity patterns.

### **Methods**

We used National Health Insurance Service cohort data in South Korea from 2002 to 2019. Patients who aged 40 or older, had records more than 5 years, and had two or more chronic diseases with a prevalence of 1% or more were included in the analysis. We only included disease pairs with Pearson correlation coefficient greater than 0 and edges (the number of patients in each pair) greater than the minimum number of possible edges in the Network Analysis. The strength of association between diseases was defined by Salton Cosine Index (SCI). The node (disease) centrality was measured based on eigenvector, degree, betweenness, and closeness. All analyses were conducted after stratification by sex and age (40-49, 50-59, 60-69, 70 or more).

### **Results**

The study population was 169,408 men and 189,508 women. The two most associated disease pairs in male were gastroesophageal reflux disease-gastritis and duodenitis and low back pain-osteoarthritis in the age 40-49, and low back pain-osteoarthritis and low back pain-benign prostatic hyperplasia in the remaining age groups. In female, low back pain-osteoarthritis was included in the two most associated disease pair in all age groups, the other pair was gastroesophageal reflux disease-gastritis and duodenitis in the age 40-49 and 50-59, and cataracts-low back pain in the age 60-69 and age 70 or more. The top two central diseases based on eigenvector method in male groups were low back pain and benign prostatic hyperplasia, and female groups were osteoarthritis and low back pain.

### **Conclusions**

The diseases included in highly associated pairs showed high centrality in all sex and age groups. Understanding multimorbidity could have a chance to develop clinical guidelines for aged population.



**Associations of Actigraph Sleep Characteristics with Blood Pressure Among Older Adults**

Maria Springall De Pablo\* Maria Springall De Pablo Diane S. Lauderdale

Previous findings have been mixed about whether sleep duration, quality and timing are linked to blood pressure (BP), but very few studies of adults have used actigraph sleep measures rather than self-reported sleep, and none have included older adults. Studies with actigraphy have reported cross-sectional associations in midlife between shorter sleep, more disrupted sleep, and later sleep midpoint and higher BP. In the National Social Life, Health and Aging Project cohort, we conducted a cross-sectional and longitudinal analysis examining 1) whether actigraph-measured sleep characteristics are associated with BP, and 2) whether they are associated with 5-year change in BP. Subjects were 714 older US adults (62-90 years), 506 of whom survived to 5-year follow up and participated. BP was an average of 2 recordings and sleep an average of 3 nights. Sleep characteristics were duration as both a linear and quadratic variable to explore U-shaped associations, sleep percentage (the percentage of time spent sleeping between first falling asleep and last awakening), and categories of sleep onset, midpoint and waking times. Multivariable linear models were adjusted for age, race, gender, obesity, smoking, and hypertension medication use (from a complete medication log). Our results indicate a U-shaped cross-sectional and J-shaped longitudinal relationship between duration and BP. Later sleep start times were associated cross-sectionally with higher systolic BP (SBP), while early sleep start times were associated with greater longitudinal SBP increase. Midpoint and wake times and sleep percentage were not significantly associated with BP. These results provide insight on the contradictory literature concerning sleep as a predictor of BP, with possibly different associations related to subject age. Our findings further support recommended intermediate sleep durations for cardiovascular health, and provide insight to sleep's role in the pathogenesis of increased BP.

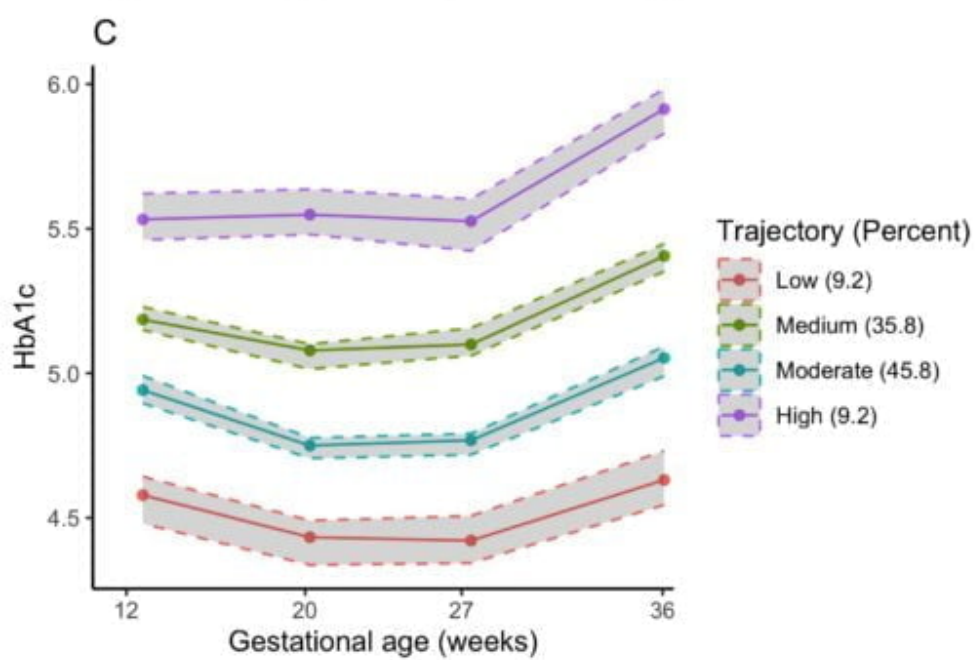
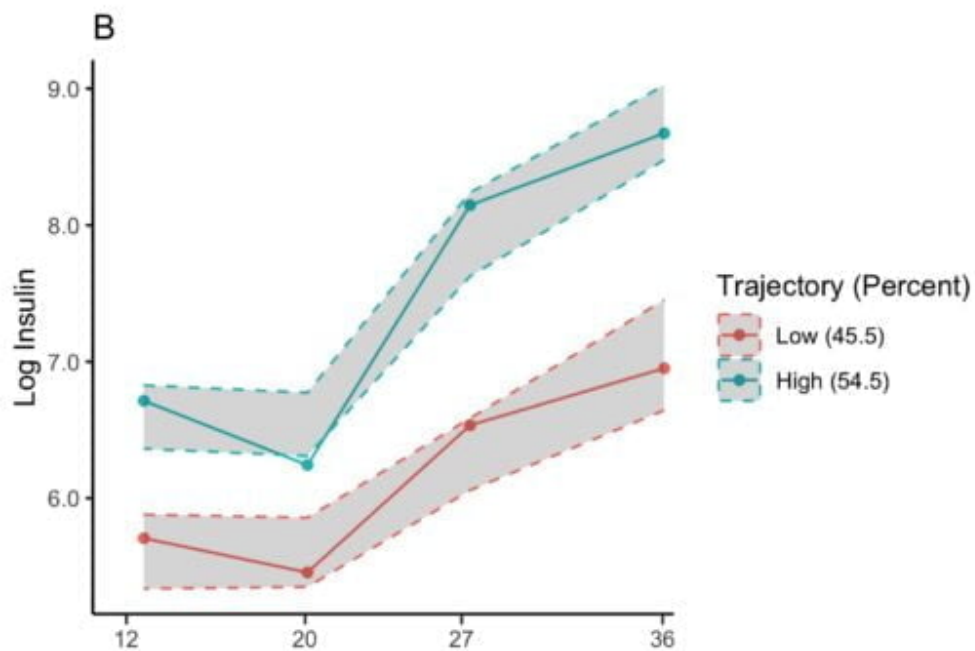
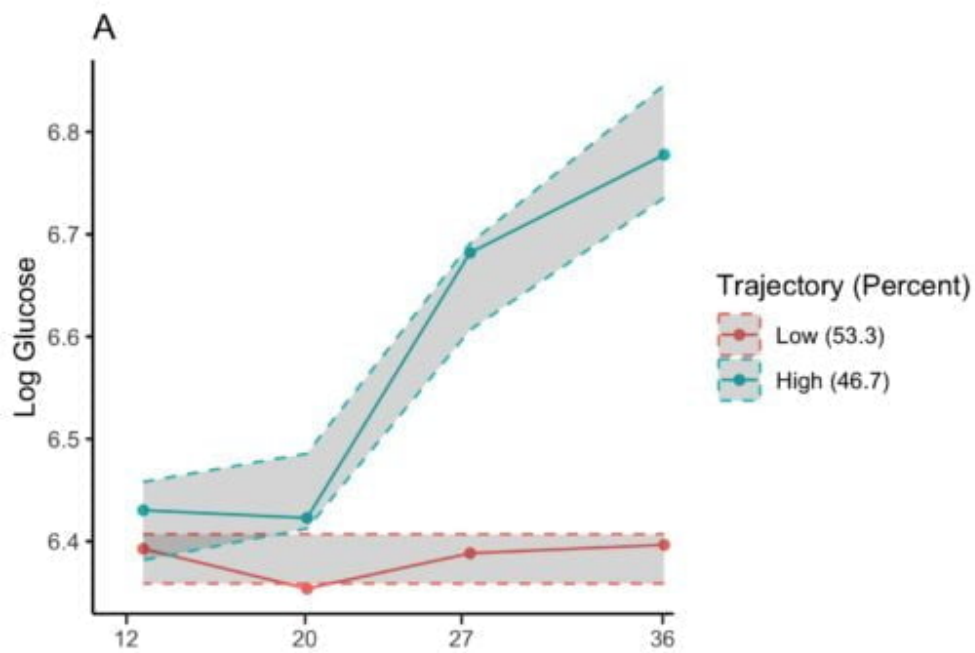
**Gestational trajectories of glycemc biomarkers and placental epigenetic aging: findings from a multi-ethnic pregnancy cohort study** Tesfa Dejenie Habtewold\* Tesfa Dejenie Habtewold Cuilin Richard J. Biedrzycki Katherine L. Grantz Una Grewal Fasil Tekola-Ayele

**Background:** Maternal prenatal glycemia status is critical for maternal and fetal health, yet its impact on placental aging is unclear. This study investigated whether longitudinal trajectories of glycemc biomarkers during pregnancy are associated with placental epigenetic aging in race/ethnicity-pooled and -stratified pregnant women.

**Methods:** Glycemc hemoglobin (hbA1c), glucose, and insulin were measured in maternal plasma from blood collected at four consecutive gestation times in the NICHD Fetal Growth Studies - Singletons (n=301; 77 White, 72 Black, 102 Hispanic and 50 Asian). Placental epigenetic age was estimated using Mayne's clock, control placental clock (CPC), robust placental clock (RPC), and refined RPC (rRPC). Placental epigenetic age acceleration (PAA) was estimated by regressing epigenetic age upon gestational age. The trajectory of each glycemc biomarker was determined by group-based trajectory modeling and its association with PAA was tested using covariate-adjusted linear regression.

**Results:** Four hbA1c (low, medium, moderate, and high), two glucose (low and high), and two insulin (low and high) trajectories were identified. Glycemc trajectories were not associated with PAA in the full sample. Among black women, compared to low trajectory, medium and moderate hbA1c trajectories were associated with increased PAA (Mayne's clock:  $\beta_{\text{moderate}}=1.60$ ,  $p=0.01$ ; CPC clock:  $\beta_{\text{medium}}=0.79$ ,  $p=0.03$ ; CPC clock:  $\beta_{\text{moderate}}=0.73$ ,  $p=0.03$ ), whereas high hbA1c trajectory was associated with decreased PAA (rRPC clock:  $\beta_{\text{high}}=-1.41$ ,  $p=0.02$ ). Among white women, medium hbA1c trajectory was associated with increased PAA (Mayne's clock:  $\beta_{\text{medium}}=1.35$ ,  $p=0.04$ ). Among Hispanic women, high glucose trajectory was associated with increased PAA (RPC clock:  $\beta_{\text{high}}=0.36$ ,  $p=0.03$ ).

**Conclusion:** Persistently elevated glycemc levels during pregnancy may be linked to accelerated or decelerated placental aging, which vary by race/ethnicity.



**Heterogeneity in estimated effects of statin use on dementia incidence by socio-demographic modifiers: an emulated trial design in a large health care database using 10 years of follow-up** Minhyuk Choi\* Minhyuk Choi Maria Glymour Scott Zimmerman Erin Ferguson Catherine Schaefer Ronald Krauss Paola Gilsanz Travis Meyers Thomas Hoffmann Neil Risch

**Introduction:**

Statins, used to manage cholesterol, are among the most common prescriptions for older adults. Statin use may reduce risk of dementia through cardiovascular mechanisms, but prior studies have conflicting findings. Important socio-demographic factors (education, income, race/ethnicity, gender) that confound or modify estimates may help explain prior inconsistent results.

**Methods:**

Data are from Kaiser Permanente Northern California (KPNC) members (n=202,171) who completed the California Men's Health Survey (2002-2003) or the Research Program on Genes, Environment and Health survey (2007).

New initiation of statin medication was the primary exposure. Racial/ethnic identity (White, Black, Asian, Hispanic, Other), education (less than high school versus high school or more), income category (5 levels), and gender were evaluated as modifiers. Dementia diagnoses were obtained from medical records. Propensity scores were calculated from major comorbidities, socio-demographic variables, and lab measures, all measured prior to exposure.

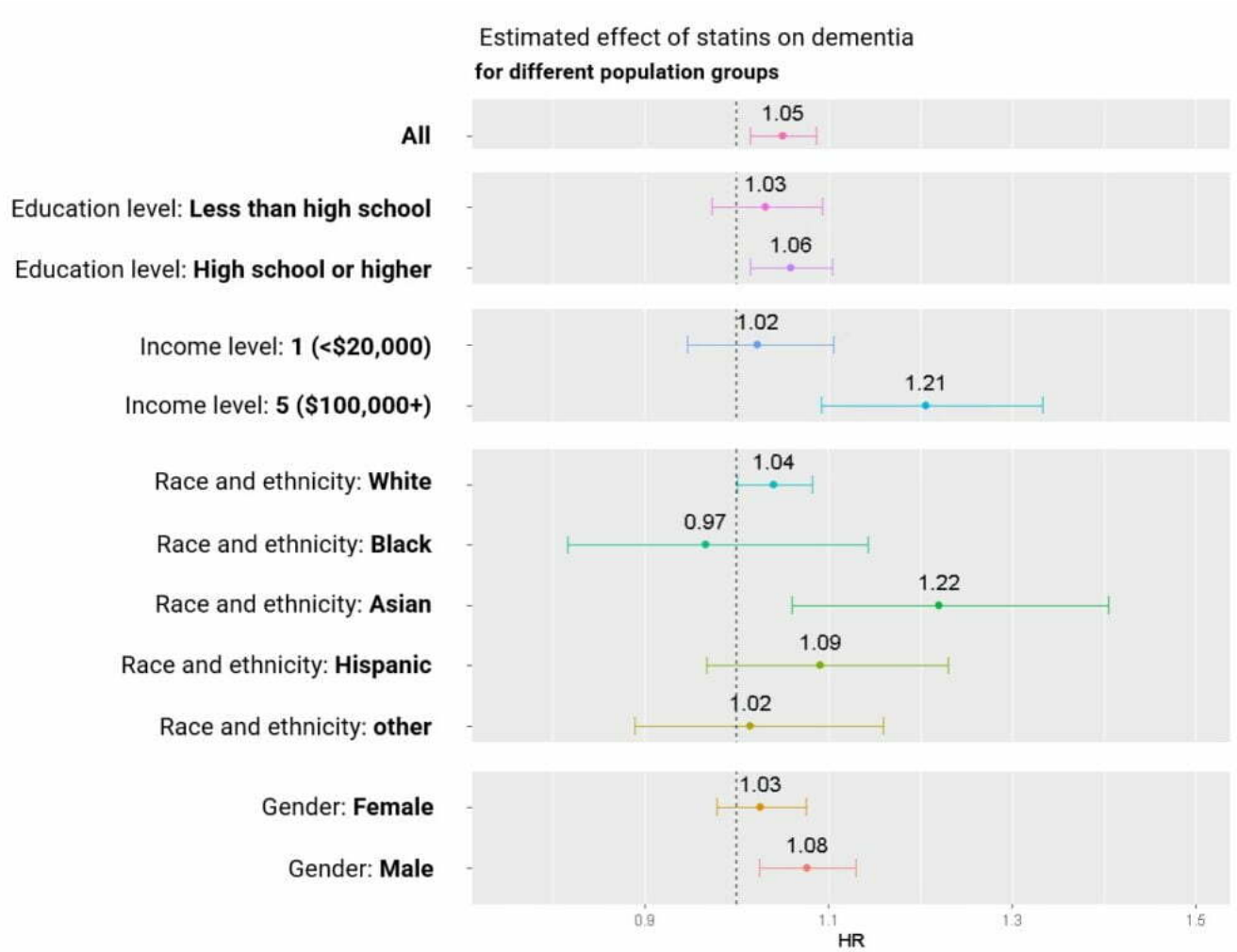
We used an emulated trial design, comparing new statin initiators to non-initiators and allowing new trials to launch each month from survey completion through 2010. Follow-up of each month's trial occurred through 12/2010, until dementia incidence, or censoring due to end of study, membership, or death. We fit inverse probability weighted Cox proportional hazards models and adjusted for age and propensity score decile.

**Results:**

Effect of statins on dementia for Asian members (HR:1.22; 95% CI:1.06,1.41) was higher than White members (HR:1.04; 95% CI: 1.00,1.08). Dementia risk associated with statin use was also higher among those with higher income (lowest income, HR: 1.02; 95% CI: 0.95,1.11; highest income, HR:1.21; 95% CI: 1.09,1.33). We found no evidence of effect modification by education, or gender.

**Discussion:**

Our findings suggest clinically modest differences in effects of statins on dementia across socio-demographic background.



**Midlife adherence to the Dietary Approaches to Stop Hypertension (DASH) diet and late-life subjective memory complaints in women** Yixiao Song\* Yixiao Song Fen Wu Sneha Sharma Tess V. Clendenen Sandra India-Aldana Yelena Afanasyeva Yian Gu Karen L. Koenig Anne Zeleniuch-Jacquotte Yu Chen

**Background:** The Dietary Approaches to Stop Hypertension (DASH) diet is associated with a lower risk of hypertension, a risk factor for cognitive impairment. Current evidence is limited regarding the role of the DASH diet on subjective memory complaints (SMCs), a self-reported, validated precursor of cognitive dysfunction.

**Objective:** To examine the association between the DASH diet and late-life SMCs.

**Methods:** We included 5116 women (mean age at enrollment, 1985-91: 46 y) from the New York University Women's Health Study. The DASH diet score was determined based on dietary data collected at enrollment. Self-reported SMCs were assessed in 2018-2020 by a 6-item questionnaire. We assessed the association of quartiles and per-SD difference of the DASH score with report of 2 or more SMCs.

**Results:** Women in the third and fourth quartile of DASH scores at baseline had a reduction of 21% (OR = 0.79; 95% CI: 0.66-0.95) and 17% (OR = 0.83; 95% CI: 0.69-0.99) in the odds of having 2+ SMCs later in life, respectively, compared with those in the bottom quartile, after adjusting for baseline demographics and follow-up health conditions. Per-SD difference in DASH scores was associated with an OR of 0.93 (95%CI: 0.87-0.99) for 2+ SMCs. The inverse association between DASH scores and having 2+ SMCs was stronger among non-white women and women without a history of cancer (p-value for interaction=0.003 and 0.005, respectively). Among DASH components, intake of sweets was positively related to SMCs, while intake of fruits (including fruit juices), vegetables (excluding potatoes), and legumes/nuts were inversely related to SMCs. Similar associations were observed in analyses with Inverse Probability Weighting to account for potential selection bias.

**Conclusion:** Higher adherence to the DASH diet in midlife was associated with lower prevalence of later-life SMCs in women. Protective factors for hypertension, such as the DASH diet, may benefit cognitive function.

**Comparative performance of different frailty measures using electronic health records in predicting mortality of older patients diagnosed with non-small cell lung cancer** Thao Minh Tu\* Thao Tu Thi Ngoc Tran Hyunsoon Cho

**Objective:** Many frailty tools have been developed, but their performances in cancer cohorts are still unknown. This study aimed to compare the ability of four frailty measures to predict overall mortality for older patients with non-small cell lung cancer (NSCLC), using electronic health records (EHR).

**Materials and Methods:** We retrospectively analyzed 4253 patients aged  $\geq 65$  newly diagnosed with NSCLC in 2007-2018 and followed up until December 2020. Four frailty instruments were Ellis 27-blood-test frailty index (FILAB), FI-combined by 21 laboratory tests and 19 clinical deficits, 28 health problems of Clegg eFI, and Falcon IMWG-F from Charlson comorbidity index, ECOG performance status, and age. We dichotomized frailty scores by using Youden index. Cox regression model and time-dependent area under ROC curves (AUC) were used to estimate the predictive ability of models with and without frailty, adjusting for age, sex, and SEER stage in total population and subgroups stratified by treatment and SEER stage.

**Results:** Overall, frailty is significantly associated with all-cause mortality regardless of frailty measures, the highest increase AUCs were seen in FILAB for 6-month death (0.771 vs. 0.731) and 1-year death (0.781 vs. 0.757). IMWG-F outperformed others in predicting long-term mortality with  $AUC > 0.7$  for 2-year mortality in localized stage group. FI-combined can be useful in the surgery-only group with AUCs ranging from 0.754 to 0.783 for 5 years follow-up. FILAB had the most significantly discriminative power for short-term mortality in distant stage and chemotherapy-only groups, 6-month AUCs were 0.712 and 0.723 respectively.

**Conclusion:** Frailty based on laboratory tests can be considered for advanced-stage NSCLC older patients, while frailty measures comprised of comorbidities and functional status are most appropriate for early-stage NSCLC, suggesting the different application of frailty measures in clinical practice for oncology screening and decision-making.

**Association of Spousal and Child Availability with Mid- to Late-life Memory Function and Decline among Older Adults in England and the United States, 2004-2018** Tsai-Chin Cho\*

Tsai-Chin Cho Xuexin Yu Lindsay Kobayashi

**Background:** Spouses and children are key sources of social support, but it is unclear how their joint availability may influence later-life memory, a key marker of dementia risk. Whether their effects on memory may vary between England and the US – two high-income countries with dissimilar social safety nets – is unknown.

**Methods:** We examined the relationships between family availability and memory of adults aged  $\geq 51$  in the US Health and Retirement Study (HRS;  $n=4,436$ ) and English Longitudinal Study of Aging (ELSA;  $n=3,474$ ) from 2004-2018. Spouse and child availability were assessed every four years from 2004-2012 (for ELSA and HRS cohort one) or 2006-2014 (for HRS cohort two) as spouse disability status, any coresident child, and any child with frequent social contact. Memory was measured biennially from 2012 or 2014 to 2018 using a harmonized 20-point word recall scale. We used sampling-weighted, multivariable mixed-effects linear models to estimate the associations of spouse and child availability and their interactions with memory function and rate of decline over time.

**Results:** The individual effects of spouse and child availability on later-life memory function and decline were close to null. However, among older adults who had a spouse with a disability, having coresident children (vs no child) was associated with worse baseline memory in the US yet better baseline memory in England (US:  $\beta=-10.34$ , 95% CI = [-17.62, -3.06]; England:  $\beta=4.41$ , 95% CI = [0.15, 8.66]; Figure 1), and having children with frequent contact (vs no child) was associated with slower memory decline in the US but not in England (cross-national interaction P-values  $< 0.001$ ; Figure 1).

**Conclusions:** Child availability may protect against later-life memory function in England and memory decline in the US, especially for older adults whose spouse has a disability. Cross-national differences in the health effects of family availability may imply potential effect modification by social welfare contexts.



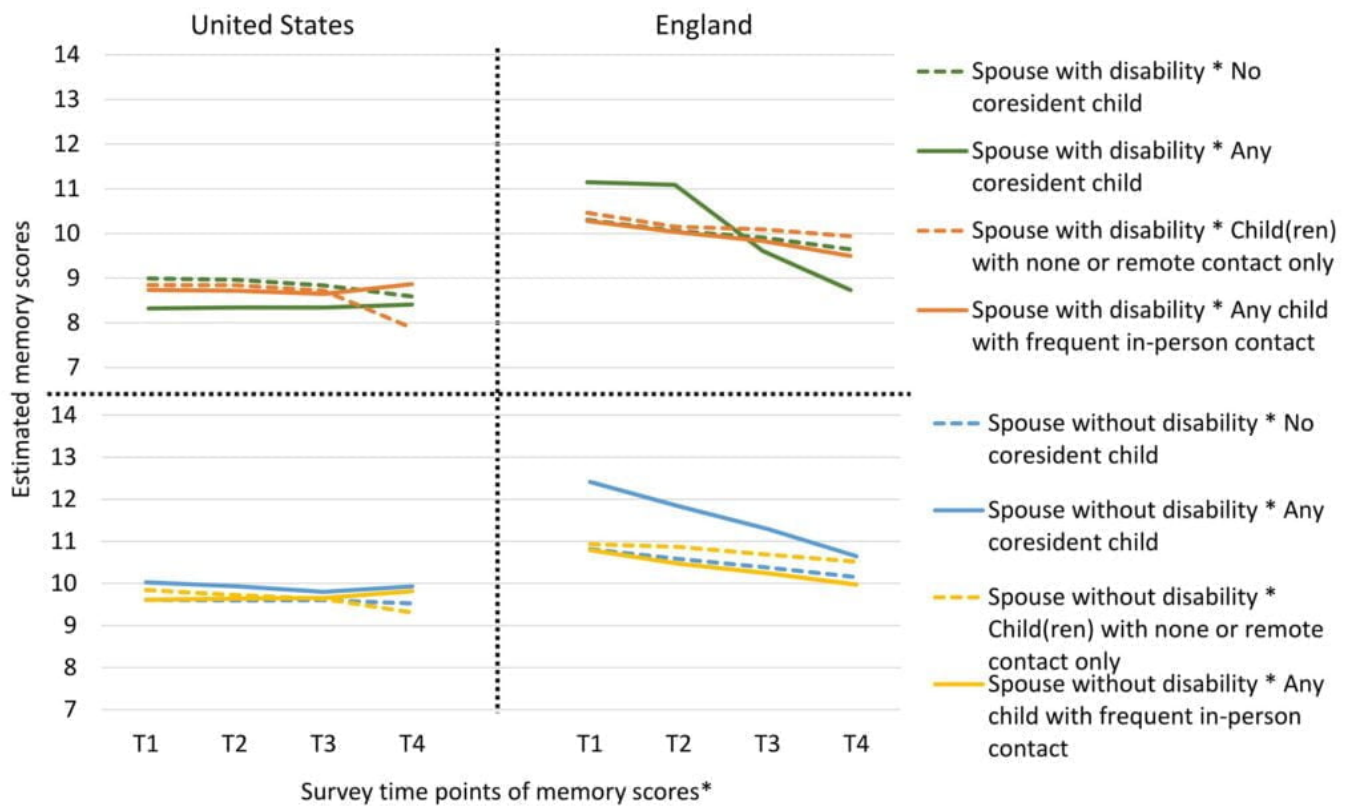


Figure 1. Estimated memory functioning scores from 2012 to 2018, by country. The models were adjusted for age, age<sup>2</sup>, sex, foreign-born status, race/ethnicity, marital status, number of children, educational attainment, within-population income quintiles, labor force status, number of depressive symptoms, number of ADL or IADL limitations, number of self-reported doctor-diagnosed health conditions, and poor self-reported general health. \* The memory scores were obtained biennially from 2012 (T1) to 2018 (T4) for ELSA and HRS cohort one; and from 2014 (T1) to 2018 (T3) for HRS cohort two.

**Incidence of SGLT2I medication adverse events among older adults with multimorbidity** Iju

Shakya\* Iju Shakya Richa Joshi Andrew R Zullo Sarah D Berry

Background: Sodium-glucose cotransporter-2 inhibitors (SGLT2I) are used to treat type 2 diabetes (T2DM), and have also been shown to improve cardiac function. Due to their multiple health benefits, prescription of SGLT2I is on the rise. However, adverse events associated with SGLT2I have been reported including urinary tract infection (UTI) and diabetic ketoacidosis (DKA). Understanding the occurrence of these adverse events is important, especially for vulnerable older adults with multimorbidity. We describe the incidence of UTI and DKA among SGLT2I users in multimorbid nursing home residents.

Methods: We conducted a retrospective cohort study including all adults aged  $\geq 66$  years enrolled in fee-for-service Medicare and with T2DM living in nursing homes between 2013 and 2019. All individuals were new SGLT2I users, defined as having a first dispensing of SGLT2Is after 6 months without any SGLT2I in Medicare Part D claims. UTI and DKA were identified using Part A hospital claims. New users were followed until an outcome, Medicare disenrollment, or death, whichever occurred first. Cumulative incidences and incidence rates of UTI and DKA were estimated non-parametrically.

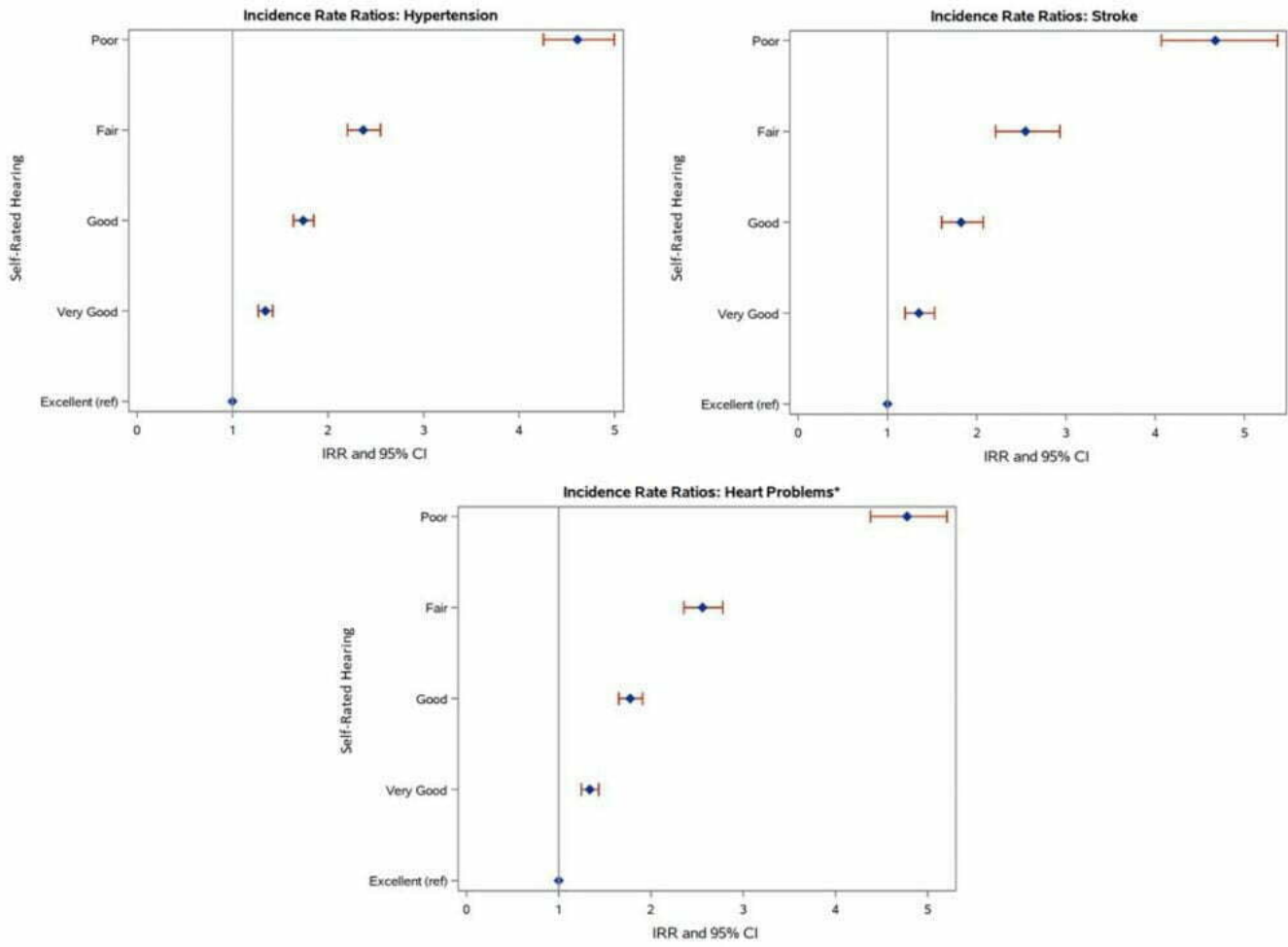
Results: Among 2,493 new SGLT2I users, mean age was 77.8 years (SD: 7.6), 60% were female, and 78% were White. Co-morbidities were common (40% had dementia, 29% heart failure). During a mean follow-up of 8 months, 60 new users experienced a hospitalized UTI (2.4%) and <11 experienced DKA (<1%). The incidence rate of hospitalized UTI and DKA was estimated to be 8.3 per 100,000 person years and 1.1 per 100,000 person years, respectively.

Conclusions: Hospitalized UTI and DKA were rare among nursing home residents with new SGLT2I use. Although the incidence rates were low, identifying risk factors for these adverse events among older adults with multimorbidity on SGLT2Is is important to identify potential subgroups where harms of treatment may outweigh benefits.

**Self-rated hearing and cardiovascular risks among older adults** Nasya Tan\* Nasya Tan  
Lindsay Kobayashi Philippa Clarke

Hearing loss is one of the most common conditions affecting older adults in the United States. Approximately 1 in 3 people between ages 65-74 have some type of hearing loss and nearly half of those aged 75+ report having difficulty hearing, yet little research has examined how hearing loss is related to cardiovascular disease in older adults. We thus compared incidence rates of self-reported physician-diagnosed hypertension, stroke, and heart problems (e.g., heart attacks, coronary heart disease, congestive heart failure, etc.) according to self-rated hearing at baseline among middle-aged and older US adults. Utilizing data from over 23,000 adults aged  $\geq 51$  years in the population-based US Health and Retirement Study from 1992-2018, we specified Poisson regression models with robust standard errors and sampling weights to obtain incidence rate ratios (IRRs) for cardiovascular health outcomes among adults with different levels of self-rated hearing loss (poor; fair; good; very good; excellent). After adjusting for age, sex/gender, race/ethnicity, health coverage, education, and total household wealth, results showed that compared to those with excellent self-rated hearing, IRRs for those with very good, good, fair, or poor hearing steadily increased for all three cardiovascular outcomes, respectively (Figure 1). Those with poor hearing had higher than four-fold increased incidence of hypertension (IRR=4.61, 95% CI=4.25, 5.0), stroke (IRR=4.67, 95% CI=4.07, 5.37), and heart problems (IRR=4.78, 95% CI=4.38, 5.21), compared to those with excellent hearing. These results are the first population-based estimates of cardiovascular disparities among middle-aged and older adults with hearing loss in the US. Further research should consider modifiable factors that may be key to preventing cardiovascular disease among the growing number of older adults with hearing difficulties in the US.

**Figure 1.** Forest plots of IRRs for hypertension, stroke, and heart problems\* according to self-rated hearing levels.



\* Heart problems include heart attack, coronary heart disease, angina, congestive heart failure, or other heart problems.

**Estimating the effects of early adulthood alcohol use on late life cognition using a synthetic lifecourse cohort** Scott Zimmerman\* Scott Zimmerman Peter T Buto Katrina Kezios Jillian Hebert Anusha M Vable Adina Zeki Al Hazzouri M Maria Glymour

Few data sources include high quality measures of both youth alcohol use and late life memory. We generated a synthetic cohort fusing the early-to-mid life National Longitudinal Study of Youth 1979 (NLSY) and the mid-to-late life Health and Retirement Study (HRS), thus generating a data set spanning adolescence to old age, and evaluated the effect of youth alcohol use on later life memory and memory decline.

We combined data from NLSY (born 1957-1965) and HRS participants (ages 50-56 at baseline, born 1954-1966). The primary outcome consisted of longitudinal immediate and delayed word-list recall in HRS. Exposure was amount of alcohol use (none; light-to-moderate: <8 drinks/week for women, <15 for men; or heavy) and binge drinking in the last 30 days, measured in 1983 in NLSY. To impute youth alcohol use, HRS participants were matched with up to 10 NLSY participants based on harmonized demographic, health and behavior variables measured in both data sets at similar ages. We used linear mixed models to estimate the association of early life alcohol use with memory at age 50 and rate of change in memory for each imputation, and pooled estimates and variances using Rubin's rules.

Samples included 42,233 HRS and 12,686 NLSY participants. We identified quality NLSY matches for 29,763 HRS enrollees. Relative to light-to-moderate non-binge drinking, other early life drinking patterns were not associated with cognition at age 50 (heavy non-binge drinkers  $b=0.04$ , 95%CI (-0.45, 0.54); binge drinkers  $b=0.01$ , 95%CI (-0.27, 0.28); nondrinkers  $b=-0.05$ , 95%CI (-0.33, 0.24)) or rate of cognitive decline (heavy non-binge drinkers  $b=-0.22$ ; 95%CI (-0.86, 0.42); binge drinkers ( $b=-0.055$ ; 95%CI (-0.347, 0.238)); nondrinkers  $b=0.016$  (-0.309, 0.341)).

Although requiring strong assumptions, data fusion can offer new insights about early determinants of cognitive aging that would not be possible in any single cohort. Future work will further evaluate the robustness of the synthetic cohort.

**The association between HIV status and the multimorbidity among older South African adults: a retrospective cohort study** Shengruo Zhang\* Shengruo Zhang Chenkai Wu

**Background:** HIV is associated with a wide range of outcomes, such as respiratory symptoms, widespread pain, and poor cognitive conditions. However, how HIV relates to multimorbidity is not completely understood, especially in less developed areas. We examined the association between HIV and multimorbidity among middle-aged and older adults in South Africa.

**Methods:** Data were from the Health and Aging in Africa: A Longitudinal Study of an INDEPTH community (HAALSI). We followed the cohort for 4 years, identified HIV status from the lab tests, and measured multimorbidity as two or more chronic conditions (a total of nine conditions included). The blood samples with a viral load of fewer than 200 copies/ml or not detected were considered to be on ART. We used a logistic regression model to examine the association between HIV status (individuals without HIV, with HIV on ART, and with HIV not on ART) at baseline and incident multimorbidity in the follow-up among persons with none or one chronic condition at baseline, adjusting for sex, age, and education.

**Results:** We included 4556 participants (2460 females; median age: 62 years, IQR: 52 – 72), including 3511 living without HIV, 533 living with HIV on ART, and 440 living with HIV and not on ART. At baseline, around 85% of individuals had one or more conditions. Neither persons with HIV on ART (OR: 0.91, 95% CI: 0.71, 1.18) nor those living with HIV not on ART (OR: 0.80, 95% CI: 0.61, 1.07) had higher odds of multimorbidity than those not living with HIV. After adjusting for each chronic disease at baseline, both those who had HIV on ART (OR: 1.00, 95% CI: 0.77, 1.30) and not on ART (OR: 0.88, 95% CI: 0.66, 1.17) were not associated with multimorbidity than the non-infected reference group.

**Conclusions:** We did not find an association between HIV and multimorbidity among middle-aged and older adults in South Africa. Further studies are needed to elucidate the mechanisms behind the link between chronic illnesses and HIV.

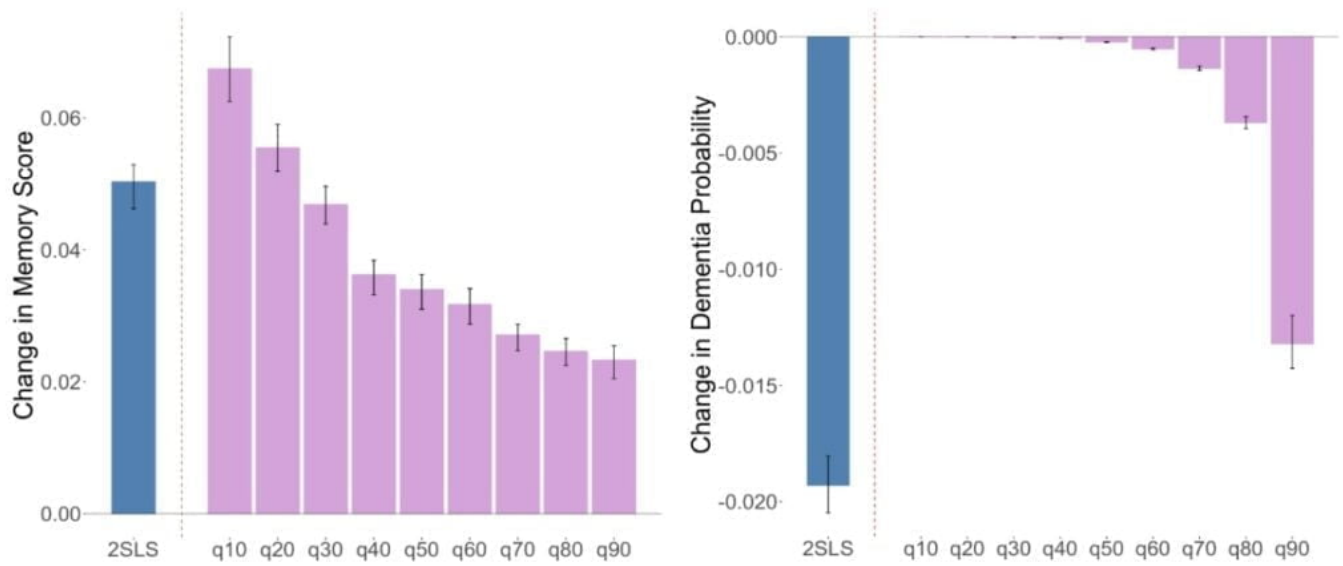
**Distributional impact of increased post-secondary educational attainment on later-life cognition: Evidence from a natural experiment** Jillian Hebert\* Jillian Hebert Amanda Irish Aayush Khadka Rita Hamad Maria Glymour Anusha Vable

Dementia incidence is declining in the US, but continues to disproportionately impact those with less education. Studies suggest population-level increases in educational attainment may be driving the decline; however, little work has established a causal link between educational attainment and dementia incidence. We leverage variation in expansion of 2- and 4-year colleges in US counties between 1940-1982 to test for a causal relationship between post-secondary educational attainment and later-life cognition.

For US-born Health and Retirement Study participants (1995-2018) ages 51 or older (N = 6,374), we instrumented participant's post-secondary education using total number of 2- and 4- year colleges in their county of residence at approximately age 17. Outcomes were algorithmically-defined measures of memory score and dementia probability. Analytic models were 2-stage least squares (2SLS) and conditional quantile regressions (CQR), and incorporated region fixed effects, state and individual covariates, and bootstrapped confidence intervals.

In our analytic sample (mean age 65.3 years (SD 9.4); 59.6% female), there was a strong relationship between the instrument and educational attainment (F-statistic = 134.9). Results from the 2SLS model suggest each year of post-secondary education increased memory scores ( $\beta = 0.05$ , 95% CI: 0.05, 0.05); CQR results showed that increases were larger for participants with lower memory scores (Figure). 2SLS estimated slight decreases in dementia probability ( $\beta = -0.02$ , 95% CI: -0.02,-0.02), while CQR models estimated greater reductions for those with higher dementia probabilities.

Additional years of post-secondary education especially benefited those with lower memory scores or higher dementia probabilities. Findings suggest policies to increase post-secondary education are promising population-level mechanisms to reduce dementia incidence among those at highest-risk.



**Figure.** 2-stage least squares (2SLS) and conditional quantile regression (10th-90th) results for memory score (left) and dementia probability (right). For x-axis labels, q10 is equivalent to the 10th quantile. Please note that the y-axis is on a different scale for each cognition measure.



## **Peripheral Immune Function and Alzheimer's Disease: A Living Systematic Review and Critical Appraisal** Chihua Li\* Chihua Li Rebecca C. Stebbins Grace A. Noppert Allison E. Aiello

### **Background**

There is a growing literature reporting relationships between markers of peripheral immune function and Alzheimer's Disease (AD) in humans. Our review summarizes characteristics and findings of previous studies, appraises their quality, and formulates recommendations for future research.

### **Methods**

We searched electronic databases of PubMed, PsycINFO, and Web of Science and references of previous reviews to identify studies focusing on peripheral immune function and AD up to September 1<sup>st</sup>, 2022.

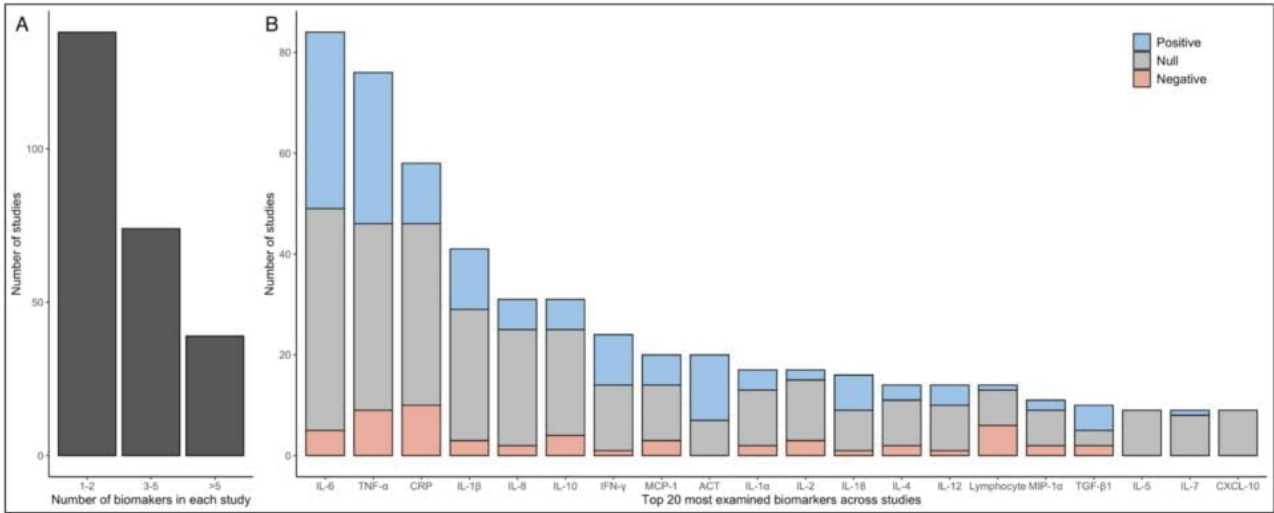
### **Findings**

In total, 251 studies met our inclusion criteria. Studies were predominantly cross-sectional (n=223, 88.8%) and clinical (n=229, 91.2%). 152 different peripheral immune biomarkers were examined. The five most frequently examined included IL-6, TNF- $\alpha$ , CRP, IL-1 $\beta$ , IL-8, and IL-10, with 31 to 84 studies examining the relationship of AD with each biomarker. Over half of these studies reported null associations for these biomarkers. Among these five biomarkers, TNF- $\alpha$  and IL-6 were more likely to be associated with AD compared to others across studies. Only a small proportion of studies (n=12, 4.8%) were deemed to be of high quality based on a modified Newcastle-Ottawa scale. The main methodological problems included lack of representative samples, small sample size, short follow-up, too few biomarkers, poor control selection, and lack of confounding adjustment.

### **Interpretation**

We found that multiple markers of peripheral immunity were associated with AD. The most common markers significantly associated with AD were IL-6 and TNF- $\alpha$ . Yet, existing research included substantial methodological limitations. Further, there is a lack of population-based studies and many key immune markers, such as T cell markers of immunosenescence, have not been widely assessed. Future studies should focus on collecting peripheral immune markers in population-based studies and expand to include cell-mediated markers of immunosenescence.

**Summary of reported findings across included studies on peripheral immune biomarkers and Alzheimer's Disease**



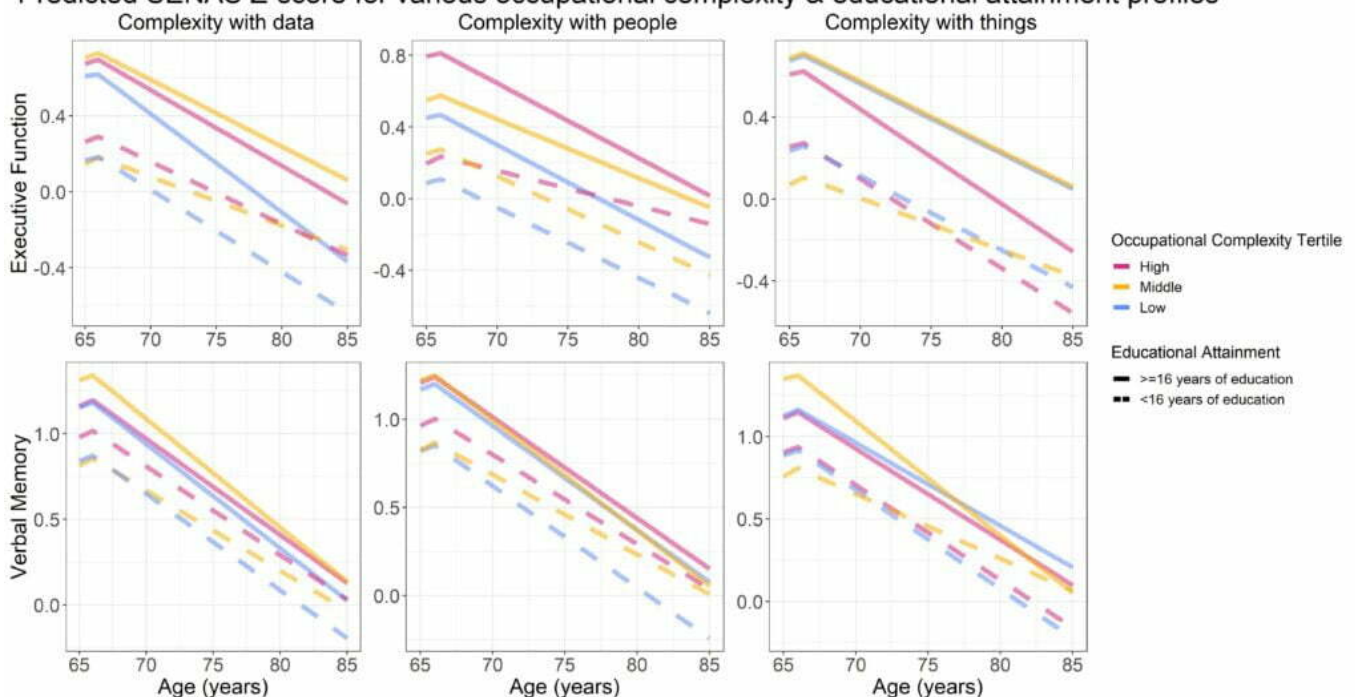
Note: A. Number of studies by how many peripheral immune biomarkers were examined in each study (1-2, 3-5, and over 5 biomarkers).  
 B. Number of studies for each of the top 20 most examined peripheral immune biomarkers stratified by reported associations (positive, null, and negative)

## Examining joint effects of educational attainment and occupational complexity on late-life cognitive function and rate of decline in a racially diverse cohort of older adults

Joseph Fong\* Joseph Fong L Paloma Rojas-Saunero Taylor Mobley Yenee Soh Paola Gilsanz Ruijia Chen M Maria Glymour Rachel A Whitmer Dan Mungas Elizabeth Rose Mayeda

**Background:** Education and occupational complexity are associated with higher cognitive function and may be associated with slower rate of cognitive decline. We estimated joint effects of educational attainment and occupational complexity on later-life cognitive function and rate of decline. **Methods:** The Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study includes long-term Kaiser Permanente Northern California members aged 65+ years. Education was self-reported (high:  $\geq 16$  years, low:  $< 16$  years). Self-reported main occupation was linked with occupational complexity scores from the Dictionary of Occupational Titles (3 domains: complexity with data, people, and things) and operationalized as tertiles for each domain (highest; middle; lowest). We created composite measures of education-occupational complexity per domain. Executive function and verbal episodic memory (z-standardized) were assessed over 3 waves. We used linear mixed effect models with age as timescale and random intercepts and slopes. Models accounted for practice and mode effects and adjusted for baseline age, sex, parental education, and race/ethnicity. **Results:** The sample ( $n=1463$ ) averaged age 75.2 years at baseline and 2.8 years of follow-up. More education and greater occupational complexity were associated with higher baseline cognitive function but rate of decline was similar across education-occupational complexity groups. For example, those with high education and high occupational complexity with data had higher mean baseline executive function ( $b=0.54$  [95% CI: 0.42, 0.67] standardized units), but similar mean rate of change ( $b=0.03$  [95 CI: -0.15, 0.22] standardized units/year) vs. low education and low occupational complexity with data. **Conclusion:** More education and higher occupational complexity are associated with higher cognition among older adults, but estimated effects on rate of cognitive decline were imprecise. Additional data may provide clearer evidence.

Predicted SENAS Z-score for various occupational complexity & educational attainment profiles



All models were adjusted for baseline age, sex, parental education, race/ethnicity, practice effects, and mode effects.  
Predictions for participants who are Asian, female, parents attained  $>8$ th grade, and completed interview in-person

**Overall and sex-specific effect of berberine for the treatment of dyslipidemia in adults: a systematic review and meta-analysis of randomized placebo-controlled trials** Jie V Zhao\* Jie V Zhao Joseph E Blais Xin Huang

**Background:** Berberine is a nutraceutical that can improve lipid metabolism. Berberine may also affect sex hormones and exert sex-specific lipid-modifying effects, which has been overlooked. This study aimed to comprehensively review the efficacy and safety of berberine in adults for the treatment of dyslipidemia with consideration of potential sex disparity.

**Methods:** We searched Medline, Embase, Wanfang, CNKI, ClinicalTrials.gov, and the WHO International Clinical Trials Registry Platform from inception to 13 December 2022. No language restrictions were applied. Eligible studies were randomized controlled trials in adults that compared berberine versus placebo and measured blood lipids or lipoproteins.

Mean differences (MD) were estimated using inverse variance weighting with random effects models for lipid outcomes. Risk of bias was assessed using the Cochrane risk of bias tool for randomized trials. Adverse events (AEs) were described narratively. Primary outcomes were low-density lipoprotein (LDL) cholesterol, total cholesterol, triglycerides, high-density lipoprotein (HDL) cholesterol, and apolipoprotein B. Secondary outcomes were gastrointestinal and muscle-related adverse events.

**Results:** 18 studies (n=1,788 participants), mainly conducted in mainland China and Hong Kong (15 studies [83%]), were included with treatment durations ranging from 4 to 24 weeks. Berberine reduced LDL cholesterol (-0.46 mmol/L, 95% CI -0.62 to -0.30, 14 studies, n=1,447), total cholesterol (-0.48 mmol/L, 95% CI -0.63 to -0.33, 17 studies, n=1,637), triglycerides (-0.34 mmol/L, 95% CI -0.46 to -0.23, 18 studies, n=1,661) and apolipoprotein B (-0.25 g/L, 95% CI -0.40 to -0.11, 2 studies, n=127). Berberine increased HDL cholesterol by 0.06 mmol/L (95% CI 0.00 to 0.12, 13 studies, n=1,248). Notably, the effect on HDL cholesterol was different in women (0.11 mmol/L, 95% CI 0.09 to 0.13) from that in men (-0.07 mmol/L, 95% CI -0.16 to 0.02). Among 16 studies that reported AEs, no serious AEs were reported for berberine. Gastrointestinal AEs were reported in 12 studies and tended to be more frequent in participants allocated to berberine versus placebo (2-23% vs. 2-15%).

**Conclusions:** Berberine produces small reductions in LDL cholesterol, triglycerides, and apolipoprotein B, with potential sex-specific effects on HDL cholesterol. Large-scale trials that consider sex disparity and assess clinical outcomes are required.

**Causal mediation analysis of exposure to environmental tobacco smoke at home and atopic dermatitis risk among adolescents in Kuwait** Saeed Akhtar\* Saeed Akhtar Saad A-Shanfari  
Hussain Booalayan Mosa Abdulrasool Abdulwahab Boujarwa Abdullah Al-Makimi Omar Alkandery

**Background:** Exposure to environmental tobacco smoke at home (EETSH) among adolescents has been shown to be associated with atopic dermatitis. However, the mechanisms underlying this link are uncertain. This study sought to quantify the contributions of EETSH to atopic dermatitis risk through multiple pathways after accounting for the effects of pre-exposure covariates.

**Methods:** During October 2015, a cross-sectional study was conducted by using a self-administered, modified version of the International Study of Asthma and Allergies in Childhood questionnaire for data collection from adolescents enrolled in nine high schools in Hawalli - one of the six governorates of Kuwait. Data were collected on EETSH ( $\geq 1$  smokers at home vs. none), atopic dermatitis (yes vs. no) and sociodemographics. Causal mediation analysis was conducted by implementing a nonparametric inverse odds-weighting method with computation of bootstrap standard errors to estimate the natural direct effect (NDE), natural indirect effect (NIDE) and total effect (TE) of EETSH on atopic dermatitis risk after accounting for the effects of pre-exposure covariates including sex and nationality. The sensitivity analyses were conducted to examine the robustness of the results to the influence of unobserved confounding.

**Results:** Of 746 participants, 74.8% were Kuwaiti, 50.1% female, 12.4% regular smokers and 54% had EETSH. The prevalence of atopic dermatitis was 14.9%. EETSH had a significant TE on atopic dermatitis risk (OR = 1.62; 95% CI: 1.10, 2.38;  $P = 0.014$ ). After accounting for the influences of pre-exposure covariates, causal mediation analysis showed that EETSH had a significant TE (OR = 1.57; 95% CI: 1.01, 2.42;  $P = 0.043$ ), marginally significant NIDE jointly mediated by asthma and self-smoking (OR = 1.12; 95% CI: 1.00, 1.26;  $P = 0.058$ ) with a proportion of mediated risk of 29.6% and nonsignificant NDE (OR = 1.40; 95% CI: 0.90, 2.17;  $P = 0.133$ ) on atopic dermatitis risk. Sensitivity analyses showed negligible influences of any unobserved confounding on parameters' estimates.

**Conclusion:** Voluntarily adapting a smoke-free home rule may protect adolescents from EETSH, smoking initiation, reduction of asthma risk and atopic dermatitis risk. If implemented, future studies may contemplate impact evaluation of such intervention.

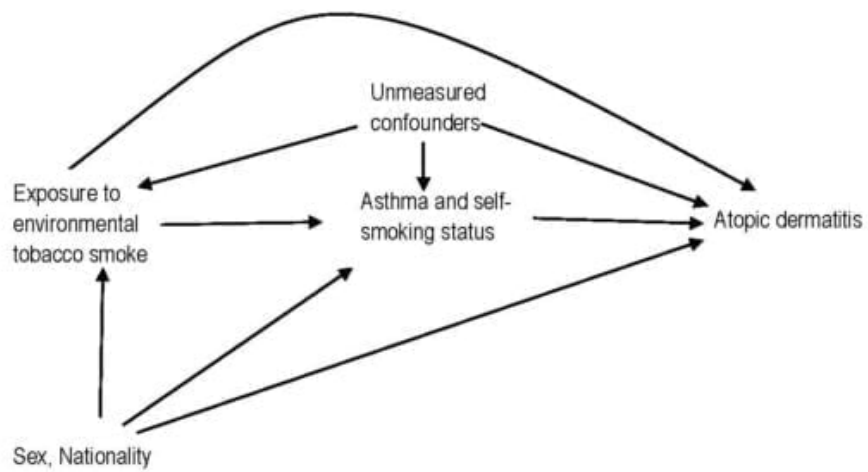


Figure 1. Directed acyclic graph for hypothesized environmental tobacco smoke exposure effect on the atopic dermatitis risk mediated by asthma and self-smoking status conditional on sex among adolescents in Kuwait

**E-cigarette, cigarette, dual e-cigarette/cigarette use and self-rated health** Olatokunbo Osibogun\* Olatokunbo Osibogun

**Objective:** To examine the relationship of e-cigarette, cigarette, and dual cigarette/e-cigarette use with self-rated health. **Methods:** Using data from Wave 1 (2013-2014) and 5 (2018-2019) of the Population Assessment of Tobacco and Health Study, we analyzed a cohort of adults aged 18 years and older from Wave 1 (N=16,224; weighted N= 197,547,497); and followed them to Wave 5 for their self-rated health. The exposure, tobacco use, assessed at Wave 1 was categorized as non-use of tobacco products (reference), e-cigarette only, cigarette only, and dual use of e-cigarette/cigarettes. The outcome, self-rated health, was categorized as suboptimal (fair/poor) and optimal (good/very good/excellent [reference]) health. The relationship was assessed using multivariable logistic regression analyses in 3 models. Model 1 was unadjusted, model 2 adjusted for sociodemographic characteristics, and model 3 additionally adjusted for tobacco dependence and past-month alcohol consumption. Odds ratios (ORs) with 95% confidence intervals (95% CI) were estimated using `svy` commands in STATA. **Results:** Among non-users, 9.8% reported suboptimal self-rated health compared to 14.6%, 20.5% and 20.9% among e-cigarette only, cigarette only and dual users respectively. In the unadjusted model, compared to non-use of tobacco products, e-cigarette only (aOR: 1.57, 95% CI: 1.18-2.11), cigarette only (aOR: 2.38, 95% CI: 2.15-2.64) and dual cigarette/e-cigarette (aOR: 2.43, 95% CI: 2.04-2.92) had higher odds of reporting suboptimal self-rated health. Associations were attenuated in subsequent models, and no longer statistically significant in the fully adjusted model. **Conclusions:** In this nationally representative sample of US adults, there was no statistically significant association between e-cigarette, cigarette and dual use and suboptimal self-rated health. Further research is needed to assess the relationship of e-cigarette and dual use of e-cigarette/cigarette with self-rated health.

**Is the association of chronotype with adolescent behavior problems mediated through social jetlag?** Mia Zhu\* Mia Zhu Henry Oliveros Constanza Marín Mercedes Mora-Plazas Eduardo Villamor

**INTRODUCTION:** Social jetlag has not been formally studied as a mediator of the relation between chronotype and behavior. We examined the associations of chronotype with behavior problems and the mediating role of social jetlag in a cross-sectional study of 957 Colombian adolescents.

**METHODS:** We assessed chronotype as the midpoint of bedtime and waketime on socially free days by parental report, and behavior through the Youth Self-Report (YSR) and the parent-completed Child Behavior Checklist (CBCL) questionnaires. We defined social jetlag as the difference between natural sleep-wake cycles and socially restricted sleep-wake cycles. We estimated adjusted mean differences with 95% CI in externalizing, internalizing, attention, social, and thought problem scores per one-hour change in chronotype using linear regression. We then stratified analyses by sex. Causal mediation analyses were conducted using the counterfactual framework.

**RESULTS:** Later chronotype was related to behavior problems. Eveningness was associated with higher adjusted mean YSR scores (unit difference per hour) in externalizing behavior (1.0; 95% CI: 0.6, 1.5), internalizing behavior (0.6; 95% CI: 0.2, 1.1), attention problems (0.2; 95% CI: 0.0, 0.3), social problems (0.4; 95% CI: 0.1, 0.8), and thought problems (0.3; 95% CI: 0.1, 0.6). Similar patterns were observed with the CBCL. The association of chronotype with somatic complaints and social problems was stronger in boys. Later chronotype was related to social jetlag, but social jetlag was only associated with somatic complaints and attention problems, and mediated 16% and 26% of their corresponding associations with chronotype.

**CONCLUSION:** Later chronotype is associated with behavior problems in adolescence. Social jetlag does not substantially mediate these associations. Future identification of potential mediating factors in the chronotype-behavior pathways could inform interventions to address behavior problems related to eveningness.



**The outperformance of machine learning by human intuition: resolving a paradox with unmeasured confounding** Aaron Sarvet\* Aaron Sarvet Mats Stensrud

In a precision-medicine system, decision rules might be algorithmically individualized based on an optimal regime previously learned from data. However, there is some resistance to the notion that such a system will result in better outcomes, compared to existing human-decision rules: existing care providers often will have access to relevant information for decision-making that is not recorded in the observed data. This is the essence of unmeasured confounding.

We present methodology for leveraging human intuition, given by the intended treatment values, by identifying a *superoptimal* regime using data generated by either nonexperimental or experimental studies, and clarify when a fusion of such data is beneficial. The *superoptimal* regime will indicate to a care provider precisely in which cases expected outcomes would be maximized if the care provider would override the optimal regime recommendation and, importantly, those cases when the optimal regime recommendation should be followed regardless of the care-provider's assessment.

Furthermore, we illustrate how *superoptimal* regime methodology may be alternatively applied for the systematic surveillance of public health paradoxes. As an example, we consider the historic case of Ignaz Semmelweis, whose observations of paradoxes with puerperal fever precipitated a hygiene revolution in clinical medicine.

**LATEBREAKER**

Big Data/Machine Learning/AI

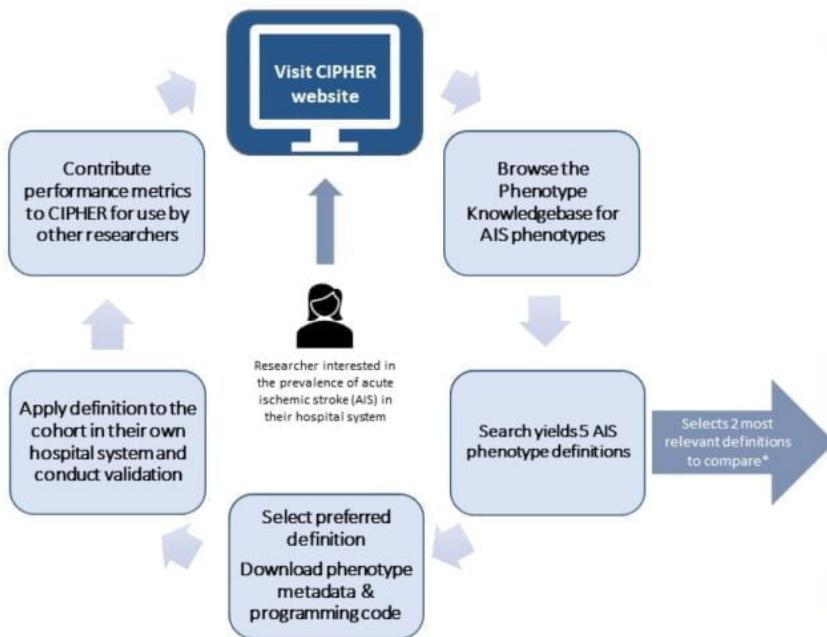
**Streamlining Development and Replication of Electronic Health Records (EHR)-based Phenotypes** Vidisha Tanukonda\* Vidisha Tanukonda Ashley Galloway Jacqueline Honerlaw Yuk-Lam Ho Francesca Fontin Jeffrey Gosian Monika Maripuri Michael Murray Rahul Sangar Edward Zielinski Laura Davies David Heise Keith Connatser Jeremy Cohen Sumitra Muralidhar Kelly Cho

Although electronic health records (EHR) data is frequently used by researchers, EHR-based phenotype development can be time and resource intensive. Created by phenomics experts and the Department of Veterans Affairs (VA), the Centralized Interactive Phenomics Resource (CIPHER), is an online knowledgebase of EHR-based phenotype algorithms and metadata. CIPHER has currently collected over 5000 phenotypes developed on various EHR systems, spanning 10 data classifications and 21 disease domains. Phenotypes are cataloged based on algorithm components, data source, validation status, method, programming language, and context of development. CIPHER aims to provide a standardized, searchable platform to optimize phenotype reproducibility, consistency, and scalability across health systems.

Researchers can utilize CIPHER's complex search to identify and compare phenotypes, and select the most applicable definition for their use case. For example, a search of acute ischemic stroke (AIS) in the CIPHER phenotype knowledgebase results in 5 different AIS definitions, ranging from machine-learning models to rules-based definitions (**Figure**). Upon selecting a definition, the phenotype metadata and programming code can be downloaded for deployment in another cohort. If a chart review is performed to evaluate the accuracy of the definition in the new cohort, the resulting performance metrics can be shared with CIPHER and updated in the phenotype catalog entry.

CIPHER contributes to big data innovation by streamlining phenotype development, and enabling replication and dissemination of phenomics knowledge. In addition to the phenotype library, CIPHER contains tools to assist researchers in developing their own phenotypes and provides an interface for capturing and contributing phenotype metadata. While CIPHER began as an internal resource for VA researchers, a public facing website will be accessible to the wider phenomics community in April of 2023.

Figure: Utilizing CIPHER to Compare and Apply Acute Ischemic Stroke Phenotype Definitions

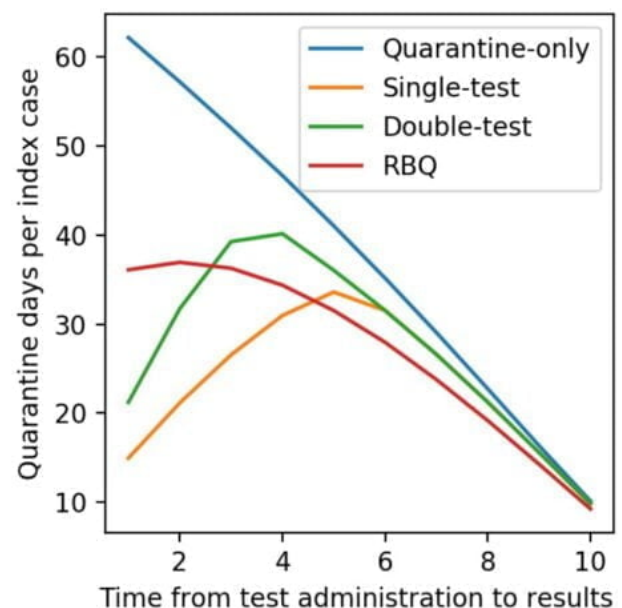
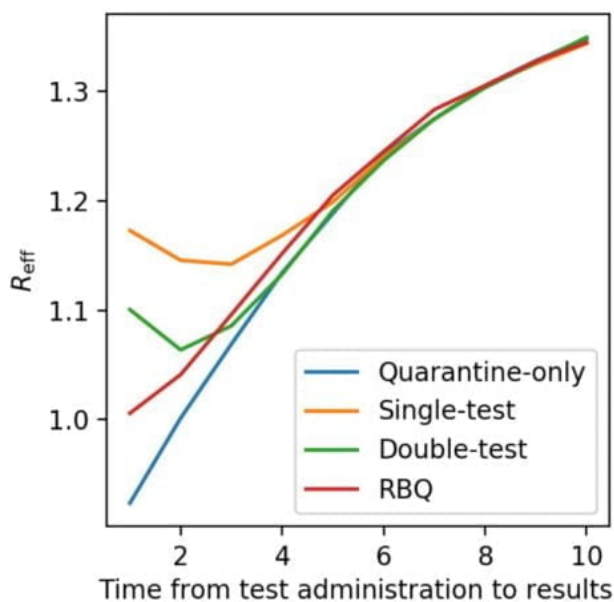


	Stroke Definition 1	Stroke Definition 2
<b>Phenotype Definition</b>	Uses structured and unstructured data from EHR data to yield probability of AIS	Rules based algorithm yields a "Yes"/"No" phenotype status based on presence of ICD code
<b>Method</b>	Machine learning - supervised	Rules-based
<b>Population</b>	All VA Users	All VA Users
<b>Publication</b>	Yu S, Chakraborty A, Liao KP, et al. Surrogate-assisted feature extraction for high-throughput phenotyping. J Am Med Inform Assoc. 2017;24(e1):e143-e149.	Tirschwell DL, Longstreth WT. Validating administrative data in stroke research. Stroke. 2002;33:2465-2470.
<b>Algorithm Components</b>	ICD-9 codes: 434.x and 436  ICD-10 codes: I63.X, I66.X9, I67.89  Concept Unique Identifier: C0038454_stroke	ICD-9 codes: 433.x1, 434 [excluding 434.x0] and 436  ICD-10 codes: I63.xx9, I63.20, I63.22, I63.30, I63.40, I63.50, I63.59, I67.89
<b>Algorithm Validation</b>	Validated	Validated
<b>Performance Metrics</b>	Sensitivity N/A Specificity N/A NPV 0.571 PPV 0.9 AUC 0.842	Sensitivity 0.957 Specificity 0.892 NPV N/A PPV 0.833 AUC N/A

\*Brief example illustrating a subset of the metadata available on CIPHER  
 AIS- Acute Ischemic Stroke; AUC- Area Under the Curve; CIPHER- Centralized Interactive Phenomics Resource; EHR- Electronic Health Data; ICD- International Classification of Diseases; NPV- Negative Predictive Value; PPV- Positive Predictive Value; VA- US Department of Veteran's Affairs

**Designing Efficient Contact Tracing Through Risk-Based Quarantining** Dinh Song An Nguyen\* Marie-Laure Charpignon Dinh Song An Nguyen Jonathan Gruber Milind Tambe Maimuna Shahnaz Majumder Andrew Perrault

In the early stages of a pandemic, specific decisions about the optimal allocation of intervention resources must be made quickly with only a scarce amount of information on disease dynamics. One such intervention is contact tracing, which becomes challenging in the presence of asymptomatic transmission and superspreading. These phenomena can result in varying infection risks for different contacts, which cannot be accounted for in standard epidemiological compartmental models. In this study, we introduce and implement risk-based quarantine (RBQ) using data-driven agents based models (ABMs), wherein each cluster of individuals with a common source of exposure is continuously monitored for symptoms, and those clusters where no individual shows symptoms are released early. Given information available early during a simulated COVID-19 outbreak, RBQ identifies optimal intervention policies, yielding a 30% reduction in the amount of quarantine time served by individuals infected with SARS-CoV-2, while still achieving a reduction in transmission similar to standard policies. We are currently extending our model to Ebola and mpox to understand the interaction of this strategy with ring vaccination. RBQ is both more effective and less cost-prohibitive than test-driven release policies and should be considered in the future as a more optimal option for contact tracing early in an outbreak.



**Dataset shift in COVID-19 mortality prediction: a multicentric study of all Brazilian regions**

Roberta Wichmann\* Roberta Wichmann Kevin Anderson Ruperto Mateo Panduro Fernando Timoteo Fernandes Alexandre Chiavegatto Filho

During the early COVID-19 pandemic there was high medical and managerial complexity, with several heterogeneous clinical protocols at the hospital level. It is increasingly important for the development of machine learning algorithms to understand whether the predictive models trained in other healthcare institutions are suitable for a given hospital, before putting them into practice. This study aimed to apply monitoring methodologies to identify the presence of dataset shift, using data from 5,178 patients with a positive RT-PCR test for COVID-19 in 18 different hospitals, covering all five Brazilian regions. Patient data was collected between March and August 2020. Training and testing datasets were used to apply the monitoring methodologies, generated by 8 different strategies for predicting mortality from COVID-19. We used the Population Stability Index (PSI) statistic to identify the presence of dataset shift in the training and test set, using the following 8 prediction strategies: 1) Training using data from one hospital and testing with 30% of the same hospital; 2) Training using all hospitals except the specific hospital; 3) Training on hospitals in the same region; 4) Training on hospitals of other regions; 5) Training on all other hospitals plus 70% of the specific hospital; 6) Training on 70% of the specific hospital plus the same absolute number of all other hospitals; 7) Training on 70% of a specific hospital plus same absolute number of hospitals from the same region; 8) Training on 70% of a specific hospital plus the same absolute number of other hospitals from the same region. Our study found higher levels of dataset shift for strategies 2 to 8, while in strategy 1 there were very low levels of dataset shift. We also identified the specific variables that presented higher dataset shift, i.e., c-reactive protein, respiratory frequency, and diastolic blood pressure. The presence of dataset shifts will be an important challenge for the clinical application of machine learning algorithms, but its presence can be assessed by repurposing statistical techniques.

**Uncertainty in machine learning predictions: Conformal prediction with applications**

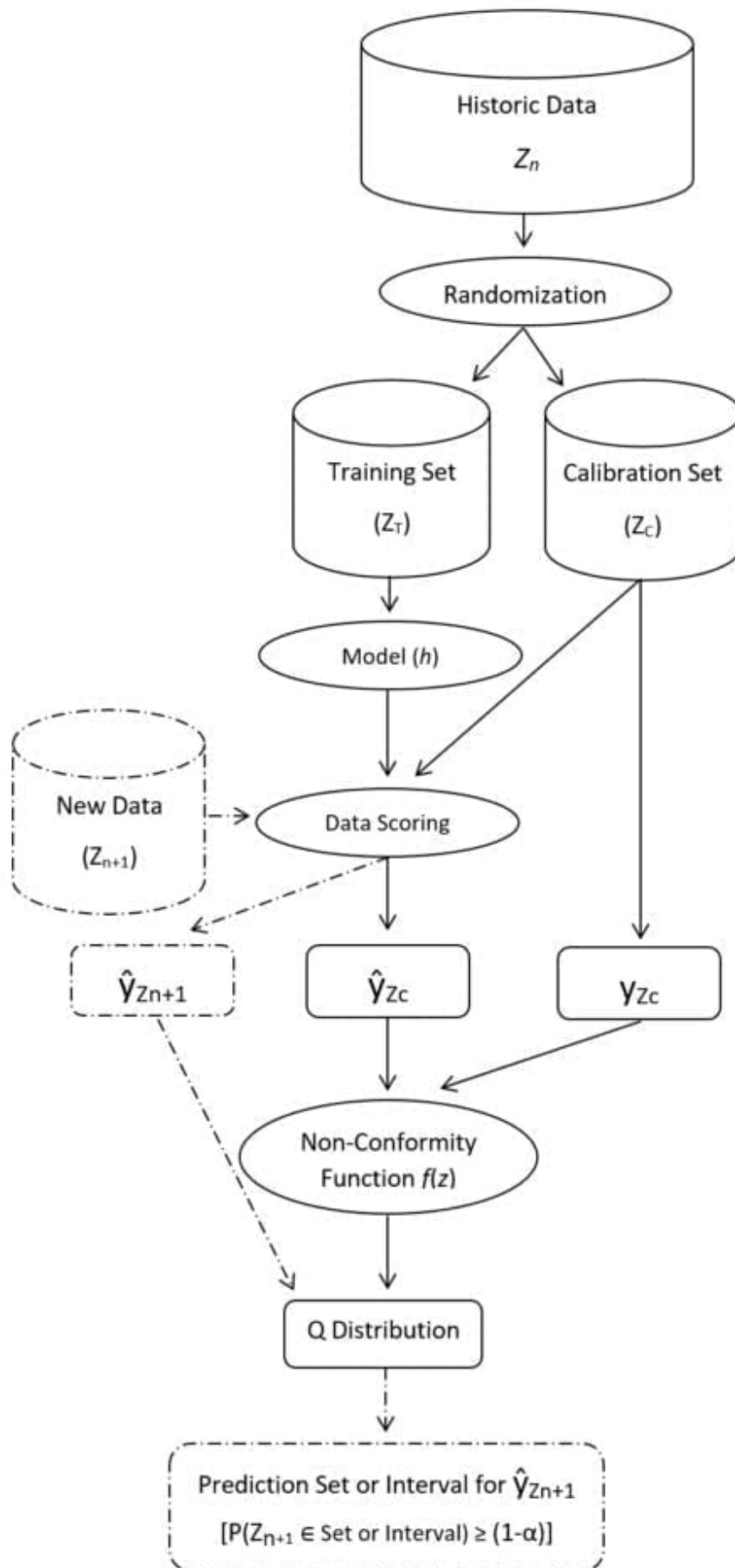
Hayden Smith\* Hayden Smith

**Background:** A historic limitation of using machine learning (ML) algorithms in the field of epidemiology has been the inability to easily calculate prediction intervals. Advances have been made to understand estimate uncertainty using approaches like conformal intervals. Objective: to describe a process for creating conformal intervals and provide applications.

**Methods:** A review of functions and software packages for creating conformal intervals was conducted for Python and R software. In addition, details for applications to regression and classification settings were documented. Lastly, a use case will be presented at the conference based on National Trauma databank records predicting hospital length of stay and inpatient mortality using random forest with conformal intervals.

**Results:** Conformal intervals are nonparametric, finite sample valid, and model agnostic, which means they can be applied to deep learners and tree ensembles as well as traditional approaches. Their only assumption is the exchangeability of observations (i.e., no temporal ordering of data). The inductive conformal predictive process entails fitting a model ( $h$ ) to a training set ( $Z_t$ ), then using a calibration set ( $Z_c$ ) along with a nonconformity function ( $f(z)$ ; loss function) to get scores for constructing a probability distribution ( $Q$ ) in establishing prediction regions ( $\gamma$ ) for a defined interval ( $1 - \alpha$ ), see Figure. Next, coverage bounds and credibility estimates can be estimated for new data ( $Z_{n+1}$ ), which should be similar to  $Z_c$ . Applications are available for regression and classification, but outputs differ (e.g., intervals for regression and set of probable labels for classifiers). Established packages include 'nonconformist' and 'MAPIE' in Python and 'conformal' in R.

**Conclusions:** With black box ML algorithms performing better than traditional approaches in some prediction spaces, conformal intervals can be used to provide prediction coverage for these estimates.



**Figure:** Schematic layout of inductive (split) conformal prediction process.

New data path has a dashed outline;  $Z$  = data;  $Q$  = quantile distribution

**A population-based study of colorectal cancer survival in the five regions of Georgia** Meng-Han Tsai\* Meng-Han Tsai Justin X. Moore Caitlyn Grunert Daramola N. Cabral

**Background:** Colorectal cancer (CRC) is responsible for the third most cancer deaths in Georgia; however, CRC incidence and death vary within the geographic regions of Georgia. Significantly higher CRC mortality was observed in the Clayton, West Central, East Central, Southeast, and Northeast regions of Georgia. We sought to examine the 5-year CRC survival rates and determinants of survival among CRC patients in these five regions of Georgia.

**Methods:** We performed retrospective analysis using data from the 1975-2016 Surveillance, Epidemiology, and End Results program aggregated to the region level. Five-year CRC survival was calculated and stratified by the five regions of Georgia, using Kaplan-Meier curve with log-rank test. Cox Proportional Hazard regression was used to examine the impact of demographic, tumor characteristics, and treatment modality on CRC survival in these five regions.

**Results:** Among 11,023 eligible CRC patients, 5-year CRC survival was lowest in the Clayton (65.9%) compared to the West Central (69.0%), East Central (68.2%), Southeast (70.5%), and Northeast regions (69.5%) (p-value=0.02). Low survival was found in the Clayton region compared to the West Central (HR, 1.11; 95%CI, 1.01-1.24) region, adjusted for demographics, tumor characteristics, and treatment modality. Among Clayton Georgians, age at diagnosis (HR, 1.02; 95%CI, 1.01-1.04), grade 3 & 4 tumors (HR, 2.23; 95%CI, 1.65-3.02), and distant stage (HR, 22.0; 95%CI, 16.8-28.8) were negatively associated with CRC survival.

**Conclusions:** In Georgia, we observed place-based differences in CRC survival. Factors associated with higher risk of CRC death among Clayton Georgians included older age at diagnosis, high-grade tumors, and distant stage CRC. Our study provides important evidence to clinicians, public health professionals, and all relevant stakeholders in furthering the development of CRC screening interventions aimed at CRC early detection and outcomes, particularly for Clayton Georgians.



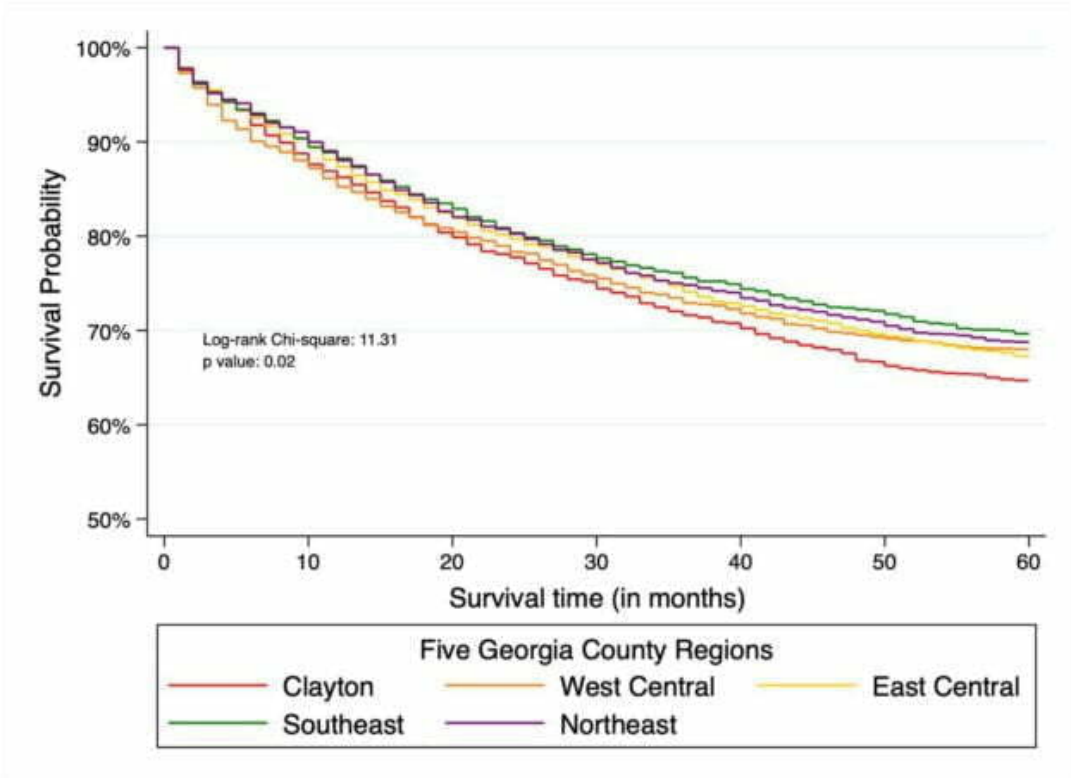


Figure 1. Kaplan Meier CRC survival curves in the Clayton, West Central, East Central, Southeast, and Northeast regions of Georgia. Abbreviation: CRC, colorectal cancer.

**The Impact of Duffy Antigen Receptor for Chemokine (DARC) Genotypes on CD8+ T Cell Infiltration in Breast Tumors from Black Women**

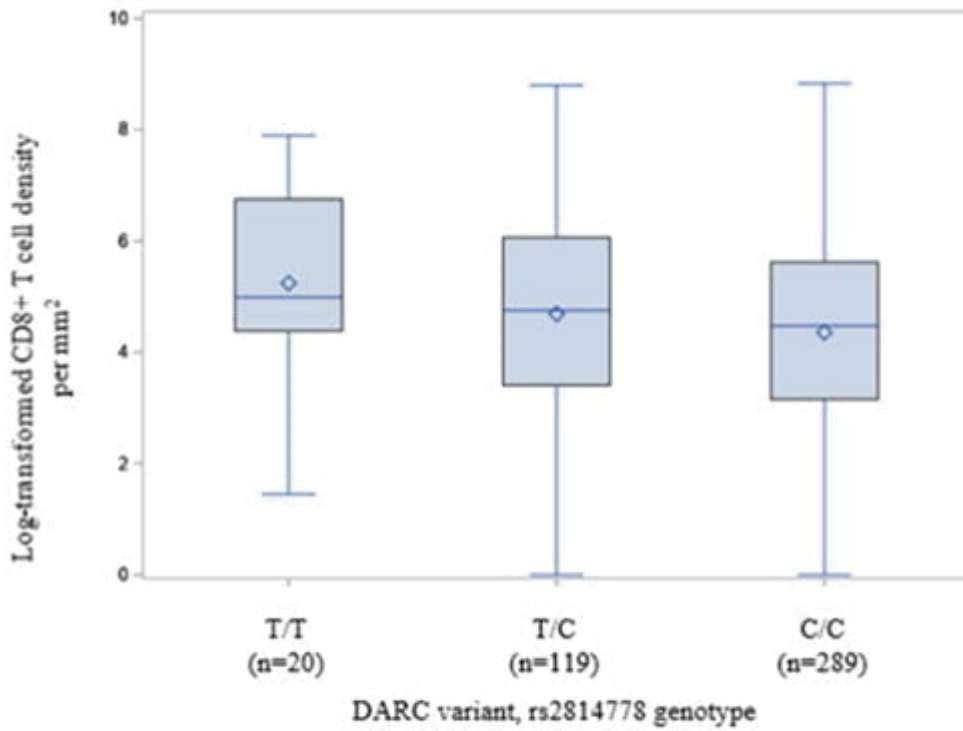
Nisha M. Nair\* Nisha Nair Angela Omilian  
Lucas Mendicino Wiam Bshara Elisa V. Bandera Chi-Chen Hong Song Yao Jo L. Freudenheim  
Christine B. Ambrosone

**Introduction:** The Duffy-null CC genotype of the DARC gene (rs2814778), which confers protection from malaria in sub-Saharan Africa, is present in ~ 70% of US Blacks. Given that DARC is a determinant of certain cytokines, chemokines and white blood cell counts in blood, and breast tumors from Black women have high levels of CD8+T cells with exhausted phenotypes, we aimed to determine if DARC genotype may influence CD8+ T cell density in Black women.

**Methods:** Tissue microarrays of breast tumors from 428 Black women with incident primary breast cancer were stained for CD8+ T cells by immunohistochemistry and evaluated in relation to DARC genotypes, obtained from the Illumina Human Exome Beadchip v1.1. We used multivariable linear regression to assess associations between genotypes and log-transformed CD8+ T cell density, with adjustment for age, hormone receptor status, and tumor stage, grade, and size.

**Results:** Homozygous Duffy-null (CC) was the major genotype (67.5%) in these Black women with breast cancer; homozygous wildtype TT genotype was present in 4.7%. CD8+ T cell densities were lowest among women with a CC genotype (median: 87.0 per mm<sup>2</sup>) and highest in TT genotypes (146.6). Furthermore, in regression models, log-transformed CD8+ T cell densities were highest in those with TT (Beta: 0.93 [95% CI: 0.08, 1.78]) and TC/TT (0.40 [0.02, 0.78]) genotypes, compared to those with CC genotypes. Each wildtype T allele was associated with a significant additive increase in log-transformed density (0.38 [0.07, 0.69]).

**Conclusions:** Breast tumors from Black women carrying genotypes of wildtype T alleles had significantly higher CD8+ T cell densities than those with homozygous Duffy-null, suggesting that Duffy-null alleles may not promote tumor immune cell infiltration, despite the study's limited sample size. Future work will expand to larger populations and determine if DARC genotypes are associated with exhausted T cell phenotypes.



**Figure 1. Distribution of log-transformed CD8+ T cell density levels among 428 Black women with breast cancer according to DARC genotype.** Box plots displaying the mean, median, quartiles, and minimum and maximum observations of log-transformed densities for each genotype. The diamond symbol represents the mean. The CC genotype represents the homozygous Duffy-null genotype.

**Inorganic arsenic in drinking water and bladder cancer: a case-control study in Northern Chile** Estela Blanco\* Estela Blanco Craig Steinmaus Catterina Ferreccio

**BACKGROUND AND AIM:** Exposure to arsenic (As) in drinking water is an established cause of bladder cancer, with strongest evidence available for high levels of exposure. Questions remain regarding risk at lower levels of exposure. Between 2014-2018, we conducted a bladder cancer incident case-control study in Northern Chile. Northern Chile is an ideal place to study health effects of As exposure because the population was highly exposed before 1970 (up to 900 µg/l), after which levels rapidly reduced.

**METHODS:** We analyzed 301 bladder cancer cases and 876 population-based controls with data collected on lifetime exposure to As and potential confounders. We linked participant-reported residences to water arsenic measurements obtained from government agencies and calculated lifetime exposure (mg) and lifetime average (lifetime exposure/ age at evaluation), not including exposures during the 5 years prior to participation. Exposure metrics were categorized into quartiles. We tested whether odds of exposure to higher levels of As in drinking water were different among cases compared to controls. Initial causal models adjusted for age and education. Because of a potential for bias (i.e., imbalance in age distribution among controls), we also fitted population-weighted logistic models and adjusted for education level.

**RESULTS:** Adjusted odds ratios (OR) for quartile of lifetime accumulated exposure to arsenic concentrations in water (<0.79, 0.79-3.05, 3.06-8.63, and  $\geq$  8.64 mg) were 1.00, 0.81 [95% confidence interval (CI), 0.50-1.31], 1.32 (0.85-2.05), and 5.78 (3.85-8.69), respectively. Results were similar, although attenuated, in population-weighted models: 1.00, 0.66 [95% confidence interval (CI), 0.41-1.06], 1.04 (0.66-1.62), and 3.72 (2.51-5.60).

**CONCLUSIONS:** In accordance with evidence implying greater risk only at the highest exposure levels, we observed increased odds of being in the highest exposure quartile of As among cases of bladder cancer compared to population controls.

**Associations between pregnancy-related factors and birth characteristics with risk of rare uterine cancer subtypes: A Nordic population-based case-control study** Jazmine Abril\*

Jazmine Abril Britton Trabert Henrik Toft Sørensen Steinar Tretli Anne Gulbech Ording Laura Madanat-Harjuoja Ingrid Glimelius Mika Gissler Anders Ekbohm Anders Engeland Rebecca Troisi Tom Grotmol Tone Bjørge

Uterine sarcomas (US) are a group of rare tumors that account for 3-7% of all uterine cancers. Compared to the most common uterine malignancy (i.e., epithelial endometrial cancer [EEC]), US are highly aggressive with a poor prognosis. Because of the low incidence and histopathological heterogeneity, the etiology of this diverse group of malignancies is not well understood. Previously, US included malignant mixed Mullerian tumors (MMT), but recent clinical data suggest that MMT share features with EEC. Together with recent changes in classification of US, risk factors for US and MMT are largely unknown, although reproductive factors are likely involved. We conducted a pooled case-control study utilizing linked data from nationwide and population-based medical birth and cancer registries in Denmark, Finland, Norway and Sweden. We evaluated the association between pregnancy-related factors and birth characteristics and risk of US (n=736) and MMT (n=234), compared with associations for EEC (n=10,215) to evaluate potential etiologic similarities across a spectrum of uterine cancer diagnoses. We used multinomial logistic regression to estimate the associations between pregnancy and birth characteristics and risk of US, MMT, and EEC compared with up to 10 matched controls (n=111,528). Having a very-low-birth-weight infant (<1500 vs 2500-3999 grams: 2.83 [1.61-4.96]) and gestational diabetes (OR [95% CI]: 1.98 [0.86-4.56]) were associated with a higher risk of US. A recent pregnancy appeared to be associated with lower risks of both MMT (<10 vs ≥30 years since last pregnancy: 0.66 [0.20-2.23]) and EEC (0.35 [0.30-0.41]) but not US (1.33 [0.90-1.98], p-het<0.05). Associations for MMT and EEC were more similar than between either MMT or EEC and US. As such, our findings differ from previous research when leiomyosarcomas (i.e., MMTs) were grouped with all US. Further research is still needed to identify additional risk factors for US to better understand this fatal disease.

**The Joint Effects of Persistent Poverty, Race and Ethnicity, and Rurality on Stage of Breast Cancer at Diagnosis: A SEER Study** Nita H. Mukand\* Nita Mukand Scarlett Lin Gomez

**Background:** The impact of residing in persistent poverty (PP) neighborhoods, where greater than 20% of residents live below the federal poverty level over a sustained period, on breast cancer (BC) outcomes has not been examined. Our objective was to assess the association between residence in census tracts (CTs) with varying durations of poverty and BC stage at diagnosis and how the effect of PP differed by rurality and race and ethnicity.

**Methods:** We identified 436,535 women aged 18 years and older diagnosed with stage I-IV first primary unilateral breast cancer from 2010 through 2018 in 18 population-based Surveillance, Epidemiology and End Results Program registries. First, we stratified by rurality, then we used logistic regression to estimate the odds ratio (OR) and 95% confidence intervals (CIs) of stage III and IV BC versus stages I and II BC for a joint variable comprised of PP status (i.e., CTs in poverty from 1980-2010) and race/ethnicity. Our model adjusted for age at diagnosis.

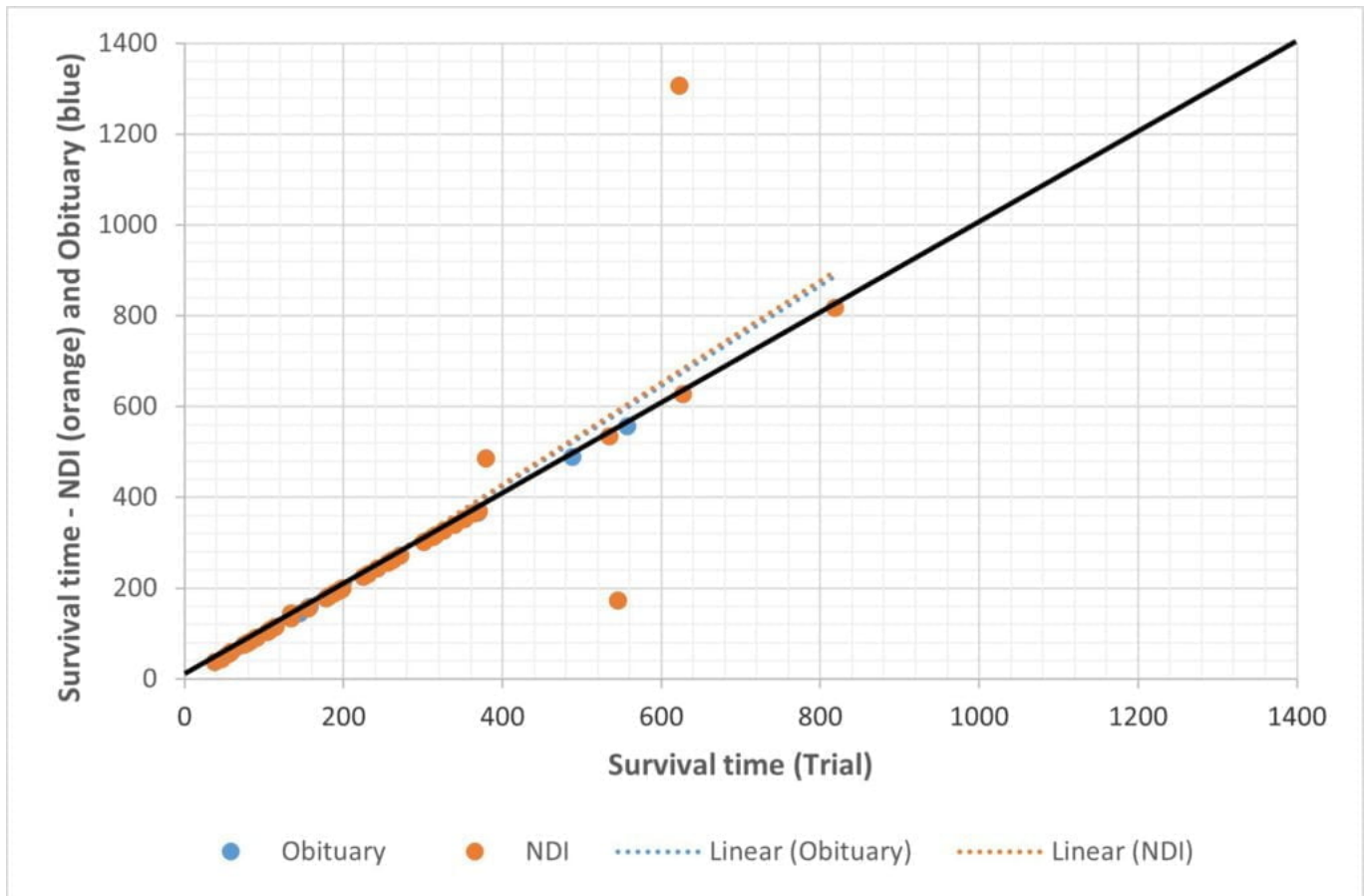
**Results:** Of those included, 6.7% resided in CTs that were persistently impoverished. 8.6% of non-PP and 22.9% of PP tracts were rural. Women residing in PP CTs were more likely to be Non-Hispanic Black (37.0%) or Hispanic (21.1%) than in non-PP CTs (9.4% Black, 11.5% Hispanic). Regardless of PP status, women residing in urban CTs generally had higher odds of stage III/IV BC. Compared to white women residing in non-PP CTs, Black and Hispanic women residing in PP CTs had an OR of 1.92 (95% CI 1.83-2.01) and 1.70 (95% CI 1.59-1.80) respectively.

**Conclusion:** Women residing in urban persistently impoverished CTs had the highest odds of later stage disease. Further study to identify modifiable social and structural characteristics driving worse outcomes in persistently impoverished urban areas is warranted.

**Evaluation of the validity of a multi-source approach to identifying deaths among older adults diagnosed with advanced cancers and enrolled in randomized clinical trials**

Jennifer L. Lund\* I-Hsuan Su Jenna Cacciatorre Rachael Tylock Saloni Sharma Sharon Peacock Hinton Paul R. Duberstein Laura C. Hanson Supriya G. Mohile Jennifer L. Lund

Mortality data can complement other primary endpoints from clinical trials. Yet, identifying death after trial completion is challenging, particularly in large, multi-site trials, as no comprehensive vital status source exists in the United States. We developed a , multi-source approach to capture death data for participants living with advanced cancer in two randomized trials. We then evaluated agreement across sources using the trial data as the reference standard. Individuals aged 70+ years with incurable solid tumors or lymphoma and at least one aging-related condition were enrolled from October 2014-March 2019 (NCT02107443; NCT02054741). Study coordinators requested death data at one-year after trial enrollment. Trial participants gave consent to link information to external sources. We developed an approach for sequential death capture using: (1) active trial follow-up up to 1-year per protocol, (2) then linkage to the National Death Index (NDI), and (3) finally online obituary searches. In a random sample of 50 participants who died during trial follow-up, we estimated sensitivity of death capture using the NDI and obituary search sources and graphed scatter plots of survival times to assess agreement. There were 1169 participants enrolled in the two trials; mean age was 77 years; 46% were female and 89% identified as Non-Hispanic White; gastrointestinal (30%) and lung (26%) were the most common cancer ; median survival was 1.1 years. In total, 609 participants died during trial follow-up. The sensitivity for death capture was 92% for the NDI and 94% for the obituary searches compared with the trial data. The figure shows excellent agreement between survival times assessed using the three sources. Extending the value of trials in older adults with advanced cancer through linkage with external death data is feasible and accurate. Future work should evaluate agreement between sources over longer time horizons and in other disease settings.





**Air pollution and the risk of second primary lung cancer among lung cancer survivors: The Prospective UK Biobank Cohort Study** Sophia Luo\* Sophia Luo Eunji Choi Anna Graber-Nadich Julie Wu Joel Neal Heather Wakelee Summer Han

**Background:** Lung cancer survivors have a high risk of developing second primary lung cancer (SPLC). While ambient air pollution has shown an association with the risk of initial primary lung cancer (IPLC), its effect on SPLC risk is unknown. We aimed to examine whether exposure to residential ambient air pollution is associated with the risk of SPLC, using data from the large, prospective, population-based UK Biobank cohort study.

**Methods:** The UK Biobank study enrolled ~500,000 participants in 2006-2010. We identified 2812 IPLC cases who were diagnosed and followed through 2017. In the UK Biobank, the annual average exposures to ambient air pollutants, including particulate matter (PM)<sub>10</sub>, PM<sub>2.5</sub>, and nitrogen dioxide (NO<sub>2</sub>), were measured in 2007 (PM<sub>10</sub> and NO<sub>2</sub>) and/or in 2010 (PM<sub>10</sub>, NO<sub>2</sub>, and PM<sub>2.5</sub>) based on high-resolution geospatial data that tracked participants' residential addresses over follow-up. We applied cause-specific Cox (CSC) regression to evaluate the association between SPLC risk and each air pollutant, adjusting for smoking status and IPLC age at diagnosis and histology. Sensitivity analysis was restricted to those who lived at the same address through their follow-up.

**Results:** Of 2812 IPLC patients, 100 (3.6%) developed SPLC over 7347 person-years. The 5-year cumulative incidence of SPLC was 3.33% (95% confidence interval, [2.65%-4.01%]). CSC regression analysis showed that lung cancer survivors exposed to a high PM<sub>10</sub> level ( $\geq 20 \mu\text{g}/\text{m}^3$  based on the WHO guideline cutoff) have a significantly increased SPLC risk (hazard ratio [HR], 3.33;  $p=0.004$ ). When restricting to only those who remained at the same location through their follow-up, a stronger association was observed (HR=5.85;  $p=0.0027$ ). PM<sub>2.5</sub> did not show a significant association with SPLC, likely due to a lack of available data.

**Conclusions:** Long-term exposure to PM<sub>10</sub> pollution may increase the risk of SPLC in lung cancer survivors and may help identify those at the highest risk of developing SPLC.

**Long-term socioeconomic consequences of early cancer diagnosis** Amanda S. Thomas\*

Amanda Thomas Eric Grodsky Chandra L. Muller John Robert Warren

Cancer is the second most common chronic disease in the US, affecting almost 40% of the population over the course of a lifetime. Although millions of Americans have survived cancer, we know very little about how the experience of being diagnosed with and surviving—especially relatively early in life—impacts people’s subsequent social and economic well-being. In this study we aim to estimate the impact of early- and mid-life cancer diagnosis and recovery on subsequent occupational, education, and economic attainments.

One reason we know so little about this question is that previous data sources have lacked life course-long longitudinal data on cancer diagnosis, survival, social and economic outcomes, and key confounding factors (e.g., education, family background). High School and Beyond (HSB) is a large (n~25,500) nationally representative cohort study of high school sophomores and seniors from 1980. Follow-up for this cohort is through 2021, with previous follow-ups in 1982, 1984, 1986, 1992, and 2014. HSB contains the diagnosis, initiation, and treatment of cancer; measures of mid- and late-life social and economic outcomes, and key confounders. Of the approximately 13,900 responding to the 2021 survey almost 13% (n = 1,770) reported that they have ever been diagnosed with cancer. Of those reporting cancer, the most common types were skin (n=630), breast (n=350), and prostate (n=130). Age at diagnosis varies, with approximately 34% below age 45 during treatment (childhood, young adulthood) and the rest in middle age (> 45 years). HSB also includes information about timing and nature of cancer deaths; important for modeling selective survival.

Our outcomes—measured at age ~60 in 2021—include occupational socioeconomic standing, later-life educational attainment, financial precarity, and marital status. Analyses will model these outcomes as a function of age and type of cancer diagnosis (net of key confounders) and will handle selective mortality from cancer.

**Cancer mortality deficits in the US during the COVID-19 pandemic** Anika T. Haque\* Anika Haque Paul S. Albert Hae-Rin Kim Neal D. Freedman Amy Berrington de González Meredith S. Shiels

**Background:** Fewer cancer deaths than expected were reported in the US during the COVID-19 pandemic (March-December 2020). To assess if there was a true deficit of cancer deaths during this time, we estimated whether cancer death rates were significantly different during the COVID-19 period, after accounting for temporal trends and seasonal patterns.

**Methods:** Age-specific cancer death counts by month (2011-20) were obtained from publicly available death certificate data from the CDC; population estimates for corresponding years were ascertained from the US Census Bureau. We fit a Poisson regression model to assess if there was a significant change in cancer death rates from March-December 2020 compared to prior years. We assessed statistical significance of the effect of COVID-19 on seasonal patterns in death rates with a Wald Chi-Squared test. We estimated the IRR for the COVID-19 period compared to the pre-COVID-19 period; adjusted for seasonal patterns and linear time trends by cancer type and age group.

**Results:** During March-December 2020, there was a significant deficit of cancer deaths in the US among 55-64 and  $\geq 75$ -year-olds. By month, cancer death rates were 2% lower than expected from March-June 2020 among those aged 55-64 years. Among  $\geq 75$ -years-old, cancer death rates were 2-3% lower than expected from March-July and December. Cancer death rates were significantly lower during some months of 2020 for bladder ( $\geq 75$ ), breast (25-34,35-44), esophagus (45-54), pancreas (55-64), colorectal and anal ( $\geq 75$ ), liver (55-64,65-74), and lung ( $\geq 75$ ) cancers.

**Conclusion:** Cancer death rates were significantly lower than expected during the early months of the COVID-19 pandemic among 55-64 and  $\geq 75$ -year-olds. As the deficits coincide with months with significant increases in COVID-19 deaths, and were restricted to the older age-groups, these apparent deficits in 2020 were most likely due to competing risks.

**Assessing physicians' recommendations for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) testing among minority populations in Greater Philadelphia and New York City** Thoin F Begum\* Thoin Begum Vidya S Patil Lin Zhu Hemi Park Ming-Chin Yeh Evelyn González Marilyn A Fraser Steven Zhu Nathaly Rubio-Torio Grace X Ma Yin Tan

Deaths from liver cancer are on the rise and disproportionately affect minority racial/ethnic groups. In this study of 576 participants, we examined differences in sociodemographic factors and associations with physicians' recommendations for Hepatitis B Virus (HBV) and Hepatitis C Virus (HCV) screening among minority populations in the US. Using Poisson regression with robust variance estimation we evaluated associations between physicians' recommendations for screening and patients getting blood tests as outcomes, adjusted for sociodemographic factors for Hispanic Americans (HA), African Americans (AA), and Asian Pacific Americans (APA). We found that HAs were significantly likely to have never gotten a blood test for either HBV or HCV (RR=1.25,95%CI:1.05,1.49). AAs were less likely to have a physician recommend screening for HBV or HCV, but more likely to get a test done for HCV (RR=1.42,95%CI:0.83,2.44), albeit without statistical significance. APAs were significantly more likely to receive a screening recommendation for HBV (RR=1.10,95%CI:1.01,1.20) and getting a blood test (RR=1.57,95%CI:1.06,2.33). Physician recommendations are strongly associated with test receipt. Future efforts to improve adherence should target trainees, emphasize the importance of obtaining relevant histories, especially for high-risk patients, and inform them about the risk factors and the role sociodemographic factors may play in developing liver cancer.

**Longitudinal patterns of claims-based frailty trajectories in older women with stage I-III breast cancer undergoing adjuvant chemotherapy** Emilie D Duchesneau\* Emilie D Duchesneau Katherine Reeder-Hayes Dae Hyun Kim Jessie K Edwards Til Stürmer Keturah R Faurot Jennifer L Lund

## Introduction

Some older women with breast cancer (BC) are at elevated risk of physical decline during treatment while others are more resilient. Physical resiliency refers to the ability to recover following a stressor. We estimated longitudinal trajectories of a Medicare claims-based proxy for frailty in older women with BC undergoing adjuvant chemotherapy (ACT).

## Methods

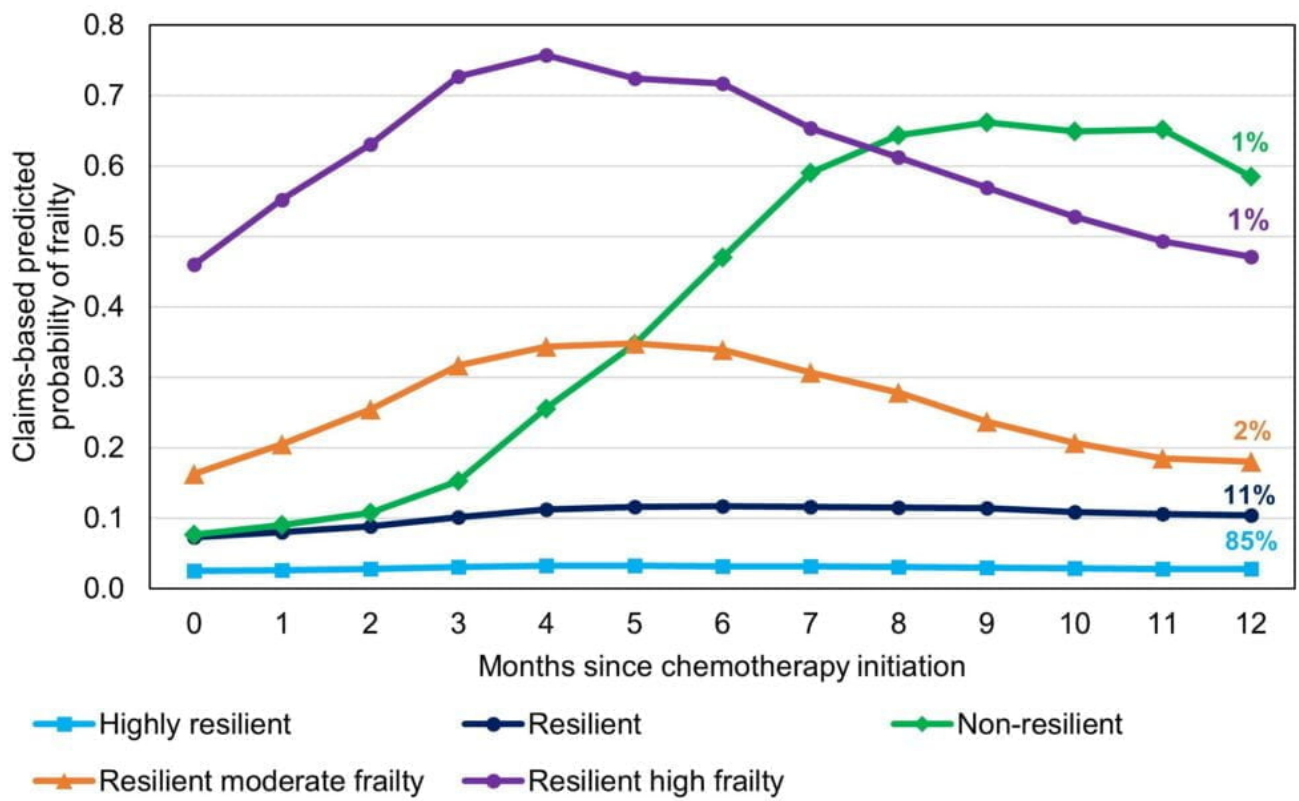
The sample included women (65+ yrs) with stage I-III BC undergoing ACT in the SEER cancer registries with linkage to Medicare claims. We used a claims-based measure (Faurot frailty index), to estimate frailty probabilities during each month from ACT initiation for 1 year. We used k-means clustering to identify patterns of frailty trajectories allowing for 2-7 clusters and selecting the final model based on aligned box criterion.

## Results

Our final model (21,525 women) resulted in 5 trajectories (**Fig**). A “highly resilient” group (85%) had low frailty throughout follow-up, experiencing a slight increase (month 0-5: 0.025-to-0.033) followed by a decrease (month 12: 0.028). A “resilient” group (11%) experienced a small increase in frailty (month 0-6: 0.073-to-0.117), followed by a decrease (month 12: 0.104). A “non-resilient” group (1%) initiated ACT with moderate frailty (0.076) that increased to high frailty without evidence of recovery (month 12: 0.585). A “resilient moderate frailty” group (2%) initiated ACT with moderate frailty, experiencing an increase in frailty (month 0-5: 0.163-to-0.348), followed by a decrease (month 12: 0.180). A “resilient high frailty” group (1%) had high frailty throughout follow-up that increased from month 0-5 (0.460-to-0.757), then decreased (month 12: 0.471).

## Conclusion

Of the 5 clusters of claims-based frailty trajectories in women with BC receiving ACT, 4 demonstrated resiliency. A small percentage of women experienced sustained increases in frailty. Identifying risk factors for a lack of resilience may drive pre-treatment management decisions that can improve outcomes.



**Assessment of efficacy of first, second- and third-line targeted therapies in Non-Small Cell Lung cancer compared to chemotherapy: a systematic review** Ruchir Raman\* Ruchir Raman  
Christina Ludema

## Background

In the most recent GLOBOCAN report, lung cancer has been reported to contribute to an estimated 1.8 million (18%) of all global cancer-related deaths. Non-small cell lung cancer (NSCLC) accounts for 80-85% of all lung cancer cases, is diagnosed at an advanced stage ( $\geq$  III b) and is a leading cancer mortality cause worldwide.

Historically, patients with metastatic NSCLC have been limited to traditional cytotoxic chemotherapy which provide limited benefits in survival outcomes and are associated with significant toxicities. In recent years, the treatment algorithm has shifted for many patients, with targeted therapies providing a renewed sense of optimism for late-stage NSCLC patients.

Targeted therapies have been heralded as a significant improvement in certain clinical patient outcomes late-stage NSCLC treatment over chemotherapy. However, there have also been concerns and questions raised regarding whether targeted therapies actually provide an overall benefit in key outcomes compared to chemotherapy. A systematic review could pave the way forward for future research in this area.

## Methods

For the systematic review, study designs including clinical trials, randomized controlled trials (RCTs) or cluster-RCTs, and cohort studies that specifically evaluated targeted therapies vs cytotoxic chemotherapy in NSCLC patients having level 1 evidence of driver mutations were included. If sufficient heterogeneity is found, subgroup analyses will be performed on the following participant/intervention characteristics

- Age
- Gene
- Smoking status
- Cancer Stage
- ECOG performance scale
- Histology

## Results and Conclusions

As of Jan 2023, 1161 records have been identified in PUBMED using the above search strategy. A full protocol has been written including search strategy, inclusion criteria and, information abstraction. Review of the papers for inclusion in this systematic review is underway.

**Occupational Benzene Exposure and Cancer Risk among Chinese Men: A Report from the Shanghai Men's Health Study** Douglas DeMoulin, PhD GSP\* Douglas DeMoulin Hui Cai, MD PhD Loren Lipworth, ScD Wei Zheng, MD PhD Xiao-Ou Shu, MD PhD

**Objective:** To assess the associations of occupational exposure to benzene with the risk of cancers of the lung, liver, kidney, stomach, and myeloma, lymphoma, and leukemia.

**Methods:** This analysis used baseline survey data collected in the Shanghai Men's Health Study, a population-based cohort study of 61,482 men aged 40-74 between 2002-2006 and followed for cancer incidence through end of 2016. Job-exposure matrices, constructed by industrial hygienists specifically for the study population, were used to estimate job-related benzene exposure intensity and industry-specific probability of benzene exposure based on the longest job held. Multivariable Cox regression analyses were used to estimate hazard ratios (HR) and 95% CI for developing cancers of interest in association with occupational benzene exposure, adjusting for demographic characteristics and known risk factors.

**Results:** A total of 1,463 and 844 men had high intensity job-related and high industry-specific probability benzene exposures, respectively. During 15 years of follow-up, a total of 1,145 lung, 656 stomach, 446 liver, 244 kidney cancer cases, and 247 leukemia, lymphoma, myeloma cases were documented. Higher intensity of job-related benzene exposure was associated with significantly increased lung cancer risk (HR=1.61, 95%CI=1.16-2.24) as well as myeloma, lymphoma, and leukemia (HR=1.94, 95%CI=1.06-3.57) compared to no exposure. Working in industries with a high probability of benzene exposure was similarly associated with a 65% increased risk of lung cancer (95% CI=1.08-2.52) and a 2.14-fold increased risk of myeloma, lymphoma, and leukemia (95% CI=1.01-4.54). Occupational benzene exposure was not associated with risk of liver, kidney, and stomach cancers.

**Conclusion:** Occupational benzene exposure was associated with 1.6 to 2.1- fold increased risk of lung cancer and myeloma, lymphoma, and leukemia among Chinese men. Additional analyses are ongoing, and results will be presented at the conference.



**Induction/latency of cancer after environmental disaster: the importance of selecting appropriate reference populations** Brandon Vaeth\* Rachel Zeig-Owens Brandon Vaeth David Goldfarb Charles B Hall Rachel Zeig-Owens

**BACKGROUND:** Increased cancer incidence has been reported among World Trade Center (WTC)-exposed responders with incidence rate ratios (IRRs) of some cancers as compared to the New York State (NYS) population have varied over time. The study objective was to evaluate the impact of using different reference populations when assessing temporal trends, as temporal trends can vary across reference populations.

**METHODS:** Participants from the WTC Combined Rescue/Recovery Cohort were observed from 3/12/02 to 12/31/15. The most common cancer was incident prostate cancer, which was used for initial analyses. Person-time accruals began 6 months after enrollment into a WTC cohort and ended at death or 12/31/15. Incidence data were obtained via linkages with 13 state cancer registries. We used Poisson regression to estimate IRRs and 95% CIs controlling for age, race/ethnicity and calendar year; changepoints in IRRs were estimated using profile likelihood. IRRs and changepoints were estimated for WTC-exposed compared with the following reference populations: SEER21, NYS and New York City (NYC).

**RESULTS:** IRRs for prostate cancer were similar using either NYC, NYS and SEER21 as reference populations. When compared to NYC, no significant changepoint was found (IRR for the whole study period was 1.31 (95%CI 1.24-1.40)). Compared to NYS, we estimated a changepoint in 2006, while compared to SEER21 the changepoint occurred in 2007 (NYS 2002-2006: IRR=1.01 (95% CI 0.85-1.20), 2007-2015: IRR=1.23 (95%CI 1.16-1.32); SEER21 2002-2007: IRR=1.12 (95%CI 0.98-1.30), 2008-2015: IRR=1.41 (95%CI 1.32-1.50)).

**DISCUSSION:** In estimating cancer induction/latency after an acute environmental exposure event, findings can be sensitive to the choice of the comparison population. Our initial findings suggest reference populations may influence the timing and statistical significance for changepoint estimation. Future analyses will assess other cancer subtypes and explore analyses with multiple changepoints.

**LATEBREAKER**

Cancer

**Could residual confounding be biasing the association between the consumption of foods by their degree of processing and the risk of head and neck cancer in the European Prospective Investigation into Cancer study?** Fernanda Morales Berstein\* Fernanda Morales Berstein Inge Huybrechts George Davey Smith Caroline Relton Carolina Borges Rebecca Richmond Tom Richardson Marc Gunter Vivian Viallon Carine Biessy Corinne Casagrande Bertrand Hemon Nathalie Kliemann Manon Cairat Jessica Blanco Lopez Aline Al Nahas Kiara Chang Christopher Millett Eszter Vamos Paolo Vineis Fernanda Rauber Renata Bertazzi Levy Diana Barbosa Cunha Pietro Ferrari Paul Brennan Antonio Agudo Paula Jakszyn Ana Goncalves Soares

**Background:** Negative control analyses, which are expected to produce null results, can be used to detect residual confounding. In this study, we aimed to investigate residual confounding in the associations between the consumption of unprocessed/minimally processed foods, processed foods and ultra-processed foods and the risk of head and neck cancer (HNC).

**Methods:** Our study included 450,111 European Prospective Investigation into Cancer cohort participants, of which 850 were incident cases of HNC. We used Cox proportional hazard models to investigate the associations between the consumption of unprocessed/minimally processed foods, processed foods and ultra-processed foods and the risk of HNC. Models were stratified by age at recruitment, sex, and centre, and adjusted for education, physical activity, height, smoking status, and alcohol intake. We also performed a negative control outcome analysis with accidental deaths as the outcome to assess the possibility of residual confounding.

**Results:** A 10% g/d higher consumption of ultra-processed foods was associated with an increased risk of HNC (HR=1.25, 95%CI 1.15-1.36), while a higher consumption of unprocessed/minimally processed foods was associated with a lower risk of HNC (HR=0.86, 95%CI 0.80-0.92). In contrast, there was no evidence of an association between the consumption of processed foods and the risk of HNC (HR=1.02, 95%CI 0.93-1.12). In our negative control outcome analysis, higher ultra-processed food consumption was associated with accidental deaths (HR=1.12, 95%CI 1.02-1.23).

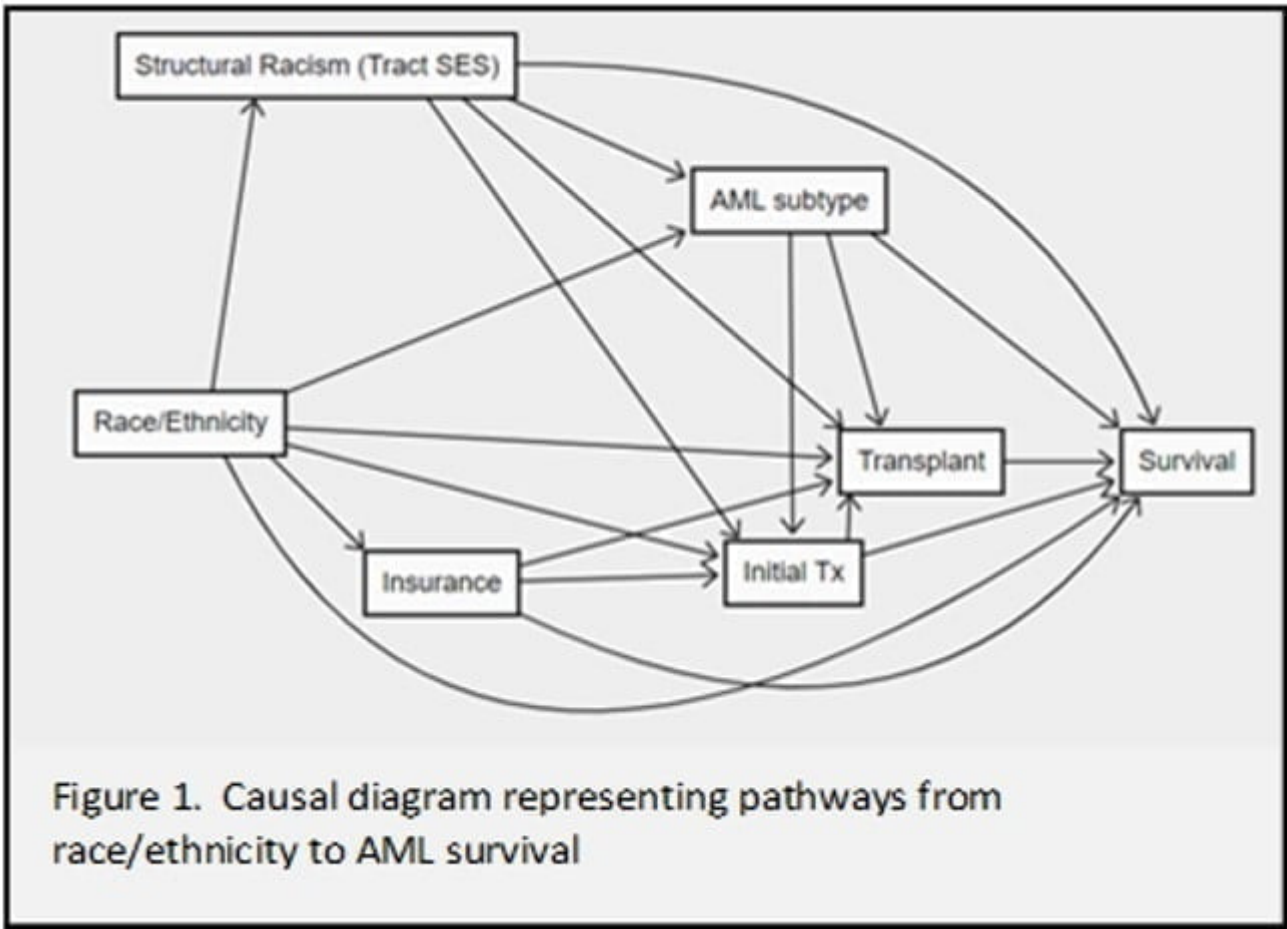
**Conclusions:** Our findings suggest that reducing the intake of ultra-processed foods in favour of unprocessed/minimally processed foods may confer protection against HNC. Nevertheless, our results may be influenced by residual confounding, as indicated by the negative control analysis. Therefore, our findings should be regarded with caution until they are replicated in settings with other underlying confounding structures.

**Birth Certificate Reported Smoking and Childhood Cancer: A Registry-Based Analysis with Probabilistic Bias Analysis** Allison Domingues\* Allison Domingues Erin Marcotte Logan Spector

**Background:** Though the carcinogenic properties of tobacco smoke and smoking are well documented, previous studies of maternal smoking and childhood cancer risk have been inconclusive in some cancers and null in others, such as acute lymphoblastic leukemia. However, case-control studies comprised the majority of prior research and thus were limited by the potential for recall bias, selection bias, and limited sample sizes. **Objective:** This analysis aimed to elucidate this relationship through a large, pooled analysis (over 10,000 cases and 25,000 controls) of existing registry-based case-control studies with a probabilistic error correction of smoking misclassification. **Methods:** The association between binary (yes/no) maternal smoking as reported on birth certificates and childhood cancer (defined by International Classification of Childhood Cancer category) was investigated using unconditional logistic regression controlling for parental education, parental race/ethnicity, and parental age. These analyses were also repeated stratified by potential mediators such as birth defects in children, birth weight, and maternal BMI. Where data was available, additional analyses were conducted for smoking by trimester and cigarettes per day also using unconditional logistic regression. A probabilistic error correction was enacted for smoking status using information on the sensitivity and specificity of birth record reported smoking in existing literature. **Results:** In preliminary analysis, maternal prenatal smoking was inversely associated with acute myeloid leukemia, astrocytoma, and retinoblastoma before misclassification-adjustment. Smoking was not found to be associated with lymphoid leukemias. After misclassification-adjustment, the inverse associations observed were slightly attenuated. **Discussion:** Mechanisms that may result in the observed inverse association between maternal smoking and certain childhood cancers warrant future study.

**A structural equations approach to examining the role of structural racism on survival disparities for adult acute myeloid leukemia.** Garth H Rauscher\* Garth Rauscher Ivy Elizabeth Abraham Anand Ashwin Patel Madelyn Burkart Eshana Shah Ami Dave Jessica K. Altman Stephanie B. Tsai Melissa L. Larson Wendy Stock Sarah Monick Maryam Zia Stephanie Berg Vedavyas Gannamani Amani Erra Matthew Kroll Irum Khan

**INTRODUCTION:** Adult acute myeloid leukemia is a hematologic cancer with a generally poor prognosis, and for which patients not only die from the disease itself but from complications that arise from treatment (e.g., high intensity chemotherapy and allogeneic stem cell transplant). Racial and ethnic disparities in AML survival are well documented but not well understood. Structural racism is a fundamental cause of health inequities and may play a role in AML survival disparities. In a previous cross-sectional analysis of the Chicago Area Leukemia Registry, four census tract-based measures of socioeconomic status (SES) accounted for all of the AML death disparity for AA and Hispanic vs. White patients. **METHODS:** For 822 AML patients, we used structural equations models (SEM) to tease out contributions of tract SES along the multiple potential causal paths for AML death disparities. We used multivariable, modified ordinary least squares to place results on a public health scale. Tumor subtype, receipt of high-intensity induction chemotherapy, and receipt of allogeneic stem cell transplant were the main clinical intermediates. **RESULTS:** Black patients were 22 percentage points more likely to have an aggressive AML subtype and tract SES accounted for 100% of this disparity ( $p=0.006$ ). Black patients were 7 percentage points less likely to receive high-intensity chemotherapy and tract SES accounted for 51% of this disparity ( $p>0.20$ ). Black patients were 21 percentage points less likely to receive a transplant and tract SES did not appear to account for any of this disparity. Together, Black patients were 14 percentage points more likely to die of the disease and tract SES accounted for 71% of the death disparity ( $p=0.04$ ). **CONCLUSION:** The three main clinical intermediates that drive AML outcomes have different etiologies, whereby structural racism contributes substantially to tumor subtype and induction therapy disparities but does not contribute to transplant disparities.



**Neighborhood differences in associations between nativity and prudent dietary pattern in the ENCLAVE study** Candyce Kroenke\* Candyce Kroenke Rhonda Aoki Brittany Morey Alice Guan Jacqueline Torres Lawrence Kushi Bette Caan Scarlett Gomez Alison Canchola Katherine Lin Samantha Garcia Stacey Alexeeff

**Neighborhood differences in associations between nativity and prudent dietary pattern in the ENCLAVE Study**

Candyce Kroenke, Rhonda Aoki, Brittany Morey, Alice Guan, Jackie Torres, Lawrence H. Kushi, Bette Caan, Scarlett Gomez, Alison J. Canchola, Katherine Lin, Samantha Garcia, Stacey Alexeeff

Background: Residence in co-ethnic neighborhoods may slow acculturation leading to maintenance of healthier diet in immigrants. We examined neighborhood differences in associations between nativity and diet in diverse women with breast cancer.

Methods: We harmonized and pooled data from three cohorts (Pathways, Life After Cancer Epidemiology, and Community Health Initiative) in the ENCLAVE study (R01CA230440, PI: Kroenke), including 6,184 Northern California women diagnosed with invasive breast cancer from 1996-2013. Census-tract-level neighborhood factors from the American Community Survey (socioeconomic status (nSES), percent race, percent immigrants) and Dun and Bradstreet business data (percent of sociocultural institutions that are ethnic-serving) were matched to participant residence. We used multinomial logistic regression to examine self-reported nativity and quartiles of a prudent dietary pattern in 4,895 (3,712 non-Hispanic White (NHW) (312 foreign-born), 725 Asian (530 foreign-born), and 458 Hispanic (178 foreign-born)) women, overall and by neighborhood factors and race.

Results: Foreign-born women were more likely to be represented in the highest quartile (Q4 vs. Q1) of the prudent dietary pattern (odds ratio (OR)=2.47, 95% confidence interval (CI): 1.94-3.14) than US-born women. The association appeared stronger in low (OR=3.45, 95% CI: 1.99-5.97) vs. high (OR=2.22, 95% CI: 1.69-2.92) nSES neighborhoods (p-interaction=0.003) and for high (vs. low) percent Hispanic neighborhoods (p-interaction=<0.001). Patterns were most evident in NHW and Hispanic women. Other statistical interactions by neighborhood variables were nonsignificant. In direct effects analyses, we noted a strong inverse association between high percent Hispanic, but not low nSES, and prudent diet consumption.

Conclusion: Foreign-born women had healthier dietary patterns than US-born women, seen most strongly among those living in low nSES or high percent Hispanic neighborhoods.

**9/11 Evacuation and risk of lung cancer and non-Hodgkin lymphoma among Lower Manhattan residents 14 years after the World Trade Center (WTC) terrorist attacks** Jiehui Li\* Jiehui Li Rebecca Kehm Janette Yung James Cone

It is well known that WTC dust contained carcinogens that have been linked with lung cancer (eg, cadmium, asbestos, PAHs) and non-Hodgkin lymphoma (NHL) (eg, benzene). Yet, among residents who were living in the affected area on 9/11, it is not known if cancer risk is associated with whether they evacuated from their residence as a result of the WTC disaster. To examine the association of evacuation with lung cancer and NHL, we studied 9,706 adult residents who lived near ground zero, enrolled in the World Trade Center Health Registry in 2003-04, and were followed through 12/31/2015. Evacuation was defined as leaving home as a result of the WTC disaster. Cancers diagnosed after enrollment through 2015 were identified from 10 state cancer registries. Adjusted hazard ratios (AHR) were estimated separately for Lung cancer and NHL using Cox models that were stratified by age on 9/11 to control for the PH violation and adjusted for race/ethnicity, gender, smoking status, education, and history of medical condition. We calculated person-years (PY) starting 6 months after enrollment and ending on event date, death date, or 12/31/2015. We also evaluated models with PY starting on 1/1/2007. There were 65 lung cancer (48% were non-Hispanic White) and 39 NHL (79% were NH-White) cases identified as first-time primary cancers during the full follow-up period. Residential evacuation was not associated with lung cancer risk when PY started 6 months after enrollment (AHR=0.60, 95% CI=0.34-1.06). However, when PY started in 2007, evacuation became significantly associated with lower lung cancer risk (AHR=0.45, 0.22-0.90). Limiting sample to NH-White, we found that evacuated residents had significantly lower risk of NHL compared to those not evacuated when PY started 6 months after enrollment (AHR=0.36, 0.18-0.73), as well as when PY started in 2007. Our findings suggest that WTC exposure might have been reduced by evacuation from residence, thus leading to lower risk in both cancers.

**Life's simple 7 and its association with trajectories in depressive symptoms among urban middle-aged adults** May A. Beydoun\* May Beydoun Michael Georgescu Sharmin Hossain Hind A. Beydoun Marie T. Fanelli-Kuczmariski Michele K. Evans Alan B. Zonderman

*Background.* The American Heart Association Life's Simple 7 (LS7) is a composite metric assessing cardiovascular health on a scale of 0-14 comprised of nutrition, physical activity, cigarette use, body mass index, blood pressure, cholesterol and glucose.

*Methods.* Using data from the Healthy Aging in Neighborhoods of Diversity across the Life Span study [n=1,465, Age at visit 1 (v1:2004-2009): 30-66y, 41.7% male, 60.6% African American], we investigated associations of trajectories in depressive symptoms (2004-2017) with Life's simple 7 scores after ~8.6 years follow-up (2013-2017). Analyses used group-based zero-inflated Poisson trajectory models and multiple linear or ordinal logistic regression.

*Results.* Overall and among women, "high declining depressive symptoms" vs. the "low declining" group was associated with 0.67-0.83 lower scores on LS7 total score (P<0.001) in analyses adjusted for age, sex, race and the inverse mills ratio. This effect was markedly attenuated to 0.45-0.62 score-points (P<0.001) upon adjustment for socio-economic factors and to 0.27-0.45 score-points (P<0.010) in fully adjusted analyses. An association between elevated depressive symptoms over time ("high declining" vs "low declining) and LS7 total score was detected among African American adults ( $\beta \pm SE$ :  $-0.281 \pm 0.131$ ,  $p=0.031$ , full model). Moreover, the "high declining" vs. "low declining" depressive symptoms group was associated with a lower score on LS7 physical activity.

*Conclusions.* In summary, poorer cardiovascular health, particularly less-than optimal physical activity, was linked to chronically elevated depressive symptoms, overall and among women.



**Potential mediating effects of uric acid and insulin resistance on the association between sugary drinks intake and continuous risk score for adolescent metabolic syndrome** WU, PEI-WEN\* Pei Wen Wu

The aggregation of cardiometabolic abnormalities predisposes adolescents to cardiovascular disease in adulthood. Sugar-sweetened beverages (SSBs) are a major source of dietary fructose intake. Clinical studies have shown that the process of fructose metabolism involves increased insulin resistance (IR) and uric acid (UA), both of which are associated with metabolic disorders. In this study, we investigated the potential mediating effects of UA and homeostatic model assessment of IR (HOMA-IR) on the association between SSB consumption and continuous risk score of adolescent metabolic syndrome (MetS). We studied 1454 adolescents aged 12-16 years who were randomly selected from 36 junior-high schools in Taiwan. Comprehensive data on sociodemographic factors, dietary and physical parameters, and anthropometric and cardiometabolic outcomes were measured. We used confirmatory factor analysis (CFA) to investigate the underlying structure of MetS and to develop a CFA-based continuous risk score for MetS. Structural equation modeling was used to assess the effect of UA and HOMA-IR on the association between SSB intake and MetS risk score. After controlling for confounding variables, daily intake of >500 mL bottled SSBs and hand-shaken SSBs (hs-SSB) were both associated with higher MetS risk scores. UA and HOMA-IR levels explained 67.9% and 32.1% of the indirect effect of >500 mL/day hs-SSB intake on the MetS risk score, respectively. Our study provides data to illustrate the role and effect of UA and HOMA-IR on the relationship between SSB consumption and clustering of adolescent metabolic dysfunctions.

**Association between uric acid levels and cardiovascular and renal outcomes among incident gout patients in Singapore** wei-yen lim\* Wei-Yen Lim Moses Yidong Lim Hwee Pin Phua Weixiang Lian Htet Lin Htun Kok Ooi Kong Irwin Clement Alphon Wai Hoong Chung Richard Meng Kam Lee Zhi Ying Chie

## Background

We investigate the independent relationship between baseline uric acid level with Acute Myocardial Infarction (AMI), Stroke, End Stage Renal Failure (ESRF) and mortality among individuals with an incident gout diagnosis and seen at the specialist outpatient clinics of an acute care tertiary hospital in Singapore.

## Methods

A retrospective hospital-based cohort of incident gout patients diagnosed between 2007-2017, identified through (i) primary discharge diagnosis, (ii) diagnosis from the Rheumatology specialist clinic and (iii) a combination of patient history at Rheumatology specialist clinic with use of urate lowering therapy or colchicine. Baseline uric acid levels were assessed and the cohort was categorised by quartile of uric acid levels. Outcomes were ascertained through data linkage with the National Registry of Diseases Office. Cox proportional hazards and Weibull regression models were used to estimate HR and 95% CI, with adjustment for age, gender, race, Charlson Comorbidity Index score, and presence of hypertension, hyperlipidaemia and diabetes.

## Results

The final cohort consisted of 2,866 incident gout patients. At the end of follow-up, there were 800 deaths and 362, 218 and 191 incidences of AMI, ESRF and stroke respectively. Using the lowest UA quartile as a reference, being in the highest UA quartile was associated with a significantly increased risk of mortality (HR: 1.49, 95% CI:1.23-1.81) and incident ESRF (HR: 2.82, 95% CI:1.89-4.20), and a non-significantly increased risk of incident AMI (HR:1.33, 95% CI:0.99-1.78). The p for trend for all 3 outcomes was significant (<0.001, <0.001, and 0.033 respectively). No significant association was found between uric acid quartile and risk of incident stroke.

## Discussion & Conclusions

This study found a higher risk of mortality and ESRF in incident gout patients with higher baseline uric acid level.

**The longitudinal change in metabolic syndrome status and its determinants in adolescents**

Yun Chen\* Yun Chen

Insulin resistance-associated pathophysiological mechanisms operate on excessive accumulation of cardiometabolic risk factors and trigger metabolic syndrome (MetS). Nevertheless, MetS may change its condition as adolescents transition into young adulthood. We conducted a study to examine the potential structure of longitudinal change in MetS and investigate its determinants. A community cohort of 1638 adolescents recruited from 3 regions with diverse economic levels was assessed for MetS using 4 diagnostic criteria to evaluate changes in MetS status over a 2.5-year follow-up period. Polytomous logistic regression models were used to assess the association between changes in MetS condition and cardiometabolic determinants. MetS status was unstable between baseline and follow-up. Among adolescents without MetS at baseline, 4.4% had incident MetS at follow-up. Among adolescents with MetS at baseline, 58.3% transformed to normal and 41.7% persisted MetS at follow-up. High systolic blood pressure (SBP) was associated with an increased risk of incident MetS. Low levels of triglycerides, SBP and fasting plasma glucose were associated with an elevated probability of MetS remission. For each MetS component, adolescents with a positive status at baseline had a higher risk of maintaining a positive status after 2.5 years than a negative status at baseline, with elevated triglycerides and central obesity showing a  $\geq 9.3$ -fold risk. Our findings revealed that changes in metabolic risk factors had an influence on the transformation of MetS status in adolescents. This supports early identification and intervention of each risk component of MetS in adolescents.

**The relation of fatty acids with ischemic heart disease and lifespan in men and women using Mendelian randomization** C Mary Schooling\* C Mary Schooling Man Ki Kwok Jie V Zhao

**Background:** Observationally polyunsaturated fatty acids (PUFA) and their sub-species have health benefits compared to saturated fatty acids (SFAs); randomized controlled trials suggest less benefit. To clarify, we assessed the association of major fatty acids and their sub-species with ischemic heart disease (IHD) overall and lifespan sex-specifically, given differing lifespan by sex, using uni- and multi-variable Mendelian randomization.

**Methods:** We obtained strong ( $p\text{-value} < 5 \times 10^{-8}$ ), independent ( $r^2 < 0.001$ ) genetic predictors of fatty acids from genome wide association studies (GWAS) in a random subset of 114999 UK Biobank participants. We applied these genetic predictors to the Cardiogram IHD GWAS (cases=60,801, controls=123,504) and to the FinnGen consortium (cases=31640, controls=187152) for IHD replication and to UK Biobank for lifespan based on parental attained age (fathers=415311, mothers=412937). We used sensitivity analysis and assessed sex differences where applicable.

**Results:** PUFA was positively associated with IHD in Cardiogram (odds ratio (OR) 1.23, 95% confidence interval (CI) 1.05 to 1.44, which replicated in FinnGen (OR 1.31, 95% CI 1.14 to 1.51). PUFA was inversely associated with lifespan in men (-0.76 years, 95% CI -1.34 to -0.17) but not women (0.20, 95% CI -0.32 to 0.70). These associations remained after allowing for MUFA or SFA. Findings were similar for omega-6s and linoleic acid. Independent associations of SFA, MUFA or omega-3s with IHD overall or with lifespan in men and women were limited.

**Conclusion:** PUFAs, via specific subspecies, may contribute to IHD and disparities in lifespan. Sex-specific dietary advice might be a start towards personalized public health and addressing inequities.

**Beta-Blocker Initiation under Dobutamine Infusion: A Target Trial Emulation with Observational Data** Yuichiro Mori\* Yuichiro Mori Kosuke Inoue Hiroyuki Sato Shingo Fukuma**Background**

In patients with advanced heart failure requiring dobutamine infusion, it is usually recommended to initiate beta-blockers after weaning from dobutamine. However, beta-blockers are sometimes initiated concurrently with dobutamine infusion in the real world. It is unknown whether dobutamine weaning should be prioritized over beta-blocker initiation.

**Objectives**

The study investigated the association between initiating beta-blockers under dobutamine infusion and survival outcomes.

**Methods**

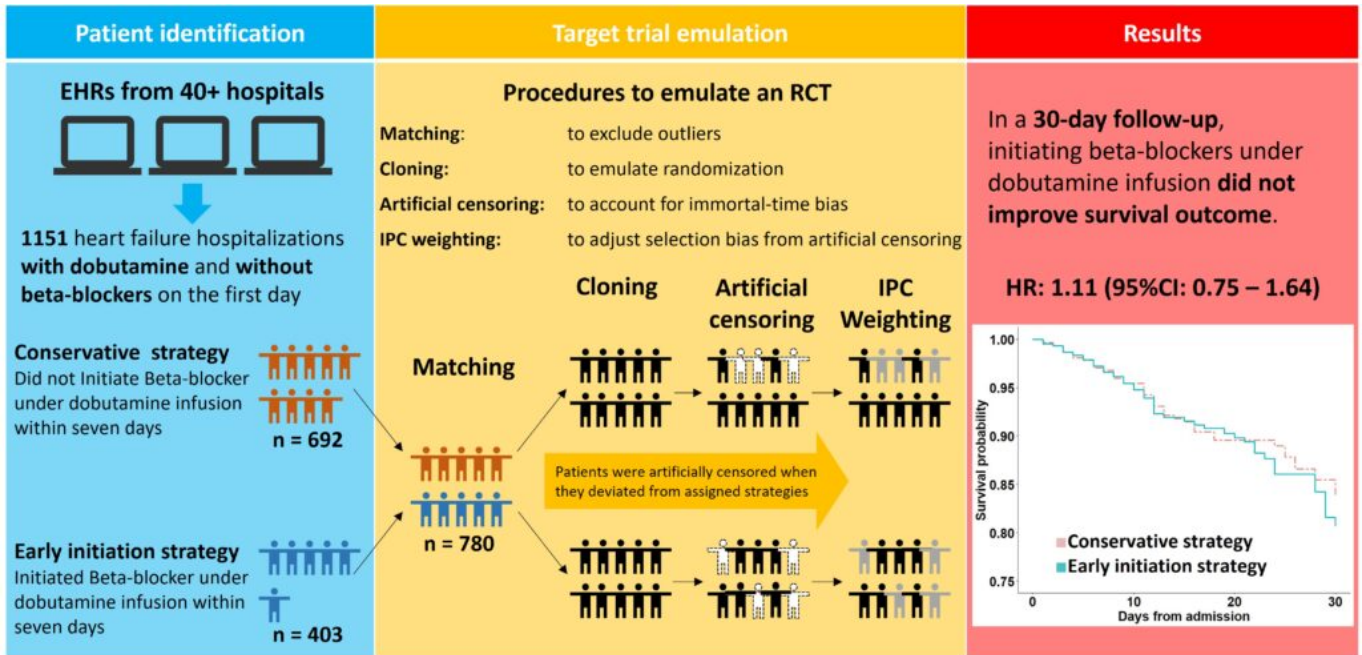
The present observational study with a multicenter diagnosis procedure combination database emulated a pragmatic randomized controlled trial of beta-blocker initiation under dobutamine infusion. First, 1151 patients on dobutamine and not on beta blockers were identified on the day of heart failure admission (day 0). Patients who initiated beta blockers under dobutamine infusion by day 7 (early initiation strategy) were 1:1 matched to those who did not (conservative strategy). Then, the methods of cloning, censoring, and weighting were applied to emulate the target trial. Patients were followed up for 30 days. The primary outcome was all-cause mortality.

**Results**

Among 780 matched patients (median age, 81 years), all-cause in-hospital death was observed in 90 (11.5%) patients. The estimated all-cause mortalities in the early initiation strategy and the conservative strategy were 19.3% (95% confidence interval: 10.6–30.7) and 16.2% (9.2–25.3), respectively (difference: 3.1% [-9.0–16.8]). The results were consistent when we used different grace periods (i.e., 5 and 9) instead of 7 days

**Conclusions**

The present observational study emulating a pragmatic randomized controlled trial found no association between beta-blocker initiation under dobutamine infusion and survival improvement.



**Comparison of Estimated Cardiorespiratory Fitness Among Volunteer Firefighters and Their State-Specific General Population** Nimit Shah\* Nimit Shah Jason Roy Sara A. Jahnke Olivia Wackowski Alberto J. Caban-Martinez Jefferey L. Burgess Judith M. Graber

Objective: Firefighting is a physically demanding occupation requiring optimal cardiorespiratory fitness (CRF), a cardiac health and firefighting performance indicator. Yet suboptimal CRF (< 12 metabolic equivalents (METs)) is often reported among volunteer firefighters, who comprise 65% of the US fire service. This cross-sectional study compares CRF among volunteer firefighters from the Firefighter Cancer Assessment and Prevention Study (CAPS) and their state general population data (Behavioral Risk Factor Surveillance System, BRFSS), by applying a previously published and validated CRF estimation model.

Methods: CAPS volunteer firefighters from 7 states completed a detailed health survey (2019-2022). We estimated CRF using self-reported age, sex, body mass index (BMI), and physical activity. We adapted this model to employed BRFSS respondents. To account for CAPS demographics distribution and the model's estimation limits, for both groups, the inclusion criteria were: 18-65 years old, male, non-Hispanic white, and BMI  $\leq 40$  kg/m<sup>2</sup>. We compared mean CRF among firefighters and their state BRFSS using 95% CIs.

Results: Firefighters (n=419, state range: 19-188) had a mean age of 42 years (95% CI: 40.7, 43.3) and CRF of 10.1 METs (95% CI: 9.9, 10.4). We observed high prevalence for: moderate physical activity (76.6%, 95% CI: 72.5, 80.7), obesity (41.8%, 95% CI: 37, 46.5), and suboptimal CRF (73.7%, 95% CI: 69.5, 78). Compared to their state BRFSS participants, firefighters had higher prevalence of moderate physical activity (CAPS vs. BRFSS range: 71.6-90.3 vs 47.4-64.9%) but similar CRF (range: 9.8-11.4 vs. 10.1-10.5 METs) and obesity prevalence (range: 27.1-33 vs. 26.3-52.2 %), except for 1 state with higher obesity.

Conclusion: High prevalence of suboptimal cardiac health indicators was seen in the CAPS and BRFSS participants which may adversely impact health. For volunteer firefighters, this may also adversely affect the health and safety of the communities they serve.

**Longitudinal Dietary Fluoride Exposures in Association with Cardiometabolic Outcomes in Mexican School-Aged Children**

Sandra India Aldana\* Sandra India Aldana Elena Colicino  
Alejandra Cantoral Preciado Andrea A. Baccarelli Martha María Téllez Rojo Maricruz Tolentino  
Robert O. Wright Damaskini Valvi

**Background/Aim**

Fluoride intake is ubiquitous and constitutes a long-term exposure during childhood. Experimental research suggests fluoride-induced lipid disturbances that affect cardiometabolic health; however, epidemiological studies have been scarce and mostly cross-sectional. We evaluated associations between repeated dietary fluoride exposure and cardiometabolic outcomes in Mexican children.

**Methods**

Dietary-derived fluoride measurements from food frequency questionnaires were obtained at ages 4, 6 and 8 years for ~500 children from the Programming Research in Obesity, Growth, Environment and Social Stressors (PROGRESS) cohort. Using covariate-adjusted linear mixed-effects and linear regression models, we assessed the associations of fluoride exposure ( $\log_2$ -transformed and in tertiles) on cardiometabolic risk components measured at ages 4, 6 and/or 8, including body fat (%), lipids (total cholesterol, high and low-density lipoprotein [HDL and LDL in mg/dL] and  $\log$ -transformed triglycerides), glucose, and age- and sex-adjusted z-scores of body mass index (BMI), waist circumference (WC), and blood pressure (BP). We also calculated a cardiometabolic risk score using the z-score sum of WC, BP, glucose, and triglycerides-to-HDL ratio.

**Results**

A doubling of fluoride intake at age 4 was associated with an annual increase in triglycerides [ $\beta=2.08$  (95% CI: 0.43, 3.76)], body fat [ $\beta=0.20$  (95% CI: 0.01, 0.38)], total cholesterol [ $\beta=1.39$  (95% CI: 0.46, 2.33)], and LDL [ $\beta=0.85$  (95% CI: 0.00, 1.69)] between ages 4-8 years. At age 6, fluoride intake was associated with higher HDL [ $\beta$  per-fluoride-doubling=4.25 (95% CI: 1.51, 7.00)]. Cross-sectional analyses at age 8 indicated that higher tertiles of fluoride exposure were associated with higher z-BMI (p-trend=0.025), triglycerides (p-trend=0.012), glucose (p-trend=0.037), and cardiometabolic risk score (p-trend=0.044). Some of these associations were stronger in boys compared to girls (p-interaction<0.05).

**Conclusion**

Dietary fluoride exposure at ages 4 and 8 years was associated with adverse cardiometabolic outcomes in school-aged children. Further longitudinal studies are needed to corroborate these findings and associations at later ages.



**The associations of genetically predicted alanine with coronary artery disease and its risk factors: a Mendelian randomization study** Xin Huang\* Xin Huang Jie V. Zhao

**Background** Alanine is an amino acid commonly used as nutritional and exercise supplement and plays a key role in glucose-alanine cycle. Observationally, alanine is associated with higher risk of coronary artery disease (CAD) and impaired lipid profile. However, large randomized controlled trials testing its health effects are lacking.

**Objective** Using Mendelian randomization to assess the unconfounded associations of alanine with CAD and its risk factors.

**Methods** We applied genetic variants that were strongly associated with plasma level of alanine to the largest available genome-wide association studies (GWASs) of CAD (143,745 cases and 622,308 controls in total), diabetes (97,321 cases and 777,137 controls in total), blood glucose, lipids (LDL-cholesterol, HDL-cholesterol, triglycerides, total cholesterol and apolipoprotein B) (more than 0.5 million Europeans), blood pressure and body mass index. Given the potential sex disparity, we conducted sex-specific analysis in the UK Biobank. We used inverse variance weighting in the main analysis, and weighted median, MR-PRESSO, and MR-RAPS in the sensitivity analysis.

**Results** Genetically predicted alanine was not associated with the risk of CAD, but associated with higher risk of diabetes (OR:1.33, 95%CI:1.03-1.72), glucose level (0.10, 95%CI:0.02-0.18), LDL-cholesterol (0.10, 95%CI:0.05-0.15), triglycerides (0.27, 95%CI:0.13-0.42), total cholesterol (0.17, 95%CI:0.09-0.24), apolipoprotein B (0.03, 95%CI:0.01-0.05), and blood pressure (1.17, 95%CI:0.31-2.04 for systolic BP; 0.97, 95%CI:0.49-1.45 for diastolic BP) overall. Alanine may have sex-specific effects on lipid profile, it increased HDL-cholesterol in men but not in women, while increased total cholesterol in women but not in men.

**Conclusions** Our study suggests alanine may not be beneficial for cardiovascular health. The associations of alanine with lipid profiles appear to be more pronounced in women. Further studies are needed to clarify the mechanisms.

**LATEBREAKER**

Cardiovascular

**Intensified Systolic Blood Pressure Control May Lower Left Ventricular Hypertrophy in Children after Kidney Transplantation: a Longitudinal Investigation of 4C-T Study** Rizky Indrameikha Sugianto\* Rizky Indrameikha Sugianto Carl Grabitz Nima Memaran Karolis Azukaitis Anke Doyon Daniela Thurn-Valsassina Franz Schaefer Bernhard M. W. Schmidt Anette Melk

## Introduction

About 40% of children demonstrate left ventricular hypertrophy (LVH) one year after kidney transplantation (KTx). LVH is a strong predictor for cardiovascular mortality. Blood pressure (BP) is the main determinant of left ventricular mass early after KTx. Specific recommendations on BP goals in pediatric KTx recipients based on prospective data are currently not available. We aimed to assess the effect of BP control expressed by the cumulative exposure of systolic BP on the dynamics of left ventricular mass index (LVMI).

## Methods

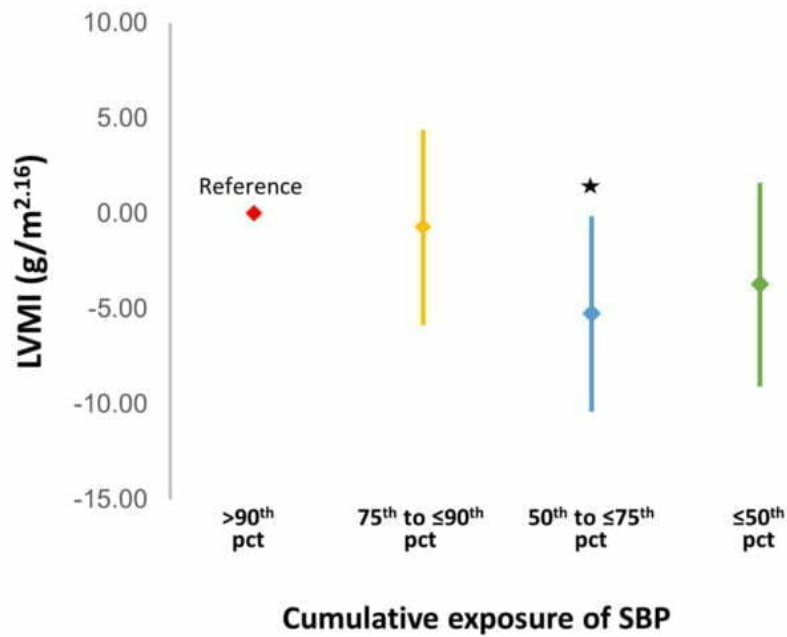
Ninety-six children (64 males)  $\geq 9$  months post-KTx from the 4C study ([4C - Kidney Disease Study: About 4C \(4c-study.org\)](#)) were included. BP and echocardiographic LVMI assessments were performed every 6 and 12 months, respectively. Only patients with two visits or more were included (median/maximum follow-up time of 2.5/7 years). The cumulative exposure of systolic BP z-scores was calculated for each visit after the baseline as time-averaged area under the curve of BP z-scores (cAUC-SBP). cAUC-SBP was then translated and categorized into percentiles of  $\leq 50^{\text{th}}$ ,  $50^{\text{th}}$  to  $\leq 75^{\text{th}}$ ,  $75^{\text{th}}$  to  $\leq 90^{\text{th}}$ , and  $> 90^{\text{th}}$ . Linear mixed regression model of LVMI ( $\text{g/m}^{2.16}$ ) for the exposure of cAUC-SBP adjusted for time since baseline, age, sex, estimated glomerular filtration rate, body mass index z-score, LVMI at baseline was performed.

## Results

At baseline, LVMI was  $49.7 \pm 12.7 \text{ g/m}^{2.16}$  and 64% (n=61) of patients showed LVH. Compared to patients with cAUC-SBP of  $> 90^{\text{th}}$  percentile, those with cAUC-SBP of  $50^{\text{th}}$  to  $\leq 75^{\text{th}}$  showed an LVMI reduction of  $-5.24 \text{ g/m}^{2.16}$  (p=0.007) and those with  $\leq 50^{\text{th}}$  showed a tendency of reduction ( $\beta = -3.70 \text{ g/m}^{2.16}$ ; p=0.067). Patients with cAUC-SBP of  $75^{\text{th}}$  to  $\leq 90^{\text{th}}$  did not show a significant reduction (Fig. 1).

## Conclusion

Continuous exposure to systolic BP values below the  $75^{\text{th}}$  percentile may lead to regression of LVH suggesting a stricter BP control in pediatric KTx recipients. This calls for evidence from a randomized controlled trial.



★ Significantly different from the reference

Both models were adjusted for sex, time since baseline, LVMI at baseline, and age, body mass index z-score, estimated glomerular filtration rate at respective visits

Figure 1. Estimates (95% CI) of LVMI depending on the categories of cumulative exposures to systolic BP. Each category was compared to the reference category ( $\geq 90^{\text{th}}$  percentile).

**Networked wealth and mortality in the Agincourt Health and Demographic Surveillance System 2009 - 2018** Keletso Makofane\* Keletso Makofane Eric Tchetgen Tchetgen Mary Bassett Lisa Berkman

## Background

Though wealth embedded in social networks appears to shape health over and above the wealth held by individuals, past epidemiologic studies have not assessed this causal relationship directly. Drawing on auto-g-computation - a newly-developed method for causal inference in networks - we examined the spillover effect of household wealth on mortality among family members.

## Methods

We analysed cohort data collected from 2009 to 2018 by the Agincourt Health and Demographic Surveillance system (AHDSS) located in Mpumalanga, South Africa. The AHDSS conducts an annual survey of about 21 000 households, collecting information on births, deaths, migrations, family relationships, and wealth. Constructing a sociocentric social network using these data, we estimated the Average Total Effect (ATE) of household wealth on deaths, decomposing it into an Average Direct Effect (ADE) and Average Spillover Effect (ASE). We estimated these quantities separately for all deaths, deaths among children (<5 years old), premature deaths (among ages 15-59), and deaths among elders (60+).

## Results

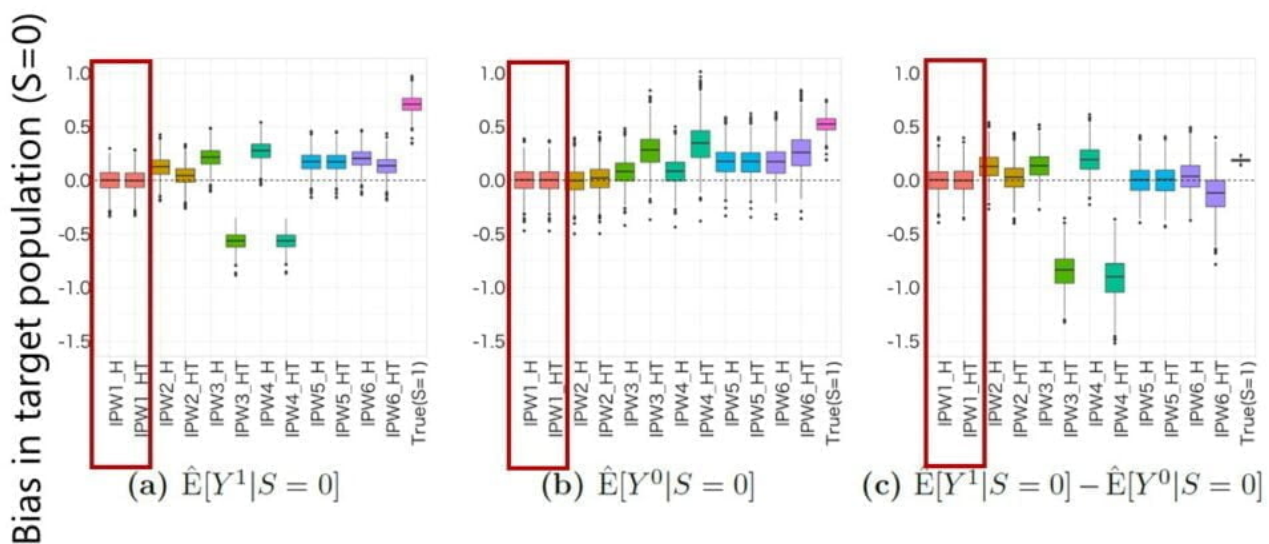
Over the study period, 8750 individuals died. Overall, a one standard deviation increase in household wealth led to an ATE of -0.61% (95% CI: -0.74 to -0.48,  $P < 0.001$ ), an ADE of -0.53% (95% CI: -0.63 to -0.42,  $P < 0.001$ ) and an ASE of -0.08% (95% CI: -0.18 to 0.01,  $P = 0.075$ ). For premature mortality, these effect estimates were -0.37% (95% CI: -0.47 to -0.26,  $P < 0.001$ ), -0.29% (95% CI: -0.37 to -0.21,  $P < 0.001$ ), and -0.08% (95% CI: -0.15 to 0.00,  $P = 0.038$ ), respectively.

## Conclusions

Results provide evidence for the protective effect of household wealth on premature mortality across family relationships.

**Transporting causal effects estimated from observational studies with preexisting exposures** Tomohiro Shinozaki\* Tomohiro Shinozaki Yuki

Transporting the effects of an exposure from one study population to another target population provides insight into the practical public health implications of interventions on said exposure. This transportation is often derived from data obtained through randomized trials, yet may also necessitate the utilization of observational studies. Regardless of the study design, a fundamental assumption for transportability is that outcome predictors are distributed similarly across the study and target populations, and are measured in both groups otherwise. Although the major difference between randomized and observational studies is the need to adjust for confounding, more nuanced issues arise. First, observational studies typically compare already measured exposures, which may affect participation in the study sample. Second, the observational study additionally collects information on confounders, which are typically not fully measured in a target population. In these settings, the distributions of confounders only measured in a study population vary across study and target populations. This can result in the failure of common methods for transporting results from randomized trials, such as g-computation and inverse probability weighting (IPW), due to incomplete measurement of confounder data in the target population. To address this issue, we derive the additional identifiability conditions and propose a modified IPW estimator that incorporates sampling weights into estimates of exposure propensity scores. Through simulation studies comparing various IPW methods, we demonstrate that our proposed estimator yields unbiased estimates even when sampling probabilities are dependent on exposure and confounders, while existing methods produced biased results (Figure). Thus, the transportation of effects estimated from observational studies involving preexisting exposures necessitates a more thorough examination beyond simple adjustment for confounding factors.



**Figure.** Simulation results of proposed (IPW1) and existing (IPW2 to 6) inverse probability weighting estimators for transportation. “True (S=1)” means the true effects in study samples.

**Addressing the longitudinal component of surgical interventions in randomized control trials** Chelsea Messinger\* Chelsea Messinger Kerollos Wanis Arin Madenci

Investigators conducting causal inference research on surgical interventions have typically ignored pre- and post-surgical aspects of interventions when specifying treatment strategies. Doing so may limit the usefulness of effect estimates to decision makers since, in reality, there are usually longitudinal post-surgical or surgery-adjacent components of treatment that affect patient outcomes. This is true for both randomized and observational studies comparing surgical interventions, and for those comparing surgical with non-surgical treatments. Leaving these longitudinal components unspecified and failing to measure adherence to them might result in lack of transportability of counterfactual mean estimates and/or misinterpretation of effect estimates.

To illustrate this, we use the example of rotator cuff tear, for which physical therapy (PT) is a core part of treatment that affects functional outcomes. Consider a randomized trial comparing surgical repair with conservative management for functional improvement. We describe four scenarios: one where both prescribed PT course and PT adherence are the same between treatment groups, one where PT course is the same but adherence differs, one where PT course differs but adherence is the same, and one where both differ. Under each scenario, there are unique challenges for interpreting effect estimates and transporting these estimates to clinical practice, particularly if PT course is not specified and/or adherence is not measured.

We suggest three recommendations for improving causal effect estimation of surgical interventions in trials. First, investigators should fully describe the surgical as well as pre- and post-surgical interventions in the trial. Second, investigators should report adherence to both assigned surgical treatment and post-treatment interventions. Finally, investigators should consider surgery-adjacent components of treatment when computing estimates of risk under a specified adherence level.

**Association between Breast Cancer and Dementia among the Population in Taiwan: A Nationwide Population-Based Retrospective Cohort Study** Yen-Chun Chou\* YEN-CHUN CHOU  
Yu-Ching Chou Sui-Lung Su

**Background:** Breast cancer (BC) is the most commonly occurring malignancy in women. There is increasing evidence show a significant inverse association between dementia and cancer. Nevertheless, only limited study population and without focusing on specific cancer in previous studies. Thus, we aimed to identify the incidence of dementia with breast cancer in population-based Taiwanese cohort.

**Methods:** The cases were identified as the first recorded diagnosis of breast cancer (ICD-9-CM codes: 174) between 1996 and 2013 from Taiwan's National Health Insurance Research Database (NHIRD). Each selected case of breast cancer was compared with sex-matched and age-matched comparison subjects. The first diagnosis of dementia (ICD-9-CM codes: 290, 292, 294, 331) until the end of 2013 was tracked in both groups. Estimated the hazard ratios (HRs), adjusted hazard ratios (aHRs), and 95% confidence intervals (CIs) for risk of dementia in the breast cancer group and comparison group using Cox proportional hazard models. All of the statistical analyses were performed using SAS statistical software, version 9.4.

**Results:** The incidence of breast cancer was 64.41 among dementia patients per 10,000 person-years. The incidence rate was 0.46 among men and 10.98 among women per 10,000 person-years. The incidence rate of BC was higher in women. After stratifying age into 5 groups, we found that the incidence rate of BC per 10,000 person-years was 2.46 in 20-29 years old, 4.39 in 30-39 years old, 9.38 in 40-49 years old, 8.12 in 50-59 years old and 5.34 in  $\geq 60$  years old. Patients have highest incidence rate of BC when age is over 60 years old. Also, incidence rate of BC was 7.56, 5.88 and 5.55 by visiting 0 time,  $\leq 3$  times and  $> 3$  times in clinical visits respectively.

**Conclusion:** The prevalence of dementia had limited influence on the breast cancer patients. Dementia might be a protective factor in patients with breast cancer.

**Inconsistent consistency: evaluating the well-defined intervention assumption in applied epidemiologic research** Sharon Schwartz\* Jerzy Eisenberg-Guyot Katrina L. Kezios Seth J. Prins

**Introduction:** For many researchers, satisfying the well-defined intervention (WDI) assumption is required for causal inference. However, no studies have systematically evaluated the assumption's treatment in the applied epidemiologic literature. Thus, we assessed how researchers using g-methods interpreted and applied the WDI assumption in epidemiologic studies. **Methods:** We reviewed observational epidemiologic studies that: 1) used g-methods in a primary study aim, and 2) that were published from 2000-2021 in epidemiology journals with the six highest 2020 impact factors. First, among 151 included studies, two reviewers assessed if authors aimed to estimate an intervention effect or a different estimand. Next, among studies that aimed to estimate an intervention effect, the reviewers assessed if authors: 1) specified a WDI supported by their data, 2) discussed key aspects of the WDI assumption, like consistency, and 3) interpreted their findings as corresponding to an intervention effect. **Results:** Sixty-four percent of studies stated an explicit causal contrast, but just 21% stated their contrast in terms of an intervention (i.e., aimed to estimate an intervention effect). Of those that aimed to estimate an intervention effect, almost none (10%) stated *how* their exposure would be intervened upon or changed, although for most (68%), the *how* likely mattered for consistency (i.e., for the intervention's effect on the outcome). Moreover, of studies that aimed to estimate an intervention effect, just 61% discussed the consistency assumption, and just 45% interpreted their findings as corresponding to an intervention effect. Finally, just 35% of studies that aimed to estimate an intervention effect were determined to have a WDI. **Discussion:** Our review found inconsistency between prevailing guidance regarding satisfying the WDI assumption and researchers' operationalization of it in practice, with studies aiming to estimate an intervention effect rarely specifying a WDI.



**Height as a protective factor against Alzheimer's disease: a Mendelian randomization****analysis** Jack Taylor\* Jack Taylor Kristine Yaffe Shea J Andrews

**Introduction:** Meta analyses have identified height, a trait influenced by both genetic and environmental factors in early life, as a risk factor associated with Alzheimer's disease. Here we use Mendelian randomization (MR) analysis to further investigate this causal relationship.

**Methods:** Two sample MR was used to obtain causal estimates of height on AD, using GWAS summary statistics from the GIANT consortium and the International Genomics of Alzheimer's Project. Independent ( $r^2 < 0.001$ , 10mb window) genome-wide significant single nucleotide polymorphisms ( $p < 5 \times 10^{-8}$ ) were included as genetic instruments ( $n = 770$ ). MR methods included inverse variance weighted (IVW), weighted median, weighted mode, and MR Egger. Cochran's Q test was used to test for heterogeneity; the MR-Egger intercept for pleiotropy; and Radial MR to identify individual variants that were outliers.

**Results:** Genetically predicted height was associated with a reduced risk of AD (IVW OR [95% CI]: -0.11 [-0.16, -0.05],  $p = 6.7e^{-5}$ ), however there was evidence of heterogeneity and pleiotropy. After outlier removal ( $n = 2$ ), height remained significantly associated with reduced risk of AD (IVW OR [95% CI]: -0.12 [-0.17, -0.07],  $p = 6.3e^{-6}$ ), with sensitivity analyses showing the same direction of effect.

**Discussion:** Genetically predicted height was protective against AD. Potential mediating factors may explain this effect. Future analyses will incorporate multivariate MR methods to evaluate potential mediators, such as intracranial volume or nutritional intake.

Children's health: autism spectrum disorders

**Association between prenatal air pollutant exposure and autism spectrum disorders in young children: a matched case-control study in Canada** Hwashin Hyun Shin\* Hwashin Hyun Shin Malia SQ Murphy Kasim E Abdulaziz Éric Lavigne Erica Erwin Yanfang Guo Alysha LJ Dingwall-Harvey David Stieb Mark C Walker Shi-Wu Wen

**Background:** The direction and magnitude of association between maternal exposure to ambient air pollutants across gestational windows and offspring risk of autism spectrum disorders (ASD) remains unclear. We sought to evaluate the time-varying effects of prenatal air pollutant exposure on ASD.

**Methods:** We conducted a matched case-control study of singleton term children born in Ontario, Canada from 1-Apr-2012 to 31-Dec-2016. Provincial birth registry data were linked with applied behavioural analysis services and ambient air pollutant datasets to ascertain prenatal exposure to nitrogen dioxide (NO<sub>2</sub>), ground-level ozone (O<sub>3</sub>), particulate matter (PM<sub>2.5</sub>), and ASD diagnoses. Covariate balance between cases and controls was established using coarsened exact matching. Conditional logistic regression was used to assess the association between prenatal air pollutant exposure and ASD. Distributed lag non-linear models (DLNM) were used to examine the effects of single-pollutant exposure by prenatal week. Sensitivity analyses were conducted to assess the impact of study design on the observed findings.

**Results:** The final sample included 1,589 ASD cases and 7,563 controls. Compared to controls, cases were more likely to be born to mothers living in urban areas, delivered by Caesarean section, and assigned male sex at birth. NO<sub>2</sub> was a consistent and significant contributor to ASD risk after accounting for co-exposure to O<sub>3</sub>, PM<sub>2.5</sub> and covariates. The odds ratio per interquartile range increase was 2.1 (95%CI 1.8-2.3) pre-conception, 2.2 (2.0-2.5) for the 1st trimester, 2.2 (1.9-2.5) for the 2nd trimester, and 2.1 (1.9-2.4) for the 3rd trimester. In contrast, findings for O<sub>3</sub> and PM<sub>2.5</sub> with ASD were inconsistent. Findings from DLNM and sensitivity analyses were similar.

**Conclusions:** Exposure to NO<sub>2</sub> before and during pregnancy was significantly associated with ASD in offspring. The relationship between prenatal O<sub>3</sub> and PM<sub>2.5</sub> exposure and ASD remains unclear. Further investigation into the combined effects of multi-pollutant exposure on child neurodevelopment is warranted.

**Biomarkers of glucose homeostasis as mediators of the relationship of body mass index and waist circumference with COVID-19 outcomes among postmenopausal women:**

**Women's Health Initiative** Hind A. Beydoun\* Hind Beydoun Ted K.S. Ng May A. Beydoun Aladdin H. Shadyab Su Yon Jung Christy Costanian Nazmus Saquib Farha S. Ikramuddin Kathy Pan Alan B. Zonderman JoAnn E. Manson

**Background & Aims:** Systematic reviews, meta-analyses and Mendelian randomization studies suggest that cardiometabolic diseases may be associated with COVID-19 risk and prognosis, with evidence implicating insulin resistance (IR) as a common biological mechanism. As driving factors for IR, we examined body mass index (BMI) and waist circumference (WC) among postmenopausal women in association with COVID-19 outcomes (positivity and hospitalization), and the role of glucose homeostasis as a mediator of this relationship.

**Methods:** Associations of BMI and WC at baseline (1993-1998) with COVID-19 outcomes collected at Survey 1 (June-December, 2020) and/or Survey 2 (September-December, 2021) were evaluated among 42,770 Women's Health Initiative (WHI) participants (baseline age: 59.36 years) of whom 16,526 self-reported having taken  $\geq 1$  COVID-19 test, with 1,242 reporting  $\geq 1$  positive COVID-19 test and 362 reporting  $\geq 1$  COVID-19 hospitalization. We applied logistic regression and causal mediation analyses to sub-samples with available fasting biomarkers of glucose homeostasis (glucose, insulin, Homeostatic Model Assessment for Insulin Resistance, Homeostasis Model Assessment for  $\beta$ -cell function, Quantitative Insulin-sensitivity Check Index, Triglyceride-Glucose index (TyG)) at baseline, whereby 57 of 759 reported COVID-19 test positivity and 23 of 1,896 reported COVID-19 hospitalization.

**Results:** In fully adjusted models, higher BMI, WC and TyG were associated with COVID-19 test positivity and hospitalization. Glucose concentrations mediated associations of BMI and WC with COVID-19 positivity, whereas TyG mediated BMI and WC's associations with COVID-19 hospitalization.

**Conclusions:** Obesity and central obesity markers collected an average of 24 years prior were associated with COVID-19 outcomes among postmenopausal women. Glucose concentration and TyG partly mediated these associations.

**Prevalence and predictors of COVID-19 stigma within a population-based sample of adults with COVID-19 in Michigan** Soomin Ryu\* Soomin Ryu Samhita Chaubal Paula Guro Elizabeth J. King Robert Orellana Nancy L. Fleischer Jana L. Hirschtick

**Background:** Many individuals with COVID-19 face stigmatization, even after recovery. Growing evidence suggests that COVID-19 stigma is negatively associated with health outcomes. However, few studies have examined who is at risk of experiencing COVID-19 stigma.

**Methods:** Using a population-based probability sample of adults with confirmed SARS-CoV-2 infection in Michigan prior to March 1, 2022, we examined the prevalence and predictors of COVID-19 stigma. COVID-19 stigma was measured by respondents answering affirmatively to any of the three items due to people thinking they might have COVID-19: “you were treated badly,” “people acted as if they were scared of you,” and “you were threatened or harassed.” Potential predictors included sex, age group, race/ethnicity, income, education, employment status, smoking status, body mass index, preexisting conditions, hospitalization, and COVID-19 symptom severity. We conducted a modified Poisson regression with robust standard errors to estimate associations between potential predictors and COVID-19 stigma.

**Results:** 38.1% of respondents (n=2,696) reported experiencing COVID-19 stigma. Adults who were female (aPR:1.22, 95% CI:1.10-1.36) versus male, 18-34 (aPR:1.39, 95% CI:1.11-1.74) or 35-44 years old (aPR:1.63, 95% CI:1.29-2.05) versus aged 65 or over, non-Hispanic Black (aPR:1.18, 95% CI:1.00-1.40) versus non-Hispanic White, had severe COVID-19 symptoms (aPR:1.23, 95% CI:1.11-1.37) versus asymptomatic/mild symptoms, and had a preexisting psychological/psychiatric condition (aPR:1.29, 95% CI:1.13-1.48) versus not were more likely to experience COVID-19 stigma.

**Conclusion:** Continuing to monitor for stigma following COVID-19 illness, especially in already vulnerable populations, may provide useful insight for public health anti-stigma campaigns.

**Modeling the impact of masking as a standalone intervention during a COVID-19 outbreak**

Alice E. Arcury-Quandt\* Alice E. Arcury-Quandt Harry Hochheiser Catherine L. Haggerty Mark S. Roberts Marnie Bertolet

Wearing a face mask or cloth face covering is an effective way to prevent COVID-19 transmission. However, the effectiveness of masking as a standalone intervention is unknown. Mask effectiveness studies have either been controlled laboratory experiments or population studies that cannot separate the effect of masking from control measures, such as stay-at-home orders. Estimating the isolated impact of masking will help guide decision making during future COVID-19 outbreaks.

We are developing an agent-based model to simulate a hypothetical future outbreak of a COVID-19 variant in an urban county in the US. The effectiveness of masking to reduce the probability of becoming infected and transmitting infection will be implemented stochastically. Based on published data, effectiveness will vary by 20%-70%, representing different mask types and imperfect or inconsistent use. The population will be segmented into healthcare workers, service industry workers, and K-12 educators, based on Bureau of Labor Statistics data; students using empirical data; and all others. Mask use will vary from 0%-100% in increments of 10% for all population segments. The model will be run for each combination of mask use and population segment 1,000 times. The distributions of cases, hospitalizations, and deaths for these combinations will be assessed to determine the impact of masking by rate of uptake. Masking levels will also be compared to published masking behaviors in prior COVID-19 outbreaks.

Using these results, we will better understand whether masking, in the absence of other strategies, is a viable method for controlling COVID-19 outbreaks and if the rate of masking required to end an outbreak approaches published rates. We will also explore the extent to which masking in schools or among healthcare or service industry workers affects population-level transmission. This information can be used by decision makers to guide mask mandates or recommendations in future outbreaks.

**Impact of the first year of the COVID-19 pandemic on cigarette smoking among New Yorkers overall and by race/ethnicity and employment status** Muhammad Salim\* Muhammad Salim Levi Waldron Elizabeth Kelvin

**Background:** Findings on the impact of the COVID-19 pandemic on cigarette smoking have differed, with some reporting increases and others decreases in smoking, suggesting that context is important.

**Methods:** We assessed the impact of the first year of the COVID-19 pandemic on cigarette smoking among New York City (NYC) residents overall and if this impact varied by race/ethnicity and employment status. We used 2020 (pandemic year 1) and 2019 (pre-pandemic reference) NYC Community Health Survey data to compare current and heavy smoking, using logistic regression, and the average number of cigarettes smoked per day, using linear regression, by year. We tested for interaction between year\*race/ethnicity and year\*employment, and stratified models when interaction was significant. Analyses were adjusted for complex sampling and weighted to the NYC population.

**Results:** Prevalence of heavy smoking (aOR=0.7, p=0.04) and the average number of cigarettes smoked per day ( $a\beta=-0.9$ , p<0.001) decreased in 2020 compared to 2019. The decrease in prevalence of current cigarette smoking (any quantity) was not statistically significant (aOR=0.9, p=0.22). However, we found significant interaction between employment and year for current smoking (interaction p-value range: 0.04-0.41). After stratifying on employment status, we found that being a current smoker decreased in 2020 among those actively employed (OR=0.8, p=0.11) and unemployed (OR=0.6, p=0.01) but increased among those not in the work force (OR=1.2, p=0.16) and did not change among those self-employed (OR=1.0, p=0.88).

**Conclusions:** Heavy smoking decreased overall in the first year of the COVID-19 pandemic in NYC but this pattern varied by employment status, which may explain why previous studies varied in the direction of the association they found.

**Did COVID-19 Bring Changes to Inter-Unit Patient Transfer Patterns within Hospitals?** Eric Lofgren\* Kaniz Madhobi Ananth Kalyanaraman Deverick Anderson Rebekah Moehring Elizabeth Dodds-Ashley

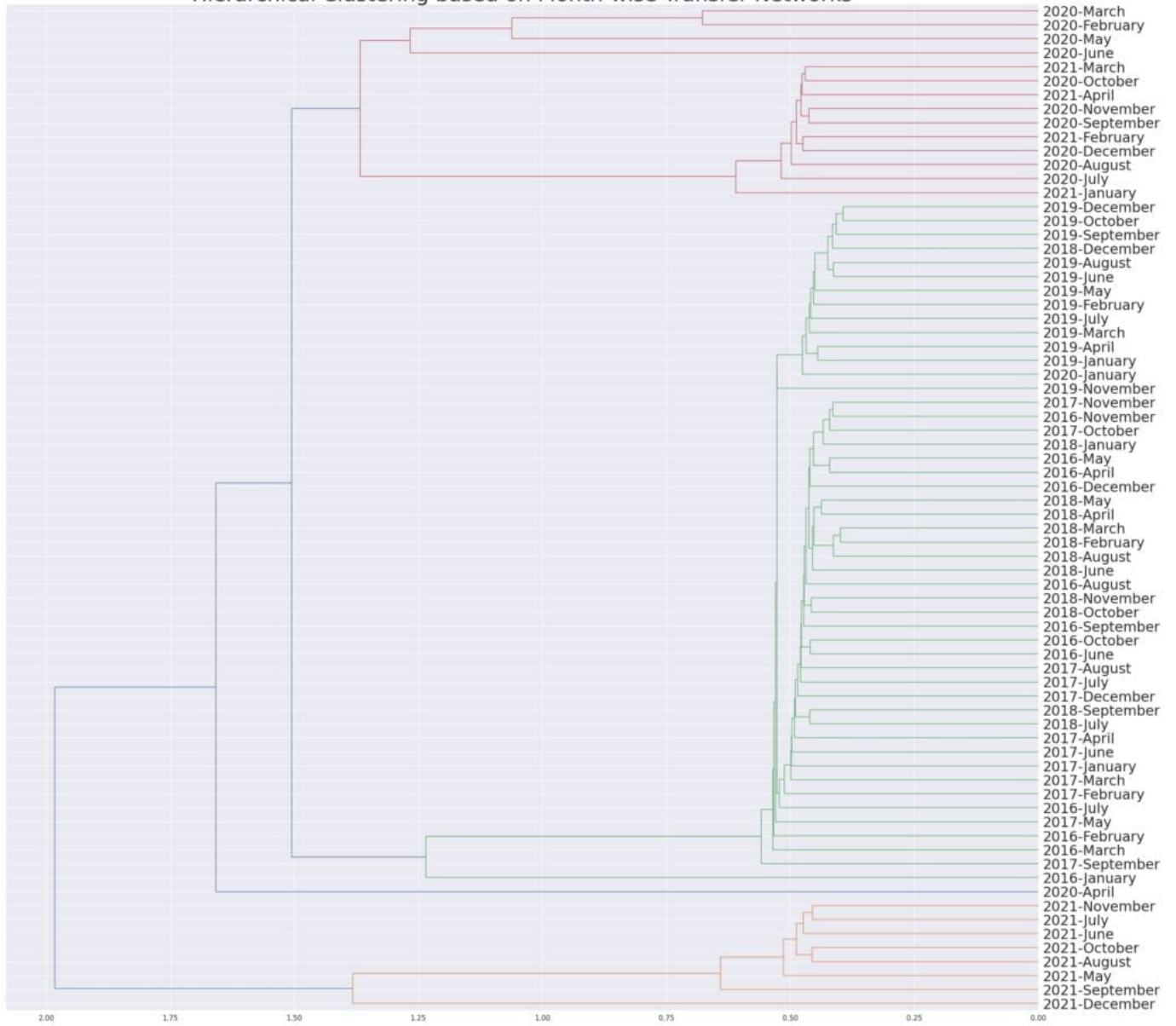
**Background:** To understand how the COVID-19 pandemic affected healthcare settings, we evaluated unit to unit transfer patterns of patients within the Duke University Hospital between January-2016 to December-2021. We evaluated monthly inter-unit transfer patterns to test whether these patterns vary between pre-pandemic vs. pandemic phases.

**Methods:** In our transfer network, each node represents a unit and an edge between nodes represents patient transfers between two units, yielding 36 nodes. Each edge is assigned a normalized weight based on the number of patients moved between the units. For the 6-year period we constructed 72 monthly transfer networks. Then we computed an L2-based distance between every pair of networks and subsequently clustered those networks using the distance score.

**Results:** We found one large cluster encompassing all the pre-pandemic period from January-2016 to January-2020 while the pandemic networks were grouped into a number of smaller clusters. We observed a small cluster containing February and March of 2020 while April-2020 was clustered alone. May and June of 2020 grouped together and from July-2020 to April-2021 we see a second large cluster. Finally May to December-2021 was clustered together.

**Conclusion:** This study quantifies the impact of the pandemic on patient transfers within the hospital. Our results suggest that COVID-19 radically altered intra-hospital patient transfers, and the appearance of a second “pandemic period” cluster from May to December-2021 suggests that while the healthcare system has left the acute period of early 2020 behind, it has not yet returned to pre-pandemic norms. Patient transfer networks represent an underused source of automatically collected hospital data. Further analysis might help to determine more optimal strategies for healthcare systems adapting to emergencies, suggest preemptive actions that might be taken for units that are susceptible to disruption due to public health emergencies.

### Hierarchical Clustering based on Month-wise Transfer Networks





**Covid-19 case fatality rates higher among Arab Americans compared to non-Hispanic whites, non-Hispanic blacks, Hispanics and Asians** Florence Dallo\* Florence Dallo Tiffany Kindratt Randell Seaton Julie Ruterbusch

Covid-19 case-fatality rates (CFR) have been estimated for non-Hispanic blacks, Asians, Hispanics and non-Hispanic whites. According to the federal government, non-Hispanic whites include anyone from Europe, North Africa or the Middle East (from hereafter referred to as Arab Americans). Arab Americans, for example, have not been included in the discourse. Two major reasons Arab Americans have been omitted are: Arab Americans are categorized as non-Hispanic white by the federal government; therefore, it is not possible to identify Arab Americans in health records and establish a valid numerator or denominator. To overcome this barrier, and in effort to better understand the burden of morbidity and mortality among Arab Americans, our team and other investigators have used place of birth or ancestry information from national data or merged surname lists with state or hospital data. A recently published article that used the surname list with state data showed that Covid-19 cases were two to three times higher among Arab Americans than any other group in Michigan. The current study estimates age-specific and sex-adjusted CFR for Arab Americans, non-Hispanic whites, non-Hispanic blacks, Hispanics and Asians 18 years of age or older. We used data from March 1, 2020 to July 30, 2021 from Michigan Vital Records and the American Community Survey (ACS) for the numerators in this study. This dataset was merged with an Arab and Chaldean (Iraqi Catholic) surname database and put through an algorithm to identify probable Arab ancestry. ACS data were used for the population size denominators in this study. The CFR increased with age for every racial and ethnic group. For individuals between the ages of 60-79, CFR were 10.01 for NH Blacks, 8.76% for Asians, 6.02 for Hispanics, 5.26 for Arab Americans and 3.90 for NH Whites. For those 80 years of age or older, Arab Americans had higher CFR (30.72%) compared to any other racial or ethnic group. This study suggests that the severity of Covid-19 is higher among Arab Americans compared to other groups. Targeted intervention and prevention efforts need to be designed, implemented and evaluated to ensure that Covid-19 does not continue to disproportionately affect the minority, immigrant and underserved population of Arab Americans.

**Association between sedentary behavior and subjective stress in university students during the COVID-19 pandemic: 24 h movement behavior and metabolic syndrome (24 h-MESYN) study**

Marcus Vinicius Nascimento-Ferreira\* Marcus Vinicius Nascimento-Ferreira Luiz Fernando de Oliveira ; Ana Clara Arrais Rosa Alaiana Marinho Franco Francisco Leonardo Torres-Leal Heráclito Barbosa de Carvalho

**Objective:** To assess the association between sedentary behavior and subjective stress in university students during the COVID-19 pandemic.

**Methods:** A sample of 195 university students (68.7% females; 44.6% aged between 21 to 25 years; 65.8% enrolled in a health sciences degree; 24.5% enrolled in the 1<sup>st</sup> to 3<sup>rd</sup> semester) was recruited. Data were collected during the first semester of 2021 in the city of Imperatriz, Maranhão, Brazil (Gini Index of 0.56). We collected online data using the Perceived Stress Scale (14-item) and South American Youth/Child Cardiovascular and Environmental (SAYCARE) sedentary behavior questionnaire (10-item). We assessed scores of positive and negative stress dimensions as outcomes (representing perceived self-efficacy and helplessness, respectively) and the time spent in five sedentary behaviors (TV viewing, using a computer, studying, playing electronic games and passive commuting [on weekdays and weekends]) in hour(s) per day as exposure. The potential confounding variables were biological sex; age; ethnicity; maternal education; degree program (health sciences degree or other undergraduate degree), shift (morning, evening, night or integral), time ( $\leq 3^{\text{rd}}$  semester or  $> 3^{\text{rd}}$  semester) and number of classes enrolled. We assessed the associations using multilevel linear regression models. To retain variable in the multivariate model, we adopted a significance level of  $p \leq 0.20$ .

**Results:** After adjusting the models, the time spent in TV viewing ( $\beta = -0.55$  [95% CI -0.94 to -0.16]) and studying ( $\beta = 0.49$  [95% CI 0.08 to 0.91]) were associated with the positive dimension of stress perception; as well as, TV viewing ( $\beta = 0.52$  [95% CI 0.06 to 0.98]) was associated with the negative dimension.

**Conclusion:** TV viewing was related with worsened perceived stress during the COVID-19 pandemic in university students from low-income region by decreasing self-efficacy and increasing helplessness perception. Studying time improved the perceived self-efficacy.

**Risk of sudden hearing loss following a positive COVID-19 test with hospitalization** Kelly M. Reavis\* Kelly M. Reavis Garnett P. McMillan Rachel Phillips Peter Steyger William Messer Timothy Hullar Kathleen F. Carlson

Our objective was to estimate the association between COVID-19 and sudden hearing loss in military Veterans. Past studies have noted new onset and progression of hearing loss after COVID-19 but lacked individuals without COVID-19 for comparison. We conducted a historical cohort study using Veterans Affairs electronic health record data between March 2020 - October 2022. The study sample includes Veterans (n=2,014,313) who were tested for SARS-Cov-2, the causative virus for COVID-19, and were free from a history of sudden hearing loss. Veterans were classified as having a negative test result (69%), a positive test result without hospitalization within 30 days of the test date (27%), or a positive test result with hospitalization within 30 days of the test date (4%) and were followed for incident sudden hearing loss. Among those who were hospitalized, we explored the association between COVID-19 treatments (low- and high-flow oxygen, extracorporeal membrane oxygenation, dialysis, ventilation, and vasopressors) and sudden hearing loss. Adjusted incidence rate ratios (aIRR) and 95% confidence intervals (CI) were estimated using binary logistic regression. We identified 1,422 cases of sudden hearing loss. Veterans who were hospitalized after a positive test had a 40% (95% CI: 7-84%) increased risk of sudden hearing loss compared to those with a negative test. No increased risk was observed among those testing positive but without hospitalization (aIRR: 0.95; 95% CI: 0.8-1.1). Hospitalized Veterans receiving high-flow oxygen (aIRR: 1.5, 95% CI: 0.8-2.7) and dialysis (aIRR: 2.4, 95% CI: 0.9-6.7) may be more likely to have sudden hearing loss compared to those not receiving these treatments. These results suggest an increased risk of sudden hearing loss among Veterans hospitalized for COVID-19. High-flow oxygen and dialysis treatments for COVID-19 may be indicators of underlying pathology that contribute to hearing loss and research into possible mechanisms is warranted.

**Estimating Rt for COVID-19 using wastewater surveillance data in New York, USA** David A. Larsen\* Dustin Hill Joe Moran Brittany L. Kmush Mary B. Collins Mohammed Alazawi Ian Bradley Christopher J. Gobler Hyatt Green Tabassum Insaf Mian Wang Yinyin Ye David A. Larsen

*Background* SARS-CoV-2 viral fragments detected in wastewater can show estimated levels of COVID-19 disease in a community and the direction of disease transmission in the near future. These data can be used to estimate the reproductive number at a particular point in time ( $R_t$ ).

*Methods* We evaluate four methods for using wastewater to estimate  $R_t$  for COVID-19 including fitting the trend in wastewater to the trend in cases, using wastewater to predict cases then using predicted case to determine  $R_t$ , substituting cases with a wastewater quantification in the  $R_t$  equation, and using the ratio change in wastewater over time as a pseudo  $R_t$  value.

*Results* Each  $R_t$  value was determined for 60 counties in New York State during the COVID-19 pandemic using data from 2020 to 2022. Values were compared to each other and to  $R_t$  values from case data using RMSE.

*Discussion and implications* The  $R_t$  can be used to estimate the epidemic curve and wastewater has become a more accurate method for estimating disease levels in a community. Using wastewater to calculate  $R_t$  can inform public health policy and by providing different methods of calculating  $R_t$ , the best method for a given situation can be selected based on time and resources.

**Self-reported health and multi-level characteristics of internal migrants from the most wealthy city in South Korea during the COVID-19 pandemic** Ikhan Kim\* Ikhan Kim Duwon

**Background:** This study aimed to identify the characteristics of internal migrants from Seoul, the most wealthy city in South Korea, at the individual, household, and district levels during the COVID-19 pandemic.

**Method:** We utilized the Korea Welfare Panel data from 2018 to 2020. The entire study period was divided into pre-pandemic (2018-2019) and post-pandemic (2019-2020). Between subjects who had not internally migrated and those who had, inbound and outbound from Seoul, sociodemographic characteristics, self-reported health status, and life events at the individual, household, and district levels were compared for each period. Age-stratified sensitivity analysis was conducted (25-39, 40-54, 55-74 years old), considering the propensity for internal migration based on the life course perspective. A pseudo-population was created using the inverse probability weights to account for sample attrition.

**Results:** Before the COVID-19 pandemic, people who migrated within Seoul had better self-reported health than those who stayed or moved outside Seoul. However, during the pandemic, the health status of those who moved within Seoul was worse than other groups. Before and during the epidemic, the health of those who moved outside Seoul was continuously poor. Additionally, movers' overall characteristics at various levels worsened during the pandemic period. According to stratified analyses, during the pandemic, the 55-74 age group experienced an increase in the residence move of those with poor health and low socioeconomic status. Besides, the percentage of participants who responded moving was due to increased housing market pressure and economic instability.

**Conclusions:** This study found an association between the COVID-19 pandemic and a rise in vulnerable people's internal migration, particularly among the older. It is required to conduct further research on the effects of internal migration on vulnerable populations.

**Impact of the COVID-19 pandemic on emergency transports due to occupational injuries in Nagoya, Japan: An interrupted time series analysis** Akihiko Narisada\* Akihiko Narisada  
Tomohiro Umemura Nauta Yamanaka Kohta Suzuki

**Background:** The COVID-19 pandemic has had a major impact on the work environment. Occupational injuries during the pandemic are not known enough. While the decrease in work production activities may have reduced the number of occupational injuries, major changes in the work environment may have also increased the risk of occupational injuries for those vulnerable to change, such as the older workers. Thus, the aim of this study is to examine the impact of the pandemic on occupational injuries by age group in a large Japanese city.

**Methods:** We used public administrative data from Nagoya, a city of 2 million people in Central Japan, from April 2016 to March 2022 (almost all emergency transport is provided by public services in Japan). Pandemic onset was defined as from April 2020. Using an interrupted time series analysis, we analyzed the change in the incidence rate of emergency transports due to occupational injuries during the pandemic by age group, taking into account seasonality and trends.

**Results:** A total of 4,116 emergency transports due to occupational injuries occurred in Nagoya during April 2016 to March 2022. Analysis of all age groups showed a 17% decrease in emergency transports due to occupational injuries during the pandemic period (Incidence Rate Ratio (IRR): 0.83, 95%CI: 0.70 - 0.98). Subgroup analysis by age group showed a 28% decrease in incidence rate in the younger age group under 50 years (IRR: 0.72, 95%CI: 0.59 - 0.89), while there was no significant change in the older age group over 50 years (IRR: 0.98, 95%CI: 0.77 - 1.23).

**Conclusions:** During the COVID-19 pandemic period, there was an overall decrease in emergency transports due to occupational injuries, but no change in the older age groups. As the workforce in Japan is aging, further study of injuries among older workers during the pandemic period is needed.

**LATEBREAKER**

COVID-19 Pandemic

**Angiotensin Converting Enzyme 2 (ACE2) Expression as a Risk-Factor for SARS-CoV-2 Transmission in Concurrent Hospital Associated Outbreaks** Aidan Nikiforuk\* Aidan Nikiforuk Kevin Kuchinski Katy Short Susan Roman Mike Irvine Natalie Prystajecy Agatha David Patrick Inna

**Background:** The severe acute respiratory coronavirus two (SARS-CoV-2) possesses a strong affinity for its host cellular receptor angiotensin converting enzyme two (ACE2), which explains the virus's propensity for widespread human-to-human transmission. We investigate the relationship between a patient's nasopharyngeal *ACE2* transcription and secondary transmission within a series of concurrent hospital associated SARS-CoV-2 outbreaks in British Columbia, Canada.

**Methods:** Epidemiological data from the outbreak investigations were merged with laboratory results and viral lineage calls from whole genome sequencing, to reconstruct concurrent outbreaks using transmission network analysis. *ACE2* transcription and RNA viral load were measured by quantitative real-time polymerase chain reaction. The transmission network was resolved to calculate the number of secondary cases. Multivariable analyses using Poisson and Negative Binomial regression models was performed to estimate the association between *ACE2* transcription the number of SARS-CoV-2 secondary cases.

**Results:** The transmission network provided  $n = 76$  potential transmission events across  $n = 103$  cases. Bivariate comparisons found that on average *ACE2* transcription did not differ between patients and healthcare workers ( $P = 0.86$ ). High *ACE2* transcription was observed in 98.6% of transmission events where either the primary or secondary case had above average *ACE2*. Multivariable analysis found that the association between *ACE2* transcription and the number of secondary transmission events differs between patients and healthcare workers. In health care workers negative binomial regression estimated that a one unit change in *ACE2* transcription decreases the number of secondary cases ( $B = -0.13$  (95%CI: -0.25 to -0.018) adjusting for RNA viral load. Conversely, in patients a one unit change in *ACE2* transcription increases the number of secondary cases ( $B = 0.18$  (95% CI: 0.010 to 0.37) adjusting for RNA viral load. Sensitivity analysis corroborated these results.

**Conclusion:** Our study suggests that *ACE2* transcription has a positive association with SARS-CoV-2 secondary transmission in admitted inpatients, but not health care workers during concurrent hospital associated outbreaks and should be considered a risk-factor for viral transmission among inpatients.

**LATEBREAKER**

COVID-19 Pandemic

**Job loss and job instability during the COVID-19 pandemic and the risk of depression and anxiety among Swedish employees** Sandra Blomqvist\* Sandra Blomqvist Linda Magnusson Hanson

The COVID-19 pandemic led to permanent and temporary job losses but inconsistency exists about the mental health consequences of different types of employment transitions. In particular, knowledge is scarce concerning furloughs, which was a common job protection strategy worldwide during this crisis. Here, we studied associations between different types of job instability and loss during the pandemic in relation to depression and anxiety.

A subset of participants from the Swedish Longitudinal Occupational Survey of Health were contacted in February 2021 and in February 2022. A total of 1635 individuals participated in either or both waves and had been working before the pandemic. Exposure to; i) workplace downsizing, ii) furlough, or iii) unemployment/job loss were investigated in relation to the Generalized Anxiety Disorder 7 item and the Patient Health Questionnaire 9 items scales, using logistic regression models with cluster-robust standard errors. Sociodemographic factors and prior mental health problems were controlled for and effect modification was tested for sex and prior mental health problems.

While furlough was unrelated to mental health, experiencing workplace downsizing during the pandemic was associated with an increased risk of anxiety (adjusted Odds Ratio (OR)=2.09, 95% Confidence interval (CI)=1.08-4.05). Job loss/unemployment increased the risk of depression (OR=1.91, 95% CI=1.02-3.57) compared to being stably employed, but crossed unity when considering prior mental health status. No effect modification by sex or by prior mental health problems was found.

This study suggests that while job loss and downsizing during the COVID-19 pandemic were associated with depression and anxiety, respectively, being furloughed was not. These results are supportive of short time work allowance schemes, as implemented in Sweden during the COVID-19 pandemic, as a strategy for job protection and prevention of mental disorders among employees during economic crises.



**LATEBREAKER**

COVID-19 Pandemic

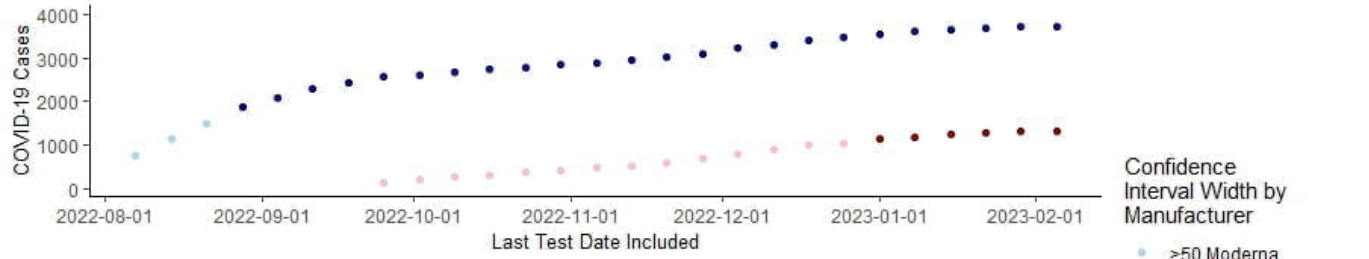
**Precision of Vaccine Effectiveness in the Setting of Low Vaccine Coverage** Lauren Roper\*  
Lauren Roper Katherine E. Fleming-Dutra Allison Arich Ciesla Ryan E. Wiegand Amadea Britton  
Ruth Link-Gelles

Vaccine effectiveness (VE) studies are essential to monitor performance of COVID-19 vaccines outside the setting of clinical trials. On Jun 18, 2022, children aged 6 months-4 years became eligible for monovalent Pfizer-BioNTech or Moderna COVID-19 vaccination. By Feb 22, 2023, about 10% of children aged 2-4 years had initiated a primary series. Low vaccine coverage can result in biased VE estimates that are imprecise and difficult to interpret due to low statistical power. CDC has used a precision threshold of  $\leq 50$  percentage points (pp) for reporting of VE estimates, regardless of vaccine coverage. We assessed stability and interpretability of VE estimates using a large national pharmacy SARS-CoV-2 testing program. We estimated VE against symptomatic infection in children aged 3-4 years using tests conducted from Aug 1, 2022, to Feb 5, 2023. To assess VE stability and precision over time, we assessed VE cumulatively by week (e.g., Aug 1-7, Aug 1-14, Aug 1-21, etc.), assuming that each additional week of data would increase sample size, thereby narrowing confidence intervals (CI). VE against symptomatic SARS-CoV-2 infection and CIs were calculated as  $1 - \text{OR} \times 100$  separately for complete primary series of Moderna (2 doses; analytic start date Aug 1, 2022) and Pfizer-BioNTech (3 doses; analytic start date Sep 19, 2022). ORs were calculated using multivariable logistic regression. Point estimates became less variable as CI widths narrowed to  $< 50$  pp even in the setting of low vaccine coverage (Figure). CIs narrowed more quickly for the Moderna analytic period compared to Pfizer analytic period, likely due to higher COVID-19 incidence during Aug 2022 leading to increased power from greater case accrual. This suggests that even in the setting of low vaccine coverage, increasing case accrual allowed stabilization of VE point estimates and interpretable CIs in this large national testing platform.

Figure depicting cumulative cases accrual and VE against symptomatic SARS-CoV-2 infection and 95% confidence intervals of a complete monovalent primary series of Moderna and Pfizer-BioNTech in 3-4 year olds, by week from August 1, 2022- January 30, 2023, using data from the Increasing Community Access to Testing Program.

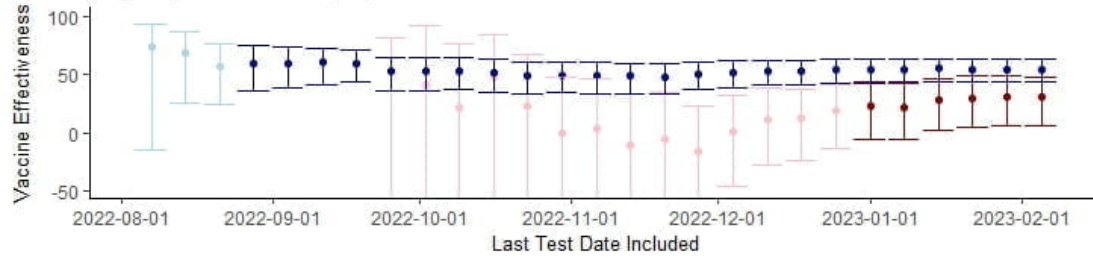
### A COVID-19 Case Accrual (3-4yo)

August 1, 2022 - February 5, 2023



### B Vaccine Effectiveness (3-4yo)

August 1, 2022 - February 5, 2023



**Association of the COVID-19 Pandemic and SARS-CoV-2 Infection During Pregnancy with Maternal and Infant Outcomes, South Carolina, 2018-2021** Jihong Liu\* Jihong Liu Maria Sevoyan Yiwen Shih Peiyin Hung Xiaoming Li

**Background:** This study aims to examine the associations of SARS-CoV-2 infection and the COVID-19 pandemic with maternal and infant outcomes.

**Methods:** Data came from the South Carolina (SC) COVID-19 Cohort, novel linkages of statewide COVID testing and vital records data for all women giving a singleton birth during pre-pandemic (01/2018-02/2020) (n=101,517 births) and peri-pandemic (03/2020-12/2021) (n=81,372 births) periods. SARS-CoV-2 infection was categorized as no COVID-19 testing, COVID-19 positive, or COVID-19 negative during pregnancy and intrapartum. Based on self-reported symptoms, COVID-19 severity was classified into three groups: asymptomatic, mild, and moderate/severe symptoms. Multivariable logistic regressions were used to examine the differences in maternal and infant outcomes by pandemic period and SARS-CoV-2 infection status.

**Results:** During the pandemic, 8.3% of birthing people in SC were infected by SARS-CoV-2. Among COVID-positive cases, 56.4% were asymptomatic, 30.6% had mild symptoms, and 13% had moderate/severe symptoms. Compared with pre-pandemic, significant increases were observed in low birthweight (<2500 grams, adjusted OR (aOR): 1.04, 1.01-1.08), preterm birth (<37 weeks, aOR: 1.03, 1.00-1.07), NICU admission (aOR: 1.10, 95% CI: 1.06-1.13), gestational diabetes (aOR: 1.16, 95% CI: 1.11-1.20), and gestational hypertension (aOR: 1.08, 95% CI: 1.05-1.12) during the pandemic. Compared with pre-pandemic, birthing people with COVID infection also had increased odds of preterm birth (aOR: 1.14, 1.05-1.24), NICU admission (aOR: 1.23, 1.13-1.34), and gestational hypertension (aOR: 1.21, 1.12-1.32). Compared to asymptomatic people, people with moderate/severe symptoms had increased odds of preterm birth (aOR: 1.42, 1.13-1.78).

**Conclusions:** Adverse maternal and infant health outcomes were increased during the COVID pandemic and were higher among people with SARS-CoV-2 infection, especially those with moderate/severe symptoms.

## **Long-term cardiac symptoms of COVID-19: a systematic review and meta-analysis** Chihua Li\* Chihua Li Boya Guo Chenya Zhao Grace A Noppert

### **Background**

There is growing body of literature on the long-term cardiac symptoms following COVID-19 infection. We conducted a systematic review and meta-analysis to synthesize and evaluate related evidence to inform clinical management and future studies.

### **Methods**

We searched two preprint and seven peer-reviewed article databases from January 1, 2020 to January 8, 2022 for studies investigating cardiac symptoms that persisted for at least 4 weeks among individuals who got COVID-19. A customized Newcastle-Ottawa scale was used to evaluate the quality of included studies. Random-effects meta-analyses were performed to estimate the proportion of symptoms with 95% confidence intervals (CI), and stratified analyses were conducted to quantify the proportion of symptoms by study characteristics and quality.

### **Results**

A total of 101 studies describing 49 unique long-term cardiac symptoms met the inclusion criteria. Based on quality assessment, only 16% of the studies (n=16) were of high quality, and most studies scored poorly on sampling representativeness. The two most examined symptoms were chest pain (10.1%, 95% CI: 6.4-15.5) and arrhythmia (9.8%, 95% CI: 5.4-17.2). Stratified analyses showed that studies with low-quality score, small sample size, unsystematic sampling method, and cross-sectional design were more likely to report high proportions of symptoms, as compared to high-quality studies. For example, the proportion of chest pain was xxx in low-quality studies as compared to high-quality studies where chest pain was reported among 4.0% (95% CI: 1.3-12.0) individuals and arrhythmia was reported among 2.7% (95% CI: 1.0-6.3) individuals. Similar patterns were observed for other cardiac symptoms including hypertension, cardiac abnormalities, myocardial injury, thromboembolism, stroke, heart failure, coronary disease, and myocarditis.

### **Discussion**

There is a wide spectrum of long-term cardiac symptoms following COVID-19. Findings of existing studies are strongly related to study quality, size and design, underscoring the need for high-quality epidemiological studies to characterize these symptoms and understand their aetiology.

Meta-analysis results of top two most reported symptoms: chest pain and arrhythmia, using a random effects model.

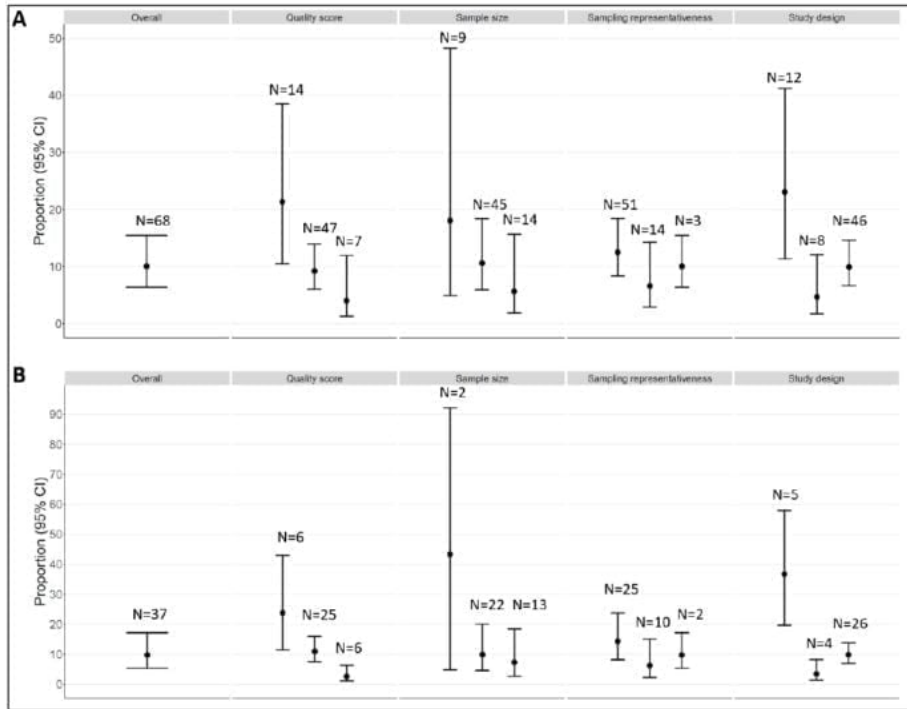


Figure 3A: Chest pain, 3B: Arrhythmia. Stratified by quality score (low, medium, high), sample size (30-99, 100-999,  $\geq 1000$ ), sampling representativeness (online survey and single hospital, multiple hospitals, national studies), and study design (cross-sectional, retrospective cohort, prospective cohort). 2 studies (Case series: n=1, Case control: n=1) were not included in chest pain - study design, and 2 studies (Case control: n=2) were not included in arrhythmia study design.

**Does a change in economic status have an effect on anxiety, depression, and suicide ideation during the COVID-19 pandemic in South Korean adults?** Jin-Young Nam\* Jin-Young Nam

**Introduction:** Coronavirus disease (COVID-19) has affected global economic changes and mental health outcomes. However, gender differences in the relationship between economic status change and mental health outcomes during the pandemic are unclear. Therefore, we investigated whether changes in economic status affect depression, anxiety, and suicidal ideation by gender.

**Methods:** This cross-sectional study used data from the COVID-19 National Mental Health Survey 2021 in South Korea. We used the Generalized Anxiety Disorder 7-items (GAD-7) scale for measuring anxiety, the Patient Health Questionnaire-9 scale for measuring depression, and self-reported questionnaires for investigating suicide ideation and suicide ideation due to COVID-19.

**Results:** Of the 2,000 participants, those with a worse change in economic status had a 2-fold higher risk of GAD; 1.9-fold, depression; 1.8-fold, suicide ideation; and, 2.7-fold, suicide ideation due to COVID-19 (GAD: PR 2.05, 95% CI 1.55–2.71; depression: PR 1.87, 95% CI 1.49–2.34; suicide Ideation: PR 1.76, 95% CI 1.44–2.14; COVID-19-related suicide ideation: PR 2.73, 95% CI 1.89–3.93). Women who experienced worsening in the economic status had a 2.6-fold higher risk of GAD (PR 2.58, 95% CI 1.75–3.80) and a 3.5-fold higher risk of suicide ideation due to COVID-19 (PR 3.46, 95% CI 1.99–6.02).

**Conclusion:** Worse economic changes negatively affected mental health during the COVID-19 pandemic. Women who experienced a decline in their financial status during the pandemic had a higher risk of suicidal ideation due to COVID-19. Prevention and intervention efforts are needed to support economically vulnerable people, who are at a higher risk of severe mental health outcomes due to the pandemic.

Table 3. Subgroup analysis of the association between financial status change and mental health problems by gender, age, and income

	Anxiety				Depression				Suicide Ideation				Suicide Ideation due to COVID-19			
	The change of economic status				The change of economic status				The change of economic status				The change of economic status			
	Better or similar		Worse		Better or similar		Worse		Better or similar		Worse		Better or similar		Worse	
	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
<b>Gender</b>																
Men	1.00	1.66	1.11	2.49	1.00	1.86	1.32	2.62	1.00	1.73	1.27	2.37	1.00	2.27	1.38	3.72
Women	1.00	2.58	1.75	3.80	1.00	1.95	1.45	2.64	1.00	1.83	1.42	2.37	1.00	3.46	1.99	6.02
<b>Age group</b>																
20-29	1.00	-	-	-	1.00	-	-	-	1.00	-	-	-	1.00	-	-	-
30-39	1.00	-	-	-	1.00	1.61	0.98	2.63	1.00	1.71	1.09	2.69	1.00	5.17	1.91	14.03
40-49	1.00	1.98	1.06	3.67	1.00	1.40	0.88	2.22	1.00	1.76	1.14	2.71	1.00	2.86	1.23	6.67
50-59	1.00	2.48	1.06	5.81	1.00	2.65	1.33	5.29	1.00	1.99	1.12	3.54	1.00	1.58	0.53	4.69
60+	1.00	2.52	1.21	5.25	1.00	1.96	1.10	3.48	1.00	2.02	1.25	3.25	1.00	-	-	-
<b>Annual household income (USD)</b>																
< 30,000	1.00	1.72	0.98	3.02	1.00	1.45	0.95	2.21	1.00	1.82	1.27	2.61	1.00	2.72	1.42	5.19
30,000-49,999	1.00	2.33	1.50	3.60	1.00	2.08	1.48	2.93	1.00	1.67	1.20	2.32	1.00	3.08	1.73	5.48
50,000 +	1.00	1.89	1.20	2.99	1.00	2.72	2.72	3.10	1.00	1.90	1.36	2.68	1.00	3.03	1.60	5.76

## **What Pandemic? Stress as Demotivation for Adhering to Public Health Guidelines to Reduce Contacts During the COVID-19 Pandemic** Keeley Morris\* Keeley Morris Gillian Tarr

Pandemic fatigue, or the demotivation to adhere to public health guidelines for limiting the spread of COVID-19, became a significant public health concern early in the pandemic. This study examined the time-varying effect of stress on contacts as an early indicator for pandemic fatigue during the first 6 months of the COVID-19 pandemic.

### Methods

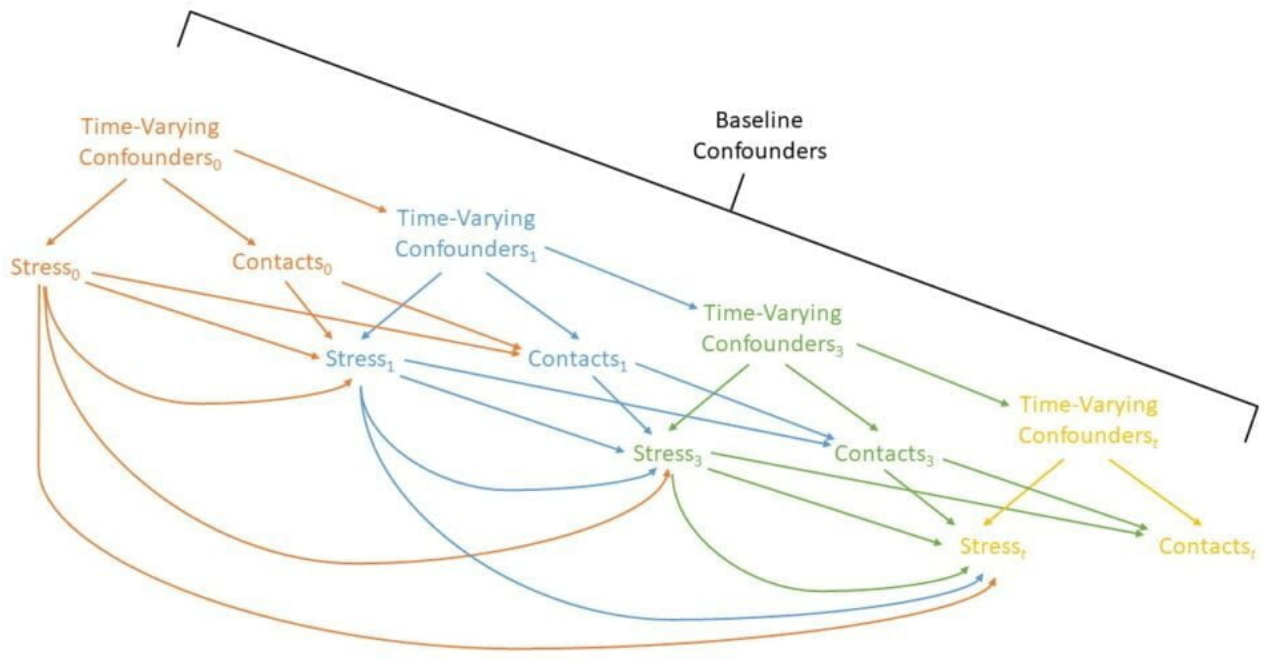
We conducted a longitudinal survey of 1,001 families with children (C1) and 340 adults over age 55 (C2), April-October 2020. Stress, measured by the Kessler-6, was selected as a psychological driver of pandemic fatigue based on the Stress and Coping Model and the WHO Framework for Pandemic Fatigue. We applied GEE to examine the overall effect of stress, modeled using a 2-knot spline, on weekly non-work, non-household contacts. We adjusted for stress history and time-varying sociodemographic and psychological confounders using marginal structural models (Figure). We examined pandemic fatigue with an interaction between stress and week.

### Results

In C1 we found that for people with the lowest (Kessler-6 <5) and highest levels of stress (Kessler-6 >11), each additional unit of stress resulted in lower contact rates (RR 0.91; 95% CI 0.80, 1.02 and RR 0.93; 95% CI 0.83, 1.04 respectively) while people with moderate stress (Kessler-6 5-11) showed higher contact rates (RR 1.06; 95% CI 0.99, 1.14). Results from C2 showed the same pattern. For both cohorts, we observed little change in the effect of stress over time.

### Conclusions

We did not find evidence of stress-driven pandemic fatigue during the first 6 months of the pandemic. Overall, we found that changes in stress were associated with higher or lower contacts depending on a person's stress level, though the results were imprecise. People with moderate stress had more contacts for every point increase in Kessler score within this range. These results may be used to target potential populations for future work to reduce disease transmission.





**Evaluating the impact of sickle cell disease on COVID-19 susceptibility and severity: an application of causal inference methods** Jiajun Luo\* Jiajun Luo Christopher O. Olopade Habibul Ahsan Jayant Pinto Briseis Aschebrook-Kilfoy

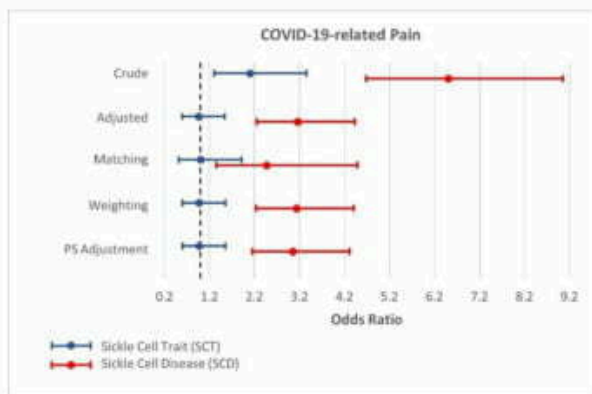
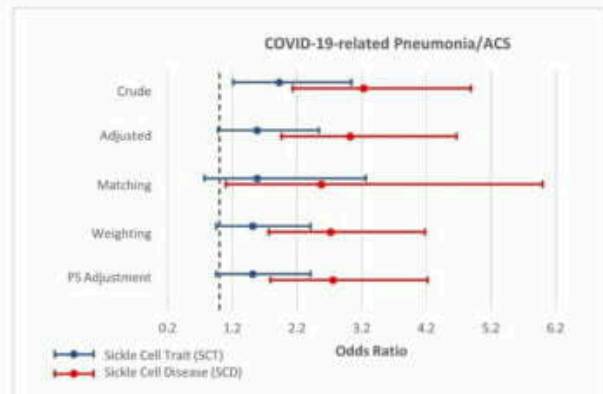
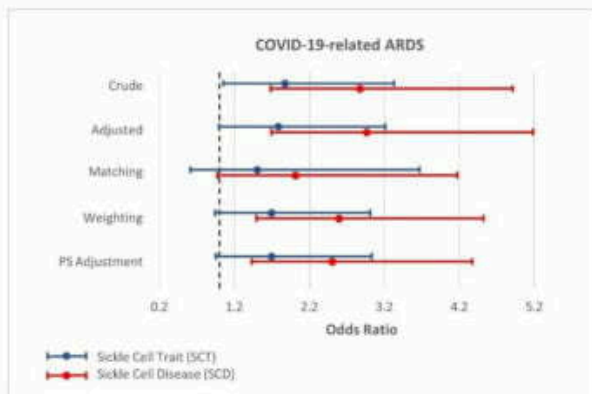
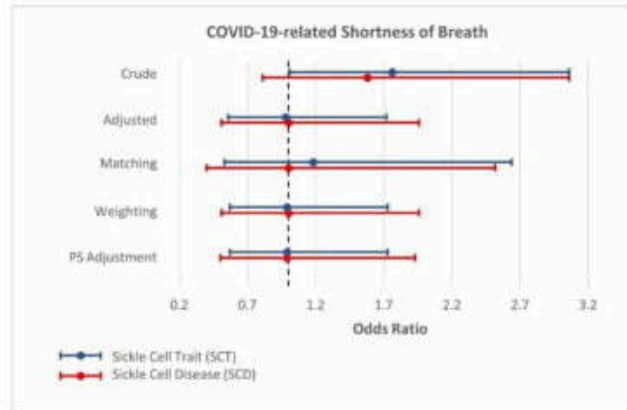
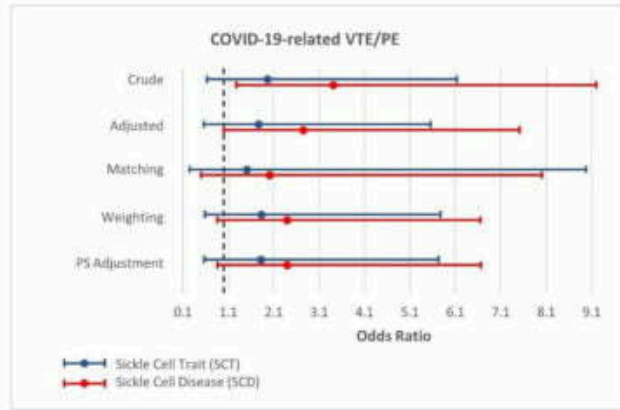
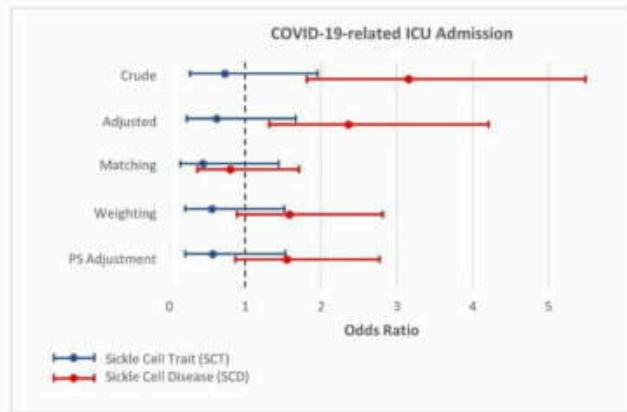
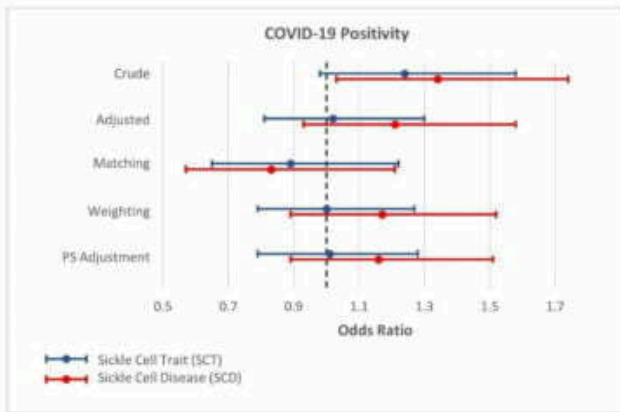
**Background:** Sickle cell trait/disease (SCT/SCD) are enriched among Blacks and associated with various comorbidities. The overrepresentation of these characteristics prevents traditional regression approach obtaining convincing evidence for the independent effect of SCT/SCD on other health outcomes.

**Objective:** To investigate the association between SCT/SCD and COVID-19-related outcomes using causal inference approaches that balance the covariates.

**Methods:** Electronic health record data from the University of Chicago Medicine between March 2020 and December 2021 were used. Medical conditions were identified using ICD-10 codes. Five approaches, including two traditional regression approaches (unadjusted and adjusted) and three causal inference approaches (covariate balancing propensity score (CBPS) matching, CBPS weighting, and CBPS adjustment), were employed.

**Results:** A total of 112334 patients were included in the study, among which 504 had SCT and 388 SCD. Patients with SCT/SCD were more likely to be Black, younger, female, non-smokers, and had diabetes, heart failure, asthma, and cerebral infarction. Causal inference approaches achieved a balanced distribution of covariates while traditional approaches failed. Across the approaches, SCD was consistently associated with COVID-19-related pneumonia (odds ratios (OR) estimates, 3.23 (95% CI: 2.13-4.89) to 2.57 (95% CI: 1.10-6.00)) and pain (OR estimates, 6.51 (95% CI: 4.68-9.06) to 2.47 (95% CI: 1.35-4.49)). While CBPS matching suggested an association between SCD and COVID-19-related acute respiratory distress syndrome (OR=2.01, 95% CI: 0.97-4.17), this association was significant in other approaches (OR estimates, 2.96 (95% CI: 1.69-5.18) to 2.50 (95% CI: 1.43-4.37)). No association was observed between SCT and COVID-19-related outcomes in causal inference approaches.

**Conclusion:** Using causal inference approaches, we provide comprehensive evidence for the link between SCT/SCD and COVID-19-related outcomes.



**SARS-CoV-2 Infections and Severe Maternal Morbidity in the United States: A National Retrospective Electronic Health Records Cohort Study** Jihong Liu\* Jihong Liu Peiyin Hung  
Tianchu Lyu Chen Liang Adiba Promiti Yiwen Shih Jiajia Zhang Xiaoming Li

**Background:** To examine the associations of SARS-CoV-2 infection, its severity and timing, with risks of severe maternal morbidity (SMM).

**Methods:** We used electronic health records (EHR) from the National COVID Cohort Collaborative (N3C), a clinical data repository from >75 healthcare systems across 50 states, restricting to women who gave a live birth between March 1, 2020 and May 31, 2021 (209,289 childbirths). COVID severity was determined using the WHO Clinical Progression Score (CPS): mild (CPS: 1-3) and moderate/severe (CPS: 4-10). SMM during pregnancy through 42 days postpartum was defined as diagnoses or procedures suggestive of any of the 20 CDC-recommended SMM indicators (excluding blood transfusion) using EHR phenotyping protocol. Log-binomial models were used to estimate adjusted relative risks (aRR) of SMM.

**Results.** The cohort was 30.6 years old ( $\pm 5.9$ ), racially diverse (17.1% Black, 19.6% Hispanic, 5.4% Asian, and 8.1% other races), of which 9% were infected by SARS-CoV-2. Of COVID cases, 65.3% were mild, 34.7% were moderate/severe COVID; 71.3% were first infected during pregnancy, and 28.7% infected at delivery or <42 days after delivery. SMM rate was 148.5 cases per 10,000 births with a higher prevalence among Black births (260.0 cases) than White births (120.5 cases). Compared to those without COVID, SARS-CoV-2 infection was associated with increased risks of SMM (aRR: 1.91, 95% CI: 1.73-2.10). SMM risks were higher among those with mild symptoms (aRR: 2.05, 1.84-2.28), those with moderate/severe symptoms (aRR: 1.65, 1.41-1.94), those infected during pregnancy (aRR: 1.26, 1.10-1.43), and those infected at delivery or early postpartum (aRR: 3.61, 3.20-4.08).

**Conclusions.** SARS-CoV-2 infection, its severity, and especially the diagnosis at delivery or early postpartum were associated with increased risks of SMM. These findings suggest an urgent need to prevent and intervene SARS-CoV-2 infections among birthing people to prevent SMM in the US.

**Self-Reported Condom Use Among Washington State Residents Prior to and During the COVID-19 Pandemic: An Analysis of BRFSS Data** Mary Jewell\* Mary Jewell Sonya Jampel Mary Grace Casagrande Kristjana Asbjornsdottir Alyson J. Littman

**Background:** COVID-19 has significantly impacted healthcare access and sexual behavior, but little is known about how COVID-19 affected condom use. During COVID-19, condom use may have been impacted by decreased access to reproductive health services or changes in rates of sex. The objective of this study is to investigate whether condom use in Washington State changed during a time of pandemic restrictions compared to a pre-pandemic period.

**Methods:** We used Behavioral Risk Factor Surveillance System (BRFSS, N = 11,684) survey data from Washington State to assess changes in the prevalence of condom use by time of interview pre-COVID-19, before the Washington State lockdown (Jan 1, 2019 - Mar 23, 2020, n = 7,708) and during COVID-19, after the first state lockdown (Mar 24, 2020 - Dec 31 2020, n = 3,976). We used Poisson regression and included age, income, and rurality as confounders, and we considered rurality and HIV risk behavior as potential effect modifiers. We also assessed changes in the prevalence of reported sex during the same periods using Poisson regression.

**Results:** Prevalence of condom use increased from 21.1% pre-COVID-19 to 21.5% during COVID-19, a relative increase of 2% (PR: 1.02, 95% CI: 0.92, 1.12, p = 0.072). We did not find meaningful effect modification by any covariate. Compared to pre-COVID-19 (88.5%), a smaller proportion of respondents reported having sex in the last 12 months during COVID-19 (85.0%), a relative decrease of 4% (PR: 0.96, 95% CI: 0.94, 0.98; p < 0.001).

**Conclusions:** The prevalence of reported sex declined during COVID-19, but among sexually active individuals, condom use remained resilient to the challenges caused by the COVID-19 pandemic in Washington State. As our reproductive and sexual health system faces increased challenges due to human and non-human caused events, other sexual health services may use these results to inform future actions.

**Multilevel Analysis of 2020 Election Results on the Relationship Between COVID-19 Vaccine Uptake in Nursing Home Residents and their subsequent COVID-19-associated Mortality in Louisiana, December 2021 to December 2022** Erica Washington\* Erica Washington Susanne Straif-Bourgeois

Background:

Vaccines protecting against SARS-CoV-2 infection have been documented as effective for reducing mortality against COVID-19. A September 2021 report by The Kellogg Family Foundation noted a divide in vaccine uptake where county-level data COVID-19 vaccinations lagged in locations with voting patterns supporting the 2020 republican presidential candidate. The present aim is to determine if the 2020 presidential election affected the relationship between nursing home COVID-19 vaccination rates and COVID-19-associated mortality among Louisiana nursing home residents.

Method:

The independent and dependent variables were nursing home resident vaccination rates and resident COVID-associated mortality rates, respectively, reported cumulatively by December 2021. November 2020 parish-level election results were exported from the Louisiana Secretary of State website. Nursing home data reported to the Center for Medicaid and Medicare Services (CMS) were linked by parish to election results. Nursing home ownership type was linked by CMS certification number in consideration of facility-level policies that may affect vaccine uptake. Data were analyzed using a multilevel generalized linear mixed model using the GLIMMIX procedure in SAS.

Results:

A total of 279 nursing homes were in the data set. Seventy-one (25.44%) parishes had election results favoring the democratic candidate. An average of 10.85 nursing home residents died of COVID-19 per nursing home. Skilled nursing facilities affiliated with hospitals were associated with the lowest average resident deaths (mean = 1.61; SD = 1.27). Compositional and multilevel models were adjusted for ownership type and election outcome (second-level predictor). Model fit statistics, including the interclass correlation coefficient, showed that the compositional model was the most appropriate.

Discussion:

6.93% of the variability in resident nursing home deaths was explained by the final model ( $r^2$ ). Nursing home resident deaths did not differ significantly by parish-level political leaning ( $p=0.06$ ). These results may be confounded by COVID-19 outbreak waves before vaccines were available. Nursing home staff vaccine uptake may be more appropriate to proxy election-vaccine attitudes; however, mortality data for that group may be inconsistent.

**COVID-19 mitigation policies and mental health of 9/11 survivors in the early months of the COVID-19 pandemic** Kacie Seil\* Kacie Seil Sungwoo Lim Robert Brackbill Sean Locke

COVID mitigation policies during the early months of the pandemic may be associated with mental health. We hypothesized that living in a state with stringent COVID mitigation policies (e.g., New York State PAUSE) would have a negative mental health impact. World Trade Center Health Registry data from a longitudinal cohort of 9/11 survivors were used in this study. The Wave 5 (W5) survey from April 2020-January 2021 coincided with the early months of the pandemic. We compared enrollees living in New York (NY - stringent COVID policies) to those living in Florida (FL - looser COVID policies) who completed the W4 survey in 2015-16 and the W5 survey in 2020-21. Outcomes were non-specific psychological distress (NSPD) (K6 scale) and depression (PHQ-8 scale). To analyze potential effects of COVID policies, we conducted a difference-in-differences (DID) analysis, examining changes in outcomes from W4 to W5. Propensity score matching using baseline demographic and clinical characteristics (e.g., age, history of stroke) created two comparable groups (N=1,255 per group). Mixed-effect DID models controlling for confounders were run. In W4, FL enrollees had a mean K6 score of 4.43, and NY enrollees had a mean score of 4.60. Between W4 and W5, after accounting for baseline scores and potential confounding, the K6 score increased by 0.32 more points in the NY group vs. the FL group ( $p=0.042$ ), indicating NY enrollees' NSPD increased more than the FL enrollees. Similarly, in W4, FL enrollees had a mean PHQ-8 score of 5.93 vs. NY enrollees with a mean score of 6.21. In W5, the PHQ-8 score increased by 0.39 more points in the NY group compared to the FL group ( $p=0.028$ ). Future analyses will assess clinical significance and attempt to more directly link observed changes to COVID policies versus other stressors. Results suggest that more stringent COVID mitigation policies may have led to higher stress and depressive symptoms among 9/11 survivors.

**COVID-19 booster vaccination by race, ethnicity, and frailty among 11.3 million older adults** Kaleen Hayes\* Kaleen Hayes Daniel Harris Andrew Zullo Vincent Mor

**Background:** Racial and ethnic disparities existed in the initial uptake of COVID-19 vaccines. It is unknown whether these disparities persist for booster vaccines, and whether racial and ethnic differences in receipt may be further modified by frailty – an age-related syndrome known to increase the risk of poor outcomes from COVID-19.

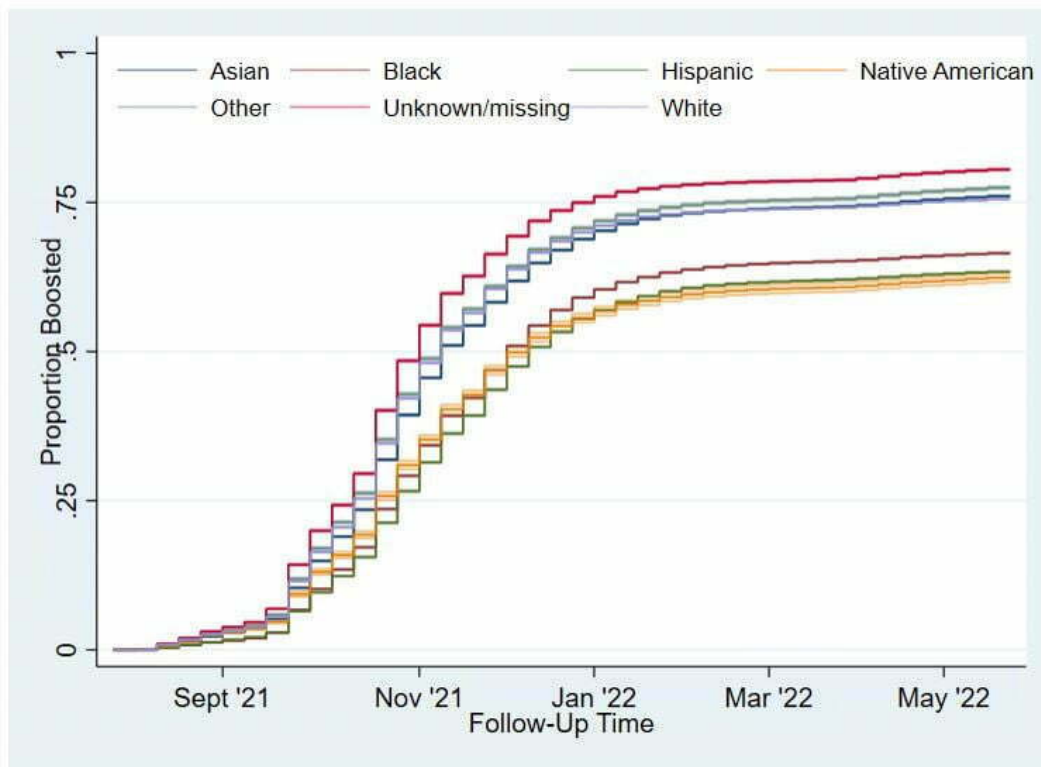
**Objective:** To examine racial and ethnic disparities in COVID-19 booster vaccine receipt overall and by frailty.

**Methods:** We conducted a retrospective cohort study using linked Medicare claims, CVS Health, and Walgreens data. We included community-dwelling Medicare beneficiaries aged  $\geq 66$  years who received 2 doses of an mRNA vaccine (BNT162b2, mRNA-1273) between 1/1/2021 and 8/1/2021. We followed beneficiaries from 8/1/2021 until the booster vaccination, death, Medicare disenrollment, or end of follow-up (5/15/2022). We estimated the cumulative incidence of booster vaccination using Kaplan Meier methods and RRs for booster uptake between groups using generalized linear models (Poisson distribution, log link, and offset for follow-up time) and adjustment for age, sex, and geographic region. We assessed differences in booster uptake by frailty (non-frail, prefrail, or frail per the Frailty Index) using interaction terms.

**Results:** We identified 11,340,298 eligible beneficiaries with 2 mRNA vaccines (mean age 76 years, 60% female, 78% White, 38% prefrail, 6.5% frail). Overall, 74% of the cohort received a booster, but we observed variation by race and ethnicity (White=76%; Asian=76%; Black=67%; Hispanic=64%, Figure 1). Compared to White patients, Black (RR=0.76 95%CI=0.75-0.76) and Hispanic patients (RR=0.70 95%CI=0.69-0.70) had lower booster vaccine receipt, while Asian patients were similar (RR=0.98 95%CI=0.97-0.98). Racial and ethnic disparities were larger among non-frail patients than prefrail/frail patients.

**Conclusions:** Racial and ethnic disparities in COVID-19 booster vaccination exist, especially for those who are not frail.

**Figure 1.** Cumulative incidence of COVID-19 booster vaccinations by race and ethnicity among 11,340,298 million eligible Medicare beneficiaries aged 66 years or older.





**National U.S. claims-based cohort study of the safety of adenoviral vector COVID-19 vaccination during pregnancy** Annette Regan\* Annette K. Regan Sheena G. Sullivan Flor M. Munoz Onyebuchi A. Arah

Compared to non-pregnant adults, pregnant people are at greater risk of complications from COVID-19 and are, therefore, a priority group for immunization. Results from several epidemiological studies support the safety of vaccination during pregnancy with mRNA COVID-19 vaccines. However, few studies have investigated the safety of vaccination with an adenoviral vector COVID-19 vaccine (Johnson & Johnson/Janssen® in the U.S.) during pregnancy. We constructed a claims-based cohort study using the Merative® Marketscan® Commercial Database, which includes health insurance claims for outpatient and inpatient care for commercially insured U.S. individuals. We included all pregnancies with a date of pregnancy end from February 27, 2020 (date of Janssen® authorization) through September 30, 2021, using a previously validated algorithm to identify pregnancy outcomes. We classified pregnancies as vaccinated if they had a date of Janssen® vaccination during pregnancy. We searched outpatient and inpatient medical claims records for ICD-coded pregnancy-related and post-vaccination events, including thrombosis or thrombocytopenia during pregnancy.

Among 144,724 eligible pregnancies, we identified 436 (0.3%) pregnancies exposed to the Janssen® COVID-19 vaccine; 50% of vaccinations occurred during the third trimester, and 36% occurred during the second trimester. Preliminary analyses showed that 83% of unvaccinated and 80% of vaccinated pregnancies ended in live birth. We identified no cases of ICD-coded thrombosis or thrombocytopenia in vaccinated individuals and 93 cases among unvaccinated individuals. These initial results highlight the ability to use large medical claims records to investigate the health effects of uncommon vaccine exposures during pregnancy. Comprehensive multi-country studies will likely be needed to evaluate the risks of rare outcomes associated with adenoviral vector COVID-19 vaccination during pregnancy.

**Role of genetic ancestry on the relationship between genetic risk score of type 2 diabetes mellitus and birth weight**

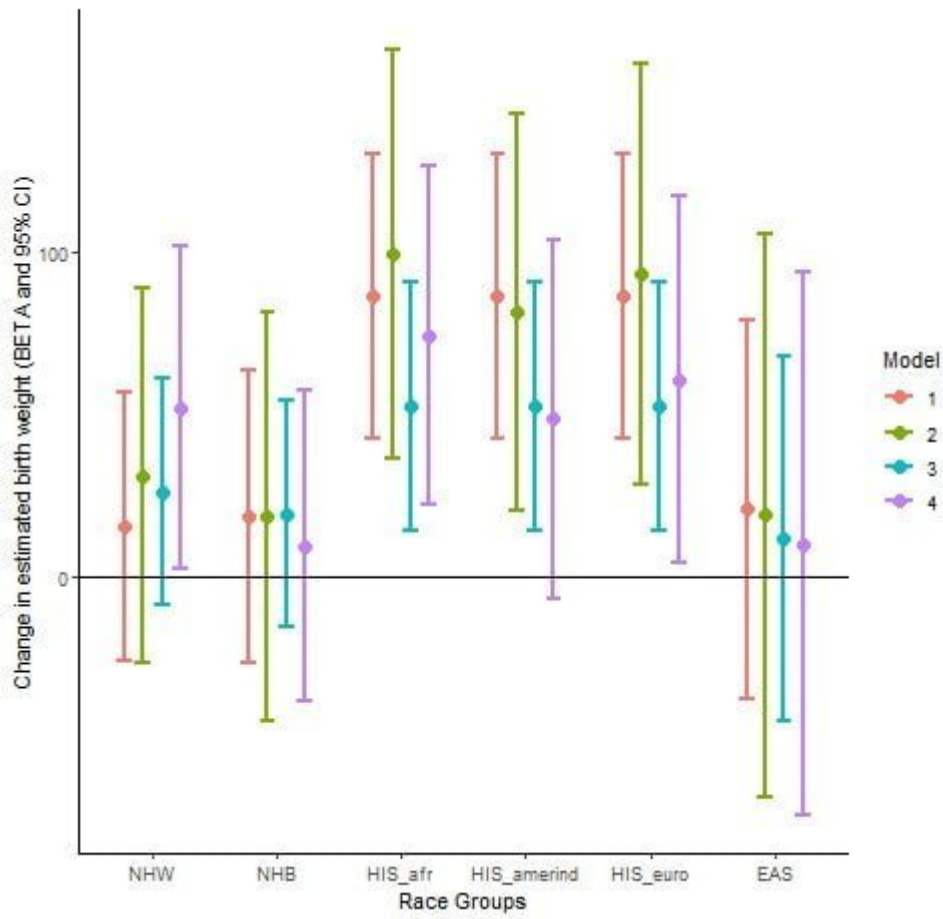
Tesfa Dejenie Habtewold\* Tesfa Dejenie Habtewold Richard J. Biedrzycki Fasil Tekola-Ayele

**Introduction:** Women's genetic risk score for type 2 diabetes mellitus ( $GRS_{T2D}$ ) has been associated with birth weight; however, the role of genetic ancestry in the relationship is unclear. We investigated whether the association of  $GRS_{T2D}$  with birth weight varies based on maternal genetic ancestry composition.

**Methods:** 1,935 pregnant women self-identified as Hispanic (n=531), White (n=601), African American (n=587), and Asian (n=216) from the NICHD Fetal Growth Studies - Singletons were included.  $GRS_{T2D}$  was calculated using 338 variants associated with T2D in the largest trans-ethnic study. The proportions of African, European, Amerindigenous, and East Asian genetic ancestry in the maternal genome were calculated. For each ethnic group, we assessed change in birthweight per unit increase in  $GRS_{T2D}$  using linear regression models without and with genetic ancestry proportion: model 1 included sex, gestational age, nativity, insurance, educational status, marital status, age, and parity; model 2 additionally included genetic ancestry, and  $GRS_{T2D}$ -genetic ancestry interaction term.

**Results:** Among Hispanics,  $GRS_{T2D}$  was significantly associated with birthweight in the model without genetic ancestry (beta [95% Confidence Interval] = 53 [14, 91] gram (gm)), and strengthened in the model with European ancestry (61 [4, 118] gm), but became weaker and non-significant in the model with Amerindigenous ancestry (49 [-7, 104] gm). Among Whites,  $GRS_{T2D}$  was not associated with birthweight in the model without genetic ancestry (26 [-9, 61] gm) but became stronger and significant in the model with European ancestry (52 [2, 102] gm). No associations were significant among African Americans and Asians in models without or with African and East Asian ancestry, respectively.

**Conclusion:** The performance  $GRS_{T2D}$  differed with genetic ancestry even within a self-identified ethnic group, which may be due to gene-environment interplays and limited non-European discovery genomic studies.



**Trends in Emergency Department (ED) visits among people with diabetes, United States, 2011-2020** Loredana Santo\* Loredana Santo Susan M. Schappert Jill J. Ashman

In the United States, diabetes was the eighth leading cause of death in 2020. The prevalence of diabetes among US adults increased steadily from 2001 to 2020, impacting health care utilization. The objective of this study was to assess recent ED visit trends for people with diabetes. **Methods:** Visit rates of people with diabetes were analyzed using nationally representative data from the 2011-2020 National Hospital Ambulatory Medical Care Survey. Time points were grouped into 2-year intervals to increase estimate reliability. Visit rates were calculated using the civilian noninstitutionalized population of the US. **Results:** The annual average number of ED visits by people with diabetes ranged from 11.5 million in 2011-2012 (8.6% of all ED visits) to 18.3 million in 2019-2020 (13.0% of visits). The ED visit rate for people with diabetes increased from 37.4 visits per 1000 people in 2011-2012 to 56.4 in 2019-2020. Children under 18 years represented only 1.0% of visits by people with diabetes in 2019-2020. Visit rates did not change among children (2.7 in 2011-2012 and 2.6 in 2019-2020) but increased among adults from 48.4 in 2011-2012 to 72.0 in 2019-2020. The visit rate increased from 118.3 in 2011-2012 to 139.5 in 2019-2020 for people with Medicare and from 45.9 to 72.5 for people with Medicaid. No change in trends was seen for people with private or no insurance. Visit rates were higher for those with Medicare or Medicaid compared with private or no insurance during 2011-2020. Non-Hispanic Black people had the highest visit rates across the study period. In 2019-2020, their rate was 104.3 compared with non-Hispanic White people (54.9), Hispanic people (41.1) and non-Hispanic people of other races (32.9). Increasing trends from 2011 to 2020 were found for race and Hispanic origin. **Conclusion:** ED visit rates by people with diabetes increased over 2011-2020 among adults. Disparities in ED use by race and ethnicity and insurance subgroups persisted over the same period.

**Public Health Funding's Impact on Type 2 Diabetes in Ontario, Canada** Mohamed Mohamed\*  
Mohamed Mohamed Roman Pabayo Brendan Smith

**Background**

Increasing diabetes rates worldwide are a major public health concern. This has led to major monetary expenses, as it costs the Canadian healthcare system \$30 billion annually. While previous research has looked at the association between public health funding and health outcomes, few have studied public health funding's impact on type 2 diabetes risk. This study's objective is to estimate the association between public health funding per capita at the public health unit level, and the odds of type 2 diabetes among adults living across health regions in Ontario, Canada.

**Methods**

We conducted a cross-sectional study using data from the 2013 Canadian Community Health Survey, a population-based representative survey that annually collects health data. Public health funding data for mandatory programs in Ontario was collected for the 34 public health units. Area-level characteristics of the regions which PHUs serve were obtained from the 2011 Canada Census. Multilevel modeling was used to estimate the association between public health funding per capita and the odds for type 2 diabetes, adjusting for individual level and area level covariates.

**Results**

Mean public health funding per capita across the health regions was 45.1 CAD (SD = 12.5), with a range of 29.8 to 80.1 CAD. The mean prevalence of type 2 diabetes across the health regions was 9.3% (SD = 0.02), with a range of 5.9 to 12.9. An SD-unit increase in public health funding per capita was associated with an increase in odds of type 2 diabetes (OR = 1.08, 95% CI = 1.00, 1.17).

**Conclusion**

Results from the study showed public health unit funding per capita had an unexpected effect on type 2 diabetes, indicating that greater public health funding was associated with an increased odds of type 2 diabetes among Ontarians. It's possible that increased public health funding is a good thing since it's being directed to where there's more type 2 diabetes prevalence present.

**The investigation of incidence rate in diabetes patients with lichen planus: a descriptive study for 14 years in Taiwanese population.** Yu-Ching Chou\* Yen-Lin Li Chien-An Sun

**Background:** According to the statistics, diabetes was ranked 5th among cause death in Taiwan. Lichen planus is a chronic inflammatory disease that involves the skin and oral mucosa. There are some data throws some light on its association with various systemic and metabolic disorders. However, secular trend studies of diabetes with lichen planus are limited. This descriptive study examined the incidence of diabetes with lichen planus in a large-scale, population-based Taiwanese cohort.

**Methods:** From 2000 to 2013. We identify 977 new cases with lichen planus in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating the incidence rates of diabetes with lichen planus in different characteristics, including sex, age groups and periods. We evaluated the change in the incidence rates over 14 years by linear trend analysis for assessing long tern trends.

**Results:** The incidence of diabetes was 224.14 among lichen planus patients per 10,000 person-years. The incidence rate was 240.8 and 209.5 among men and women per 10,000 person-years respectively. The incidence rate of diabetes was higher in men. After stratifying age into 5 groups, we found that the incidence rate of diabetes per 10,000 person-years was 22.3 in 20-29 years old, 111.97 in 30-39 years old, 152.58 in 40-49 years old, 400 in 50-59 years old and 444.88 in  $\geq 60$  years old. Patients have higher incidence rate of diabetes when age is increasing. Also, incidence rate of diabetes was 229.94 and 218.69 by visiting 1 time and  $>1$  times in lichen planus clinical visits respectively.

**Conclusion:** Diabetes had a severe impact on our life cause its rank of cause death. We found that incidence rate of diabetes with lichen planus is steadily rising through the data analysis base on NHIRD. For future study, we could further investigate the association between lichen planus and diabetes.

**Keywords:** Lichen planus, National Health Insurance Research Database (NHIRD), Diabetes

**Glycaemic control and one-year risk of potentially avoidable hospitalisations among adult type 2 diabetes patients: a cohort study** Wei-Yen Lim\* Wei-Yen Lim Htet Lin Htun Weixiang Lian Hwee Pin Phua Moses Yidong Lim Timothy Peng Lim Quek Daniel Ek Kwang Chew

**Aims:** We evaluated the relationship between glycaemic control over a 2-year period and potentially avoidable hospitalizations (PAH) in the subsequent year in a cohort of diabetics managed at the outpatient clinic of a tertiary hospital

**Methods:** Data from a retrospective closed cohort of adult type 2 diabetes patients with  $\geq 3$  HbA1c tests over two years measured between 2009 and 2017 were used. The outcome of PAH was defined using Agency of Healthcare Research and Quality criteria. Glycaemic control was assessed using mean HbA1c, and by classifying patients into HbA1c trajectory classes using group-based trajectory modelling. Modified Poisson regression was used to assess the relationship between glycaemic control and PAH.

**Results:** A total of 14923 patients (mean age:  $62.9 \pm 12.8$  years; 55.2% men) were included. Four HbA1c trajectories were observed; low-stable (n=9854, 66.0%), moderate-stable (n = 3125, 20.9%), high-decrease (n=1017, 6.8%), and high-persistent (n=927, 6.2%). Compared to the low-stable trajectory, moderate-stable (RR 1.15, 95%CI 1.00-1.32), high-decrease RR 1.54, 95%CI 1.32-1.81) and high-persistent trajectories (RR 1.97, 95%CI 1.59-2.45) were associated with increasing risks of PAH. These risks were highest for PAHs defined as diabetes-related and chronic. Compared to patients with a mean HbA1c of 6.0–6.9%, patients with higher mean HA1c had higher risks of PAH: HbA1c 7.0-7.9% RR 1.08, 95%CI 0.95-1.22, HbA1c 8.0-8.9% RR 1.12, 95%CI 0.97-1.29, HbA1c  $\geq 9.0\%$  RR 1.51, 95%CI 1.32-1.73) p for trend 0.002. The increase in risks were highest for diabetes-related PAH.

**Conclusion:** Better glycaemic control was significantly associated with a lower subsequent risk of PAH. Patients in the high-decrease HbA1c trajectory had a lower risk of PAH compared to those in the persistent-high category, suggesting that risk of PAH related to poor glycaemic control is potentially reversible.

**Applications of environmental mixture methods on associations with persistent organic pollutants exposures: A scoping review** SHudi Pan\* Shudi Pan Bruna Rubbo Brittney Baumert Victoria Quon-Chow Carmen Chen Max Aung Erika Garcia David Conti Leda Chatzi

**Background and aim:** All humans are exposed to multiple chemicals simultaneously at any given time point or cumulatively across their lifetimes. Chemicals are highly correlated and potentially have antagonistic or synergistic effects in mixtures. Persistent Organic Pollutants (POPs) are environmentally and biologically persistent synthetic chemicals widely used in daily life such as flame retardants and pesticides. Recently through the application of novel statistical methods, such as Bayesian Kernel Machine Regression (BKMR) and Weighted quantile sum regression (WQS), several epidemiological studies have focused on associations between adverse health outcomes and mixtures of POPs as opposed to single POP exposure.

**Methods:** We summarized articles that investigated associations between the overall effects of POP mixtures and various health outcomes in PubMed and Embase from January 2011 to August 2022. We focused on five chemical classes of POPs: Organochlorine Pesticides (OCPs), polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs), per- and polyfluoroalkyl substances (PFASs), 5) polychlorinated dibenzo-p-dioxins (PCDDs) and polychlorinated dibenzofurans (PCDFs).

**Results:** We identified 185 studies for review. The majority of eligible studies were in the United States (n = 73, 39.5%). The most frequently studied health outcome is developmental (n = 53, 28.6%). Most articles used BKMR (n = 81) and WQS (n = 49) to estimate the overall effects of mixtures. Through these methods, researchers usually estimated overall effects of single chemical class, like PFASs (n = 72) and OCPs (n = 59); however, sixty-four articles estimate the overall effects of all POPs from different chemical classes, as well as incorporated other type of chemicals such as heavy metals (n = 17), and other non-persistent chemicals (n = 16).

**Conclusion:** We recommend a standardization of POPs combination in mixtures for better comparisons between studies for future research.



**An exploration of the impact of air pollution on systolic blood pressure percentiles in children (3-9 years of age)** Celeste D. Butts\* Celeste Butts Kristen M. Rappazzo Keia Sanderson Cathrine Hoyo Chantel L. Martin

Air pollution is a leading environmental health concern and early life exposures may have life-long implications. Prenatal air pollution exposure has been reported in association with blood pressure (BP) percentiles and elevated BP in children, which are important predictors of future hypertension and consequently increased risk of cardiovascular (CV) disorders. However, the existing data is sparse and most previous studies used measures from a single day. Trajectory modeling, which groups individuals with similar health outcomes over time, may be more useful for targeting wide-reaching clinical interventions. Our objective was to explore associations between  $\text{NO}_2$ ,  $\text{PM}_{2.5}$  and  $\text{O}_3$  and systolic BP percentile trajectories for 884 children in the Newborn Epigenetic Study, a diverse North Carolina cohort, and to explore differences by race. Harvard and CMAQ pollutant estimates were assigned by census tract across 90 days preconception, trimesters and the entire pregnancy. We used multinomial logistic regression to estimate associations between the air pollutants and trajectory group membership (low stable [referent] (41%), low increasing (17%), high stable (30%) or high decreasing (12%)) adjusting for age, race, education and season of conception. In main effects models, we saw a suggested 12% increased odds of high stable group membership with preconception  $\text{PM}_{2.5}$  exposures. In the offspring of Black gestational parents (n=433), preconception  $\text{PM}_{2.5}$  exposures were associated with increased odds of high stable group membership [OR: 1.26 (1.08, 1.46)] (Harvard) and [OR: 1.23 (1.08, 1.41)] (CMAQ), while in the offspring of White gestational parents (n=241), we saw a suggested ~10% decreased odds of high decreasing group membership with  $\text{NO}_2$  exposures across all time points. Overall, our results suggest that air pollution may be related to BP percentile trajectories. Our findings may be of clinical importance given the impact of early cardiometabolic outcomes on future CV health.

**Mercury and Nickel Exposure is Associated with Sleep Problems in Children Aged 6-14****Years Old** Kelsey M Maclin\* Kelsey Maclin Lonnie Sears, PhD John Myers, MS Kristina Zierold, PhD

**Background and Aim:** Sleep problems in children can result in learning problems, negative emotions, and impact neurodevelopment. Research investigating sleep problems and environmental pollutants has been conducted in adults, for which certain metals have been associated with circadian functions in the sleep-wake cycle. Limited research has been conducted to investigate the association between heavy metals and children's sleep. Therefore, the objective of this study was to investigate the association between heavy metal exposure and sleep problems in children aged 6 to 14 years old.

**Methods:** This was a community-based cross-sectional study with children residing near two coal-fired power plants in Kentucky. Parent-reported sleep problems were defined as ever having difficulty falling asleep or remaining asleep. Heavy metal body burden was determined from toenail samples analyzed by Inductively coupled plasma mass spectrometry (ICP-MS). Toenails reflect 6-12 months of exposure. To assess the association between several heavy metals and parent-reported sleep problems, two statistical approaches were used: the Wilcoxon test and logistic regression.

**Results:** There were 283 children enrolled in this study and 18% of children had sleep problems. 26% of children self-identified as nonwhite, and there were slightly more males than females. Based on nonparametric tests, exposure to higher levels of mercury and nickel was associated with sleep problems ( $p=0.02$  and  $p=0.06$  respectively). Multivariable logistic regression supported these findings.

**Conclusions:** No literature has reported an association between nickel and mercury and sleep problems in children. Our study found that children exposed to nickel and mercury were more likely to report sleep problems compared with children not exposed. Further research needs to be conducted to confirm this finding and to understand how exposure to nickel and mercury may be associated with sleep problems in children.

**Iron status does not Mediate the Association of an Industry-Relevant Metal Mixture with IQ in Italian Adolescents** Samantha Schildroth\* Samantha Schildroth Linda Valeri Baoyi Shi Alexa Friedman Roberta F. White Katarzyna Kordas Donatella Placidi Robert O. Wright Donald Smith Roberto G. Lucchini Megan Horton Birgit Claus Henn

**Background:** Metals have been associated with adverse neurodevelopmental outcomes in children.

Epidemiological evidence suggests that these associations may be mediated by essential nutrients like iron (Fe). However, few studies have investigated Fe status as a possible mediator of a metal *mixture* with neurodevelopment.

**Methods:** We used cross-sectional data from 383 adolescents (10-14 years) in the Public Health Impact of Metals Exposure Study. Manganese (Mn), chromium (Cr), and copper (Cu) were quantified in hair; lead (Pb) was quantified in whole blood using ICP-MS. Ferritin, a marker of Fe status, was quantified in serum using immunoassays. The Wechsler Intelligence Scale for Children (WISC) was administered to assess intelligence quotient (IQ). We used Bayesian Kernel Machine Regression Causal Mediation Analysis (BKMR-CMA) to estimate natural direct effects (NDEs) and natural indirect effects (NIEs), adjusting for *a priori* selected confounders. Betas ( $\beta$ ) and 95% credible intervals (CIs) were estimated.

**Results:** Median concentrations for Mn, Cr, Cu, Pb and ferritin were 0.08  $\mu\text{g/g}$ , 0.05  $\mu\text{g/g}$ , 9.4  $\mu\text{g/g}$ , 1.3  $\mu\text{g/dL}$  and 27.0  $\text{ng/mL}$ , respectively. Although individual metals (e.g., Cu, Pb) were associated with IQ, there was limited evidence that the overall mixture was materially associated with IQ. The NDE, reflecting the direct association not mediated through Fe status for an increase in the overall mixture from its 25<sup>th</sup> to 75<sup>th</sup> percentiles, was null for verbal IQ ( $\beta=-0.30$ , 95% CI= -2.28, 1.52), performance IQ ( $\beta=0.06$ , 95% CI=-1.31, 1.54), and full-scale IQ ( $\beta=-0.05$ , 95% CI=-1.56, 1.40). There was no evidence of mediation by Fe status, where the NIEs for each IQ scale were null.

**Conclusion:** In this Fe-replete population, there was no evidence that the metal mixture was jointly associated with IQ through either direct or indirect pathways. Fe-deficient populations may be more susceptible to metals neurotoxicity, and should therefore be examined in future studies.

**Association of gaseous ambient air pollution and brain volumes in the ARIC cohort** Katie Lynch\* Katie Lynch Melinda C. Power Erin E. Bennett Qi Ying Eun Sug Park Xiaohui Xu Richard L. Smith Duanping Liao Joel D. Kaufman Eric A. Whitsel

**Introduction:** Growing evidence links air pollution to late-life cognitive health, but the limited research on gaseous pollutants yields mixed results. We explored the associations between gaseous pollutants and MRI markers of neurodegeneration in participants of the Atherosclerosis Risk in Communities (ARIC) study, with attention to the potential influence of exposure estimation approach and confounding by study site.

**Methods:** Our sample included up to 1,665 ARIC participants recruited from 4 U.S. sites in 1987-89 (Forsyth County, NC; Jackson, MS; the suburbs of Minneapolis, MN; and Washington County, MD) who had valid brain MRI data from Visit 5 (2011-13), required exposure data, complete covariate data, and were in large race-site categories. We estimated 10-year (2001-10) mean carbon monoxide (CO), nitrogen dioxide (NO<sub>2</sub>), nitrogen oxides (NO<sub>x</sub>), and 8- and 24-hr ozone (O<sub>3</sub>) concentrations at geocoded participant addresses using multiple approaches. We estimated site-specific associations between pollutants and regional brain volumes using adjusted linear regression. We combined them in inverse variance-weighted, random-effects meta-analyses. We compared combined associations with those from analyses that neither stratified by nor adjusted for site.

**Results:** Combined associations were generally null regardless of exposure estimation approach. Relatively consistent (and occasionally marginally significant) point estimates suggesting associations between higher CO or NO<sub>2</sub>/NO<sub>x</sub> and lower temporal lobe volume were seen. Contrary to primary analyses, models that did not adjust for study site often yielded significant summary estimates.

**Conclusion:** We did not find strong evidence of gaseous pollutant-brain volume associations regardless of exposure estimation method. Results would benefit from evaluation in larger samples. Limited exposure variability within site may limit power to detect associations. Not adjusting for location may lead to spatial confounding.

**Augmenting the Premature Mortality Population Risk Tool (PreMPoRT) with urban environmental data to evaluate predictive performance benefits of environmental measures in risk prediction models** Lief Pagalan\* Lief Pagalan Helen Stylianou Mackenzie Hurst Meghan O'Neill Stacey Fisher Lori Diemert Hong Chen Jeffrey Brook Andy Hong Laura C. Rosella

**Introduction:** Environmental factors have been shown to impact premature mortality (death before age 75); however, it is not known how the inclusion of environmental factors improves prediction for premature mortality in the general population. We augmented the Premature Mortality Population Risk Tool (PreMPoRT) with environmental determinants to predictive performance impacts.

**Methods:** Sex-specific Weibull survival models were developed by linking the 2000-12 Canadian Community Health Survey (CCHS) cycles to the Canadian Vital Statistics Death Database to predict the 5-year incidence of premature mortality for adults 18-74 in cities. Base models included sociodemographics, health behaviors, and health-related variables (e.g., chronic conditions). Using residential postal code, we added environmental data to base models, including air pollution, greenspace, temperature, and neighborhood-level socioeconomic and walkability indices. The 2000-08 cycles were used as a training set, which was then spatially validated using 2000-08 holdout Forward Sortation Areas and temporally validated using 2009-12 cycles.

**Results:** The analytic sample included 126,000 females and 108,000 males, with 1.3% and 1.9% premature mortality, respectively. Adding environmental data to base models did not change discrimination and calibration. Minimal models with just age and environmental variables maintained fair-to-good discrimination and calibration with a slight loss in performance (Table 1). In females, minimal models had C-indices of 0.75 and 0.79 in spatial and temporal validation, respectively, versus 0.84 and 0.87 in base models; in males, 0.80 and 0.80 versus 0.85 and 0.86. Discrimination, calibration slopes, and calibration-in-the-large were similar across all models.

**Conclusion:** Adding environmental data to the premature mortality prediction model showed no performance gains, but using age and environmental predictors alone produced fair-to-good discrimination and calibration.

**Table 1. PreMPoRT Predictive Performance Measures Using CCHS Cohort Restricted to Census Metropolitan Areas**

Split	Performance Measure	Target (Range)	Female (n = 126,000)			Male (n = 108,000)		
			Base Model	Base Model + Environmental	Age + Environmental	Base Model	Base Model + Environmental	Age + Environmental
Development	Sample Size		62,000 (49.2%)			54,000 (50.0%)		
	Premature Deaths		1.3%			1.9%		
	Nagelkerke R <sup>2</sup>	1 (0–1)	0.1110	0.1133	0.0599	0.1028	0.1058	0.0620
	Integrated Brier Score	0 (0–1)	0.0059	0.0059	0.0063	0.0081	0.0081	0.0086
	C-Index	1 (0–1)	0.8726	0.8754	0.8144	0.8540	0.8572	0.8031
	Discrimination Slope	Higher is Better	0.0927	0.0950	0.0212	0.0908	0.0946	0.0304
	Calibration-in-the-Large	0	-0.0008	-0.0008	-0.0006	-0.0010	-0.0010	-0.0009
	Calibration Slope	1	1.0000	1.0000	1.0000	1.0000	1.0000	1.0000
Spatial Validation	Sample Size		23,000 (18.3%)			20,000 (18.5%)		
	Premature Deaths		1.3%			2.0%		
	Nagelkerke R <sup>2</sup>	1 (0–1)	–	–	–	–	–	–
	Integrated Brier Score	0 (0–1)	0.0059	0.0060	0.0061	0.0092	0.0093	0.0099
	C-Index	1 (0–1)	0.8379	0.8324	0.7506	0.8456	0.8429	0.8060
	Discrimination Slope	Higher is Better	0.0642	0.0640	0.0144	0.0894	0.0904	0.0309
	Calibration-in-the-Large	0	-0.0016	-0.0015	-0.0016	0.0022	0.0020	0.0019
	Calibration Slope	1	0.9729	0.9473	0.7879	1.0489	1.0230	1.0388
Temporal Validation	Sample Size		41,000 (32.5%)			34,000 (31.5%)		
	Premature Deaths		1.1%			1.8%		
	Nagelkerke R <sup>2</sup>	1 (0–1)	–	–	–	–	–	–
	Integrated Brier Score	0 (0–1)	0.0053	0.0053	0.0055	0.0086	0.0086	0.0090
	C-Index	1 (0–1)	0.8706	0.8670	0.7880	0.8552	0.8532	0.7950
	Discrimination Slope	Higher is Better	0.1015	0.0952	0.0212	0.0835	0.0838	0.0292
	Calibration-in-the-Large	0	-0.0042	-0.0030	-0.0031	-0.0015	-0.0013	-0.0023
	Calibration Slope	1	1.0188	0.9950	0.9753	1.0507	1.0151	0.9721

**Female base model:** Age, self-rated health, household income, education, body mass index, smoking, physical activity, chronic obstructive pulmonary disease and emphysema, heart disease, diabetes, cancer, stroke effects. **Male base model:** Age, self-rated health, marital status, household income, education, smoking, arthritis, chronic obstructive pulmonary disease and emphysema, heart disease, cancer, stroke effects, Alzheimer’s disease. **Environmental variables:** Households and dwellings index, material resources index, age and labour force index, immigration and visible minority index, active living environment index, nitrogen dioxide, ozone, particulate matter 2.5 microns in diameter and less, normalized difference vegetation index, annual highest temperature, annual lowest temperature, annual number of heat event starts based on average temperature, annual number of days in heat events based on average temperature, annual number of cool event starts based on average temperature, annual number of days in cool events based on average temperature. **Sample size rounding:** Sample sizes for preliminary results were rounded to the nearest thousand to comply with Statistic Canada Research Data Centre vetting procedures.

**An extension of the Quantile G-computation method to estimate joint causal effects of time-varying air pollutant mixtures on survival outcomes** Juwel Rana\* Juwel Rana**An extension of the Quantile G-computation method to estimate joint causal effects of time-varying air pollutant mixtures on survival outcomes**

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**BACKGROUND:** Quantile g-computation (QGcomp) is one of the available multipollutant analytic methods that may estimate the causal effects of environmental pollutant mixture exposures at fixed time points. However, these are rarely applied in air pollution studies and cannot handle time-varying pollutant mixtures which may introduce collider stratification and time-dependent biases.

**OBJECTIVES:** To fill these knowledge gaps, this study extends the QGcomp via Monte Carlo-based parametric g-computation to estimate the causal joint effects of time-varying air pollutant mixture on nonaccidental death in Canada.

**METHODS:** We simulate a cohort study of 10,000 to 100,000 participants  $\geq 25$  years old at enrollment followed for up to 5 years. The geoscience-derived annual air pollutant estimates (2012-2016) of outdoor PM<sub>2.5</sub> mass and seven PM<sub>2.5</sub> components (i.e. black carbon, sulfate, ammonium, nitrate, organic matter, sea salt, and mineral dust for North America) are time-varying mixtures. The study simulates nonaccidental death, a discrete time-to-event outcome, based on the Canadian Census Health and Environment Cohorts 2016, with increasing complexity in the air pollutant mixture-outcome associations. The study controls for simulated age, sex, race/ethnicity, individual-level income, and educational attainment as baseline/time-fixed confounders and neighborhood-level unemployment rate and mean household income as time-varying confounders. We estimate average joint causal risk difference, causal attributable risk difference, and causal dose-response. We examine and compare bias, empirical standard error (SE), and confidence interval (CI) coverage in different exposure-response scenarios. Moreover, how these estimates are impacted by the number of time points, in the presence of interactions among air pollutants, high collinearity among air pollutants, non-linear exposure-outcome relationships, and effect measure modification (EMM).

**RESULT:** The extended QGcomp for time-varying multipollutant can produce the least biased joint and independent effect estimates with reliable SE and CI coverage and can detect true dose-response relationships, interaction effects, and EMM.

CONCLUSION: Our approach will help to account for time-varying environmental mixtures in estimating the joint causal effect which addresses collider stratification and time-dependent confounding biases.



**Comparison of historical redlining HOLC grade exposure assessment metrics for differing spatial scales** Monica P. Jimenez\* Monica P. Jimenez Adrien A. Wilkie Christine L. Gray Kristen M. Rappazzo Thomas J. Luben

Background and Aim: Around the mid-1930s, the Home Owners' Loan Corporation (HOLC) ranked urban neighborhoods as least to most desirable in terms of perceived mortgage stability. When evaluating the impacts of this racist practice (i.e., redlining), studies have not assessed potential misclassification to HOLC grades when individual-level locational information is unavailable. We evaluate how assignment of HOLC grades differs across spatial scales within five historically redlined cities in North Carolina (NC).

Methods:

Using geocoded NC birth records (2003-2015), we created and compared HOLC grade designations at spatial scales of individual residential address, census block group (CBG), census tract (CT), and ZIP code. At the 4 different scales, addresses were assigned HOLC grade A (Best), B (Still desirable), C (Declining), or D (Hazardous). For residential address, we used a "point-in-polygon" approach to assign geocoded addresses to an HOLC grade. HOLC grade was assigned to CBG, CT, and ZIP code based on the grade of the HOLC polygon(s) covering the majority of the land area. We used Pearson correlation coefficients ( $r_p$ ) and ranked classifications (Kappa statistics) to compare the designations made at different spatial scales.

Results:

Our analysis included 39330 residential addresses; 3311 (8.4%) in grade A, 5776 (14.7%) in grade B, 20204 (51.4%) in grade C, and 10039 (25.5%) in grade D. Assignments to HOLC grade using CBG or CT were well-correlated with HOLC grade using residential address ( $r_p=0.77$  for CT and  $r_p=0.78$  for CBG); correlations were lower for ZIP code ( $r_p=0.56$ ). The weighted kappa statistic also showed there was a greater degree of agreement to HOLC designation when comparing CBG to residential address compared to CT or ZIP code (Figure 1).

Conclusions: This comparison of HOLC grade assignment metrics suggests that the use of CBG or CT, rather than residential address, may be feasible. The use of ZIP code is less feasible in North Carolina.

**Figure 1: Percent agreement and non-agreement of HOLC designation based on residential address compared with designation based on census block group, census tract, or ZIP code of residence**

Residential Address	HOLC Grade by Residential Address (%)				TOTAL (%)	
	A	B	C	D		
Residential Address	8.4	14.7	51.4	25.5	100	

Residential Address	HOLC Grade by Block Group (%)				TOTAL (%)	% Non-agreement
	A	B	C	D		
<b>A: Best</b>	<b>73.4</b>	6.9	14.6	5.2	100	26.6
<b>B: Still desirable</b>	3.9	<b>55.5</b>	33.6	7.1	100	44.5
<b>C: Declining</b>	1.5	2.6	<b>75.2</b>	20.7	100	24.8
<b>D: Hazardous</b>	0.0	0.0	6.0	<b>94.0</b>	100	6.0
<b>TOTAL (%)</b>	7.5	10.1	46.3	36.1	<b>100</b>	Weighted Kappa = 0.70

Residential Address	HOLC Grade by Census Tract (%)				TOTAL (%)	% Non-agreement
	A	B	C	D		
<b>A: Best</b>	<b>68.0</b>	9.8	20.4	1.8	100	32.0
<b>B: Still desirable</b>	4.4	<b>58.1</b>	36.3	1.2	100	41.9
<b>C: Declining</b>	1.3	3.7	<b>84.3</b>	10.7	100	15.7
<b>D: Hazardous</b>	0.1	1.0	22.2	<b>76.7</b>	100	23.3
<b>TOTAL (%)</b>	7.1	11.5	56.0	25.4	<b>100</b>	Weighted Kappa = 0.69

Residential Address	HOLC Grade by ZIP Code (%)				TOTAL (%)	% Non-agreement
	A	B	C	D		
<b>A: Best</b>	<b>60.8</b>	1.0	36.4	1.8	100	39.2
<b>B: Still desirable</b>	8.6	<b>24.7</b>	63.0	3.7	100	75.3
<b>C: Declining</b>	2.1	5.0	<b>87.3</b>	5.7	100	12.7
<b>D: Hazardous</b>	0.0	1.8	65.2	<b>32.9</b>	100	67.1
<b>TOTAL (%)</b>	7.5	6.7	73.8	12.0	<b>100</b>	Weighted Kappa = 0.43

\* bolded percentages = agreement with individual residential address

**Modification of the associations between gestational lead exposure and autistic behaviors by maternal folate status** Josh Alampi\* Josh Alampi Bruce Lanphear Amanda MacFarlane Youssef Oulhote Joseph Braun Tye Arbuckle Janice Hu Gina Muckle Lawrence McCandless

Maternal folic acid (FA) intake may attenuate associations between gestational exposure to certain chemicals and autism/ autistic behaviors, but this has not been assessed for lead. We examined whether the relationship between gestational blood-lead levels (BLLs) and autistic behaviors was modified by folate, child sex, and maternal methylenetetrahydrofolate reductase (*MTHFR*) 677C>T genotype.

We used data from the Maternal-Infant Research on Environmental Chemicals (MIREC) study, a Canadian pregnancy and birth cohort (2008-2011). We assessed autistic behaviors in 601 3-4-year-old children using the Social Responsiveness Scale-2 (SRS-2), where higher scores denote more autistic-like behaviors. We measured BLLs and plasma-folate concentrations during the first and third trimesters of pregnancy. We also assessed maternal *MTHFR* 677C>T genotype and FA supplementation (12-16<sup>th</sup> weeks' gestation). We estimated confounder-adjusted associations between log<sub>2</sub>-transformed BLLs and SRS scores by child sex, gestational folate status, and maternal *MTHFR* 677C>T genotype.

Third-trimester BLLs were associated with increased SRS scores ( $\beta$  per 2-fold increase = 2.68, 95% CI: 0.36, 5.00) among mothers who consumed <400  $\mu\text{g}$  FA/day. Associations were null ( $\beta$  = -0.23, 95% CI: -1.16, 0.69) among mothers with adequate FA supplementation (400-1000  $\mu\text{g}$  FA/day) (p-int= 0.02). Third-trimester plasma-folate concentrations (<10<sup>th</sup> vs. 10<sup>th</sup>-80<sup>th</sup> percentile) similarly modified these associations (p-int< 0.001). Third-trimester BLL-SRS associations were also stronger among mothers who possessed two *MTHFR* 677C>T single nucleotide polymorphisms than those with none (p-int= 0.05). These variables also modified first-trimester BLL-SRS associations but to a lesser extent.

Our results suggest that maternal folate status (measured with FA supplementation, gestational plasma folate concentrations, and *MTHFR* 677C>T genotype) modified the associations between gestational lead exposure and childhood autistic behaviors.

**LATEBREAKER**

Environment/Climate Change

**Development and initial validation of the ACCLIMATES surveillance tool: Assessing climate change-related chronic disease vulnerability in Alberta, Canada** Brian Steele\* Brian Steele  
Brooke Sidney Kaitlyn Menard Okan Bulut Samuel Lowe Roman Pabayao Shelby Yamamoto

**Background.** Climate change poses significant threats to population health. Environmental features impacted by climate change (e.g. pollution, temperature) are associated with the development of chronic disease. There is a need to develop surveillance tools that measure environmental factors and social environments across urban and rural settings. None have been developed for use in Canada. We introduce a measurement tool developed in Alberta, Canada (pop. 4.4 million) and demonstrate initial validation.

**Methods.** Potential indicators of exposure, sensitivity, risk, and adaptive capacity included area-level environmental measures (green/blueness, vegetation, meteorological data, pollution, industrial proximity) from satellite and ground-based sources, census sociodemographic variables (sex, age, ethnicity, income/labor, dwellings, immigration, language), and health/social services access from government data.

Principal component factor (PCF) analysis was conducted. Variables with high missingness were excluded, as were variables with high uniqueness ( $\geq 0.6$ ). Following PCF, we used stepwise selection (based on AIC) with zero-inflated negative binomial regression using robust standard errors to study the association between predicted area-level factor scores with the frequency of diabetes, myocardial infarction, chronic obstructive pulmonary disease, and dementia in physician claims from 2015-2017.

**Results.** Of 254 potential variables, 210 were included in the PCF, achieving 95% provincial coverage. 15 factors accounted for 72.6% of the variance. For each outcome, models had the best fit with all 15 factors included. The majority of factors were significantly associated with the frequency of the outcomes, though the strength of associations varied across the final models.

**Conclusion.** Future directions for development, validation, and implementation are discussed, including domain-specific indicators, estimates of risk, and alternative methods for dimensionality reduction.

**An investigation of the association between trace elements in well water and congenital anomalies in North Carolina infants from 2003 - 2015** Celeste D. Butts\* Celeste Butts Jessie P. Buckley Andrew F. Olshan Nina E. Forestieri Rebecca C. Fry Lauren A. Eaves Alexander P. Keil

Birth defects, or congenital anomalies, impact >100,000 US births annually and are the leading cause of infant mortality. While genetic factors may contribute to their development, the role of environmental factors, including trace elements, is not as clearly understood. Contaminated drinking water is a major source of trace element exposures. This is of particular concern for the >2 million NC residents relying on unregulated private drinking well water as their primary drinking water source. Our objective was to examine independent and joint associations between 11 trace elements (As, Cd, Pb, Ca, Cl, Cr, Cu, Fe, Mg, Mn, Zn) in residential well water and the prevalence of non-chromosomal congenital anomalies in 1,293,227 live births. Exposures were multiply imputed to address lower reporting limits and averaged over census tracts before linking to births. We used adjusted logistic regression to estimate independent associations between trace element exposure (dichotomized as  $\geq 90$ th or  $\leq 50$ th percentile) and anomalies, and we used quantile g-computation to estimate the change in odds of an anomaly per simultaneous 1-quartile increase of all elements. Higher exposure to Cl [OR: 1.1 (95% CI: 1.1, 1.1)], Pb [OR: 1.1 (95% CI: 1.0, 1.1)], and Ca and Fe with similar estimates, and lower exposure to Mg [OR: 0.95 (95% CI: 0.91, 0.98)], Cr, and Mn were associated with higher odds of any anomaly. Stratified models showed lower odds of any anomaly with Mg and increased odds with Cl exposures for Non-Hispanic Whites, with suggestions of lower odds with Cl in Non-Hispanic Blacks, Hispanics, and Asian Pacific Islanders. In the mixture analysis, Cl and Mg had the strongest positive and negative associations with any anomaly, respectively. Overall, results suggest that well water contamination may have a complex role in the etiology of congenital anomalies and if causal, suggest that simple interventions that reduce all trace elements, like filtration, could have mixed results.

**Agricultural Exposures and Risk of Childhood Neuroblastoma: A Systematic Review and Meta-Analysis** Emma Hymel\* Emma Hymel Abraham Degarege Jordan Fritch Paraskevi Farazi Krishtee Napit Don Coulter Cynthia Schmidt Shinobu Watanabe-Galloway

While neuroblastoma accounts for 8% of childhood cancers, it causes 15% of childhood cancer deaths in the United States. The role of agricultural exposures in the development of neuroblastoma is unclear. We conducted a systematic review and meta-analysis of studies examining the relationship between agricultural exposures and neuroblastoma. MEDLINE, EMBASE, Scopus, and Google Scholar were searched in February 2022, identifying 742 publications. Seventeen articles met the inclusion criteria; all were published between 1985-2020 and included 14 case-control, one cross-sectional, and two cohort studies. Random effects models were used to calculate summary odds ratios (sORs) and 95% confidence intervals (CIs). An increased odds of developing neuroblastoma with parental exposure to any pesticides (sOR=1.25, 95% CI: 1.03-1.48; 4 studies), insecticides (sOR=1.55, 95% CI: 1.19-1.91; 3 studies) and residential exposure to crops/vegetables (sOR=1.04, 95% CI: 1.01-1.06; 2 studies) was seen. Heterogeneity was low in all analyses and no publication bias was evident. No significant associations were found with agricultural occupations, herbicides, and agricultural dusts. The studies were limited by exposure measurements and small sample sizes. Further studies are needed to explore mechanisms in the development of neuroblastoma in children with parental agricultural exposures, especially pesticides, and to improve methods of measuring agricultural-related exposures.

**Influence of weather and environment on the effectiveness of water, sanitation, and handwashing interventions on childhood diarrheal disease and enteric infections in rural Bangladesh** Anna Nguyen\* Anna Nguyen Jessica A. Grembi Marie Riviere Gabriella Barratt

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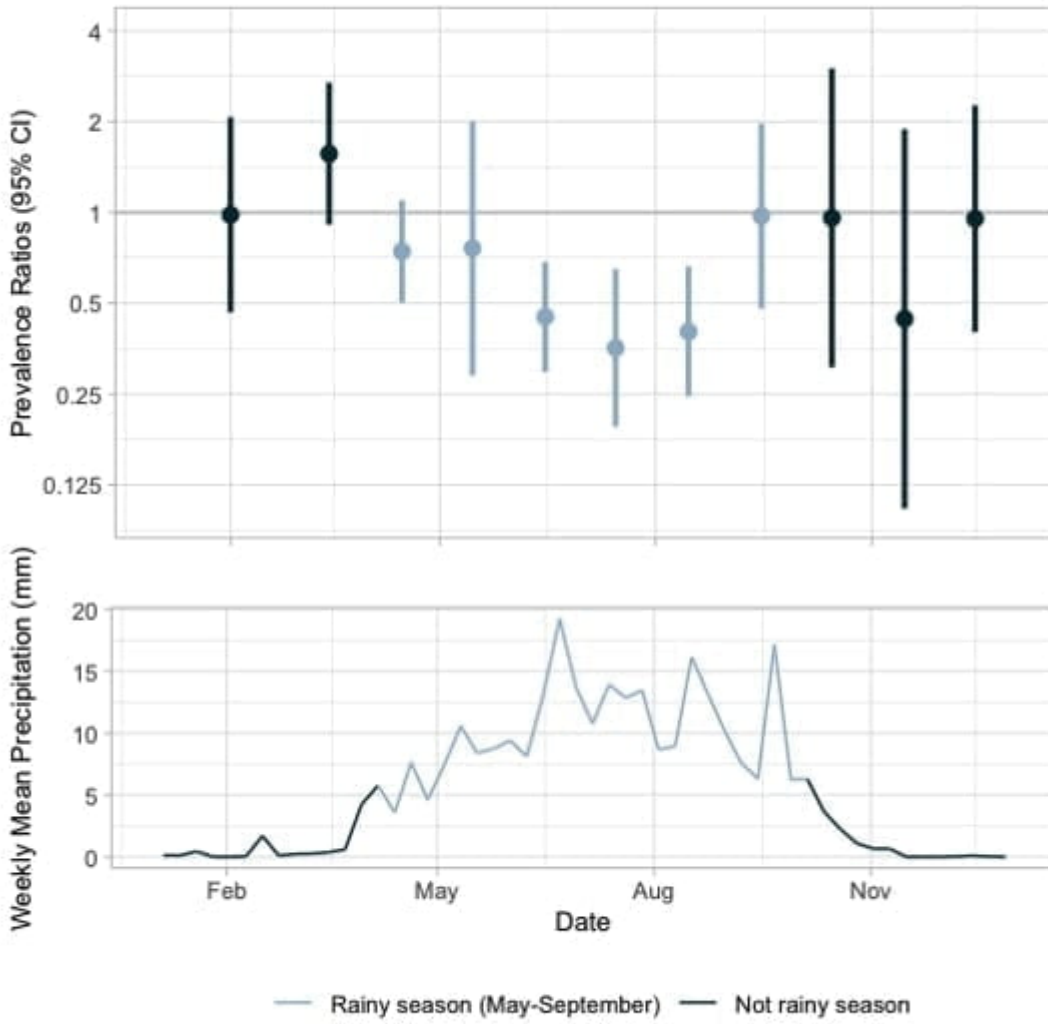
*Background:* Diarrhea is a leading cause of child morbidity and mortality in rural Bangladesh. Water, sanitation, and hygiene (WASH) interventions aim to reduce exposure to enteric pathogens, and weather and environment may impact effectiveness. We investigated whether weather and environmental variables modified the effect of low-cost, point-of-use WASH interventions on diarrheal disease, *Giardia* infection, and soil-transmitted helminths (STH) infection.

*Methods:* We analyzed data from a cluster-randomized trial in rural Bangladesh that measured the diarrhea, *Giardia*, and STH prevalence in children 0-2 years from 2012-2016. We matched remote sensing data on temperature and precipitation to households by location and date. We estimated prevalence ratios (PR) for WASH interventions vs. control under different environmental conditions using generative additive models and targeted maximum likelihood estimation.

*Results:* WASH interventions more effectively prevented diarrhea when there was heavy rain in the previous week (heavy rainfall PR = 0.38, 95% CI 0.23-0.62 vs. no heavy rainfall PR = 0.77, 95% CI 0.60-0.98) and during the rainy season, when effectiveness peaked at a PR of 0.35 (95% CI 0.19-0.65). WASH interventions were also more effective against STH infections under heavy rain (PR 0.36, 95% CI 0.19-0.68 vs 0.92, 95% CI 0.77-1.10), with the strongest effect modification for hookworm infections (PR 0.32, 95% CI 0.17, 0.64 vs 0.82, 95% CI 0.64-1.05). There was moderate effect modification by weekly minimum temperature for *Giardia* infection, where the PR was 1.11 (95% CI 0.91-1.30) at 12.3°C and 0.81 (95% CI 0.64-0.99) at 21.0°C.

*Discussion:* WASH interventions were most effective against childhood diarrhea and STH infections under high precipitation and against *Giardia* infections under high temperatures. Targeting WASH intervention promotion to periods with greater rainfall may prevent the largest number of infections in children in similar settings.

### WASH effectiveness against diarrhea, by month and season



\* Combined estimates for January and February due to small sample size



**Racial and ethnic disparities in the association between short-term increases in ambient PM<sub>2.5</sub> concentrations and temperature with stillbirth among Medicaid enrollees: A time-stratified, case-crossover study** Stefania Papatheodorou\* Matthew Shupler Krista Huybrechts Michael Leung Yaguang Wei Joel Schwartz Sonia Hernandez-Diaz Stefania Papatheodorou

**Background:** Studies examining the association between prenatal exposure to ambient fine particulate matter (PM<sub>2.5</sub>), temperature and stillbirth risk in the US typically focus on long-term (e.g. trimester) rather than short-term (e.g. days, weeks) exposures. Racial/ethnic heterogeneity in the effect of short-term increases in PM<sub>2.5</sub> or temperature on stillbirth have also been understudied.

**Methods:** Within the Medicaid Analytic eXtract (MAX) dataset, 118,632 stillbirths from 2000-2014 were linked to zip code-level average daily outdoor PM<sub>2.5</sub> concentration and temperature. A time-stratified, case-crossover design using a distributed lag non-linear model (0 to 6-day lag) estimated the odds of stillbirth associated with increases in exposures, with an index date set at two days prior to the stillbirth date of diagnosis. Disparities in the association by maternal race/ethnicity (Black, White, Hispanic, Asian, American Indian) and median household income were assessed.

**Results:** A 10 µg/m<sup>3</sup> increase in average daily PM<sub>2.5</sub> concentration was associated with increased odds of stillbirth on the index date (lag 0) (1.10% (95%CI:[0.22,1.98]) through lag 3 (0.45% 95%CI:[0.01,0.89]) and over the entire lag period (lag 0-6) (3.17% 95%CI:[0.07,6.37]). The temperature-adjusted odds of stillbirth due to PM<sub>2.5</sub> from lag 0 to 4 days and lag 0-6 days was higher among Black individuals (lag 0-6: 9.31% 95%CI:[3.45,15.51]) than White individuals (lag 0-6: -2.75% 95%CI:[-8.43,3.29]). Within the lowest income zip codes, a stronger association existed with PM<sub>2.5</sub> among Black mothers (e.g. lag 0-6: 14.13% (95%CI:[4.51,24.65]) compared with White mothers (e.g. lag 0-6: 2.88% 95%CI:[-8.26,15.38]). A 1°C temperature increase was not associated with stillbirth risk.

**Conclusion:** Short-term increases in PM<sub>2.5</sub> exposures were associated with stillbirth among Medicaid recipients, particularly Black enrollees. Racial/ethnic minorities are more vulnerable to environmental exposures exacerbated by climate change.



**Prenatal exposures to polycyclic aromatic hydrocarbons and school-aged executive****function: results from a U.S. multi-cohort study** Yu Ni\* Yu Ni Alexis Sullivan Adam A. Szpiro

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Nguyen Sheela Sathyanarayana Emily S. Barrett Nicole R. Bush Qi Zhao Daniel A. Enquobahrie

Christopher Simpson Shaikh I. Ahmad Jessica A. Arizaga Brent R. Collett Karen J. Derefinko

Kurunthachalam Kannan Kaja Z. LeWinn Catherine J. Karr

**Background:** Executive function, which enables problem-solving, focused attention, and planning, develops rapidly in childhood. Environmental exposures have been linked to executive function impairment, but evidence related to prenatal polycyclic aromatic hydrocarbons (PAH) is limited.

**Methods:** We examined this association in 967 mother-child dyads from two U.S. cohorts in the ECHO-PATHWAYS Consortium. Seven mono-hydroxylated PAH metabolites were measured in mid-pregnancy urine. Three executive function domains were measured at age 8-9: cognitive flexibility, working memory, and inhibitory control. A composite score quantifying overall performance was further calculated. We fitted linear regressions adjusted for socio-demographics, maternal health behaviors, and psychological measures, and examined modification by child sex and stressful life events in pregnancy. Bayesian kernel machine regression estimated the interactive and overall effects of the PAH mixture.

**Results:** Most associations were null, including those of individual PAH metabolites as well as mixtures. Contrary to our hypotheses, we found some evidence of positive (i.e., protective) associations. Children experiencing higher 2-hydroxyphenanthrene exposure in utero were more likely to have better inhibitory control [ $\beta$ : 0.71 (95%CI: 0.02, 1.39) per 2-fold increase]. Higher prenatal 1/9-hydroxyphenanthrene exposure was associated with better cognitive flexibility [ $\beta$ : 0.7% (95%CI: 0.04%, 1.5%) per 2-fold increase], and this association was stronger in subgroups with medium to high 2-hydroxynaphthalene exposures. No modification by child sex or maternal stress was indicated.

**Conclusion:** We found little evidence to support an adverse association between prenatal PAH exposures and child executive function. The few positive relationships have weak biological plausibility and may be spurious due to residual confounding. Future studies should explore other windows of exposure, including the postnatal period.

**Associations between Air Pollutants and Extra-Axial Cerebrospinal Fluid Volume in Infancy**

Irena Gorski-Steiner\* Irena Gorski-Steiner Mark Shen Kelly N. Botteron Stephen R. Dager Annette M. Estes M. Daniele Fallin Heather C. Hazlett Sun Hyung Kim Robert McKinstry Robert T. Schultz Martin Styner Joseph Piven Heather E. Volk

Air pollution has been shown to have many deleterious effects on the brain, but little is known about the impact on infants' brains. Cerebrospinal fluid (CSF) functions as the cleaning system of the brain, such that efficient CSF circulation is responsible for clearing waste such as inflammatory cytokines, and potentially environmental pollutants. Excessive CSF volume in the subarachnoid space (i.e., extra-axial, EA-CSF) is a marker of deficient circulation and potentially impaired clearance of pollutants, which could have a pathological effect on brain development. We examined associations between prenatal residential air pollution exposure and EA-CSF volumes from 6-24 months of age in participants from the Infant Brain Imaging Study (IBIS). We used generalized estimating equations models with robust standard errors to discern the association between prenatal air pollution exposure (fine particulate matter [PM<sub>2.5</sub>], nitrogen dioxide [NO<sub>2</sub>], and ozone [O<sub>3</sub>]) and repeated measures of EA-CSF at 6 (N=245), 12 (N=270), and 24 (N=214) months of age, adjusted for potential confounders. We also discerned effect modification by sex and differences by trimester. In full-pregnancy average models, higher residential O<sub>3</sub> was significantly associated with lower EA-CSF (aβ: -5.7 per 10 ppb [-10.4, -0.9]), NO<sub>2</sub> was marginally significantly associated with higher EA-CSF (aβ: 5.4 per 10 ppb [-0.9, 10.8]), and PM<sub>2.5</sub> was not significantly associated with EA-CSF (aβ: -3.7 per 10 μg/m<sup>3</sup> [95% CI: -11.8, 44.5]). Estimates were similar by sex. There were higher point estimates for PM<sub>2.5</sub> and NO<sub>2</sub> in the second trimester, with a significant result for NO<sub>2</sub> (aβ: 12.7 per 10 ppb [2.9, 22.5]). Exposure to NO<sub>2</sub> may be associated with a higher volume of EA-CSF in the developing brain, while O<sub>3</sub> may contribute to a lower volume. Next steps include evaluating co-pollutant models and mixtures of air pollutants in association with EA-CSF as well as differences by downstream non-typical development.

**A genome-wide association study(GWAS) of Type 2 Diabetes(T2DM) in Taiwanese** Chia-Yu Tsai\* Chia-Yu Tsai Chia-Ni Hsiung Chien-An Sun Yu-Ching Chou

**Background:** Over the past several decades, the burden of T2DM as increased rapidly worldwide. Genetic factors contribute to the risk of developing diabetes. It is easy to know the association between single nucleotide polymorphism(SNP) and T2DM through GWAS, but rare longitudinal studies focused on Taiwanese. The objective of this study is to examine the T2DM's SNPs based on the database of Taiwan Biobank and to develop the profiling of risk genes in T2DM.

**Methods:** We conducted a retrospective nested case-control study. From 2012 to 2018, 7,757 new cases with T2DM were identified in Taiwan Biobank connected to Taiwan's National Health Insurance Research Database (NHIRD). The number of controls was 7,757 after being matched to cases by age, sex and the date of T2DM diagnosis at a 1:1 ratio. Logistic regression was used to estimate the association between SNPs and T2DM risk after adjusting BMI, Charlson Comorbidity Index(CCI), smoking, drinking, betel nut chewing and the top 10 principal components.

**Results:** Compared to the controls, the cases have poorer education, lower percentages of divorced or separated, less likely to exercise, higher percentages of smoking habit, drinking habit, betel nut chewing habit and higher CCI. In GWAS, we determined the p value at  $1.0 \times 10^{-5}$  as achieving the significance by statistics. This study shows that the variant of SNP rs59367072 and rs12470133 at LOC730100 gene, rs497257□rs484425 at RBFOX1 gene and rs6895177 at chromosome 5 are at risk of developing T2DM. The risk ratios(RRs) are 1.20, 1.19, 0.84, 0.82, 0.77, respectively.

**Conclusion:** In the past 7 years, we find out 5 new SNPs associated with T2DM and indicate the probability that LOC730100 and RBFOX gene may be new candidate genes of T2DM. The related pathways and mechanisms of LOC730100 and RBFOX gene with T2DM can be verified by experiment.

**Keywords:** Type 2 Diabetes(T2DM), single nucleotide polymorphism(SNP), genome-wide association study(GWAS)

**Preliminary Genome-Wide Association Study of colorectal cancer in metabolic syndrome patients using Taiwan Biobank** Cheng-Chih,Teng\* Cheng-Chih Teng

**Background:** Colorectal cancer (CRC) has a high incidence and high mortality rate in Taiwan. The current studies found that genetics is one of the important risk factors for colorectal cancer, and obesity and metabolic syndrome are also increasing year by year in Asia. This is also the reason for the occurrence of colorectal adenomas. This genome-wide association study (GWAS) revealed significant single nucleotide polymorphisms (SNPs) affecting colorectal carcinogenesis in patients with metabolic syndrome.

**Methods:** Data of blood samples were collected from Taiwan Biobank (TWB) to identified metabolic syndrome. Diagnosis of CRC and selecting of control group based on National Health Insurance Research Database (NHIRD). We employed a genome-wide association study design in a sample of 223 CRC cases and 2,230 controls (1:10 sex and age matched). Finally, 251,275 single nucleotide polymorphisms (SNPs) were available for the GWAS analysis to search for significant SNPs for CRC in metabolic syndrome patients.

**Results:** There were 82 of 223 colorectal cancer patients and 760 of 2,230 control group had metabolic syndrome. Overall, 1 candidate SNP rs6889488 was associated with colorectal cancer risk at the  $p < 10^{-6}$  level. With a lower threshold for preliminary significance to  $p < 10^{-5}$ , 16 suggestive association signals were observed in the GWAS. One of above, SNP rs34103243 located in intron of TRIM44 which is associated with several other cancers, and the other SNP rs1908795 located in intron of SEMA6D is associated with breast cancer.

**Conclusion:** In summary, we reported 17 suggestive loci associated with colorectal cancer in metabolic syndrome patients. These findings provided new insights into the potential mechanisms between colorectal cancer and metabolic syndrome. These preliminary findings require further validation in a larger sample size.

**Keywords:** Colorectal cancer (CRC), Metabolic syndrome, National Health Insurance Research Database (NHIRD), Taiwan Biobank (TWB).

**LATEBREAKER**

Global Health

**Screening for severe acute malnutrition using mid-upper arm circumference: a regression discontinuity analysis** Huiyu Hu\* Huiyu Hu Mamadou Ouattara Ali Sié Mamadou Bountogo Valentin Boudo Elodie Lebas Till Bärnighausen Kieran S. O'Brien Benjamin F. Arnold Thomas M. Lietman Catherine E. Oldenburg

**Objective**

Community-based screening for severe acute malnutrition (SAM) in children aged 6-59 months relies on mid-upper arm circumference (MUAC) measurements. Children with MUAC < 11.5 cm in screening programs are referred to community-based management of acute malnutrition programs - for further workup and enrollment in a SAM treatment program. We examined the efficacy of SAM screening for prevention of all-cause mortality and improving nutritional status (measured by MUAC) at 6 months using a regression discontinuity design.

**Methods**

All children in 241 communities in rural Burkina Faso were screened every 6 months using MUAC and vital status was assessed. Children with MUAC < 11.5 cm were identified by the study's mobile data application and referred. Using MUAC as the running variable and a threshold of 11.5 cm, we utilized a regression discontinuity design to evaluate the efficacy of MUAC screening on mortality and follow-up MUAC. Under some assumptions, this design allows for estimation of the causal effect of MUAC-based screening for SAM among children who are close to the threshold (11.5 cm) for referral. We fit generalized linear mixed-effects models using 3 bandwidths around the threshold (10.5-12.5 cm, 9.5-13.5 cm, 8.5-14.5 cm).

**Results**

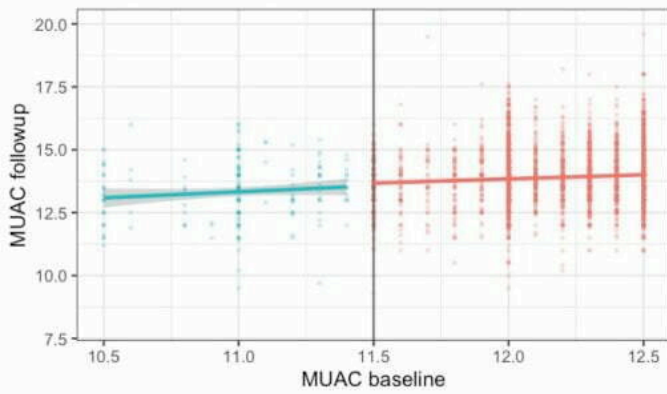
We found no evidence of an effect of screening and referral for SAM on all-cause mortality or nutritional status as measured by MUAC at 6 months, with results broadly consistent across bandwidths. At the narrowest bandwidth, 6-month mortality was similar for children below and above the threshold (OR = 1.18, 95% CI 0.11 to 12.26) and mean MUAC at 6 months after screening was similar (mean difference -0.11 cm, 95% CI -0.46 to 0.23).

**Conclusions**

This analysis does not support an effect of mass screening using MUAC for prevention of mortality or nutritional status. Children who screened positive may not have received care, underscoring the importance of ensuring that children with SAM are linked to care.

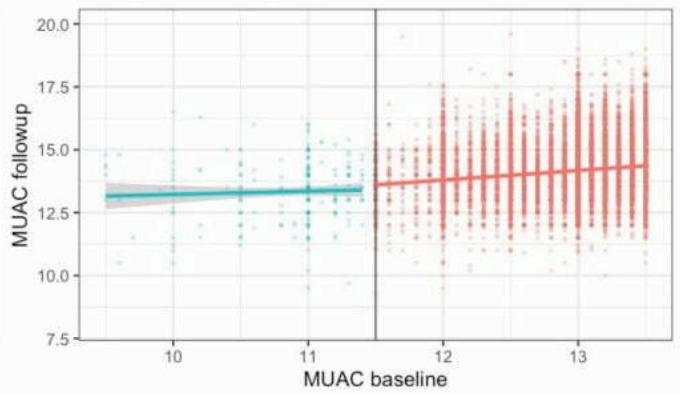
**A** Range: 10.5 to 12.5 cm (N = 5375)

Slope below threshold = 0.45;  
Slope above threshold = 0.32;  
Difference at the cutoff = -0.11



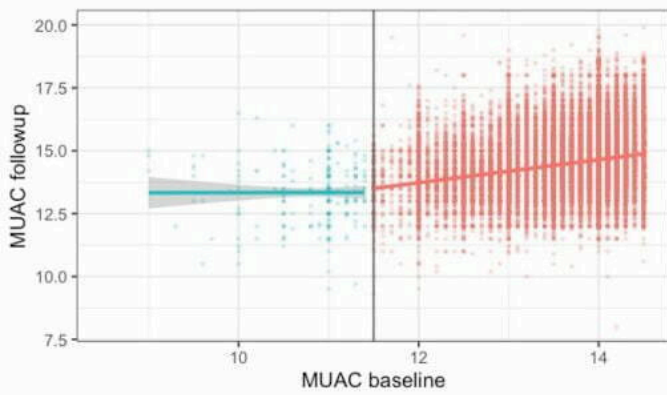
**B** Range: 9.5 to 11.5 cm (N = 34651)

Slope below threshold = 0.11;  
Slope above threshold = 0.36;  
Difference at the cutoff = -0.2



**C** Range: 8.5 to 14.5 cm (N = 105388)

Slope below threshold = 0.01;  
Slope above threshold = 0.45;  
Difference at the cutoff = -0.16





**Mediating effects of inequitable gender norms on intimate partner violence and contraceptive use in a cluster randomized control trial in Niger: A causal inference mediation analysis**

Sabrina C. Boyce\* Sabrina Boyce Alexandra M. Minnis Julianna Deardorff Sandra I McCoy Dana E Goin Sneha Challa Nicole E. Johns Sani Aliou Mohamad I Brooks Abdoul-Moumouni Nouhou Holly Baker Jay G. Silverman

Reducing gender inequity, a deeply-rooted driver of poor health globally, could benefit a wide range of health outcomes, but critical gaps remain in the evidence about how to change the gender norms that drive gender inequity. A four-arm cluster randomized control trial was conducted to evaluate effects of the Reaching Married Adolescents (RMA) in Niger intervention (small group; household visits; both offered; neither) on married adolescent girls and their husbands in Dosso, Niger (baseline: 1042 dyads; 24 mos. Follow-up: 737 dyads; 2016-2019). This study seeks to understand if changes in social norms were the mechanisms behind intervention effects on increasing modern contraceptive use and decreasing intimate partner violence (IPV). We assessed for mediation using an inverse odds weighting approach. In the small group intervention, of the total effect on IPV prevalence (8% reduction), indirect effects via gender norms change were associated with a 2% decrease (95% CI: -0.07, 0.12; 22.3% of the total effect) and direct effects with a 6% decrease (95% CI: -0.20, -0.02). For household visits, of the total effect on contraceptive use (20% increase), indirect effects were associated with an 11% decrease (95% CI: -0.18, -0.01) and direct effects with a 32% increase (95% CI: 0.13, 0.44). For the combination arm, of the total effects on contraceptive use (19% increase), indirect effects were associated with a 9% decrease (95% CI: -0.20, 0.02) and direct effects with a 28% increase (95% CI: 0.12, 0.46). The present study contributes experimental evidence that the small group RMA intervention reduced IPV partially via decreasing perceived inequitable gender norms. Effects on contraceptive use appear to not be mediated by inequitable gender norms. These results open the “black box” around mechanisms through which the RMA small group intervention works and provide evidence supporting the importance of changing underlying social norms to reduce IPV.

**Resilience modifies the association between childhood adversity and perinatal depression among pregnant women in Kenya** Linxuan Wu\* Linxuan WU Julia Dettinger Lauren Gomez Grace C. John-Stewart John Kinuthia Anna Larsen Marwa Motongori Nancy Ngumbau Ben Ochieng Felix Abuna Jillian Pintye

**Background** Adverse childhood experiences (ACEs) are associated with negative health outcomes later in life, including perinatal depression. Resilience may impact the relationship between ACEs and depression during the perinatal period. Few data are available on ACEs, perinatal depression, and resilience from low- and middle-income countries.

**Methods** We evaluated the association between ACEs and perinatal depression using data from a longitudinal study that enrolled HIV-negative women during pregnancy at 8 clinics in western Kenya to be followed for 5 years. ACEs and resilience were measured using the Adverse Childhood Experiences International Questionnaire (ACE-IQ) and the Brief Resilient Coping Scale (BRCS), respectively. High ACE-IQ scores were defined as scores  $\geq 6$ . BRCS scores were grouped into low (4-13), medium (14-16), or high (17-20) resilience levels. Perinatal depression was assessed by the Center for Epidemiologic Studies Depression Scale Revised (CESD-10) at study visits up to 9 months postpartum. Perinatal depression was defined as having at least one study visit with CESD-10 score  $\geq 10$ . Modified Poisson regression was used to evaluate the effect modification by resilience on the association between ACEs and perinatal depression.

**Results** Among the 1152 pregnant women included in this analysis, the median age was 26.8 years (IQR 23.1-27.2), the median number of living children was 3 (IQR 2-4), and the median ACE-IQ score was 4 (IQR 3-6). Overall, 370 (31.7%) had a high ACE-IQ score, 363 (31.1%) experienced perinatal depression, and 327 (28.0%) were high resilience copers. Having a high ACE-IQ score was associated with a 23% increased risk of perinatal depression comparing women with lower ACE-IQ scores (PR=1.23, 95% CI 1.03-1.47). Resilience modified the association between ACEs and perinatal depression ( $p < 0.05$ ). Specifically, the association between ACEs and perinatal depression was strongest among low (PR=1.47, 95% CI 1.02-2.13) and medium (PR=1.43, 95% CI 1.10-1.87) resilience copers; high ACE-IQ scores were not associated with perinatal depression among high resilience copers (PR=0.88, 95% CI 0.64-1.21).

**Conclusions** Our findings suggest that higher resilience may buffer against the negative effect of ACEs on perinatal mental health.

**Phthalate exposure in children with asthma and the influence of exposure to environmental tobacco smoke: a pooled analysis using the HHEAR Data Repository** Sofia Bengoa\* Sofia Bengoa Jeanette Stingone Susan Teitelbaum

The HHEAR (Human Health Exposure Analysis Resource) Data Repository houses deidentified data from environmental and exposome health studies. Data is harmonized to a common vocabulary via an interdisciplinary HHEAR ontology to facilitate comparisons, data pooling, and performing meta analyses.

We evaluated associations between environmental smoking exposure and urinary concentrations of mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP), mono(2-ethyl-5-oxohexyl) phthalate (MEOHP), mono ethylhexyl phthalate (MEHP), monobenzyl phthalate (MBzP), mono isobutyl phthalate (MiBP), mono-n-butyl phthalate (MnBP), and monoethyl phthalate (MEP) in a pooled cross-sectional analysis of asthmatic children using variables harmonized from three HHEAR studies. Additionally, associations between exacerbated asthma symptoms and phthalate exposures within environmental smoking exposure strata were investigated.

Phthalates were measured in spot urine collected from 264 children across the three studies. Asthma diagnosis was either from information collected at the study site or caregiver reported physician diagnosis. Wheezing and environmental smoking exposure were caregiver reported. Crude and adjusted logistic regression models were used to estimate the odds ratios (ORs) per one log<sub>10</sub> unit change in phthalate concentration.

Of 264 children, 116 (43.9%) had environmental smoking exposure. Compared with concentrations in those without environmental smoking exposure, MEOHP and MnBP were associated with environmental smoking exposure ( $p < 0.05$ ): OR = 2.40 (95% CI 1.38-4.16) and OR = 1.59 (95% CI 1.03-2.45) per log<sub>10</sub> unit increase, respectively. There were no associations between wheezing and phthalate concentration when stratified by smoking exposure.

Environmental smoking exposure is associated with greater phthalate exposure in children with asthma across three harmonized studies. Diverse datasets allow for investigations with larger sample sizes and greater exposure variability.

**Differences in Non-Pharmacologic Chronic Low Back Pain Care across Race and Ethnicity in People with Opioid Use Disorder** Fiona Bhondoeckhan\* Fiona Bhondoeckhan Brandon Marshall Amal Trivedi Theresa Shireman Jessica Merlin Patience Moyo

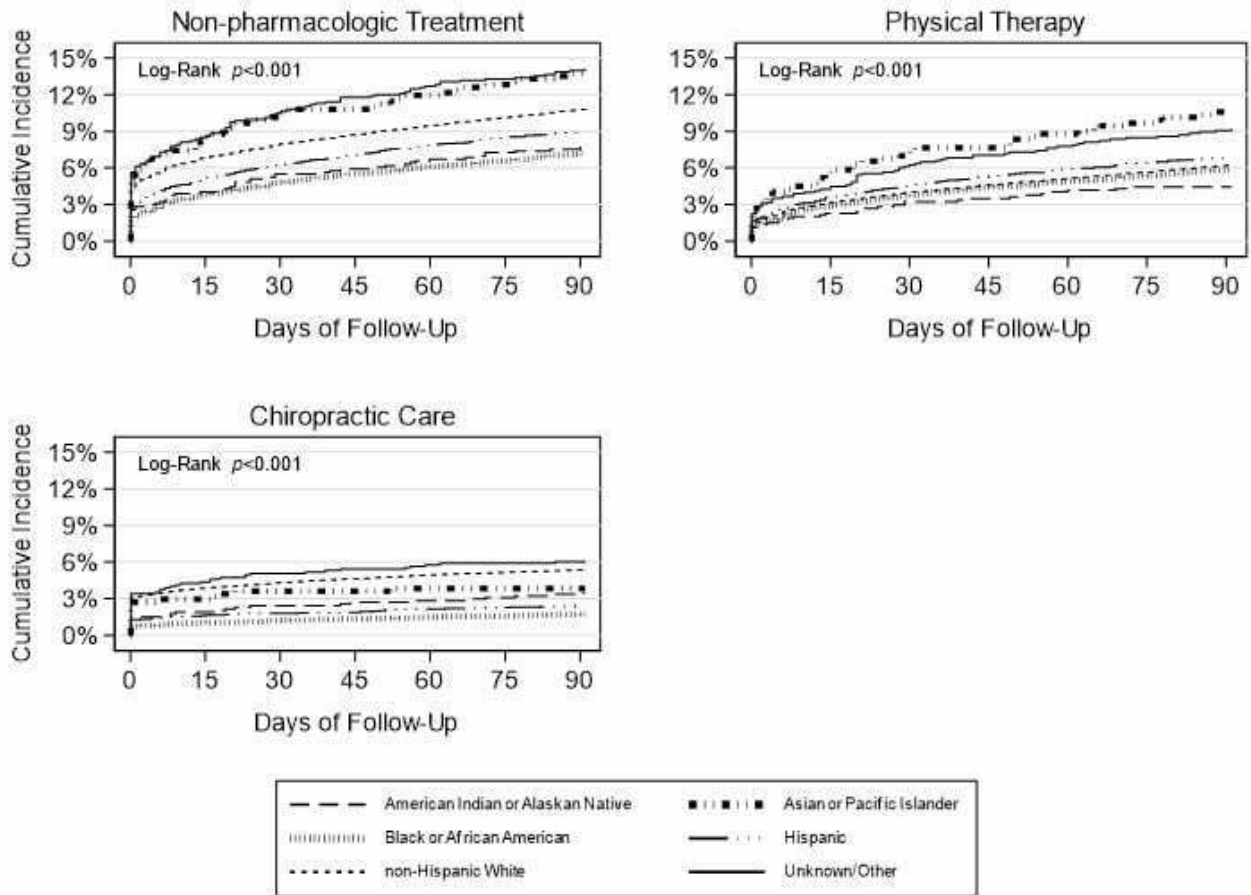
*Background:* Non-pharmacologic pain care is important among people with comorbid chronic low back pain (cLBP), the most common chronic pain, and opioid use disorder (OUD) in whom pharmacologic therapies may be risky. There are also known racial/ethnic disparities in pain care. In this context, we investigated racial/ethnic differences in non-pharmacologic pain care among people with comorbid cLBP and OUD.

*Methods:* In a 20% national sample of fee-for-service Medicare data (2016-2018), we identified beneficiaries with comorbid cLBP and OUD using ICD-10 codes. The independent variable was race/ethnicity, and the outcome was receipt of Medicare-covered non-pharmacologic services for physical therapy (PT) or chiropractic care within 3 months of cLBP diagnosis. Time to outcome was expressed in days on Kaplan-Meier curves. Multilevel logistic regressions evaluated the association between race/ethnicity and receipt of non-pharmacologic care, adjusting for confounders and accounting for state and county clustering.

*Results:* Among 69,362 beneficiaries with comorbid cLBP and OUD, 10.2% received PT or chiropractic care within 3 months of diagnosis. Use was highest for Asian/Pacific Islanders (13.7%) and non-Hispanic Whites (10.8%) and lowest for American Indian/Alaskan Natives (7.7%) and Black/African Americans (7.3%). Time to PT or chiropractic care was longest for Black/African Americans (median=13 days) and shortest for non-Hispanic Whites (median=5 days). After adjustment, American Indian/Alaskan Natives (OR=0.66, 95%CI=0.50-0.88), Black/African Americans (OR=0.72, 95%CI=0.66-0.79), and Hispanics (OR=0.74, 95%CI=0.66-0.83) had lower odds of receiving PT or chiropractic care relative to non-Hispanic Whites.

*Conclusion:* Non-pharmacologic pain care was low and differed by race/ethnicity among Medicare beneficiaries with comorbid cLBP and OUD, highlighting the need for targeted patient, provider, and system-level interventions to promote equitable and appropriate pain management.

**Figure:** Cumulative incidence of non-pharmacologic treatment, physical therapy, and chiropractic care by race/ethnicity.



**Adverse childhood experiences and self-rated Health: Exploring effect modification by age, sex and race/ethnicity** Olatokunbo Osibogun\* Olatokunbo Osibogun

**Objective:** This study investigated whether age, sex, or race/ethnicity modifies the association between adverse childhood experiences (ACEs) and self-rated health in a nationally representative population data. **Methods:** Data from the 2020 and 2021 Behavioral Risk Factor Surveillance System were used to explore the association between ACEs and self-rated health among 185,731 (weighted N= 47,862,016) adults  $\geq$  18 years. ACEs, the independent variable, were assessed from 11 questions related to childhood emotional abuse, physical abuse, sexual abuse, and household dysfunction. Response options were coded as no = 0 or yes = 1. An ACE composite score was calculated using responses ranging from 0 to 11 and categorized as 0 (reference), 1, 2, 3, or  $\geq$ 4. The dependent variable, self-rated health, included responses of excellent, very good, good, fair, and poor, which were grouped as optimal (excellent/very good/good [reference]) and suboptimal (fair/poor) health. Multivariable logistic regression was conducted testing the interaction between age, sex, and race/ethnicity with ACEs while controlling for sociodemographic factors, the number of chronic diseases, mental health distress days, heavy alcohol consumption, smoking status, and physical activity. **Results:** Increasing number of ACEs had statistically significant higher odds of suboptimal self-rated health in a graded manner after adjusting for potential confounders except for 1 ACEs (1 ACEs: aOR: 1.09 [1.00-1.20]; 2 ACEs: aOR:1.16 [95% CI: 1.03-1.30]; 3 ACEs: 1.17 [1.03-1.32]; and  $\geq$ 4 ACEs: 1.39 [CI: 1.26-1.53]). There was a significant interaction with age\*ACEs at  $p < 0.001$ . Younger age (18-24 years) had the strongest association (aOR: 3.26 [CI: 1.97-5.40]) for  $\geq$ 4 ACEs compared to the older age groups (25-34: 1.66 [1.22-2.27]; 35-44: 1.56 [1.18-2.07]; 45-54: 1.21 [0.95-1.56]; 55-64: 1.25 [1.02-1.54] and  $>65$ : 1.21 [1.03-1.41]). There was no effect modification by sex and race. **Conclusion:** These findings underscore the importance of developing age-appropriate trauma-informed intervention strategies. It is also essential to consider ACEs in designing health-promoting interventions to improve overall health.

**Trend analysis of racial group-specific esophageal cancer incidence, mortality, and county-level risk factors in the state of Mississippi between 2003 and 2019** Yingxi Chen\* Yingxi Chen Angel Walker Christian Abnet Meredith Shiels Wayne Lawrence Tanya Funchess Deirdre Rogers Monica Webb Hooper

**Background:** Esophageal cancer is one of the most aggressive cancers. The aim was to describe trends in esophageal cancer incidence and mortality, and county-level factors in the state of Mississippi from 2003 to 2019 by sex, race, and geolocation.

**Methods:** This study used data from the Mississippi Cancer Registry, linked to county-level data from the Behavioral Risk Factor Surveillance System, the American Community Survey, and the Institutes for Health Metrics and Evaluation. We estimated trends in age-standardized incidence (ASR) and mortality rates (AMR), mortality incidence rate ratio, and average annual percent change (AAPC) in rates by sex, race, and geolocation. We further calculated relative risks for each county-level factor including smoking, obesity, college degree completion, unemployment rate, and median household income ranking within the state.

**Results:** Between 2003 and 2019, Black men had the greatest reduction in esophageal cancer incidence and mortality ( $ASR_{2019}=10.5$ ,  $AMR_{2019}=7.3$  per 100,000;  $AAPC_{incidence}=-3.7\%$ ,  $P<0.001$ , and  $AAPC_{mortality}=-4.9\%$ ,  $P<0.001$ ) despite high rates. The reduction was largely driven by decreases in the non-Delta region ( $ASR_{2019}=9.3$  per 100,000,  $AAPC_{incidence}=-4.2\%$ ,  $P<0.001$ ), while incidence rate remained high among Black men in the Delta region ( $ASR_{2019}=15.4$  per 100,000,  $AAPC_{incidence}=-1.8\%$ ,  $P=0.3$ ). The rates among White men were relatively stable ( $ASR_{2019}=8.5$ ,  $AMR_{2019}=7.6$  per 100,000;  $AAPC_{incidence}=0.18\%$ ,  $P=0.7$ ,  $AAPC_{mortality}=-0.4\%$ ,  $P=0.6$ ). County-level smoking prevalence ( $P=0.002$ ) and median household income ranking ( $P=0.001$ ) were significantly associated with esophageal cancer incidence.

**Conclusions:** We observed a substantial reduction in esophageal cancer incidence and improvement in mortality among Black Mississippians from 2003 to 2019. However, the high rates among Black men residing in the Mississippi Delta highlight the importance of targeted interventions to address structural factors underlying this disparity.

**Access to symptom screening and severe symptom risk among cancer patients with severe psychiatric illness** Laura Davis\* Laura Davis Rinku Sutradhar Michaela Bourque Antoine Eskander Chistopher Noel Elie Isenberg-Grzeda Simone Vigod Natalie Coburn Julie Deleemans James Bolton Wing Chang Julie Hallet Alyson Mahar

**Introduction.** Cancer patients with severe mental illness (SPI) are at a greater risk for health inequalities. Symptom screening has the potential to improve symptom burden and cancer outcomes among patients with SPI. We determined rates of symptom screening with the Edmonton Symptom Assessment System (ESAS) and symptom burden in cancer patients with SPI.

**Methods:** This was a retrospective cohort study using linked administrative databases of adults diagnosed with cancer from 01-01-2007 to 08-31-2020. Individuals who had a history of mental illness but did not meet the definition of SPI were excluded. An SPI was measured in the 5 years prior to cancer diagnosis and categorized as inpatient, outpatient, or no SPI. Outcomes were defined as <sup>31</sup> ESAS screening and <sup>31</sup> moderate-to-severe symptom among those who completed <sup>31</sup> ESAS assessment. Cause-specific and Fine and Gray competing events models were used for both outcomes, controlling for age, sex, rural residence, year of diagnosis and cancer site.

**Results:** Of 389,870 cancer patients, 4049 (1%) had an inpatient SPI and 9775 (2.5%) had an outpatient SPI. Individuals with inpatient SPI were least likely to complete an ESAS (67.5%) compared to those with outpatient SPI (72.3%) and without SPI (74.8%). Compared to those without SPI, individuals with an inpatient or outpatient SPI had a lower incidence of symptom screening records after accounting for the competing risk of death (multivariable sHR 0.78 (95%CI 0.74-0.80) and 0.89 (95%CI 0.86-0.90) respectively). Compared to those without SPI, individuals with inpatient and outpatient SPI status had a consistently significantly higher risk of reporting high symptom scores across all symptoms.

**Conclusions:** Individuals with inpatient and outpatient SPI are less likely to be screened for ESAS and report higher symptom scores. Understanding the disparity in ESAS screening for patients with SPI and cancer is a vital step toward providing equitable cancer care to this population.



**The incidence of anemia in chronic kidney disease patients: a nationwide descriptive study in Taiwan** Yu-Ching Chou\* Pei Jie Lin Chien-An Sun

**Background:** In Taiwan, the prevalence rate of chronic kidney disease (CKD) is 11.9%. Anemia has been recognized as a common phenomenon in CKD. However, secular trend studies of anemia with CKD are limited. This descriptive study examined the incidence of anemia with CKD in a large-scale, population-based Taiwanese cohort.

**Methods:** We conducted a descriptive study. From 2000 to 2013, 17,115 new cases with CKD were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating the incidence rates of anemia with CKD in different sex, age groups and periods. For long term trends, we assessed the change in the incidence rates over 14 years by linear trend analysis.

**Results:** The incidence of anemia was 51.3 among CKD patients per 10,000 person-years. The incidence rate was 37.7 among men and 66.75 among women per 10,000 person-years. The incidence rate of anemia was higher in men. After stratifying age into 5 groups, we found that the incidence rate of anemia per 10,000 person-years was 39.67 in 20-30 years old, 47.11 in 30-40 years old, 58.06 in 40-50 years old, 37.79 in 50-60 years old and 55.05 in  $\geq 60$  years old. Patients generally have higher incidence rate of anemia when age is increasing. Also, incidence rate of anemia was 1127.93, 1190.13, 1262.37, and 1192.38 by visiting 0 time,  $\leq 3$ times, 4 - 37 times, and  $\geq 38$  times in CKD clinical visits respectively.

**Conclusion:** In the past 14 years, the incidence of anemia had a profound impact on our life. By means of the big data, our finding suggested incidence rate of anemia with CKD is steadily rising. For future study, we need to test hypothesis for evaluating the correlation between CKD and anemia.

**Keywords:** Chronic kidney disease (CKD), National Health Insurance Research Database (NHIRD).

**Educational attainment and incident alcohol-attributable acute and chronic emergency department visits in Ontario and Alberta, Canada: A population-based prospective cohort study** Alessandra Andreacchi\* Alessandra Andreacchi Erin Brendan

**Background:** Socioeconomic inequities in 100% alcohol-attributable harm have been observed in many high-income countries. However, it is unclear whether these inequities are driven by alcohol-attributable conditions that are acute (e.g., poisonings) or chronic (e.g., liver cirrhosis). We estimated the association between socioeconomic position (SEP) and 100% alcohol-attributable emergency department (ED) visits separately for acute and chronic conditions.

**Methods:** A population-based prospective cohort study was conducted among current and former alcohol consumers aged 15-64 living in Ontario and Alberta who participated in the Canadian Community Health Surveys (CCHS, 2000-08) linked to ED records through 2017. SEP was measured using educational attainment (<high school, high school, some post-secondary vs. post-secondary). Fine & Gray sub-distribution hazard models estimated sex-specific associations between education and incident 100% alcohol-attributable acute and chronic ED visits, separately, with all-cause mortality as a competing risk (n=119,800; 51% female). Models were adjusted for age, rurality, marital status, immigration status, race, cycle and province.

**Results:** Among males, a gradient was seen between lower education and alcohol-attributable ED visits. Those with <high school compared to post-secondary education had 2.9 (95%CI:2.0-4.1) and 6.9 (95%CI:3.9-12.1) times greater risk of 100% alcohol-attributable acute and chronic ED visits. Among females, those with <high school compared to post-secondary education had 2.3 (95%CI:1.5-3.5) and 2.4 (95%CI:1.2-5.0) times greater risk of 100% alcohol-attributable acute and chronic ED visits.

**Conclusion:** Low SEP was associated with an increased risk of 100% alcohol-attributable ED visits, with greater social inequities for chronic than acute conditions among males. These findings can inform sex-specific policies to reduce social inequities in alcohol harm.

**Assessing the impact of equity factors in a population-based prediction model: the Chronic Disease Population Risk Tool (CDPoRT)** Kitty Chen\* Kitty Chen Kathy Kornas Laura C. Rosella

**Background:** Chronic disease is among the leading causes of worldwide mortality. Predicting chronic disease incidence at a population level is important to inform overall future chronic disease burden and opportunities for prevention. The aim of the study was to estimate the future burden of chronic disease in Ontario, Canada using a population-level risk prediction algorithm and model population-level interventions for high-risk equity subgroups.

**Methods:** The validated Chronic Disease Population Risk Tool (CDPoRT) estimates the 10-year risk of major chronic diseases using population survey data. CDPoRT was applied to data from the 2017-2018 Canadian Community Health Survey to predict baseline 10-year risk and incidence of chronic disease in the Ontario population aged 20+, and among equity-deserving groups. CDPoRT was then used to model population-level prevention scenarios of 2% and 5% risk reductions targeting high-risk equity groups.

**Results:** Baseline chronic disease risk was highest among those with less than secondary school education (37.52%), severe food insecurity (19.51%), low income (21.17%), and extreme workplace stress (24.64%). CDPoRT predicted 1,415,429 new chronic disease cases in Ontario from 2017-2018 to 2027-2028. Reducing chronic disease risk by 2% and 5% prevented 330 and 1,520 cases among those with less than secondary school education, prevented 3,820 and 14,880 cases among low income populations, and prevented 820 and 2,780 cases among food insecure populations. Large reductions of 112,510 and 258,500 cases were found by targeting individuals with extreme workplace stress.

**Conclusion:** Each of the four scenarios predicted a considerable reduction in chronic disease cases, which supports the need for targeted interventions for priority subgroups. Prediction models that consider the upstream determinants can guide policy, programming, and community designs in understanding underlying structural factors affecting chronic disease burden.

**Spatial Inequities in COVID-19 Vaccination in Los Angeles by Neighborhood-level Race and Income** Usama Bilal\* Angela D'Adamo Jane Miller Usama Bilal

**Objective:** Vaccination is a key intervention to mitigate the impacts of the COVID-19 pandemic, but there is evidence of spatial inequities in vaccination. We examined the associations between neighborhood-level income and racial/ethnic composition and COVID-19 vaccination coverage in Los Angeles from the start of vaccination rollout through September 2021.

**Methods:** We used data for 535 neighborhoods (zip-code tabulation areas) in the Los Angeles Metropolitan Area from the 2015-2019 American Community Survey and the California Department of Public Health. We created choropleth maps of vaccination coverage, income, and racial/ethnic composition by neighborhood. We compared average vaccination coverage by neighborhood-level income and racial/ethnic using ANOVA and ANCOVA.

**Results:** Neighborhoods of medium and high income experienced average COVID-19 vaccination rates about 8 and 14 percentage points higher than those of low-income neighborhoods, respectively. COVID-19 vaccination rates varied by racial/ethnic classification of neighborhoods. Majority non-Hispanic Asian/Pacific Islander neighborhoods had the highest mean vaccination rates (83%), and majority Hispanic or non-Hispanic Black neighborhoods had the lowest vaccination rates (both around 65%). Within each racial/ethnic composition group, vaccination rates were higher in neighborhoods with higher income, but these differences were only statistically significant in non-Hispanic white and Mixed neighborhoods ( $p < 0.001$ ). One cluster of low-income Hispanic and non-Hispanic Black neighborhoods around Inglewood experienced particularly low vaccination (40-73%) compared to surrounding White, Asian/Pacific Islander, and mixed race/ethnicity neighborhoods (73%-100%).

**Implications:** Results provide support for social policies that target increasing vaccination in low-income, Hispanic, and Black neighborhoods in Los Angeles. These may be useful strategies to mitigate disparities in COVID-19 severity.

**Relative Prevalence of Adverse Childhood Experiences in High School Students by Disaggregated Asian Ethnicity** Isabel J. Ricke\* Isabel Ricke Ruby H.N. Nguyen Julia Tindell Lauren Martin Nancy E. Sherwood

**Background.** Adverse childhood experiences (ACEs) have been associated with adverse health outcomes later in life. Previous studies have found that while Asian children experience fewer ACEs on average, Asian children may have higher prevalence for certain ACEs. There may also be heterogeneity in the number and type of ACEs experienced by different Asian communities.

**Objectives.** To determine whether specific ACEs are more prevalent among Asian/Asian American children compared to children of any other race, and whether patterns emerge when investigating disaggregated Asian race data.

**Methods.** Self-reported ACEs from the 2019 Minnesota Student Survey were examined in 80,456 9<sup>th</sup> and 11<sup>th</sup> grade children. Asian/Asian American children were asked to best describe their ethnicity from Minnesota's ten most prominent Asian/Asian American communities. Data were stratified by sex and race (Asian versus any other race). Prevalence ratios were estimated from logistic regression models adjusted for age, sex and sexual orientation.

**Results.** Asian children, on average, reported fewer total ACEs than children of any other race but they more often reported physical abuse (adj. PR=1.37, 95% CI: 1.28-1.48) and witnessing domestic violence (adj. PR=1.26, 95% CI: 1.14-1.39) than their non-Asian counterparts. Household alcohol abuse was less often reported by Asian students, but disaggregated data showed an increased prevalence ratio for each of the Southeast Asian groups (Hmong, Lao, Vietnamese, Burmese and Karen) relative to students of any other race. Asian students' higher physical abuse prevalence was driven by Asian Indian, Chinese, Filipino and Vietnamese students; Filipino and Hmong students were more likely to report exposure to domestic violence.

**Conclusions.** Examining the total number of ACEs may misrepresent the differential impact of specific types of ACEs in Asian communities. In addition, within the Asian race, there are heterogeneous types of ACEs experienced.

**Evaluation Framework For Chicago's Hypertension Surveillance: Survey vs Electronic Health Record Data** BreAna Pipkins\* BreAna Pipkins Ajanta Patel Theresa Walunas**Evaluation Framework For Chicago's Hypertension Surveillance: Survey vs Electronic Health Record Data**

BreAna Pipkins, MPH<sup>1</sup>, Theresa Walunas, PhD<sup>2</sup>, and Ajanta Patel<sup>1</sup>, MD, MPH

1. Chicago Department of Public Health
2. Northwestern University- Feinberg School of Medicine

**BACKGROUND:**

Chicago Department of Public Health (CDPH) monitors chronic disease prevalence trends. According to Healthy Chicago Survey (HCS) data, 30% of adult Chicagoans had ever been diagnosed with hypertension in 2021. It is not known if HCS hypertension prevalence estimates are under/overestimated. Further, electronic health record (EHR) data is becoming available for disease prevalence estimates but may vary from survey estimates. We aim to conduct a surveillance system evaluation by comparing survey data against EHR data.

**METHODS:**

We developed a framework to guide our surveillance system evaluation. Our framework is informed by national guidelines for evaluating public health surveillance systems. It includes 3 methodological steps to compare 2020-2021 HCS data against EHR data from CDC's 2020-2021 MENDES data and Northwestern's 2015-2020 CAPriCORN data. Step 1, identify strengths and limitations of each system. Step 2, compare population size, representativeness, data completeness of each system, using SAS 9.4 to perform simple statistics. Step 3, develop data flowcharts and conduct stakeholder interviews with CDPH Epidemiologists and external data aggregators to evaluate each systems' timeliness, usability, simplicity, acceptability, sustainability, and cost.

**RESULTS:**

Hypertension prevalence is estimated as 30% using HCS and 17% using unpublished CAPriCORN data; CDC MENDES estimate is pending. Our framework sets up our evaluation of survey vs EHR surveillance systems to understand the difference in prevalence estimations of Chicago's adult hypertensive population. Preliminary results indicate more individual people are sampled in EHR-based data networks but are oversampled with affluent, white, older people. EHR systems also tend to be more complex in data flow and require more human effort.

## DISCUSSION:

The findings from the final evaluation will strengthen our understanding of each system, enrich the way we explain their differences, result in more informed decisions around acquiring new EHR data, and strengthen our descriptive reporting when publishing prevalence indicators.

**Agreement of preoperative diagnoses of endometriosis and adenomyosis for hysterectomy with the corresponding post-operative pathology report by race/ ethnicity groups**

Joacy Gerard Mathias\* Joacy Gerard Mathias Whitney R Robinson Natalie Rivadeneira Lauren G anderson Michael J Green

**Introduction** Endometriosis and adenomyosis are painful, chronic, often misdiagnosed gynecological conditions affecting reproductive-aged women. However, it remains unclear how much diagnostic accuracy has improved with improved imaging and other diagnostic techniques. We assessed agreement of preoperative diagnoses of endometriosis and adenomyosis with the related post-operative pathology report for 1753 premenopausal patients who underwent a hysterectomy for non-cancerous indications, hypothesizing that there would be notable differences between pre-surgical diagnoses and post-operative findings from the pathology report.

**Methods** Using electronic health record (EHR) data from 1,753 hysterectomy patients (aged 18-44 years) treated in a large healthcare system in the US South between 2014 and 2017, we calculated percent agreement between preoperative indication for endometriosis and adenomyosis among premenopausal non-Hispanic Black, non-Hispanic White, and Hispanic patients. We calculated observed agreement between the main indication for surgery noted in pre-surgical EHR notes and the post-surgical EHR pathology report.

**Results** The overall percentage of observed agreement was 84.6% for endometriosis and 69.6% for adenomyosis. For example, 84.6% of the time endometriosis diagnosis was consistently absent as a main indication in pre-surgical notes and in the pathology report or endometriosis diagnosis was consistently present as a pre-surgical main indication and found on pathology.

**Conclusion** There was moderate but incomplete agreement between pre-operative indication and pathology findings for endometriosis and adenomyosis. These results highlight challenges in accurate diagnosis of advanced, symptomatic gynecologic disorders.



**Comparing lifetime polyvictimization and mental health outcomes in women with vs without incarceration histories: A population based latent class analysis** Sandra P. Arevalo, PhD\* Sandra Arevalo Qianwei Zhao

**Purpose:** This study uses data from the Add Health, a national and longitudinal survey, to identify women with (n = 418) and with no incarceration histories (n = 5,099) to compare lifetime trauma exposure and risk for distal mental health and substance use outcomes in women with vs. without incarceration histories.

**Method:** With a detailed list of traumas that captures the category (e.g., sexual, physical, psychological), the perpetrator (parent, partner, other), and timing (e.g., childhood, adolescence, adulthood) of the exposure, we used Latent Class Analysis to identify distinct groups of polytrauma exposure in the two groups of women. Multivariate logistic regressions examine the association between class membership and mental health (depressive symptomatology, PTSD, anxiety, suicidal ideation, and suicide attempt), and substance misuse (alcohol, marijuana, and other illicit drug misuses) outcomes, after adjusting for relevant covariates.

**Results:** we identify a unique pattern of trauma exposure characterized by high exposure to multiple types of childhood abuse that persisted during the preschool and middle childhood years in the group of women with incarceration histories. Different groups of polytrauma exposure were associated with distinctive mental health and substance misuse outcomes among women with incarceration histories, but not in women without incarceration histories.

**Conclusion:** Our findings highlight the common prevalence of polyvictimization exposure in both women with and without histories of incarceration; and point to distinct patterns created by the type, frequency, and timing of the trauma exposure, and their distinct associations to distal psychological health outcomes, and possibly criminal justice involvement.

**Using latent profile analysis to categorize states into typologies of structural racism**

Stephanie Veazie\* Stephanie Veazie Elleni Hailu Corinne A. Riddell

**Background:** Structural racism is a key driver of Black-White health inequities; however it is a complex construct that is difficult analyze due to its multi-dimensionality.

**Objective:** Classify US states into 3 typologies of structural racism using a latent profile analysis tool previously applied to smaller geographies in Minnesota.

**Methods:** We collected five-year average (2015-2019) data on Black-White residential segregation (index of dissimilarity), educational attainment ratios, employment ratios, income (index of concentration at extremes [ICE]), homeownership ratios, and incarceration ratios by state from Census Bureau, Bureau of Justice Statistics, and America's Health Rankings websites. We fit a latent profile model specifying 3 classes and describe characteristics of each class.

**Results:** 13 states were classified as typology 1 (T1), 18 as typology 2 (T2), and 20 as typology 3 (T3). Each typology had inequities in all domains. There was a geographic pattern in states' classification, with T1 consisting of Midwestern states, T2 consisting of Western and Northeastern states, and T3 consisting of Southern states. T1 states had the largest inequities in incarceration (T1 RR marginal mean: 9.4 vs T2: 6.1 vs T3: 4.1), educational attainment (T1 RR: 0.54 vs T2: 0.73 vs T3: 0.64), employment (T1 RR: 0.93 vs T2: 0.97 vs T3: 0.95) and residential segregation (T1 index of dissimilarity: 68.6 vs T2: 62.5 vs T3: 58.1). T2 states had the largest inequities in income (T2 ICE: 0.30 vs T1: 0.27 vs T3: 0.16) and homeownership (T2 RR: 0.42 vs T1: 0.48 vs T3: 0.59). T3 states had the smallest inequities in 4 domains (residential segregation, income, incarceration and homeownership).

**Conclusion:** Our analysis classifies states into typologies of structural racism largely along geographic lines. Future research should compare these typologies to state-level health inequities thought to be impacted by structural racism, such as infant mortality, cardiovascular disease, and homicide.



**Educational disparities in dementia prevention: Do diet and physical activity strategies benefit everyone?** Chelsea Liu\* Chelsea Liu Yuan Ma Albert Hofman Melinda C. Power Priya Palta Casey M. Rebholz James R. Pike Thomas Mosley A. Richey Sharrett M. Maria Glymour Rebecca F. Gottesman

**Background:** Due to structural barriers to health outside of lifestyle factors, achieving optimal levels of diet and physical activity may be less effective in preventing dementia for socially vulnerable populations, such as those with low educational attainment. We hypothesized that 1) midlife diet and physical activity have weaker associations with dementia risk among those with low educational attainment, and that 2) divergence in dementia risk among those with different education levels is likely mediated through pathways *other than* midlife diet and physical activity.

**Methods:** The study population included 13,368 Black and White adults aged 45-64 in the Atherosclerosis Risk in Communities Study. Education was categorized as grade school, high school without graduation, high school graduate or equivalent, college with or without graduation, and graduate or professional school. Midlife diet quality was measured using the Healthy Eating Index-2015 (HEI-2015). Moderate-to-vigorous physical activity (MVPA) was assessed using the Modified Baecke Physical Activity Questionnaire. Dementia was ascertained via a detailed neurocognitive battery, informant interview, adjudicated review, telephone assessment or surveillance of hospitalization and death records.

**Results:** Over an average of 22.7 years of follow-up in the study population, higher HEI-2015 was associated with lower risk of dementia only among those with graduate or professional school-level education, while the association between MVPA and dementia did not vary by education level. Neither HEI-2015 nor MVPA substantially mediated the education-dementia association.

**Conclusions:** The effectiveness of behavior change on dementia risk may be lower among those without the social and financial capital afforded by education, and may exacerbate inequalities. Thus, future intervention design should take into account whether lifestyle strategies for dementia prevention are equitable in different study populations.

**Maternal and perinatal health disparities among Middle Eastern and North African and non-Hispanic White women and children in the United States**

Tiffany Kindratt\* Tiffany Kindratt Florence J. Dallo Kyrah K. Brown

Few studies have evaluated the health of Middle Eastern and North African (MENA) American women and children. This study determined the odds of well-visits, preventive behaviors during pregnancy, and low birthweight among foreign-born MENA women and children compared to US-born and foreign-born non-Hispanic White women and children after adjusting for selected covariates. We analyzed 2000-2018 National Health Interview Survey data (n=411,709 women, n=3,908 pregnant, n=311,961 children). Outcomes included well-woman visits (past 12 months; ages 18+ years); dentist visits (past 6 months) and current smoking among pregnant women; and low, moderately low, and very low birthweight among children. Age, family income, education, marital status, and health insurance were covariates. Over half (53.4%) of foreign-born MENA women were of childbearing age (ages 18-45) compared to 47.7% US-born and 43.2% foreign-born non-Hispanic White women. Statistically significant differences were found when comparing income and health insurance among women and children ( $p$ 's<.05). The odds of completing a well-women visit were 0.73 times lower (95%CI=0.38-0.89) among foreign-born MENA women compared to US-born non-Hispanic Whites after adjusting for covariates. There was no statistically significant difference in dental visits among foreign-born MENA and US-born non-Hispanic White pregnant women. No foreign-born MENA pregnant women reported current smoking. Foreign-born MENA children had higher odds of low (OR=1.65; 95%CI=1.16-2.35) and moderately low birthweight (OR=1.78; 95%CI=1.19-2.66) compared to US-born non-Hispanic White children after adjusting for covariates. There were no statistically significant differences in very low birthweight. MENA Americans are classified as White by the federal government. Results demonstrate that the health of foreign-born MENA women and children differs from their White counterparts.

**The Association Between Household Income Changes and Cardiovascular Disease in Postmenopausal Women** Miremad Moafi-Madani\* Miremad Moafi-Madani Mary B Roberts Muhammad Baig Yaser Mokhayeri Michael J LaMonte Charles B Eaton

**Objective:** Lower household income is associated with higher incident cardiovascular disease (CVD). However, there is limited research on the association between income changes and cardiovascular outcomes, especially among older women. In this study, we intended to examine the association between change patterns in total household income and the risk of CVD.

**Design:** The Women's Health Initiative (WHI) is a large prospective cohort that recruited 161,808 women aged 50 to 79 years nationwide in 40 clinical centers between 1993 and 1998. In this analysis, we used total household income variables from baseline and Year 6. Participants were followed up until March 31, 2018.

**Exposure:** The baseline and Year-6 household income were collected as 8- and 13-level categorical variables, respectively. We used the midpoints of each level's bracket in order to categorize participants into three groups: those who experienced their household income decrease by more than 50%, increased by more than 50%, and remained unchanged or changed by less than 50% during the first 6 years of follow up.

**Outcomes:** Our primary outcome was incident CVD (MI, fatal CHD, HF, and stroke) during a mean follow-up time of 11 years starting after Year-6 data collection, using the Cox proportional hazard model to calculate unadjusted hazard ratios and adjusted for age, baseline household income, racial/ethnic groups, education, marital status, employment status, BMI, total leisure-time physical activity, and the alternative healthy eating index (AHEI-2010).

**Results:** Of the 64,736 participants who had available household income data at both time points (mean [SD] age at baseline was 63 [7.2] years, 3906 and 2269 participants were Black and Hispanic) 10,470 participants (16%) were in the decreased income group, 37,652 participants (58%) remained unchanged or experienced a change below 50%, and 16,614 participants (26%) experienced an increased income greater than 50%. In our fully-adjusted model, participants with a decreased income had a significantly higher risk of incident CVD compared with participants whose incomes remained relatively unchanged (hazard ratios: 1.16; 95% CI, 1.06-1.27). Participants with an increased household income did not have a lower risk of incident CVD. (hazard ratios: 1.03; 95% CI, 0.96-1.11)

**Conclusion:** A significant decrease in household income over 6 years was associated with a higher risk of incident CVD during 11 years, while increased income was not associated with a lower risk of subsequent incident CVD.

**Characterizing high-cost healthcare users among adults with back pain in Ontario, Canada: A population-based cohort study** Jessica Wong\* Jessica Wong Pierre Côté Andrea Tricco Tristan Watson Laura Rosella

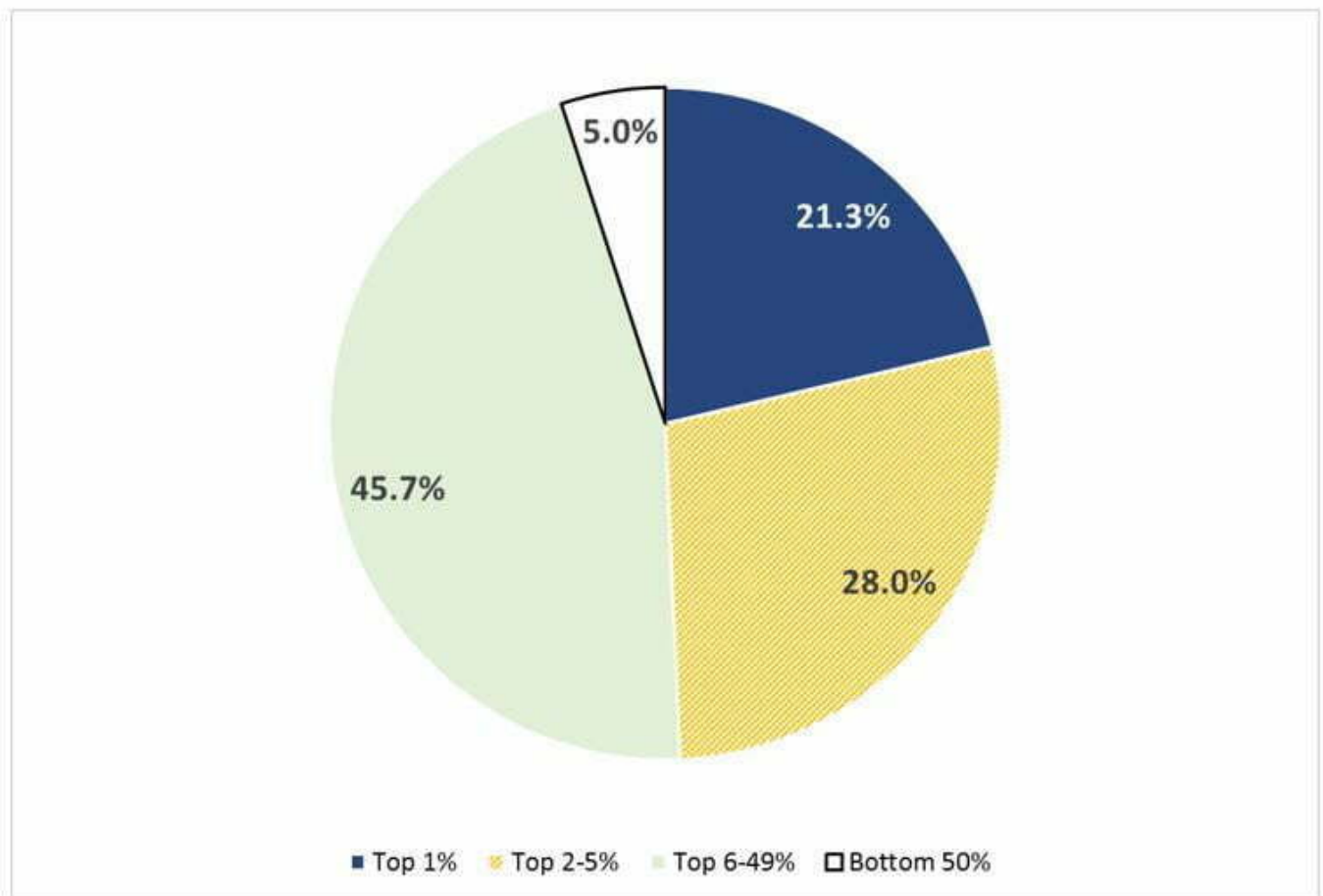
**Background:** Some patients with back pain contribute disproportionately high healthcare costs; however, characteristics of high-cost users with back pain are not well defined. We described high-cost healthcare users based on overall costs among a population-based cohort of adults with back pain within the Ontario government single-payer health system across sociodemographic, health and behavioural characteristics.

**Methods:** We conducted a population-based cohort study of Ontario adult respondents of the Canadian Community Health Survey (CCHS) with back pain (2003-2012), linked to administrative data. Respondents were ranked based on gradients of healthcare costs (top 1%, 2-5%, 6-50%, bottom 50%) for 1-year following the CCHS survey, with high-cost users defined as top 5%. We used multinomial logistic regression to investigate sociodemographic, health and behavioural characteristics associated with the four cost groups.

**Results:** We included 36,605 adult respondents with back pain. Top 5% of cost users accounted for 49% (\$4 billion CAD) of total healthcare spending, with inpatient hospital care as the largest contributing service type (~40% of total costs). In the multivariable model, top 5% high-cost users were more likely to be aged  $\geq 65$  years ( $OR_{top1\%}=16.6$ ;  $OR_{top2-5\%}=44.2$ ), lowest income quintile ( $OR_{top1\%}=3.6$ ;  $OR_{top2-5\%}=1.8$ ), chronic disease ( $OR_{top1\%}=3.8$ ;  $OR_{top2-5\%}=1.6$ ), highest Aggregated Diagnosis Groups quintile measuring comorbidities ( $OR_{top1\%}=25.4$ ;  $OR_{top2-5\%}=13.9$ ), and fair/poor self-rated general health ( $OR_{top1\%}=6.7$ ;  $OR_{top2-5\%}=4.6$ ) compared to bottom 50% users.

**Conclusions:** High-cost users among adults with back pain account for nearly half of all healthcare spending over a 1-year period. Among adults with back pain, high-cost users are associated with older age, lower income, comorbidities, and fair/poor general health. Findings identify a high risk group for back pain to inform healthcare and public health strategies that target upstream determinants in Canada.

**Figure 1.** Distribution of healthcare spending over a 1-year period in adults with back pain based on four cost ranking groups (top 1%, top 2-5%, top 6-49%, bottom 50%), among pooled participants surveyed from 2003 to 2012, Canadian Community Health Survey, Ontario, Canada (n=36,605).





**Claims and cost responsibility trends for high deductible insurance plan participants in the New Hampshire Limited Use Commercial Health Care Claims data.** Keith\* Keith Dookeran  
Mark Brunk-Grady

Background: High-deductible health plans (HDHPs) are popular in the US due to their potential to curb rising healthcare costs and involve higher out-of-pocket costs for consumers which are associated with lower utilization of health services. Data on longitudinal trends for claims and cost responsibility for adult HDHP participants is however scarce, and it is also unclear whether this might vary by income level.

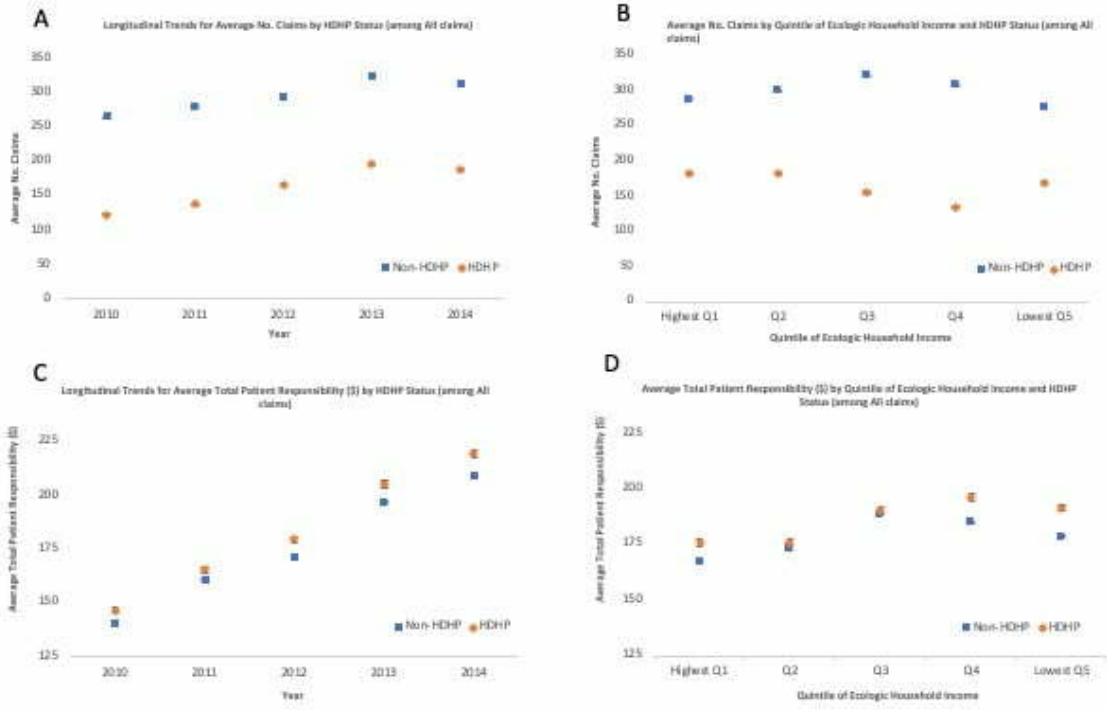
Methods: We used multivariable Poisson regression models with the Huber/White/Sandwich linearized estimator of variance and predictive margins (reported as counts with 95% Confidence Intervals) to develop select stratified estimates of (a) the average number of claims per enrollee (claims), and (b) the average total participant responsibility per enrollee visit (cost in \$; i.e., the sum of in-network and out-of-network values) for adult (age  $\geq 18$  years) HDHP participants in the New Hampshire Limited Use Commercial Health Care Claims data for the 5-year period 2010-14. Final models were fully adjusted for other plan types, year, age, and quintile of ecologic income. Our final dataset consisted of 2,047,481 claim records in 40,636 HDHP participants overall.

Results: Figure 1 shows results. HDHP participants were seen to have significantly fewer claims within each year strata, although the claims levels appeared to rise over time for both HDHP and non-HDHP participants [Panel A]. Although claims appeared lower for HDHP participants overall, fewest claims were made by HDHP participants in the in the three lowest income strata [Panel B]. In addition, HDHP participants were seen to have significantly higher participant responsibility within each year strata, and the levels appeared to rise over time for both HDHP and non-HDHP participants [Panel C]. However, the highest participant responsibility values were observed for HDHP participants in the 2 lowest income strata [Panel D].

Conclusion: Overall, fewest claims and highest cost responsibility were observed in HDHP participants from amongst the lower income strata and suggest disparate impact.

**Figure 1:  
Panels A-D**

[HDHP – High Deductible Health Plan]



**Estimating the Impact of Access to the Rashtriya Swasthya Bima Yojana (RSBY) Health Insurance Program on Adverse Pregnancy Outcomes in India: 2004 - 2019** Caroline Joyce\*  
Caroline Joyce Deepti Sharma Arnab Mukherji Arijit Nandi

**Background:** India has high rates of maternal and neonatal mortality but does not have a universal health insurance scheme. In 2008 the central government launched the RSBY program, created specifically for families at or below the poverty line. The goal of RSBY is to increase access to hospital services for families who cannot afford them. The RSBY program covers specific inpatient services, e.g. in-hospital childbirth, identified as imperative for lowering maternal and neonatal morbidity and mortality.

**Aim:** This research project examines whether access to the RSBY program reduces social inequalities in maternal and reproductive health outcomes.

**Methods:** This study uses data from three district-representative health surveys with similar target populations, sampling designs, and survey instruments giving a combined sample of 2,085,733 pregnancies that occurred between 2004 and 2019 inclusive. The primary outcomes of interest were whether the pregnancy resulted in an abortion, miscarriage, or stillbirth. District-level access to RSBY was assigned as a binary outcome starting with the month it was first introduced. A difference-in-differences (DD) approach was used to estimate the impact of providing access to the RSBY program on pregnancy outcomes, as well as whether these effects vary by socioeconomic position. To measure the impact RSBY access had on social inequality, treatment effects were estimated by quintiles of household income.

**Results:** We hypothesize that women in the lowest wealth quintile who had access to RSBY will have lower rates of stillbirth compared to women without. Additionally, we hypothesize that rates of induced abortion will be higher among women with access to RSBY compared to women without.

**Conclusion:** As India expands health insurance access through the expanded PM-Ayushman Bharat scheme, this research study will provide critical evidence about whether RSBY had an equitable impact on pregnancy outcomes among women in India.

**Food deserts and COVID-19: A national associational analysis** Matthew Lavallee\* Matthew Lavallee Isaacson Michel Caitlin O'Connor Nadia N. Abuelezam

**Background:** Food deserts (FD), areas with limited access to fresh food, have received attention in the health services literature. Prior work has found that FD are strongly associated with adverse health outcomes, particularly COVID-19. Additionally, the COVID-19 pandemic had detrimental impacts on social determinants of health, such as food insecurity. We examined how pre-existing FD are associated with COVID-19 risk factors and incidence, nationally.

**Methods:** We restricted our analysis to Medicare recipients due to the increased risk for severe COVID-19 cases in this population. All outcome data was acquired from claims data made available by Dartmouth's Atlas of Health Care (DAoHC) at a hospital service area (HSA) level. Data on FD was made available by the U.S. Department of Agriculture. Our outcomes included: the proportion of people in the HSA over 65 years old living with two or more risk factors for COVID-19 in 2018 and the monthly incidence rates of COVID-19 (per 1000) in 2020. Our analysis included two models: 1) a linear regression to estimate the relationship between FD and the proportion of people living with risk factors; 2) a fixed effect model which estimates the association between FD and COVID-19 incidence rate with controls for time.

**Results:** We analyzed 3435 HSAs nationally, flagging those with greater than or equal to the median proportion of people in FD as being FD HSAs (N=1715, 49.9%). Monthly COVID-19 incidence rates ranged from 0 to 123 per 1000 Medicare beneficiaries, and the proportion of people living with 2 or more risk factors ranged from 1% to 22% across HSAs. We found that FD were associated with a 3.7% decrease in the proportion of highest-risk people before the pandemic and an 8.0% decrease in COVID-19 incidence rates.

**Discussion:** There is a need for continued examination of the relationship between food insecurity and infectious disease spread, nationally, especially in the context of the COVID-19 pandemic.

**Associations between the sweetened beverage tax implementation in Seattle, Washington and changes in supermarket interior marketing displays**

Nicole Asa\* Nicole Asa Melissa A. Knox Vanessa M. Oddo Lina Pinero Walkinshaw Brian E. Saelens Nadine Chan Jessica C. Jones-Smith

Sugar-sweetened beverages (SSBs) are a significant contributor to added sugar intake, leading to adverse health outcomes such as type 2 diabetes, obesity, and cardiovascular disease. There has been increased global attention and increased emphasis on decreasing added sugar intake, leading to SSB taxes. SSB taxes are hypothesized to affect consumption by raising prices, thus promoting a decreased demand for SSBs. Little is known about SSB taxes impact on beverage marketing in the retail environment. We assessed changes in large food stores interior marketing displays before and 12-months after the implementation of Seattle's Sweetened Beverage Tax, which went into effect January 1, 2018. This study used a quasi-experimental design with stores in Seattle exposed to the tax, while stores in a comparison area were unexposed. Poisson difference-in-difference (DID) models estimated the degree to which the presence and variety of interior beverage marketing displays in Seattle change from before to after the tax compared to displays in a non-taxed comparison area, overall and by beverage type. There were no significant changes in overall SSB or non-SSB interior marketing displays in Seattle versus the comparison area. By beverage type, there was a significant relative decrease in displays for diet soda (DID=0.79, 90%CI=0.65, 0.97), and a significant relative increase in displays for diet energy drinks (DID=1.78, 90%CI=1.03, 3.09). Identifying how the SSB tax affects beverage marketing is important to understand the mechanisms by which the SSB tax plays a role in reducing consumption of SSBs and thus further contributing to the reduction in related adverse health outcomes. There was mixed evidence that stores changed beverage interior marketing displays in response to Seattle's Sweetened Beverage Tax.

**Voluntary blood donation preferences in China: a discrete choice experiment** Stephen W. Pan\* Stephen Pan Chuqing Cao Jing Wang Tianyu Guo Xinwen Hu Stephen W. Pan

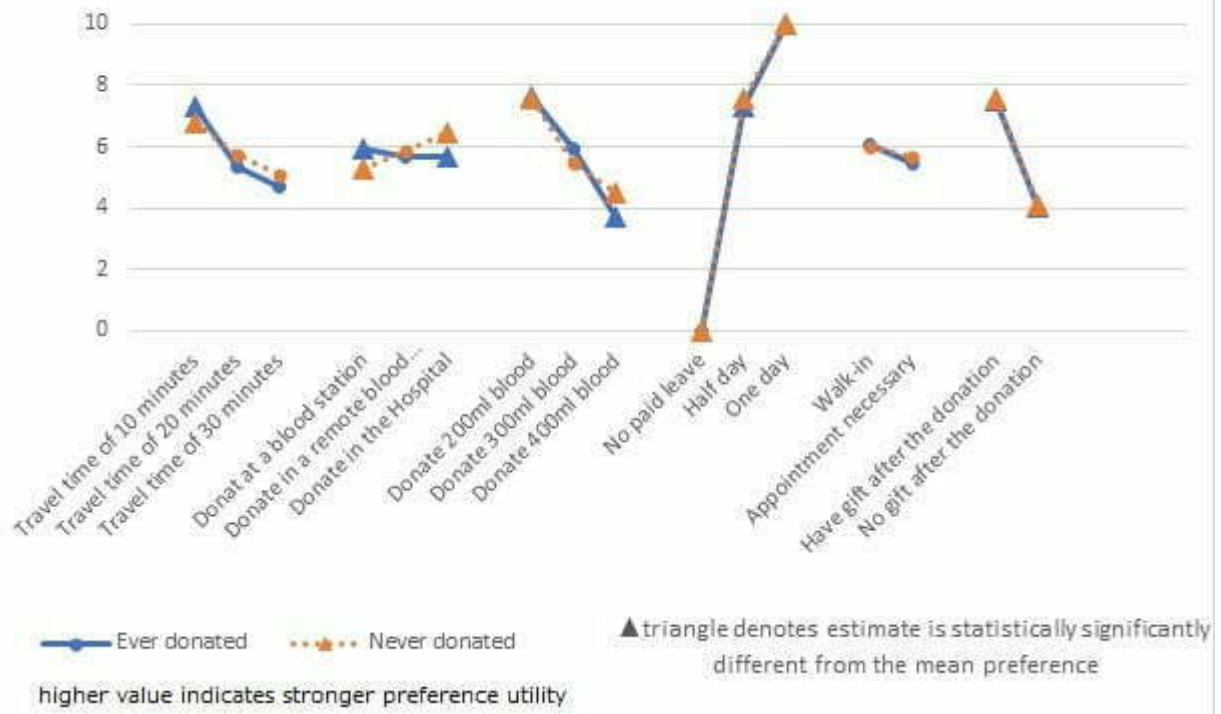
**Background:** Due partly to an aging population, China is facing an increasingly dire blood shortage crisis that will require greater voluntary blood donations. A better understanding of blood donation preferences can help inform blood donation policies and potentially increase donations. We used an online survey and discrete choice experiment to identify the most influential facilitators and barriers to voluntary blood donation in China.

**Method:** First, we identified seven structural attributes (travel time, venue, donation volume, paid leave, scheduling, gifts) that were hypothesized to influence voluntary blood donation; attribute selection was based on literature review, personal experience, and qualitative interviews. Second, a d-efficient design matrix with 36 choice sets was developed. There were four different choice sets in each of nine blocks, and each participant was randomly assigned to a block. Participants were asked to complete four choice sets and in each choice set, they were asked to choose from three options: two voluntary blood donation scenarios and a “Do not donate blood” option. Study participants were recruited through an online survey platform company in China. Voluntary blood donation preferences and preferences by blood donation history were estimated with random-parameter logit models and interaction terms.

**Results:** In 2022, 1185 individuals enrolled into the study. Most participants had at least college education (92%). Generally, participants had the strongest preference for longer paid leave, lower blood donation volumes, and gifts after donation (see figure). Based on interaction analyses, previous donors have a stronger preference for the blood donation station, compared to those who have never donated.

**Conclusion:** Results suggest that paid leave after voluntary blood donation, lower blood donation volumes, and small gifts could encourage more voluntary blood donation among higher educated individuals living in China.

Figure: Scaled preference utility estimates of blood donation preferences in China, by donation history (n=1185 )



**Effects of a Federal Smoke-Free Housing Policy on Lower Respiratory Tract Infections in Older Adults Living in New York City Public Housing** Jonathan Burke\* Jonathan Burke Elle Anastasiou Leopoldo Segal Andrea Titus Lorna E. Thorpe

**Background:** Smoke-free housing (SFH) policies aim to reduce the adverse health effects of secondhand smoke exposure, but few studies have examined the health impacts of these policies. We assessed the effect of a 2018 federal SFH rule for public housing authorities on the rate of lower respiratory tract infections (LRTIs).

**Methods:** Using 2015-2019 housing data from Coredata.nyc and claims data from New York's Statewide Planning and Research Cooperative geocoded to the Census Block Group (CBG) level, we evaluated the policy's impact on older residents (age 50+) of New York City Housing Authority (NYCHA) units compared to other subsidized housing units not subject to the federal rule. We employed propensity score matching to achieve strong balance and overlap on CBG-level age, sex, race/ethnicity, poverty, education, and housing density using five-year American Community Survey averages. We utilized a Difference-in-Difference (DiD) model with matched data to estimate the Average Treatment Effect on the Treated of the SFH policy on LRTI rates after a one-year washout period.

**Results:** Matched NYCHA (n=104; 65,339 housing units) and control (n=220; 122,969 units) CBGs had large proportions of residents that were Black (37.2 vs 36.8%), Hispanic (51.6 vs 51.2%), and earned <100% federal poverty line (41.2 vs 41.8%). NYCHA CBGs had higher average pre-intervention (10.4 vs 6.6 LRTIs per 1,000 people per three-month-period) and post-intervention LRTI rates (7.8 vs 4.7) than control CBGs. 17 months after policy introduction, the weighted DiD model estimated that the SFH policy prevented a negligible number of LRTIs (0.8 per 1,000 people per three-month-period; 95% CI: -1.1, 2.8) in NYCHA housing units.

**Conclusion:** The SFH policy did not reduce LRTIs in older adults in the early period after its introduction in New York City. This should be reevaluated with longer-term data given gradual implementation and time needed for reversal of pathologic changes in the respiratory tract.



**Outcomes of Physician- versus Midwife-Attended Births: Variation by Race/Ethnicity and Place** Laura Chen\* Laura Chen

**Background:** Midwifery has been proposed as a potential avenue to mitigate adverse birth outcomes and severe racial and ethnic disparities in maternal and child health in the United States, where pregnancy and childbirth are heavily medicalized. Currently, policies that define midwives' role in healthcare vary widely between states. Few studies have evaluated how birth attendant type affects birth outcomes depending on maternal race/ethnicity, or how state-level midwifery policies may exert influence on this relationship.

**Methods:** Analyzing 2014 birth data (n=2,593,795) from the National Vital Statistics System, we use propensity-weighted multivariable logistic regression to test the association between physician versus midwife attendant and various birth outcomes (including preterm birth, low/very low birthweight, and low Apgar score), as well as how this association may vary by maternal race/ethnicity. We then use random effects models to explore the state-specific effects of state midwifery policy climate in each of the 50 states and D.C. (as measured using the Midwifery Integration Scoring System) on these relationships between birth attendant, maternal race/ethnicity, and outcomes.

**Results:** Even after controlling for differential risk profiles of physician- and midwife-attended births, midwife attendant was associated with lower odds of all adverse birth outcomes studied. Midwives were also particularly protective for Black mothers relative to White mothers across a variety of outcomes. Moreover, states with more integrative midwifery policy tended to have higher birthweights than states with more restrictive policy, even after accounting for compositional differences of each state.

**Conclusion:** A more comprehensive effort to integrate midwives and the midwifery model of care into the healthcare system may help advance maternal and child health and health equity in the US.

**Patient-provider relationships and antiretroviral therapy adherence among women with HIV, Miami-Dade County, Florida, 2021-2022** Mary Jo Trepka\* Mary Jo Trepka Melissa K. Ward Kristopher P. Fennie Diana M. Sheehan Sofia Fernandez Tan Li Michele Jean-Gilles Gladys Ibanez Tendai Gwanzura Ekperereka Nawfal Aaliyah Gray Mary Catherine Beach Robert Ladner

**Background:** Adherence to antiretroviral therapy by people with HIV is critical to meet the US National HIV/AIDS Strategy's goal of 95% viral suppression. Compared with men, women with HIV disproportionately experience adverse socioeconomic factors such as low education and poverty and thus need supportive health care services. This cross-sectional study assessed the role of patient-provider relationship on adherence to antiretroviral therapy among women with HIV in Miami-Dade County, Florida.

**Methods:** Adult women in the Ryan White Program participated in telephone surveys between June 2021-March 2022. Patient-provider relationship was measured, in part, using the Health Care Relationship (HCR) Trust Scale and communication items from the Consumer Assessment of Health Care Providers and Systems. Adherence was measured with 3 self-reported items (number of missed doses, frequency of compliance to prescription, and subjective rating of adherence) and classified as  $\geq 90\%$  in the last month. In addition to age and race/ethnicity, variables associated with adherence with a  $p$ -value  $\leq 0.2$  in bivariate analysis were entered into a multivariate logistic regression model, using backwards selection with  $p$ -value  $< 0.15$  as the threshold for the final model.

**Results:** Of 560 cis-gender women, 33.2% were Hispanic, 28.0% Haitian, and 35.4% Non-Hispanic Black; 71.6% were  $\geq 90\%$  adherent. In the final model, adherence was significantly associated with HCR Trust Score (adjusted OR [aOR] 1.30; 95% CI 1.07-1.59) and high provider communication scores (aOR 1.99; 95% CI 1.14-3.46 for high vs. low and aOR 2.58; 95% CI 1.18-5.63 for moderate vs. low). Excellent perceived health, absence of significant depressive symptoms, no alcohol use in last 30 days, and no transportation problems were also associated ( $p < 0.05$ ).

**Conclusion:** High quality patient-provider relationships and services for substance use and mental health are needed to support antiretroviral therapy adherence for women.

**PrEP uptake and bacterial sexually transmitted infections: applications of marginal structural models and quantitative bias analysis to evaluate risk compensation** Nguyen K. Tran\* Nguyen Tran Seth L. Welles Jason A. Roy David J. Brennan Esther Chernak Neal D. Goldstein

**Background:** While pre-exposure prophylaxis (PrEP) has contributed to declines in HIV infection, studies indicate that it may also increase rates of bacterial sexually transmitted infections (STI) among gay, bisexual, and men who have sex with men (GBM) through risk compensation. However, longitudinal studies evaluating this phenomenon have been limited. We aimed to assess the effect of PrEP uptake on rates of bacterial STI among GBM.

**Methods:** Data were from the iCruise Study, an online longitudinal study of Ontarian GBM from July 2017 - April 2018. PrEP uptake and bacterial STI were based on self-reported measures collected in the baseline and follow-up surveys. We used marginal structural models with inverse probability of exposure and attrition weights to examine the relation of PrEP uptake and rate of bacterial STI including chlamydia, gonorrhea, and syphilis. Quantitative bias analysis was used to evaluate the sensitivity of estimates to nondifferential outcome misclassification.

**Results:** The analytic sample included 535 HIV-negative, cisgender GBM. Participants were followed for a total of 1623.5 person-months. About 13.1% (n = 70) took PrEP during over follow-up. After accounting for confounding and selection bias, PrEP uptake was associated with an increased incidence rate of gonorrhea (IRR = 3.75, 95% CI: 1.50, 9.35). We did not find evidence to indicate a relation of PrEP uptake with any bacterial STI (IRR = 1.53, 95% CI: 0.72, 3.99), chlamydia (IRR = 0.97, 95% CI: 0.43, 2.33), or syphilis (IRR = 0.96, 95% CI: 0.23, 4.02). In quantitative bias analysis, the median IRR for gonorrhea was 2.36 (95% SI: 1.08, 5.06).

**Conclusions:** We only observed increased rate of gonorrhea incidence among GBM using PrEP to those who did not, but these estimates were sensitive to outcome misclassification. Findings support current guidelines for STI testing, integrating bacterial STI risk reduction with PrEP care, and the potential use of doxycycline post-exposure prophylaxis.

**The unique and joint contributions of intimate partner violence and male HIV partner status on adolescent girls' and young women's risk of living with HIV: a pooled analysis of cohabiting couples from 35 surveys in sub-Saharan Africa (2000-2020)** Salome Kuchukhidze\*

Salome Kuchukhidze Dimitra Panagiotoglou Marie-Claude Boily Souleymane Diabaté Jeffrey W Eaton Heidi Stöckl Rhoda K Wanyenze Mathieu Maheu-Giroux

## Background

Adolescent girls and young women (AGYW) are three times as likely to acquire HIV, and twice as likely to be living with HIV than men of the same age in sub-Saharan Africa. Intimate partner violence (IPV) may partly explain this. However, few studies examining IPV-HIV accounted for male partners' HIV status. We aimed to understand whether experiencing IPV in the past year adds to AGYW's risk of living with HIV, beyond the risk resulting from their partners' HIV status.

## Methods

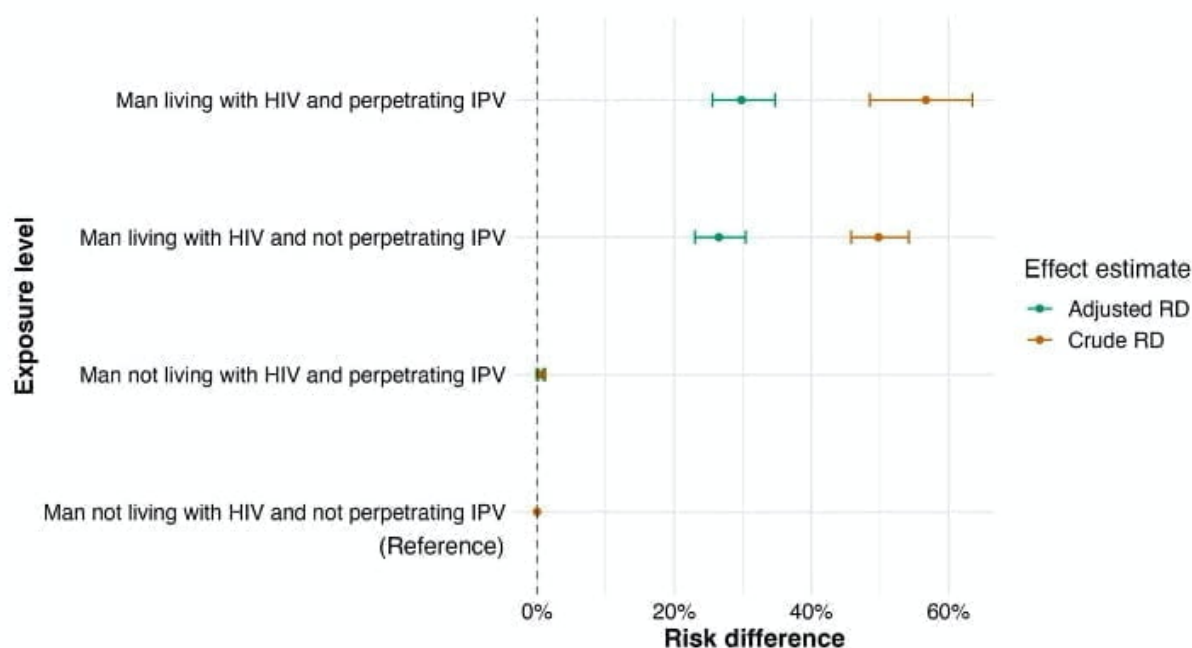
We pooled data from all nationally representative, cross-sectional surveys with information on past-year physical and/or sexual IPV and HIV biomarkers to create a dataset of cohabiting couples (women aged 15-24 and their current male partners) in sub-Saharan Africa (2000-20). We used marginal standardization with generalized estimating equations and robust standard errors to calculate crude and adjusted risk differences (RD) of the impact of male partner HIV status on AGYW's HIV status, with IPV as an effect measure modifier (EMM). We calculated 95%CI via bootstrapping. Models were adjusted for AGYW's age, wealth, residence (rural/urban), lifetime number of sex partners and survey fixed effects. Additive EMM was assessed via Relative Excess Risk due to Interaction (RERI).

## Results

Thirty Demographic and Health Surveys and 5 Population-based HIV Impact Assessment were pooled ( $N_{\text{couple}}=17,834$ ). AGYW whose partners lived with HIV had 27% higher risk of HIV seropositivity compared to AGYW whose partners neither lived with HIV nor perpetrated IPV (aRD=27%;95%CI:23-30%; Fig 1). Using the same reference, AGYW whose partners perpetrated IPV and lived with HIV had a 30% higher risk of HIV (aRD=30%;95%CI:26-35%). RERI was 1.03 (95%CI:0.97-1.08) indicating an additive EMM.

## Conclusion

AGYW experiencing IPV have a small added risk of living with HIV, beyond the effect of their partners' HIV status. Interventions for IPV may mitigate HIV risk among AGYW whose partner is HIV seropositive.



**Figure 1.** Unique and joint contributions of male partner HIV status and male partner perpetrated physical and/or sexual intimate partner violence (IPV) to HIV status among adolescent girls and young women (AGYW). We present crude and adjusted risk differences. Reference category is man who are not living with HIV and do not perpetrate intimate partner violence.

*Model adjusted for AGYW's age (continuous), wealth quintile, AGYW's education (none, primary, secondary, higher), residence type (rural, urban), AGYW's lifetime number of sexual partners (0-1; 2, 3+), survey identifier.*

**Methylation markers for anal cancer screening: a repeated cross-sectional analysis among people living with HIV, 2015-2016**

Anjali Vasavada\* Anjali Vasavada Rachel L. Winer John Lin  
Stephen E. Hawes Judith N. Wasserheit Helen Stankiewicz Karita Jeffrey T. Schouten Stephen L.  
Cherne Ruanne Barnabas

**Background:** People living with HIV (PLWH) are at highest risk of anal cancer and will benefit from optimized screening practices for early disease detection. We compared host DNA methylation markers in high-grade squamous intraepithelial lesions (HSIL) versus samples negative for intraepithelial lesions (NILM) or low-grade intraepithelial lesions (LSIL) in PLWH.

**Methods:** We recruited PLWH identifying as male aged  $\geq 18$  years undergoing high-resolution anoscopy (HRA) in Seattle, Washington, between 2015-2016. Anal samples were collected for HPV genotyping and pyrosequencing methylation (genes ASCL1, PAX1, FMN2, and ATP10A); clinical data were abstracted from medical records. We assessed associations between methylation and presence and extent of HRA HSIL using generalized estimating equation logistic regression, adjusting for covariates. Marker panels using HPV DNA and methylation were also evaluated to predict prevalent cytologic/histologic detected HSIL.

**Results:** We analyzed 125 samples from 85 participants (mean age 50.3, SD 10.2 years). ASCL1 (aOR per 1 unit increase mean percent methylation:1.07, 95%CI:1.01-1.13) and FMN2 (aOR per 1 unit increase mean percent methylation:1.12, 95%CI:1.06-1.19) methylation were significantly associated with cytologic/histologic detected HSIL versus NILM/LSIL. ASCL1 (aOR:1.06, 95%CI:1.01-1.11) and FMN2 (aOR:1.07, 95%CI:1.02-1.10) methylation were positively associated with increasing HRA HSIL extent. A panel combining methylation (ASCL1 and FMN2) and HPV DNA (HPV16, HPV18, HPV31) improved sensitivity (78.2%) and specificity (73.9%) for cytologic/histologic HSIL detection compared to methylation markers alone.

**Discussion:** Increasing levels of DNA methylation of ASCL1 and FMN2 were positively associated with HSIL detection in PLWH. Host gene methylation testing shows promise as an effective screening and triage tool for anal cancer.

### Cardiometabolic health among HIV-exposed and HIV-unexposed infants in South Africa

Madelyn Frey & Sophie Lazar\* Angela Bengtson Hlengiwe Madlala Mushi Matjila Gregory Petro Zandile Maqwatini Azetta Fisher Landon Myer

In utero exposure to HIV and antiretroviral therapy (ART) may influence cardiometabolic health in HIV-exposed but uninfected (HEU) children. After enrollment at 24-28 weeks gestation in Cape Town, South Africa we followed HIV-unexposed (HU) and HEU children for up to 26 months postpartum. Infant anthropometry was assessed by trained research assistants and converted to age- and sex-adjusted z-scores. Pre-prandial blood samples were collected to assess glucose, insulin, lipids and insulin resistance using the Homeostatic Model Assessment (HOMA-IR). In multivariable analyses, we compared cardiometabolic health by HIV exposure status and post-conception ART regimen (dolutegravir (DTG) versus efavirenz (EFV). Among 208 children (n=100 HU, n=108 HEU), 75% had  $\geq 1$  laboratory measure at an average age of 10 months (SD 4.2). Of HEU children, 54% were born to mothers on post-conception ART (n=42 DTG, n=17 EFV) and 95% had a laboratory value. Compared to HU, HEU children had lower BMI (0.9 vs 1.4), weight-for-age (0.5 vs 1.0), weight-for-length (WLZ; 0.8 vs 1.4), but not length-for-age z-scores (-0.2 vs -0.05, Table). HU children had a higher proportion of overweight (WLZ >2 SD, 23% vs 15%) or obese (WLZ >3 SD, 10% vs 5%), than HEU children. Few children (n=3) were underweight (WLZ <-2 SD). HEU children had marginally higher HOMA-IR (0.9 vs 0.6) and insulin (3.5 vs 3.0 mIU/L) but not glucose (4.2 vs 4.3 mmol/L) than HU children, adjusted for age. There were also no differences in anthropometry, glucose metabolism or lipids by ART regimen, but sample size was limited. In this cohort of HU and HEU children, few children were underweight, but HIV exposure led to lower weight at an average of age 10 months. Despite this, HEU children had higher insulin and insulin resistance levels while maintaining similar glucose levels, possibly suggesting early adaptive changes in glucose metabolism. Ongoing follow-up of cardiometabolic health in HEU and HU children is needed.

**Table. Cardiometabolic health by HIV exposure and ART regimen among infants in Cape Town, South Africa**

	HIV-unexposed	HIV-exposed	RD (95% CI)	Post-conception DTG	Post-conception EFV	RD (95% CI)
	mean (SD)	mean (SD)		mean (SD)	mean (SD)	
<b>Glucose Metabolism</b>	n= 81	n=76		n=30	n=8	
HOMA-IR	0.6 (0.6)	0.9 (1.7)	0.3 (-0.1, 0.8)*	0.8 (0.7)	0.7 (0.5)	-0.1 (-0.7, 0.6)*
Fasting plasma glucose, mmol/L	4.3 (0.5)	4.2 (0.5)	-0.1 (-0.2, 0.1)*	4.4 (0.6)	4.0 (0.4)	-0.3 (-0.8, 0.2)*
Fasting Insulin, mIU/L	3.0 (2.8)	3.5 (3.6)	1.5 (-0.2, 3.3)*	4.0 (3.5)	3.8 (2.6)	0.0 (-2.9, 2.9)*
<b>Lipids</b>	n= 81	n=73		n=28	n=7	
LDL cholesterol, mmol/L	2.0 (0.7)	1.8 (0.7)	-0.2 (-0.4, 0.0)*	1.6 (0.6)	1.8 (0.9)	0.0 (-0.6, 0.6)*
HDL cholesterol, mmol/L	1.0 (0.2)	0.9 (0.2)	-0.1 (-0.1, 0.0)*	1.0 (0.3)	1.3 (0.4)	0.0 (-0.3, 0.3)*
Total cholesterol, mmol/L	3.5 (0.8)	3.3 (0.8)	-0.1 (-0.1, 0.0)*	3.2 (0.6)	3.4 (0.9)	0.0 (-0.5, 0.6)*
Triglycerides, mmol/L	1.1 (0.5)	1.2 (0.7)	-0.1 (-0.1, 0.0)*	1.5 (0.9)	1.4 (0.9)	0.0 (-0.8, 0.8)*
<b>Anthropometry</b>	n=100	n=108		n=42	n=17	
BMI z-score <sup>1</sup>	1.4 (1.5)	0.9 (1.4)	-0.5 (-0.9, -0.2)	0.8 (1.3)	0.4 (1.7)	-0.4 (-1.2, 0.5)
WAZ-score <sup>1</sup>	1.0 (1.3)	0.5 (1.2)	-0.5 (-0.8, -0.2)	0.4 (0.9)	0.1 (1.4)	-0.4 (-1.0, 0.3)
WLZ-score <sup>1</sup>	1.4 (1.5)	0.8 (1.3)	-0.6 (-0.9, -0.2)	0.8 (1.2)	0.5 (1.6)	-0.4 (-1.1, 0.4)
LAZ-score <sup>1</sup>	-0.05 (1.4)	-0.2 (1.5)	-0.2 (-0.6, 0.2)	-0.1 (1.6)	-0.4 (1.7)	-0.2 (-1.1, 0.7)
Weight category	n (%)		RR (95%)	n (%)		RR (95%)
Not overweight (WLZ $\leq$ 2 SD) <sup>1</sup>	67 (67.0)	87 (80.6)	1.00	32 (82.1)	14 (82.4)	1.00
Overweight (WLZ >2 SD) <sup>1</sup>	23 (23.0)	16 (14.8)	0.6 (0.4, 0.9)	5 (12.8)	2 (11.8)	1.0 (0.3, 3.5)
Obese (WLZ >3 SD) <sup>1</sup>	10 (10.0)	5 (4.6)		2 (5.1)	1 (5.9)	

DTG: dolutegravir; EFV: efavirenz. <sup>1</sup>z-scores based on child sex and age, according to WHO guidelines \*Adjusted for child age in months.

**The Mediating Role of Diabetes in the Relationship Between Body Mass Index and Infection: A Population-Based Cohort Study** Fang-Wen Lu\* Hsien-Ho Lin Fang-Wen Lu Yen-Tsung Huang Yi-Ting Huang Bo-Chen Liu Bo-Siang Zeng Yi-Cheng Chang

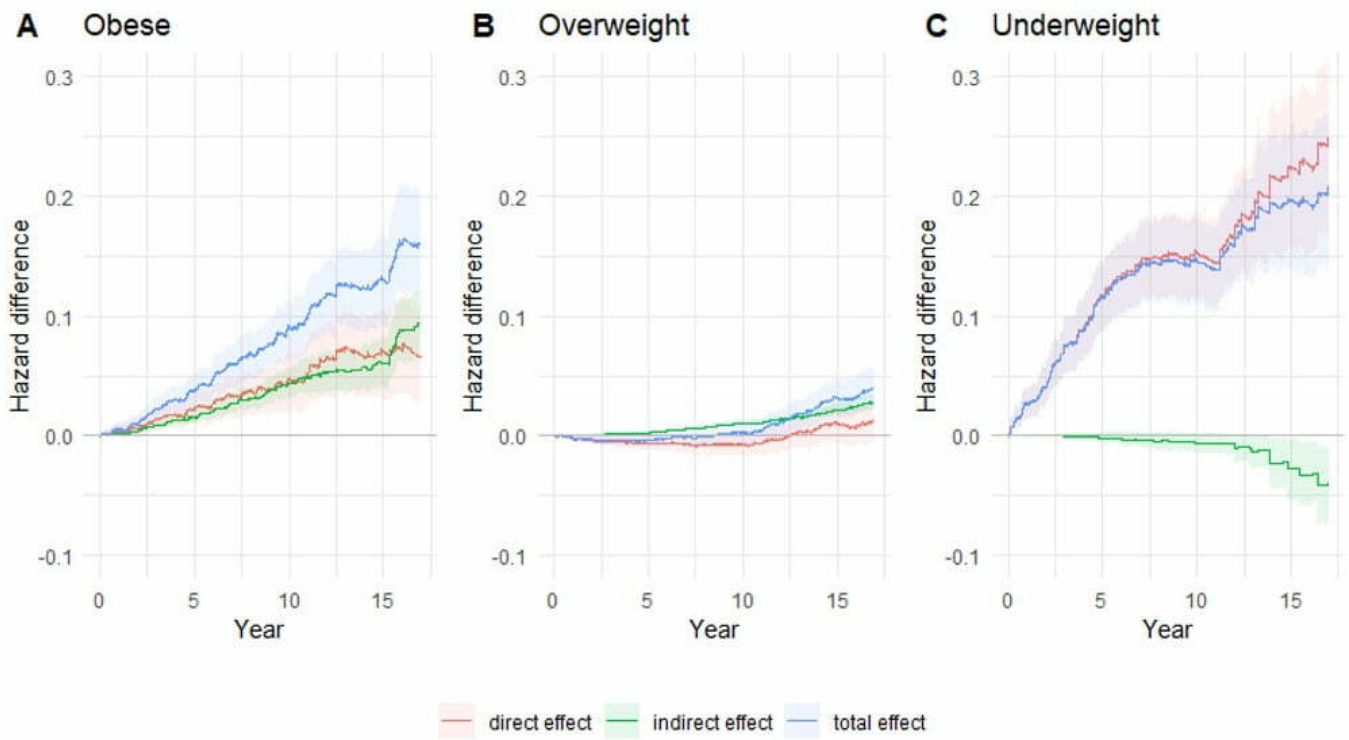
**Background:** Mounting evidence suggests that extreme body mass index (BMI) (e.g. underweight or obese status) and diabetes increase the overall risk of infections. However, the mediating role of diabetes in the relationship between BMI and infections has not been assessed. Therefore, the purposes of this study were to (i) quantify the association between BMI and the overall risk of infections, and (ii) estimate the indirect effect of BMI on infections mediated through diabetes.

**Methods:** The cohort included 52,391 participants from the National Health Interview Survey (NHIS) conducted in Taiwan. Incident diabetes and hospitalized infections were identified from Taiwan's National Health Insurance Research Database (NHIRD). Cox regression was used to quantify the association between BMI and the risk of infections. To estimate the indirect effect of BMI on infections mediated through diabetes, a non-parametric causal mediation model was adopted to calculate the cumulative hazard differences. Stabilized inverse probability weighting was used to adjust for confounding. Two types of hypothesis tests, a weighted log-rank test and an intersection-union test, were conducted to test the significance of the overall mediation effect across the study period. Integration was used to calculate the proportion of mediation.

**Results:** During the follow-up period, 5,501 (10.50%) individuals developed diabetes, and 7,709 (14.71%) individuals had hospitalized infections. Compared to the normal-weight population, the hazard ratios were 1.45 (95% confidence interval [CI], 1.32-1.59) for the underweight group and 1.60 (95% CI, 1.46-1.74) for the obese group. The indirect effects in the underweight, overweight, and obese groups were all statistically significant, with the obese group having the highest hazard difference. Incident diabetes mediated 47.24% (95% CI, 0%-78.80%) of the relationship between obese status and infection risk.

**Conclusions:** The relationship between obesity and infection was significantly mediated through diabetes; the proportion of mediation was around 50%. Diabetes control strategies may help reduce the burden of infections due to obesity.





**Fig.** 95% CI of the total, direct and indirect effects (cumulative hazard differences) for (a) obese, (b) overweight, and (c) underweight group (vs. normal-weight)

**Analysis of invalid vaccine dose administration among U.S. children: National Immunization Survey-Child 2020** Alexandria N Albers\* Alexandria Albers Sarah Y Michels Rain E Freeman Jason M Glanz Matthew F Daley Sophia R Newcomer

**Background:** Young children are recommended to receive multiple vaccinations against 15 diseases, with most vaccinations requiring multiple doses to achieve optimal disease protection. Vaccine series have minimum age and interval requirements, and doses provided outside recommended parameters are considered invalid. We quantified the prevalence of and factors associated with invalid childhood vaccine doses.

**Methods:** We analyzed provider-verified vaccination records of children ages 19-35 months from the 2020 National Immunization Survey-Child. Doses were invalid if administered before the recommended minimum age, or if the minimal interval between doses was not met. A multivariable logistic regression model was used to identify demographic, socioeconomic, or household factors associated with receipt of at least one invalid dose. Analyses accounted for complex survey design, including weighting to represent national estimates.

**Results:** In analyses of 19,342 children, 428 (weighted percent: 2.3%, 95% CI:1.9-2.7) had at least 1 invalid dose, and most were attributed to doses in the hepatitis B (HepB) (n=184, 44.1%), diphtheria-tetanus-acellular-pertussis (DTaP) (n=107, 30.5%), and pneumococcal (PCV) (n=115, 20.0%) vaccine series. Within each series, 53.7% of PCV, 64.4% of HepB, and 44.0% of DTaP invalid doses were due to final doses administered when the child was too young. Additionally, 85.9% of DTaP, 36.0% of HepB, and 26.3% of PCV invalid doses were due to final dose interval violations. Reasons for invalid doses were not mutually exclusive. None of the demographic, socioeconomic, or household factors were significantly associated with the receiving one or more invalid doses.

**Conclusion:** Our analyses indicate less than 3% of U.S. children may be considered undervaccinated due to invalid doses. Broader implementation of electronic health record- or immunization information system-based clinical decision support tools could help reduce invalid vaccine administrations.

**Using individual, contextual, and dyadic information to identify infection sources for Carbapenem resistant *Klebsiella pneumoniae* cases in a long-term care facility.** Hannah Steinberg\* Hannah Steinberg Evan Snitkin Jon Zelner

Carbapenem resistant *Klebsiella pneumoniae* (CRKP) is a healthcare-associated infection causing diverse manifestations of disease including pneumonia, bloodstream infections, and wound infections, as well as asymptomatic colonization. CRKP infection is dangerous for individuals with compromised immunity and other underlying health conditions, making individuals in long-term care facilities a population at high risk for both infection and adverse outcomes. Despite its importance, not much is known about the determinants of individual-level CRKP infection risk in such facilities. We developed and compare multiple models for describing the genomic relatedness of isolates obtained from CRKP cases in a long-term acute care hospital (LTACH). We analyzed a dataset in which 260 patients of an LTACH were sampled for CRKP colonization or infection every two weeks from June 2012-June 2013, and all positive isolates were subjected to whole genome sequencing. 255 individuals (98%) were colonized, 180 of whom were colonized with the dominant strain type 258, which was used in analyses. We compare three measures of genomic relatedness (single nucleotide variant distance, closest genomic distance, and membership in the same genomic cluster). All of these measures are meant to capture the likelihood that two cases are linked by transmission, with lower genomic distance generally indicating a higher likelihood of direct transmission. All models were adjusted for calendar time and included a random intercept for each potential donor to capture unobserved heterogeneity in infectiousness. In all three models, sharing a room or residing on the same floor during the potential transmission period predicted smaller genomic distance and cluster co-membership between pairs, with sharing a room as the strongest predictor of genomic similarity. This work suggests that decolonization and other infection prevention efforts should focus on close within-facility contacts of CRKP patients.

## Impact of Exposure to Potentially Contaminated Hospital Beds and Hospital Rooms on Risk of Hospital-onset Clostridioides difficile Infection: A Four-Way Decomposition Analysis

Radhika Prakash-Asrani\* Radhika Prakash Asrani Lucy S Witt Jessica Howard-Anderson Elizabeth Overton Jesse T Jacob

**Background:** Clostridioides difficile spores can remain on hospital environmental surfaces despite appropriate cleaning measures. We examined the risk of a patient developing hospital-onset C. difficile infection (HO-CDI) when staying in a hospital bed that had a previous occupant with CDI (“contaminated bed”) and if this relationship is mediated by and/or has interaction from being exposed to a room which had a previous occupant with CDI (“contaminated room”).

**Methods:** We retrospectively identified HO-CDI cases in two academic medical centers from 4/2018–8/2019. We defined a bed (or room) as “contaminated” if it was previously occupied by a patient with CDI within the last 90 days (Fig 1). We conducted mediation analyses allowing for four-way decomposition of the effect of contaminated bed on HO-CDI, mediated by and/or with interaction from exposure to a contaminated room, adjusting for hospital length of stay and admission to the intensive care unit.

**Results:** Of 25,032 hospital encounters, we identified 237 cases of HO-CDI (0.9%). In unmediated adjusted analyses, being exposed to a contaminated bed was associated with developing HO-CDI (OR 1.51, 95% CI: 1.15, 1.97). The total excess relative risk was 0.45 (95% CI: 0.05, 0.85), of which 62% was attributable to mediated interaction from being in a contaminated room (Excess Relative Risk 0.28, 95% CI: –0.03, 0.59). The overall proportion of HO-CDI mediated was 78% (95% CI: 59, 98).

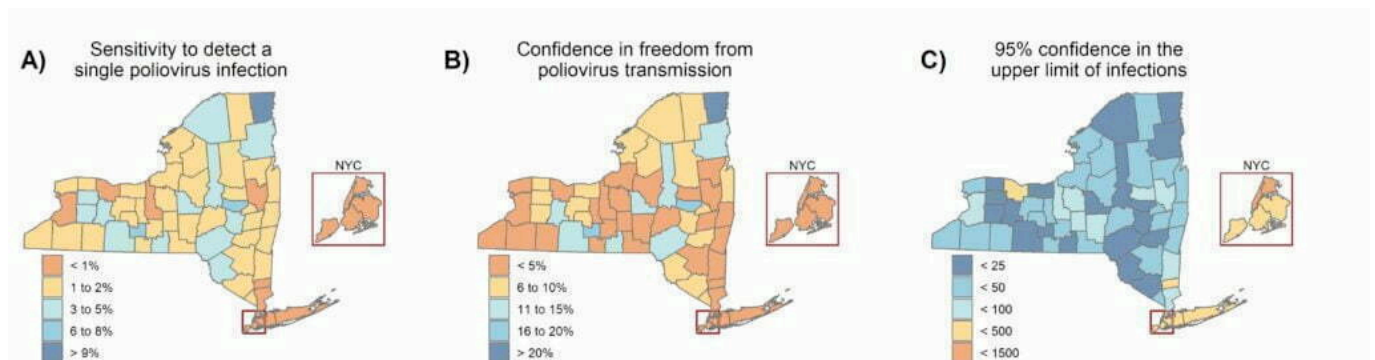
**Conclusion:** Occupying a hospital bed with a prior occupant who had CDI is a risk factor for developing HO-CDI. This relationship is both mediated by and has interaction from residing in a hospital room that previously contained a patient with CDI.



Figure 1. Exposure to a C. difficile “contaminated” bed. Beds are considered contaminated starting with the positive C difficile test of an occupant (green occupant). The bed remains contaminated for 90 days in this figure. Subsequent patients were only considered to have an associated HO-CDI if they developed their infection within seven days of occupying a contaminated bed and after at least three days in the hospital (orange occupant). Occupants were required to have spent only one night in a contaminated bed to have an associated CDI. The blue occupant did not develop CDI.

**Considerations in designing wastewater (environmental) surveillance for poliovirus** David A. Larsen\* David Larsen Dustin Hill Mohammed Alazawi Dana Chatila Christopher Dunham Catherine Faruolo Brandon Ferro Alejandro Godinez Brianna Hanson Tabassum Insaf Dan Lang Dana Neigel Milagros Neyra Nicole Pulido Max Wilder Nan Yang Brittany Kmush Hyatt Green

Wastewater (environmental) surveillance is commonly used in the global polio eradication initiative in countries at risk of polio transmission. Recent polio outbreaks in New York State and London, England have prompted wastewater surveillance in those countries, but questions remain regarding how to interpret non-detections of poliovirus in wastewater. We estimate a sensitivity of detection of poliovirus in wastewater to inform the sensitivity of wastewater surveillance for poliovirus throughout New York State. Estimated sensitivity to detect a single poliovirus infection was low, < 11% at most wastewater treatment plants and < 3% at most counties across the state. However, the maximum threshold for the number of infections present in the context of non-detection of poliovirus in wastewater was much lower than the expected number of cases observed before a paralytic case. With the majority (81%) of communities with polio vaccine coverage < 70% covered by the state's wastewater surveillance network, we propose baseline prospective wastewater surveillance that can both confirm the absence of a polio threat in the community and be escalated in the case of poliovirus detection.



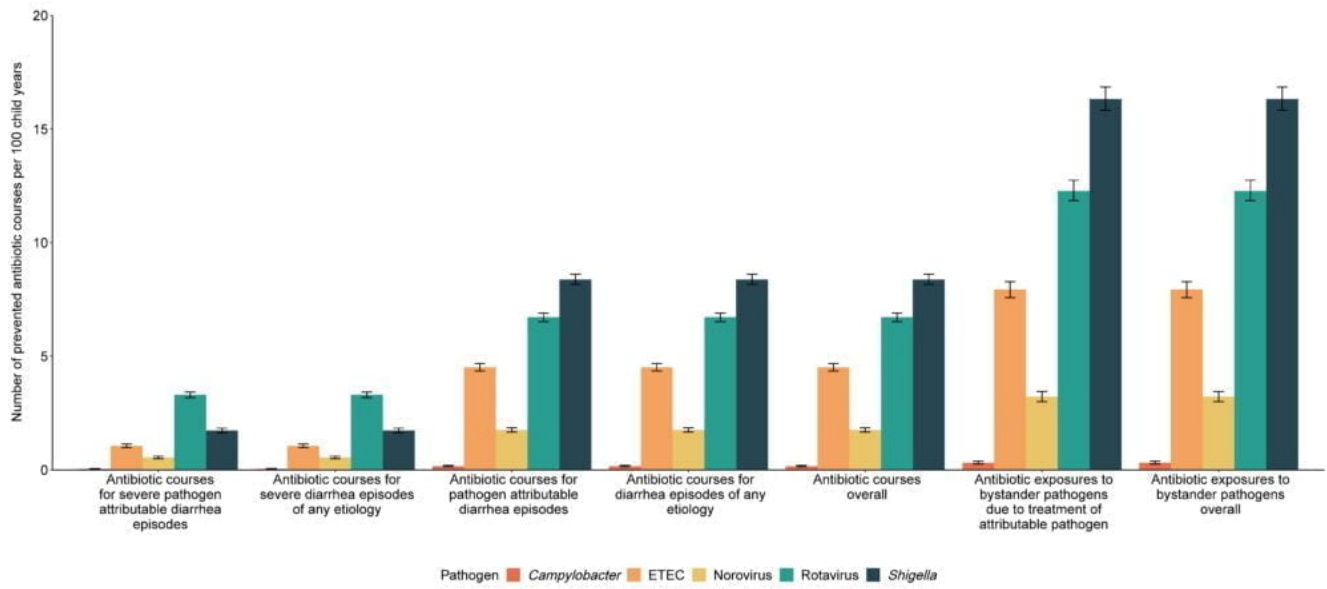
**Impact of vaccines for diarrhea on antibiotic use: a simulation study** Stephanie A. Brennhofer\* Stephanie Brennhofer James A. Platts-Mills Sarah E. Elwood Elizabeth T. Rogawski McQuade

Vaccines against diarrheal pathogens may reduce selection pressure for antimicrobial resistance (AMR) by reducing antibiotic use. We estimated the impact of hypothetical vaccines against *Campylobacter jejuni/coli*, enterotoxigenic *E Coli* (ETEC), norovirus GI/GII, rotavirus, and *Shigella* on antibiotic use and exposure for pathogens present asymptomatically at time of treatment (i.e., bystander exposure) among children from 5 sites in the MAL-ED birth cohort study.

We analyzed 3029 diarrhea episodes and 12918 antibiotic courses in 1119 children. We used Monte Carlo simulations to estimate the impact of two-dose vaccines for each pathogen on antibiotic use and bystander exposure. We simulated the administration of the norovirus and rotavirus vaccines at 2 and 4 months and the *others* 6 at 9 months of age. All vaccines were assumed to be 60% efficacious against severe disease and 40% efficacious against non-severe disease 14 days after the second dose.

The *Shigella* vaccine prevented 8.4 antibiotic courses per 100 child years followed by rotavirus at 6.7 courses, ETEC at 4.5 courses, norovirus at 1.7 courses, and *Campylobacter* at 0.2 courses (Figure). While the *Shigella* vaccine prevented the most antibiotic exposures, the rotavirus vaccine prevented the most treatments of severe diarrhea episodes. The impact on bystander exposure was larger; 16.3 (*Shigella*), 12.3 (rotavirus), 7.9 (ETEC), 3.2 (norovirus), and 0.3 (*Campylobacter*) exposures per 100 child years to antibiotics were prevented through vaccination. However, the percent reductions in overall antibiotic use were minimal, ranging from 0% (*Campylobacter*) to 1% (*Shigella*).

*Shigella* and rotavirus vaccines would likely make the largest reductions in antibiotic use for diarrhea compared to other enteric vaccines. While preventing a small proportion of antibiotic use overall, these vaccines could have substantial ancillary benefits on bystander pathogen exposure and AMR due to frequent antibiotic use in this population.



**Feasibility and optimal sampling frequency of oral herpes simplex virus shedding among immunosuppressed populations: a pilot study among solid organ transplant recipients**

Molly Fischer\* Molly Fischer Margaret Green Stacy Selke Amanda Phipps Christine Johnston Steven Pergam

**Background**

Herpes simplex virus (HSV) frequently reactivates during immunosuppression in transplant recipients and may be a risk factor for adverse post-transplant outcomes. Understanding HSV viral kinetics is important for advancing research to improve post-transplant outcomes. We describe the characteristics of oral HSV shedding among solid organ transplant (SOT) recipients to determine the optimal sampling frequency for future longitudinal studies.

**Methods**

HSV-1 seropositive SOT recipients self-collected oral swabs 3 times daily for 6 weeks and recorded the presence of any oral symptoms or clinical lesions in a diary. Swabs were tested for HSV using RT-PCR. The number of shedding episodes, viral copies and the proportion of swabs with HSV DNA detected were calculated as a measure of viral reactivation. A shedding episode was defined as  $\geq 1$  consecutive DNA-positive swabs both preceded and followed by 2 consecutive negative swabs.

**Results**

A total of 15 participants enrolled (n=8 liver, n=7 kidney, median age 58.5 years). Sample collection was high among study participants with a median of 122 swabs collected per person (range: 85.7-101.6% of expected swabs). Most participants (n=12, 80%) experienced at least 1 shedding episode during the study period, with a median per-person shedding rate of 8.8% (range: 0-33.6%). There were 32 total shedding episodes (median 2 per person); 23 were asymptomatic. For episodes of known duration, median length was 21.8 hours (IQR: 11.4-46.1 hours). Most shedding episodes (59.4%) lasted >24 hours; few episodes lasted  $\leq 12$  hours (18.8%).

**Discussion**

Daily collection of oral swabs for HSV detection is feasible and subclinical oral HSV shedding occurs frequently among SOT recipients. Our pilot findings suggest that twice daily sampling may be sufficient to detect most shedding episodes.



**Estimating the beginning of the 2022-2023 influenza season in the United States using methods to estimate the time-varying reproduction number of influenza** Sarabeth Mathis\*  
Sarabeth Mathis Pragati Prasad Rebecca Borchering Sinead Morris Michael A. Johansson Matthew Biggerstaff

**Introduction:** During the COVID-19 pandemic, the time-varying reproduction number ( $R_t$ ) has been a pivotal tool for determining whether COVID-19 cases and hospitalizations are likely increasing or decreasing.  $R_t$  estimates for influenza could serve as an important metric for detecting changes in dynamics of seasonal epidemics in real time. We adapted methods to estimate  $R_t$  to determine jurisdictions where influenza hospital admissions were likely increasing during the 2022-2023 influenza season.

**Methods:** We used national- and state-level data for daily influenza hospital admissions from the Health and Human Services (HHS) Protect dataset and adapted methods to estimate  $R_t$  from those developed during the COVID-19 pandemic. Our approach applied the Cori et al.  $R_t$  calculation method and used sequential sampling to propagate uncertainty from the  $R_t$  estimates and serial interval distribution to generate uncertainty bounds. We used an estimate of five days from illness onset to hospitalization, and a gamma-distributed serial interval with a mean of 3.6 days. We calculated the probabilities that  $R_t$  would be greater than 1 for each state and nationally, with probabilities above 0.6 used to indicate when influenza hospitalizations were likely increasing. We applied this approach to HHS admission data from July 26, 2022, until December 13, 2022.

**Results:** Nationally, the mean  $R_t$  stayed below 1 from late July through August 2022 and fluctuated around 1 during September. The probability that  $R_t$  was above 1 first exceeded 0.6 on September 24 for the United States and remained above this threshold until December 13. States in the South Census Region were the first to exceed 0.6 on September 29, followed by other regions starting in late October.

**Conclusion:** Influenza activity began atypically early in the 2022-2023 season. Our  $R_t$  estimation method was able to identify likely increases in influenza activity nationally in late September before substantial increases were observed in other influenza surveillance indicators. Efforts to estimate  $R_t$  routinely could be useful for public health planning to determine when influenza transmission is likely increasing.

**Expanding antibiotic treatment to patients with moderate cholera disease could reduce community transmission - a modeling study** Sharia Ahmed\* Sharia Ahmed Iza Ciglenecki Andrew Azman Daniel T Leung Lindsay T Keegan

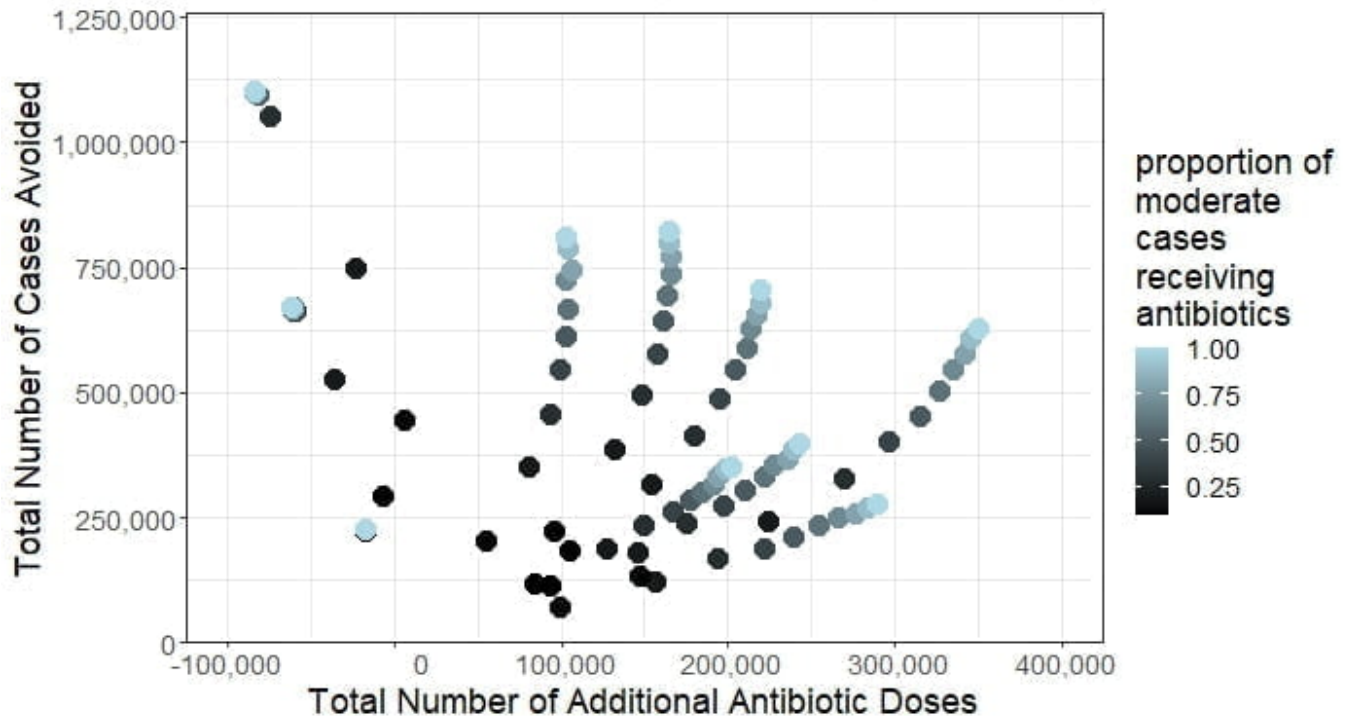
Cholera outbreaks continue to occur worldwide and remain an important cause of diarrhea morbidity and mortality. Under current guidelines, all cholera patients receive rehydration therapy, but only severely dehydrated patients receive antibiotics, which decrease the volume of stool and duration of shedding, thereby reducing transmission. Once rehydrated, all cholera patients are discharged back into the community. Here, we modeled the impact on community transmission of expanding antibiotic treatment to include moderately dehydrated cholera patients.

We built an SEIR model to simulate a cholera outbreak in a fully susceptible population to quantify the impact of expanded antibiotic treatment. We assumed that non-antibiotic-treated infected individuals continue to shed pathogen after symptoms resolve, but that severely and moderately dehydrated patients who receive antibiotics stop contributing to transmission after presenting to care. We employed Latin-hypercube sampling to explore a range of possible parameter values.

We found that treatment of moderately dehydrated cholera patients with antibiotics reduced the total number of cases in a cholera outbreak. On average, treating no moderately dehydrated cholera cases resulted in 60% (sd=0.25) of the total population being infected with cholera. However, when 40% and 80% of moderately dehydrated cases were treated with antibiotics, we found only 45% (sd=0.28) and 40% (sd=0.28) of the total population was infected during the outbreak, respectively. In approximately 20% of simulations, expanded antibiotic eligibility led to fewer doses being used over the full course of the outbreak, though this was highly variable.

Through this simulation model, we provide early evidence that expanding antibiotics to moderately dehydrated cholera patients could have a substantial impact on reducing community transmission and therefore morbidity and mortality of cholera outbreaks.

# Total Number of Cases Avoided Over Entire Outbreak



**LATEBREAKER**

Infectious Disease

**Herpes zoster vaccine and the risk of stroke: a population-based cohort study using linked data from the Clinical Practice Research Datalink in England** Kathryn Richardson\* Kathryn Richardson Yoon K Loke Helen I. McDonald Helen Parretti Jemma L Walker Fawziah Lalji

**Background:** Several studies report herpes zoster (HZ) infection associated with short-term excess stroke risk. In England the HZ vaccine has been licensed to 70-79 year olds since September 2013. We aimed to examine if HZ vaccine is associated with lower stroke rates in this age group compared to unvaccinated patients. **Methods:** We conducted a matched cohort study of patients aged 70-80 years registered with general practices in England from Clinical Practice Research Datalink Aurum with linkage to hospital admissions, death certificate and deprivation data. We compared patients with first HZ vaccination (index date) from 2013-19, to patients unvaccinated between 2007-12, matched on age, sex, index month and index day. Patients were followed until the first of: death, stroke diagnosis, leaving the GP practice, 30 days before last data collection, March 2020 (in vaccinated), August 2013 (in unvaccinated), or 5 years post index date. We excluded those with previous stroke or <12 months prior GP registration. Hazard ratios (HR) for incident stroke for vaccinated compared to unvaccinated patients were estimated using Cox proportional hazards regression, adjusted for many potential confounders. We also compared vaccinated patients to an active comparator of first influenza vaccination when eligible for the HZ vaccination during 2013-19. **Results:** We recorded 16,281 and 21,216 strokes among 678,110 vaccinated and 678,110 matched unvaccinated patients. The adjusted HR (95% CI) for incident stroke in HZ vaccinated patients compared to unvaccinated patients was 0.90 (0.85-0.95). Similarly, the adjusted HR (95% CI) in HZ vaccinated patients compared to 712,715 patients given an influenza vaccination (active comparator) was 0.87 (0.85-0.90). The HRs did not vary consistently by age, sex, or immunosuppression. **Conclusions:** HZ vaccine is associated with a 10-13% reduced stroke risk in patients aged 70-80 years. Uptake of this vaccine should continue to be promoted to older people.

**Place Matters: Exploring the Relationship between Social Conditions and Causes of Injury- and Violence-Related Death in North Carolina** Ty Lautenschlager\* Ty Lautenschlager Shabbar Ranapurwala Shana Geary

## Background

North Carolina (NC) experienced a 23% increase in injury and violence-related deaths between 2016-2020. We examined the association between census tract social vulnerability and injury- and violence-related deaths.

## Methods

Geocoded death certificate data (2016-2020) from NC were used to identify deaths from falls, medication/drug overdose (OD), homicides, motor vehicle traffic collisions (MVT), and suicides. We used Poisson regression to calculate rates, ratios, and 95% CI of the association of the Social Vulnerability Index (SVI) of a census tract with injury- and violence-related deaths. SVI integrates socioeconomic status, household composition, race/ethnicity, housing, and transportation from a census tract. We compared the lowest SVI grouping (least vulnerable) to the highest SVI grouping (most vulnerable) census tracts. We used generalized estimation equations to account for county-level clustering and adjusted for sex, education, rurality, and age.

## Results

The OD death rate in the least vulnerable tracts was 13.3/100K person-years (95% CI: 12.6-14.1), and for the most vulnerable tract was 25.3/100K (24.1-26.5). The rates were 11.4 (10.9-12.0) vs 18.2 (17.4-19.0)/100K for MVT deaths, 16.5 (14.6-18.6) vs 27.3 (26.1-28.4)/100K for homicides, 13.1 (12.2-14.0) vs 12.6 (11.6-13.6)/100K for falls-related deaths, and 16.6 (15.9-17.3) vs 14.3 (13.5-15.2)/100K for suicide deaths among the least and most vulnerable tracts, respectively. Compared to least vulnerable tracts, most vulnerable tracts had greater deaths from OD [RR=1.32 (95% CI: 1.21-1.45)], homicides [1.46 (1.24-1.73)], and MVT [1.31 (1.23-1.40)]; and lower deaths from falls [0.81 (0.73-0.91)] and suicides [0.79 (0.72-0.85)].

## Conclusion

There is an increased burden of OD, homicide, and MVT deaths in highly vulnerable census tracts. However, low vulnerability tracts are at higher risk of fall and suicide deaths. SVI can help outline the disproportionate burden and prioritize need at census tract level.

**The Mental Health Consequences Before and After a Historic Police Killing in Minneapolis in Black and White Communities** Jeanie Santaularia\* Jeanie Santaularia Ryan Larson Christopher E. Robertson Christopher Uggen

Police violence, a form of structural racism, is a fundamental cause of health inequity. The direct and indirect exposure of police violence leads to a variety of negative health outcomes such as anxiety, depression, trauma symptoms, and suicide attempts. Given the long history of police violence and brutality, the high profile police killing of George Floyd is likely to have an aftermath of negative health consequences, particularly among Black people in Minneapolis. Our study evaluated the rate of mental health diagnoses after the murder of George Floyd on May 25th, 2020 in Black and white communities in Minneapolis, Minnesota. All results are based on the Minnesota Hospital Association discharge data merged to data from the Minnesota Department of Natural Resources, the Minneapolis Police Department, and the American Community Survey. We analyzed the data using interrupted time series models at the week-level and random-effects panel models at the ZCTA-week level to assess the change in mental health diagnoses in response to the murder of George Floyd. All final models were adjusted for weather, police use of force incidents, police stops, officer-involved shootings, the inception of COVID-19 State of Emergency order, and the introduction and conclusion of this Stay-at-Home order. After adjustment, we find a 0.23 per 100,000 increase in mental health conditions among Black people in the immediate post-murder period, followed by a weekly decline (-.007) in mental health diagnoses. By comparison, we find a 0.06 per 100,000 increase in mental health conditions among white people in the immediate post-murder period, followed by a weekly decline (-.004) in mental health diagnoses. These findings speak to the traumatizing effects of police violence and the short- and longer-term public health consequences for communities, particularly Black communities.

**Change in rate of sport-related catastrophic traumatic brain injuries among U.S. high school football athletes after enactment of return-to-play laws** Erin Shore, MPH\* Erin Shore Shabbar I. Ranapurwala, PhD, MPH, BHMS Jingzhen (Ginger) Yang, PhD, MD Johna Register-Mihalik, PhD, LAT, ATC, FACSM, FNATA Kristen L. Kucera, PhD, MSPH, ATC, LAT

**Introduction:** By 2014, all 50 states and Washington DC had enacted laws to mitigate severe consequences of traumatic brain injury (TBI) in youth sports. This study assessed the change in rate of catastrophic sport-related TBIs among US high school football athletes after enactment of return-to-play (RTP) laws. **Methods:** A quasi-experimental negative-controlled interrupted time series analysis was performed among US high school football athletes from academic years (AY) 2000-2021. Data from 3 sources, the National Center for Catastrophic Sport Injury Research (NCCSIR), National Federation of State High School Associations, and Policy Surveillance Program at the Temple University Beasley School of Law Temple University were merged and analyzed. The presence of an RTP law was coded 1 if a law was enacted and 0 otherwise. The outcome was rate of catastrophic sport-related TBIs and the negative control was sudden cardiac arrest (SCA) among high school football athletes. Time was standardized with AY of law enactment coded as 0. We performed single series and negative-controlled interrupted time series analysis using both TBI and SCA data. **Results:** From AY2000-AY2021, 245 catastrophic TBIs and 97 incidences of SCA were reported among US high school athletes. The rate of catastrophic TBI in AY2000 was 1.58 (95%CI: 1.07, 2.09) per 100,000 athlete-seasons, which slowly increased until the law enactment followed by an immediate absolute decline in the rate of -0.50 per 100,000 athlete-seasons (95%CI: -1.19, 0.19) and the sustained decline in trend of -0.08 (95%CI: -0.18, 0.03) per 100,000 athlete-seasons per year. Compared to the rate of SCA, a greater absolute difference in rate (-0.58, 95%CI: -1.45, 0.29) of TBI and a greater change in sustained trend (-0.14, 95%CI: -0.27, -0.001) were observed. **Conclusions:** Post law-enactment, there was a large immediate decrease in the rate of catastrophic TBIs followed by a sustained change in rate of injury of catastrophic TBIs.

**Bicycle infrastructure and the incidence rate of bicyclist crashes with cars per distance ridden and intersections entered in Atlanta: a case-control study with Strava data** Michael Garber\* Michael Garber Kari Watkins W. Dana Flanders Michael Kramer Felipe Lobelo Steve Mooney David Ederer Lauren McCullough

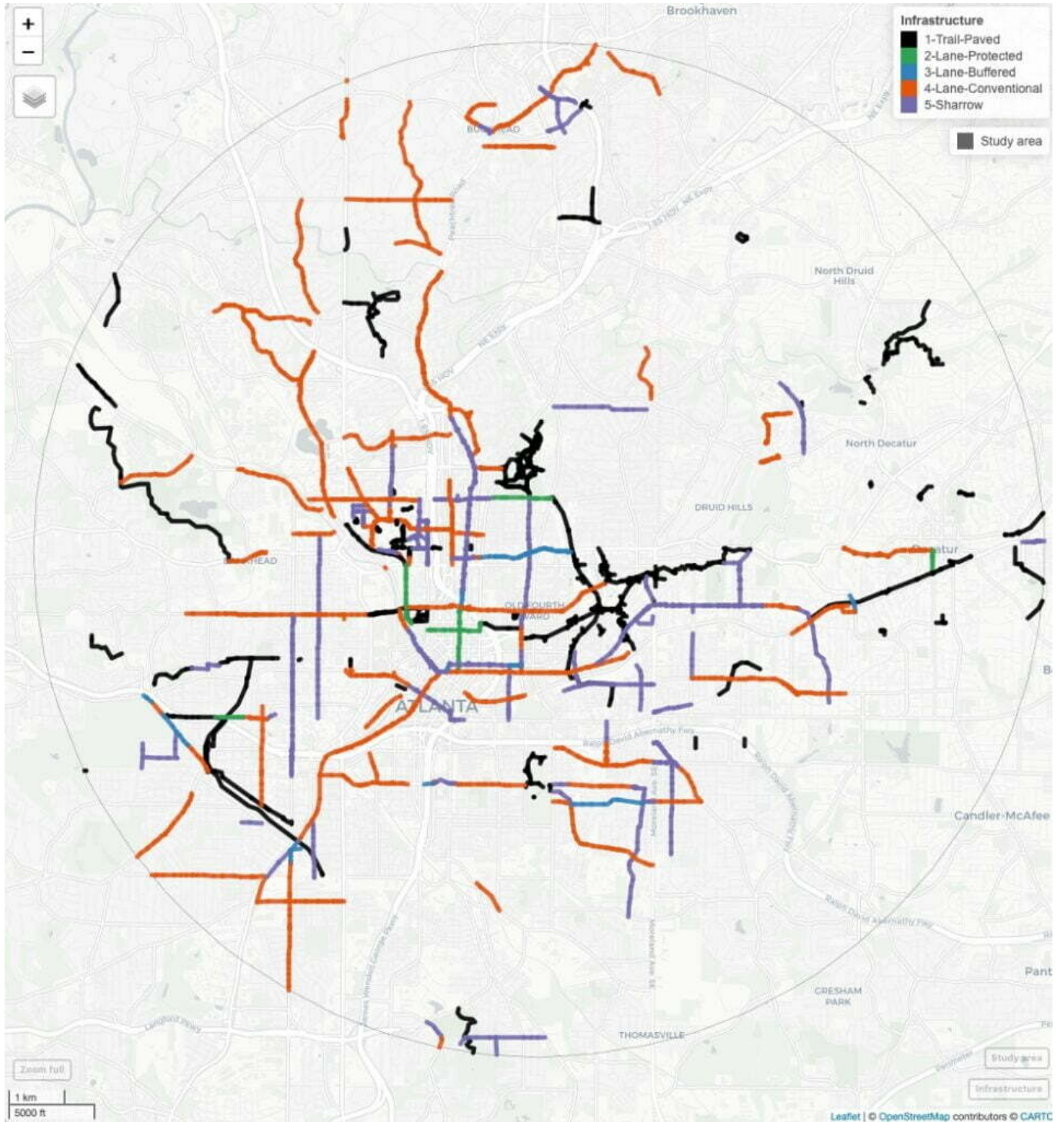
Bicycling has individual and collective health benefits. Safety concerns are a deterrent to bicycling. Incomplete data on bicycling volumes has limited epidemiologic research investigating safety impacts of bicycle infrastructure, such as protected bike lanes.

In this case-control study, set in Atlanta, Georgia between 2016-10-01 and 2018-08-31, we estimated the incidence rate (IR) of a police-reported bicyclist crash (n=124) with a motor vehicle on several types of infrastructure (off-street paved trails, protected bike lanes, buffered bike lanes, conventional bike lanes, and sharrows) among bicycle-distance ridden on segments and among intersection entries. To estimate underlying bicycling (the control series), we used a sample of high-resolution bicycling data from Strava, an app, combined with data from 15 on-the-ground bicycle counters to adjust for possible selection bias in the Strava data.

Compared with segments without infrastructure, after adjusting for Strava use and roadway type, buffered bike lanes had a lower estimated IR (incidence rate ratio (IRR)=0.0 [95% confidence interval: 0.0, 0.0]), but conventional bike lanes (IRR=2.1 [1.0, 4.2]) and sharrows had a higher estimated IR (IRR=2.4 [0.9, 4.9]), while the estimated IR on protected bike lanes was slightly lower (IRR=0.7 [0.0, 2.7]). Among intersection entries, the estimated adjusted incidence proportion ratio among those originating from off-street paved trails was 0.5 (0.0, 2.3), 1.9 (0.0, 5.3) from protected bike lanes, 11.7 (0.0, 37.8) from buffered bike lanes, 2.8 (1.5, 5.1) from conventional bike lanes, and 1.1 (0.3, 2.2) from sharrows.

Results highlight the importance of installing infrastructure appropriate for its context and the limitations of infrastructure absent other safety measures, such as reducing motor-vehicle speeds.





**Cumulative neighbourhood socioeconomic status and risk of premature injury death**

Emmalin Buajitti\* Emmalin Buajitti Laura C. Rosella

*Background*

Neighbourhood socioeconomic context (SES) is an important predictor of health outcomes. Injury-related deaths (suicide, homicide, and accidents) have a well-established socioeconomic gradient. Most studies focus on neighbourhood exposure at time of death, despite the potential for cumulative or historical neighbourhood effects. We used comprehensive data linkages in Ontario, Canada to assess the relationship between longitudinal residential SES and injury mortality.

*Methods*

We identified Canadian Community Health Survey respondents, aged 18 to 74, interviewed between 2000 and 2012 (n=158,074). We captured neighbourhood income quintile at interview, and subsequent years, using encounter-based postal codes from Ontario's single-payer health care system. Annual cumulative neighbourhood exposures were created using a time-weighted average.

Injury deaths were identified from vital statistics data based on ICD-10 codes (V01-Y98). Respondents were followed until December 31 2018, age 75, emigration, or death. We used time-dependent, cause-specific Cox models, with up to 20 annual measures of cumulative SES. Adjusted models included age, sex, survey cycle, immigrant status, self-rated health, smoking, physical activity, alcohol, and education.

*Results*

About 68% of respondents moved at least once during follow-up, with a mean of 2.3 moves per person. Cumulative neighbourhood SES was associated with large differences in premature injury mortality, and higher risks among long-term low-income residents (Hazard Ratio (HR) for lowest income=1.6; 95%CI 1.09, 2.35), though the relationship was non-linear (Fig. 1). This association persisted after adjusting for variables that may influence selection into low-income neighbourhoods (HR 1.16, 95%CI 0.76, 1.76), and attenuated when using non-cumulative neighbourhood exposures.

*Conclusion*

Our findings suggest that persistent exposure to low-income neighbourhoods is associated with increased risk of premature death from injury.

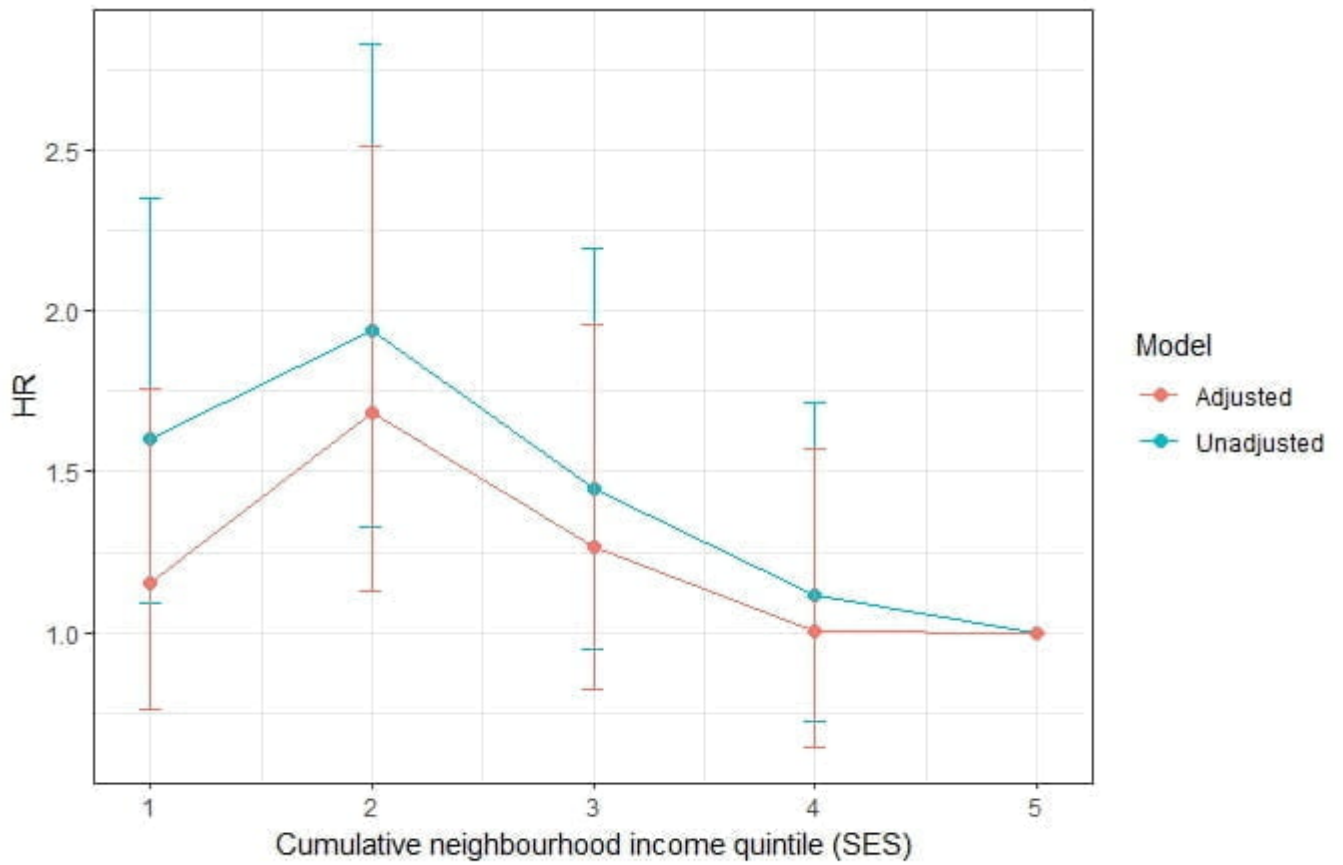


Figure 1. Hazard Ratio (HR) for risk of premature injury death, Ontario CCHS respondents ages 18 to 74, 2000 to 2012 (n=158,074)

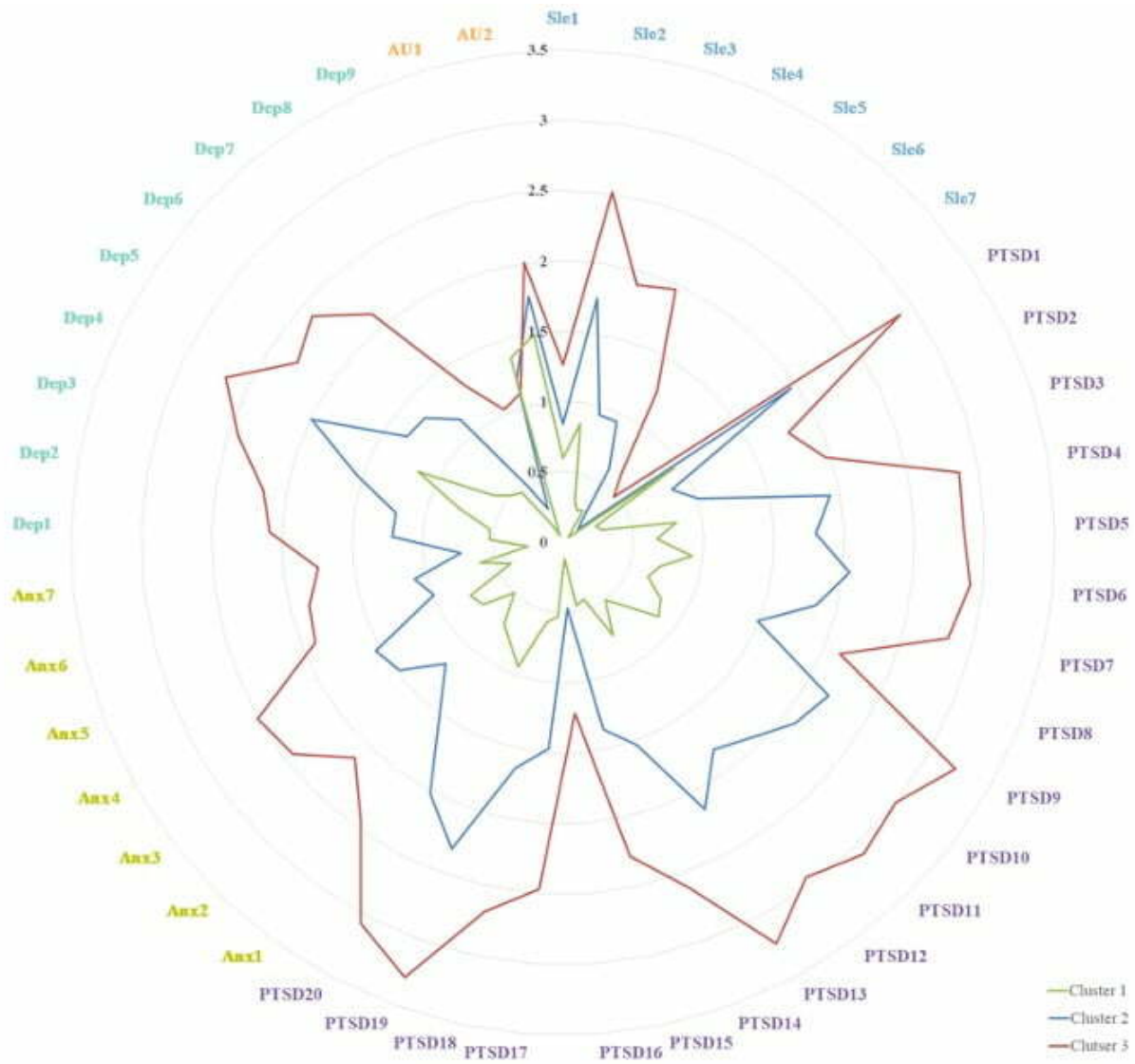
**Determinants of resilience and unfavorable mental health outcomes of violence: a nationwide representative cross-sectional study** Fenfen Ge\* Fenfen Ge Yue Wang Thor Aspelund Unnur Anna Valdimarsdóttir

**Background** Violence against women is a serious global health problem and associated with a range of adverse mental health outcomes. There is scarcity of transdiagnostic data-driven approaches to facilitate understanding of varying mental health symptom-burden following violence. We used machine learning to disentangle resilience and unfavorable mental health problems clusters among women who had experienced violence and identify predictors of these.

**Methods** Participants were 11,338 women who reported having experienced violence during their lives in the Stress-And-Gene-Analysis (SAGA), a nationally representative study in Iceland. We used information on participant's self-reported mental health symptoms, including posttraumatic stress disorder, depression, anxiety, trauma-related sleep, and binge drinking. We further used information on 31 candidate features/covariates covering social demographic, social economic, adverse childhood experiences (ACEs), childhood health, resilience, health related behaviors, perceived social support and violence-related information. We used K-means to identify mental health clusters and both logistic regression and XGBoost to investigate the importance of each feature for the clusters.

**Findings** We identified three distinct clusters, including 41% of women with low symptom burden while 59% with unfavorable or high symptoms burden (i.e., subthreshold and severe symptomology). Both models have good performance, the C-statistic was 0.84 for the logistic regression model and mean (SE) area under the curve was 0.81 (0.01) for XGBoost model. Identified risk factors of unfavorable cluster were younger age, shorter time since the violence exposure, being exposed multiple times to violence, unemployment, experience of certain ACEs (i.e, sexual abuse and emotional abuse/neglect), while identified protective factors were high coping ability and support from family members.

**Interpretation** A large proportion of women who experience violence suffers from multiple mental health symptoms while high coping ability and support from family members are associated with lower probability of such adverse outcomes.



**Evaluating virtual care to improve follow-up for survivors of sexual assault and intimate partner violence presenting for urgent care at emergency departments** Katherine Muldoon\*  
Katherine Muldoon Olivia Mercier Kari Sampsel

**Background:** Sexual assault and intimate partner violence (IPV) are traumatizing experiences. Of the few who present to emergency departments (ED) for urgent care, even fewer return for follow-up. The objective of this study was to evaluate the effectiveness and acceptability of virtual care to improve follow-up care for survivors.

**Methods:** In 2021, The Ottawa Hospital began a virtual care follow-up program for survivors of sexual assault and IPV who presented to the ED. This mixed methods study compares quantitative programmatic data from 2018 (before virtual care was available) to 2021 (when virtual care was introduced). Log-binomial multivariable regression models were used to compute adjusted risk ratios (aRR) and 95% confidence intervals (CI) to estimate changes in follow-up care. Qualitative interviews were conducted among consenting survivors who attended a virtual follow-up.

**Results:** 786 patients were included in this analysis, there were 482 (61.3%) cases of sexual assault, 322 (41.0%) of physical assault, and 726 (92.4%) occurred among women. In 2018, 367 patients were seen and 145 (39.51%) attended a follow-up. In 2021, 419 patients were seen and 219 (52.27%) attended follow-up. In 2021, there were 114 (27.2%) who attended a virtual follow-up appointment. After adjusting for the type of assault (sexual and/or physical assault), follow-up increased in 2021 vs 2018 (ARR: 1.28, 95% CI:1.11-1.49). Qualitative narratives among 9 survivors who attended virtual follow-up revealed that virtual care was acceptable, more convenient, and many preferred being in their own safe space. Barriers included lack of privacy and lack of safety if they lived with the perpetrator.

**Conclusion:** This study documented a 12% increase in follow-up appointments following the introduction of virtual care. Under safe and appropriate circumstances, virtual care is an innovative way to provide trauma-informed care for survivors of sexual assault and IPV.

**The cumulative effects of cyber aggression and bullying on depression in a sample of middle school smartphone users** Andrew Ryan\* Andrew Ryan Marizen Ramirez

**Introduction:** Violent experiences can accumulate and have long-term impacts, but little is known about the effects of cyberaggression exposure in youth who may or may not have experienced violence in other spaces like the neighborhood or school. We examined if weekly cyberaggression exposure affect depression levels in middle school youth with and without previous bullying victimization.

**Methods:** Students from two Iowa middle schools filled out a baseline survey in fall 2014 that included questions on phone use, bullying victimization during the two months before baseline, and a modified version of the Center for Epidemiologic Studies Depression Scale (CESD). A follow-up survey was administered in late spring 2015. During follow-up from January through May 2015, students with smartphones were asked to participate in weekly Ecologic Momentary Assessments of cyberaggression. Generalized linear models with Gamma distribution provided estimates of the difference in baseline to follow-up changes in mean CESD score between those who did and those who did not report cyberaggression.

**Results:** A total of 167 students completed a baseline or follow-up survey. Among the 66 students who responded to at least one weekly cyberaggression survey, 24 (36%) reported no cyberaggression, 28 (42%) were victims and witnesses, 12 (18%) were witnesses only, and 2 (3%) were victims only. The median CESD score at baseline and follow-up was 18. Among students who were bullied before the baseline survey, the proportional increase in the CESD from baseline to follow-up was 42% greater among those who witnessed and were victims of cyberaggression compared to those with no cyberaggression experience. A similar effect was not observed among those who were not previously bullied.

**Conclusion:** The increased sensitivity to cyberaggression among those with previous bullying victimization suggests a cumulative effect of bullying and cyberaggression exposure on depression symptoms.

**LATEBREAKER**

Injuries/Violence

**The use of Extreme Risk Protection Orders to prevent violence in Oregon: Preliminary evidence** Shauna Rakshe\* Shauna Rakshe Kathryn Freeman Susan DeFrancesco Kathleen Carlson

Extreme Risk Protection Order (ERPO) laws have received increasing attention as a tool to prevent firearm suicide and homicide, including mass shootings. However, ERPO usage is little understood. We abstracted data from all ERPO petitions filed in Oregon, from implementation of the ERPO law in January 2018 through December 2022 (n=650), using the Oregon Judicial Case Information Network database. ERPO petitions were filed in 29 of 36 counties (80.6%, range 0-106 per county), against respondents 17-96 years of age (median: 38). Of ERPOs filed, 78.3% were initially granted. While only 16.2% of respondents in initially-granted ERPOs requested a hearing, when a hearing was held, nearly half (48.4%) of ERPOs were dismissed. The majority of ERPO petitions were motivated by threat of harm to both respondent and others (n=327, 50.3%), followed by threat of harm to others-only (n=219, 33.7%) or respondent-only (n=81, 12.5%). During the 5-year period, 72 (11.1%) ERPO petitions cited threats of mass violence as a motivating factor, including 39 (6.0%) petitions citing threats to schools or college campuses. ERPOs filed by law enforcement officers were more often granted than those filed by family/household members (95.9% vs 71.4%) or by intimate partners (39.1%). ERPOs were slightly more likely to be granted when filed for threats of mass violence (93.2%) than for threats of harm to both respondent and others (81.0%), to others-only (73.1%), or to respondent-only (88.9%). Further analyses will examine contextual factors related to ERPO petitions and their outcomes, at both the individual- and community-levels. Preliminary findings to date suggest that ERPOs are being used in Oregon to prevent self-harm, assault, and mass violence, but that the public may need assistance in engaging effectively with the ERPO process.



**The risk of depression after the cardiovascular event of spouse: A nationwide study in Japan** Toshiaki Komura\* Toshiaki Komura Kosuke Inoue

**Background:** The association between cardiovascular disease (CVD) and depression is well established. However, there's limited evidence about whether and the extent to which the spouse's CVD affects the partner's mental health.

**Methods:** We conducted a nationwide cohort analysis including pairs of married couples aged 20 years or older from a claim database of the Japan Health Insurance Association between 2015 and 2021. ICD-10 codes were used to identify the onset of composite CVD (stroke, heart failure, and myocardial infarction) and depression between 2016 and 2021. Subjects whose spouse experienced incident CVD were matched to controls whose spouse did not experience CVD based on age, sex, income, and the onset date of spouses' CVD. Multivariable Cox proportional hazard models were applied to investigate the association between spouses' CVD and subjects' depression in the following period adjusting for comorbidities of subjects and spouses.

**Results:** Among 141,912 matched pairs of married couples (mean age, 59.11), the onset of a spouse's CVD between 2016 and 2021 was observed among 70,956 pairs (50%) and the partner's depression was observed among 2,487 pairs (1.75%). A spouses' CVD was associated with the subjects' depression (adjusted HR [95% CI] = 1.10 [1.01 to 1.19]). Particularly, subjects with previous history of CVD showed increased hazard ratios of depression after their spouse's CVD (adjusted HR [95% CI] = 1.95 [1.50 to 2.52]) while those without the previous history of CVD did not show the association.

**Conclusion:** The spouses' onset of CVD was associated with the increased risk of the subjects' depression. Our findings indicate that comprehensive mental care is needed for family members of CVD patients, such as cross-field collaboration of cardiologists and psychiatrists and expansion of supportive tools for caregivers.

**Religious activity and psychological distress among college students in East China: a longitudinal causal mediation analysis** Stephen Pan\* Stephen Pan Brian J. Hall Wanqi Wang

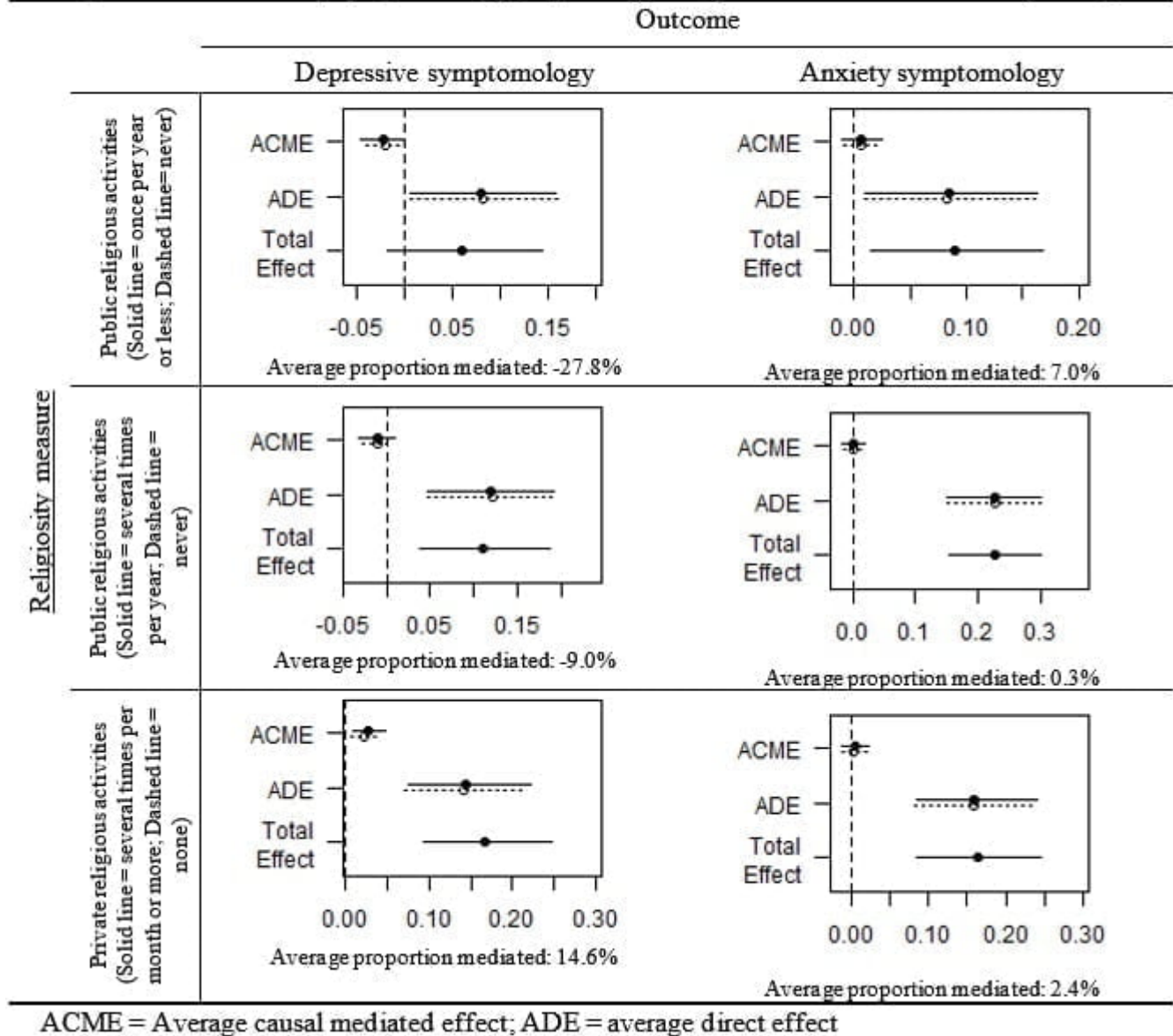
**Background:** Longitudinal research of religious activities and psychological distress in China is extremely limited. We conducted a four-wave cohort study with Chinese college students, a population vulnerable to psychological distress. The aims were to examine associations between religious activity and psychological distress, and potential mediation by social support.

**Methods:** In 2020, 806 first-year college students  $\geq 18$  years old in Suzhou, China completed a baseline online survey (t0). Follow-up surveys were administered at 4 months [t1], 8 months [t2], and 12 months [t3]. Psychological distress was measured by depressive and anxiety symptom severity using the Patient Health Questionnaire-4. Public and private religious activity (of any religious faith tradition) was measured with the Duke University Religiosity Index. To address missing data, we used multiple imputation with 100 imputed datasets. Generalized estimating equations were used to assess associations between religious activity [t1; t2] and depressive and anxious symptomologies [t2; t3]. Causal mediation analysis was used to assess effects of religious activity [t1] on depressive and anxious symptomologies [t3], via indirect effects of putative mediators [t2]. Baseline control covariates included depressive and anxious symptomologies [t0] and frequency of religious activities during childhood and at baseline[t0], among other measures.

**Results:** Engaging in private religious activities (several times per month vs none) was significantly associated with depression (AOR: 2.46, 95% CI: 1.03 - 5.86; E-value: 4.36) and anxiety (AOR: 3.16, 95% CI: 1.36 - 7.33; E-value: 5.77). Social support mediated 14.6% of the association between private religiosity and depression.

**Conclusion:** Private religious activities may increase incidence of depressive and anxious symptomology among freshman college students in China. Social support may be mediating associations between private religiosity and depressive symptomology.

**Figure: Causal mediation analysis of social support as putative mediator [t2] for religiosity [t1] on depressive and anxiety symptomology [t3] among college students in East China (n=806)**



**Assessing Trends in Internalizing Symptoms among Marginalized Racial and Ethnic Adolescents: Results from the Monitoring the Future Survey 2005-2020** Navdep Kaur\*  
Navvdep Kaur Paris B. Adkins-Jackson Victoria Joseph Mia Campbell Katherine M. Keyes

## **Introduction**

Depressive symptoms have rapidly accelerated among recent US birth cohorts progressing throughout adolescence, yet there remains little understanding of trends among racialized and minoritized groups. Depressive symptoms are the most prevalent health conditions among adolescents, and racialized and minoritized groups may experience depressive symptoms due to the deleterious effects of structural racism. We examine all racialized groups using within-group analyses to observe trends in high depressive symptoms across cohorts.

## **Methods**

2005-2020 Monitoring the Future survey data, a nationally representative and annual cross-sectional survey of students in 8<sup>th</sup>, 10<sup>th</sup>, and 12<sup>th</sup> grade (n=613,513). Using a composite of four depression items (dichotomized at the 75<sup>th</sup> percentile), we model high depressive symptoms by age group and additive interaction between birth cohort and race/ethnicity.

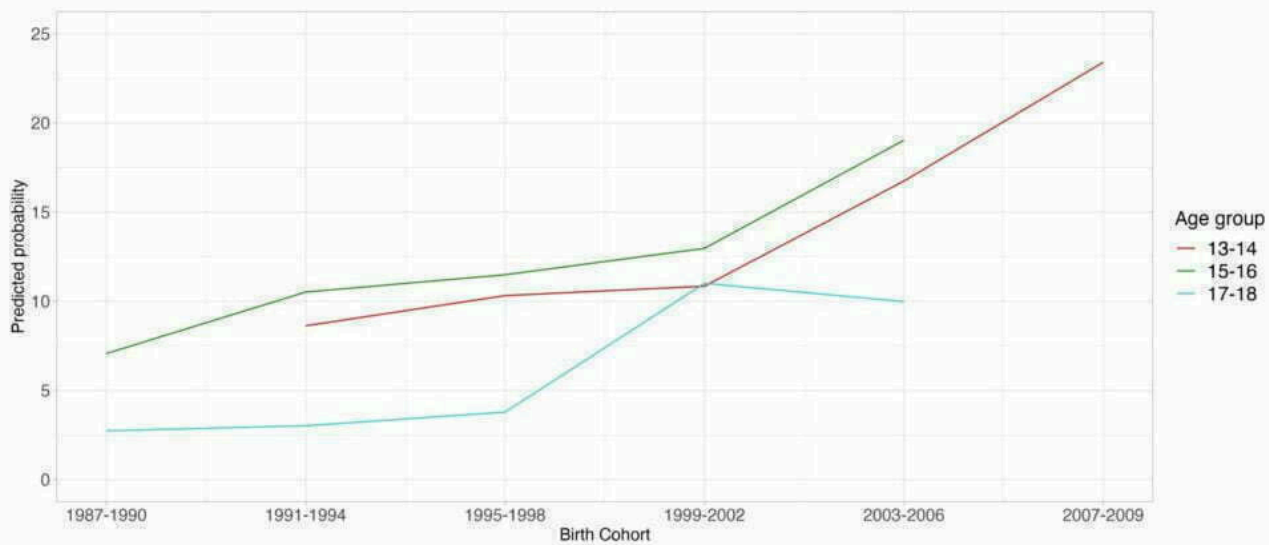
## **Results**

Overall, high depressive symptoms increased from 6.50% to 14.31% across the study period, with increases driven by cohort effects. Cohorts effects were particularly concentrated among adolescents racialized as Indigenous and Hispanic White. Among Indigenous adolescents, the 2003-2006 birth cohort had higher increases in depressive symptoms compared to other groups born in those years (interaction beta: 0.027, 95% C.I. 0.012-0.024). A similar magnitude of excess increase was observed for Hispanic white adolescents born 2003-2006 (interaction beta: 0.025, 95% C.I. 0.011-0.039).

## **Conclusion**

Depressive symptoms are increasing among US adolescents by birth cohort, with concentrated increases among Indigenous and Hispanic adolescents. Public health efforts to reduce disparities may consider barriers such as structural racism that may disproportionately impact the mental health of racialized and minoritized adolescents while reducing access to culturally competent mental health providers and school-based mental health services.

Figure 1. Predicted probability of experiencing depressive symptoms among Indigenous students in the Monitoring the Future Study (2005-2020), by birth cohort and age



**Sex Differences in Psychopathology Following Traumatic Experiences in a Danish Population-Based Cohort** Sophie Selbe\* Sophie Selbe Jamie L. Gradus Yasmin Barrientos Kofman Jennifer Sumner Peter Szentkúti Timothy L. Lash Sandro Galea Henrik Toft Sørensen

**Background:** Research on posttraumatic psychopathology has focused primarily on posttraumatic stress disorder (PTSD). Women are more likely to be diagnosed with PTSD than men, but sex differences in other forms of posttraumatic psychopathology are less well examined. This study examined the sex-specific incidence of psychopathology within 5 years of experiencing a potentially traumatic event (PTE) using data from the population of Denmark.

**Methods:** Our study included a cohort of 1,398,026 individuals who had experienced PTE and a comparison cohort of 420,544 individuals who had experienced a non-traumatic stressor. Using data from the Danish electronic health registries, we calculated the 5-year incidence of nine categories of ICD-10 psychiatric disorders and standardized morbidity ratios (SMR) comparing the trauma cohort to the stressor cohort with regard to psychopathology outcomes.

**Results:** Following PTE, the most common diagnosis for men was substance use disorder (7.4%), while for women it was depression (3.2%). Among interpersonal PTE (i.e., physical assault, pregnancy-related trauma, suicide of family member, multiple traumas), men had the strongest association between physical assault and schizophrenia/ psychotic disorders (SMR=18, 95% CI=16, 19) while for women, the strongest association was between physical assault and personality disorders (SMR=16, 95% CI=15, 18). Among noninterpersonal PTE (i.e., fire or explosion, transport accident, exposure to toxic substance/medical complications, traumatic brain injury), the strongest associations were between exposure to toxic substances/medical complications and personality disorders for men (SMR=20, 95% CI=19, 21) and for women (SMR=21, 95% CI=20, 21).

**Conclusion:** Sex differences in posttraumatic psychopathology other than PTSD may not be as pronounced as what has been shown among persons with PTSD. Additional results that highlight the few disorders for which sex differences were found will be presented.

**Longitudinal trends in mental wellbeing among multiracial/ethnic adults in the U.S.** Sarah Forthal\* Sarah Forthal Seth Prins

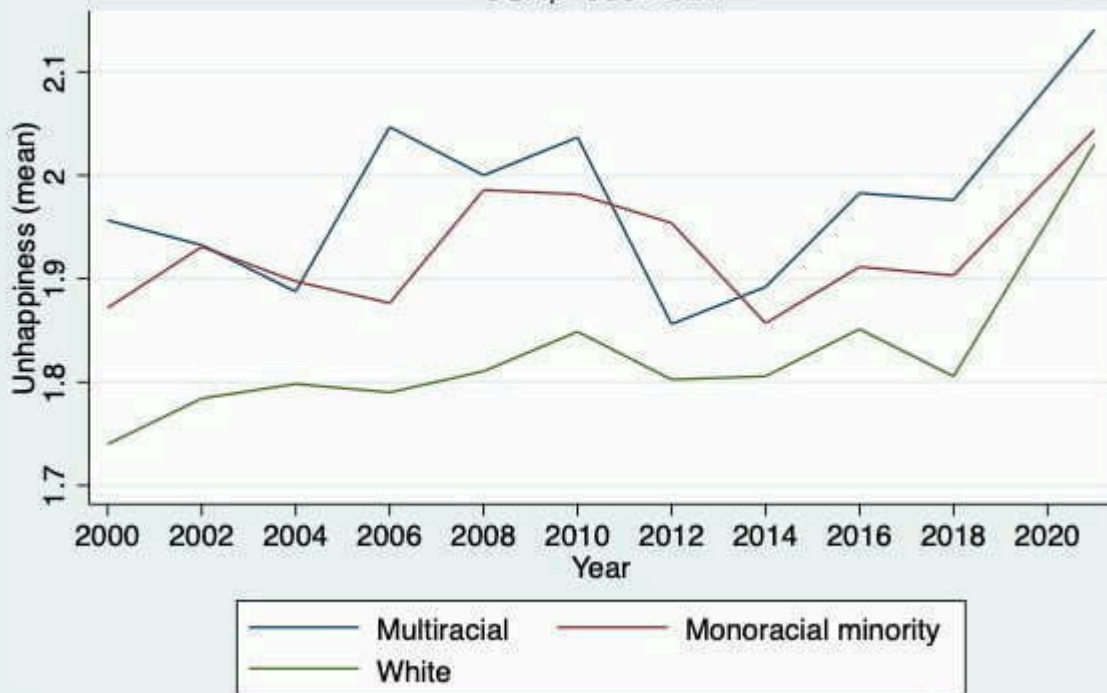
**Introduction:** Public health has increasingly acknowledged its responsibility to address long-standing racial and ethnic mental health disparities in the U.S. However, these efforts have largely overlooked the fast-growing multiracial/ethnic population, who may experience the consequences of a racialized society uniquely.

**Methods:** Using repeated cross-sections from the U.S. nationally representative General Social Survey, we compared trends in mean self-reported unhappiness and days of poor mental health between multiracial/ethnic, monoracial/ethnic minority, and monoracial white adults (minimum N=1,974; maximum N=4,510). Both measures were collected biennially: unhappiness from 2000-2021 and days of poor mental health from 2002-2006 and 2010-2018. Participants were classified as multiracial/ethnic if they self-identified as more than one racial/ethnic category and monoracial/ethnic if they self-identified as one racial/ethnic category.

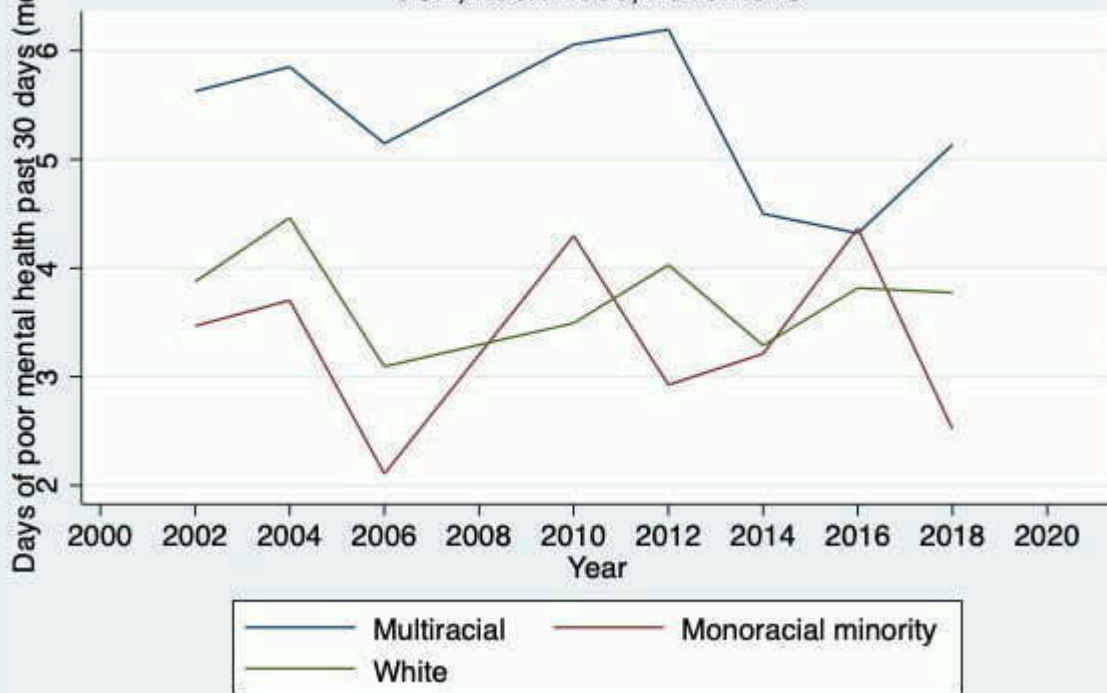
**Results:** Multiracial/ethnic adults comprised 5% of the sample in 2000; this grew to 9% in 2016 but decreased to 7% in 2021. Multiracial/ethnic adults had consistently elevated days of poor mental health compared to monoracial/ethnic minority and white adults (except 2016, when levels were equivalent for multiracial/ethnic and monoracial/ethnic minority adults). Until 2014, multiracial/ethnic adults reported similar unhappiness levels to monoracial/ethnic minority adults but higher than monoracial white adults. However, a gap between multiracial/ethnic and monoracial/ethnic minority adults appeared to emerge in 2016, with multiracial/ethnic adults reporting increasingly more unhappiness until 2021.

**Conclusions:** Multiracial/ethnic adults in the U.S. may have unique mental health needs that are not adequately appreciated by current research agendas. Efforts to study and reduce disparities should give greater attention to this population.

Unhappiness among multiracial and monoracial adults  
USA, 2000-2021



Poor mental health among multiracial and monoracial adults  
USA, 2002-2006, 2010-2018





## **The Mediating Role of Racism on the Longitudinal Relationship Between Ethnicity and Mental Health** Kishan Patel\* Kishan Patel

**Background:** The relatively poor mental health of minority ethnic groups in the UK is well documented, but the ethnicity gap has been shown to widen throughout the life-course. Therefore, the differing life experiences of ethnic minority young people and their white counterparts have been identified as a contributing factor of the worsening of ethnic minority mental health. One such factor is exposure to racial discrimination, whether experienced first-hand (primary), or second-hand (vicariously). This study aims to fill a current research gap by linking three datasets and quantifying the longitudinal impacts of primary and vicarious racial discrimination on the mental health of ethnic minority people in UK households.

**Methods:** Data was drawn from the Understanding Society longitudinal study, comprising of the core, ethnic minority boost, and family matrix datasets. The analytic sample comprised of all ethnic minority participants with information at baseline, and at least one measure of high psychological distress across the follow-up period (n=9945; 53.4% female). Initial descriptive analyses were conducted to provide an overview of the sociodemographic characteristics of the analytic sample, including household size, history of migration, and numbers of family members within and outside the household. Mediation analyses were employed to quantify the extent to which experiences of primary and vicarious racism alter the longitudinal relationship between ethnic minority status and changes in mental health. Further analyses focussed on sub-types of racial discrimination experienced, and sensitivity analyses restricted models to incidences of racial discrimination identified as severe, and further cases of repeated discrimination.

**Findings:** Early findings indicate an increased worsening of mental health over time for persons who had experiences of either primary or vicarious racism.

**Psychological distress modifies the association between household financial constraints and perceived posttraumatic growth: Evidence from the COVID-19 Southern Cities Study**

Emily Goldmann\* Emily Goldmann Nadim Akter Kabeer Majhu Izzah Nazir Daniel Hagen

Posttraumatic growth - positive psychological change that may follow disaster and other potentially traumatic event experience - has been documented during the COVID-19 pandemic. However, few studies have examined the impact of concomitant stressors on perceived posttraumatic growth (PPTG), and the role of psychological distress on this relationship. Data came from the COVID-19 Southern Cities Study, a probability-based survey of adult residents of five metropolitan statistical areas (MSA) in the U.S. South collected May-June 2020 (n=1,727). Five variables representing domains of PPTG (strengthened relationships, created new possibilities, helped identify personal strengths, created spiritual change, increased appreciation of life) were assessed for the prior two weeks using the sum score of the Complementary and Integrative Research Lab Pandemic Impact Questionnaire (C-PIQ), with item response options ranging from 1 (not at all) to 5 (extremely). Household financial constraint was present if there was "fairly" or "very often" not enough money in the household for rent/mortgage, food, utilities, transportation, or healthcare in the past 30 days. Past-week psychological distress was indicated where Patient Health Questionnaire (PHQ)-4 score  $\geq 6$ . Mean PPTG score was 11.9 ( $SE=0.2$ , range 5-25), with 29.5% reporting a constraint and 21.0% experiencing distress. In linear regression models accounting for complex survey design, adjusted for age, gender, race/ethnicity, marital status, education, and MSA, experiencing a constraint was associated with greater PPTG ( $B=2.1$ ,  $SE=0.5$ ,  $p<0.001$ ). In stratified models, this association was present among those with distress ( $B=4.4$ ,  $SE=0.8$ ,  $p<0.001$ ) but not those without distress ( $B=1.0$ ,  $SE=0.6$ ,  $p=0.082$ ). PPTG may reflect an approach to coping with distress related to stressors, rather than a positive outcome on its own. Additional research is needed to understand long-term effects of PPTG on functioning and well-being.

**Suicide rates before and during the COVID-19 pandemic: a systematic review and meta-analysis** Ana Paula da Cunha Varella\* Ana Paula da Cunha Varella Eve Griffin Zubair Kabir*Objectives*

Although there is extensive research on the effects of the pandemic on mental health issues such as depression and anxiety, the influence on the incidence of suicide is still not comprehensively addressed. Moreover, the current literature suggests divergent results. Therefore, we aimed to thoroughly synthesize evidence of the impact of the COVID-19 pandemic on suicide rates worldwide.

*Methods*

A systematic review and meta-analysis were performed, following a detailed search strategy and predefined eligibility criteria. Quality appraisal and risk of bias were assessed through a Joanna Briggs Institute tool; certainty of estimates was assessed using the GRADE tool. Pooled proportions of suicide rates using a random-effect model for two time-periods (pre and during COVID-19 pandemic) were estimated. We defined “during pandemic” as any calendar period from the onset of the COVID-19 pandemic, whether few months or full year, and the “pre-pandemic” period as any calendar period 10 years before the COVID-19 pandemic. Differences in rates were formally tested using a heterogeneity test. A-priori subgroup analyses (by gender and WHO region) and publication bias were assessed.

*Results*

A total of 34 studies were included in the review capturing suicide data from over 40 countries and regions. The meta-analysis outputs did not indicate a significant change in suicide rates during the COVID-19 pandemic. The pooled suicide rate in pre-pandemic period was 11.38(95% CI 9.35-13.42) and in the period during the pandemic was 10.65(95% CI 8.61-12.68). Stability in suicide rates across gender and WHO-specific regions was observed.

*Discussion*

No significant change in suicide rates was observed during the COVID pandemic from a global perspective. A longer follow-up can provide different explanations on suicide trends globally. Improvements in data reporting, specifically with implementation of real-time surveillance, are imperative to provide adequate suicide prevention and support.

**Advances in telehealth in outpatient mental health treatment settings: Faster growth in urban US states, 2014-2020** George Pro\* George Pro Brian Fairman Don Willis Jure Baloh Brooke EE Montgomery

### Introduction

Mental health treatment utilization is low, and progress in promoting treatment uptake has been slow. Telehealth promises to increase mental health treatment use. Much of the national discourse has focused predominately on rural behavioral health systems, but urban residents may also benefit from telehealth access. Better understanding the pace of telehealth adoption in more urban states may inform resource allocation and intervention design. This national study investigated changes in telehealth in mental health treatment facilities, and how changing rates varied by state rurality.

### Methods

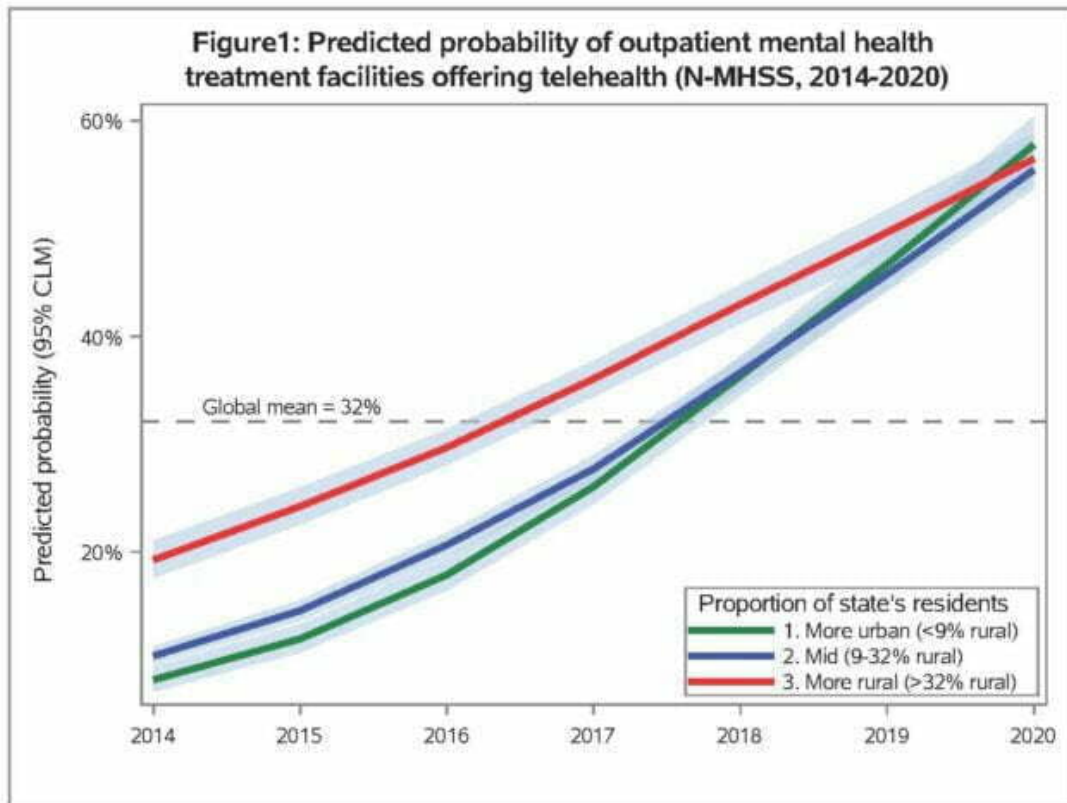
We used data from the US National Mental Health Services Survey (2014-2020) to identify outpatient treatment facilities (n~4,500 per year) offering telehealth. We used logistic regression to model if telehealth availability was associated with time, adjusting for facility-level covariates. We defined state rurality as low/mid/high based on the national mean +/- one standard deviation. We further explored the interaction between time and rurality and predicted the probability of telehealth availability based on our model.

### Results

A third (32%) of outpatient facilities offered telehealth which increased each year (OR=1.34, 95% CI=1.30-1.37). States with larger urban populations experienced the fastest increase in offering telehealth. More rural states had the highest probability of offering telehealth from 2014-2018, but more urban states outpaced them by 2020 (58% for <9% rural; 55% for 9-32% rural; 56% for >32% rural) (Figure 1).

### Discussion

Telehealth is growing across the US, but faster in urban than in rural states. While the need for behavioral health system strengthening in rural areas remains, urban residents in need of mental health services also face barriers and may benefit from a wider range of treatment modalities. The value and prospects of telehealth extend beyond any single geographic area.



**Neighborhood deprivation and mental health indicators among GuLF Study participants**

Sam J. Neally\* Sam Neally Kaitlyn G. Lawrence Emily J. Werder Braxton Jackson II Kate Christenbury Lawrence S. Engel Dale P. Sandler

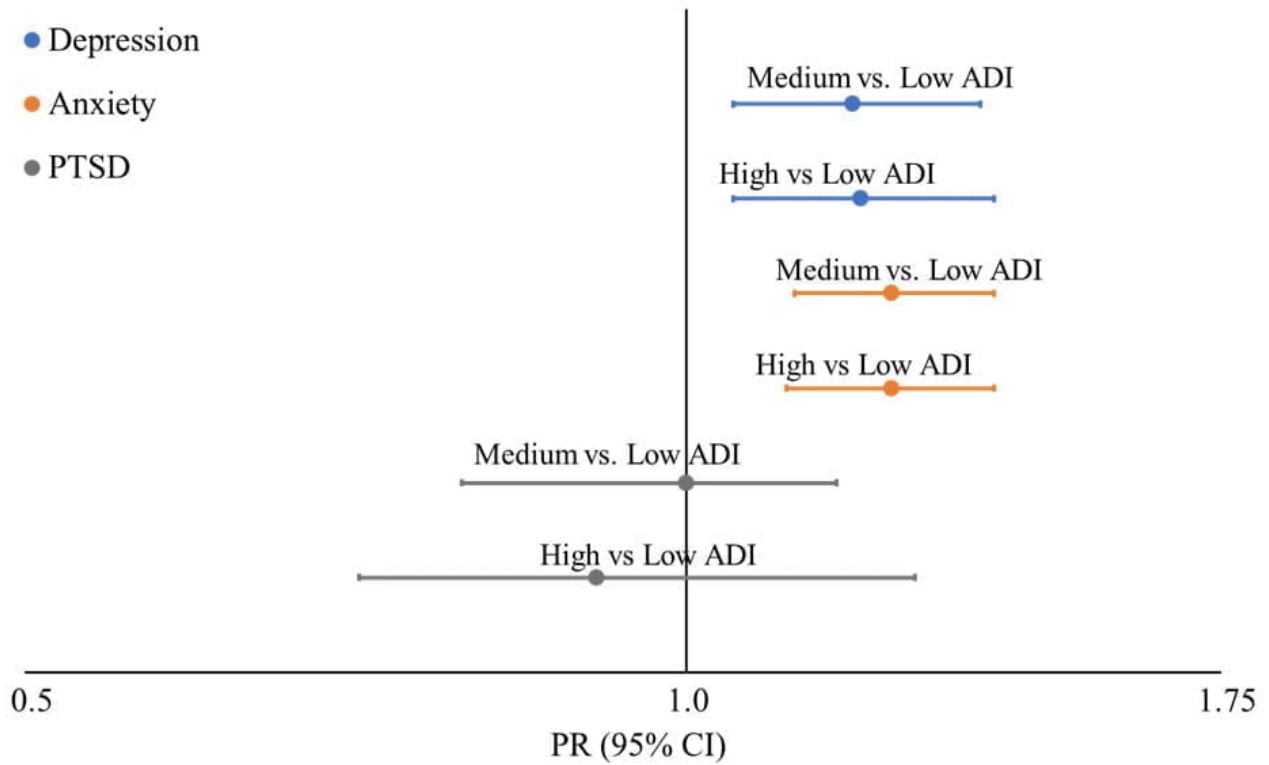
**Background:** Neighborhood socioeconomic position (NSEP) is associated with poor mental health (MH). However, few studies have assessed NSEP in relation to multiple MH dimensions.

**Aim:** We examined associations of NSEP with depression, anxiety, and PTSD among adults living in US Gulf Coast states.

**Methods:** The Gulf Long-Term Follow-up (GuLF) Study (2011-2013) is a prospective cohort study of oil spill cleanup workers and nonworkers following the 2010 *Deepwater Horizon* disaster (N=32,608). At enrollment participants reported sociodemographic, health, and lifestyle information. 11,193 participants living in 5 Gulf States (44% of eligible) completed a home visit including standardized psychosocial questionnaires. We analyzed data from 9,055 participants with complete information on MH and covariates. NSEP was measured at the census block group level using the 2013 Area Deprivation Index (ADI). ADI national percentiles (1-100, with 1 = least deprivation) were linked to participant residences and categorized as low (<50<sup>th</sup>), medium (50<sup>th</sup>-<75<sup>th</sup>), and high (≥75<sup>th</sup>). Depression was measured with the Patient Health Questionnaire-9 (PHQ-9, ≥10), anxiety with the Generalized Anxiety Disorder Questionnaire-7 (GAD-7, ≥10), and PTSD with the Primary Care PTSD Screen for DSM-5 (PC-PTSD-5, ≥3). Multivariable log binomial regression estimated PR and 95% CI for associations between ADI and MH outcomes, adjusted for demographic, individual-level SES, and oil spill cleanup employment factors.

**Results:** Compared to low ADI, higher ADI was associated with greater depression (PR<sub>med</sub>:1.19, CI=1.05-1.36; PR<sub>high</sub>:1.20, CI:1.05-1.38) and anxiety (PR<sub>med</sub>:1.24, CI:1.12-1.38; PR<sub>high</sub>:1.24, CI:1.11-1.38). ADI was not associated with PTSD (PR<sub>med</sub>: 1.02, CI=0.81-1.28; PR<sub>high</sub>: 0.96, CI=0.75-1.21).

**Conclusions:** NSEP contributes independently to depression and anxiety even after accounting for individual SEP characteristics.



**Figure 1. Effects of high and medium compared to low neighborhood socioeconomic deprivation on prevalence of mental health outcomes, adjusting for individual confounders<sup>1</sup>**

<sup>1</sup>Age, gender, race, ethnicity, marital status, income, education, oil spill cleanup employment

**Video Game and Social Media Use and Mental Health Outcomes during the COVID-19****Pandemic** Phillip Hegeman\* Phillip Hegeman Sherine El-Toukhy

**Introduction:** We examined the associations between social media and video game use and mental health outcomes during the COVID-19 pandemic.

**Methods:** Data came from a non-nationally representative survey of US adults ( $N=5559$ ) in 2022. Adjusting for demographics, we ran linear regression models of hours/day of gaming and social media use onto three standardized outcomes: depression, social isolation, and stress. We also ran logistic regression models of binary outcomes for depression and social isolation (i.e., moderate/severe vs. mild/within normal limits, defined as scoring greater vs. less than 1 SD above the general population mean, respectively).

**Results:** Daily gaming and social media hours were positively associated with depression ( $\beta_{\text{gaming}}=0.015$ ,  $\beta_{\text{social media}}=0.015$ ) and stress ( $\beta_{\text{gaming}}=0.009$ ,  $\beta_{\text{social media}}=0.009$ ), while social isolation was only associated with social media ( $\beta=0.009$ ). Daily gaming (OR=1.025 per one hour of use) and social media (OR=1.030) hours were positively associated with moderate/severe depression, and social media hours were significantly associated with moderate/severe social isolation (OR=1.025). Compared to non-users of social media, those who reported using social media >8 hours per day (11.89% of the sample) had >27% increase in the odds of scoring in the moderate-to-severe depression range.

**Conclusions:** Time spent on digital platforms was associated with adverse mental health outcomes during the COVID-19 pandemic. Associations differed by digital platform, where social media hours, but not gaming, were significantly associated with social isolation. The magnitudes of associations were small, but increases in adverse outcomes with each additional hour were noteworthy for heavy users. Despite the social underpinnings of gaming and social media platforms that might have heightened their use during the COVID-19 pandemic, their adverse associations with mental health outcomes warrant consideration during public health crises and beyond.



**Associations Between Feelings of Sadness and Current Binge Drinking Among Youth Using the Youth Risk Behavior Survey (2017, 2019, 2021)** Elena Penedo\* Elena Penedo Vanora

Binge drinking can lead to several acute and long-term negative outcomes including alcohol poisoning, motor vehicle accidents and injury, and altered neurological development among adolescents. Substance use and mental health are both complex issues that can coexist in adolescent populations. We aim to assess the association between reported feelings of sadness and current binge drinking among a representative sample of youth in Texas. We pooled data from the 2017, 2019, and 2021 Texas Youth Risk Behavior Survey and restricted to students that answered “Yes” or “No” to the question “During the past 12 months, did you ever feel so sad or hopeless almost every day or for two weeks or more in a row that you stopped doing some usual activities?”. We used weighted logistic regression analysis to assess the association between feelings of sadness and current binge drinking, adjusting for age, sex, grade in school, and race/ethnicity. Overall, 39.1% of students reported feelings of sadness, with 65.5% being female and 34.5% male. The percentage of binge drinking overall was 11.9%, with 54.8% being female and 45.2% male. Among those that reported current binge drinking, 36.7% were in 12th grade, 26.5% in 10th grade, 23.1% in 11th grade, and 13.7% in 9th grade. Compared to those who answered “No”, participants that reported “Yes” to feelings of sadness (AOR: 2.38, 95% CI: 1.95, 2.91) were more likely to report current binge drinking. Compared to non-Hispanic Whites, non-Hispanic Blacks (AOR: 0.28, 95% CI: 0.16, 0.5), Hispanics (AOR: 0.62, 95% CI: 0.47, 0.81), and non-Hispanic other (AOR: 0.42, 95% CI: 0.22, 0.77) were less likely to report binge drinking. Findings highlight the importance of policies and interventions that promote mental health to help mitigate adverse substance use related outcomes among adolescents. Further investigation is necessary to better understand the intricate relationship between mental health and alcohol use disorders, such as binge drinking in adolescents.

**Mediating role of social capital in the relationship of social contacts and happiness in Taiwan: A comparative cross-sectional study between 1997 and 2017** Wu, Yun-Hsuan\* Yun-Hsuan Wu Yang, Yun-Chieh Tsai, Meng-Han

**Introduction:**

Previous evidence showed that social contacts and social capital were associated with happiness, which plays a part in achieving mental health. However, it is unclear whether social capital could mediate the relationship between social contacts and happiness and whether the underlying mechanism would change over 20 years based on the rapidly changing society in Taiwan.

**Method:**

Data from the 1997 (n=2,678) and 2017 (n=1,726) Taiwan Social Change Survey (TSCS) were utilized. The happiness score was our outcome of interest and the exposure of interest was the number of daily social contacts. Three standardized measures of position generator (extensity, upper reachability, and range) were used to measure social capital as the mediator. Structural equation models (SEM) were performed to assess the mediating role of social capital on the association between social contacts and happiness.

**Results:**

Happiness score was significantly lower in 2017 comparing to 1997 (p-value<0.001). We found that the direct effect of social capital on happiness was continuously significant across 20 years (1997:  $\beta = 0.003$ , p-value=0.01; 2017:  $\beta = 0.05$ , p-value <0.001). In 1997, social contacts had not only the direct effect ( $\beta = 0.03$ , p-value <0.001) but also the indirect effect ( $\beta = 0.004$ , p-value=0.01) on happiness. However, social contacts only had the indirect effect on happiness ( $\beta = 0.006$ , p-value=0.01) in 2017. Nevertheless, the total effect of social contacts on happiness through social capital was significant in both 1997 and 2017.

**Conclusion:**

Social capital plays an important mediating role in the relationship between social contacts and happiness, and it has the positive effects of social contacts on happiness among Taiwanese. Further the potential mechanism between social contacts, social capital and happiness may change over time. Maintaining social contacts and expanding social capital have potential beneficial to mental health.

**LATEBREAKER**

Mental Health

**Increased Incidence of Breast Cancer in Women Patients with Schizophrenia: Data of 959,008 Women from the Korea National Health Insurance Service** Ji Su Yang\* Ji Su Yang

**Objective:** This study aimed to evaluate the risk of breast cancer in schizophrenia patients compared with controls from other psychiatric patients and the general population. Also, we explored the association between the duration of antipsychotic use and breast cancer development in schizophrenia patients.

**Methods:** We utilized the medical claim data of women aged 18 to 80 in the Korean national health information database from 2007 to 2018. The schizophrenia cases (ICD code F20 or F25 with antipsychotics prescription) were compared with 1) women with other psychiatric diseases (F10-F19, F30-F69) (control 1) and 2) the general population groups (control 2), matched by index date (date of the first diagnosis of schizophrenia) and age at the index date at a ratio of 1:1:2 (cases=239,752; control 1=239,752; control 2=479,504). Cox proportional hazard model was used to estimate the hazard ratio of breast cancer, adjusting for insurance premiums and medical comorbidities. In addition, the association between the duration of antipsychotic use and the incidence of breast cancer was assessed with landmark analysis in schizophrenia cases.

**Results:** The hazard rate of breast cancer was 1.23 times higher in the schizophrenic group than in the general population (95% CI 1.17-1.30, p value<.0001) even after adjusting for medical comorbidity and insurance level. In comparison with the psychiatric patient group, the HR was 1.10 (95% CI: 1.04-1.28, p value<.001). As a result of stratification by the age at first diagnosis of schizophrenia, only patients diagnosed with schizophrenia at the ages from 40 to 65 showed a statistically significant increased hazard ratio of breast cancer. (HR=1.33, 95% CI [1.24-1.43], p value<.0001). In patients with schizophrenia, the risk of breast cancer was significantly increased in those who took antipsychotics for 1 year or more than in those who took antipsychotics for less than 6 months after full adjustment (1-3 years: HR=1.57, 95% CI [1.28-1.93]; 3-4 years: HR=1.84, 95% CI [1.49-2.28]; ≥4 years: HR=1.70, 95% CI [1.40-2.07]).

**Conclusion:** Patients with schizophrenia have a significantly higher risk of breast cancer compared to patients with other psychiatric disorders or the general population, and this association is prominent in middle-aged women. Among schizophrenia patients, long-term use of antipsychotics seems to increase the risk of breast cancer.

**LATEBREAKER**

Mental Health

**Longitudinal association between types of peri-traumatic responses and subsequent mental health in South Korean patients with COVID-19: Real-world data from the public mental health service** Hyejin Kim\* Hyejin Kim Dongkyu Lee Minyoung Sim Sun Jae Jung

**Background:** A number of studies have reported the long-term psychiatric sequelae of COVID-19. Peri-traumatic responses that COVID-19 patients exhibit following diagnosis may be linked to subsequent mental health, but empirical evidence is lacking. Here, we aim to assess the global trajectory of mental health in clients with COVID-19 throughout counseling sessions, as well as identify the association between severity and types of peri-traumatic responses to COVID-19 and global mental health over time.

**Methods:** We analyzed real-world data of 515 COVID-19 patients in South Korea who received public telecounseling from the Korean National Center for Disaster Trauma. A therapist evaluated peri-traumatic responses following COVID-19 diagnosis and its four subtypes (cognitive, emotional, behavioral and physiological responses) before intervention was initiated. Every counseling session, the Clinical Global Impression Severity Scale (CGI-S) was used by the therapist to assess the client's global mental health. Using longitudinal linear mixed models, we estimated whether the severity and types of peri-traumatic responses affect subsequent mental health throughout counseling sessions. Sex stratification was also conducted.

**Results:** The trajectory of CGI-S scores during counseling was heterogeneous by individual, but scores decreased globally over time. Peri-traumatic responses ( $\beta = 0.05$  [95% CI: 0.04 to 0.07]) and prior psychiatric disorders ( $\beta = 0.40$  [0.23 to 0.58]) were positively associated with subsequent CGI-S scores. Cognitive response was the strongest predictor of subsequent CGI-S scores (standardized  $\beta = 0.25$  [0.18 to 0.32]), followed closely by emotional response (standardized  $\beta = 0.24$  [0.17 to 0.32]). In women, these associations were highlighted, whereas in men, only emotional responses were linked to subsequent CGI-S scores.

**Conclusion:** Patients with COVID-19 who exhibit cognitive and emotional responses in the early stages of the disease may require more than brief telecounseling.

Table. Associations of the peri-traumatic response and its subtypes with CGI score among COVID-19 patients (Subject  $n = 515$ , Observation  $n = 2,219$ )

<i>Predictors</i>	Std. Beta	SE	95% CI	<i>p</i> value
<i>Total (subject n=515, observation n=2,219)</i>				
Sum score	0.317	0.036	0.246 - 0.388	<.0001
Emotional responses	0.243	0.038	0.169 - 0.317	<.0001
Cognitive responses	0.240	0.037	0.168 - 0.312	<.0001
Behavioral responses	0.174	0.035	0.105 - 0.244	<.0001
Physical responses	0.156	0.037	0.084 - 0.229	<.0001
<i>Men (subject n=169, observation n=725)</i>				
Sum score	0.206	0.072	0.065 - 0.346	0.004
Emotional responses	0.224	0.065	0.096 - 0.353	0.001
Cognitive responses	0.064	0.067	-0.068 - 0.195	0.342
Behavioral responses	-0.038	0.061	-0.158 - 0.082	0.533
Physical responses	0.049	0.062	-0.073 - 0.171	0.428
<i>Women (subject n=346, observation n=1,494)</i>				
Sum score	0.381	0.045	0.293 - 0.470	<.0001
Emotional responses	0.259	0.047	0.168 - 0.351	<.0001
Cognitive responses	0.310	0.039	0.234 - 0.386	<.0001
Behavioral responses	0.212	0.043	0.129 - 0.296	<.0001
Physical responses	0.228	0.046	0.138 - 0.317	<.0001

For all analyses, a cluster-robust (sandwich) estimator was used for SE calculation to control for interfamilial correlation within the data. All continuous variables were standardized for comparison. The presented model adjusted for random effect of intercept and time along with fixed effect of intercept, time, counselor IDs (total  $n=35$ ), baseline year (2020, 2021 and 2022), gender, age group (over 50s vs. under 50s), living alone, residence (metropolitan city, local city and abroad), COVID-19 stage (acute, subacute and chronic phase), number of COVID-19 stressors, prior psychiatric disorders and prior physical illnesses.

Abbreviation: Std., standardized; SE, standard error; CGI, Clinical Global Impression Scale-Severity

**LATEBREAKER**

Methods/Statistics

**Identifying Comorbidity Patterns among Police Officers using medications: a Latent Class Analysis** JA GU\* JA GU Luenda E. Charles Desta Fekedulegn Samantha Service John M. Violanti

*Objective:* Police officers are exposed to high levels of occupational stress. Such exposure may lead to adverse physical and mental health outcomes resulting in the need for various medications. This study aims to identify comorbidity patterns among police officers based on their medication use.

*Methods:* Participants were 300 officers from the Buffalo Cardio-Metabolic Occupational Police Stress Study (2010-2014). We used Latent Class Analysis (LCA), a statistical method for finding classes of participants based on their behaviors, to describe the comorbidity patterns of our cohort. LCA was conducted on 11 commonly used medications. The number of comorbidity patterns was determined by comparing G-squared, Akaike Information Criterion (AIC), Bayesian Information Criterion (BIC), Consistent AIC, Adjusted BIC, and entropy statistics in LCA.

*Results:* The frequency of medication use taken by officers: hypertension (23.7%), hyperlipidemia (20.0%), arthritis (32.3%), diabetes (2.3%), depression (11.7%), anxiety (4.0%), sleep disorders (6.0%), allergies (7.3%), asthma (5.0%), antibiotics (4.3%), and NSAID (39.0%). With LCA, we identified five comorbidity patterns: 1) "Excellent health" (n=101, 33.7%) reporting no medication use, 2) "Good health" (n=44, 14.7%) with one medication (mostly anti-hypertensive), 3) "Moderate health" (n=54, 18.0%) with two medications (mostly lipid-lowering, anti-inflammatory, or arthritis), 4) "Fair health" (n=34, 11.3%) with two or three medications (mostly anti-hypertensive, lipid-lowering, or depression and anxiety), and 5) "Poor health" (n=67, 22.3%) with three or more medications (mostly anti-hypertensive, lipid-lowering, arthritis, or anti-inflammatory).

*Conclusion:* Our study identified five comorbidity patterns of officers with major medication groups. Medication use pattern can serve as a good indicator of an individual's comorbidity profile and may provide clinical direction for targeting health problems in this occupational group.

**LATEBREAKER**

Methods/Statistics

**A comparison of three area-level indices of neighborhood deprivation and socioeconomic status and their applicability to breast cancer mortality** Lauren E. Barber\* Lauren Barber  
Rebecca Nash Maret L. Maliniak Lauren E. McCullough

**Background:** Neighborhood deprivation and socioeconomic indices are widely used in public health. How they compare, especially in regards to health outcomes, is unclear. We estimated correlations between the Area Deprivation Index (ADI), neighborhood deprivation index (NDI), and Yost index, and compared their association with breast cancer mortality.

**Methods:** ADI, NDI, and Yost index were measured for Georgia census block groups using 2011-2015 data on indicators from six domains (Fig 1): poverty, income, occupation, housing, employment, and education. ADI was obtained from the Neighborhood Atlas. We used American Community Survey data and principal components analysis to create the NDI and Yost index. Pearson correlation coefficients were calculated overall for the three indices and for indicators within each domain. Indices were linked to 37,760 women identified by the Georgia Cancer Registry as having a breast cancer diagnosis between 2010-2017. We estimated hazard ratios (HR) and 95% confidence intervals (CI) for the association between each index, assessed in quintiles, and breast cancer mortality using Cox proportional hazards regression.

**Results:** ADI, NDI, and Yost index were well correlated: absolute value of correlation coefficients  $>0.77$ . Indicators within a domain showed moderate to high correlation. The average correlation coefficient, taking the absolute value, of indicators in the poverty, income, housing, occupation, and education domains were 0.37, 0.83, 0.36, 0.69, and 0.78, respectively. Over follow-up, 2,754 women died from breast cancer. Each index was similarly associated with breast cancer mortality (most vs. least deprived: HR=1.34, 95% CI 1.17-1.55 for ADI; HR=1.30, 95% CI 1.13-1.49 for NDI; HR=1.35, 95% CI 1.17-1.56 for Yost index).

**Conclusion:** This is the first comparison of all three indices. By understanding their correlations and associations with health outcomes, researchers can better determine which index is most appropriate for analysis.

Neighborhood deprivation and socioeconomic indices				
Domains	Indicators	ADI	NDI	Yost index
Poverty	% individuals below poverty line			
	% individuals below 150% poverty line			
	% individuals below 200% poverty line			
	% families below poverty line			
	% individuals receiving public assistance			
	% HH receiving public assistance			
	% female-headed households with children age <18 years			
	% single-parent households with children age <18 years			
	% households without phone			
	% households without plumbing			
% households without car				
Income	% household income <\$35,000			
	Median family income			
	Median household income			
	Income disparity			
Occupation	% employed in managerial/administrative jobs			
	% individuals ≥16 in white-collar jobs			
	% blue-collar jobs			
Housing	% housing crowding			
	% owner occupied housing			
	Median home value			
	Median rent			
Employment	Median monthly mortgage			
Education	% individuals unemployed			
	% individuals age >25 without a high school degree or GED			
	% individuals age ≥25 with <9 years education			
	% individuals age ≥25 with ≥12 years education			
	Education index			

**Figure 1.** A visual representation of the domains and indicators used to construct the three neighborhood deprivation and socioeconomic indices, the Area Deprivation Index (ADI), neighborhood deprivation index (NDI), and Yost index.



**Impact of potential confounders for occupational radiation exposure and cancer incidence among radiologic technologists** Won Jin Lee\* Won Jin Lee Ye Jin Bang Young Min Kim Eun Jin Jang

**Background:** Confounding is essential in observational epidemiology, particularly in low-dose radiation studies. The confounding effects have been observed differently for each population group. We examined the impact of potential confounders on cancer risk from occupational radiation exposure and the magnitude and direction of these potential confounding estimates among radiologic technologists.

**Methods:** The study included 4,308 radiologic technologists who participated in the questionnaire survey-based cohort study (2012–2013) that investigated non-radiation factors and 19,408 radiation technologists from the registration-based cohort study (1996–2011) enrolled in the National Dose Registry that obtained non-radiation factors by multiple imputations. Non-radiation factor items, including smoking status, alcohol intake, body mass index (BMI), exercise, sleep duration, shift work, personal medical examination, and past medical history, were selected as potential confounders. We quantified the confounding effects of cancer risks on radiation exposure based on a linear dose-response model. To determine whether a given risk factor caused confounding on the estimate of the baseline model, we compared the estimated measure of the association before and after adjusting for non-radiation factors.

**Results:** In the questionnaire survey-based cohort, the ERR per 100 mSv of the baseline model for the association between radiation dose and cancer risk was 0.58 (95% CI: -0.91, 2.07, 10-years lagged) after adjusting for sex, attained age, birth year, and years of employment duration. Directly adjusted for confounding by smoking (ERR/100mSv=0.58), alcohol intake (0.57), BMI (0.64), exercise (0.55), sleep (0.62), shift work (0.53), personal medical examination (0.52), and past medical history (0.70), but the trend was not statistically significant. In the registration-based cohort, the baseline ERR per 100mSv estimate was 0.12 (95% CI: -0.34, 0.57). After indirectly adjusting for the imputed non-radiation factors by smoking (ERR/100mSv=0.13), alcohol intake (0.12), BMI (0.11), exercise (0.12), sleep (0.13), and shift work (0.13), there was no significant difference compared to the estimation of the baseline model.

**Conclusions:** We found little evidence of factors with statistically significant confounding effects on risk per unit dose of cancer between directly and indirectly confounder-adjusted effects. However, cautious interpretation is needed due to the possibility that unmeasured confounders or insufficiently measured confounding factors cannot be excluded.

## **Do Community Capacity Building Programs Impact Household Food Insecurity? Results from a Cohort of Newly enrolled Food Banks Users**

Mabel Carabali\* Elsurry Pérez Mabel  
Carabali Geneviève Mercille Marie-Pierre Sylvestre Federico Roncarolo Louise Potvin

**Background:** Community-based capacity building programs (CCBP) have been expanded in high income countries to address issues related to poverty and household food insecurity (HFI). Yet, the effects of CCBP on HFI among food bank (FB) users has not been documented.

**Methods:** To examine whether CCBP use influenced household food security (HFS) 12 month after enrolment in a FB program, we conducted a 12-month longitudinal analysis (2018-2020) of *Pathways study*, a cohort of newly registered food bank users (n=1,000) from four regions of Quebec, Canada. HFS was measured using the Health Canada's Household Food Security Module and was categorized into three levels: food security, moderate food insecurity, and severe food insecurity. A dichotomous outcome variable reflecting change in HFS status over 12 months (from HFI to HFS) was created. The main exposure was the use of at least one CCBP (i.e., individual follow-up, job search service, educational courses, or personal development activities). Longitudinal Targeted Maximum Likelihood Estimation with stabilized inverse probability of treatment and censoring weights were used to account for time-varying confounders and selection bias. Baseline covariates included age, gender, race, country of origin, household composition and educational level, length of FB use before enrolment, and profiles of alternative food sources utilization. Time-varying covariates included annual household income, presence of stressful life events, and self-reported physical and mental health at baseline and at 12 months of follow-up. Sensitivity analysis included stratified analysis by rural and urban settings.

**Results:** Analyses are currently ongoing. Preliminary results suggest that the use of at least one CCBP is associated with switching from HFI to HFS after one year of food donations use (ATE; 0.25: IC 0.17; 0.33).

**Conclusion:** There is a potential effect of CCBP use on food security among new food bank users, further research on sustainability is needed.

**Identifying intersecting characteristics of Canadians using homecare** Afshin Vafaei\* Afshin Vafaei Susan P. Phillips

**Background:** What research designs best identify characteristics of Canadian older adults who accessed state-funded formal or individually arranged informal care? Does accounting for intersecting characteristics deepen meaning of findings?

**Methods:** As there is no single quantitative design to assess intersectionality we compared two standard methods. Using the Canadian Longitudinal Study on Aging, we performed recursive partitioning regression tree analysis using Chi-Squared automatic interaction detection (CHAID) and multivariate logistic regression to evaluate the impact of socioeconomic (SES), family-related, physical and psychological factors and social/material deprivation on care use. **Results:** Using CHAID, diminished function indicated by Activities of Daily Living (ADL), was most strongly aligned with formal care. Age, living arrangement, having no partner, depression and chronic medical conditions playing a lesser role. Notably, sex/gender, were not determinants. Characteristics aligned with informal care also included country of birth and years since immigration. Both 'trees' showed low risk of misclassification (4.6% and 10.8% for formal and informal care, respectively). Logistic regression models after adjustment for mutual confounding effects mirrored the CHAID findings. For example, limitations in ADL, the first splitter in the trees also showed a high estimated odds of using care (OR=4.4; 95%CI:3.9-4.8).

**Conclusions:** Our CHAID intersectionality analysis identified nuanced relationships between many factors involved in care use. Although considered marginalized, women, immigrants, or those of lower SES utilized formal care equitably. Need, primarily medical but also arising from living arrangement, rather than SES factors or sex predicted formal care. In this study, intersectional analyses did not enrich findings. Nevertheless, using regression, alone, interconnections between various social locations will be invisible and will, therefore, be missed.

**Revisiting the Population Attributable Fraction** Mark Klose\* Mark Klose Stephen R. Cole Paul N. Zivich

The population attributable fraction (PAF) measures estimated reduction in caseload under a theoretical exposure intervention. We formalize the PAF through potential outcomes, with special consideration for combining study level association estimates with population level exposure estimates. The PAF variance must propagate uncertainty from both causal risk ratio estimation and exposure proportion to construct valid confidence intervals; we provide and compare delta method, bootstrap, and robust variance estimators.

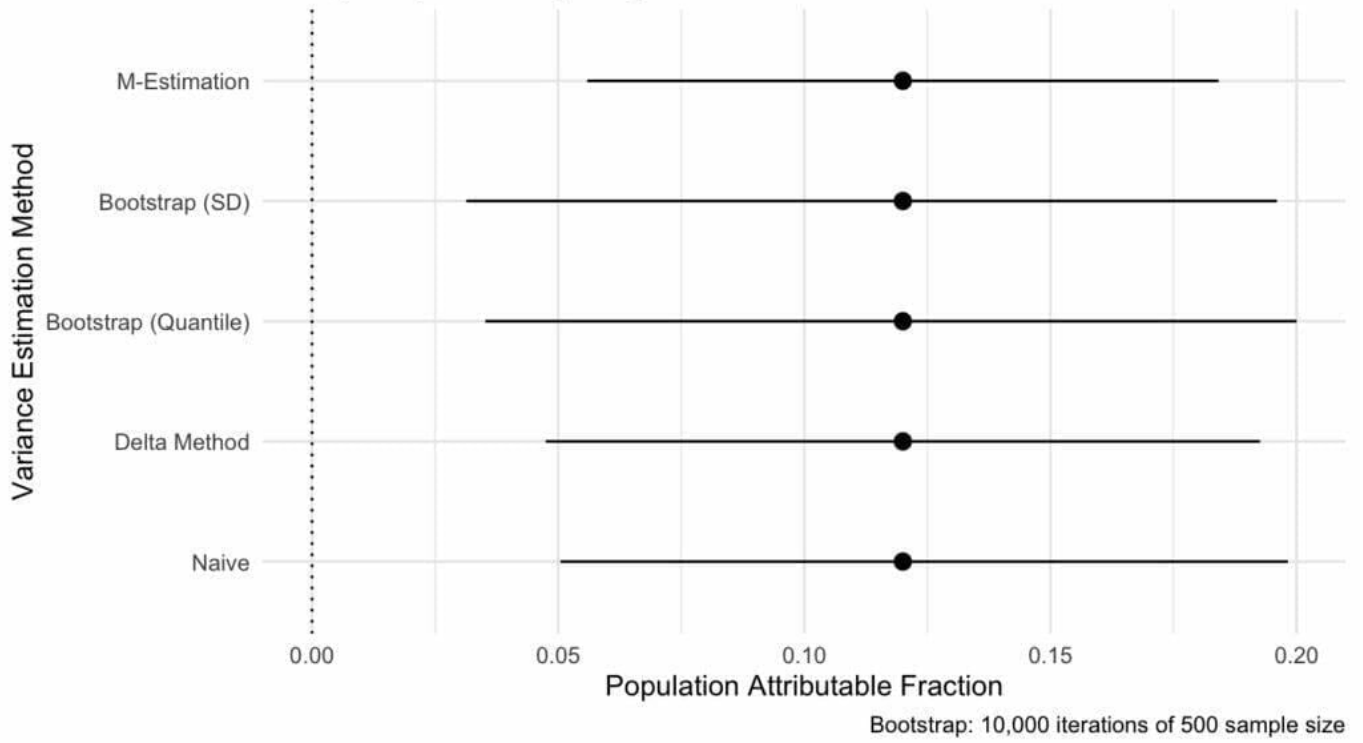
The motivating example is from the Women's Interagency HIV Study, where  $N=1,164$  women with known status of injection drug use (IDU) history were followed for 10.8 years or until the composite outcome of AIDS diagnosis or death occurred. Approximately 39.7% of the study sample had history of IDU, compared to 19.7% of women diagnosed with HIV in 2020 from CDC estimates. The risk of AIDS diagnosis or death among individuals with IDU history is 1.69 times the risk among individuals without IDU history when estimated by inverse probability weighting, with treatment propensity modeled by logistic regression incorporating nadir CD4 count, age, and an indicator of Black race.

The figure graphs estimates and confidence intervals by variance estimation method. About 12% of cases are attributable to a history of injection drug usage; the data are compatible with PAF intervals of (4.7%, 19.3%), (3.5%, 20.0%), (3.1%, 19.6%), and (5.6%, 18.4%) under the delta method, bootstrap 2.5th and 97.5th percentile, bootstrap standard deviation, and M-Estimation, respectively.

The population attributable fraction estimands used by Levin and Miettinen hide assumptions about the target population and sampling method, leading to conflicting advice about mathematical characteristics like additivity, distributivity, and sequential application. Formalizing with potential outcomes addresses limitations such as interventions affecting covariate distributions and defining attribution.

# Population Attributable Fraction and Intervals

History of Injection Drug Usage on AIDS or Death in WIHS Cohort, 1995-2006



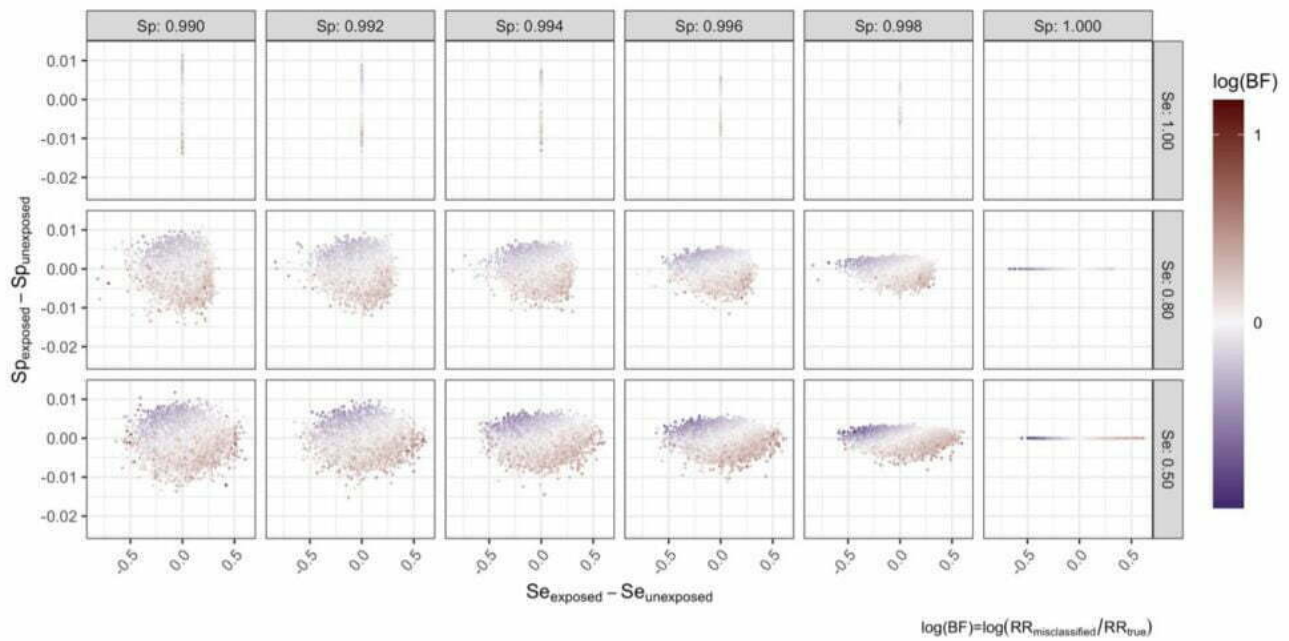
**Non-differential misclassification of outcome under near-perfect specificity: a simulation study** Thomas P. Ahern\* Thomas Ahern Weida Ma

**Background:** Misclassification of a dichotomous outcome will not bias risk ratio estimates when specificity is 100% and the imperfect sensitivity is non-differential. This mathematical convenience is used to support arguments against the impact of information bias, and to justify exclusion of bias analyses from analytic workflows. It is not known how the integrity of this argument is threatened by small departures from either perfect specificity, non-differential sensitivity, or both.

**Methods:** We simulated true and misclassified cohort data under 288 unique scenarios with varying specificity (99% to 100% by 0.2%), sensitivity (50%, 80%, and 100%), true risk ratio (1.0, 1.5, 2.0, and 5.0), exposure prevalence (10% and 50%), and baseline risk (1% and 10%). We misclassified record-level outcomes with binomial error using scenario-specific sensitivity and specificity values. We defined degree of departure from non-differential sensitivity as the difference in realized values between exposed and unexposed. We calculated bias factors at each iteration by dividing the misclassified risk ratio by the scenario-specific true risk ratio.

**Results:** The median bias factor across all scenarios was 0.987 (range: 0.716–1.008). Median bias factors increased monotonically as values of specificity and sensitivity decreased from 100%. Bias was apparent even with specificity as high as 99.8%. Stochastic differences in sensitivity between exposed and unexposed generated substantial bias, even under perfect specificity: bias was toward the null when sensitivity was lower in exposed vs. unexposed, and bias was away from the null when sensitivity was higher in exposed vs. unexposed (Figure).

**Discussion:** Substantial bias of the risk ratio may be present when validation data indicate near-perfect specificity and non-differential sensitivity of outcome classification. Small departures from perfect specificity—which investigators may be inclined to ignore—can still result in substantial bias.



**Figure.** Magnitude of outcome misclassification bias under departure from perfect specificity and stochastically differential sensitivity/specificity. Each panel depicts results from 10,000 simulations using the corresponding values of specificity ( $Sp$ , columns) and sensitivity ( $Se$ , rows); all simulations set exposure prevalence to 10%, baseline risk to 1%, and the true risk ratio to 1.0.

**Comparing approaches to rank interventions in a network meta-analysis: application to patients with opioid dependence** Myanca Rodrigues\* Myanca Rodrigues Brittany B Dennis Mikail Malik Leen N Naji Devon Malhotra Alannah Hillmer Nitika Sanger Sameer Parpia Lehana Thabane Zainab Samaan Behnam Sadeghirad

**Background:** Despite the widespread use of network meta-analysis (NMA) to synthesize the effectiveness of multiple interventions, there is no consensus on how to rank treatments. Proposed approaches use different criteria for categorizing the hierarchical effectiveness of interventions, which may result in different conclusions. There exists a need to identify the optimal method for ranking treatments for patients with opioid dependence to inform decision-makers about the credibility and effectiveness of presented evidence.

**Methods:** We conducted a literature search from inception to September 26, 2021 to identify randomized controlled trials evaluating opioid substitution and antagonist therapies for patients with opioid dependence, and assessed intervention effectiveness for *treatment retention* through a random-effects, frequentist NMA. Treatment effectiveness was ranked using three approaches: the rank-heat plot (RHP) method which uses surface under the cumulative ranking curve values, and the minimally-and partially-contextualized methods, which use assessments regarding the quality of evidence, in conjunction with effect estimates or the magnitude of clinically-beneficial effects, respectively.

**Results:** We included 53 trials assessing 12 interventions. All approaches were similar in ranking the interventions which were the most effective (dihydrocodeine and combination medication-assisted therapy with heroin and methadone) and least effective (clonidine) at retaining patients in treatment. However, methadone ranked only moderately using the RHP and partially-contextualized approaches, but was considered 'among the most effective' interventions by the minimally-contextualized method.

**Conclusions:** Different approaches to rank treatments in NMAs may impact clinical decision-making. We suggest use of the minimally contextualized approach for this clinical population, given the arbitrary thresholds and lack of considering the quality of evidence by other methods.



Partially-Contextualized Classification	Intervention	RD (95% CI) %	Certainty	Rank-Heat Plot SUCRA values
Large beneficial effect (50%+)	DIHYCO	64 (36, 68)*	Moderate	95.5
	HERMET	55 (36, 64)*	Moderate	87.2
Moderate beneficial effect (30-49%)	HERO	46 (23, 59)*	Moderate	69
	MET	43 (28, 54)*	Moderate	65.2
	LAAM	43 (19, 57)*	Moderate	62.4
	WLUC	39 (1, 60)*	Moderate	54
	MORPH	38 (-7, 62)	Low	53.3
Small beneficial effect (10-29%)	BUP	36 (20, 48)*	Moderate	46.9
	SUBOX	28 (12, 43)*	Moderate	35.3
Small harmful effect (opposite direction)	NALT	12 (-3, 28)	Low	20.2
	CLONID	-21 (-30, 15)	Low	1.4

Figure 1a: Partially-contextualized and rank-heat plot approaches for ranking interventions

Certainty	Minimally-Contextualized Classification	Intervention	OR (95% CI)
High (Moderate to high)	Among the most effective	DIHYCO	46.34 (4.47,479.94)*
		HERMET	14.38 (4.52,45.73)*
		MET	6.48 (3.23,12.99)*
	Inferior to the most effective, but superior to the least effective	HERO	7.41 (2.57,21.38)*
		LAAM	6.25 (2.23,17.51)*
		WLUC	5.13 (1.05,25.17)*
		BUP	4.43 (2.28,8.59)*
Low (Low to very low)	May be among the least effective	SUBOX	3.20 (1.64,6.23)*
		MORPH	4.94 (0.70,34.78)
		NALT	1.67 (0.87,3.23)
		CLONID	0.26 (0.04,1.85)

Figure 1b: Minimally-contextualized approach for ranking interventions

**Abbreviations:** APLCB: placebo (reference treatment/comparator), BUP: buprenorphine, CI: 95% confidence interval, CLONID: clonidine, DIHYCO: dihydrocodeine, HERO: heroin (heroin-assisted therapy), HERMET: heroin + methadone assisted-therapy, LAAM: Levacetylmethadol or levomethadyl acetate, MET: methadone, MORPH: morphine, NALT: naltrexone, OR: odds ratio, RD: risk difference, SUBOX: suboxone, SUCRA: surface under the cumulative ranking curve values, WLUC: waitlist or usual care

**Notes:** \* represent statistically significant results. Effect estimates are for the comparisons of the intervention vs. placebo. Figure 1a is colour-coded according to partially-contextualized (columns 2-4) or rank-heat plot (column 5) rankings. Figure 1b is colour-coded according to minimally-contextualized rankings.

**Bias in the mediated association between maternal obesity and caesarean section delivery**

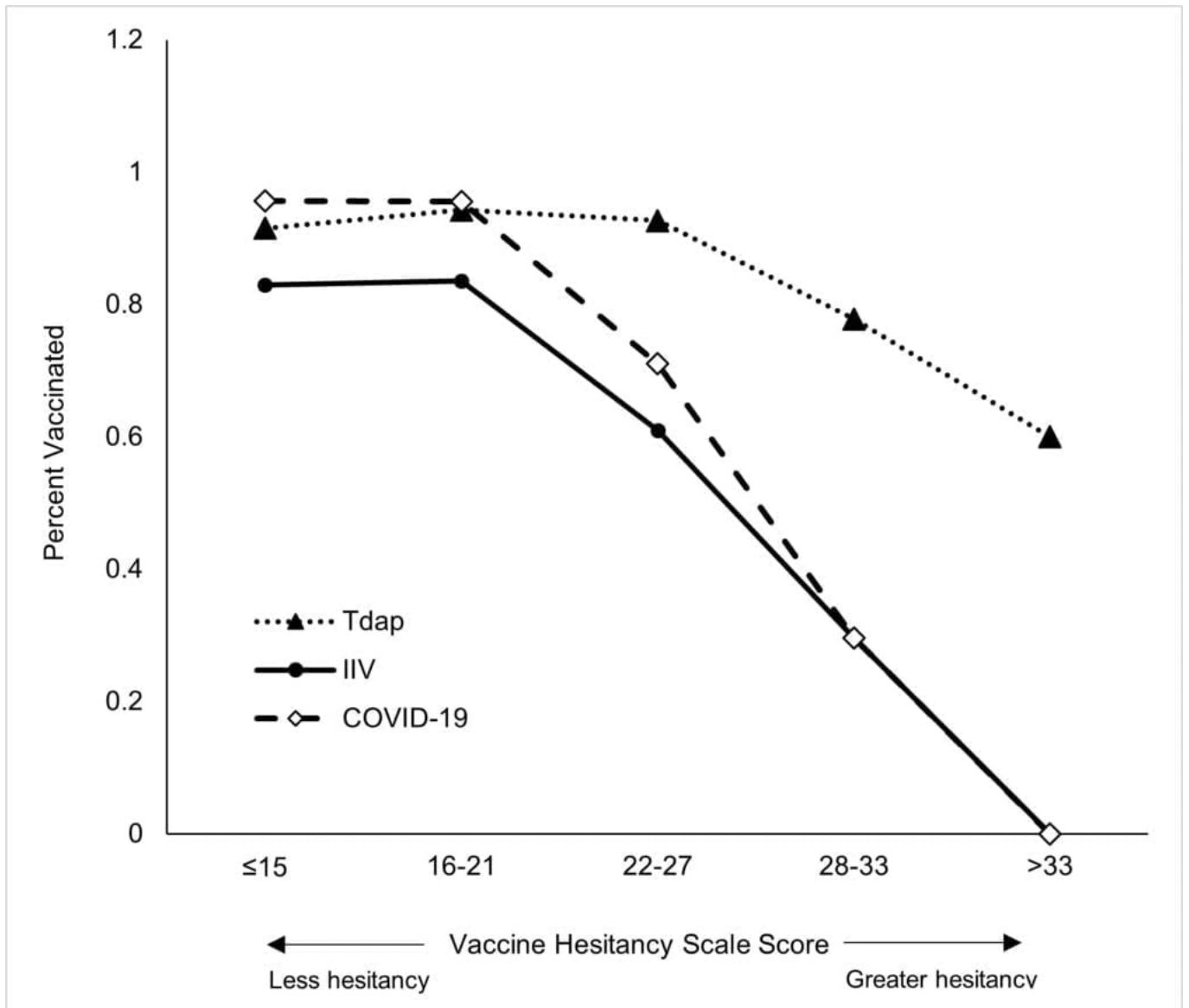
Jennifer Dunne\* Jennifer Dunne Gizachew A Tessema Amanuel T Gebremedhin Gavin Pereira

Mediation analysis is generally conducted under the assumption of no unmeasured confounding. However, bias from unmeasured confounding has the potential to distort mediated exposure-outcome associations. The aim of this simulation study was to determine the total effect of maternal obesity on caesarean section delivery when mediated by the pregnancy complication of pre-eclampsia. We also estimated the magnitude and direction of bias resulting from unmeasured confounding in this mediated association. We simulated data from an observed pregnancy cohort in Western Australia and a range of values for the prevalence of maternal obesity, pre-eclampsia, caesarean section delivery and an unmeasured confounder  $U$ . We also simulated the odds ratio for the selection effects (maternal obesity  $\rightarrow$  pre-eclampsia, pre-eclampsia  $\rightarrow$  caesarean section delivery,  $U \rightarrow$  pre-eclampsia,  $U \rightarrow$  caesarean section delivery) based on realistic assumptions. Overall, we found that conditioning on the mediator of pre-eclampsia had a negligible impact on the association between maternal obesity and caesarean section delivery. When we compared the total effect, including the influence of the mediator and unmeasured confounder, to the direct effect drawn from the observed cohort we found a negligible downward bias of 1%. By extrapolation, we conclude that the results of studies that intended to estimate the total effect of maternal obesity on caesarean section delivery are not biased by over-adjustment for pre-eclampsia.

**Measuring hesitancy toward prenatal vaccination: development of a Vaccine Hesitancy Scale for vaccination during pregnancy** Annette Regan\* Annette Regan Jeannette Comeau Ning Yan Gu Tasmiah Nuzhath Marie-Claude Couture

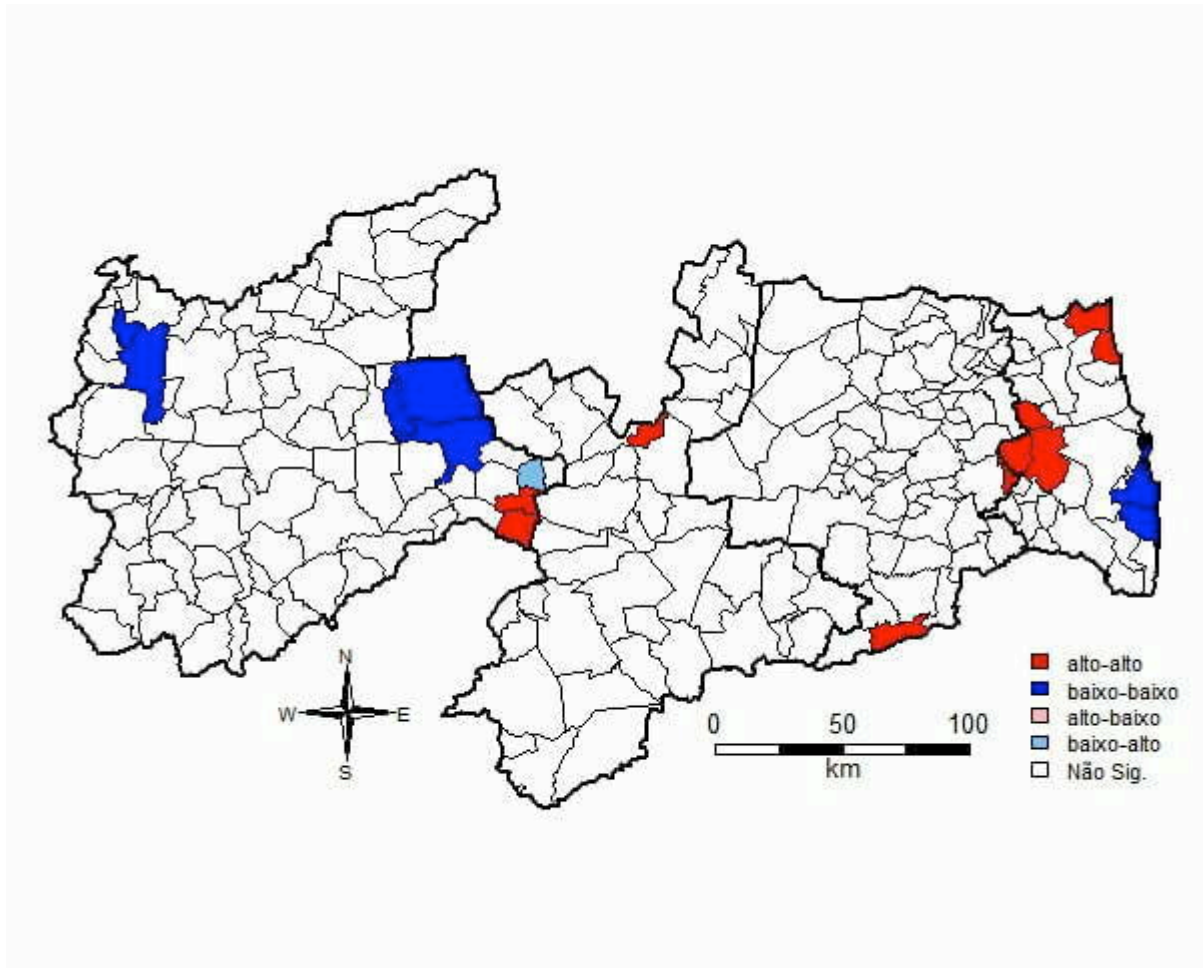
Prenatal immunization offers protection against severe vaccine-preventable diseases to newborns. However, the uptake of vaccines during pregnancy remains suboptimal, and despite extensive research on determinants and predictors of prenatal vaccination, there is currently no tool to measure hesitancy toward vaccination during pregnancy. We analyzed data from a national cross-sectional survey of 872 US adults 18-49 years of age who had given birth during the past 6 months. Participants self-reported uptake of influenza, Tdap, and COVID-19 vaccines during their most recent pregnancy and completed the adult Vaccine Hesitancy Scale (aVHS). The aVHS is a scale initially developed by the SAGE Working Group on Vaccine Hesitancy and recently modified for application to adult vaccines, with higher scores indicating greater hesitancy to vaccines. We performed confirmatory factor analysis using structural equation modeling with maximum likelihood estimators. We examined mean aVHS scores for both vaccinated and unvaccinated respondents. We also compared vaccination rates for each vaccine by aVHS quintile.

Confirmatory factor analysis indicated moderate fit of the VHS among postpartum adults (Standardized Root Mean Residual [SRMR] = 0.063; Tucker-Lewis Index = 0.856), which modestly improved after removing item 5 (SRMR 0.052; Tucker-Lewis Index = 0.882). The mean VHS score was 20.1 (range: 9 to 41) and was lower for vaccinated compared to unvaccinated respondents for COVID-19 vaccine (-5.8) and influenza vaccine (-3.7), and less so for Tdap vaccine (-2.0). We observed lower uptake of influenza and COVID-19 vaccines associated with higher aVHS scores and weaker declines in the uptake of Tdap vaccine (**Figure**). Currently available tools for measuring vaccine hesitancy in adults do not perform optimally for all vaccines recommended during pregnancy. A tool specifically designed to measure hesitancy toward prenatal vaccines is likely needed.



**spatial modeling of socioeconomic indicators in child mortality, mortality under five years rate in the state of paraíba, northeast region, brazil.** Tiago Almeida de Oliveira\* Tiago Oliveira  
Alexsandro Morais de Azevedo Gabriel Messias Santana Peixoto Mateus Santos Peixoto Hiago José  
Andrade de Albuquerque Martins Ricardo Alves de Olinda

Currently, despite the global decrease, the Infant Mortality Rate—IMR is still considered one of the major problems of Public Health worldwide, a reality present in some countries, including Brazil. The under-five mortality rate — U5MR, is an important marker that expresses socioeconomic development and deficits in environmental infrastructure. These types of mortality are related are mainly related to the manifestations of socioeconomic discrepancies and basic sanitation, which still hinder the access and use of the means of promotion, protection, and recovery of health. The Northeast region still presents the worst social indicators, in relation to the other regions of the country, being the State of Paraíba with its 223 municipalities inserted in this context. In this sense, this work aims to prove the hypothesis that there may be spatial dependence on socioeconomic indicators in the State of Paraíba, Brazil, with the mortality variables IMR and U5MR. For implement a model that is able to identify areas favorable to advances and setbacks in public policies in the last sense. For this, the methods of spatial statistics for area data is used, which allows spatial visualization of the study variables through the neighborhood matrix with spatial autocorrelation (and techniques, I of Moran Global and Local, Lisa Map and Moran scatter plot). Three different spatial regression models - SRM were used: Mixed Autoregressive Spatial Model - SAR, Spatial Error Model - SEM and Durbin Spatial Model - SDM. The choice of the best model was based on the goodness of fit test and the lowest AIC value. The SRM were also shown to be efficient in the autocorrelation structure of the IMR and U5MR and socioeconomic variables. This study showed an existence of spatial dependence among the municipalities, forming clusters in various locations. It helps the understanding of how socioeconomic variables influence mortality rates at one and five years, given their spatial dependence.



**Bias Resulting From Categorizing Continuous Exposure Variables** Chrystelle Kiang\*

Chrystelle Kiang Thomas P. Ahern Lindsay J. Collin Richard F. MacLehose Timothy L. Lash

**Introduction:** A special mechanism of information bias arises from misclassification of a continuous exposure variable. Even if the continuous exposure is measured with non-differential error, the misclassification can become differential when the exposure affects the outcome and the continuous measure is categorized. A paper often cited when discussing this bias used a simulation with a uniformly-distributed exposure; results may differ for exposures with different distributions. We adapted the previous simulation to evaluate the potential bias for a normally distributed continuous exposure, which may be more typical of epidemiologic exposures.

**Methods:** We simulated datasets with true uniform or normally distributed continuous exposure and dichotomous disease status. The measured exposure value was the sum of the continuous exposure and an error term with normal distribution with mean 0 and varied SD, and the true and measured exposure values were dichotomized. We repeated these simulations and calculated mean sensitivity and specificity over the simulations.

**Results:** We simulated scenarios of exposure with uniform and normal distributions with similar ranges, measurement error with normal distribution of mean 0 and SD of 100, 300, and 500, and expected RRs of 1.5, 2.5, and 5.0. When the exposure was distributed uniformly, differences in sensitivity and specificity between disease and non-diseased ranged from 0.02 to 0.16, with the largest difference observed when RR=5.0. When the exposure was distributed normally, the differences in sensitivity and specificity ranged from 0.00 to 0.10, with the largest difference observed when RR=5.0.

**Conclusion:** When a continuous exposure variable is distributed normally, measured with random, non-differential error, and categorized, the extent of misclassification is attenuated relative to an exposure distributed uniformly. The greatest bias arises when exposure prevalence is low and association with disease is high.

**Correcting for sampling bias in healthcare claims datasets** Alex Dahlen\* Alex Dahlen Vivek Charu

Healthcare claims databases, which aggregate claims from commercial insurers, are increasingly being used to generate real-world evidence in medical research and the FDA has recently begun to consider this style of evidence in regulatory decisions. However, these databases represent a non-random sample of the population—one that is systematically biased along racial and socioeconomic lines. These same dimensions, often referred to as social determinants of health, have also been shown to be effect modifiers for a large array of conditions and treatments in medicine, including the burden of disease, access to healthcare, and even the effectiveness of some treatments. This combination of inconsistent sampling and effect modification can give rise to external validity bias, where results generated from the claims data will fail to generalize to the underlying, target population; specifically, estimates generated from these data will be biased toward the result that is relevant to the over-sampled demographic group. Indeed, the bias can be quite large: the CDC estimates that the average US incidence of HIV (a disease that disproportionately affects people living below the poverty line) is 0.36%; the same estimate from claims data is only 0.11%. This talk has two objectives. First, to characterize the sampling bias, we will compare region-level variation in sampling rates for two of the most common claims databases (Optum and MarketScan) with region-level variation in sociodemographic indicators. The correlation coefficients in Figure 1 show that these databases both over-represent wealthier and more educated regions. Next, to understand how this sampling bias affects estimates derived from these databases, we compare prevalence estimates for a wide variety of diseases and procedures between claim data and ground truth datasets like the CDC or the AHRQ's State Inpatient Databases. Characterizing and overcoming this source of external validity bias is an essential first step to unlocking the potential of these large databases.



		Optum Sampling	MarketScan Sampling	HIV Prevalence
Population	Total Population (millions)	0.01	-0.04	0.06
	Log <sub>10</sub> Pop. Density (1/sq. mile)	0.14	-0.12	0.14
Sex	% Female	0.12	-0.06	-0.03
Race/Ethnicity	% White	0.20	0.01	-0.22
	% Black	-0.15	-0.25	0.29
	% Hispanic	-0.19	-0.25	0.06
	% Asian	0.16	0.32	-0.01
	% Other	-0.08	-0.06	-0.00
Age	% Under 18	-0.09	0.01	-0.13
	% 18 - 40	-0.21	-0.24	0.22
	% 40 - 60	0.32	0.39	-0.11
	% 60 - 80	0.14	0.08	-0.08
	% Over 80	0.12	0.01	-0.04
Household income	% < \$15k	-0.34	-0.42	0.22
	% \$15k – \$30k	-0.40	-0.33	0.15
	% \$30k – \$45k	-0.37	-0.27	0.09
	% \$45k – \$60k	-0.23	-0.06	0.02
	% \$60k – \$100k	0.10	0.35	-0.17
	% \$100k – \$125k	0.33	0.39	-0.19
	% \$125k – \$200k	0.43	0.33	-0.14
	% > \$200k	0.42	0.20	-0.04
Work & Insurance	% Unemployed	-0.29	-0.33	0.18
	% No health insurance	-0.31	-0.21	0.17
Education	% Less than High School	-0.33	-0.36	0.12
	% High School	-0.27	-0.03	-0.02
	% Some College	-0.09	0.11	-0.12
	% College	0.41	0.23	-0.02
	% Graduate	0.30	0.11	0.02
Housing	% houses that are owner occupied	0.25	0.31	-0.31
	Median house price (millions of \$)	0.36	0.10	0.02

**Detection of Temporal Trends in the Short-Term Health Effects of Air Pollution** Hwashin

Hyun Shin\* Hwashin Hyun Shin Kamal Rai Patrick Brown

We developed a new model to detect trends in the association between short-term exposure to ambient air pollutant (AP) and health outcomes such as mortality. We used daily concentrations of AP and daily counts of mortality aggregated by census division (city). We considered ground-level ozone because of its seasonal variations and considered 6 cities to ensure this study covered cities with different population sizes: 2 cities of each relatively large, medium and small population. We modeled ozone as a time-varying, 2nd-order random walk, giving two ways to characterize a trend – momentum for direction and stability for variability. We fit this model to circulatory and pulmonary mortality data across two age groups: non-senior (1-65) vs. senior (66+) over 17 years (1996-2012). We found trends in two cases for senior group only: a decreasing trend for circulatory mortality for a small city St. John, whereas an increasing trend for pulmonary mortality for a large city Toronto. This indicates the trend depended on location (city), age group, and cause (circulatory vs pulmonary). In addition, we observed three other findings. First, although the posterior means of the air pollution effect were smooth and relatively stable over time, their estimates often had large uncertainty. Second, pulmonary mortality had more time-varying associations than circulatory mortality. This may be related to seasonality in pulmonary mortality, due to factors such as the flu. Third, momentum and stability could detect linear trends only, not for non-linear trends. Further research is warranted to detect non-linear trends.

**Trajectory of longitudinal lending discrimination modifies the efficacy of a skills-based intervention in stroke survivors** Jeffrey J. Wing\* Jeffrey Wing Helen C.S. Meier Jenna I. Rajczyk Jonathan R. Powell Emily Drum Bernadette Boden-Albala

**Introduction:** Racial discrimination in the US contributes to current stroke disparities.

**Objective:** To determine if the efficacy of a skills-based intervention on systolic blood pressure (SBP) reduction in a cohort of mild/moderate strokes varied by longitudinal lending discrimination.

**Methods:** The Discharge Educational Strategies for Reduction of Vascular Events (DESERVE) intervention randomized 552 stroke survivors to skills-based intervention or usual care. Participants' addresses were geocoded and linked to census tract-level historic and present-day lending discrimination. A four-level neighborhood longitudinal lending discrimination variable was created from Home Owners' Loan Corporation (HOLC) redlining data and 2018 Home Mortgage Disclosure Act loan occurrence and cost reports: no discrimination, growing investment, declining investment, and persistent discrimination (N=315). Change in SBP by intervention status stratified by longitudinal lending discrimination category was modeled linearly with generalized estimating equations for clustering by site. To account for selection biases related to residing in a HOLC graded neighborhood and loss to follow-up inverse probability weights were used separately and in combination.

**Results:** In unweighted models, the intervention was most efficacious in declining discrimination areas (7.53 mmHg reduction; 95% CI: 0.50, 14.57) vs usual care and least efficacious in growing investment areas (7.25mmHg increase; 95% CI:-13.17, -1.33). After combined weighting, the intervention was even less efficacious in growing investment areas (17.82mmHg increase; 95% CI:-24.84, -10.81; Figure).

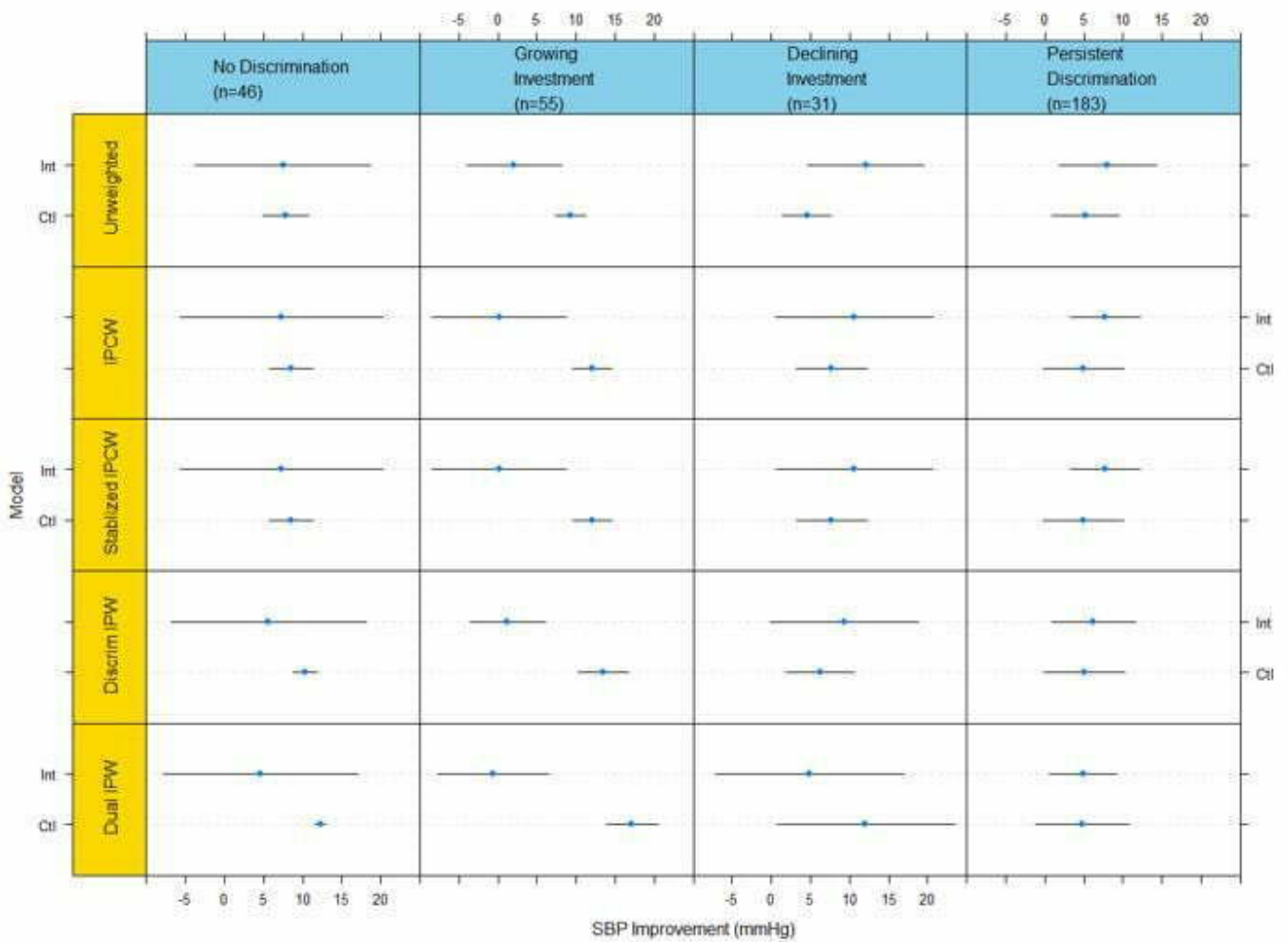
**Conclusions:** The efficacy of interventions is impacted by underlying systems of disadvantage such that contextual factors should be considered when designing trials. Accounting for selection bias demonstrated that the intervention was less efficacious for those in growing investment areas, perhaps due to the length of time residing in these areas.

**Figure.** Categorization of longitudinal lending discrimination based on historic redlining quartile and current lending discrimination (A); and Efficacy of systolic blood pressure reduction (improvement in mmHg) by category of longitudinal discrimination and intervention status (B).

**A**

Redlining Quartile	+	Current Lending Discrimination	→	Longitudinal Discrimination
Low (1)	+	No Current Discrimination	→	No Discrimination
Low (1)	+	Current Discrimination	→	Declining Investment
High (2-4)	+	No Current Discrimination	→	Growing Investment
High (2-4)	+	Current Discrimination	→	Persistent Discrimination

**B**



**A longitudinal association between perceived interpersonal racism and incident stroke in U.S. Black women** Shanshan Sheehy\* Shanshan Sheehy Hugo J Aparicio Julie R. Palmer Yvette Cozier Vasileios-Arsenios Lioutas Julie G. Shulman Lynn Rosenberg

**Background:** Black Americans experience stroke and stroke mortality at younger ages and more frequently than other racial groups. Studies examining the longitudinal association between interpersonal racism and risk of stroke are lacking.

**Methods:** In the Black Women's Health Study (BWHS), a prospective cohort study of 59,000 Black women from across the U.S., we assessed the longitudinal relation between perceived interpersonal racism and stroke incidence. On a questionnaire completed in 1997, participants reported experiences of racism in everyday life and when dealing with situations that involved employment, housing, or interactions with police. Strokes were identified through self-report on biennial questionnaires, medical records adjudication, and linkage with the National Death Index (NDI). Stroke-free participants were followed from 1997 until onset of stroke, death, loss to follow-up, or end of the study period. Cox models were used to estimate hazard ratios (HR) and 95% confidence intervals (CI), adjusting for major confounders (including education, neighborhood socioeconomic environment, and cardiometabolic factors).

**Results:** During over 22 years of follow up, 1,664 incident stroke cases were identified; among them 497 were definite cases confirmed by neurologist review and/or NDI. Multivariable HRs for participants who reported experiences of racism in the domains of employment, housing, and the police versus none were 1.49 (95%CI 1.24-1.80) based on all incident cases and 1.32 (95%CI 0.97-1.81) based on definite cases. For comparisons of women in the highest quartile of everyday interpersonal racism score relative to women in the lowest quartile, there was little evidence of an association.

**Conclusions:** Black women who reported multiple experiences of interpersonal racism in situations involving employment, housing, and the police appeared to have an increased risk of stroke, even after accounting for demographic and vascular risk factors.

**Evaluating Pathways between Dementia Risk Factors, Biomarkers of AD/ADRD, and Cognitive Function in Young Adulthood** Jennifer Momkus\* Allison E. Aiello Jennifer Momkus  
Rebecca Stebbins Yuan Zhang Y. Claire Yang Kathleen Mullan Harris

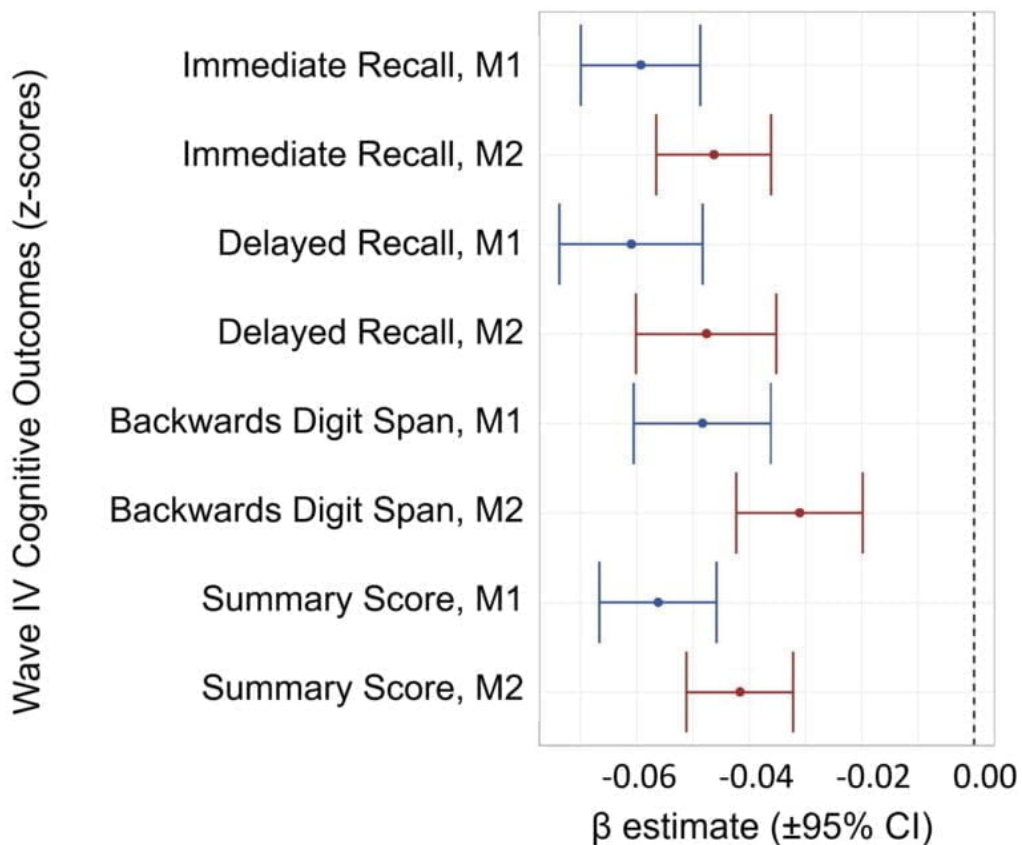
**Background:** The Cardiovascular Risk Factors, Aging, and Incidence of Dementia (CAIDE) risk score has shown significant predictive value for AD and cognitive impairment in older age populations. Yet, it is increasingly recognized that neuropathology and cognitive decline begin much earlier, including during young adulthood. Thus, there is a need to examine the utility of risk scores for AD in younger adult populations. We tested the association of the CAIDE score in predicting cognitive function in young adults and assessed whether the score was associated with biomarkers of AD/ADRD risk in young adulthood.

**Methods:** Participants were from Wave IV (ages 24-34) and Wave V (ages 33-44) of the National Longitudinal Study of Adolescent to Adult Health (Add Health). The CAIDE score was constructed based on survey and physical exam data using age, educational attainment, sex, systolic blood pressure, BMI, total cholesterol, and physical activity. Measures of word recall and digit span backwards tasks were used to assess cognitive function. We used survey-weighted linear regression to estimate the associations between CAIDE score and (1) cognitive function (2) biomarkers of inflammation and neurological damage at each wave (including C-Reactive Protein (CRP), Interleukin (IL)-6, total Tau, Neurofilament light, among others), adjusting for race/ethnicity and early life socioeconomic status (SES).

**Results:** A higher CAIDE score at Wave IV was associated with lower cognitive function at Wave IV and Wave V (see Figure 1). A higher CAIDE score was also associated with higher levels of CRP and IL-6 in both waves. Neither the Wave IV nor Wave V CAIDE score predicted markers of neurodegeneration.

**Conclusions:** Even in early adulthood, known dementia risk factors were associated with cognitive function. Chronic inflammation may play a role in this relationship. Intervention earlier in the life course may be especially effective for prevention of AD/ADRD.

Figure 1. Cross-Sectional Association between Dementia Risk Score and Cognitive Function, Add Health Wave IV (ages 24-34 years)



N=11,852, M1: Unadjusted, M2: Race/ethnicity and early life SES

**Examining associations between daily dietary intake at dinner and cardiovascular health outcomes in children three years later**

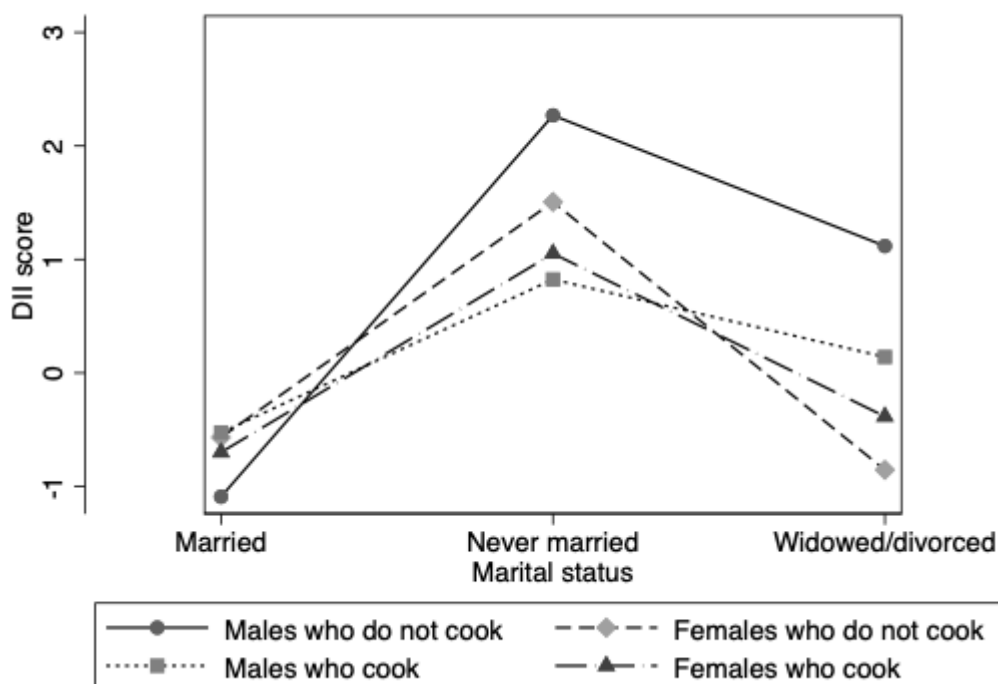
Shiwani Sapkota\* Shiwani Sapkota Allan D. Tate  
Christopher P. Carr Junia N. de Brito Amy E. Noser Vivienne M. Hazzard Alicia Kunin-Batson Jerica  
M. Berge

**Background:** Dietary intake is a major lifestyle risk factor for cardiovascular diseases (CVDs), but the role of childhood diet in relation to timing of CVD onset is not well understood. Considering the limitations of traditional dietary assessment methods (e.g., recall bias), focusing on child dietary intake during the typically largest meal of the day, the dinner meal, may be advantageous for intervention. This study used ecological momentary assessment (EMA) as a novel dietary assessment approach to examine the predictive utility of daily dietary intake at the dinner meal for cardiovascular health outcomes in children at 3 years follow-up. **Methods:** A cohort study with 350 racially/ethnically diverse children (aged 5-9 years) was conducted in Minneapolis-St. Paul, MN. Parent report of child dietary intake at dinner was measured via 7 days of EMA at baseline. Child systolic and diastolic blood pressure (BP) was measured approximately 3 years later at a single measurement visit. BP was dichotomized into elevated/not elevated (age and height-standardized BP adapted from the American Academy of Pediatrics). Multiple regression models with robust standard errors were used to examine diet-CV health relationships. **Results:** 11.7% of sample had elevated BP at follow up (9.8 years old). Greater intake of fruit juice at dinner was associated with higher odds of elevated BP in children (OR: 1.14; 95% CI: 1.02-1.28), whereas intake of dairy at dinner was associated with lower odds of elevated BP (OR: 0.90; 95% CI: 0.83-0.98). **Conclusion:** Child intake of fruit juice at dinner was a determinant of poorer pre-adolescent cardiometabolic health. Behavioral and environmental determinants of dietary intake behavior among children during dinner may be important intervention targets (home food accessibility, meal preparation, and child eating behaviors) to mitigate risk factors of CVDs during childhood to early adolescence transition.



**Association between disaster-related traumatic experiences and dietary inflammatory index among older people** Aki Yazawa\* Aki Yazawa Koichiro Shiba Sakurako Shiba Okuzono Ichiro Kawachi

Traumatic experiences such as surviving a natural disaster have long-lasting impacts on health directly and indirectly through the alteration of health behaviors. Among potential pathways, the impact of disaster-related trauma on diet has been understudied. This study investigated the relationship between disaster-related trauma, the post-disaster experience of mental illness, and change in marital status and inflammatory diet score, and how these relationships differed between genders and cooking skills among older survivors of the 2011 Great East Japan Earthquake and Tsunami ( $n = 1,341$ ). Dietary data were collected in 2020 using a self-administered diet history questionnaire (BDHQ), from which we derived a dietary inflammatory index (DII) based on 26 food/nutrient items, where higher scores indicate a pro-inflammatory diet (ranged from -5.3 to 4.5 in this sample). Housing damage due to the tsunami was associated with higher DII scores (coef. = 0.72, 95%CI 0.19, 1.26), whereas loss of friends was associated with lower DII (coef. = -0.29, 95%CI -0.56, -0.03). Post-disaster depression was associated with higher DII (coef. = 0.41, 95%CI 0.18, 0.65) conditional on pre-disaster depression. Compared to those who have a partner, those who never married (coef. = 0.45, 95%CI 0.17, 0.72) and those who were widowed/divorced after the disaster (coef. = 0.50, 95%CI 0.17, 0.84) had higher DII scores. Three-way interactions (gender x change in marital status x whether individuals prepare their meals) revealed that never-married males who do not cook had the highest DII score, followed by females who never married and do not cook, then widowed or divorced males who do not cook. Interventions to support healthy nutritional practices may assist in the long-term recovery of disaster survivors.



**Vitamin C and multiple disease outcomes in adults: a systemic review of mendelian randomization studies** Junmeng Zhang\* Junmeng Zhang Lai Ling Hui Jie V Zhao

**Background:** Vitamin C has several important functions and many health benefits; however, its protective role in multiple disease outcomes remains ambiguous. Mendelian randomization (MR) is an increasingly explored method to strengthen causal inference. This systematic review aimed to summarize the causal relationship between vitamin C and disease outcomes based on current evidence in MR studies.

**Methods:** We searched the Cochrane, Embase, and PubMed databases from inception to 23 September 2022. All published articles using the MR approach to explore potential causal relationships between circulating Vitamin C (and its metabolites) and health outcomes were included. Two reviewers independently conducted titles and abstract screening, full-text review, and data extraction.

**Results:** We included 29 MR studies investigating the causal effect of vitamin C on 53 disease outcomes, including various cancers, cardiovascular diseases, and neurodegenerative diseases. Of these 53 outcomes, 44 showed null associations. Genetically predicted higher plasma vitamin C levels (and its metabolites) have shown suggestive protective effects on colon cancer, colorectal cancer, small intestine cancer, cardioembolic stroke, peripheral arterial disease, Alzheimer's disease, and intraocular pressure; but conferred an increased risk of endometrial cancer and atrial fibrillation.

**Conclusions:** This MR review suggests that vitamin C might play a causal role in some diseases. The null associations of other outcomes cannot rule out treatment effects from high-dose vitamin C or for people deficient in vitamin C.

**LATEBREAKER**

Nutrition/Obesity

**Diet quality at 3 years of age relates to lower BMI but not blood pressure at 10 years of age**

Qihua Wang\* Qihua Wang Tian Xie Xia Huo Harold Snieder Eva Corpeleijn

**Introduction:** Adhering to a healthy diet is recommended to prevent or reverse overweight and hypertension. Primordial prevention of overweight in early childhood could be most effective, but limited evidence is available for elevated blood pressure. We aim to investigate the associations for a healthy diet with body mass index (BMI) and blood pressure (BP) in childhood.

**Methods:** In the GECKO Drenthe cohort, weight, height and BP were measured at 5 and 10 years of age. Diet was evaluated at 3 years of age using a food frequency questionnaire, and 3 diet scores were calculated, namely the Dietary Approaches to Stop Hypertension (DASH) score, Mediterranean Diet Score (MDS), and Lifelines Diet Score (LLDS). Models were adjusted for age, sex, height (only for BP), parental education level, and any smoking during pregnancy.

**Results:** From the 1077 children included in the analysis, 10.8% had overweight at 5 years and 16.5% at 10 years, while 34.5% had elevated BP at 5 years and 23.9% at 10 years. Higher DASH, MDS, and LLDS, indicating healthier diet, were all associated with lower BMI z score at 10 years of age [B and 95% CI: DASH -0.028 (-0.044, -0.013), MDS -0.055 (-0.101, -0.009), LLDS -0.013 (-0.024, -0.003)]. Higher DASH related also to lower overweight risk at 10 years of age [OR (95% CI): 0.936 (0.898, 0.976)]. Although a moderate association was found between BMI and BP, none of the diet scores were associated with BP or elevated BP at either 5 or 10 years of age.

**Conclusion:** A better diet quality at 3 years of age relates to less overweight but not lower BP at 10 years of age. Our findings suggest that healthy diet in early childhood may prevent overweight in middle childhood, but the effect on BP needs further study with longer follow up.

**Metals exposure among children living near coal-burning power plants is associated with obesity** Oludesola Ogunesan\* Oludesola Ogunesan Kristina Zierold Lonnie Sears John Myers

**Purpose:** Obesity is a public health challenge that threatens the health of children throughout the world. The prevalence of childhood obesity in the United States is approximately 20%. Children who live near coal-burning power plants are exposed to many metals, which may be risk factors for obesity. The purpose of this study was to assess the association between metals and obesity among children 6-14 years old.

**Methods:** A community-based research study design was used to collaborate with people living within a 10-mile radius of two coal-burning power plants. Children (n=280) between the ages of 6-14 years were included in the study. Nail samples were collected and analyzed using inductively coupled plasma mass spectrometry (ICP-MS). To calculate Body Mass Index (BMI), child weight and height were collected during an in-home visit. Using BMI, children were classified as underweight or healthy weight and overweight or obese. Logistic regression and Wilcoxon tests were used to evaluate the relationship between metals and obesity.

**Results:** 47% of children were overweight or obese. Among the children who were overweight or obese, 60% were obese. Our result showed that children who were overweight and obese had higher body burden of manganese (OR= 1.9; 95%CL= 1.3 - 2.5; p=0.04), nickel (OR = 1.7; 95%CL = 1.5 - 2.8; p=0.05), aluminium (OR = 1.8; 95%CL = 1.5 - 3.2; p=0.01 ), and zinc (OR = 1.9; 95%CL = 1.5 - 2.7; p=0.05 ), compared to children who were healthy weight or underweight.

**Conclusions:** Obesity in children is a public health crisis. Our study showed that metals are associated with children living near coal-fired power plants being overweight or obese. Regulations on environmental exposure from industrial sources need to be strengthened and enforced. Furthermore, our research provides an impetus for developing new regulations to protect against the harms of metals.

**Predictors of night shift work adaptation among rotating night shift workers** Anna Palomar-Cros\* Barbara Harding Ana Espinosa Maria Mata Gemma Castaño Vinyals Oscar J Pozo Manolis Kogevinas Kyriaki Papantoniou

### **Introduction:**

Which factors predict the ability to adapt to night shift work require further study. We explored differences in night shift work adaptation using melatonin levels, a common biomarker of circadian phase and disruption, among rotating night shift workers.

### **Methods:**

This study included 37 male, rotating shift workers from the automotive industry in Barcelona, sampled twice at the end of a 3-week night-shift (22:00-06:00 hrs) and 3-week day-shift (06:00-14:00 hrs) rotation. Participants collected 24-hour urine voids, wore sensors, and responded to questionnaires during each shift. We examined melatonin production from urine samples, extracting the time of peak production using cosinor analysis, a curve fitting technique. Adaptation to night shift work was defined as the difference in the individual melatonin peak production time after 3 weeks of night shifts versus after 3 weeks of day shifts. We examined whether the following factors, measured during the night shift, were associated with adaptation: light intensity; sleep duration, onset and problems; chronotype; meal timing and frequency; demographic factors; and scheduling-related factors using linear models.

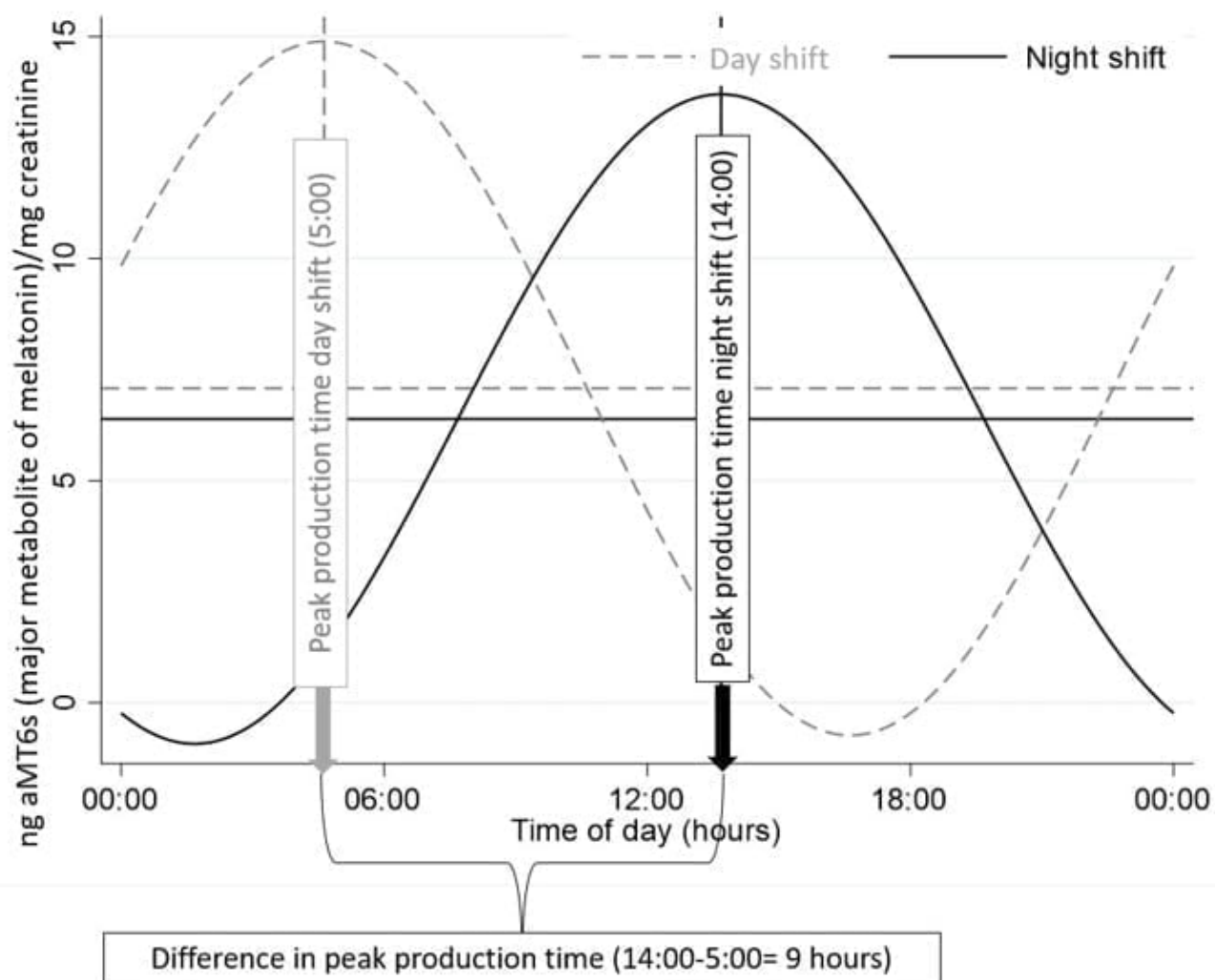
### **Results:**

Participants were 38 ( $\pm 8$ ) years of age. Melatonin peak production time was shifted by a median of 9.0 (IQR 7.1-10.5) hours during the night shift. When examining individual predictors of adaptation, we found that time of sleep onset (coeff 0.73, 95%CI 0.35, 1.10 per hour) and time of breakfast (coeff -0.29, 95%CI -0.55, -0.03 per hour) were associated with night shift work adaptation. Other factors were not associated with adaptation.

### **Conclusion:**

Time of sleep onset and time of breakfast were associated with night shift work adaptation in a slow backward rotating shift system. These results can inform sleep and meal timing interventions at the workplace to enhance circadian adaptation of shift workers.

**Figure:** How adaptation is defined in the present study using data from a hypothetical participant. Using the cosinor curves for urinary aMT6s levels, the major metabolite of melatonin, the major metabolite of melatonin, the peak production time is extracted during each shift for this participant and the difference in the individual peak production time is calculated.



**Occupational tasks associated with shoulder pain and upper extremity disability in the Johnston County Osteoarthritis Project** Elizabeth Yanik\* Elizabeth Yanik Carolina Alvarez  
Rebecca Cleveland Amanda Nelson Yvonne Golightly

Shoulder pain is a leading cause of disability. Occupations requiring high upper extremity demands may put workers at greater risk of shoulder injury and resulting pain. We examined associations of occupation with shoulder pain and upper extremity disability in the Johnston County Osteoarthritis Project (JoCoOA).

Work industry and occupational tasks for the longest job held were collected from JoCoOA participants. At a follow-up visit ranging from 4-10 years later, participants were asked about shoulder symptoms (pain, aching, or stiffness occurring most days of one month in the last year) and given a 9-item, modified Disabilities Arm Shoulder and Hand (DASH) questionnaire to categorize disability from none (0) to worst disability (4). Logistic regression and cumulative logit regression were used to estimate associations with prevalent shoulder symptoms and with worse category of disability, respectively. Models were adjusted for cohort, age, sex, race, education and time to follow-up visit. Associations stratified by sex and race were evaluated.

Shoulder outcomes and occupational data were available for 1560 JoCoOA participants with a mean age of 62 years (standard deviation=9 years). Of these, 32% were men, and 31% were Black. Compared to the managerial/professional industry, higher odds of both shoulder symptoms and worse upper extremity disability were seen for most industrial groups with physical-demanding jobs (Figure), particularly for the service industry. Work that often or always required lifting/moving >10 lb. objects was associated with higher odds of shoulder symptoms. Work that sometimes or always required heavy work standing in one place was associated with higher odds of shoulder symptoms (Figure), and this association was stronger among men and White workers.

Physically-demanding occupations were associated with increased occurrence of shoulder pain and disability. Mitigating specific physical work demands may reduce shoulder-related disability.

Figure: Associations of occupational exposures with shoulder symptoms and upper extremity disability in the Johnston County Osteoarthritis Project

Occupational exposure (modeled separately by exposure)		Shoulder Pain, Aching, or Stiffness	ModifiedDASH-9 score category
	N	OR (95% CI)*	OR (95% CI)†
<i>Occupational industry, Total N=1487</i>			
<i>Managerial and professional (ref)</i>	345	1.00	1.00
<i>Technical, sales, and administrative support</i>	421	1.12 (0.78, 1.60)	1.06 (0.81, 1.39)
<i>Operators, fabricators, and laborers</i>	313	1.68 (1.14, 2.48)	1.71 (1.25, 2.32)
<i>Service</i>	212	1.96 (1.28, 3.01)	2.23 (1.57, 3.15)
<i>Precision, production, craft, and repair</i>	183	1.45 (0.93, 2.28)	1.43 (0.99, 2.04)
<i>Farming, forestry, and fishing</i>	13	1.71 (0.50, 5.87)	0.88 (0.28, 2.70)
<i>Requires lifting, carrying, or moving objects weighing &gt;10 lbs, Total N=1555</i>			
<i>never (ref)</i>	203	1.00	1.00
<i>seldom</i>	315	1.00 (0.64, 1.58)	0.87 (0.63, 1.22)
<i>sometimes</i>	355	1.33 (0.86, 2.05)	1.04 (0.75, 1.43)
<i>often</i>	443	1.86 (1.22, 2.81)	1.14 (0.84, 1.57)
<i>always</i>	239	1.83 (1.15, 2.91)	1.29 (0.90, 1.87)
<i>Requires heavy work standing in one place, Total N=1446</i>			
<i>never (ref)</i>	881	1.00	1.00
<i>seldom</i>	228	0.88 (0.60, 1.27)	0.93 (0.71, 1.23)
<i>sometimes</i>	183	1.80 (1.26, 2.57)	1.39 (1.03, 1.89)
<i>often</i>	113	1.25 (0.79, 1.98)	1.35 (0.94, 1.96)
<i>always</i>	41	2.86 (1.48, 5.53)	1.49 (0.79, 2.81)
*Logistic model to produce adjusted ORs and (95% CI).			
†Partial proportional odds model using cumulative logits to produce adjusted OR (95% CI), with unequal slopes for education and race for the second model			
All models adjusted for baseline cohort, age, sex, race, education, and time to follow-up.			
OR=odds ratio; CI: confidence interval; ref=reference category			



## **Short-term impact of night shift work on resting heart rate among platform labours in South Korea** Juho Choi\* Juho Choi Jinha Yoon

- Background

Health and safety issues among platform labour have become an important social issue, but the studies that identified and analyzed the actual situation are rare.

Since it is well known that the incidence of various diseases, especially cardiovascular diseases, is significantly higher among night shift workers, it could be assumed that platform workers who work late at night are at higher risk of cardiovascular

Therefore, in this study, we investigated the short-term effects of the night-shift working hours on the resting heart rate measured by a wearable device among platform workers in South Korea.

### 2. Method

This study was conducted targeting designated drivers who work mainly at night among mobile platform workers. A wearable device "charge 4", developed by "Fitbit", was given and worn at all times as possible, through which the movement distance and heart rate were measured minute by minute.

The study subjects were recruited from January to February in 2022, and total 224 people participated in the study, and they wore the device for 16 weeks from March 23, 2022 to July 6, 2022.

Night shift status and night shift working hours were defined based on the distance. The time between 10:00 pm in a day and 6:00 am the next day was divided into 15-minute intervals, and when a significant movement distance (more than one meter per minute) was observed for more than 5 minutes out of 15 minutes, this period of 15 minute was defined as working hour. If total working hours were more than 2 hours, we consider that the subject worked in night in that day.

### 3. Result

For all night workers, the odds ratio for the risk of having a resting heart rate above one`s average increased significantly when the night shift working hours were 3 to 4, 4 to 5, and 6 to 8 hours, compared to those who worked 2 to 3 hours at night. In particular in the 6-8 hour night working group, the highest risk was observed compared to those who worked 2-3 hours in nights (OR=1.94, 95% CI 1.12-3.34).

### 4. Discussion

In this study, it was confirmed that the risk of resting heart rate increase above the one`s average was significantly higher for continuous night workers, especially those who worked for 3 consecutive nights and worked for more than 5 hours. However, no significant change was found with continuous night work or night work alone.

**The Relationship Between Early Economic Activity Loss and All-Cause Mortality in Young Age Workers** Byungyoon Yun\* Byungyoon Yun Juyeon Oh Jin-Ha Yoon

This study aims to examine the relationship between early economic activity loss and all-cause mortality among young age workers. This study retrospectively included participants (aged 30–39) who were first employed (including self-employed) in 2009–2011 and have never been employed before, using the National Health Insurance Service Database in Korea. Early economic activity loss was defined as participants who were unemployed or left work within 2 years. Adjusted Hazard ratios (HRs) and 95% confidence interval (CIs) of all-cause mortality by early economic activity loss stratified by gender were estimated using Cox proportional hazard models, adjusting for age, gender, income, region, disability grade, charlson comorbidity index, health service participation, and industrial classification. Among 500,545 participants (median 12-year follow-up, 53.0% women), death occurred in 4,385 participants. The proportion of early loss of economic activity were significantly higher in women, compared with men (35.7% vs. 22.9%;  $p < 0.001$ ). The proportion of early economic activity loss was significantly higher in health service non-participation group in both men and women, compared with participation group (32.3% vs 9.5% in men; 46.6% vs. 22.0% in women; all  $p < 0.001$ ). The 10-year cumulative incidences of all-cause mortality were significantly higher in early economic activity loss group in men but not in women (0.7% vs. 1.1% in men; all 0.4% in women). Adjusted HR (95% CI) of all-cause mortality by early economic activity loss was 1.31 (1.20–1.42) in men and 0.91 (0.82–1.01) in women, which infers gender difference. Our result found that early loss of economic activity is significantly associated with all-cause mortality in men but not women. Further studies regarding the gender difference on the association of economic activity status with health outcomes are needed with detailed information.

**A cross-sectional analysis of depression and precarious work scheduling practices** Colin Hawkinson\* Colin Hawkinson Sarah Vanessa Oddo Anjum Hajat Anita Minh Shanise Owens Jessie Seiler

**Background:** Last-minute scheduling practices - where workers are given little or no notice, are expected to accept last-minute cancellations, and accommodate extra shifts - have become increasingly prevalent, which may have implications for mental health. Because of gendered division of caretaking and other domestic-labor responsibilities, as well as occupational segregation, women may be disproportionately exposed to precarious scheduling practices and in turn, the deleterious consequences for mental health.

**Objective:** To describe how work schedule notice is distributed by sociodemographic characteristics and examine the association between work scheduling notice and prevalence of depressive symptoms.

**Methods:** In a cross-sectional, gender-stratified analysis of 2019 data from the National Longitudinal Study of Youth 1997 (N=4,963), we modeled the association between work schedule notice ( $\leq 2$  weeks,  $> 2$  weeks, consistent scheduling) and depressive symptoms (Center for epidemiologic studies of depression short form  $\geq 10$ ,  $< 10$ ) with multivariable modified poisson regression. We further evaluated whether the association was heterogeneous by work hour variability.

**Results:** Compared to respondents reporting  $> 2$  weeks schedule notice, those reporting  $\leq 2$  weeks schedule notice were disproportionately non-Hispanic Black or Latinx, disproportionately resided in the South and/or in a rural area. Depression was 39% more prevalent among women with schedule notice of  $\leq 2$  weeks compared to those with  $> 2$  weeks notice (*Prevalence Ratio (PR): 1.39*, 95% CI: 1.07, 1.80); no association was observed among men.

**Conclusions:** Policies to reduce precarious schedules are gaining popularity in the U.S. These policies should be evaluated for their impacts on mental health, especially among women.

**LATEBREAKER**

Occupational

**Association Between Shiftwork and Modifiable Psychosocial Workplace Exposures Among U.S. Working Adults** Desta Fekedulegn\* Desta Fekedulegn Gu Service Charles Violanti

**Objective:** Shiftwork is linked to adverse physical and mental health outcomes. The relation of shiftwork to psychosocial workplace exposures, factors that also contribute to stress, anxiety, depression, and lower productivity, is inadequately explored. We examined whether shift workers experience higher levels of hostile work environment (HWE) and low supervisory support (LSS) relative to their counterparts.

**Methods:** The study sample included all employed sample adults from the 2015 National Health Interview Survey (NHIS) (n=17,379). Questionnaire data were used to determine shiftwork (day, non-day), HWE (yes/no), and LSS (yes/no). Prevalence estimates and unadjusted and adjusted prevalence ratios (PRs) were derived using SUDAAN software to account for the complex sample design. Analysis was stratified by sex and race/ethnicity.

**Results:** Overall, prevalence of HWE was 94% higher in shift workers compared to those on day shift (PR=1.94,95%CI:1.67-2.26). This relationship was consistent across sex (males: PR=2.12,CI:1.69-2.66); females: PR=1.86,CI:1.52-2.27) but varied by race; statistically significant in Whites (PR=2.22,CI:1.83-2.70) and other races (PR=2.97,CI:1.75-5.03) but not in Blacks and Hispanics. Similarly, prevalence of LSS was 24% higher in shift workers relative to those on day shift (PR=1.24,CI:1.09-1.42) and was consistent across sex (males: PR=1.24,CI:1.01-1.52); females: PR=1.27,CI:1.06-1.51) but significant only among Whites and other races. Adjustment for demographic and lifestyle factors and work hours did not attenuate these associations.

**Conclusion:** Shift workers, irrespective of sex, experienced higher levels of hostile work environment and low supervisory support compared to day shift workers. High levels of modifiable psychosocial exposures in shift workers may compound the adverse health effects of shiftwork and should be addressed by organizations and managers. Further research is needed to understand racial differences in the associations.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Risk factors for orofacial clefts among Hispanic individuals in the United States** Erin Sley\*  
Erin Sley Tania Desrosiers Joanna Maselko Suzan Carmichael Daniela Stores-Alvarez Mollie Wood  
A.J. Agopian Mark Canfield Mimi Le Andrew Olshan

**Background**

Orofacial cleft (OFC) prevalence varies by ethnicity in the United States (US), yet most studies evaluate risk factors in populations with a large proportion of non-Hispanic White (NHW) persons. The US Hispanic population is diverse, partially because 30% are foreign-born persons. Using data from the National Birth Defects Prevention Study (NBDPS), we assessed OFC risk factors among Hispanic persons and considered the impact of acculturation.

**Methods**

NBDPS is a large case-control study in the US (1997-2011). Our analysis included 937 cases with OFCs (n=684 cleft lip with/without palate [CL/P] and 253 cleft palate alone [CP]) and 2,794 controls born to self-identified Hispanic persons. Acculturation was measured by the Proxy Acculturation Scale (PAS-3), which incorporates language spoken at home, interview language, and proportion of life lived in the US. Adjusted ORs (aORs) with 95% CIs were estimated using logistic regression to evaluate 16 risk factors ascertained during the NBDPS interview. Effect measure modification by acculturation was assessed on the additive scale for smoking, folic acid supplementation, education, and prenatal care.

**Results**

Among our sample, 35.4% completed the NBDPS interview in Spanish, 37.2% spoke Spanish at home, and 35.0% had a low (vs. high) PAS-3 score. For CL/P, the strongest associations were for pregestational diabetes (aOR=3.1, CI:1.5-6.5) and secondhand smoke (aOR=1.4, CI:1.1-1.7). For CP, the strongest associations were for secondhand smoke (aOR=1.6, CI:1.2-2.3) and high acculturation (aOR=1.5, CI:1.1-2.0). Individuals with high acculturation and <12 years of education (vs. ≥12 years) had a CP aOR of 1.5 (CI:0.9-2.6) but an expected aOR of 2.7, indicating a sub-additive effect.

**Conclusion**

Additional research that considers heterogeneity among Hispanic persons by acculturation may help identify these risk factor patterns and, subsequently, inform public health efforts to reduce OFC incidence in this population.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Risk of Stillbirth by Gestational Age for Fetuses with Specific Birth Defects** Dominique Heinke\* Dominique Heinke Anne Marie Darling Eirini Nestoridi Wendy Nembhard Susan Carmichael Drucilla Roberts Angela Lin Mahsa Yazdy

Increased fetal monitoring could prevent stillbirth of fetuses with major malformations, but data on stillbirth risk by gestational age are needed to inform clinical practice. We identified a population-based cohort of 19,176 infants and fetuses (liveborn, stillborn, or terminated) with selected major birth defects (without genetic disorders) from active surveillance programs in 9 states during 1997-2011. Clinical geneticists confirmed and classified all birth defects using abstracted medical records. We categorized gestational age (GA) as: 20-28, 29-34, 35-36, 37-40, and 41-42 completed weeks. To smooth random variability from small numbers, we estimated the stillbirth risk by GA as the conditional risk of stillbirth during the remaining pregnancy (i.e., number of stillbirths in the GA category or later divided by the number of fetuses at risk [FAR] at the start of the GA category). We summarized the level of stillbirth risk (per 1000 FAR) as follows: extreme ( $\geq 100$ ), very high (20-99), high (4-20), moderate (1-4), and low ( $< 1$ ). Stillbirth risk was highest during 20-28 weeks for all defects and lowest during 35-36 or 37-40-weeks for most defects. The stillbirth risk was extreme across all GAs for fetuses with anencephaly, bilateral renal agenesis, and limb-body-wall complex. Stillbirth risk for fetuses with amniotic bands (limbs only) and omphalocele decreased from extreme to high. Risk decreased from very high to high for those with encephalocele, small intestinal atresia/stenosis, gastroschisis, limb deficiency, holoprosencephaly, spina bifida, Dandy-Walker malformation, diaphragmatic hernia and cleft lip with cleft palate. Fetuses with esophageal atresia had a high stillbirth risk across all GAs, while the risk decreased from high to moderate for those with hydrocephaly and cleft lip or palate alone. These estimates may be of immediate value for parent counseling and informing the timing of additional monitoring for affected pregnancies.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Prenatal Phthalate Exposure and Anogenital Distance in Male and Female Infants at 12 Months** Nicole Salvi\* Nicole Salvi Yuyan Wang, PhD Mengling Liu, PhD Linda G. Kahn Leonardo Trasande, MD, MPP Akhgar Ghassabian, MD, PhD

**Introduction**

Anogenital distance (AGD) is a proxy measure for *in utero* androgen exposure. Higher exposure to phthalates—commonly used plasticizers that are known endocrine disruptors—during the fetal period of sexual development has been associated with shorter AGD in males. The impact of prenatal phthalate exposure on female AGD is understudied.

**Methods**

Data were from the NYU Children's Health and Environment Study, a NYC birth cohort (2016-2019). Phthalate metabolites were quantified in maternal urine samples collected at <18 weeks of gestation. We measured anus to clitoris (AGD<sub>AC</sub>) and anus to fourchette (AGD<sub>AF</sub>) distances in female infants, and anus to scrotum (AGD<sub>AS</sub>) distance, anus to penis (AGD<sub>AP</sub>) distance, and penis width in male infants around 12 months. We examined associations of 12 phthalate metabolites, phthalic acid, and 2 phthalate groupings,  $\Sigma$ di(2-ethylhexyl)phthalate (DEHP) metabolites and  $\Sigma$ anti-androgenic phthalates, with infant AGD, adjusted for infant age, weight-for-length Z scores, and urinary dilution.

**Results**

416 infants had both phthalate exposure and AGD data (214 males and 202 females). In males, higher mono(carboxy-isononyl) phthalate (mCINP) was associated with shorter AGD<sub>AP</sub> (parameter estimate,  $b=-0.329$ , 95%CI: -0.585, -0.072) and higher monobutyl phthalate (mBP) with shorter penile width ( $b=-0.002$ , 95% CI: -0.004, -0.0001). In female infants, higher mBP and mono-isobutyl phthalate (mIBP) were associated with longer AGD<sub>AC</sub> ( $b=0.024$ , 95%CI: 0.0003, 0.048 and  $b=0.023$ , 95%CI: 0.001, 0.045, respectively). We observed a negative association between  $\Sigma$ anti-androgenic phthalates and penile width in male infants and a positive association between  $\Sigma$ anti-androgenic phthalates and AGD<sub>AC</sub> in female infants.

**Conclusion**

Negative associations of phthalate exposure with AGD<sub>AP</sub> and penile width in male infants and positive associations with AGD<sub>AC</sub> in female infants suggest that the effect of prenatal phthalate exposure on fetal reproductive development varies by sex.



**The timing, duration, and severity of nausea and vomiting of pregnancy and adverse birth outcomes in the National Birth Defects Prevention Study** Nina Schrager\* Nina Schrager  
Martha Werler Samantha Parker

**Background:** Nausea and vomiting of pregnancy (NVP) occurs in approximately 70% of women, with varying severity and duration. Observed associations between NVP and birth outcomes, including preterm birth, small for gestational age (SGA), and low birth weight are inconclusive.

**Objective:** To determine whether NVP is associated with adverse birth outcomes.

**Methods:** We used ten years of control data from the population-based, multisite National Birth Defects Prevention Study (1997-2006) to evaluate whether self-reported NVP according to timing, duration, and severity was associated with preterm birth (<37 weeks), SGA (<10%ile), and low birth weight (<2500 grams). A novel composite score (0-10 points) assigned greater severity to more frequent symptoms and to vomiting over nausea. Scores were categorized as mild (1-3), moderate (4-7), and severe (8-10) for each trimester. Odds ratios (aOR) and 95% confidence intervals (CI) were adjusted for sociodemographic, reproductive (e.g., parity, folic acid use), and medical factors (e.g., diabetes, hypertension, smoking, BMI).

**Results:** Neither mild nor first trimester NVP was associated with any of the outcomes of interest. Compared to people with no NVP at any point of pregnancy, odds of preterm birth were increased for people with any second trimester NVP (aOR: 1.21, 95% CI: 1.00, 1.46), any third trimester NVP (aOR 1.47, 95% CI: 1.22, 2.00), and NVP lasting all three trimesters of pregnancy (aOR: 1.49, 95% CI: 1.10, 2.03). Severe third trimester NVP was associated with increased odds of SGA (aOR: 1.55, 95% CI: 1.08, 2.24) and preterm birth (aOR: 1.54, 95% CI: 1.08, 2.20). Neither trimester-specific NVP nor severe NVP were associated with low birth weight (aORs ranged from 0.82 to 1.05).

**Conclusion:** Mild NVP and NVP limited to early pregnancy appear to have no effect on preterm birth, SGA, or low birth weight. Long-lasting NVP, severe NVP, and NVP later in pregnancy are associated with increased risk of preterm birth and SGA.

**Using Perinatal Periods of Risk Analysis to Identify Disparities in Fetal-Infant Mortality Rates in Pennsylvania, 2009-2018** Zeinab Baba\* Zeinab Baba Heather Edelblute

**Background:** Reducing infant mortality is an objective of Healthy People 2030. In 2018-2019 Pennsylvania's infant mortality rate was 25th nationally. Identifying disparities in fetal-infant mortality rates (FIMR) through a Perinatal Periods of Risk (PPOR) analysis provides avenues for addressing disparities at four stages of fetal and infant development.

**Methods:** The sample consisted of deaths reported in fetal and linked birth-death records in Pennsylvania for 2009-2018 grouped into 5-year time periods. Analyses were performed using SAS version 9.4. Implausible combinations of birthweight and gestational age were excluded along with records with fetal death < 24 weeks or birthweight < 500 grams. The reference group were fetal and infant deaths to mothers who were residents of Pennsylvania, non-Hispanic White, age 20 or older, and with a high school diploma or more (n=4,528). The target group were fetal and infant deaths to non-Hispanic Black mothers in Pennsylvania (n=2,274). FIMR per 1,000 for each PPOR section was calculated.

**Results:** Excess mortality in the target group for each PPOR section was calculated by subtracting the FIMRs for the reference group from the target group. The maternal health/prematurity section saw an increase in FIMRs over time. The maternal care section showed a slight decrease in excess mortality over time and the newborn care section saw elimination of excess mortality. Excess mortality decreased in the infant care section over time though the disparity was not eliminated. Overall, the total FIMRs decreased but excess mortality increased from 2.32 per 1,000 in 2009-2013 to 2.42 per 1,000 in 2014-2018.

**Conclusions:** There has been progress in reducing FIMRs in Pennsylvania and the PPOR analysis indicates there is excess mortality in non-Hispanic Black women related to maternal health and infant prematurity. Further investigations are needed to identify maternal and child factors where public health interventions can reduce this disparity.

Perinatal Periods of Risk – **EXCESS IN TARGET GROUP COMPARED TO REFERENCE** – Pennsylvania (2009-2013 and 2014-2018)

	Fetal Death (24 weeks and older)	Neonatal (0-27 days)	Post-natal Death (28-364)
Birthweight (500g-1,499g)	<b>Maternal health/prematurity</b> 2009-2013 excess FIMR = 2.32 2014-2018 excess FIMR = 2.42		
Birthweight (1,500+ g)	<b>Maternal Care</b> 2009-2013 excess FIMR = 0.30 2014-2018 excess FIMR = 0.28	<b>Newborn Care</b> 2009-2013 excess FIMR = 0.36 2014-2018 excess FIMR = 0.00	<b>Infant Health</b> 2009-2013 excess FIMR = 1.58 2014-2018 excess FIMR = 1.12
	2009-2013 Overall Excess Fetal-Infant Mortality Rate = 4.56 per 1,000 2014-2018 Overall Excess Fetal-Infant Mortality Rate = 3.82 per 1,000		

\*FIMR is per 1,000

**Maternal Postpartum Depressive Symptoms and Infant Growth Indices** Xuanxuan Zhu\*

Xuanxuan Zhu Jihong Liu Prema S. Bhattacharjee Bo Cai Sara Wilcox

**Background.** Previous studies are inconclusive about associations between maternal postpartum depression and infant growth. Most studies have examined major postpartum depression and ignored subclinical postpartum depressive symptoms. Further, many studies have focused on mothers with normal pre-pregnancy body mass index, even though women with overweight/obesity are more likely to have elevated postpartum depressive symptoms. This study aims to evaluate the longitudinal effect of maternal depressive symptoms among overweight/obese mothers on infant growth in the first year of life.

**Methods.** Data came from a randomized controlled trial designed to promote healthy weight gain during pregnancy and postpartum weight loss among women who were overweight/obese before pregnancy. The Edinburgh Postpartum Depression Scale (EPDS) assessed depressive symptoms at 6 months after delivery. Infants' weight, length, head circumference, arm circumference, triceps skinfold, and subscapular skinfold were measured at 6- and 12-postpartum months. Their z-scores were obtained to show the growth indices. Linear mixed models were used to assess the aforementioned association.

**Results.** Of 170 mother-infant dyads, the mean age of mothers was 29.9 years ( $\pm$  5.0) with 43.5% being Black. The mean EPDS score was 4.1 ( $\pm$  4.2). After adjusting for covariates, EPDS scores were negatively associated with infants' mean of length-for-age z-scores at 12-months of age ( $\beta$  = -0.05, 95% CI: -0.09, -0.01, p-value = 0.01). Maternal depressive symptoms were not associated with other infant growth indices at either 6- or 12- months postpartum.

**Conclusion.** Having more postpartum depressive symptoms was negatively associated with infant's length during the first year of life. It is necessary to raise awareness among women and their families to pay more attention to maternal mental health since better mental health is not only good for mothers but also translates to better growth outcomes for infants.

**Pregnancy and birthing experiences of young adult Black pregnant women during COVID-19: Qualitative findings of desired pregnancy supports** Ashley Hill\* Ashley Hill Phoebe Balascio Mikaela Moore Fahmida Hossain Natacha De Genna

**Introduction:** The purpose of this work is to document pregnancy and birthing experiences of young, Black pregnant women during the COVID-19 pandemic in one geographic area to make recommendations for improving young Black women's pregnancy and birthing experiences.

**Methods:** Participants for this research were recruited through The YoungMoms Study (R01 DA04640101A1, PI De Genna), and included Black or biracial participants ages 16-23. Individual interviews were conducted to assess pre-, peri-, and post-natal healthcare system encounters; experiences of structural and obstetric racism and discrimination in healthcare settings while obtaining prenatal care; attitudes around healthcare systems and medical professionals; effects of COVID-19 pandemic on participants lives and the impact of enacted healthcare policies in their perinatal experience; substance use changes during pregnancy; and coping mechanisms for stress.

**Results:** Four themes emerged from participant experiences of racial discrimination in healthcare settings; (1) awareness of historical racism that influences perinatal care; (2) clinical providers assume participant substance use and enact contraceptive coercion; (3) clinical providers question validity of Black women's birthing complaint; and (4) Young Black pregnant women know and will express what they desire in their perinatal experience if asked.

**Conclusions:** This study identified consistent themes around young Black women's encounters with structural racism and intersectional bias from healthcare providers during the COVID-19 pandemic. By centering the perspectives and experiences of this overlooked population, public health researchers and clinical providers can utilize anti-racist frameworks to create more equitable, just practices in reproductive healthcare.

**Periconceptional intakes of micronutrients involved in folate metabolism may further reduce risk of neural tube defects in offspring: A United States population-based case-control study of women meeting the folic acid recommendations**

Julie M. Petersen\* Julie Petersen Rashida S. Smith-Webb Gary M. Shaw Suzan L. Carmichael Tania A. Desrosiers Eirini Nestoridi Anne Marie Darling Samantha E. Parker Maria D. Politis Mahsa M. Yazdy Martha M. Werler

**Background.** Neural tube defects (NTDs) occur in offspring of some women who consume folic acid for prevention. Other micronutrients involved in methylation or folate metabolism may further protect against NTDs. We investigated whether intakes of B6, B12, choline, betaine, methionine, thiamine, riboflavin, and zinc, alone or in combination, were associated with NTD risk in offspring of women meeting the folic acid recommendations.

**Methods.** Data were from the National Birth Defects Prevention Study (US population-based, case-control), restricted to 1999-2011 deliveries with daily maternal periconceptional folic acid supplementation or estimated dietary folate equivalents  $\geq 400$   $\mu\text{g}$ . Cases were NTD-affected livebirths, stillbirths, or terminations ( $n=1227$ ). Controls were livebirths without a major birth defect ( $n=7095$ ). Each micronutrient was categorized as higher or lower intake based on food frequency questionnaire data and self-reported supplement use. We estimated NTD associations for higher versus lower intake of each micronutrient with ORs and 95% CIs, adjusted for age, race/ethnicity, education, and study center. In secondary analysis, we stratified by offspring sex.

**Results.** NTD associations were weak to modest for each micronutrient in isolation but were considerably stronger with concurrent higher intakes of multiple micronutrients. For instance, NTD odds were halved with higher intakes of  $\geq 4$  versus  $\leq 1$  of the micronutrients (OR 0.53, 95% CI 0.33, 0.86). The strongest association was observed with concurrent higher intakes of B6, B12, choline, betaine, and methionine (OR 0.26, 95% CI 0.09, 0.77) compared with higher intake of  $\leq 1$  micronutrient (Figure). Associations comparing higher intakes of  $\geq 4$  versus  $\leq 1$  of the micronutrients were slightly stronger among females.

**Conclusion.** Our findings support that NTD prevention, in the context of folic acid fortification, can be augmented through intakes of methyl donors and other micronutrients involved in folate metabolism.

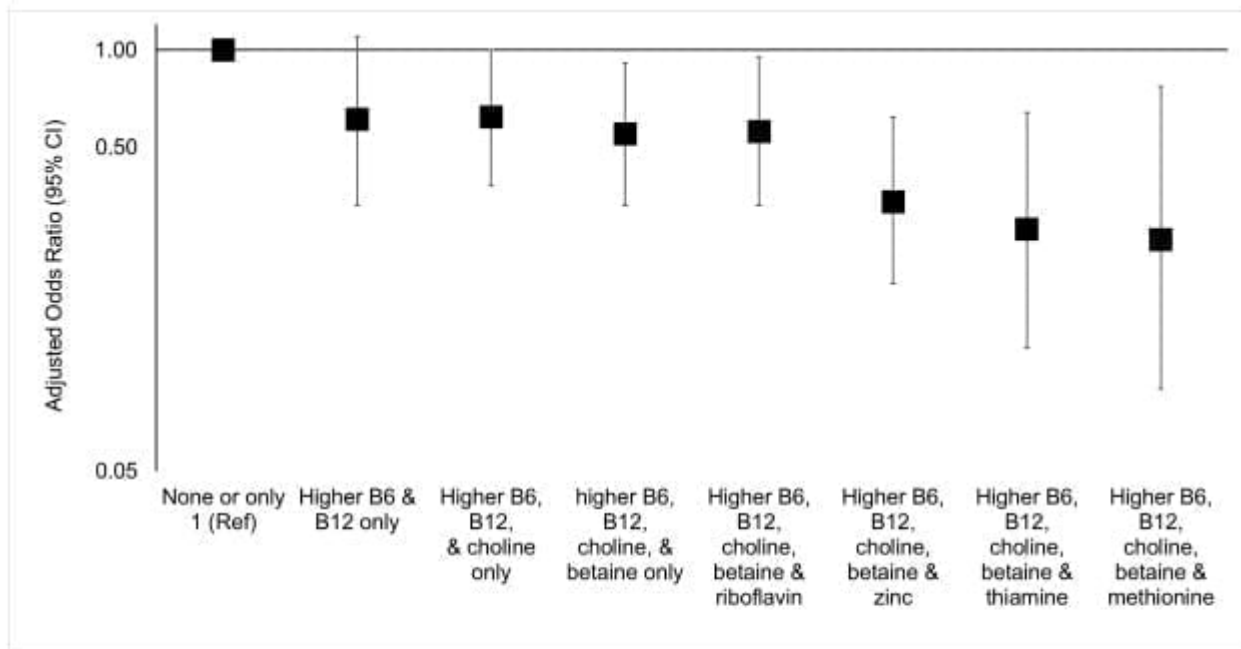


Figure. Neural Tube Defect Associations for Specific Groups with Concurrent Higher Intakes of Methyl Donors and Other Micronutrients Involved in Folate Metabolism

Data were from the National Birth Defects Prevention Study (1999-2011). To categorize each micronutrient intake (as higher or lower intake), we used a combination of information from diet and supplements. ORs and 95% CIs were estimated using unconditional logistic regression with Firth's penalized likelihood adjusted for age, race/ethnicity, education, and study center. The y axis is on the log scale. The reference group for all comparisons is intake in the higher range for none or only one of the micronutrients of interest.

**Chronic hypertension during pregnancy and adverse obstetrical and neonatal outcomes**

Stephanie Leonard\* Stephanie Leonard Brielle L. Formanowski Ciaran S. Phibbs Scott A. Lorch  
Elliott K. Main Katy Backes Kozhimannil Molly Passarella Brian T. Bateman

**Objectives.** Our study objective was to evaluate associations between chronic hypertension and adverse obstetrical and neonatal outcomes. **Methods.** This population-based study used linked vital record and patient discharge data from all live and stillbirths occurring in California (2008-2018), Michigan (2008-2020), Pennsylvania (2008-2014), and South Carolina (2008-2020). We used multivariable log-binomial regression models to estimate risk ratios and population attributable risk (PAR) percentages with 95% confidence limits for associations between chronic hypertension and several obstetrical and neonatal outcomes, selected based on prior evidence and pathological pathways. We adjusted models for demographic factors (race/ethnicity, payment method, educational attainment), age, and body mass index, and conducted analyses stratified by race/ethnicity. **Results.** The study included 7,463,325 births, of which 167,777 (2.2%) were complicated by chronic hypertension. Chronic hypertension was associated with several adverse obstetrical and neonatal outcomes (Table), with the largest PAR percentages observed for preeclampsia/eclampsia (26.9; 95% CI: 26.7, 27.1), acute renal failure (19.7; 95% CI: 18.6, 20.8), and pulmonary edema (13.1; 95% CI: 11.1, 15.1). Estimated risk ratios were overall similar across racial/ethnic groups, but PAR percentages varied. The adjusted PAR percentages (95% CI) for severe maternal morbidity—a widely used composite of acute severe events—for people who were American Indian, Asian, Black, Latinx, Pacific Islander, White, and Multirace/other were 6.1 (1.4, 10.6), 4.8 (4.1, 5.5), 12.1 (11.2, 12.9), 5.1 (4.7, 5.4), 15.5 (9.5, 21.1), 4.2 (3.8, 4.5), and 7.2 (5.7, 8.8), respectively. **Conclusion.** Chronic hypertension in pregnancy substantially increases the risk of many adverse obstetrical and neonatal outcomes, and contributes to racial/ethnic disparities in these outcomes for people who are Black or Pacific Islander.



**Table. Associations between chronic hypertension and obstetrical and neonatal outcomes.**

<b>Outcome</b>	<b>Crude RR (95% CI)</b>	<b>Adjusted RR (95% CI)</b>	<b>Adjusted PAR % (95% CI)</b>
<b>Obstetrical</b>			
Preeclampsia/eclampsia	17.8 (17.6, 17.9)	13.9 (13.7, 14.0)	26.9 (26.7, 27.1)
Mode of birth			
Spontaneous vaginal	Reference	Reference	Reference
Operative vaginal	0.88 (0.85, 0.91)	1.03 (0.99, 1.06)	0.04 (-0.01, 0.08)
Unplanned cesarean	2.48 (2.45, 2.51)	1.44 (1.42, 1.45)	1.13 (1.10, 1.16)
Planned cesarean	2.51 (2.48, 2.54)	1.33 (1.32, 1.34)	0.94 (0.91, 0.96)
Placental abruption	1.90 (1.83, 1.97)	1.83 (1.76, 1.90)	1.90 (1.74, 2.05)
Postpartum hemorrhage	2.11 (2.04, 2.17)	1.80 (1.74, 1.85)	2.05 (1.91, 2.19)
Cerebrovascular event	6.62 (6.08, 7.21)	4.91 (4.46, 5.40)	10.5 (9.50, 11.5)
Pulmonary edema	8.03 (6.94, 9.30)	6.36 (5.35, 7.55)	13.1 (11.1, 15.1)
Acute renal failure	12.3 (11.5, 13.1)	9.56 (8.84, 10.3)	19.7 (18.6, 20.8)
Severe maternal morbidity	4.10 (3.98, 4.23)	3.31 (3.20, 3.42)	6.01 (5.76, 6.26)
<b>Neonatal</b>			
Stillbirth	2.30 (2.15, 2.47)	1.97 (1.83, 2.12)	2.51 (2.16, 2.86)
Small-for-gestational age ( $<10^{\text{th}}$ percentile)	1.47 (1.46, 1.49)	1.61 (1.59, 1.63)	1.26 (1.22, 1.30)
Gestational age at birth			
23-27 wk	5.20 (5.02, 5.39)	3.85 (3.70, 4.00)	6.54 (6.25, 6.83)
28-31 wk	5.91 (5.75, 6.06)	4.96 (4.82, 5.10)	7.91 (7.68, 8.15)
32-36 wk	3.38 (3.34, 3.42)	2.95 (2.91, 2.99)	3.61 (3.56, 3.67)
37-42 wk	Reference	Reference	Reference
Birthweight			
$<1500$ g	6.18 (6.05, 6.32)	4.98 (4.86, 5.10)	8.50 (8.30, 8.71)
1500-2499 g	3.16 (3.12, 3.20)	3.03 (2.99, 3.08)	3.65 (3.58, 3.71)
$\geq 2500$ g	Reference	Reference	Reference
Congenital anomaly			
Cardiovascular	2.44 (2.21, 2.69)	2.58 (2.33, 2.87)	3.27 (2.75, 3.78)
Other anomaly	2.68 (2.54, 2.82)	2.63 (2.49, 2.78)	3.62 (3.33, 3.92)
None	Reference	Reference	Reference

CI, confidence interval; PAR, population attributable risk; RR, risk ratio

**Adverse Birth Outcomes: A Comparative Analysis among Black Mothers enrolled in Des Moines, Iowa Healthy Start Initiative** Kendria Kelly-Taylor\* Kendria Kelly-Taylor Anne Wallis Kira Taylor Muriel Harris Brian Guinn Cynthia Winn

Existing population-based studies suggest foreign-born (FB) Black women present more favorable birth outcomes in comparison to US-born (USB) Black women with varying risk profiles. Limited literature has investigated this relationship among mothers who participate in Healthy Start; a federally funded program initiated to reduce infant morbidity and mortality in high-risk communities in the US. This study sought to explore the relationship between maternal nativity status and adverse birth outcomes, preterm birth (PTB), and small for gestational age (SGA) among Black mothers who participated in Des Moines Healthy Start Initiative. Secondary data from the years 2000 to 2021 (n= 1,233) were ascertained. Mothers who self-identified as Black/African American with a singleton live birth and 18 years or older were included in the analysis. Multivariable logistic regression models were utilized. Analysis was done using SAS 9.4. Among the sample, 904 (73.3%) were USB, and 329 (26.7%) were FB. There was a significant difference (p-value <.05) in education, marital status, prenatal care (PNC), parity, and drug and alcohol use. FB mothers reported a higher proportion of marriage (58.4% vs 28.1%), income level above \$20,000 (53.3% vs 17.81%), and prenatal care (60.5% vs.46.9%). A significant difference was observed in PTB rates among USB (18.4%) and FB (11.9%) mothers (p-value <.0085). The odds of PTB were 65% time higher among USB mothers (cOR:1.65 CI: 1.2-2.4), yet; the effect attenuates in the final model adjusting for income, marital status, maternal age, PNC, and drug/alcohol use (OR:1.18 CI: 0.8-1.8). No significant association was observed for SGA. The findings suggest that socioeconomic and behavioral risk factors influence adverse birth outcomes, irrespective of nativity status, among this study population. The findings support the development of culturally appropriate programmatic interventions that target risk factors specified to Des Moines, Healthy Start clientele.

**Association between gestational weight gain and three-dimensional fetal organ volumes in the NICHD Fetal 3D Study** Kathryn Wagner\* Kathryn Wagner Zhen Chen Stefanie Hinkle Jessica Gleason Wesley Lee William Grobman Roger Newman John Owen Daniel Skupski Daniel He Roger Gore-Langton Seth Sherman Cuilin Zhang Jagteshwar Grewal Katherine Grantz

Inadequate and excessive gestational weight gain (GWG) are associated with smaller and larger estimated fetal weight (EFW), respectively. However, it is unclear whether GWG's association with EFW is due to a global increase or specific fetal measures.

The NICHD Fetal 3D Study was a diverse, prospective US pregnancy cohort. Maternal pre-pregnancy weight was self-reported and subsequent weight was measured at each study visit and abstracted from prenatal records (median=19 measures). Up to five 3D ultrasounds were completed across gestation, from which fetal organ volumes were obtained. Among pregnancies with at least one GWG and ultrasound measure (n=2158), linear mixed models were used to separately estimate fetal organ volumes and maternal weight trajectories across gestation. Estimated GWG at the end of each trimester was defined as "inadequate," "adequate," or "excessive" based on the 2009 IOM guidelines. Linear regression was used to examine the association between trimester-specific GWG categories and fetal organ volumes at 14-, 28-, and 39-weeks' gestation, adjusted for known covariates.

Inadequate, compared to adequate, second trimester GWG was associated with a smaller lung volume (Table). In a sensitivity analysis among those delivering at term and without pregnancy complications (n=1519), findings persisted. Specifically, inadequate, compared to adequate, first trimester GWG was associated with a smaller lung volume and lung volume:EFW ratio (Table). There were no associations between GWG categories and all other organ volumes (e.g., cerebellar, kidney, & liver volumes and volume:EFW ratios).

Inadequate GWG up to 28 weeks' gestation was associated with smaller lung volume in a diverse pregnancy cohort with repeated GWG and 3D ultrasound measures. Prior studies have found that inadequate GWG is associated with increased risk of offspring asthma, but it is unknown whether smaller fetal lung volumes translate to changes in short- and long-term function.

Table. Adjusted association between adequacy of gestational weight gain according to the Institute of Medicine's 2009 guidelines and fetal 3D organ volumes at each trimester; Fetal 3D Study.

Fetal Growth Outcome	n	First Trimester - IOM Guidelines				Second Trimester - IOM Guidelines				Third Trimester - IOM Guidelines			
		Inadequate vs. Adequate		Excessive vs. Adequate		Inadequate vs. Adequate		Excessive vs. Adequate		Inadequate vs. Adequate		Excessive vs. Adequate	
		$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value	$\beta$ (95% CI)	p-value
<b>Total Analytic Sample<sup>a</sup></b>													
Lung volume, cm <sup>3</sup>	513	-0.01 (-0.07, 0.05)	0.74	-0.01 (-0.06, 0.04)	0.68	<b>-1.17</b> <b>(-2.07, -0.27)</b>	<b>0.01</b>	0.15 (-0.71, 1.00)	0.73	-0.85 (-2.23, 0.53)	0.23	0.36 (-1.08, 1.80)	0.63
Lung volume: EFW	510	-0.0004 (-0.001, 0.0001)	0.11	-0.0003 (-0.0007, 0.0001)	0.19	-0.0005 (-0.001, 0.0001)	0.08	0.0001 (-0.0005, 0.0007)	0.71	-0.0003 (-0.0006, 0.0001)	0.20	0.0001 (-0.0003, 0.0005)	0.60
<b>Standard Population<sup>b</sup></b>													
Lung volume, cm <sup>3</sup>	366	<b>-0.07</b> <b>(-0.14, -0.002)</b>	<b>0.04</b>	-0.009 (-0.06, 0.05)	0.74	-0.80 (-1.74, 0.13)	0.09	-0.05 (-1.01, 0.92)	0.92	-0.88 (-2.37, 0.62)	0.25	-0.89 (-2.58, 0.80)	0.30
Lung volume: EFW	364	<b>-0.0008</b> <b>(-0.002, -0.0002)</b>	<b>0.01</b>	-0.0004 (-0.0009, 0.0001)	0.13	-0.0005 (-0.001, 0.0002)	0.14	-0.0001 (-0.0008, 0.0006)	0.80	-0.0003 (-0.0007, 0.0001)	0.16	-0.0003 (-0.0008, 0.0002)	0.19

Boldface indicates statistical significance at <0.05

Adjusted for: maternal age, race/ethnicity, education, parity, infant sex, cotinine, and gestational weight gain in the previous time period (where applicable)

<sup>a</sup>Total analytic sample excludes women missing all gestational weight gain and fetal 3D ultrasound measures, without a live birth (i.e., congenital malformations, miscarriage, or pregnancy termination), and who were lost to follow-up, refused, moved, or were ineligible after enrollment.

<sup>b</sup>Standard population excluded women with pregnancy complications, including preterm delivery (<37 weeks), gestational diabetes, and hypertensive disorders, and neonatal conditions including congenital anomalies and death.

**Does Selection Bias Explain Reduced Odds of Hypospadias with Exposure to Tobacco**

**Smoke During Pregnancy?** Jacob Kahrs\* Jacob Kahrs Mollie E. Wood Nedghie Adrien Julie M. Petersen Elizabeth C. Ailes Amy Herring Meredith Howley Samantha E. Parker Maria D. Politis Paul A. Romitti Gary M. Shaw Andrew F. Olshan National Birth Defects Prevention Study

A meta-analysis of 15 case control studies of maternal smoking and offspring hypospadias found a pooled odds ratio (OR) of 0.9 (95% confidence interval [CI] 0.85, 0.95). We evaluated whether selection bias due to differential participation may explain this finding using previously published results from the National Birth Defects Prevention Study (NBDPS), a large population-based case control study in the United States (US).

We conducted deterministic bias analyses with a range of bias parameters reflecting selection fractions representing differential participation that varied by both case/control status and smoking. We then used the resulting fractions to simulate source populations from which cases and controls were drawn and estimated selection bias adjusted ORs for the association between smoking and hypospadias. Simulated source population estimates of smoking prevalence were drawn from the Pregnancy Risk Assessment Monitoring System.

The original published NBDPS OR for active smoking in pregnancy was 0.8 (95% CI 0.7, 1.0). Selection bias adjusted ORs remained below 1.0 if the selection fraction of smoking-exposed cases was lower than exposed controls and/or the selection fraction of smoking-unexposed cases was greater than the unexposed controls. Selection bias adjusted ORs moved toward or across the null in scenarios where smoking-exposed case mothers were less likely to participate than unexposed case mothers. When simulated participation was similar to observed participation for NBDPS (65% of hypospadias cases, 64% of controls) and smoking prevalence was similar to the US birthing population (e.g., 21%) but was higher in cases than controls (e.g., 25% vs 20%), the selection bias adjusted OR could be as high as 1.33.

Realistic differences in participation for smoking-exposed versus unexposed cases and controls may explain previously observed reduced odds of hypospadias associated with maternal smoking.

**Perinatal Depression and Adverse Child Growth Outcomes in Low- and Middle-Income****Countries: A Systematic Review and Meta-Analysis** Stefania Papatheodorou\* Hyelee Kim

Elizabeth Carosella Shradha Chhabria Aliya Moreira Dana Naamani Brennan Ninesling Bizu Gelaye

Aisha K. Yousafzai Stefania Papatheodorou

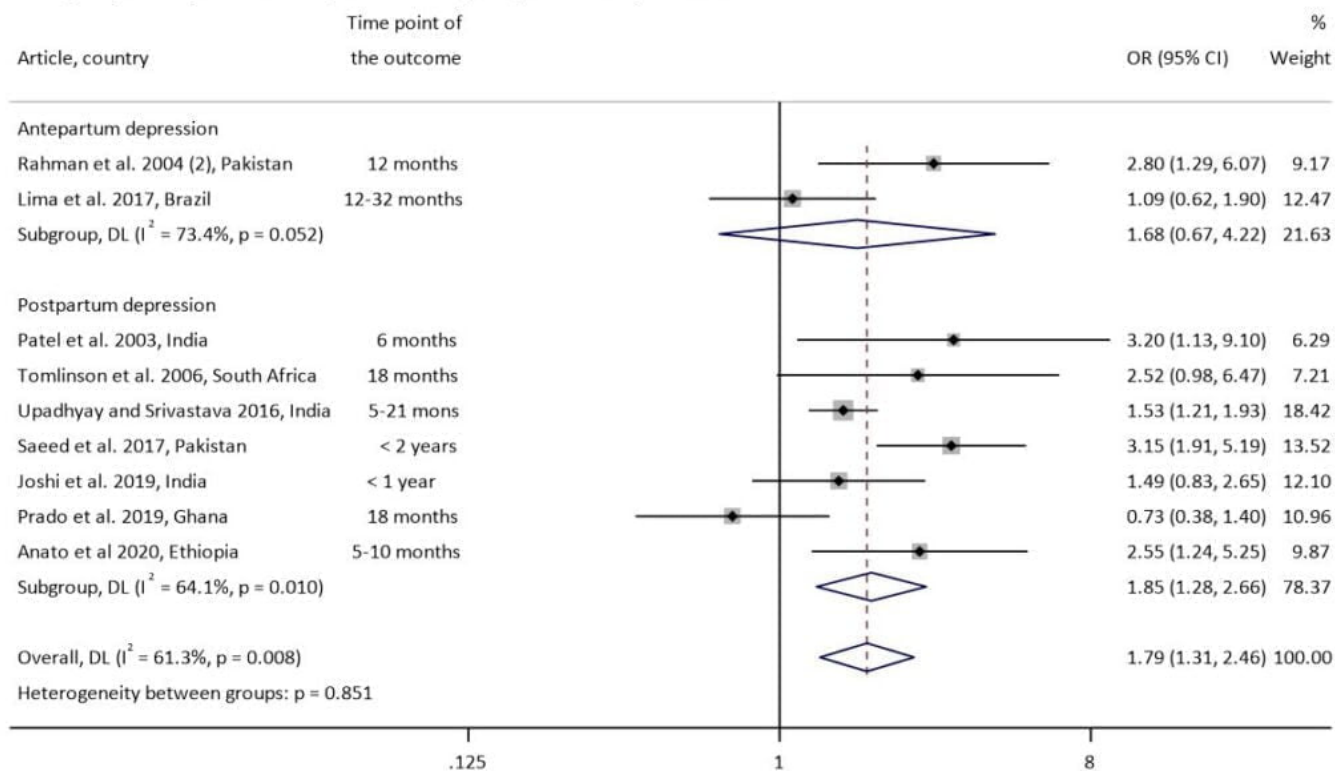
**Background and objectives:** Perinatal depression (PND), which encompasses antepartum and postpartum depression of mothers, impairs both women's health and child nutrition, particularly in low- and middle-income countries (LMICs). We aimed to meta-analyze the associations between PND and adverse child growth outcomes in LMICs.

**Method:** Nine electronic databases (PubMed, EMBASE, Google Scholar, Web of Science, CINAHL Plus, Global Health Database, WHO Regional Databases, PsycINFO, and LILACS) were assessed. To prevent the reverse causation, we selected studies where PND was assessed during pregnancy until 1 year after birth, and child growth was measured after PND assessment. For PND, we selected studies that used a validated screening tool or clinical interview. Studies reported outcomes of stunting, wasting, underweight, or overweight/obesity in children aged 6 to 32 months were included. Study characteristics and effect estimates were extracted from each study and pooled using random-effects models (PRISMA registration number: CRD42021246803).

**Results:** Seventeen papers met our inclusion criteria, representing 11 countries and 15,520 mother-baby pairs. Children of mothers with PND were more likely to be stunted (n=9, OR 1.79, 95% CI 1.23, 2.46) and underweight (n=9, OR 2.73, 95% CI 1.92, 3.91). However, the pooled for both stunting and underweight were not statistically significant: RR for stunting=1.04 (n=7, 95% CI: 0.92, 1.17) and RR for underweight=1.12 (n=7, 95% CI 0.97, 1.30). There were insufficient studies pertaining to the consistent measure of associations between PND and wasting or overweight/obesity.

**Conclusions:** In this study, we found suggestive evidence that PND is associated with an increased risk of stunting and being underweight among children aged up to 32 months. Nonetheless, there were limited studies, and more research should be done on LMICs. Prioritizing prevention, screening, and treatment of PND may help reduce adverse child growth outcomes.

**Figure. Meta-analysis of OR for stunting between mothers with and without perinatal depression (n=9): subgroup analysis of antepartum vs. postpartum depression**



**Associations between gestational exposure to air pollution and birthweight in a North Carolina birth cohort** Alison K Krajewski\* Alison K. Krajewski Thomas J. Luben Joshua L. Warren Kristen M. Rappazzo

Previous studies reported birthweight (BW) is associated with exposure to criteria air pollutants. Due to the variability in the magnitude of reported associations, we used quantile regression to evaluate the magnitude of the association between gestational exposure to fine particulate matter (PM<sub>2.5</sub>), nitrogen dioxide (NO<sub>2</sub>), or ozone (O<sub>3</sub>) and BW among term births in a North Carolina birth cohort from 2003-2015 (n:1,252,811). Modeled daily PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> concentrations were aggregated to census tract, linked to residential address at delivery, and averaged across each trimester of pregnancy. Quantile regression estimated the change (and 95% CI) in mean BW across deciles of BW per 1-unit increase in PM<sub>2.5</sub>, NO<sub>2</sub>, or O<sub>3</sub>, adjusted for gestational parent marital status, race/ethnicity, age at delivery, and Medicaid status. The daily mean (SD) concentrations were 10.9 (2.2) µg/m<sup>3</sup> for PM<sub>2.5</sub>, 15.8 (6.6) ppb for NO<sub>2</sub>, and 41.6 (3.5) ppb for O<sub>3</sub>. During the first and third trimesters, we observed higher BW with higher PM<sub>2.5</sub> concentrations across all deciles, but lower BW with higher PM<sub>2.5</sub> concentrations during the second trimester across all but the highest decile. Generally, we observed higher BW with higher NO<sub>2</sub> concentrations and lower BW with higher O<sub>3</sub> concentrations across trimesters and deciles of BW. Overall, the largest magnitude quantile regression coefficients for lower BW associated with higher air pollutant concentrations were for second trimester PM<sub>2.5</sub> exposure and first and second trimester O<sub>3</sub> exposure, whereas the largest magnitude coefficients for higher BW were for higher NO<sub>2</sub> concentrations during each of the three trimesters. While the overall magnitude of associations with BW were relatively small across pollutants and trimesters, evaluating these associations may help to identify critical windows of exposure that have the greatest risk to changes in BW.



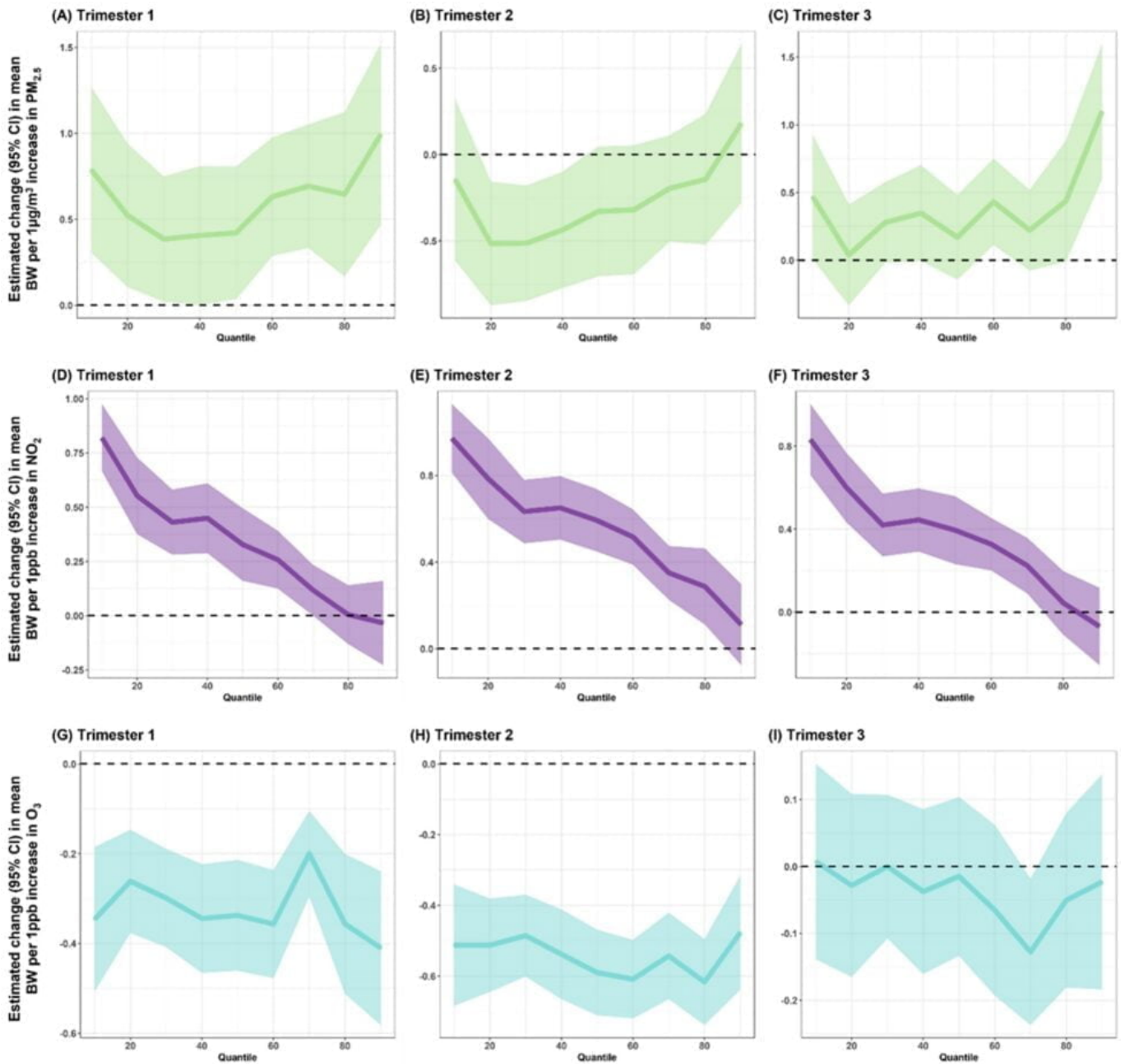


Figure 1A-I: Estimated change (95% CI) in mean BW across deciles of BW per 1-unit increase in PM<sub>2.5</sub>, NO<sub>2</sub>, or O<sub>3</sub> by trimester of gestational exposure.

**Toward defining healthy gestational weight gain for pregnant people with high BMI:****estimated effects on size for gestational age** Janne Boone-Heinonen\* Janne Boone-Heinonen

Dang Dinh Shuling Liu Jean O'Malley Teresa Schmidt Jonathan Snowden Rachel Springer Sarah-

Truclinh Tran Kimberly K Vesco

**Background:** Gestational weight gain (GWG) recommendations differ by pre-pregnancy body mass index (BMI), but are uniform for any BMI $\geq$ 30 kg/m<sup>2</sup> and, among those with BMI $\geq$ 30, for trimesters 2 and 3. Yet BMI $\geq$ 30 encompasses a broad range with varying GWG patterns and risks. We estimated the effects of trimester-specific GWG on size for gestational age (small and large, compared to appropriate; LGA, SGA, AGA) in pregnant people with high BMI (Class I, II, and III obesity).

**Methods:** We examined 20,162 pregnancies from people with BMI 30-34.9 (n=11,751), 35-39.9 (n=5,180), or  $\geq$ 40 (n=3,231) kg/m<sup>2</sup> receiving care from a national network of community health centers. In pre-pregnancy BMI-stratified analysis, we calculated trimester-specific weight change using latent piecewise trajectory models. We then modeled SGA and LGA (vs AGA) as a function of GWG trajectory parameters (intercept; trimester 1, 2, and 3 slopes) and maternal characteristics using multinomial logistic regression.

**Results:** Greater GWG was generally associated with higher odds of LGA and lower odds of SGA, but with notable exceptions. First, trimester 1 GWG was inversely associated with LGA for those with BMI 35-39.9 or  $\geq$ 40 [OR (95% CI): 0.78 (0.70, 0.86), 0.80 (0.72, 0.89)]. This finding mainly reflects lower odds of LGA with *less weight loss*, as average trimester 1 slopes were negative in trajectory models, especially in higher BMI groups (average slopes: -0.1, -0.2, -0.2 lb/week). Second, greater trimester 2 GWG was associated with *higher* odds of SGA in those with BMI $\geq$ 40 [OR (95% CI): 1.35 (1.16, 1.58)]. Finally, BMI groups varied in which trimester of GWG was most strongly associated with greater odds of LGA or SGA.

**Discussion:** Findings were largely consistent with prior evidence for lower BMI groups, but unexpected findings suggest a need for further study of potential adverse effects of early pregnancy weight loss and differential effects of GWG in trimester 2 vs 3 in pregnant people with higher BMI.

**Evaluating the Association Between Dental Health and Flourishing Among Adolescents in the United States** Chelse Spinner\* Chelse Spinner

**Introduction:** An adolescent's ability to flourish may be influenced by physical and mental health, as well as other social determinants of health, including access to health services. Dental health is a major component of overall health, as the burden of poor dental health can significantly affect physical, social, and mental health outcomes. Adolescents are considered at risk due to their increased likelihood to experience dental caries, poor oral hygiene, and limited access to dental care services. Thus, research is needed to ascertain if there is a significant clinical association between dental health and flourishing. This study evaluates the association between dental health and flourishing among adolescents.

**Methods:** This study analyzed data from the combined 2018-2019 National Survey of Children's Health. A multivariable logistic regression model was developed to model the association between dental health and flourishing. We examined dental health characteristics, characteristics of adolescents, and parent/household characteristics among 30,935 adolescents, ages 10-17, that were or were not considered to be flourishing.

**Results:** After adjusting for various socio-demographic characteristics, adolescents with fair/poor oral health had a 75% increased odds of not flourishing compared to adolescents with excellent oral health (OR, 1.75; 95% CI, 1.33-2.29). Among adolescents that met 0 family resilience items, there was an 83% increased odds of not flourishing compared to adolescents that met all 4 family resilience items (OR, 1.83; 95% CI, 1.38-2.42).

**Conclusion:** Adolescents that experience poor oral health and lack family resilience, are more likely to not flourish compared to adolescents with excellent oral health and family resilience. Findings highlight the need for understanding the relationship between oral health status, family resilience, and flourishing among adolescents, to further improve the quality of care for this at-risk population, and to better inform models of dental care for adolescents.

**Racial Disparities in Maternal Exposure to Ambient Air Pollution During Pregnancy and Prevalence of Congenital Heart Defects**

Olufunmilayo Arogbokun Knutson\* Olufunmilayo Arogbokun Knutson Thomas Luben Jeanette Stingone Lawrence Engel Chantel Martin Andrew Olshan

**Background:** Birth defects are the primary cause of infant mortality in the United States. However, the causes of birth defects are largely unknown. Environmental factors, such as air pollution, are among potential causes. Racial disparities in pollution exposure and congenital heart defects (CHDs) have been identified, but disparities in their association have not been explored. **Methods:** We conducted a cohort study to investigate the relationship between select air pollutants and CHDs using North Carolina birth certificate and birth defect registry data from 2003-2015 (N=1,225,285). Maternal air pollution exposure was determined using the Environmental Protection Agency's Downscaler Model. A 7-week average of particulate matter <2.5 microns (PM<sub>2.5</sub>) and ozone exposure at the geocoded address at birth was estimated for each pregnancy during weeks 3-9. CHDs included in our study were: pulmonary valve atresia/stenosis, Tetralogy of Fallot (TOF), and atrioventricular septal defects. Single-pollutant and co-pollutant log-binomial models were created for the entire study population and stratified by race, limited to non-Hispanic Black and non-Hispanic White women to investigate disparities. **Results:** Positive associations between both pollutants and CHDs were observed in adjusted co-pollutant categorical models not stratified by race. An increasing concentration-response association was found for PM<sub>2.5</sub> and TOF (Quartile 4 aPR: 1.46; 95% CI: 1.06, 2.03). Elevated aPRs were present in the pulmonary valve atresia/stenosis model as well; however, there was no concentration-response trend. The pattern of association for PM<sub>2.5</sub> and pulmonary valve atresia/stenosis was stronger for babies of non-Hispanic Black women. **Conclusion:** PM<sub>2.5</sub> and ozone exposure early in pregnancy may increase the prevalence of certain CHDs. Air pollution exposure may impact non-Hispanic Black and non-Hispanic White pregnancies differently, though more epidemiologic studies are needed to confirm findings.

**The associations of prenatal agricultural farm work with fetal overgrowth and pregnancy complications in State of Arizona birth records** Kimberly L. Parra\* Kimberly Parra Robin B. Harris Leslie V. Farland Paloma Beamer Melissa Furlong

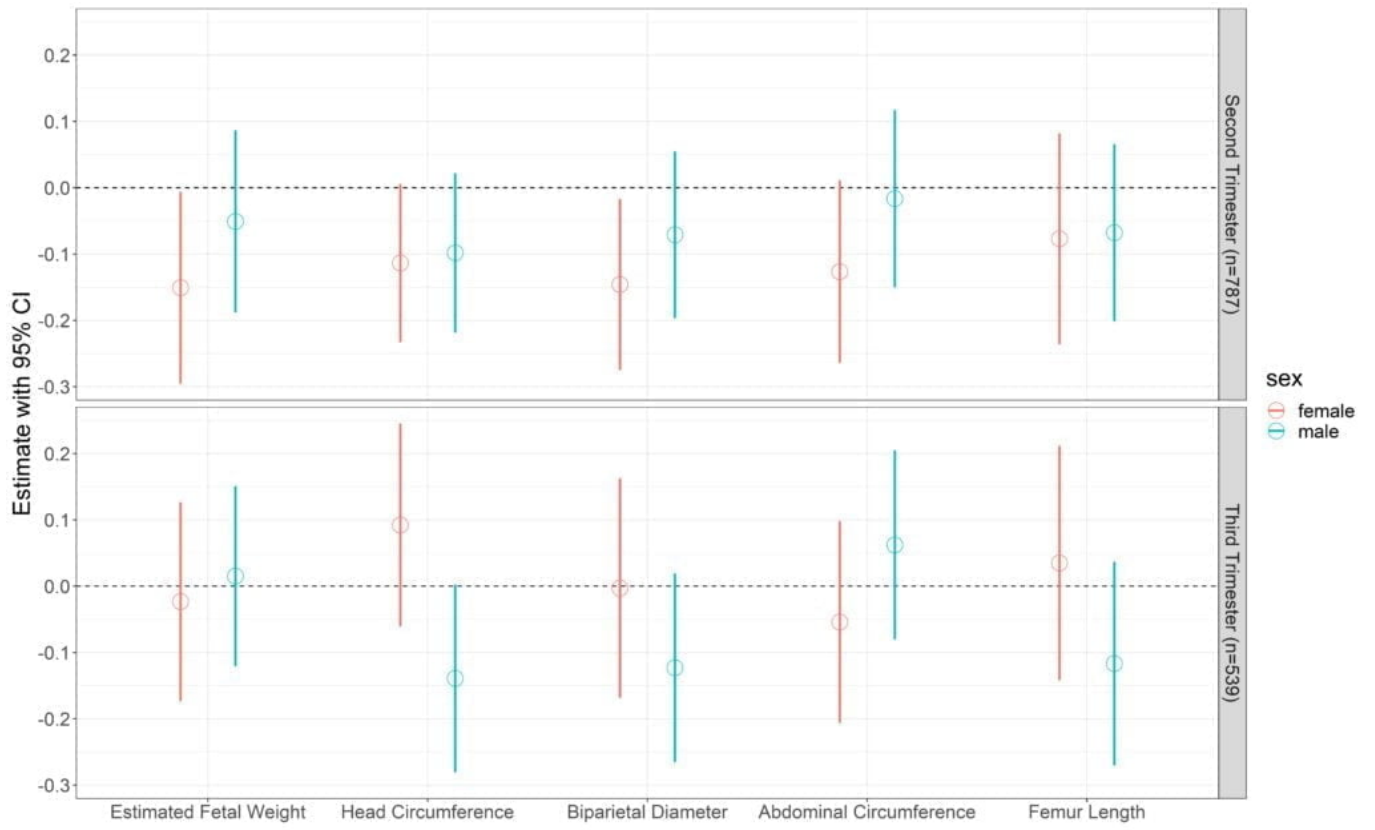
Pregnant agricultural workers are a marginalized and understudied group with high occupational exposures. However, there has been little characterization of their pregnancy and birth outcomes. We sought to examine fetal growth outcomes for neonates delivered to agricultural workers in Arizona. Using 2006-2013 Arizona birth certificates with parental occupational, we identified live-birth singletons (N=623,185) by agricultural worker household status. Logistic regression models estimated adjusted Odds Ratios (aOR) of household status with neonatal outcomes: macrosomia (>4,000 grams), postterm birth (>41 weeks), low birth weight (LBW <2,500 grams), pre-term birth (PTB <37 weeks), large for gestational age (LGA), small for gestational age (SGA), and 5 min-APGAR score (<7). The mean gestational age was 39 weeks (SD  $\pm$ 1.6) and birthweight was 3,320 grams ( $\pm$ 519.0). Compared to non-agricultural households, newborns of agricultural households (n=6,371) had a higher risk of macrosomia, (aOR 1.15, 95% CI: 1.05, 1.26), LGA (aOR 1.12, 95% CI: 1.03, 1.22), postterm birth (aOR 1.20, 95% CI: 1.09, 1.33), and low 5-min APGAR score (aOR 1.39, 95% CI: 1.07, 1.81), whereas LBW (aOR: 0.85, 95% CI: 0.76, 0.96) and PTB (aOR: 0.82, 95% CI: 0.74, 0.92) were inversely related. These findings suggest that having a parent working in agriculture or farming increased the likelihood of fetal overgrowth and low APGAR score.

**Daily physical activity and nocturnal glucose in pregnant people with gestational glucose intolerance** Bethany G. Rand\* Bethany Rand Jill M. Maples Scott E. Crouter Christina M. Peterson Nikki B. Zite Kimberly B. Fortner Samantha F. Ehrlich

**PURPOSE:** This study examined the relationships of daily minutes (min) of moderate to vigorous intensity physical activity (MVPA), light intensity activity (LPA), and total activity (MVPA + LPA) with nocturnal (12AM- 6AM) glucose levels in individuals with gestational glucose intolerance (GGI). **METHODS:** Data come from the Project Wellness pilot randomized controlled trial (i.e., baseline). Participants concurrently wore a Dexcom G6 continuous glucose monitor and an ActiGraph CentrePoint Insight Watch activity monitor for 7 days. The TwoRegressions algorithm estimated min by min metabolic equivalents of task (METs) for periods in which the devices were worn, and mins per day at  $\geq 3.0$  METs and  $<3$  METs, indicative of MVPA and LPA, respectively, were summed. PROC MIXED in SAS, with an autoregressive covariance structure, estimated the associations of 10 min blocks of MVPA, LPA, and total activity with nocturnal: mean glucose, percent time in range (TIR; 60-99 mg/dL), and glucose area under curve (AUC). AUC was calculated in R, using 12AM glucose as the starting point and the trapezoid method. **RESULTS:** Nine participants with mean gestational age 31 weeks [standard deviation (SD) 1.8] contributed a total of 66 days of data. On average, they amassed 56 mins of daily MVPA (SD 32) and 321 mins of LPA (SD 98). Mean nocturnal glucose was 88 mg/dL (SD 13) and TIR 86% (SD 28). For each 10 min increase in MVPA, there was a 1.5 mg/dL increase in mean nocturnal glucose ( $P = .004$ ), a 3.3% decrease in TIR ( $P = .03$ ), and a 26,575 mg/dL increase in AUC ( $P = .02$ ). Estimates for LPA and total activity did not attain statistical significance. Mean nocturnal glucose and AUC also increased with each passing day (both  $P < .02$ ). **CONCLUSION:** Findings suggest that MVPA may negatively affect nocturnal glucose levels in pregnant people with GGI. Future studies with concurrent dietary intake data are needed to investigate the potential role of compensatory behaviors in this population.

**Prenatal Organophosphate Pesticide Exposure and Fetal Biometry** Eleanor Medley\* Eleanor Medley Leonardo Trasande Mrudula Naidu Yuyan Wang Akhgar Ghassabian Linda G. Kahn Sara Long Yelena Afanasyeva Kurunthachalam Kannan Shilpi Mehta-Lee Whitney Cowell

Organophosphate (OP) pesticide exposure during pregnancy may be associated with reduced fetal growth, though studies are limited and results have been mixed. We aimed to investigate associations between prenatal OP pesticide exposure and fetal biometry and determine if associations vary by fetal sex. In the New York University Children's Health and Environment Study cohort, prenatal urinary concentrations of 6 dialkyl phosphate (DAP) metabolites of OP pesticides were measured at 3 time points. Fetal biometrics were obtained from ultrasounds in the second (n=793) and third (n=543) trimesters. Estimated fetal weight and biometry z-scores were calculated using Intergrowth-21<sup>st</sup> standards. Covariates included age, education, race/ethnicity, parity, pre-pregnancy BMI, and tobacco exposure. Associations between pregnancy-averaged, creatinine-adjusted, log-transformed  $\Sigma$ DAP and fetal biometry z-scores were determined through linear models for each ultrasound timepoint and stratified by child sex. In the second trimester, one log-unit increase in  $\Sigma$ DAP was associated with lower estimated fetal weight (-0.15 SD; 95% CI: -0.29, -0.01), head circumference (-0.11 SD; CI: -0.23, -0.004), biparietal diameter (-0.15 SD; CI: -0.27, -0.02), and abdominal circumference (-0.13 SD; CI: -0.26, 0.01) measures in females. In the third trimester, one log-unit increase in urinary  $\Sigma$ DAP was associated with lower head circumference (-0.14 SD; CI: -0.28, 0.001), biparietal diameter (-0.12 SD; CI: -0.26, 0.02), and femur length (-0.12 SD; CI: -0.27, 0.04) measures in males. Most of these associations remained consistent when the sample was restricted to participants without gestational diabetes, pre-eclampsia, or pregnancy-induced hypertension. Our results suggest that prenatal OP pesticide exposure is negatively associated with fetal growth and affects fetal biometry trajectories in a sex-specific manner, with females affected earlier in gestation and males affected later in gestation.





**LATEBREAKER**

Pharmacoepidemiology

**Comorbid disease and other clinical factors contributing to patterns of endocrine therapy adherence in premenopausal breast cancer patients**Kirsten M. Woolpert\* Kirsten Woolpert  
Julie A. Schmidt Dóra K. Farkas Thomas P. Ahern Deirdre P. Cronin-Fenton**Background:**

Patients with hormone receptor positive breast cancer are recommended at least five years of adjuvant endocrine therapy. Side effects and barriers to care can influence adherence to these treatments. We evaluated tumor characteristics, treatments, and baseline comorbid conditions in relation to patterns of adjuvant endocrine therapy adherence among premenopausal women with breast cancer.

**Methods:**

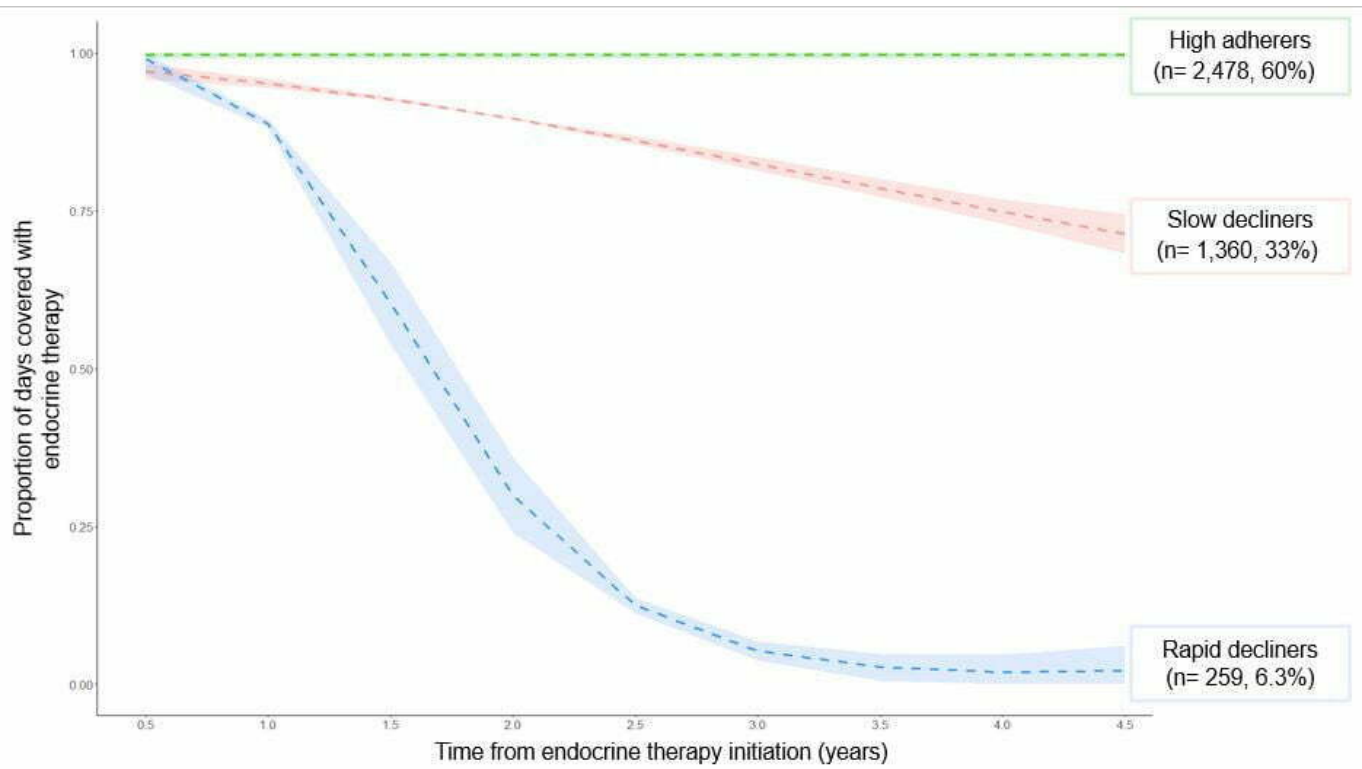
We enrolled 4,097 premenopausal, stage I-III breast cancer patients registered in the Danish Breast Cancer Group who were indicated to take endocrine therapy (2002-2011). We linked to Danish population-based and medical registries to obtain information on clinical characteristics and prevalent comorbid diseases. We fit group-based trajectory models to define patterns of endocrine therapy adherence for 4.5 years following initiation. We modeled associations between clinical factors and adherence trajectories *via* multinomial logistic regression.

**Results:**

We identified three distinct adherence patterns (Figure 1) — high adherers (60%), slow decliners (33%), and rapid decliners (6.3%). Compared with high adherers, rapid decliners were more likely to have stage I disease (vs. stage II or III; OR: 2.2, 95% CI: 1.7, 2.9), disease not indicated for chemotherapy (vs. indicated chemotherapy; OR: 4.4, 95% CI: 2.2, 8.9), no positive lymph nodes at biopsy (vs. one or more positive lymph nodes; OR: 2.1, 95% CI: 1.6, 2.7), and prevalent comorbid disease (Charlson Comorbidity Index  $\geq 1$  vs. 0; OR: 1.9, 95% CI: 1.3, 2.8).

**Conclusions:**

Several clinical factors were associated with poor adherence in this cohort, particularly less severe cancer and a higher comorbidity burden. Future analyses will look at specific comorbid diseases, non-cancer medication use, and socioeconomic position in relation to endocrine therapy adherence patterns, which may inform interventions to improve adherence.



**Figure 1.** Group-based trajectories of endocrine therapy adherence in a cohort of 4,097 premenopausal breast cancer patients in Denmark (2002–2011)

**Geographically Weighted Associations Between Household Income and Racial Disparities in Substance Use Arrest Rates** Nora Clancy Kelsall\* Nora Clancy Kelsall Spruha Joshi John R. Pamplin II

As of 2021, overdose deaths in New York City are at an all-time high. Overdose rates vary considerably across neighborhoods and race/ethnicities, with the greatest rates being among Black New Yorkers. Nonetheless, despite its association with increased overdose risk, the criminalization of drug use continues to be prominent in New York City. In addition to dramatic racial inequities, there are also distinct geographic patterns in drug and alcohol related arrest rates that may contribute towards racial and geographic patterns of overdose risk. Little is understood about the factors that contribute to the distribution of these disparities across neighborhoods. Using American Community Surveys and New York City Open Data, we used linear and geographic weighted regression to investigate the association between census-tract level median household income and drug and alcohol related arrest rate difference between racial groups, adjusting for proportion of the census tract population under 25. Preliminary results investigating arrest disparities between individuals identifying as Black and white show that increased median household income is statistically significantly associated with greater racial disparities in arrest rates for all years. On average, a \$10,000 increase in median household income was associated with an increase in Black-white rate difference of 119 arrests per 1,000 people. Geographically weighted regression illustrated an effect modification by space as median income was associated with racial disparities in arrest in Lower and Midtown Manhattan, and Manhattan-adjacent parts of Brooklyn, Queens, and Staten Island, but not in the Bronx or more distal parts of the outer boroughs. Our findings suggest that racial inequities in substance use policing are most pronounced in high income areas, which has implications for future public health and harm reduction interventions.

**Perceived stress and markers of ovarian reserve among subfertile women** Lidia Minguez Alarcon\* Lidia Minguez Alarcon Paige L. Williams Irene Souter Jennifer B. Ford Russ Hauser Jorge E. Chavarro

**Background:** We investigated whether self-reported psychological stress was associated with markers of ovarian reserve among subfertile women.

**Methods:** This observational study included 520 women seeking fertility care at the Massachusetts General Hospital who enrolled in the Environment and Reproductive Health (EARTH) study between 2005 and 2019. Women completed the short version of the validated Perceived Stress Scale 4 (PSS-4), which assesses psychological stress. Ovarian reserve markers included Antral Follicle Count (AFC), circulating serum levels of day-3 follicle stimulating hormone (FSH) and anti-Müllerian hormone (AMH) assessed in a subset of participants (n=185). We fit linear regression models to evaluate the association between psychological stress and markers of ovarian reserve while adjusting for confounders.

**Results:** We observed that higher total PSS4 scores were negatively associated with AFC and serum AMH levels in analyses adjusted for age, BMI, race, smoking, education, physical activity, and type of infertility diagnosis. Specifically, women in the second and third tertiles of stress had lower mean AFC compared to women in the lowest tertile of psychological stress score (2<sup>nd</sup> tertile: -7% (95% CI= -20%, -13%); 3<sup>rd</sup> tertile: -6% (95% CI= -11%, -1%)). Women in the second and third tertiles of total PSS4 scores also lower mean serum AMH compared to women in the lowest tertile (2<sup>nd</sup> tertile -24% (95% CI= -43%, -9%); 3<sup>rd</sup> tertile: -24% (95% CI= -34%, -5%)). These associations varied by several socioeconomic factors and were observed primarily among women who were younger, belonging to minority races, with a college degree, or with annual household income <\$100,000.

**Conclusions:** Higher perceived stress was negatively associated with AFC and serum AMH levels, and these associations varied by several socioeconomic factors. These results add to the existing epidemiologic literature on health effects of psychologic stress in women.

**Effect Measure Modification of Smoking Patterns in Pregnancy on Postpartum Depression by Antenatal Depression Status based on a Directed Acyclic Graph (DAG)** Anthony Kondracki\* Anthony Kondracki Jennifer Barkin Bonzo Reddick Matthew Valente

**Background:** Pregnancy and postpartum are periods of increased maternal vulnerability to depression. Women with symptoms of depression tend to smoke during pregnancy and postpartum and smoking is one of the major risk factors for depression. Limited research has focused on how changes in smoking behavior during pregnancy affect postpartum depression when modified by antenatal depression. **Objective:** The aim of this study was to investigate the average causal effects of naturally varying self-reported maternal smoking patterns on postpartum depression (PPD) modified by antenatal depression status (effect measure modifier) using a directed acyclic graph (DAG). **Methods:** A sample of participants with singleton live births (N=56,227) was drawn from the 2017-2018 Pregnancy Risk Assessment Monitoring System (PRAMS) survey dataset. Based on self-reported smoking behavior, seven unique mutually exclusive categories reflecting dimensions of timing and intensity of smoking behavior in pregnancy were used as exposure variables. We employed a causal directed acyclic graph (DAG) to illustrate the relationships between variables, to identify adjustment strategies, and improve estimates of causal effects in the effect measure modification process. Effect measure modification was defined in terms of counterfactuals to support causal inference. Multivariate logistic regression models were fitted with weighted data to assess main effects of smoking patterns on PPD and interaction effects with antepartum depression status, using minimally sufficient set of observed covariates (i.e., race/ethnicity, age, education, health insurance, prenatal care, and low birthweight) for adjustment. The synergy index (SI) and 95% CIs based on a delta method tested interaction effects on an additive scale. The analyses were repeated with multiply-imputed data for comparison. **Results:** Most women (33.6%) smoked at high intensity ( $\geq 10$  cigarettes/day) in early and late pregnancy and these women had the highest prevalence of postpartum depression (23.7%) and antenatal depression (37.2%). Applying a DAG allowed presentation of interactions between variables, account for assumptions and potential confounders incorporated in a DAG to guide the modeling strategy. The main estimated effects of smoking on PPD were significantly greater for high intensity smokers in early and late pregnancy (aOR 1.80; 95% CI: 1.47, 2.19) and the interaction effects for the effect measure modification indicated significantly higher odds of PPD for increasers (aOR 9.72, 95% CI: 1.73, 54.60) and quitters-low in early pregnancy (aOR 7.40, 95% CI: 4.35, 12.57). The synergy index (SI), interpreted as the excess risk due to exposure to both factors with interaction and without interaction, was 2.06 (95% CI: 1.89, 2.23). **Conclusions:** Using a DAG revealed and explained collider bias and the advantages of confounder selection and conditioning using statistical models. Combining biological plausibility and a DAG's theory specified by graphical criteria and supported by causal assumptions we attempt to explain causal inferences and draw conclusions about estimates. Findings from this study may help improve our understanding of how different maternal smoking patterns contribute to PPD in women with antenatal depression to reduce its incidence and prevalence.

**Association Between Exposure to Bisphenols and Phthalates and Female Time to Pregnancy and Subfecundity: Findings from a NYC Pregnancy Cohort** Mia Charifson\* Mia Charifson Linda Kahn Eunsil Seok Shilpi Mehta-Lee Mengling Liu Leonardo Trasande

Bisphenols and phthalates are endocrine-disrupting chemicals commonly found in consumer products and linked to reproductive health and fertility. The goal of this study was to investigate the relation of female bisphenol and phthalate exposure with time to pregnancy (TTP) and subfecundity (TTP >12 months) in the New York University Children's Health and Environment Study (n=400). Chemicals were creatinine-adjusted and imputed below the limit of detection (LOD) as LOD/√2. We used discrete Cox and logistic regression models to estimate associations for each quartile of chemicals measured in first-trimester urine with TTP and subfecundity. To assess the relative importance of each chemical on these outcomes, we employed a novel partial linear single-index mixture model. All models were adjusted for age, body mass index, parity, race/ethnicity, nativity, pre-pregnancy alcohol and folic acid use, and hospital site. Consistent with prior literature, we found little evidence of a link between bisphenols and fecundity, but we unexpectedly observed some positive associations at low doses (Q2 vs. Q1 TTP Fecundability Ratio [FR]: 1.58 [95% confidence interval: 1.16, 2.15]; Subfecundity Odds Ratio [OR]: 0.30 [0.10, 0.77]). Phthalates were consistently associated with longer TTP (lower FR) and higher odds of subfecundity, although the only group with statistically significant results in all quartiles of exposure was the anti-androgenic phthalates (Q4 vs. Q1 TTP FOR: 0.65 [0.47, 0.89]; Subfecundity OR: 4.62 [1.58, 16.9]). The chemical with the highest relative contribution to TTP and subfecundity in the mixtures model was mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHHP; 75.9% and 41.4%, respectively), an anti-androgenic phthalate. Results were robust to several sensitivity analyses. Overall, we found evidence of negative associations between phthalates and fecundity, warranting further investigation into potential mechanisms and recommendations for public health.

## Count Them In: A Descriptive Epidemiological Study of Pregnant and Parenting Students

**Attending Chicago Public Schools** Katie Nikolajuk\* Katie Nikolajuk Ronus Hojjati Esther Bier Justine Britten Tristan Banks Thalia Chicojay Amy K Johnson

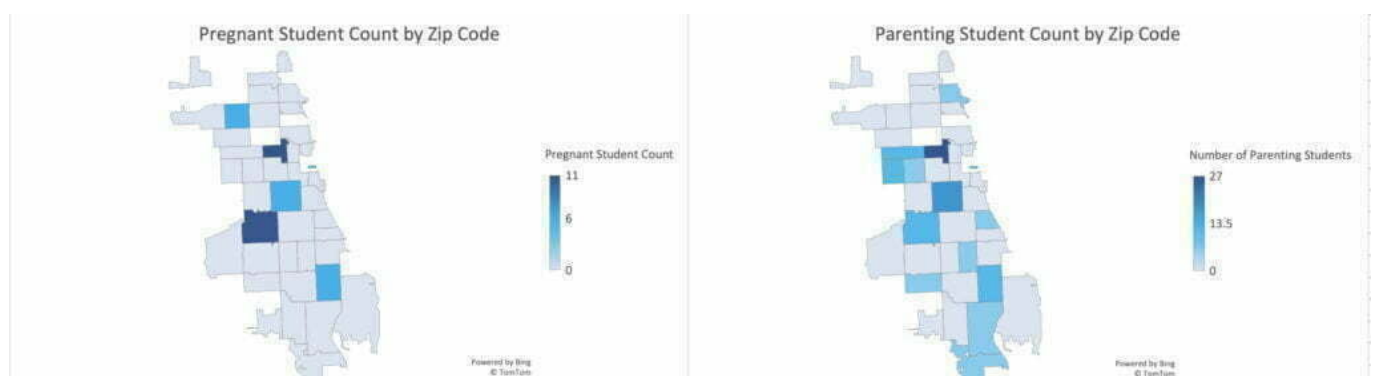
**Background:** In Chicago Public Schools (CPS), 5.8% of African American students reported a pregnancy experience compared to 3.7% of white students. Yet, CPS does not report the number of pregnant and parenting young people (PPY) enrolled each school year. Limited descriptive epidemiological data on PPY contributes to an overlooked public health problem and inhibits improving additional public health outcomes.

**Methods:** We developed a survey documenting PPY enrollment during the 2021-2022 school year by assessing three topics: 1. The number of pregnant students, and the number of parenting students: 2. current school wide PPY data collection and 3. Ideal data collection methods. The sampling frame included all CPS high schools (N=162).

**Results:** 95 participants completed the survey across 92 schools. PPY enrollment was highest in Brighton Park, Chatham, and Pilsen on the South side, West Town on the West side, and The Loop in Downtown. Portage Park on the Northwest side had more pregnant students while Ashburn, Englewood, Grand Boulevard, Riverdale, and Roseland on the South side, and Austin, Humboldt Park, and West Garfield Park on the West had more parenting students.

PPY (including men, women, and transgender men and women) are more likely to encounter public health issues including community violence, delayed first trimester prenatal care, preterm birth, sexual assault, cervical cancer, prostate cancer, smoking during pregnancy, sexually transmitted infections, and lower educational attainment, leading to increased poverty, which contributes to population health outcomes. Collecting PPY enrollment data is crucial to assess incidence and prevalence of these outcomes.

**Conclusion:** This study collected data on components of descriptive epidemiology by examining PPY enrollment to determine feasibility of collecting this data and establishing need for further PPY supports. This data is an essential step to studying public health problems where PPY are at higher risk.



**LATEBREAKER**

Reproductive

**Exploring U.S. state abortion policy trajectories from 1970 - 2014 using sequence analysis**

Leah Koenig\* Leah Koenig Lucia Pacca Rita Hamad Anusha Vable

**Context and Objective:** The national abortion landscape changed dramatically in 2022 when the *Dobbs v. Jackson Women's Health* U.S. Supreme Court decision led to abortion care being banned in at least 13 states. However, even before *Dobbs*, state abortion policies have been implemented for decades. We characterized U.S. states' abortion policy trajectories from 1970–2014.

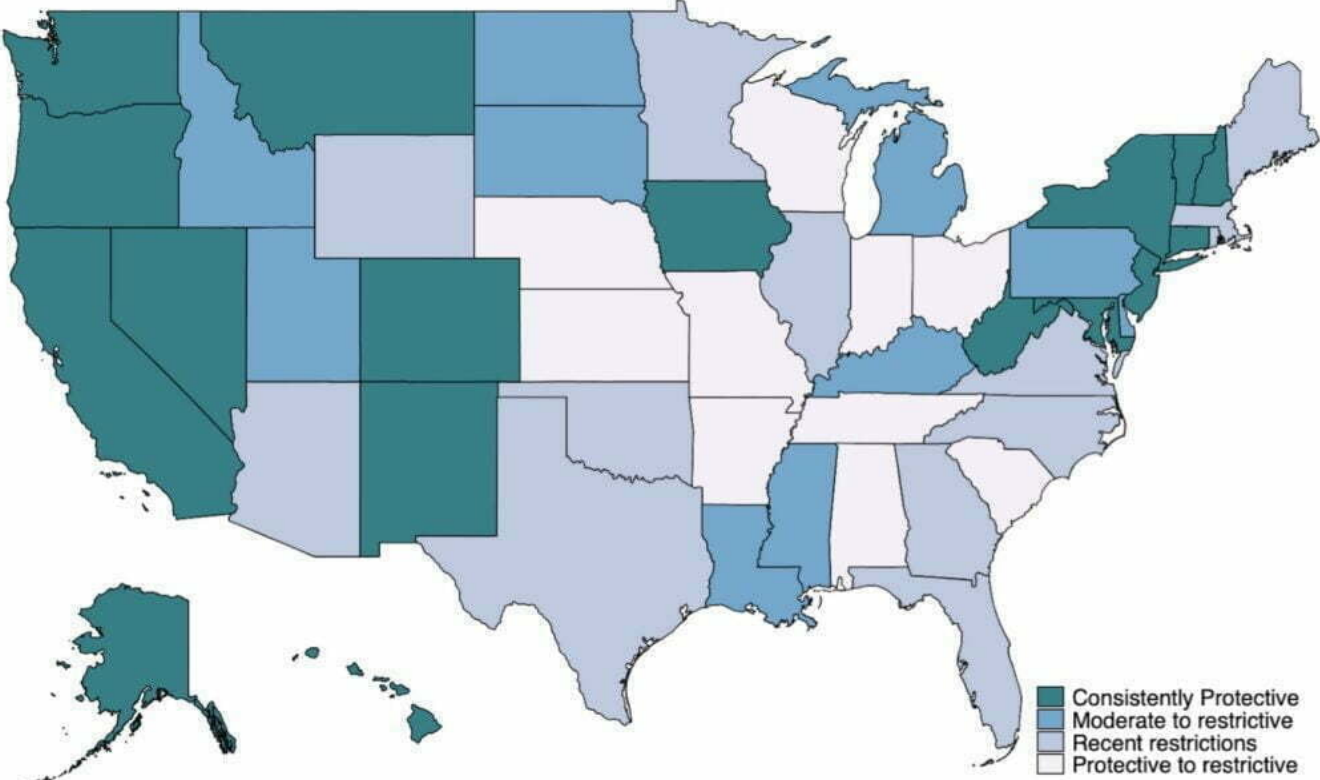
**Methods:** We examined state policy data from all U.S. states from 1970 to 2014. We calculated a continuous index of abortion policy permissiveness, reflecting the total number of protective abortion policies minus the number of restrictive abortion policies each year in each state. Each year, the index was re-scaled from 0–1. We categorized this measure into quintiles ranging from very protective to very restrictive. We used sequence analysis to measure similarities between state abortion policy trajectories across the study period, and hierarchical clustering to identify groups of states with similar policy trajectories.

**Results:** State abortion policies were largely moderate or protective from the 1970s to 1990s and became more restrictive in some states starting in the mid-1990s. We identified four distinct clusters of abortion policy trajectories: 1) moderate to restrictive, 2) protective to restrictive, 3) recent restrictions beginning in the mid-2000s, and 4) consistently protective. Moderate to restrictive states, protective to restrictive states, and states that implemented recent restrictions were predominantly located in the South and Midwest. Consistently protective states were most likely to be on the East and West coasts.

**Conclusions:** Even prior to the *Dobbs* decision, abortion policy had been growing more restrictive in many U.S. states, especially in the period between the 1990s and 2014. Abortion policies have become increasingly polarized over time such that reproductive autonomy is increasingly curtailed and determined by state of residence.



Results from sequence analysis and hierarchical cluster analysis depicting state abortion policy trajectories from 1970 – 2014



**LATEBREAKER**

Reproductive

**Establishing the relationships between adiposity and reproductive factors: a multivariable mendelian randomization analysis.** Claire Prince\* Claire Prince Laura D Howe Gemma C Sharp Abigail Fraser Rebecca C Richmond

Few studies have investigated associations between adiposity and reproductive factors using causal methods, both of which have a number of consequences on disease. Here we assess whether adiposity at different points in the lifecourse affects reproductive factors differently and independently, and the plausibility of the impact of reproductive factors on adiposity.

We used genetic data from UK Biobank and other consortia for eight reproductive factors: age at menarche, age at menopause, age at first birth, age at last birth, number of births, being parous, age first had sexual intercourse and lifetime number of sexual partners, and two adiposity traits: childhood body size and adulthood body mass index (BMI). We applied multivariable mendelian randomization to account for genetic correlation and estimate causal effects of childhood and adulthood adiposity, independently of each other, on reproductive factors. Additionally, we estimated the effects of reproductive factors, independently of other relevant reproductive factors, on adulthood adiposity.

We recently found a higher childhood body size leads to an earlier age at menarche, which in turn leads to higher adulthood BMI. Furthermore, we find contrasting and independent effects of childhood body size and adulthood BMI on age at first birth (Beta 0.22 SD (95% confidence interval 0.14,0.31) vs -2.49 (-2.93,-2.06) per 1 SD increase), age at last birth (0.13 (0.06,0.21) vs -1.86 (-2.23,-1.48) per 1 SD increase), age at menopause (0.17 (0.09,0.25) vs -0.99 (-1.39,-0.59) per 1 SD increase), and likelihood of having children (Odds ratio 0.97 (0.95,1.00) vs 1.20 (1.06,1.37) per 1 SD increase)

We highlight the importance of untangling the effects of exposures at different timepoints across the lifecourse, as demonstrated with adiposity, where accounting for measures at one point in the lifecourse can alter the direction and magnitude of effects at another time point and should therefore be considered in further studies.

**Characterizing Idiopathic Pulmonary Fibrosis Prevalence within World Trade Center Rescue/Recovery Workers** Alexandra Mueller\* Alexandra Mueller Rachel Zeig-Owens Krystal Cleven Brandon Vaeth David Prezant Alexandra Mueller

**Background:** The World Trade Center (WTC) disaster exposed Fire Department of the City of New York (FDNY) rescue/recovery workers to dust containing various metals and toxicants. WTC exposure is associated with adverse respiratory outcomes. Idiopathic pulmonary fibrosis (IPF) is considered to be an emerging occupational hazard for firefighters, though currently, only one WTC study has been conducted using self-reports of IPF. As it may be progressive in nature and is associated with a decline in lung function and early mortality, understanding the extent and severity of IPF within this cohort is imperative for understanding how to best drive treatment and care.

**Objective:** A descriptive study to evaluate and characterize the prevalence of IPF within WTC-exposed rescue/recovery workers from FDNY.

**Methods:** 90 WTC-exposed FDNY firefighters and EMS providers without sarcoidosis who had a chest computed tomography (CT) scan that fit the case criteria for IPF were included in the study. Case criteria were derived from American Thoracic Society guidelines. Descriptive statistics were used to evaluate the cohort.

**Results:** Of the 14,474 FDNY WTC-exposed responders, 90 males (0.64%) were diagnosed with ILD. 50% (n=45) arrived at the disaster site on 9/11/01, and 47% (n=42) arrived within the next two weeks. Mean age on 9/11 was 52.8 years (SD=9). Mean forced vital capacity (FVC) was 3.6 liters (SD=1). Mean FVC percent predicted was 89.8% (SD=23). Compared with the rest of the WTC-exposed population, FVC percent predicted, which controls for age, height, sex, and race, was not significantly different ( $p=0.6$ ).

**Conclusion:** The prevalence of IPF among FDNY WTC-exposed rescue/recovery workers is 0.64%, greater than in the estimated U.S. general population (~0.11%-0.18%). Exploring IPF in this well-studied cohort will improve the understanding of the development, progression, and treatment of this disease.

**LATEBREAKER**

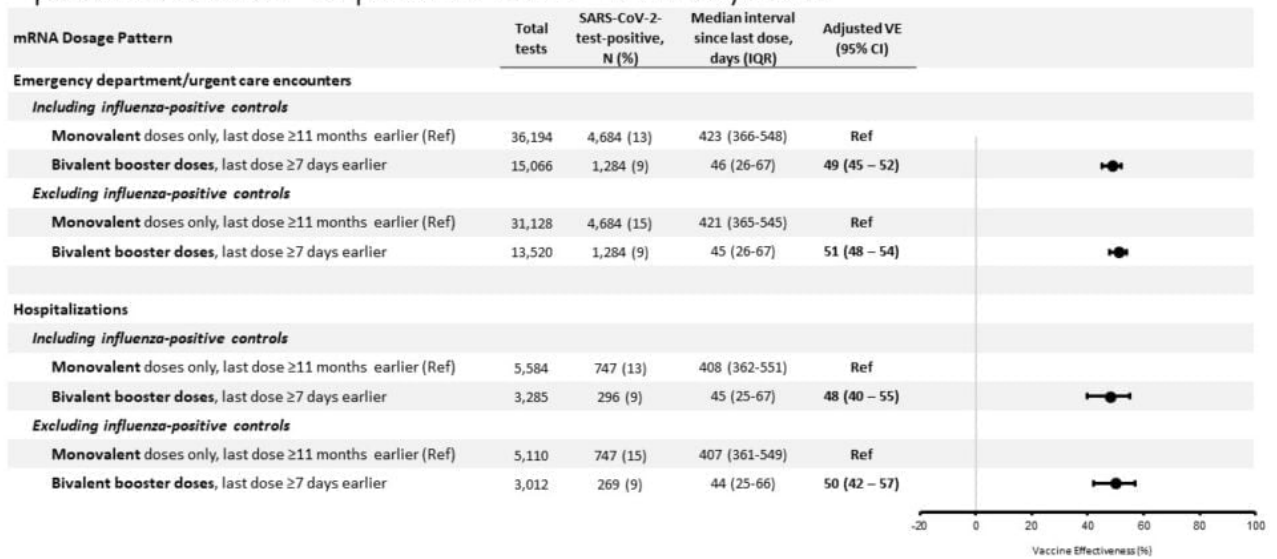
Respiratory

**Impact of exclusion of influenza-positive controls in a COVID-19 vaccine effectiveness evaluation using a test-negative design, September 2022-February 2023** Ruth Link-Gelles\*

Ruth Link-Gelles Zachary A. Weber Sarah E. Reese Toan C. Ong Gabriela Vazquez-Benitez Allison L. Naleway Nicola P Klein Peter J. Embi Shaun J. Grannis Edward Stenehjem Anupam B. Karbanda Manjusha Gaglani Mark W. Tenforde

COVID-19 vaccine effectiveness (VE) estimates have implications for policy decisions and for communicating to the public about the importance of vaccination. To mitigate potential biases due to testing practices, the test-negative design (TND) uses symptomatic SARS-CoV-2-positive individuals as cases and symptomatic SARS-CoV-2-negative individuals as controls. COVID-19 TND VE studies may have the potential for bias when influenza-positive controls are included due to correlated COVID-19 and influenza vaccine behaviors (Doll CID 2022). We used electronic healthcare record data to explore possible confounding due to inclusion of influenza-positive controls for bivalent VE against COVID-19-associated emergency department/urgent care (ED/UC) encounters and hospitalizations. Analyses included encounters during September 2022-February 2023, which was a period with high influenza activity. Cases and controls had COVID-19-like illness; cases were SARS-CoV-2-positive. In the primary analysis controls were SARS-CoV-2-negative, regardless of influenza test result. Sensitivity analyses explored the effects of excluding SARS-CoV-2-negative/influenza-positive controls (influenza testing was conducted based on decisions of treating clinicians). In the primary analysis, relative VE comparing bivalent vaccination to monovalent-only with the last monovalent dose  $\geq 11$  months prior was 49% (95% CI: 45-52%) and 48% (95% CI: 40-55%), for ED/UC and hospitalization, respectively (Figure). In the sensitivity analysis excluding influenza-positive controls, VE was 51% (95% CI: 48-54%) and 50% (95% CI: 42-57%), for ED/UC and hospitalization, respectively. In this analysis, exclusion of influenza-positive controls did not meaningfully change estimated VE; however, changes in rates of influenza among controls, or influenza vaccination coverage or VE could impact these findings and the potential bias should continue to be assessed.

Figure. *Relative VE of bivalent booster against ED/UC encounters and hospitalization among adults aged ≥18 years with and without influenza-positive controls – September 2022 – February 2023*



**Diagnostic Bias Perspectives from Rheumatologists: A Qualitative Interview Study** Shalmali Bane\* Shalmali Bane Julia Simard Patricia Rodriguez Espinosa Titilola Falasinnu

There are no definitive objective diagnostic criteria for systemic lupus erythematosus (SLE). SLE is more prevalent among women of childbearing age, however men with SLE are often described as having more severe disease and poorer outcomes. It is unclear how much of this clinical presentation is due to natural history vs diagnostic delay. In a recent experimental study, we found rheumatologists took longer and were less likely to correctly diagnose SLE in White males (78%) vs Black females (89%) when reviewing identical vignettes with race/sex randomly varied.

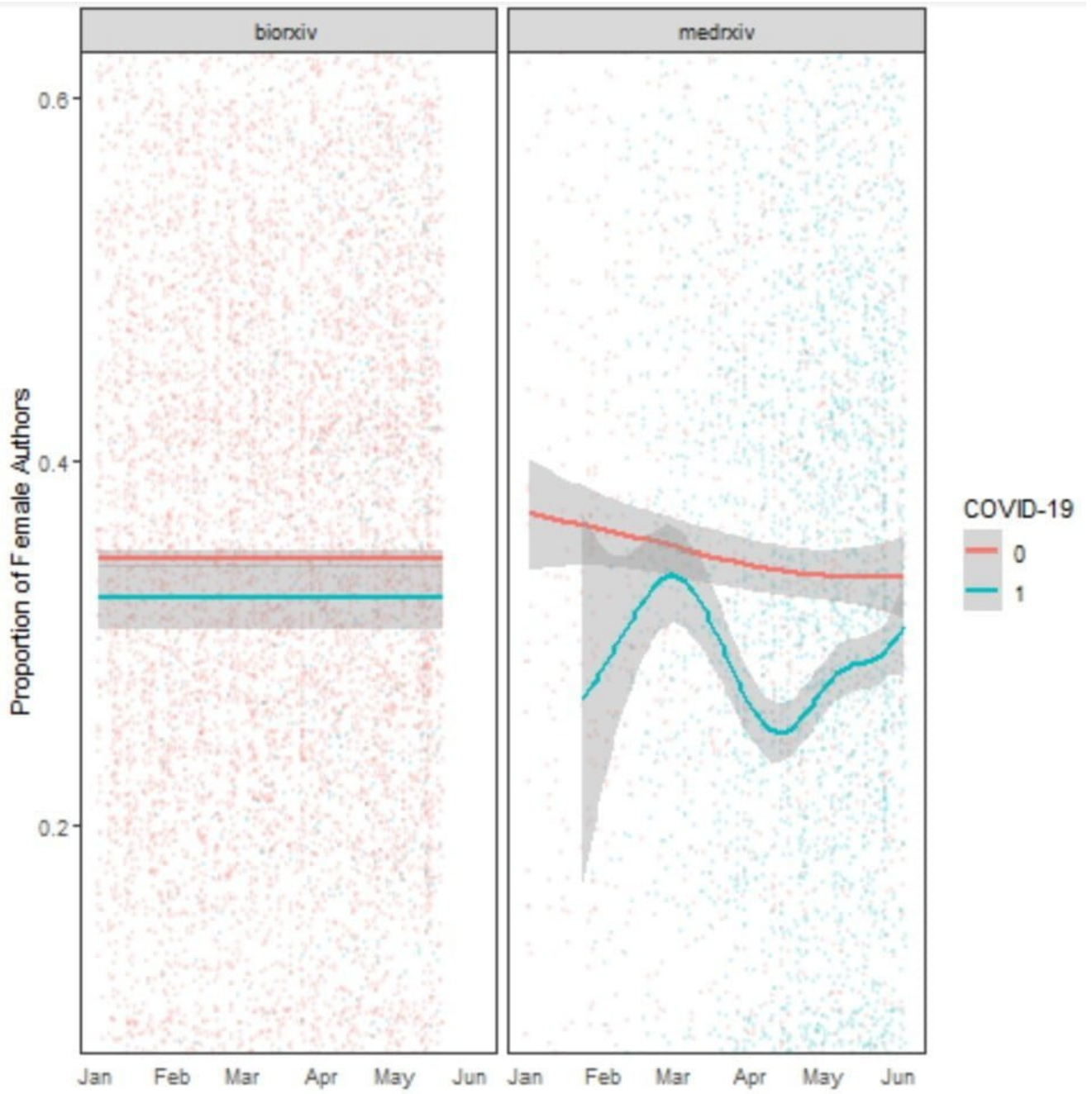
To contextualize these findings, we conducted 41 semi-structured individual interviews with rheumatology fellows and board-certified US rheumatologists, using purposeful sampling. Participants were presented with results from previous work exploring if a patient's sex and/or race influenced SLE diagnosis among rheumatologists. Interviews were conducted via web-conference. Transcribed qualitative interview data were analyzed thematically by 4 researchers, in NVivo.

Participants were 66% female and 39% were <5 years out of fellowship. Interview length ranged from 26-62 mins (Mean: 43 mins). Participants noted a range of factors contributing to SLE diagnosis including demographic factors (e.g., age, sex, or race), emphasized through curricula and exams (e.g., USMLE question vignettes). Many noted that relying on epidemiologic data shaped their pretest probability for SLE diagnosis, and that a major consequence to patients was delayed diagnosis, potentially resulting in more severe manifestations, particularly for males. Recommendations to prevent these biases included continuing education, implicit bias training, and the role of professional societies.

This study underscores the unique challenges of diagnosing SLE, with patients presenting with symptoms and serologies that vary over time with no diagnostic criteria. There is a need for training that curtails diagnostic bias in clinical decision making.

**Gender Balance and Readability of COVID-19 Scientific Publishing: A Quantitative Analysis of Preprint Manuscripts** Marie-Laure Charpignon\* Marie-Laure Charpignon Joel Park Julia Situ Liam G. McCoy Daniel K. Ebner Justin Saliccioli Leo Anthony Celi Aaron R. Kaufman

Releasing preprints is a popular way to hasten the speed of research but may carry hidden risks for public discourse. The COVID-19 pandemic caused by the novel SARS-CoV-2 infection highlighted the risk of rushing the publication of unvalidated findings, leading to damaging scientific miscommunication in the most extreme scenarios. Several high-profile preprints, later found to be deeply flawed, have indeed exacerbated widespread skepticism about the risks of the COVID-19 disease - at great cost to public health. Here, preprint article quality during the pandemic is examined by distinguishing papers related to COVID-19 from other research studies. Importantly, our analysis also investigated possible factors contributing to manuscript quality by assessing the relationship between preprint quality and gender balance in authorship within each research discipline. Using a comprehensive data set of preprint articles from medRxiv and bioRxiv from January to May 2020, we construct both a new index of manuscript quality including length, readability, and spelling correctness and a measure of gender mix among a manuscript's authors. We find that papers related to COVID-19 are less well-written than unrelated papers, but that this gap is significantly mitigated by teams with better gender balance, even when controlling for variation by research discipline. Beyond contributing to a systematic evaluation of scientific publishing and dissemination, our results have broader implications for gender and representation as the pandemic has led female researchers to bear more responsibility for childcare under lockdown, inducing additional stress and causing disproportionate harm to women in science.





## **Trends in participation in Colorectal cancer screening by smoking status in the United States, 2018.** Christian Okitondo\* Christian Okitondo Shiwani Sapkota Allan Tate

### **Background**

The US Preventive Services Task Force recommends screening adults aged 45 to 75 for Colorectal cancer (CRC). This study examines socio-behavioral opportunities for targeted CRC screening interventions. Although cancer screening has reduced mortality from many types of cancer, including CRC, lifestyle behaviors continue to pose barriers to prevention and disease management. Smoking is a highly specific risk factor for many cancers, and this study explores trends in colorectal cancer screening among never-smokers, former smokers, and current smokers in the US.

### **Methods**

This cross-sectional study examined data from the 2018 National Health Interview Survey. Adults aged 45 - 75 (N=11,123) who had never been diagnosed with cancer were included. Multivariate logistic regression was implemented, accounting for the complex survey sampling design to examine associations between self-reported CRC screening and smoking status (never smokers, former smokers, and current smokers). Sociodemographic factors included in the model were age and sex, race/ethnicity, and nativity, as well as income, education, and marital status.

### **Results**

Current smokers were less likely to have ever received CRC screening (51% vs 59%; AOR 0.70; 95% CI 0.61-0.81,  $p < 0.001$ ) than never-smokers. In contrast, former smokers were more likely to have ever received CRC screening (67% vs 59%; AOR 1.48; 95% CI 1.33-1.65,  $p < 0.001$ ) than never-smokers. Among current smokers, those who tried to quit smoking in past year were more likely to have ever screened (55% vs 49%; AOR 1.33; 95% CI 1.07-1.66,  $p < 0.05$ ) than those who never tried.

### **Conclusion**

Lower rate of CRC screening is strongly correlated with active smoking. Public health implications should emphasize smoking cessation integrated with counseling interventions on the importance of cancer screening in this high-risk group. Active smokers can therefore benefit the most from cancer screening to prevent the disease or detect it at an early stage.

**Incidence of harms following colorectal cancer screening by colonoscopy in older adults**

Jessica Chubak\* Jessica Chubak Laura Ichikawa Sophie Merchant Ronit Dalmat Rebecca Ziebell  
Christopher Jensen Jeffrey Lee TR Levin Douglas Corley Nirupa Ghai Beverly B. Green Celette Sugg  
Skinner Joanne Schottinger Erica Breslau Aruna Kamineni

The US Preventive Services Task Force recommends offering colorectal cancer screening to adults aged 45-75 but only selectively to those aged 76-85. Harms of colonoscopy are important considerations, but data are limited for older adults. We conducted a retrospective cohort study of screening colonoscopies vs. fecal immunochemical tests (FIT) among patients ages 76-85 within 4 integrated healthcare systems (2010-2019) using electronic health records and administrative data. The primary outcome was death or overnight hospitalization within 30 days. A secondary outcome included the primary outcome or any of nine diagnoses (e.g., gastrointestinal bleed, stroke). A log binomial model accounting for multiple tests per person estimated risk following colonoscopy vs. FIT. The main analysis truncated follow-up at the next lower endoscopy or procedure; however, we also examined results without truncation to include harms occurring at procedures triggered by screening. In the main analysis, patients aged 76-85 undergoing colonoscopy (N=4,465) had a 1.03% (95% CI: 0.77%, 1.37%) risk of death or hospitalization within 30 days. The risk in patients undergoing FIT (N=73,775) was similar (RD vs. FIT as reference=0.19% (95% CI: -0.11%, 0.49%)). Without truncation, the risk in colonoscopy patients was 1.63% (95% CI: 1.30%, 2.05%) with RD=0.75% (95% CI: 0.37%, 1.13%) vs. FIT patients. The secondary outcome risk in colonoscopy patients (1.23%, 95% CI: 0.95%, 1.60%) was higher than FIT patients (RD=0.34% (95% CI: 0.01%, 0.67%)) with truncation and increased to RD=0.88% (95% CI: 0.48%, 1.27%) without truncation. Results adjusted for healthcare system, age, sex, comorbidity, and body mass index were similar. Our study suggests the risk of death or hospitalization after screening colonoscopy at ages 76-85 is low and similar to a FIT-screened population. However, colonoscopy may confer an increased risk when a broader range of harms or events following downstream procedures are included.

**Subdivision model of susceptibility phase based on natural history of disease in preventive medicine** Hideo Yamazaki\* Hideo Yamazaki Soichi Sakabe Xiao Qing Hikaru Yamazaki Noriko Miyake

**Introduction:** In practical activities of community health and public health based on health promotion (HP) proposed by the World Health Organization (WHO), a primary prevention is one of the most effective ways to prevent lifestyle-related diseases (LSRDs). In general, although the young-adults have a very low incidence rate in LSRDs, the cumulative exposure to behavioral disadvantage across stages of life may be strongly associated with predispose LSRDs. However, an appraisal way for health conditions in a susceptibility phase based on the natural history of diseases has not been established yet. The present study proposes a model of the primary prevention segmentation that corresponds to the variation in the susceptibility phase in preventive medicine from a light of HP activities.

**Methods:** A self-report questionnaire consisted of 54 items was administered to the young-adults in Japan between 2015 and 2019. As analyzed data without defect values, 4,889 samples obtained from university students. A principal component analysis (PCA) was applied to valid data.

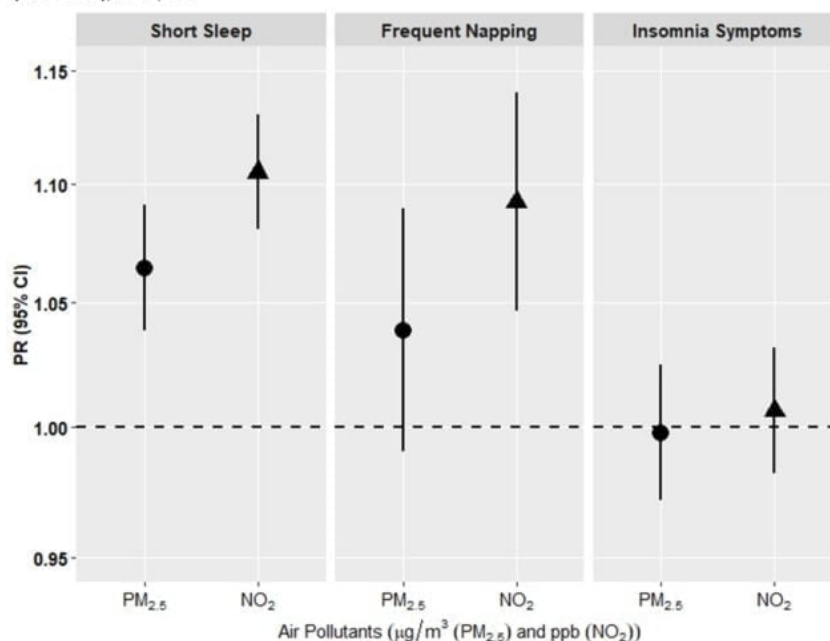
**Results:** The PCA was applied to the sample in order to extract a semihealth index (SHI) meant one's poor health condition in the susceptibility phase. Then the index score was calculated by the norm eigenvectors of the first principal component. Furthermore, a distribution of the young-adults with the semihealth condition was determined by using this score. As a result, the prevalence, sensitivity, specificity, positive predictive value, negative predictive value, and false positive rate showed 23.4%, 86.1%, 82.2%, 59.7%, 95.1% and 0.18, respectively.

**Conclusions:** The findings from this study made it possible to divide the susceptibility phase into two phases: the healthy phase and the semihealthy phase. It was pointed out that this empirical model will allow for the accurate and rapid development of measures for people who have moved from the healthy phase to the semihealthy phase.

**Air pollution and sleep health in a racially/ethnically diverse cohort of US women** Symielle A. Gaston\* Symielle Gaston Dana M. Alhasan Jennifer L. Ish Joel D. Kaufman Dale P. Sandler Alexandra J. White Chandra L. Jackson

**Background:** In the US, under-resourced communities, which are largely comprised of minoritized racial/ethnic groups, have disproportionately higher burdens of air pollutant exposure and poor sleep health. Yet, research on the interplay between racial/ethnic disparities in air pollution—a likely contributor to sleep disordered breathing—and sleep health is sparse. **Methods:** To investigate exposure to fine particulate matter (PM<sub>2.5</sub>) and NO<sub>2</sub> in relation to sleep health, overall and by race/ethnicity among US women, we used enrollment data collected in 2003-2009 from 39,682 eligible Sister Study participants. Validated spatiotemporal models estimated average ambient PM<sub>2.5</sub> and NO<sub>2</sub> concentrations at participants' homes for the year prior to their enrollment. Self-reported sleep characteristics included duration (<7 vs. 7-9 hours), napping (≥3 times/week), and insomnia symptoms. Adjusted for sociodemographic, health behavior, and clinical characteristics, PRs and 95% CIs were estimated using Poisson regression with robust variance. We performed Wald tests for additive and multiplicative interaction. **Results:** Mean±SD age was 55±9.0 years, 3.0% identified as Latina, 8.5% non-Hispanic Black (NHB), 86% non-Hispanic White, and 2.5% another race/ethnicity. NHB participants had the highest PM<sub>2.5</sub> and NO<sub>2</sub> concentrations (e.g., IQR<sub>PM<sub>2.5</sub></sub>=11-13 μg/m<sup>3</sup> NHB vs. IQR<sub>PM<sub>2.5</sub></sub>=8.7-12 μg/m<sup>3</sup> overall) and prevalence of poor sleep (e.g., short sleep: 52% vs. 28% overall). Associations did not vary by race/ethnicity (p<sub>interactions</sub>>0.05). An interquartile increase of each pollutant was associated with a higher prevalence of short sleep duration (PR<sub>PM<sub>2.5</sub></sub>=1.06 [95%CI:1.04-1.09] and PR<sub>NO<sub>2</sub></sub>=1.11 [1.08-1.13]) and frequent napping (PR<sub>PM<sub>2.5</sub></sub>=1.04 [95%CI:0.99-1.09] and PR<sub>NO<sub>2</sub></sub>=1.09 [1.05-1.14]). **Conclusion:** While air pollution was similarly associated with poor sleep across races/ethnicities, the higher exposure among NHB women offers a potential target for interventions to mitigate sleep disparities.

Figure 1. Prevalence ratios of poor sleep per IQR increase in air pollutant concentrations, Sister Study (2003-2009), N=39,682



Abbreviation: IQR (interquartile range). Models are adjusted for race/ethnicity, age category, census tract-level median household income, census region of residence, population density, physical activity, history of asthma, antidepressant use, and sleep medication use.

**Impact of racial and childhood socioeconomic position on latent class analysis-defined concurrent adverse childhood experiences in a population-based sample**

Lydia (Marcus) Post\* Lydia (Marcus) Post Dimitri Topitzes Dorothy R Pathak Young Cho Kelly Hirko Richard Houang Jamila Kwarteng Ann S Hamilton Ellen M Velie

Unlike the commonly used adverse childhood experience (ACE) index, which weights adversities equally, latent class analysis (LCA)-defined ACE clusters identify patterns of concurrent ACE exposure that may have distinct risk profiles. To our knowledge, no studies have evaluated ACE clusters by joint race and childhood socioeconomic position (cSEP). We identify ACE clusters with LCA and evaluate the joint associations of cSEP and race with ACE clusters in a population-based sample of women. **Methods:** Data are from 20-49-year-old non-Hispanic Black (NHB, n=665) and White (NHW, n=716) women in Metropolitan Detroit and Los Angeles County, 2011-2016. Race, cSEP indicators, and ACE exposure before age 13 years (caregiver(s) experienced: serious illness, divorce/separation, substance abuse, incarceration; participant experienced: loved one's death, sexual abuse, physical abuse, verbal abuse, personal everyday discrimination, vicarious everyday discrimination, physical abuse among adults in household) were recalled during in-person interviews. We identified ACE clusters via survey-weighted LCA, created a cSEP index using polychoric principal component analysis, and combined cSEP index with race to create a 6-category joint variable. We estimated ORs with 95% CIs for joint cSEP and race associations with ACE clusters using weighted multivariate logistic regression. **Results:** Three clusters emerged from LCA: low ACEs (53% of sample), high ACEs (25%), and predominantly everyday discrimination (23%). Odds of experiencing high ACEs were highest for low cSEP women (vs high cSEP NHW) irrespective of race (NHW OR=5.0, 95% CI 2.6, 9.4; NHB OR=6.1, 95% CI 3.1, 12.1). At all cSEP levels, NHB (vs high cSEP NHW) women had higher odds of everyday discrimination (e.g., high cSEP NHB OR=4.3, 95% CI 2.3, 8.0). **Conclusions:** NHB women had highest odds of experiencing everyday discrimination <13 years, irrespective of cSEP. Low cSEP was associated with higher odds of high ACEs regardless of race.

**Intergenerational educational mobility and depressive symptoms in young adulthood among a Filipino birth cohort** Elijah Watson\* Elijah Watson Thomas McDade Sera Young Christopher Kuzawa Lucia Petito

Rapid urbanization and economic development have contributed to changes in socioeconomic circumstances within and across generations, which may in turn contribute to mental health burdens. Using data from the Cebu Longitudinal Health and Nutrition Survey in the Philippines, we estimated associations between intergenerational educational mobility and depressive symptoms in young adulthood (mean age=21.5). Participant and parental educational attainment were used to cross-classify participants into stable-high (n=1,219), stable-low (n=165), upwardly mobile (n=312), or downwardly mobile (n=178) intergenerational trajectories. Depressive symptoms were measured in 2005 using a modified Center for Epidemiologic Studies-Depression scale (standardized to mean=0, SD=1). Parametric targeted maximum likelihood estimation (TMLE), adjusted for mother's age, urbanicity, household wealth, household income, gender, and mother's religion, was used to estimate marginal mean differences in depression scores by intergenerational educational mobility trajectories. Interaction terms were specified to model effect modification by gender and urbanicity. Compared with the stable-low trajectory, the stable-high trajectory was associated with lower depression scores (mean diff. = -0.44; 95% CI: -0.78, -0.09), while the upwardly mobile (mean diff = -0.07; 95% CI: -0.39, 0.29) and downwardly mobile trajectories (mean diff = -0.27; 95% CI: -0.63, 0.12) were not associated with significant differences in depression scores. When instead compared with the stable-high trajectory, downward mobility was associated with higher depression scores (mean diff. = 0.17; 95% CI: -0.02, 0.38). Our results suggest that stable-low and downward intergenerational educational mobility may contribute to poorer mental health in young adulthood. In a context characterized by rapid socioeconomic change, the potential mental health benefits of upward educational mobility may not be fully realized in young adulthood.

**Neighborhood social environment and air pollution exposure: a meta-analytic approach summarizing evidence across six prospective cohorts**

Hiwot Y. Zewdie\* Hiwot Y. Zewdie  
Carolyn A. Fahey Anna L. Harrington Claire L. Leiser Elizabeth W. Spalt Joel D. Kaufman Anjum Hajat

Air pollution exposure is linked to numerous poor health outcomes. Research on the relationships between social factors, such as racial residential segregation (RRS) and neighborhood socioeconomic status (NSES), and air pollution exposure will illuminate air pollution burden and inequitable distribution of air-pollution-related health risks.

We compiled data from six large cohorts, restricting to Black and White participants residing in urban tracts, to examine associations between the social environment (i.e., RRS, NSES) and individual air pollution exposure. Cohorts included the Multi-Ethnic Study of Atherosclerosis (n=4,889), Reasons for Geographic and Racial Differences in Stroke (n=24,498), Cardiovascular Health Study (n=3,911), Health Professionals Follow-up Study (n=33,675), Nurses' Health Study (n = 91,319), and Nurses' Health Study II (n=74,620). We used decennial census data to derive a NSES index and a novel spatial RRS measure (i.e., divergence) for participants' residing census tracts. We used national spatiotemporal models to estimate PM<sub>2.5</sub> and NO<sub>2</sub> exposures at participants' residential addresses. To pool effect sizes across adjusted cohort-specific multilevel models, we fit random-effects models using a DerSimonian-Laird estimator. Effect sizes represent a percent change in the air pollution measure per standard deviation difference in RRS or NSES.

More RRS was associated with higher air pollution exposure across all cohorts, with stronger neighborhood effects observed for NO<sub>2</sub> (Pooled % Change PM<sub>2.5</sub>=3.20, 95% CI: 1.61,4.78; Pooled % Change NO<sub>2</sub>=10.82, 95% CI: 6.22, 15.42). Similarly, greater neighborhood economic disadvantage was associated with higher air pollution exposure (Pooled % Change PM<sub>2.5</sub>=2.94, 95% CI: 1.59, 4.28; Pooled % Change in NO<sub>2</sub>=8.40, 95% CI: 5.11, 11.69).

Disadvantaged social environments were associated with higher individual air pollution exposure. Findings may be used to inform policymaking and reduce environmental health inequities.

**Association between specific maternal adverse childhood experiences and perinatal maternal mental health in a longitudinal study nested in a home visiting program** Katherine Bowers\* Katherine Bowers Alonzo Folger Lili Ding

Prior studies have identified an association between adverse childhood experiences (ACE) and maternal mental health in the perinatal period, including depression and anxiety. Home-visiting programs serve pregnant women experiencing poverty to support parenting and ultimately optimize child development. Identification of specific experiences that place women at higher risk for mental health impairment is critical to support trauma-informed care in home visiting. The Pregnancy and Infant Development Study (PRIDE) follows pregnant women participating in the Every Child Succeeds home visiting program in Cincinnati, Ohio through 18 months postnatal, collecting comprehensive data on psychosocial experiences and perinatal and child health outcomes. Among 267 women who completed a postnatal study visit we evaluated the association between specific maternal ACEs and maternal mental health as measured by the Edinburgh Postnatal Depression Scale (EPDS) and the Brief Symptom Index (BSI)-18, which measures overall distress and 3 individual aspects of distress including somatization, depression and anxiety. Overall, women with greater than 4 ACEs screened positive for depression on the EPDS ( $\geq 11$ ) at nearly twice the frequency (41.6 versus 21.9%,  $p=0.0008$ , for each additional ACE: OR=1.17, 95% CI:1.06, 1.29) and had higher scores on the BSI-18 Global Severity Index (GSI) ( $\beta=1.55$  (0.96, 2.14)). The strongest associations were observed for mothers who experienced physical abuse by family ( $\beta=8.9$ , CI: 4.8, 12.9) felt unloved or not special ( $\beta = 8.3$ , CI: 4.8, 11.7) and who had neglectful parenting ( $\beta = 9.5$ , CI: 5.1, 14.0). Associations remained adjusting for other ACEs ( $\beta = 6.2$ ,  $p=0.03$ ;  $\beta=5.1$ ,  $p=0.02$ ;  $\beta=4.6$ ,  $p=0.09$ , respectively). Though correlation exists between ACEs ( $r^2$  range .35 - .46), Variance Inflation was  $<2.5$  for all independent variables. Further analyses will be conducted to evaluate whether home visiting services may mitigate these associations.

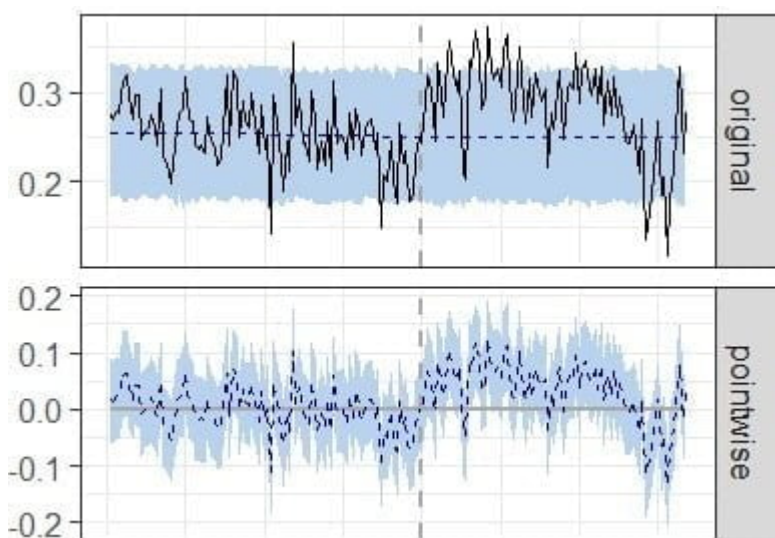


## The rise of anti-Jewish sentiment on Twitter: the impact of Kanye and Elon

Thu T Nguyen\*  
Thu Nguyen Junaid S. Smith Yulin Hswen

The media have reported a rise in anti-Semitic speech in recent months starting with public anti-Jewish statements from prominent figures such as Kanye West (first anti-Semitic tweet on October 7 2022), Kyrie Irving, and former president Trump. Elon Musk's acquisition of Twitter on October 27 further resulted in a large-scale departure of employees with key roles in content moderation. This study aims to empirically investigate changes in negative sentiment of tweets referencing Jewish people following these events. A random 1% sample of 55,336 publicly available tweets using Jewish keywords was collected using Twitter's Application Programming Interface (API). Sentiment analysis was performed using support vector machine (SVM), a supervised machine learning model.

Comparison of manually labeled and machine classified negative sentiment tweets indicated 91% model accuracy. A Bayesian structural time series model was fitted, specifying July 1 - October 7 as the pre-period, which was used to estimate the expected proportion anti-Semitic tweets from October 8-December 31 (post-period). Panel 1 of Figure 1 displays the observed (solid line) and expected (horizontal dotted line) proportion of tweets referencing Jews that were negative based on pre-Oct 8 data (vertical dotted line), and Panel 2 shows the pointwise differences between the two. After October 8, we observed a rise in proportion of tweets referencing Jews that were negative. This was sustained for several weeks and began to decline in the latter half of December. During the post-Oct 8 period, 28% of tweets referencing Jews were negative, compared to expected proportion of 25%, indicating a relative increase of 13% (95% CI: 8%, 19%). Our results align with reports indicating a rise in anti-Semitic speech following statements by public figures and changes on Twitter. Social media data can be used to examine shifts in publicly expressed sentiment about minoritized groups.



**Area-level New Deal emergency employment of teachers and late-life cognition among Health and Retirement Study Participants** Chloe Eng\* Chloe Eng David Rehkopf Maria Glymour Sepideh Modrek

**Background**

New Deal emergency employment programs in the 1930s provided funding for hundreds of thousands of teachers in response to sweeping school budget cuts of the Great Depression. We examine the association between increased area-level teacher employment through the Works Progress Administration (WPA) and late-life cognition.

**Methods**

Health and Retirement Study participants (age 50+ years) were linked to 1940 census records (n=7,725) with childhood geographic information. Average z-standardized memory and decline across biennial survey waves (1998-2018; mean follow-up: 4.4 years) were estimated as a function of enumeration district-level WPA teacher employment, as the percent increase in teachers from WPA funding past non-WPA teachers. Mixed linear regression models with random intercepts were adjusted for percent non-WPA teachers in district and individual/area-level covariates with state fixed effects.

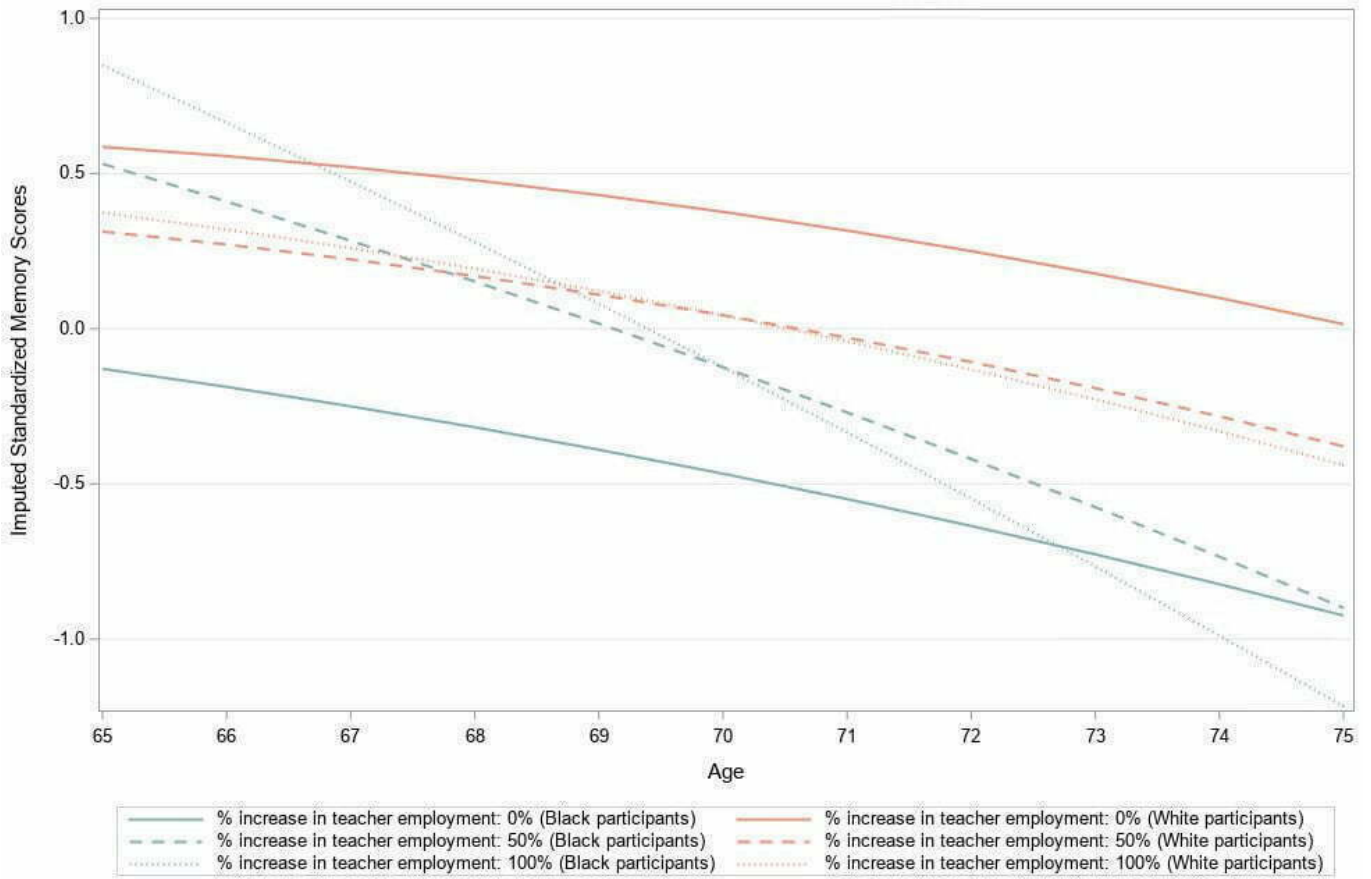
**Results**

Most (n=5,919; 76.5%) census-linked HRS participants lived in districts with at least some WPA teachers. WPA teacher employment was higher in areas with a higher density of non-WPA teachers, more Black residents, higher unemployment, and fewer homeowners. A 10% increase in teachers through the WPA was associated with 0.05 (95% CI: 0.08, 0.80) SD lower memory scores and a faster decline of up to 0.03 (95% CI: -0.05, -0.01) SD per year. Black participants had faster annual decline by 0.02 (95% CI: 0.01, 0.02) SD per 10% increase in teachers through the WPA.

**Conclusions**

Increased teacher employment through the New Deal was associated with lower late-life cognitive performance and faster decline, likely related to the allocation of New Deal funding to lower-resource areas and more so for decline in Black participants. Further research is needed to quantify whether results reflect any neutralization of pre-existing disadvantage.

**Associations between additional teacher employment through the WPA and late-life cognitive decline in race-stratified models  
(p-value for race-age-WPA interaction = 0.0295)**



**Adverse childhood experiences (ACEs) and health-related behaviors during emerging adulthood: A cross-sectional analysis of 2019-2020 Florida Behavioral Risk Factor Surveillance System (BRFSS) data.** Michelle Crozier\* Michelle Crozier Hillary Denton

**Introduction:** Adverse childhood events (ACEs) are toxic stressors before 18 years and lead to poor health in adulthood. The brain finishes developing during emerging adulthood (18-25 years), but little research exists examining the impact of ACEs on health during this important phase. We conducted a cross-sectional analysis of the association between ACEs and health seeking and risk-taking behaviors among 18-25 year olds in Florida using the 2019-2020 Florida Behavioral Risk Factor and Surveillance System (BRFSS). **Methods:** Respondents self-reported 10 ACEs and those with  $\geq 1$  ACE were considered exposed. We examined 6 outcomes (y/n): poor health, could not see a physician due to cost, received flu vaccine in past year, ever tested for HIV, 1 HIV risk behavior in past year (injection drug use, STD treatment, money for sex, unprotected sex), binge drinking in past month, and 7 covariates: sex (m/f), age (continuous), race/ethnicity (NH white, NH black, NH multiracial, NH other, Hispanic), marital status (married/widowed, divorced/separated, never married, part of unmarried couple), education (high school, some college, college), income ( $\leq \$24,999$ ,  $\$25,000-49,999$ ,  $\geq \$50,000$ ), health care coverage (y/n). We used multivariable logistic regression with survey weights in SAS 9.4. **Results:** A total of 6,075 (2019) and 8,208 (2020) emerging adults were included (54, 55% male, respectively). We observed that those with  $\geq 1$  ACE had statistically significantly greater odds of each outcome except for receiving a flu vaccine and binge drinking (no association). The strongest associations were for HIV risk behaviors (aOR<sub>20</sub>=3.70, 95% CI: 2.43-5.63) and not seeing a physician due to cost (aOR<sub>20</sub>=3.16, 95% CI: 2.02-4.96). **Discussion:** These exploratory results highlight the need for further research of emerging adulthood and show that potentially no relationship exists between ACEs and certain risky behaviors such as binge drinking, as is observed among older adults with a history of ACEs.

**LATEBREAKER**

Social

**Structural racism and cortisol as a biomarker of stress in adolescents** Helen C.S. Meier\*

Sarah Laurent Lorraine Halinka Malcoe Helen C.S. Meier

**Background:** Stress exposure during adolescence can result in negative lifelong health outcomes. No previous studies have examined historical practices of structural racism, such as redlining, in relation to present-day biomarkers of stress in adolescents.

**Objective:** We examined the association between historic redlining and a biomarker of stress in adolescents.

**Methods:** Data come from the Study of Adolescent Neural Development. A total of 175 adolescents aged 15–17 years from Chicago, Detroit, or Toledo had cortisol concentrations derived from hair samples. Historic redlining scores assessed the proportion of census tracts graded by the Home Owners' Loan Corporation (HOLC) "residential security" maps from the early 20th century multiplied by a weighted HOLC grade. Census tracts were divided into intervals based on the national distribution of redlining scores; areas not assessed by HOLC were marked as "ungraded". We used linear regression models to examine associations between redlining scores and log-transformed cortisol levels adjusted for covariates of interest including baseline city of residence and mom's age at birth.

**Results:** About half (46.5%) of the sample resided in the lowest two redlining intervals, which included tracts with HOLC gradings of "declining" or "hazardous" for investment, while 34.0% lived in ungraded census tracts. Adolescents living in tracts with the two lowest HOLC intervals had higher cortisol levels compared to those living in ungraded regions, after adjusting for covariates of interest ( $\beta=0.77$ , CI: 0.11, 1.43). A sensitivity analysis in non-Hispanic Black adolescents only showed similar results.

**Discussion:** Our study is the first to show that census tracts graded by the HOLC as declining or hazardous for investment are associated with present-day higher stress levels in adolescents. These findings provide support that historic structural racism is an upstream determinant of present-day health inequalities.

**Trajectories of childhood educational quality and late-life cognitive decline among Black and White older adults** Yenee Soh\* Yenee Soh Elizabeth Rose Mayeda Rachel L. Peterson Charles P. Quesenberry Jr. Dan M. Mungas Rachel A. Whitmer M. Maria Glymour Paola Gilsanz

## Background

The few studies evaluating effects of educational quality (e.g., attendance rates) on late-life cognitive outcomes have not incorporated information on educational quality measures at different grades. We examined state-level attendance rate trajectories during early childhood and adolescence among Black and White adults in Northern California, and their associations with late-life cognitive decline.

## Methods

Participants in the Kaiser Healthy Aging and Diverse Life Experiences cohort (n=758) reported their state of residence in 1st, 6th, 9th, and 12th grade, which was linked to historical state- and year-specific data on school attendance rates. Latent class mixture modeling analyses identified distinct attendance rate trajectories. Domain-specific cognition (executive function, verbal episodic memory, and semantic memory) was assessed up to 3 times with the Spanish and English Neuropsychological Assessment Scales. Linear mixed-effects models estimated associations between attendance rate trajectory groups and domain-specific cognitive decline (z-standardized), overall and by race.

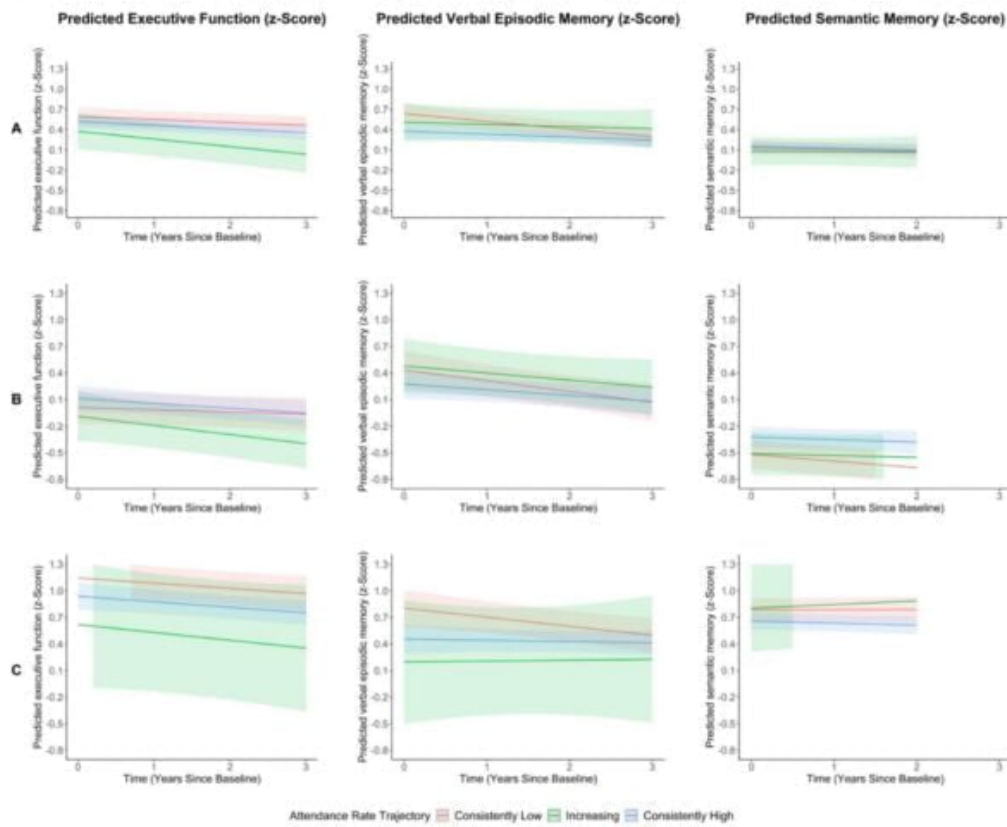
## Results

Mean participant age at start of follow-up was 75.6 years, 49.7% identified as Black, 63.1% female, and 28.1% had maternal education >12 years. Three attendance rate trajectories were identified: consistently low (32.7%), increasing (6.6%), and consistently high (60.7%). Compared to individuals attending schools in states with consistently low attendance rate trajectories (reference), individuals in consistently high trajectories had lower baseline verbal episodic memory ( $\beta$ [95%CI] = -0.26[-0.41, -0.11] SD units) and slower decline over time (0.07[0.02, 0.12] SD units/year). In race-stratified analyses, similar results were found among White participants only (Figure).

## Conclusions

Trajectories of school attendance may be differentially associated with late-life cognitive aging. Larger-scale studies are needed to confirm these preliminary findings.

**Figure. Predicted Domain-Specific Cognitive Trajectories by Attendance Rate Trajectory Group**



Trajectories represent predicted marginal means of z-scores for each cognitive domain (executive function, verbal episodic memory, semantic memory) over time in relation to attendance rate trajectory groups (Panel A: pooled sample, Panel B: Black individuals only, Panel C: White individuals only). All models include random intercepts and are adjusted for baseline age, sex, race (in pooled sample only), maternal education, time since baseline, and interaction term for time with attendance rate trajectory group. Models for executive function and verbal episodic memory additionally adjusted for practice effects and interview mode. Models for semantic memory were only available across two time points.

**Changes in air pollution exposure over time by racial residential segregation in the United States: a longitudinal multi-cohort study** Carolyn Fahey\* Carolyn Fahey Hiwot Zewdie Claire Leiser Elizabeth Spalt Joel Kaufman Anjum Hajat

## Background

While ambient air pollution has declined over time in the United States, exposure disparities by race and ethnicity persist. Racial residential segregation may contribute to differential reductions in air pollution and perpetuate related health inequities.

## Methods

We analyzed harmonized data from six longitudinal cohort studies: Nurses' Health Study (NHS), NHS II, Health Professionals Follow-up Study (HPFS), Cardiovascular Health Study (CHS), Multi-Ethnic Study of Atherosclerosis (MESA), and Reasons for Geographic and Racial Differences in Stroke (REGARDS) (N= 3,860,761 person-years). Address-level annual average NO<sub>2</sub> and PM<sub>2.5</sub> levels were estimated from national spatio-temporal models. Annual neighborhood segregation indices of multi-race divergence, Black-White dissimilarity, and single-race isolation were created from Census tract-level data. We evaluated percent changes in NO<sub>2</sub> and PM<sub>2.5</sub> over time by segregation z-score and race using log-linear generalized estimating equations adjusted for age, sex, socioeconomic status, urbanicity, region. Results for each cohort were combined using fixed effects meta-analysis.

## Results

From 2000 to 2017, mean NO<sub>2</sub> exposure decreased by 51.1 % for Black participants [from 15.8 to 7.73 ppb] and 49.3% for White participants [11.25 to 5.70 ppb]; PM<sub>2.5</sub> respectively declined by 48.4% [14.9 to 7.7 µg/m<sup>3</sup>] and 44.7% [13.1 to 7.2 µg/m<sup>3</sup>]. Among Black participants, exposure levels were consistently higher in more segregated neighborhoods, where the rate of decline lagged: each standard deviation increase in divergence was associated with 0.08% (95% CI: 0.06-0.10) and 0.05% (0.04-0.06) slower average annual declines in NO<sub>2</sub> and PM<sub>2.5</sub>, respectively, with similar trends for dissimilarity and isolation. In contrast, increasing divergence among White participants was associated with *faster* rates of decline in air pollution [NO<sub>2</sub>: -0.66% (95% CI: -0.70, -0.63); PM<sub>2.5</sub>: -0.31% (95% CI: -0.33, -0.29)].

## Conclusions

Despite improvements in air quality, Black individuals continue to experience higher levels of air pollution than White individuals, particularly in more segregated neighborhoods. These disparities may fuel enduring inequities in health outcomes, warranting further research and action on environmental injustice.



**Identifying and characterizing the social and structural determinants of health of Asian American enclaves by ethnic origin groups**

Sarah-Truclinh Tran, MPH\* Sarah-Truclinh Tran  
Janne Boone-Heinonen, PhD, MPH Sarah B. Andrea, PhD, MPH Betty T. Izumi, PhD, MPH, RD  
Miguel Marino, PhD, MS

**Background:** Asian Americans (AsA) are the fastest-growing segment of the United States (US) population and are experiencing increasing residential segregation. Neighborhood conditions of AsA enclaves are poorly understood, particularly in disaggregated AsA subgroups.

**Methods:** Using 2015-2019 American Community Survey data from 590 mainland counties with >100,000 residents, we identified Chinese, Filipino, Indian, Japanese, Korean, and Vietnamese enclaves, defined as counties with high ethnic concentration, segregation, and isolation of the specific AsA group relative to regional distributions. We then examined their area-based socioeconomic metrics (ABSM): median household income, percent (%) college educated, %foreign-born, %households in poverty, and more.

**Results:** We identified 57 ethnic enclaves. Filipino and Chinese enclaves are the most geographically dispersed. Other AsA group enclaves are disproportionately located in a single subregion (e.g., 4/8 Indian and 4/9 Vietnamese enclaves are in the South, 4/6 Korean enclaves are in the Midwest). Los Angeles County, CA is an enclave setting for all AsA groups except Indian.

Filipino and Vietnamese enclaves are in counties represented at the highest and lowest ABSM values. Most Chinese enclaves (10/13) have below-state median incomes, while most (3/4) Japanese enclaves have above-state median incomes and lower %foreign-born. Overall, counties with an AsA enclave have higher %foreign-born and %household overcrowding than non-enclave counties. Chinese, Korean, and Vietnamese enclaves have higher %poverty than their non-enclave counterparts.

**Conclusion:** There are wide variations in the geography and ABSM of AsA enclaves by ethnic origin that likely reflect differences in immigration, assimilation, and segregation histories. Results can inform local public health institutions engaging with segregated AsA groups in their jurisdictions, as well as place-based research on rapidly growing and evolving AsA ethnic groups.

Table. Descriptive statistics of the counties identified as ethnic enclaves of each Asian subgroup, 2015-2019 ACS

Subregion	County	Total population	% of the race group	D <sub>m</sub>	mP <sub>m</sub>	% Foreign-born	% College	Median income (\$)
<b>Chinese enclaves</b>								
1 New England	Hampshire County, MA	161,032	2.35	0.57	0.08	8.8	23.9	28,327
2 Mid Atlantic	Broome County, NY	193,188	1.54	0.63	0.09	7.0	15.4	26,593
3 East North Central	Delaware County, IN	115,020	0.69	0.70	0.03	2.1	13.4	22,613
5 South Atlantic	Pickens County, SC	124,029	0.80	0.65	0.04	3.6	14.9	23,331
9 Pacific	San Bernardino Co., CA	2,149,031	2.13	0.55	0.21	21.0	13.6	27,235
2 Mid Atlantic	Kings County, NY	2,589,974	8.23	0.61	0.48	36.1	22.5	31,406
4 West North Central	St. Louis city, MO	308,174	0.98	0.63	0.09	7.2	19.7	28,186
4 West North Central	Lancaster County, NE	313,158	0.95	0.60	0.09	7.8	24.8	31,293
6 East South Central	Bradley County, TN	105,749	0.58	0.75	0.04	5.8	14.1	26,412
9 Pacific	Los Angeles County, CA	10,081,570	5.06	0.63	0.53	34.0	21.2	29,985
2 Mid Atlantic	Rensselaer County, NY	159,185	1.24	0.66	0.08	5.2	18.0	36,310
6 East South Central	Madison County, MS	104,562	0.55	0.69	0.04	4.5	28.8	36,455
9 Pacific	Sacramento County, CA	1,524,553	3.98	0.55	0.24	20.9	20.4	32,275
<b>Asian Indian enclaves</b>								
1 New England	Worcester County, MA	824,772	1.76	0.67	0.17	12.1	22.0	35,350
9 Pacific	Kern County, CA	887,641	1.32	0.67	0.18	19.9	11.0	25,013
2 Mid Atlantic	Queens County, NY	2,287,388	6.54	0.67	0.57	47.2	20.2	31,992
5 South Atlantic	Columbia County, GA	150,705	1.13	0.7	0.08	7.1	22.5	36,592
5 South Atlantic	Henry County, GA	225,356	1.45	0.68	0.18	7.9	18.1	33,610
5 South Atlantic	Iredell County, NC	175,538	1.05	0.71	0.09	6.5	20.0	30,102
5 South Atlantic	Union County, NC	231,053	1.56	0.66	0.09	9.5	24.1	34,405
7 West South Central	Benton County, AR	265,759	2.1	0.73	0.17	11.6	22.0	33,141
<b>Filipino enclaves</b>								
3 East North Central	DeKalb County, IL	104,366	0.67	0.64	0.04	6.5	20.2	28,262
5 South Atlantic	Highlands County, FL	103,437	0.97	0.68	0.06	11.0	11.0	22,059
8 Mountain	Cochise County, AZ	125,867	0.76	0.56	0.04	10.8	14.2	25,573
4 West North Central	Johnson County, IA	148,577	0.48	0.59	0.02	12.0	27.7	30,486
8 Mountain	Yuma County, AZ	209,468	0.71	0.54	0.06	26.3	9.8	24,291
9 Pacific	Los Angeles County, CA	10,081,570	4.05	0.49	0.33	34.0	21.2	29,985
9 Pacific	Monterey County, CA	433,410	3.42	0.51	0.25	29.8	14.8	28,207
1 New England	Kent County, RI	163,869	0.59	0.65	0.03	6.1	21.0	37,994
6 East South Central	Boone County, KY	130,820	0.43	0.73	0.03	5.7	20.7	36,732
6 East South Central	Kenton County, KY	165,668	0.31	0.73	0.03	3.3	19.6	32,892
9 Pacific	Ventura County, CA	847,263	3.15	0.48	0.24	21.8	21.3	33,814
9 Pacific	San Diego County, CA	3,316,073	6.14	0.54	0.36	23.4	23.8	34,307
9 Pacific	San Mateo County, CA	767,423	10.88	0.62	0.52	34.9	29.0	49,128
9 Pacific	Alameda County, CA	1,656,754	6.52	0.49	0.35	32.5	27.3	43,583
9 Pacific	Napa County, CA	139,623	5.58	0.73	0.48	22.1	23.2	37,953
9 Pacific	Santa Clara County, CA	1,927,470	5.87	0.53	0.4	39.2	27.7	47,584
9 Pacific	San Francisco County, CA	874,961	5.32	0.49	0.32	34.3	34.8	52,677
<b>Japanese enclaves</b>								
9 Pacific	Los Angeles County, CA	10,081,570	1.4	0.49	0.19	34.0	21.2	29,985
1 New England	Kent County, RI	163,869	0.23	0.76	0.02	6.1	20.9	37,994
2 Mid Atlantic	Dauphin County, PA	275,632	0.2	0.79	0.04	7.7	19.2	33,232
5 South Atlantic	Iredell County, NC	175,538	0.31	0.74	0.03	6.5	20	30,102
<b>Korean enclaves</b>								
2 Mid Atlantic	Camden County, NJ	506,738	0.49	0.67	0.04	11	20.3	33,626
3 East North Central	Vanderburgh County, IN	181,291	0.32	0.75	0.05	2.8	17.9	27,095
3 East North Central	Kenosha County, WI	168,524	0.3	0.73	0.02	6.3	16.8	31,510
9 Pacific	Los Angeles County, CA	10,081,570	2.28	0.57	0.34	34	21.2	29,985
3 East North Central	Allen County, IN	372,575	0.38	0.77	0.05	6.7	18.8	30,325
4 West North Central	Platte County, MO	100,682	0.48	0.71	0.03	5.5	26.4	39,879
<b>Vietnamese enclaves</b>								
5 South Atlantic	Wicomico County, MD	102,539	0.72	0.77	0.05	8.3	15.8	27,278
7 West South Central	Potter County, TX	119,674	1.36	0.84	0.34	15.7	10.3	25,457
3 East North Central	Walworth County, WI	103,074	0.23	0.88	0.04	5.7	18.3	29,626
7 West South Central	Orleans Parish, LA	390,845	1.63	0.83	0.72	5.5	21.2	26,095
9 Pacific	Los Angeles County, CA	10,081,570	1.15	0.66	0.34	34	21.2	29,985
3 East North Central	Summit County, OH	541,334	0.3	0.85	0.07	5.2	20.6	30,799
5 South Atlantic	Spotsylvania County, VA	132,833	0.4	0.76	0.05	6.8	19.5	38,572
9 Pacific	Santa Clara County, CA	1,927,470	7.62	0.66	0.56	39.2	27.7	47,584
9 Pacific	Orange County, CA	3,168,044	7.11	0.64	0.5	30.1	26	36,135

Ethnic enclaves are defined as counties with ≥100,000 residents and ≥4 census tracts, whose ethnic concentration, segregation, and isolation indexes for the target AsA subgroup are all in the top tertile of regional distributions.

D<sub>m</sub> : Dissimilarity index measures the extent to which the Asian ethnic group and non-Hispanic white group are unevenly distributed across census tracts within the county; higher values indicate higher segregation.

mP<sub>m</sub> : Isolation index measures the extent to which the Asian ethnic members are exposed only to one another in the county; higher values indicate higher isolation.

**A longitudinal evaluation of the relationship between sense of community belonging and type 2 diabetes incidence** Sarah Mah\* Sarah Mah Laura Rosella

**Background:** There is growing interest but limited longitudinal evidence for the potential of social connections and belonging to mitigate future health challenges such as chronic disease. Our objective is to estimate the association between community belonging and diabetes incidence in a cohort study.

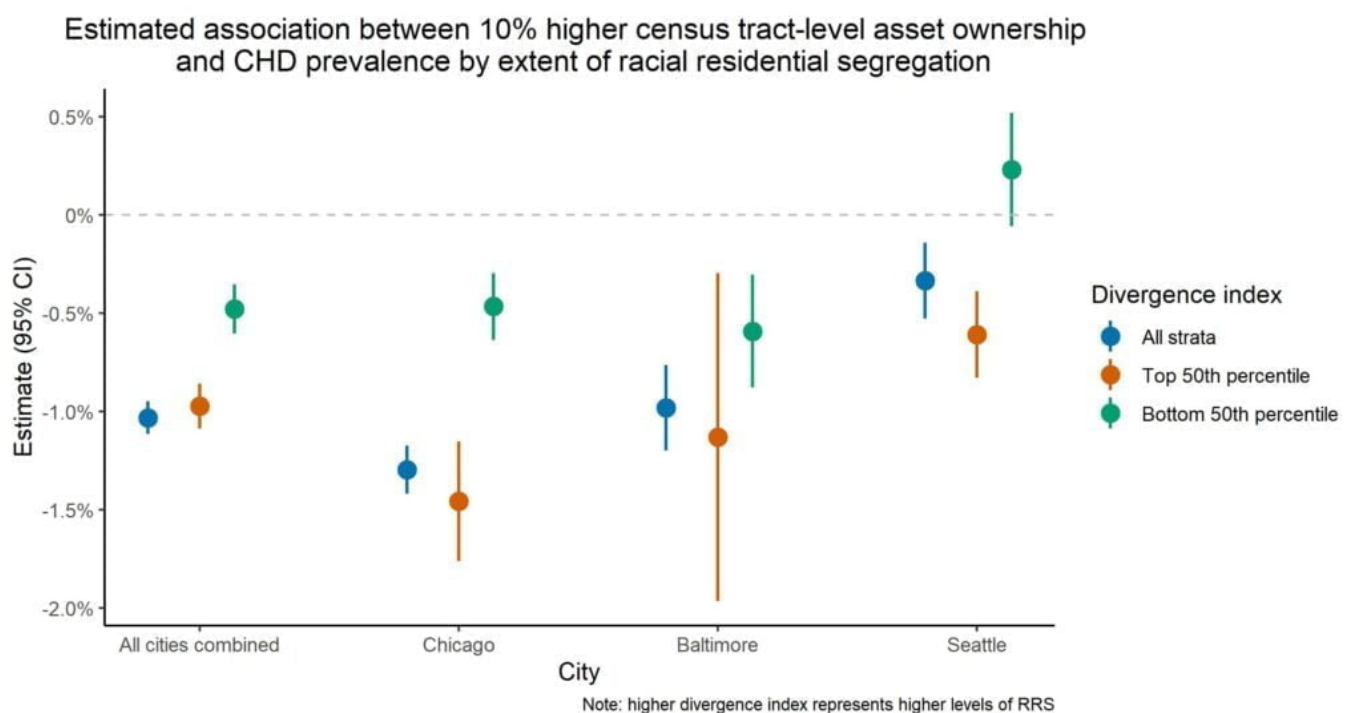
**Methods:** The cohort included Ontario respondents of the Canadian Community Health Survey (2000-2014) who were 30-84 years old, diabetes-free and rated their sense of belonging to community as being very strong, somewhat strong, somewhat weak, or very weak (N = 150 526). Individuals were linked to a validated diabetes registry in a single-payer system and followed until 31 March 2020. We modeled the relationship between sense of community belonging and 3-year diabetes incidence using cox proportional hazards models adjusting for a range of sociodemographic and behavioural confounders.

**Results:** At the end of study follow-up, 0.86% (N = 1437) of the sample developed diabetes. Those reporting a very high sense of community belonging were more likely to be older, more educated, partnered, and physically active. In contrast, those reporting a very low sense of community belonging were more likely to be younger, less educated, single, immigrant, currently smoking, and physically inactive. Compared to those reporting a somewhat strong sense of belonging, respondents with a very weak sense of belonging exhibited marginally higher risk of developing diabetes (HR 1.45, 95% CI 1.03-2.03) after adjusting for age and sex; however, the association was attenuated after adjusting for all covariates (HR 1.29, 95% CI 0.93, 1.79).

**Conclusions:** This study suggests there may be a relationship between weak sense of community belonging and higher diabetes incidence that warrants further investigation. Longer follow-up time will increase our ability to investigate the association further. The results add to the evidence examining the role that community belonging plays in population health.

**Assessing heterogeneity in the relationship between wealth, coronary heart disease, and racial residential segregation in three US cities** Andrea R Molino\* Andrea R Molino Carolyn A Fahey Kia L Davis Anjum Hajat

Wealth, from sources like asset income, can provide financial stability and reduce stress, a risk factor for poor cardiovascular health. This association may be modified by socioenvironmental factors such as racial residential segregation (RRS). This ecological study characterized the relationship between assets and coronary heart disease (CHD) examining potential effect modification by RRS in three US cities of differing sizes and RRS distributions: Chicago, Baltimore, and Seattle. We harmonized two national data sources at the census tract-level: the CDC 500 Cities Project to obtain 2017 CHD prevalences, and the 2013-2017 ACS to obtain percentages of households owning assets (interest, dividends, or net rental income). We operationalized RRS as multi-race divergence using the 2010 Decennial Census. Greater divergence represented higher RRS/racial divergence from the encompassing CBSA. We stratified tracts by top vs. bottom 50<sup>th</sup> divergence percentile using city-specific distributions, and fit linear regressions for all cities together, individually, and stratified by high vs. low divergence. 1,112 tracts were analyzed (Chicago=788, Baltimore=193, Seattle=131). Median CHD and asset ownership prevalences were 5.3% and 13.7%. Overall, 10% higher asset ownership was associated with 1.03% lower CHD prevalence (95%CI: -1.11, -0.95). The association between assets and CHD was stronger for tracts in the top 50<sup>th</sup> percentile of divergence in all cities, from -0.61% (95%CI: -0.83, -0.39) in Seattle to -1.46% (95%CI: -1.76, -1.15) in Chicago. The relationship varied notably for Seattle: 10% higher asset ownership was associated with higher CHD prevalence in low divergence tracts (0.23%, 95%CI: -0.06, 0.52). The association between wealth and cardiovascular health may depend on RRS, which may further be location specific. The assumption of homogeneity across urban areas may be flawed when examining US cities with differing historical contexts and current-day patterns of RRS.



**Associations between recent houselessness and adverse health outcomes: An outcome-wide analysis of the Veteran Aging Cohort Study** Yu Li\* Yu Li Kirsha S. Gordon Fiona Bhonodoekhan Rachel Vickers-Smith Stephen Crystal Robert D. Kerns E. Jennifer Edelman Brandon DL Marshall

**Background:** Houselessness is associated with multiple adverse health outcomes among people with HIV (PWH). However, most studies have been cross-sectional (limiting causal inference), and/or have studied only one of many clinical (e.g., viral load suppression) or patient-centered (e.g., quality of life) endpoints. We aimed to address these limitations by adapting a novel, outcome-wide analytic design developed by VanderWeele et al. to compare the effects of houselessness on multiple outcomes longitudinally. **Methods:** We used data from the Veterans Aging Cohort Study Survey Sample of PWH (2002-2004, N=1,215) to investigate whether recent houselessness measured at one time point (defined as past 4 weeks, yes vs. no) was associated with three groups of outcomes at a subsequent visit: HIV (viral load, CD4 counts, antiretroviral medication adherence), substance use (unhealthy alcohol use, any marijuana, stimulant/cocaine, and extra-medical opioid use), depression and pain interference (a measure of how much pain interferes with normal functioning), accounting for missing data with multiple imputation. **Results:** 145 (11.9%) participants reported recent houselessness at the first visit during the study period. Significant effects existed houselessness-pain interference relationship (RR: 1.38, 95% CI: [1.04, 1.82]), adjusted for demographics, baseline tobacco, and substance use: no other associations were statistically significant. **Conclusion:** We demonstrated the feasibility of conducting an outcome-wide longitudinal analysis of multiple outcomes contemporaneously using data from a large, prospective cohort of PWH. This approach avoids problems of under-reporting null effects often seen for single outcome analyses and permits comparison of effect sizes across multiple outcomes. Considering the commonly co-occurring outcomes among PWH evaluated in this study, pain interference may play an important role in maintaining housing stability.

**Comparative Effectiveness of Urine Drug Testing Schedules Alongside Opioid Agonist**

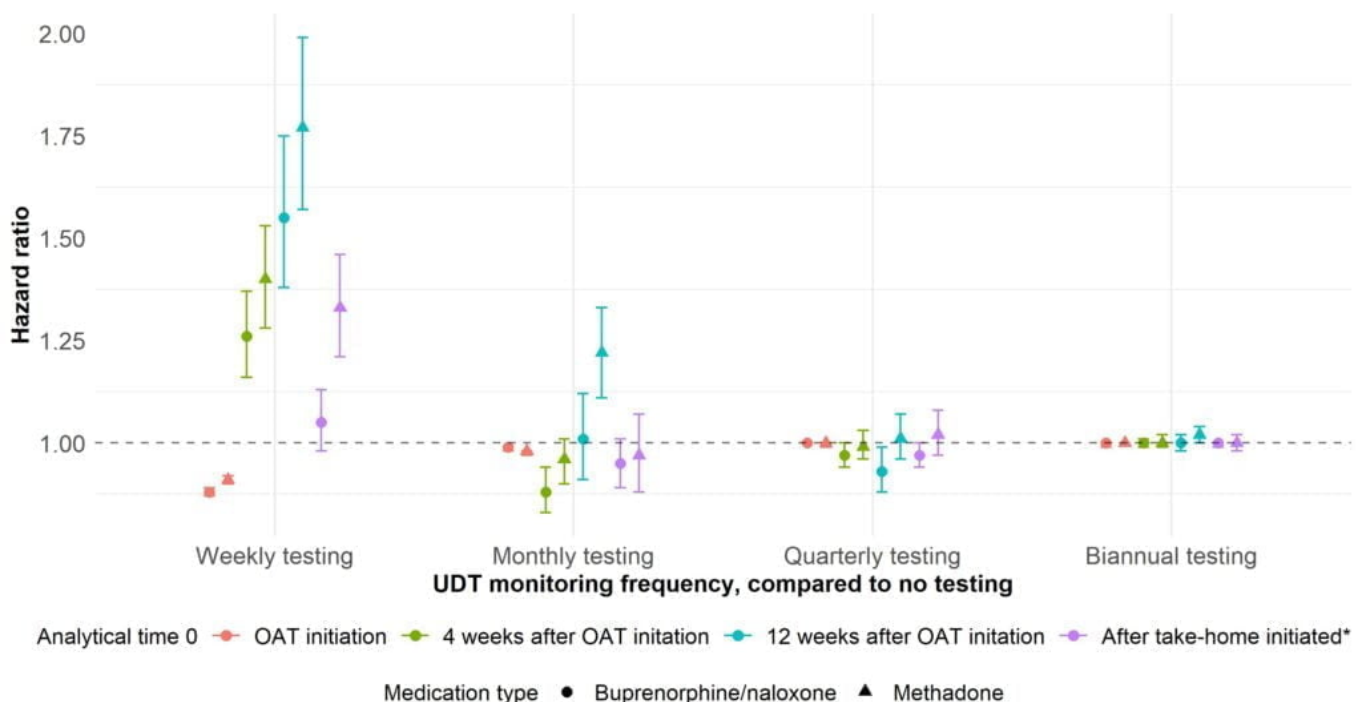
**Treatment** Megan Kurz\* Megan Kurz Bohdan Nosyk Brenda Carolina Guerra Alejos Jeong Eun Min

Background: Though it is recommended practice in most settings internationally, the evidence on the effectiveness of urine drug testing (UDT) strategies alongside Opioid Agonist Treatment (OAT) on treatment retention is unclear and randomized control trials on UDTs may not extend to real-world practice. We aimed to determine the comparative effectiveness of alternative UDT monitoring strategies as observed in clinical practice among OAT clients in British Columbia, Canada from 2010 to 2020.

Methods: We conducted a retrospective cohort study for UDT monitoring strategies and their impact on retention for individuals initiating methadone (MET) or buprenorphine/naloxone (BNX) in British Columbia from 01/01/2010-03/17/2020. Our exposure was defined as five static UDT monitoring strategies: no UDTs, weekly UDTs, monthly UDTs, quarterly UDTs and biannual UDTs. We applied a 'clone-censor-weight' approach with a marginal structural cox model to compare the impact of these strategies on OAT retention.

Results: There were 19,036 and 11,423 first time OAT initiators with MET and BNX, respectively during the study period. When compared to no UDT monitoring, weekly UDTs resulted in a 12% decrease (HR: 0.88, 95% CI: (0.87, 0.89)) in the risk of discontinuation for clients receiving BNX, with similar results for MET. Monthly UDTs marginally reduced the risk of discontinuation, but quarterly and biannual UDTs demonstrated no difference in the risk of treatment discontinuation. However, for individuals retained for at least 4 weeks, receiving weekly UDTs after the first 4 weeks of treatment increased the risk of discontinuation by 26% (1.26, (1.16, 1.37)) compared to no UDTs for BNX clients, and by 40% (1.40, (1.28, 1.53)) for MET clients.

Conclusion: Our findings suggest that weekly UDT monitoring is beneficial during induction, however frequent UDT monitoring in thereafter may increase the risk of treatment discontinuation.





**Intersectional trends of drug overdose mortality in the US and the Covid-19 shock on drug overdose death rates** Ariadne Rivera Aguirre\* Ariadne Rivera Aguirre Julian Santaella-Tenorio Magdalena Cerdá Samuel R. Friedman

**Background:** In 2021, over 100,000 people died from drug overdoses, more than any other year in US history. While most discussion of the overdose epidemic has focused on White men, trends of drug overdose death rates by race/ethnicity/sex show that overdose death rates have increased among minority groups. Furthermore, it remains understudied how overdose trends and mechanisms operate within intersectional categories of sex, race/ethnicity and Hispanic origin.

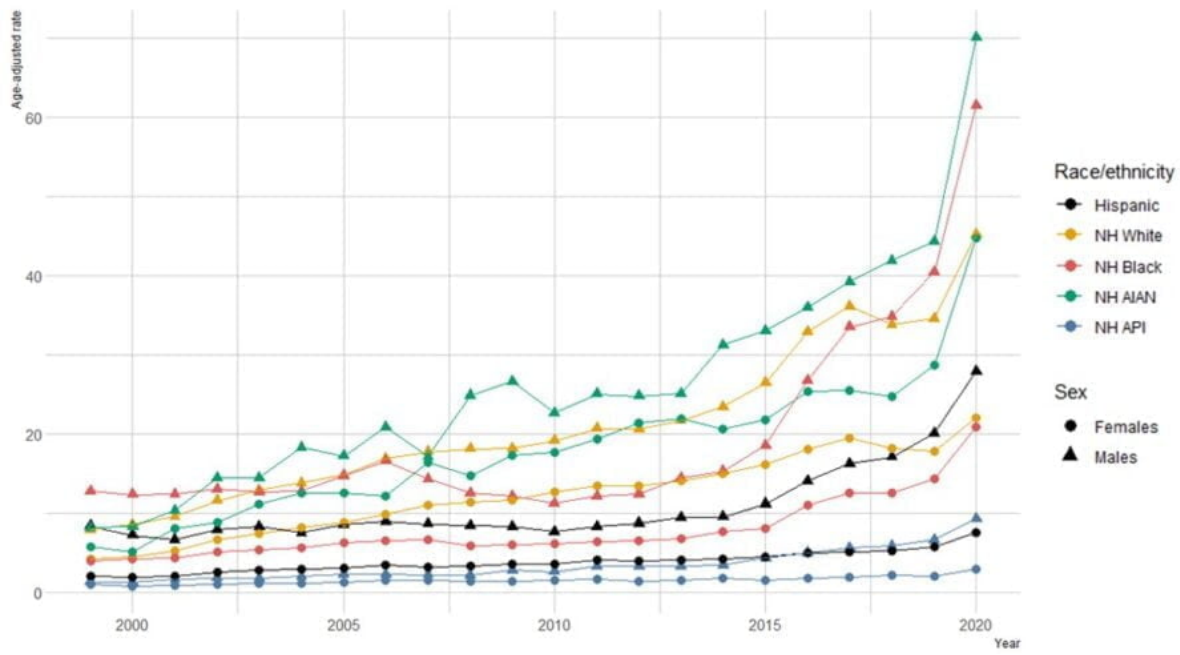
**Aims:** To describe how rates of drug overdose mortality vary intersectionally by sex, race/ethnicity and Hispanic subgroups, and estimate how the Covid-19 shock affected rates of drug overdose mortality by subgroups.

**Methods:** We calculated annual age-adjusted mortality rates by sex, race/ethnicity and Hispanic origin from 1999-2020 using restricted-use mortality data from the Multiple Cause of Death files from the CDC National Vital Statistics Program. We estimated changes in age-adjusted overdose mortality rates between 2016-2019 and compared to changes between 2019-2020 by population subgroup.

**Results:** Age-adjusted drug overdose mortality rates were higher among Non-Hispanic (NH) American Indian Alaskan Native (AIAN) men and women than among NH White counterparts (Figure 1). Since 2018, overdose mortality rates of NH Black males have been higher than mortality rates of NH White males. Among Hispanics, males of Puerto Rican origin had the highest drug overdose death rate in 2020 (68.4 per 100,000), and have had the highest overdose death rates since 1999.

**Conclusions:** Although media have focused mainly on the NH White population, these results show that the overdose crisis has also affected other population subgroups. Intersectional analysis of overdose mortality rates is critical to identify how inequalities shape the experiences and outcomes of different population subgroups.

Figure 1: Age-adjusted overdose death rates per 100,000 population by race/ethnicity and sex in the US, 1999-2020





**Longitudinal assessment of the effect of discrimination on binge alcohol drinking among older adults in the U.S.** Marie-Claude Couture\* Marie-Claude Couture Sze Yan Liu Laura Chyu Erin Grinshteyn

**Background:** Discrimination is a well-known stressor that can lead to numerous negative psychological, behavioral, and health outcomes, including unhealthy alcohol drinking as a coping mechanism. Few studies have examined whether experiences of discrimination are associated with binge alcohol drinking in a nationally representative sample of U.S. older adults.

**Methods:** Data from the 2008-2018 Health and Retirement Study were used to assess the association between (1) major lifetime experiences of discrimination (no major experience, one or more) and (2) everyday discrimination (no discrimination, low, moderate, high) with binge alcohol drinking (last three months) among older adults ( $\geq 50$  years old). Mixed-effects logistic regression models were used controlling for age, gender, race/ethnicity, depression, and self-assessed health status. Effect modification was assessed, and analyses were stratified by sex.

**Results:** The prevalence of binge drinking in the last three months was 9.8% among older women and 27.8% among older men. Older women who reported major lifetime experiences of discrimination had an increased risk of binge alcohol drinking (OR=1.53; 95% CI: 1.32-1.77). No statistically significant association was observed in older men. Everyday discrimination was associated with binge alcohol drinking among older female adults; the odds were 1.43 times higher among women reporting low levels of discrimination (95% CI: 1.26-1.62) and 1.28 times higher among women reporting moderate discrimination (95% CI: 1.12-1.46) compared with women reporting no discrimination. Low levels of everyday discrimination were associated with binge alcohol drinking in older men (OR=1.17; 95% CI: 1.05-1.31), but no association was observed among men reporting moderate or high levels of discrimination.

**Conclusion:** Major lifetime experiences of discrimination increased the risk of binge alcohol drinking in older women, but not men. Everyday discrimination was associated with binge alcohol drinking among older women, but this effect was less pronounced among older men. Further research is needed to identify gender differences in mediators connecting experiences of discrimination and binge drinking in older adults.

**Alcohol and drug harms to others: findings from the 2020 US National Alcohol Survey** Erika Rosen\* Erika Rosen William Kerr Kate Karriker-Jaffe

While harms of substance use are well-documented, less is known about secondhand harms experienced by people from others' substance use, especially for substances other than alcohol. The objectives of this study were to measure prevalence of lifetime and past 12-month harms from others' cannabis, opioid, and other drug use; document the extent to which these harms co-occur with harms from others' alcohol use; and assess associations with individuals' own substance use. This cross-sectional analysis used data from 7,799 respondents (51.6% female; 12.9% Black, 15.6% Hispanic/Latinx; mean age 47.6) in the 2019-2020 National Alcohol Survey. Harms included family difficulties, traffic accidents, vandalism, physical harm, and financial difficulties due to someone else's substance use. Prevalence estimates and chi-square statistics were calculated. Logistic regression models assessed associations between substance use and harms from others' use. Analyses were weighted to be nationally representative. Prevalence of lifetime harms from others' alcohol, cannabis, opioid, and other drug use was 34.2%, 5.5%, 7.6%, and 8.3%, respectively. Past 12-month prevalence was 6.2%, 1.8%, 2.0%, and 2.2%. Co-occurrence of harms was significant ( $p < 0.01$ ) for lifetime and 12-month harms, with 12.7%, 8.2%, and 10.0% of those reporting harms from others' alcohol use in the past 12 months reporting harms from others' cannabis, opioid, and other drug use. Exceeding drinking guidelines was associated with increased odds of past 12-month harms from others' alcohol (OR=2.09 [1.41, 3.11]) and cannabis use (OR=2.06 [0.98, 4.36]). Drug use was associated with increased odds of past 12-month harms from others' alcohol, opioid, and other drug use. There was substantial overlap of harms due to others' alcohol, cannabis, opioid, and other drug use. Associations of harms from others' substance use with an individual's substance use suggest key populations who may be particularly susceptible to these harms.

**A longitudinal analysis of flavored cigar use and cigar smoking cessation among US adults**

James H. Buszkiewicz\* James Buszkiewicz Steven Cook Hayoung Oh Richa Mukerjee Jana L. Hirschtick Nancy L. Fleischer

**Background:** Flavored cigars have grown in popularity from 2009 to 2020, accounting for over half of cigars consumed in 2020. Flavoring masks the harsh taste of tobacco and may be a key barrier to successful cigar smoking cessation. To date, there have been few longitudinal studies examining whether flavored cigar use is associated with short- or long-term cigar cessation.

**Methods:** Using data from Population Assessment of Tobacco and Health Study Waves 1-5, we examined whether flavored cigar use was associated with 30-day and 1-year cigar smoking cessation. Multivariable discrete-time survival models were fit to a sample of adult respondents (age 18+) who had a current, established cigar use at baseline and smoked cigars at least 5 or more days in the past 30 days. Models adjusted for age, sex, race/ethnicity, income, cigarette and cigar smoking intensity, and blunt use.

**Results:** At baseline, 44.3% of respondents ( = 774) were 18-34 years old, 76.7% were male, 58.1% were non-Hispanic White, 75.8% had household incomes of <\$50,000, and 51.3% smoked flavored cigars. In fully adjusted models, flavored cigar use was not associated with either 30-day (HR = 0.87, 95% CI = 0.69, 1.09) or 1-year cessation (HR = 0.97, 95% = 0.77, 1.21).

**Conclusion:** We found no evidence of an association between flavored cigar use and either 30-day or 1-year cigar smoking cessation. More work is needed to understand the dynamics of cigar smoking transitions, including initiation, cessation, and relapse, and the role flavorings may play in larger cohorts, particularly in those who exclusively use cigars or dual-use cigars and cigarettes.

**Dimensions of homeless experiences on substance use among a representative probability sample of adults experiencing homelessness in California** Ryan D Assaf\* Ryan Assaf Ryan D Assaf Eve Perry Cheyenne Garcia Margot Kushel Meghan Morris

Approximately 170,000 people experience homelessness (PEH) nightly in California (CA), representing one third of PEH in the US. Most homelessness literature comes from small service provider samples or from service utilization in areas with widespread shelter. We describe patterns of illicit drug use and assess the association between use and age at first homeless, duration, and shelter status. Using a venue-based sampling frame to create a representative sample of CA, we recruited homeless participants aged 18+ in 8 counties between 2021 to 2022. Trained staff administered questionnaires. We used logistic regression analysis to assess dimensions of homelessness and any illicit drug (cocaine, opioids, or methamphetamine) use in the past 6 months adjusting for demographics, SES, lifetime incarceration, and mental health. Overall, 3,065 participants completed the survey. Among the weighted sample, participants were primarily cisgender men (69.3%), Latinx (36.3%) with mean age of 46.6 years old (SD 72.3). Lifetime use of any illicit drug was 76.0% with 50.3% reporting past 6-month use (10.9% cocaine, 17.1% opioid, 45.8% methamphetamine). Compared to those in shelters, those who were unsheltered and those unsheltered in a vehicle had increased odds of any drug use in the past 6 months (aOR 4.74, 95%CI 4.56, 4.93; aOR 2.80, 95%CI 2.67, 2.93, respectively). Those experiencing chronic homelessness were at increased odds of drug use compared to those who were not (aOR 1.66, 95%CI 1.61, 1.72). Every 10-year increase in age of first homeless experience decreased the odds of any drug use (aOR 0.95, 95%CI 0.94, 0.96). We found that the prevalence of cocaine was lower (12.5-37.7%) whereas opioids (6.4-12.9%) and methamphetamine use (4.8-29%) were higher than prior literature among PEH; with similar positive associations with dimensions of homelessness. Housing first interventions successfully house those with substance use disorders and should be expanded to meet the need.

**Impact of Early Childhood Education Reform on Substance Use Among Youth in Portugal**

Jasleen Arneja\* Jasleen Arneja Sarah Windle Efe Atabay Ilona Vincent Sam Harper Arijit Nandi

The early life social environment impacts child development, with implications for health and wellbeing across the life course. In Portugal, publicly funded free early childhood education and care (ECEC) was introduced for 5 year-olds in 1997 and 3-4 year-olds in 2000. We assessed the impact of free ECEC access on substance use in adolescents aged 14-16, including ever use of alcohol, cannabis, and cigarettes.

We used data from WHO's Health Behaviour in School-aged Children study, a cross-sectional school-based survey of adolescents, and a difference-in-differences design. For the first difference, treated adolescents (2014/2018 HBSC survey respondents eligible for free ECEC at ages 3-5) were compared to adolescents in Portugal who were too old to benefit from free ECEC (2002/2006 respondents). For the second difference, potential controls were 14-16-year-old HBSC survey respondents in European countries without free ECEC at ages 3-5. Control countries were selected by visually assessing parallel trends in each outcome in the pre-policy period. We estimated risk differences using linear probability models adjusted for age and sex, with cluster-robust standard errors to account for school-level clustering.

The sample from Portugal comprised 5753 14-16-year-olds, of whom 29% had ever been drunk, 11% ever used cannabis, and 50% ever smoked at baseline (2002). Selected control countries varied across outcomes. Free ECEC did not impact the prevalence of ever being drunk (RD=-0.021, 95% CI -0.069, 0.027), ever using cannabis (RD=0.026, 95% CI -0.001, 0.052), or ever smoking (RD=-0.015, 95% CI -0.062, 0.031) among adolescents in Portugal.

We found little evidence that expanded ECEC affected substance use, perhaps due to the lack of granularity in the binary outcome categorization. Further, while the ECEC expansion led to increased enrollment (by 21%), the proportional change may not have been substantive enough to lead to population-level changes in adolescent substance use.

**Alcohol Use and Sexual Behavior among Women: Population-based data from 5 sub-Saharan African Countries** Domonique M. Reed\* Domonique M. Reed Sarah Gutkind Jessica Justman

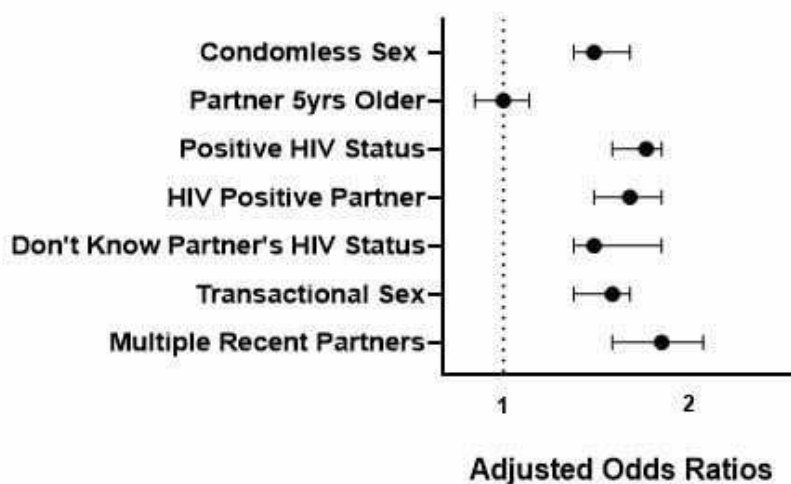
**Background:** Alcohol use is linked to sexual behavior associated with HIV acquisition. This association is well understood among diverse populations in high-income countries but is understudied among women in sub-Saharan Africa (SSA), where alcohol use is growing. We assessed alcohol use and the associations between alcohol use at last sex and risky sexual behavior among women in five SSA countries.

**Methods:** We pooled data from the 2015-2017 Malawi, Tanzania, Uganda, Zambia, and Zimbabwe Population-based HIV Impact Assessments, nationally representative household surveys. We assessed the prevalence of alcohol use frequency and number of drinks per drinking day. We used logistic regression to model associations between alcohol use at last sex with their primary partner and risky sexual behavior (condomless sex; a partner  $\geq 5$  years older; HIV positive; HIV positive partner; partner's HIV status unknown; transactional sex with partner; multiple recent partners). We weighted analyses for country-specific sampling designs.

**Results:** Among 40,158 women, 11% reported drinking monthly or less, 6% reported having 1-4 drinks per drinking day, and 15% used alcohol at last sex. Most women who drank alcohol at last sex were 25-40 years (52%), completed primary school (62%), married or cohabited (93%), and not currently pregnant (91%). Compared to women who did not report alcohol use at last sex, we found alcohol use at last sex was associated with condomless sex (adjusted odds ratio:1.4 [95% confidence interval:1.3-1.6]), being HIV positive (1.7[1.5-1.8]), having an HIV positive partner (1.6[1.4-1.8]), not knowing partner's HIV status (1.4[1.3-1.8]), engaging in transactional sex (1.5[1.3-1.6]), and having multiple recent partners (1.8[1.5-2.1]).

**Discussion:** Alcohol use among women in SSA was associated with risky sexual behavior, a similar pattern seen in high-income countries. With increasing consumption rates in SSA, sexual health interventions should emphasize alcohol-related harms.

**Figure.** Associations of Alcohol Use at Last Sex and Engagement in Risk Sexual Behavior among Women in Five sub-Saharan African Countries from 2015 to 2017



Multivariate models adjusted for age, education, country, marital status, wealth index, and current pregnancy status; Reference groups from top to bottom: 1) condom used at last sex; 2) partner <5 years older; 3) negative HIV status as documented in the PHIA survey; 4) HIV negative partner, as reported by individual; 5) HIV negative partner; 6) non-transactional sex; 7) 1 sexual partner in the last 12 months.

**Systematic review of validity of US survey measures for assessing substance use** Ruchi Bhandari\* Ruchi Bhandari Yuni Tang Erin Caswell Rowida Mohamed Natalie Wilson Edis Osmanovic Gordon Smith Summer Hartley

**Introduction:** Substance use is primarily assessed via self-report in population-based surveys in the US. The steep rise in substance use shows an urgency to assess its prevalence using valid measures. This systematic review summarizes the validity of measures to assess the prevalence of substance use in the US via population-based surveys and in clinical settings.

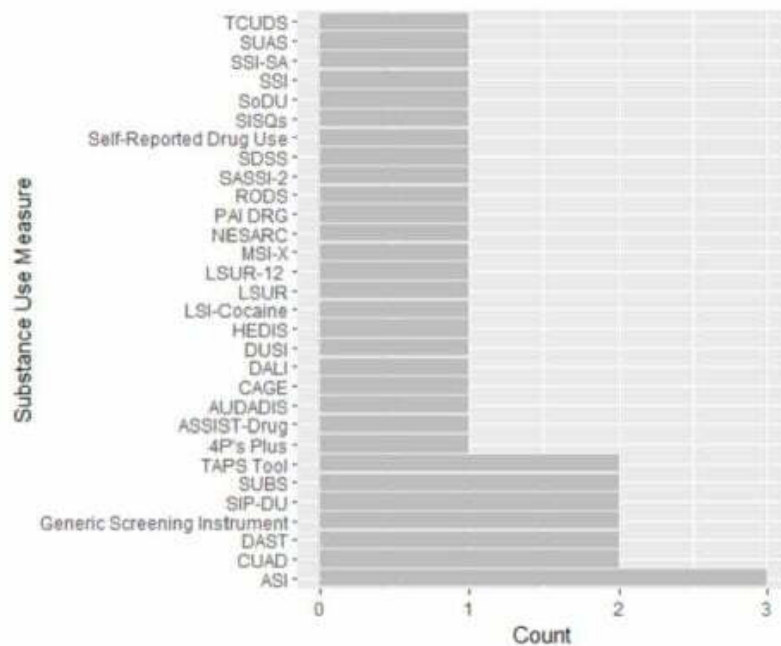
**Methods:** A literature search was performed using eight online databases. Studies, which were published in English and tested the validity of substance use measures among US adults at the population-level or in clinical settings, were eligible for inclusion in the review. A risk of bias tool was adapted to assess methodological quality. Independent reviews were conducted by the authors to assess the risk of bias and data synthesis.

**Results:** Overall, 41 studies (mean sample size was 1,192) were included in this review, in which 95% were conducted in clinical settings and 80% assessed the validity of substance use disorder screenings. Almost every study used a different survey measure. Among the 33 studies that assessed substance use disorder screening measures, 82% examined a generic substance use disorder, and the rest screened for specific disorders such as cocaine, marijuana, or opioids. Sensitivity and specificity tests were conducted in a quarter of the studies for validation and 10 studies used receiver operating characteristics curve. Risk of bias assessment found that 88% of the studies had a low risk of bias.

**Conclusion:** Findings suggest a lack of standard methods in measuring and reporting prevalence of substance use amongst US adults in both clinical and non-clinical settings. Further research is needed to examine limitations and differentials in validity of substance use survey measures.



Figure: Frequency of Survey Measures Used in Included Studies



Abbreviations in order: Texas Christian University Drug Screen (TCUDS); Substance Use and Abuse Survey (SUAS); The Simple Screening Instrument for Substance Abuse (SSI-SA); The Simple Screening Instrument (SSI); Screen of Drug Use (SoDU); Single-Item Screening Questions (SISQs); Substance Dependence Severity Scale (SDSS); Substance Abuse Subtle Screening Inventory-2 (SASSI-2); Rapid Opioid Dependence Screen (RODS); Personality Assessment Inventory Drug Problem Scale (PAI DRG); National Epidemiologic Survey on Alcohol and Related Conditions (NESARC); The Marijuana Screening Inventory (MSI-X); The Longitudinal Substance Use Recall Instrument Recall for 12 Weeks Instrument (LSUR-12); The Longitudinal Substance Use Recall Instrument (LSUR); Lifetime Severity Index for Cocaine Use Disorder (LSI-Cocaine); Healthcare Effectiveness Data and Information Set (HEDIS); The Drug Use Screening Inventory (DUSI); Dartmouth Assessment of Lifestyle Instrument (DALI); Cut down, Annoyed, Guilty, and Eye-Opener Substance Abuse Screening Tool (CAGE); The Alcohol Use Disorder and Associated Disabilities Interview Schedule (AUDADIS); Alcohol, Smoking, and Substance Involvement Screening Test-Drug (ASSIST-Drug); Parents, Partners, Past and Pregnancy Plus (4P's Plus); Tobacco, Alcohol, Prescription Medication, and Other Substance Use (TAPS Tool); Substance Use Brief Screen (SUBS); Single Question Used from Short Inventory of Problems-Drug Use (SIP-DU); Drug Abuse Screening Test (DAST); The Chemical Use, Abuse, and Dependence (CUAD); Addiction Severity Index (ASI)

**Longitudinal association between financial strain and alcohol use among middle aged and older adults in the United States, 2018-2020** Sarah Gutkind\* Sarah Gutkind Pia M. Mauro

**Background:** Alcohol use has been increasing among older US adults, urging the need to assess predictors of alcohol use change, such as financial strain (i.e., inability to meet financial needs). We examined whether financial strain predicted subsequent alcohol use in a longitudinal sample of middle-aged and older US adults.

**Methods:** We included adults ages  $\geq 51$  in the 2018 and 2020 Health and Retirement Study (HRS) core surveys and the 2019 HRS Consumption and Activities Mail Survey ( $n=3,966$ ). We used the 2018 and 2020 survey responses to define changes in any alcohol use (since last interview), alcohol use frequency (days/week in past 3 months), and binge alcohol use (days in past 3 months with  $\geq 4$  drinks) as no change 1) among never drinkers or 2) current/former drinkers, and 3) increasing or 4) decreasing use. Financial strain (none, moderate, severe) was measured in 2019. Multinomial logistic regressions estimated alcohol use changes by financial strain, adjusting for sex, age, race and ethnicity, marital status, and retirement.

**Results:** Between 2018 and 2020, most people maintained their alcohol use status, alcohol use frequency, and binge drinking frequency (6.3%, 17.9% and 6.3% increased, respectively; 6.5%, 8.2%, and 5.7% decreased, respectively). Relative to 2018, severe financial strain in 2019 (8.3%) was associated with increasing any alcohol use (adjusted relative risk ratios [aRRR]=2.62 [1.58, 4.26]) and alcohol use frequency (aRRR=1.86 [1.21, 2.85]). Moderate financial strain (40.3%) was associated with increasing alcohol use frequency (aRRR=1.38 [1.06, 1.78]). Financial strain was not associated with binge drinking changes.

**Discussion:** Moderate or severe financial strain was associated with increasing alcohol use frequency, but not binge drinking or decreases in use. Given the adverse outcomes associated with alcohol use in older adults, financial assistance programs and other interventions to reduce strain should be explored in future research.

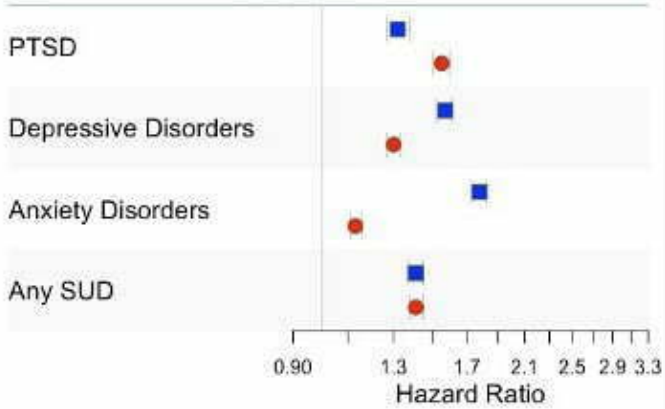
**Sex-specific associations between traumatic brain injury and non-fatal drug overdose in young adult Post-9/11 Veterans** Jennifer Fonda\* Jennifer Fonda Vladislav Bravman Jaimie Gradus Rachel Sayko Adams

**Background:** Evidence is mounting that Veterans with a history of traumatic brain injury (TBI) have a disproportionately higher risk for overdose, yet information on sex-specific associations is lacking. This study evaluated the sex-specific association between TBI and overdose, and the role of psychiatric conditions as mediators of this association. **Methods:** The sample included 1,303,649 Post-9/11 Veterans receiving care at national Veterans Affairs facilities from 2007-2019 and aged 18-65 (81% male; mean age 34 yrs). TBI was defined as a confirmed diagnosis (10%) according to VA TBI comprehensive evaluation; no TBI was defined as a negative primary TBI screen (i.e., no head injury). Non-fatal overdose (all drug and opioid-specific) was defined using ICD codes. We used Cox-proportional hazard regression to compute the sociodemographic adjusted hazard ratio (aHR) and 95% CI. Mediation analyses were conducted to examine the role of psychiatric conditions (posttraumatic stress disorder, depressive, anxiety, and substance use disorders) in this association. Separate models were run for each overdose outcome and stratified by sex. **Results:** There were 19,159 drug overdoses in the study period (11% opioid-related). Veterans with TBI had close to a 2-fold increased rate of overdose (Men: aHR = 1.94, 95% CI = 1.87, 2.03; Women: aHR = 1.75, 95% CI = 1.52, 2.01), and over a 2-fold increased rate of opioid-specific overdose (Men: aHR = 2.42, 95% CI = 2.17, 2.68; Women: aHR = 2.95, 95% CI = 2.04, 4.26), compared to those without TBI. This association was attenuated in mediation analyses for both the overall and opioid-specific outcomes (see figure). **Conclusion:** This study suggests that Veterans with deployment-related TBIs are at increased rate of overdose, with similar association of TBI and overall overdose by sex, and slightly higher TBI and opioid-specific overdose association in women. However, this association was partially attributable to co-morbid psychiatric conditions.

### Men - All Overdoses

■ Exposure: TBI vs. No TBI ● Mediator: Psychiatric Condition

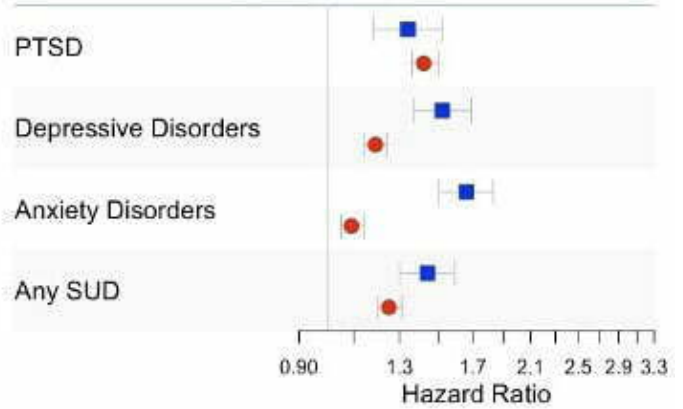
#### Mediator



### Women - All Overdoses

■ Exposure: TBI vs. No TBI ● Mediator: Psychiatric Condition

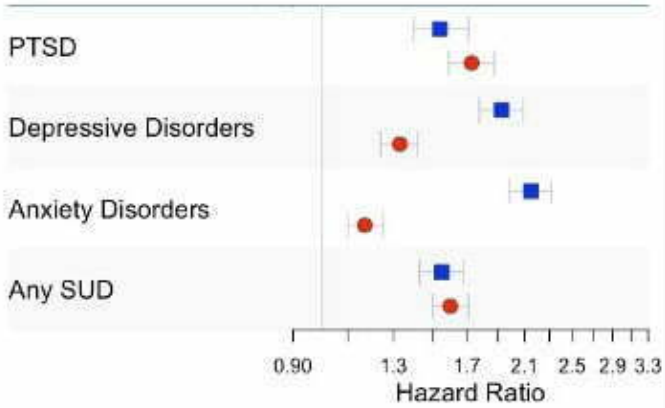
#### Mediator



### Men - Opioid Overdoses

■ Exposure: TBI vs. No TBI ● Mediator: Psychiatric Condition

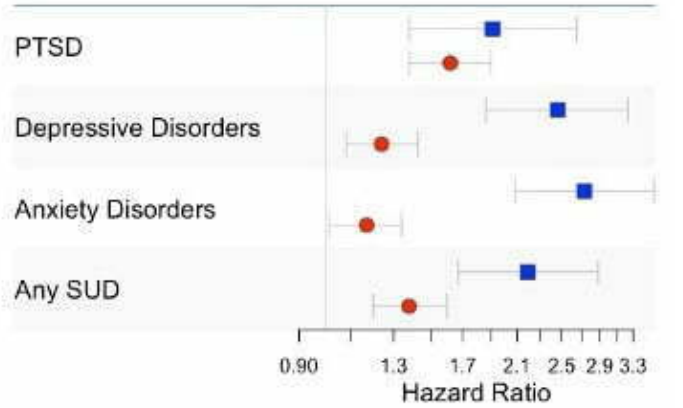
#### Mediator



### Women - Opioid Overdoses

■ Exposure: TBI vs. No TBI ● Mediator: Psychiatric Condition

#### Mediator



**Spiritual coping and substance use among college students in China: a repeated measures study** Stephen W. Pan\* Stephen Pan Wanqi Wang Stephen W. Pan

**Background:** Research from Western countries suggests that religiosity and spirituality are inversely associated with substance use among adolescents and young adults. However, there is sparse research about this relationship in China. In response, we examined the potential association between spiritual coping and substance use among college students in China.

**Methods:** In 2020, 807 first-year college students  $\geq 18$  years old in Suzhou, China completed a baseline online survey. Follow-up surveys were administered at 4 months, 8 months, and 12 months. Spiritual coping was measured by five items in the Chinese Spiritual Coping Scale. Substance use was defined as whether a person engaged in any substance use (e-cigarettes, cigarettes, imbibed alcohol) in the past three months. Generalized estimating equations were used to assess the association between spiritual coping and substance within the same wave. We adjusted for age, sex, ethnicity, residency during school year, and religious affiliation. We also conducted the analysis stratified by students with and without religious affiliation.

**Results:** Overall, spiritual coping was directly associated with substance use (AOR: 1.47, 95% CI: 1.13-1.91). Among students without any religious affiliation, spiritual coping was significantly associated with substance use (AOR: 1.48, 95% CI: 1.13-1.94). However, among students with religious affiliation, this association was not significant (AOR: 0.86, 95% CI: 0.21-3.46).

**Conclusion:** Spiritual coping appears to be associated with substance use among college students in China. Longitudinal studies are needed to elucidate the mechanisms of these associations.

**Association between electronic cigarette consumption and peer use of e-cigarettes: a meta-analysis of prospective studies** Ngoc Minh Luu\* Ngoc Minh Luu Jin-Kyoung Oh Thi Tra Bui Thanh Hai Phan

**Purpose:** To assess the association between electronic cigarette (e-cigarette) consumption and peer use of e-cigarettes by meta-analysis of prospective studies.

**Materials and methods:** We performed the search strategy on PubMed, EMBASE, and Web of Science in November 2022. We selected prospective studies reporting odds ratio (OR) or relative risk (RR) with 95% confidence interval (CI).

**Results:** This study included thirteen prospective studies, with a total of 36,893 participants in the final analysis. In the random-effects model meta-analysis of all the studies, e-cigarette use was higher in the group of participants having friends who used e-cigarettes (OR/RR = 1.76, 95% CI 1.47 to 2.10; I<sup>2</sup> = 85.7%). In the subgroup meta-analysis by type of outcome, having friends use e-cigarettes significantly increased ever use and current use of e-cigarettes. The subgroup meta-analysis by age, region, sample size, and methodological quality of study also revealed similar findings.

**Conclusion:** The current meta-analysis found that having friends use e-cigarettes was a significant factor contributing to the increased use of e-cigarettes. Interventions to prevent e-cigarette use should take this finding into consideration.

**Funding:** This research was supported by the “International Cooperation & Education Program (NCCRI NCCI 52210-52211, 2023)” from National Cancer Center, Korea.

**LATEBREAKER**

Substance Use

**Assessing social stigma towards drug use disorders related to opioids, methamphetamines, crack cocaine and alcohol** Mofan Gu\* Mofan Gu Mofan Gu Bruce Taylor Harold Pollack Odell Johnson Nickolas Zaller

Political affiliation and racial attitudes, among many other factors, potentially impact one's stigma towards substance use disorders (SUDs). Prior studies suggest that Republicans tend to agree with more punitive drug policies; in addition, race/ethnicity played a significant role in public perception of the drug epidemics. In this study, we analyzed data from the 2021 AmeriSpeak Survey (n=6,515), and assessed potential drivers behind stigma towards four types of SUDs—opioids use disorder (OUD), methamphetamine use disorder (MUD), crack cocaine use disorder (CCUD) and alcohol use disorder (AUD). We found that participants who identified as Republican in our study displayed the highest stigma towards all four SUDs. In addition, racial blindness and older age significantly increased SUD stigma, even after controlling for potential confounders. Our findings suggest that stigma towards SUD is shaped by one's living experience and cultural background. Tailored educational campaigns, as well as more resources to help SUD recovery, could potentially reduce public stigma towards SUD.

**Evaluating an approach to incorporating anti-racist pedagogy and equity, diversity and inclusion in Epidemiology courses** Jessie Seiler\* Anjum Hajat Jennifer Balkus Lucia Fraire Brandon Guthrie Christine Khosropour Merih Mehari Thomas Walton Yasaman Zia

Incorporating anti-racist pedagogical approaches is critical for improving population health and training the next generation of epidemiologists. The University of Washington Epidemiology Department developed guidance for instructors, known as course development plans (CDP), on best practices to center anti-racism and equity, diversity and inclusion (EDI) in the classroom and encourage continuing education and growth in anti-racist pedagogy.

Over the 2020-2021 academic year, instructors documented and implemented changes in their courses. Prior to the start of each academic quarter, the CDP for each class offered that quarter was reviewed by a faculty-student pair to provide additional feedback on how best to incorporate CDP guidance, a critical step that promotes instructor reflection and encourages sharing perspectives and experiences across academic hierarchies. We conducted an evaluation of the CDP process by interviewing 10 instructors, 10 teaching assistants (TAs) and conducting two focus groups among students enrolled in epidemiology courses.

Instructors were highly engaged in the CDP process and felt well-supported in their efforts to implement changes. Students appreciated efforts to improve the curriculum, which they saw as a long-term commitment to change, and the transparency and honesty about challenges of incorporating these principles into courses. Instructors reported challenges in several areas (see figure). Both students and TAs themselves said including TAs in discussions about how to better include anti-racism and EDI into the classroom would be beneficial.

Additional opportunities are planned to provide support to instructors on commonly reported challenge areas. Despite reported challenges, the CDP process provides regular touch points with instructors and opportunities for feedback from instructors and students that encourage growth. The long-term goal of the CDP process is to incorporate an anti-oppression framework into the curriculum.



Figure: Commonly reported challenges faced by instructors in CDP implementation and student perspective on that challenge.

<b>Challenge reported by instructors</b>	<b>Student perspective</b>	<b>Potential <u>next-steps</u> for instructors</b>
Recognizing and addressing microaggressions	Often <u>occured</u> within breakout rooms (for courses delivered online); Reported to instructor after the fact; Students appreciated instructors' responses when informed about microaggressions	Practice responding to microaggressions (i.e., role play); Always follow-up with entire class when alerted to clarify that microaggressions are unacceptable
Improving representation of minoritized scholars in classroom materials	Appreciated effort when combined with other elements	Encourage discussion of how identities of authors and participants (e.g., race, ethnicity, gender, sexual identity) may bias <u>particular study</u> and how students might address those sources of bias in their own work
Decentering authority in the classroom	Commended instructors' awareness of positionality and the chance to reflect on classroom norms	Consider alternate forms of <u>students</u> assessment; Maintain flexibility
Incorporating anti-racism and EDI in methods courses	Quantitative methods courses are not exempt from incorporating anti-racism and EDI	Consider how bias is introduced when racism and other forms of oppression are present in any phase of study

**Machine learning based prediction of suicidal behaviors in patients with perinatal depression: a nationwide register-based cohort study** Hang Yu\* Hang Yu Elgeta Hysaj Emma Bränn Donghao Lu

### **Background**

Previous research shows that women who suffered from perinatal depression (PND) have a higher risk of suicidal behavior throughout their lifetime. However, clinical tools for predicting suicidal behavior among patients with PND are lacking.

### **Aim**

To develop a prediction model for suicidal behavior after PND using machine learning.

### **Methods**

Leveraging nationwide Swedish register data, we included 57,848 women with PND diagnosed during 2001-2018 and identified 2,303 events of suicidal behavior up to 5 years after PND diagnosis. Based on our previous association studies, 16 predictors containing information on demographics and pregnancy characteristics were included after multiple imputation. The sample was randomly split into 80% as a training set and 20% for testing. Classification and Regression Tree (CART), Random Forest (RF), Naïve Bayes (NB) and Logistic regression (LR) were used to establish prediction models with area under the curve (AUC) assessed for prediction performance. 10-fold cross-validation was used to evaluate the algorithms on unseen data.

### **Results**

In the prediction models, the CART yielded the best performance for suicidal behavior within 5 years after PND diagnosis (AUC 0.78, 95% CI 0.76-0.81). The population that scored highest (17%) in CART model had 84% risk of suicidal behavior. LR also had a comparable performance (AUC 0.78, 95% CI 0.76-0.81), whereas RF (AUC 0.74, 95% CI 0.72-0.76) and NB (AUC 0.70, 95% CI 0.68-0.72) had relatively poor performance. Notably, suicide history was the main contributor in all four models. Other predictors like household income, gestational age and education level were also important indicators of suicidal behavior risk.

### **Conclusion**

The machine learning models have promising prediction performance for suicidal behavior after PND. Yet, further improvement is needed before clinical implementation.

**Symptoms of premenstrual disorders associated with self-harm and suicide attempts**

Sigurbjörg Anna Guðnadóttir\* Sigurbjörg Anna Guðnadóttir Edda Björk Þórðardóttir Donghao Lu  
Jóhanna Jakobsdóttir Thor Aspelund Arna Hauksdóttir Unnur Anna Valdimarsdóttir

**Objectives:**

Premenstrual disorders (PMDs) are common among women of reproductive age with documented negative impact on women's health and quality of life. Yet, limited data exist on the association between PMDs and suicidality. The aim of this study was to explore the association between PMDs and risks of suicidal behaviors.

**Methods:**

The SAGA Cohort is a nationwide representative study of women 18-69 years residing in Iceland. We conducted a cross-sectional analysis of 14,634 women who responded to the revised Premenstrual Symptoms Screening Tool as well as the WMH-CIDI about suicidal behaviors and self-harm over the lifetime. Modified Poisson regression, with adjustment for age and other confounding We estimated prevalence ratios (PR) for suicidal behaviors contrasting women with and without PMDs. The analysis accounted for multiple covariates and symptoms of co-morbid psychiatric disorders.

**Results:**

The average age of women with PMDs was 34 years while the average age of the reference group was 36 years. Women with PMDs had higher prevalence of self-harm compared to women without PMDs, (PR 1.34 (95% CI 1.24, 1.45)). Similarly, women with PMDs had higher prevalence of lifetime suicidal attempts (PR 1.57 (95% CI 1.45, 1.71)). Stratification for comorbid symptoms of anxiety and depression yielded attenuated yet statistically significant associations between PMDs and suicidal attempts and self-harm.

**Conclusions:**

The preliminary results support a link between premenstrual disorders and self-harm and suicidal attempts over the lifetime. If confirmed in further analyses and independent prospective cohorts, our findings motivate increased surveillance of women with PMDs.

**Preconception nutritional quality in pregnancy-planning and general-population cohorts:****The PrePARED Consortium** Nicole Cohen\* Emily Harville Lixuan Ji Janaki Sundaresan Cailey Cranny Ke Pan Danielle Downs Erica Gunderson Gita Mishra Abigail Pauley James Shikany Lauren Wise

The preconception period is important for nutrition, to provide physical strength for pregnancy and establish diet for optimal fetal nutrition. Understanding preconception diet ideally includes both planned and unplanned pregnancies. Diet data from 5 cohorts participating in the PrePARED consortium of preconception studies were harmonized (total N=25632). These included four general studies (Australian Longitudinal Study of Women's Health (ALSWH); California Teachers' Study (CTS); Central Pennsylvania Women's Health Study (CePAWHS), a study of rural Pennsylvania women); and the Coronary Artery Risk Development in Young Adults (CARDIA) study, a national study of young Black and Whites, which include data on both planned and unplanned pregnancies; and one study of couples planning pregnancy (Pregnancy Study Online (PRESTO), which recruited from the US and Canada without respect to location). Adherence to the International Federation of Gynecology and Obstetrics (FIGO) (include meat/chicken, fruit and vegetables, fish, dairy, whole grains, and packaged snacks/sugar-sweetened drinks), the Mediterranean diet, and other dietary patterns were calculated in each cohort. Number of recommendations, average score, and cut-offs for quantile-based scales were compared across studies. PRESTO and CTS participants were more likely to have higher education and income than other participants. PRESTO participants were more likely to meet all six of the FIGO recommendations (8.8%; median 4) than participants in the CTS (3.9%, median 4), CARDIA (1.7%, median 4), ALSWH (1%, median 3), or CePAWHS (median 2 of 4 assessed) studies. Median score on the Mediterranean diet was also higher for PRESTO. Adherence to recommendations for optimal pregnancy nutrition is low among reproductive-aged women, although it varies substantially by study population, probably due to education and other socioeconomic variables as well as pregnancy planning status.

**Differences in birth hospitalization experiences during the COVID-19 pandemic by maternal race and ethnicity, Pregnancy Risk Assessment Monitoring System, 2020** Jessica Meeker\* Regina Simeone Mehreen Meghani Jessica R. Meeker Lauren B. Zapata Romeo R. Galang Beatriz Salvesen von Essen Ada Dieke Sascha R. Ellington

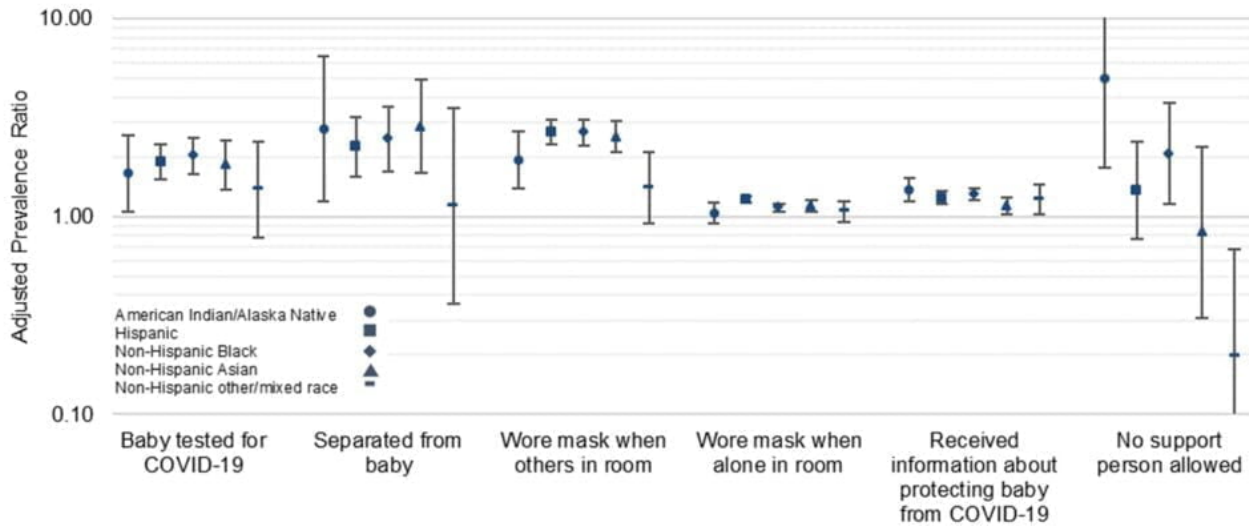
Infection prevention and control measures in healthcare settings to prevent COVID-19 transmission changed delivery of obstetric care. It is unclear how these measures were experienced among women of different racial and ethnic backgrounds.

Our analysis of the 2020 Pregnancy Risk Assessment Monitoring System (PRAMS) included 12,879 women who had a live, in-hospital birth, from April-December 2020, and responded to questions about COVID-19 related experiences during the birth hospitalization. These experiences included having their baby tested for COVID-19, being separated from their baby due to COVID-19, and not being allowed a support person during their labor and delivery, among others. Weighted percentages of birth hospitalization experiences were calculated. Adjusted prevalence ratios (aPR) estimated associations between maternal race and ethnicity and these experiences.

Overall, 12.3% of women reported their baby was tested for COVID-19, 3.6% reported they were separated from their baby, and 1.8% reported not being allowed a support person. These experiences differed by maternal race and ethnicity. Compared to non-Hispanic White women, American Indian/Alaska Native (aPR=1.6 and 2.7), Hispanic (aPR=1.8 and 2.2), non-Hispanic Black (aPR=2.0 and 2.4), and non-Hispanic Asian (aPR=1.8 and 2.9) women were more likely to report their baby was tested for COVID-19 and to report they were separated from their baby due to COVID-19, respectively (Figure). American Indian/Alaska Native (aPR=5.3) and non-Hispanic Black (aPR=2.3) women were more likely to report not being allowed a support person (Figure).

Women reported a range of birth hospitalization experiences, with variation by race and ethnicity. Hospital implementation of COVID-19 infection prevention and control measures may have been unequally experienced by racial and ethnic minorities. The impact of some hospitalization experiences on short- and long-term maternal and infant well-being is unclear.

Figure. Adjusted prevalence ratios<sup>a</sup> for the association between maternal race and ethnicity and COVID-19 birth hospitalization experiences<sup>b</sup>, Pregnancy Risk Assessment Monitoring System, 2020



- a. Models adjusted for maternal age in years (<20, 20-24, 25-34, >=35), delivery insurance (private, Medicaid, other/none), quartile of state-level government COVID-19 containment scores, and being told by a doctor that woman had COVID-19 during pregnancy
- b. Reference category is non-Hispanic white race and ethnicity

**Improving Self Esteem through the “In This Together” therapy program for survivors of domestic violence** Michaela F George\* Michaela George Sofia Esteva Leydi Lopez Umana Liliana Cervantez Molina Patti Culross Meghan Kehoe

## **BACKGROUND**

Domestic violence has demonstrated to affect around 10 million people every year in the United States. There are many forms of violence within intimate partners which can result in a victim developing psychological trauma, like low self esteem and self identity. This research study will evaluate the “In This Together” program (ITT) in order to understand if program material influences self esteem levels and parent-child relationships for families in Marin County, CA.

## **METHODS**

Data was collected using a mixed methods approach and available in Spanish and English. Intakes consisted of questionnaires and interviews of the survivor parent and willing children before the intervention. The ITT program consisted of a 10 week therapy program covering unique clinical benchmarks led by a licensed therapist once a week via Zoom. Once participants completed the program, follow-up interviews were collected to measure impact of the program.

## **RESULTS**

The materials included in the program curriculum was designed to empower and support survivor parents in their healing journey with themselves and their children. From the analysis, themes like emotional strengths, communications, family time, acceptance, and optimism were highlighted from participants. Survivor-parents have demonstrated to have an impact in their well being and self-esteem levels, resulting in them becoming more assertive in their parenting and relationships with their children.

## **DISCUSSION**

In this study we are able to gain insight on the impact the program left on participants' perspective of one-self and the relationship with their children. ITT has revealed to uplift emotion and pass down skills for parents to manage their emotional and mental wellbeing. Through ITT, participants are able to create a space of healing and acceptance, as well as knowledge to identify abuse.

**LATEBREAKER**

Women's Health

**Associations of early pregnancy plasma per- and polyfluoroalkyl substance (PFAS)****concentrations with subsequent menopausal symptoms in midlife - Project Viva** Tamarra

James-Todd\* Emma V. Preston Sheryl L. Rifas-Shiman Diana C. Soria-Contreras Lidia Mínguez-Alarcón Sharon K. Sagiv Abby F. Fleisch Jorge E. Chavarro Marie-France Hivert Emily Oken Ami R. Zota Tamarra James-Todd

**Background:** Per- and polyfluoroalkyl substance (PFAS) exposure may be associated with earlier onset of natural menopause, but associations with menopausal symptoms have not been evaluated. We examined the extent to which 1<sup>st</sup> trimester plasma PFAS concentrations are prospectively associated with midlife menopausal symptoms.

**Methods:** We studied 556 participants enrolled in the Project Viva cohort between 1999-2002 (Boston, MA) with data on 1st trimester plasma concentrations of 8 PFAS (ng/mL) and subsequent menopausal symptoms, which were assessed in midlife approximately 18 years post-pregnancy using the 11-item Menopause Rating Scale (MRS, range: 0-44). We used multivariable linear and logistic regression to estimate associations of log<sub>2</sub>-PFAS concentrations with MRS score (continuous) and individual symptoms (yes/no), respectively. Models were adjusted for age and parity at enrollment, race/ethnicity, education, age at menarche, and pre-pregnancy cycle length.

**Results:** At midlife, participants had a mean age of 52 years and MRS score of 7.9 (SD=5.7), 5% reported no symptoms, and 36% had experienced natural menopause. Each doubling in EtFOSAA concentrations was associated with a 0.49 (95% CI: 0.05, 0.94) higher mean MRS score and higher odds of depressed mood, irritability, anxiety, exhaustion, joint/muscle pain, heart discomfort, and bladder symptoms (e.g., incontinence). Higher concentrations of other PFAS (e.g., PFOA) were generally associated with higher odds of experiencing anxiety (OR=1.28; 95% CI: 1.01, 1.63), hot flashes (OR=1.19; 95% CI: 0.93, 1.53), and bladder symptoms (OR=1.33; 95% CI: 1.03, 1.72), but not with MRS score.

**Conclusion:** Our results suggest that exposure to select PFAS in pregnancy may increase the odds of experiencing certain menopausal symptoms in midlife. Future work will help disentangle the extent to which these associations may be mediated by previously reported associations of PFAS exposure with earlier onset of natural menopause.



**Polycystic Ovary Syndrome in Association with Metabolic Syndrome in Hispanic/Latinas from the Hispanic Community Health Study/Study of Latinos: Effect Modification by Inflammation and Menopause Status** Hridya Rao\* Hridya Rao Lindsay Fernandez-Rhodes Michell M. Meyer Michelle Kominiarek Martha Daviglius Linda Gallo Christina Cordero Raveen Syan Krista Perreira Gregory Talavera

**Background:** Polycystic Ovary Syndrome (PCOS), a complex endocrine-reproductive disorder, has been associated with hormones, inflammation, and Metabolic Syndrome (MetS); however, the effect of interactions between these factors on MetS have not been studied in US Hispanic/Latinas, who have a higher burden of MetS.

**Methods:** The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is a longitudinal cohort of United States Hispanic/Latinos from four urban centers. Our analytic sample included females with PCOS and MetS information (Visit 2 N=7,332). Those who had either natural or surgical menopause status were defined as being post-menopausal, and those having high-sensitivity C Reactive Protein (CRP)>3 mg/L as high inflammation. Using HCHS/SOL's complex survey sampling weights & logistic regression, we estimated the association between PCOS and MetS and its subcomponents and tested for effect-modification by menopause status and CRP. All models were adjusted for age, age<sup>2</sup>, combined study site and Hispanic/Latino background indicators, nativity and age at immigration, education, and health insurance status.

**Results:** PCOS (n=1,135) was significantly associated with MetS (OR=1.41, 95%CI:1.13-1.76), impaired fasting glucose (OR=1.25,1.05-1.49), and elevated triglycerides (OR=1.47,1.19-1.82). PCOS was associated with MetS after adjusting for menopause status and CRP (OR=1.34, 1.07-1.67). We observed effect modification by menopause status (OR<sub>PRE</sub>=1.46,1.18-1.75; OR<sub>POST</sub>=1.34,1.04-1.64) and by CRP (OR<sub>HIGH</sub>=1.41,1.08-1.74; OR<sub>LOW</sub>=1.26,0.94-1.57).

**Conclusions:** PCOS was associated with odds of MetS after adjusting for menopause status and CRP. Further analyses showed that menopause status and CRP were important effect-modifiers in the PCOS-MetS association. Pre-menopausal or high-inflammation status show effect-modification with PCOS case status in association with MetS. MetS interventions should target these factors in Hispanic/Latinas.

**Impact of neighborhood disadvantage on posttraumatic outcomes after sexual assault**

Rachel Gaither\* Rachel Gaither Tamsin Zandstra Sarah D Linnstaedt Samuel A McLean Francesca L Beaudoin

**Background**

In the US, 38 million people seek emergency care for traumatic injury every year. Motor vehicle collision (MVC) and sexual assault are two common sources of trauma, with evidence that reduced neighborhood-level socioeconomic characteristics increase posttraumatic pain after MVC. We aimed to evaluate if neighborhood disadvantage is associated with posttraumatic outcomes among women after sexual assault.

**Methods**

Women aged  $\geq 18$  ( $n=656$ ) presenting for emergency care at facilities in the US after sexual assault were followed for one year. We measured characteristics of their home neighborhood at baseline using the Area Deprivation Index (categorized into quintiles), and measured self-reported pain, anxiety, depression, and posttraumatic stress disorder (PTSD) symptoms at six weeks. We fit adjusted log-binomial regression models to examine the relationship between each clinical outcome and neighborhood disadvantage.

**Results**

Women (65% white, 26% Hispanic) residing in more disadvantaged neighborhood quintiles were more likely to be non-white and have lower annual incomes. Six weeks after trauma, the prevalence of clinically significant pain, anxiety, and depression had nearly doubled from baseline (37 vs. 19%, 56 vs. 24%, and 49 vs. 23%, respectively); 36% of women also reported PTSD symptoms. Black, Hispanic, and lower-income participants were more likely to report pre- and post-assault pain, anxiety, and depression. After adjustment for race, ethnicity, and income, no association existed between neighborhood disadvantage and any of the four outcomes.

**Conclusion**

Socioeconomic disparities were seen in pre- and post-assault levels of pain, anxiety and depression. However, neighborhood disadvantage was not associated with posttraumatic outcomes in a cohort of sexual assault survivors. Our findings contradict previous results in MVC survivors and highlight that type of trauma (accidental vs. targeted) may be an important driver of adverse posttraumatic symptoms.

**Immune dysregulation and inflammation in characterizing women with vulvodynia, depression, and both** Amy Zheng\* Amy Zheng Bernard L. Harlow Jessica Gereige

**Background:** Depression and vulvodynia are often co-morbid where diagnosis of one increases the risk for the other. The onset of depression and vulvodynia may be immune and/or stress/environmentally-induced. We explored whether vulvodynia, depression, or both occur in response to a T-Helper 1 (Th1) mediated versus T-Helper 2 (Th2) mediated immune response.

**Materials and Methods:** We analyzed data from a case-control study of clinically confirmed vulvodynia and history of depression determined through structured clinical interviews. Immune dysregulation and inflammation were categorized based on the following self-reported conditions: Rheumatoid Arthritis, Sjogren's Disease, Scleroderma, Systemic Lupus Erythematosus, Inflammatory Bowel Disease, Fibromyalgia, Osteoarthritis, Polycystic Ovarian Syndrome, Diabetes Mellitus, Uterine Fibroids, Asthma (based on medication use), Atopic Dermatitis, Allergic Rhinitis. Logistic regression analyses adjusted for marital status, body mass index, and pack years.

**Results:** Women with vulvodynia and depression had higher odds (aOR = 4.93, 95% CI: 2.19-11.1) of systemic immune dysregulation compared to women with depression only (aOR=1.61, 95% CI: 0.65-3.98) or vulvodynia only (aOR=2.45, 95% CI: 1.00-5.96). Women reporting local immune dysregulation had similar odds of depression (aOR=1.89, 95% CI: 0.99, 3.59), vulvodynia (aOR=2.12, 95% CI: 1.08, 4.18), and depression with vulvodynia (aOR=1.96, 95% CI: 0.98, 3.90). Women with Th2 inflammation had similar odds of depression (aOR=2.2, 95% CI: 1.05-4.77) and vulvodynia (aOR=2.6, 95%CI: 1.2-5.49). Women with depression and vulvodynia had similar odds ratios for Th1 (aOR=3.03, 95%CI 1.48, 6.19) and Th2 (aOR=3.14, 95%CI: 1.49-6.6).

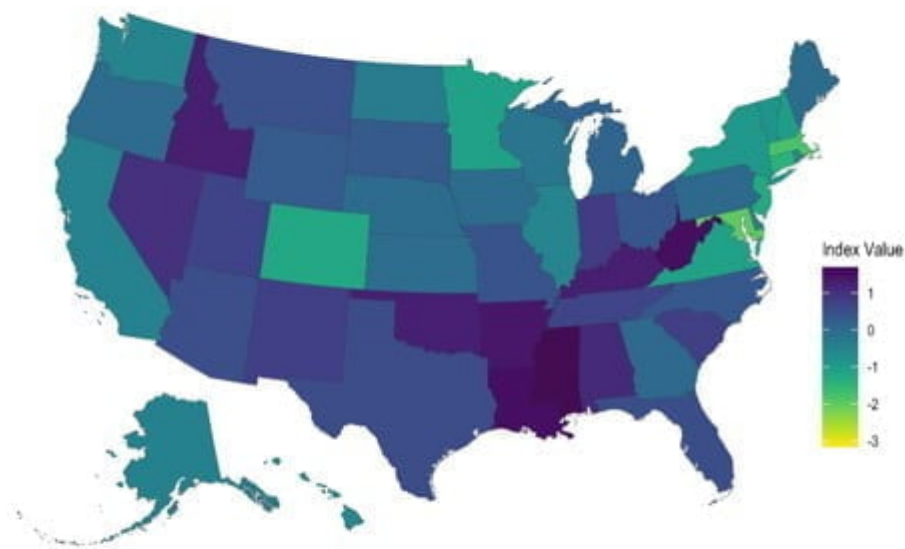
**Conclusions:** Our results suggest that an imbalance of cytokines, regardless of T-helper cell origin, can result in an increased risk of vulvodynia and/or depression. Additionally, vulvodynia and depression may share similar immune etiologies.

**State-Level Structural Sexism Linked With Elevated Risk of Use of Deceptive and Harmful Dietary Supplements Among US Women During the COVID-19 Pandemic** S. Bryn Austin\* S.

Bryn Austin Ariel L. Beccia Amanda Raffoul Destiny A. Jackson Madina Agénor Vishnudas Sarda Jorge Chavarro Jaime Hart

Use of harmful dietary supplements, such as those sold with claims promising weight-loss, cleansing/detoxing, or boosted energy and immunity, has increased during the COVID-19 pandemic among US adults, especially women. These trends have been linked to heightened experiences with psychosocial stressors (e.g., discrimination); however, the role of upstream factors, such as structural sexism, remains unknown. Data were drawn from five waves of the COVID-19 Pandemic Substudy embedded in the Nurses' Health Studies 2/3 and Growing Up Today Study (N=54,931 cisgender women; April 2020-April 2021). We constructed an index of state-level structural sexism (**Figure 1**) using data from 2018 on relevant policies and social inequalities from the Institute for Women's Policy Research (higher scores indicate higher structural sexism) and assigned each participant exposure values. Using multilevel logistic models with participant and state random intercepts adjusted for individual- (age, cohort, race/ethnicity) and state-level (percentage of population living in poverty, Index of Concentration at the Extremes) confounders, we estimated OR and 95% CI for associations between structural sexism and use of the four types of supplements across the study period. The baseline prevalence of supplement use was: weight-loss: 2.7%; immunity: 22.6%; energy: 4.4%; and cleanse/detox: 3.2%. State-level structural sexism was associated with higher prevalence of use of all supplement types. Each one standard deviation increase in structural sexism was associated with higher odds of use as follows: weight loss 25% (95% CI: 11-40%); cleanse/detox 14% (95% CI: 5-24%); energy 26% (95% CI: 14-38%); and immune 13% (95% CI: 7-20%). Our study provides novel evidence for the role of state-level structural sexism in increasing the likelihood of harmful dietary supplement use among US cisgender women during the pandemic.

**Figure.** Composite Structural Sexism Index by U.S. State\*



Data source: Institute for Women's Policy Research, 2018

\* Higher score indicates higher structural sexism score. |

**Quantifying misclassification of non-cancerous gynecologic conditions among women****undergoing hysterectomy** Eva Laura Siegel\* Eva Siegel Brianna VanNoy Roshni Rangaswamy  
Cherie Q. Marfori Ami R. Zota

Etiologies of most gynecological disorders remain poorly understood, in part because they have been under-examined in epidemiological studies. Most studies assume that medical records are the gold standard, and have not quantified outcome misclassification, even though these conditions are often mis- or under-diagnosed. Our objective is to quantify the extent of clinical misdiagnosis through pathology confirmation following hysterectomy, and to characterize whether misclassification varies by demographic and clinical characteristics.

We compared gynecologic diagnoses extracted from medical records to those deduced from pathology reports among women receiving hysterectomies for non-cancerous gynecologic conditions in 122 patients at an urban academic hospital in Washington, DC. Demographic and clinical data were available from medical histories, and women completed the symptom and health-related Uterine Fibroid Quality of Life survey (UFsQOL).

Additional uterine pathologies were confirmed by pathology in 47/122 (39%) of patients, indicating substantial clinical misdiagnosis. Of those with an initial fibroids-only diagnosis, 39/89 (44%) had undiagnosed endometriosis/adenomyosis. Of those with an endometriosis or adenomyosis-only diagnosis, 7/29 (24%) also had fibroids. White women were more likely to have received a correct diagnosis compared to women of color, as were women with higher household income (vs. lower) and non-public insurance (vs. public). Women who were misdiagnosed reported worse symptoms on the UFsQOL and poorer quality of life across UFsQOL subscales.

While medical records are assumed the gold standard for outcome measurement, the large amount of measurement error in our sample highlights the need for better non-invasive diagnostic methods for research on these disorders. We observed differential misclassification by race/ethnicity, income, and insurance type, as well as by symptom profiles, which may have added implications for clinical management.

**LATEBREAKER**

Aging

**Sociodemographic and clinical comorbidity changes among residents of assisted living facilities in Ontario, Canada** Derek Manis\* Derek Manis Paul Katz Natasha Lane Susan Bronskill Paula Rochon Samir Sinha Kali Thomas Ross Andel George Heckman David Kirkwood Andrew Costa

**Objective:** We investigate the changes in the sociodemographic characteristics, clinical comorbidities, and transitions between care settings among residents of assisted living facilities.

**Methods:** We conducted a repeated cross-sectional study using linked, individual-level health system administrative data on residents of assisted living facilities in Ontario, Canada from January 1, 2013 to December 31, 2019. We calculated counts and proportions to describe the sociodemographic characteristics and clinical comorbidities. Absolute and relative changes and trend tests were calculated to quantify the longitudinal changes in the characteristics of residents of assisted living facilities between 2013 and 2019. Closed cohorts were created for each calendar year from 2014 onwards, and Sankey plots were graphed to display transitions.

**Results:** There was a 34% relative increase in the size of residents of assisted living facilities population (56,975<sub>2019</sub> v. 42,600<sub>2013</sub>). These older adults had a consistent mean age of 87 years, and women consistently accounted for nearly two thirds of the population. The five clinical comorbidities that had the highest relative increases were: renal disease (18,032<sub>2019</sub> v. 10,844<sub>2013</sub>; 66%); other mental health conditions (33,009<sub>2019</sub> v. 21,124<sub>2013</sub>; 56%); osteoporosis (26,153<sub>2019</sub> v. 17,698<sub>2013</sub>; 48%); cardiac arrhythmias (29,940<sub>2019</sub> v. 20,424<sub>2013</sub>; 47%); and diabetes (18,136<sub>2019</sub> v. 12,494<sub>2013</sub>; 45%). On average at the end of each calendar year, 82% of residents remained in their assisted living facility, 6% were admitted to a nursing home, 1% were admitted to hospital, and 11% died.

**Interpretation:** Residents of assisted living facilities are an important older adult population that has progressively increased in clinical complexity.

**Estimating the health effects of a potential vaccine for cytomegalovirus (CMV) among older adults in the United States** Yuelin He\* Yuelin He Jessica Faul Kate Duchowny Chihua Li Rebecca Stebbins Grace Noppert

Cytomegalovirus (CMV) infection has been indicted in the etiology of multiple aging-related diseases, yet its vaccine development has been slow. Few studies have investigated the potential health effects of a CMV vaccine, particularly among older individuals.

To quantify what proportion of aging-related diseases could be prevented in the United States with a viable CMV vaccine, we used longitudinal data from the Health and Retirement Study (HRS) from 2016 to 2020. The sample included N=5,855 individuals aged 65 or above. Creating a binary indicator based on the continuous IgG antibody measure of serum CMV, we assumed a hypothetical vaccine would shift the distribution of CMV levels from the highest quartile to the lower 3 quartiles, resulting in improved immune control of CMV. We estimated attributable fractions (AF) to top-quartile CMV levels for 7 dichotomous health outcomes: cardiovascular diseases (including heart problems, stroke, high blood pressure, and high cholesterol), cancers, diabetes, and disability using a novel logistic regression-based approach which allows adjustment for continuous age. Analyses were stratified by sex and race/ethnicity.

Among female Non-Hispanic Whites (NHWs) in the top quartile of CMV IgG, 3.4 (95%CI: 1.4, 5.4)% of existing diabetes cases and 4.7 (95%CI: 0.1, 9.4)% of high cholesterol cases could be prevented if the vaccine decreased CMV IgG below the top quartile cutoff. Additionally, 2.8 (95%CI: 0.8, 4.9)% of heart problems and 1.9 (95%CI: 0.8, 3.1)% of high blood pressure cases among female NHWs and 4.2 (95%CI: 2.0, 6.3)% of heart problems and 2.5 (95%CI: 1.2, 3.8)% of high blood pressure cases among the male NHWs could be prevented. Results for Non-Hispanic Blacks and Hispanics were not significant.

Our findings provide important evidence for the potential population health impact of a vaccine for CMV and lay the groundwork for future studies to examine the impact of vaccines with varying efficacy levels across other age groups.



**Correcting MRI measures for intracranial volume: do alternative correction approaches modify associations between regional MRI measures and cognitive function?** Jingxuan Wang\* Jingxuan Wang Tanisha G. Hill-Jarrett Peter Buto Scott C. Zimmerman Erin Ferguson Yulin Yang Annie Pederson Ben Lacar Kendra D. Sims Minhyuk Choi Michelle A. DeVost Michelle R. Caunca Ruijia Chen Sarah F. Ackley M. Maria Glymour

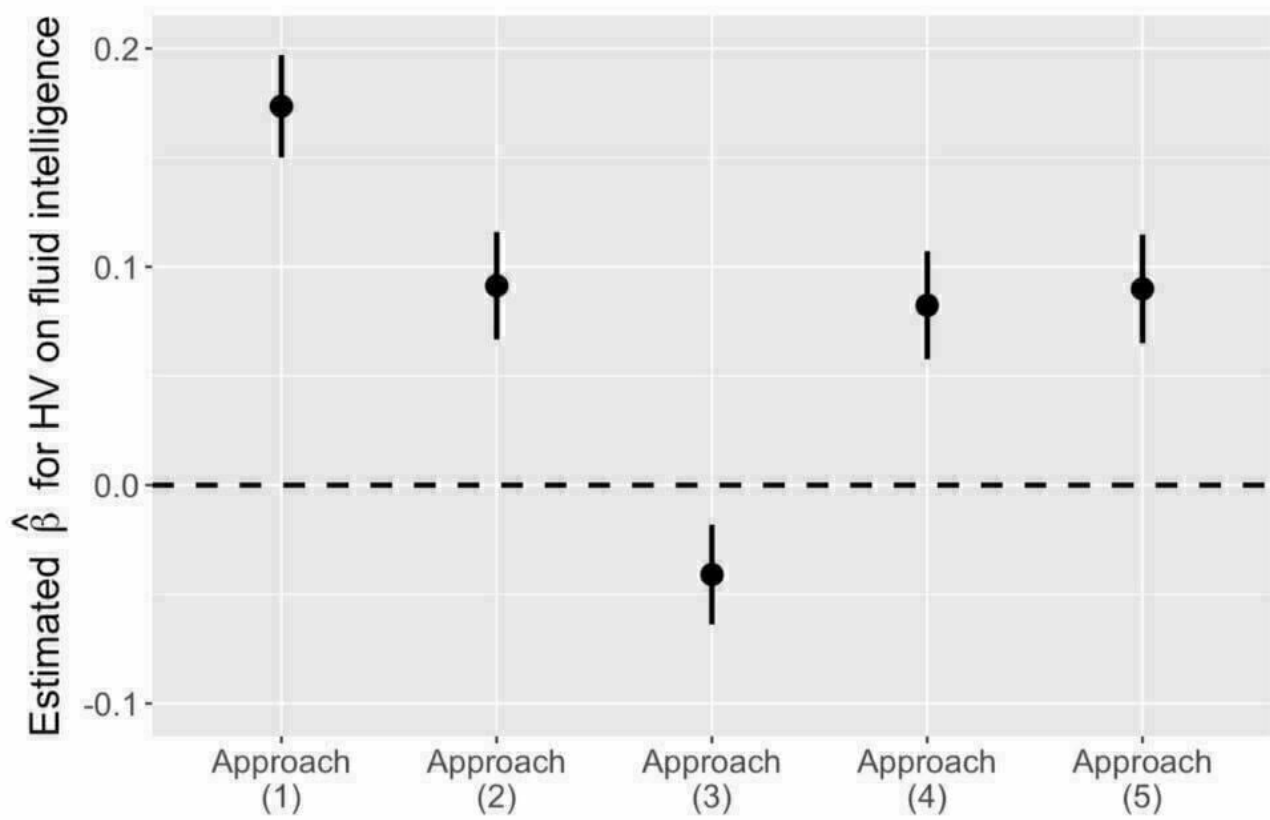
**Background:** Volumetric MRI measures such as hippocampal volume (HV) are associated with cognitive function. Adjustment of raw HV for total intracranial volume (ICV) is believed to be necessary to account for differences in head size. However, there is no consensus across studies on the best statistical approach to account for ICV when estimating the effect of HV on cognition.

**Methods:** Using cross-sectional data from 37,938 dementia-free UK Biobank participants aged 50+, we fit linear regression models of fluid intelligence with HV as the predictor, adjusting for age, age squared, gender, assessment center, education, and race. In these models, we compared the coefficients for HV from five correction approaches and used a priori knowledge from the neuropsychological literature to assess whether correction approaches produce plausible effects. The five approaches evaluated were (1) no correction, (2) adjusting for ICV as a covariate, (3) proportional-rescaling (i.e., dividing HV by ICV and multiplying by mean ICV), (4) residualizing HV by regressing on ICV, and (5) both 2 and 3. All approaches yield coefficients on the same scale (1/cm<sup>3</sup>).

**Results:** The mean age of the participants was 64.2 years (SD=7.6) and 97% were White. The proportional approach (3) indicated that larger HV is paradoxically associated with worse cognition ( $\beta$  for fluid intelligence: -0.04, 95% CI: [-0.06, -0.02]). Adjusting approach (2) ( $\beta$ : 0.09 [0.07, 0.12]), residualizing approach (4) ( $\beta$ : 0.08 [0.06, 0.11]), and adjustment with rescaling approach (5) ( $\beta$ : 0.09, [0.07, 0.11]) yielded similar estimates. Crude volume (1) yielded an estimate approximately double ( $\beta$ : 0.17 [0.15, 0.20]) that of (2), (4), and (5).

**Conclusion:** Crude HV is likely confounded by childhood growth on ICV and adult cognition via reserve or related mechanisms. Rescaling HV as a proportion of ICV without adjusting for ICV as an independent predictor may produce biologically implausible findings.

Figure: Associations of hippocampal volume with fluid intelligence scores across different ICV correction methods (approaches 1-5). The exposure was scaled to unit of  $1\text{cm}^3$ .



**Self-reported and clinical diagnoses of depression and risk of dementia over an average of 10 years of follow-up in a large multi-ethnic sample**

Erin Ferguson\* Erin Ferguson Paola Gilsanz Scott C Zimmerman Chen Jiang Vidhu Choudhary Travis Meyers Cynthia Campbell Ulrike Muench Fan Xia Catherine Schaefer M Maria Glymour

**Introduction:** Depression is a modifiable risk factor for Alzheimer's disease and related dementias (ADRD), but heterogeneity in associations by means of reporting and by race/ethnicity is unclear. We evaluated associations of self-reported and electronic health records (EHR) depression diagnoses with ADRD and tested for effect modification by race/ethnicity.

**Methods:** Analyses included 249,917 members of Kaiser Permanente Northern California aged 55+ years when surveyed in 2002 or 2007. Depression was measured using 1) survey self-report and 2) clinical diagnoses in the EHR prior to the survey. ADRD diagnoses were recorded in EHRs (ICD9/10 codes, n=33,646 through Dec 2020). We used Cox proportional hazards models to estimate hazard ratios (HRs) for the association of both measures of depression with incident ADRD, adjusted for racial/ethnic identity, sex, age, education, income, marital status, US nativity, alcohol use, smoking, and head injury. We tested for interactions between racial/ethnic identity (White, Asian, Black, Hispanic, Other) and depression. To minimize reverse causation from ADRD to depression, a sensitivity analysis omitted ADRD cases in the first 5 years of follow-up.

**Results:** Average age at survey was 70 years (SD=8.93). Prevalence of pre-survey depression diagnosis from self-reports was 12.7% (n=31,733) and from EHRs was 17.2% (n=43,008). Self-reported (HR=1.50, 95% CI:1.46-1.55) and diagnoses (HR=1.69, 95% CI:1.65-1.74) of depression both predicted ADRD. Dropping the first 5 years of follow-up attenuated estimates but all remained significant (p<0.001). Self-reported depression was associated with higher risk for Asian individuals compared to White individuals (p = 0.02). No other interactions were observed.

**Conclusion:** Depression was consistently associated with increased risk of ADRD. There was minimal interaction by racial/ethnic group. Future work will use this sample to quantify confounding and investigate depression treatment and ADRD risk.

**Evaluation of causal relationships between dementia, visual impairment, and cataracts using bi-directional Mendelian randomization** Erin Ferguson\* Erin Ferguson Peter Buto Mary Thoma Jingxuan Wang M. Maria Glymour Thomas Hoffmann H el ene Choquet Shea Andrews Kristine Yaffe Kaitlin Casaletto Willa Brenowitz

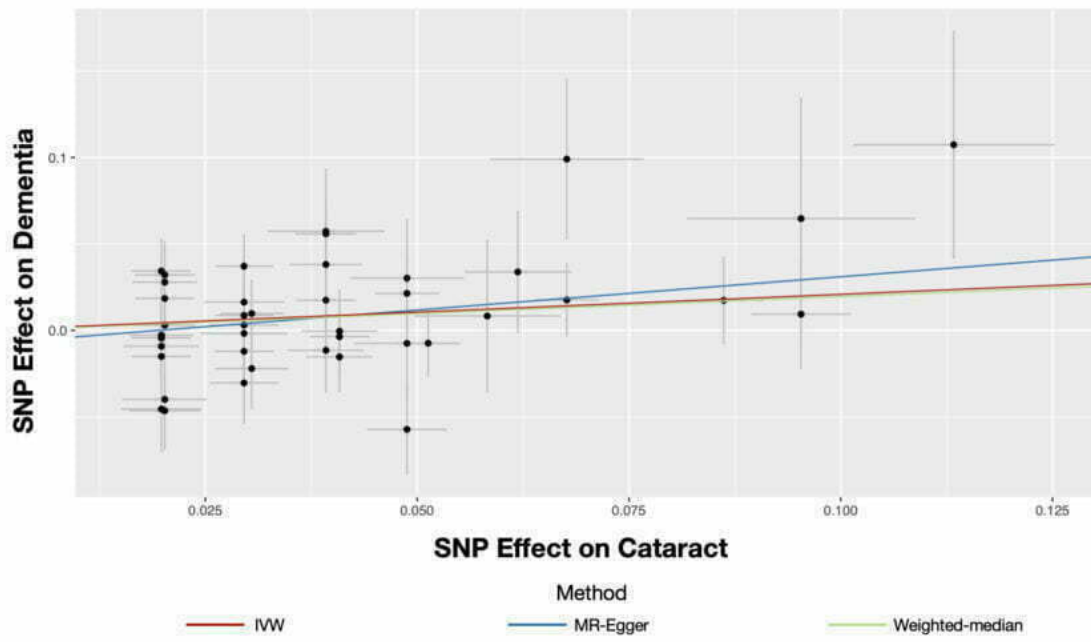
**Introduction:** Visual impairment and cataracts are emerging as potentially modifiable risk factors for Alzheimer disease (AD) and related dementias (ADRD) but establishing causality is difficult. Using Mendelian randomization (MR), we leverage variation in genetic risk of AD and cataracts to evaluate bi-directional causal effects.

**Methods:** Analyses included 496,938 UK Biobank participants aged 40-70 without dementia at assessment and with genetic data. Participants self-reported history of cataracts and 113,756 completed visual acuity exams. All-cause dementia was identified from medical records. Logistic regression adjusting for demographic/clinical confounders estimated the association between cataract and dementia. We conducted 2-sample MR with 45 genetic variants previously associated with cataracts to estimate the causal effect of cataract on dementia and 27 genetic variants previously associated with AD to estimate the reverse effect. 3 MR estimators adjusted for age, sex, and genetic ancestry were used: inverse variance weighted (IVW), MR-Egger, and weighted-median.

**Results:** The sample was an average of 56.5 years (SD=8.09) at assessment, with a cataract prevalence of 3.2% (n=16,087). Observationally, history of cataract was associated with higher dementia odds (OR=1.12; 95% CI:1.02-1.24). In MR, the IVW estimated a significant effect of cataract on higher dementia odds (OR=1.23, 95% CI:1.01-1.51). All three MR estimators produced similar estimates (Figure 1) and there was no evidence of pleiotropy (MR-Egger intercept  $\beta=-.01$ ,  $p=.41$ ). In MR for reverse causality, AD was not significantly associated with cataract (IVW OR=1.00, 95% CI: .97-1.03) or visual acuity (OR=.98, 95% CI: .93-1.03).

**Conclusion:** Using variation in genetic risk, we estimate that cataract increased risk of dementia, but AD did not affect cataract risk or visual acuity. This finding supports cataracts as a risk factor for dementia, suggesting cataract treatment may help prevent dementia.

**Figure 1.** Effect of cataract SNPs on cataract and dementia. MR estimates for the effect of cataracts are shown for inverse variance weighted (IVW), MR-Egger, which adjusts for pleiotropy, and weighted-median.



**A Data- and Simulation-Based Crosswalk from Cognitive Change to Dementia Hazard Ratios: Contextualizing Results from Trials Anti-Amyloid Antibody Drugs** Sarah Ackley\*  
Sarah Ackley Jingxuan Wang Tanisha G. Hill-Jarrett M. Maria Glymour

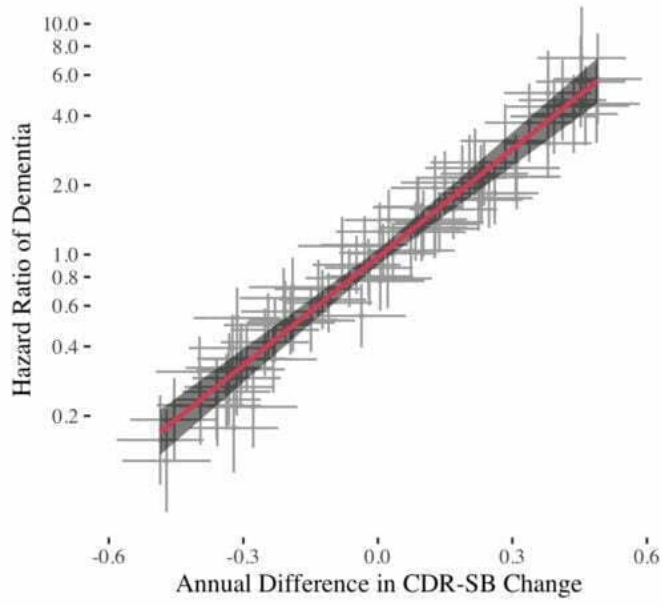
**Background:** Dementia and cognitive outcomes are inconsistently reported across studies, making head-to-head comparisons of interventions difficult. Recent anti-amyloid drug trials report change in CDR-SB, a cognitive test, as the primary outcome, while observational studies on risk factors typically report dementia hazard ratios (HRs). We present a method to crosswalk cognitive change differences to HRs. We then determine the HR that corresponds to CDR-SB change differences in the CLARITY-AD trial.

**Methods:** Alzheimer's Disease Neuroimaging Initiative (ADNI) participants with suspected or likely mild cognitive impairment at baseline were followed for up to two years. To develop a crosswalk, we iteratively randomly divided participants into two groups in such a way to generate a range of corresponding cognitive change differences and HRs. HRs for the effect of treatment on time to dementia were estimated using Cox proportional hazards models; CDR-SB change rate differences were estimated using linear mixed-effects regression (random intercepts). Effect estimates and standard errors were used to obtain a log-linear crosswalk from CDR-SB change difference to HR using a maximum likelihood estimation technique that allows for propagation of errors in coefficients through to final estimates. We then obtain a crosswalked HR for CLARITY-AD.

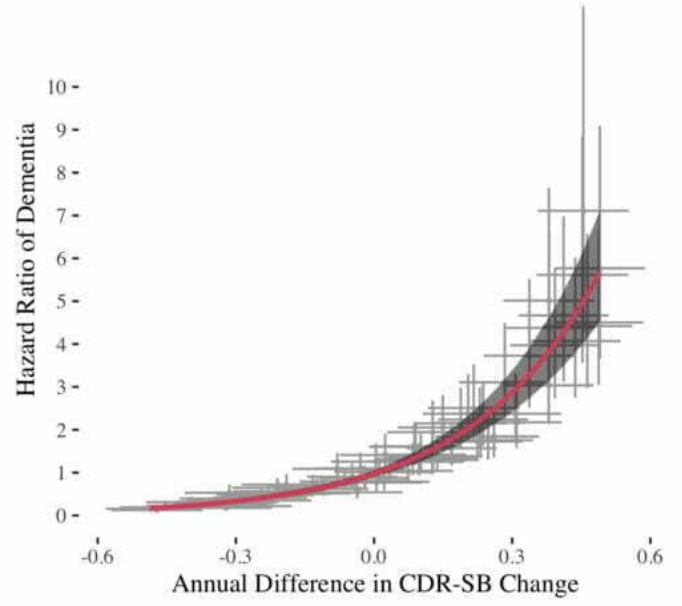
**Results:** 871 ADNI participants (3062 assessments) were followed for a median of 1.49 (IQR: 1.02-1.97) years. Based on CDR-SB change in CLARITY-AD, we obtain a crosswalked HR of 0.68, 95% CI: (0.61, 0.76); incorporating error in CDR-SB change gives a 95% CI of (0.47, 0.98). The figure shows coefficients estimated with 95% CIs, and the resulting crosswalk and 95% confidence band.

**Conclusions:** Small differences in cognitive change between groups, such as those seen in CLARITY-AD, may correspond to moderate dementia HRs. Methods to crosswalk change and time-to-event measures allow for a wide range of relevant comparisons.

Log-Linear Plot



Linear-Linear Plot



**Metal mixture and incident cognitive impairment—an application of the quantile-based g-computation method** Yijia Zhang\* Yijia Zhang Weixi Chen Liping Lu Meghan Angley Ka Kahe

*Background:* Research has shown the potential linkage between trace elements and cognitive function. However, most studies focused on individual elements. This study used quantile g-computation to study the metal mixture in relation to cognitive impairment in a cohort of US adults.

*Methods:* The study sample included 1,617 participants from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Trace Element Study. Four relatively important metals (magnesium, calcium, zinc, arsenic) were selected as mixture components by comparing the metals' t-statistic in generalized linear model trained with cross-validation. Primary outcome was defined with enhanced cognitive battery tests (ECB) to determine participant's domain-based cognitive function impairment. The association of the metal mixtures with incident impairment on ECB was evaluated using quantile g-computation, which allows flexibility to examine positive and negative joint effects of metal mixture components. Metal concentrations are divided into quartiles to estimate the ORs along with CIs. The scaled effect size of positive/negative was the sum of the coefficients of the metals contributed to that direction.

*Results:* After adjusting for all covariates, a quartile increase in the metal mixture was not associated with incident cognitive impairment defined by ECB [OR (95% CI) = 0.65 (0.38, 1.10)], presumably due to insufficient sample size. Among the four metals (Figure 1), calcium contributed on the positive direction (scaled effect size=0.16), whereas magnesium, zinc and arsenic contributed on the negative direction (scaled effect size=-0.59).

*Conclusion:* Quantile g-computation can potentially be used as a tool to study the association between metal mixtures and incident cognitive impairment and to identify harmful/beneficial constituents.



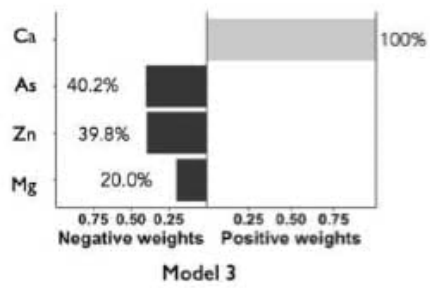


Figure 1 Weight contribution by individual element of the effect on incident cognitive impairment in positive and negative directions

**Changes in the association of Alzheimer's Disease genetic risk with social connections in middle- and older-ages**

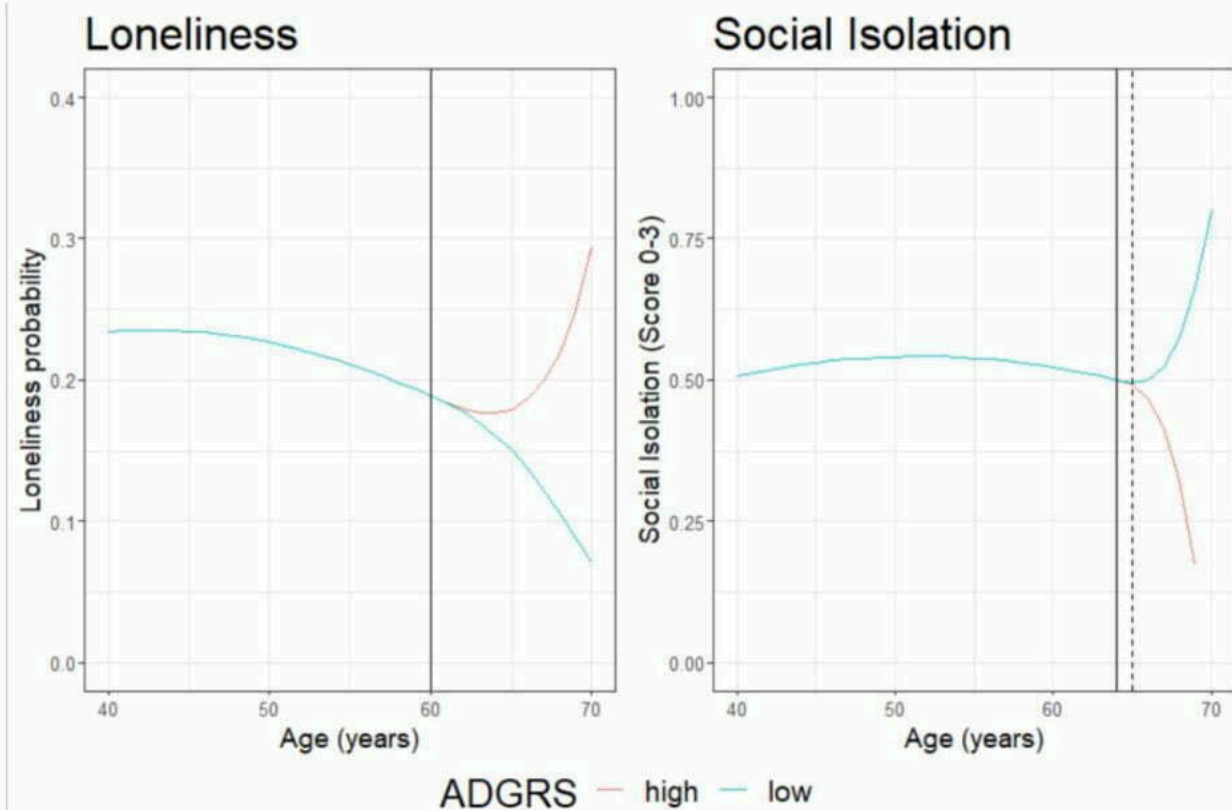
Scott Zimmerman\* Scott Zimmerman Ruijia Chen Lucia Pacca Jillian Hebert Alicia Riley Min Hee Kim Haobin Qian Annie Pederson Alice Tang Yulin Yanh Willa Brenowitz M Maria Glymour Ashwin Kotwal Jacqueline M. Torres

Social connections and dementia risk are inversely associated, but the age when these associations start to emerge and whether they reflect "reverse causation" (i.e. early dementia symptoms disrupting social connections) are unknown. Genetic risk of Alzheimer's Disease (AD) is established at conception and, as in Mendelian randomization, can be used to evaluate the age when the earliest symptoms of AD influence social connections. We aimed to determine the earliest age at which the associations of genetic risk of AD with social isolation and loneliness emerge and whether these associations were consistent with reverse causation.

We used data from UK Biobank participants aged 40+ years in 2006-2015 (n=487,194) with self-reported outcomes: i) loneliness (yes/no) and ii) social isolation (a composite of living alone, infrequent social/leisure activities, and infrequent friend/family visits; range 0-3). To evaluate the age when the association emerged, we fit generalized linear regression models, adjusted for age, sex, assessment center, genotyping array, and genetic ancestry principal components. We compared models that constrained the interaction of AD genetic risk score (AD-GRS) and age to be zero below an age threshold (from 30 to 70 years across models). We selected the threshold from the best-fitting model based on mean squared prediction error in 5-fold cross-validation.

Participants' mean (sd) age was 56.5 (8.2) years. Loneliness probability increased for high AD-GRS but decreased for low AD-GRS after age 60 (interaction  $b=0.00057$ , 95%CI (-0.00075, 0.00188) per SD of AD-GRS per year). Social isolation increased for low AD-GRS but decreased for high AD-GRS after age 64 (interaction  $b=-0.0013$ , 95%CI (-0.0025,-0.0001) per SD of AD-GRS per year).

Differences in social isolation and loneliness begin to emerge nearly two decades before the average age of AD diagnosis, but the direction of change in social isolation is not consistent with reverse causation bias.



**Figure.** Divergence Model Results for Social Connection Measures. Mean predicted outcome (loneliness or social isolation) for the study sample assigned counterfactual values of AD-GRS at high (95th percentile) or low (5th percentile) of AD-GRS. Solid lines indicate the threshold age corresponding to the best fitting model (i.e. the age of divergence in the outcome due to AD-GRS). Dashed lines indicate the youngest age at which the association between AD-GRS and the outcome was statistically significant in t-tests comparing predicted outcomes at high and low AD-GRS. Statistical significance for the interaction of ADGRS and loneliness was not observed at any age.

**Dehydroepiandrosterone sulfate and lifespan in men and women: a Mendelian randomization study using the UK Biobank** C Mary Schooling\* C Mary Schooling Jie V Zhao

**Background:** The prohormone dehydroepiandrosterone sulfate (DHEA-s) falls with age and is implicated in aging. Whether DHEA-s is a biomarker of aging or a target of intervention is unclear. Previous observational studies suggest DHEA-s could be protective in older men but are open to confounding and selection bias, particularly from inevitably only recruiting survivors.

**Methods:** We used a two-sample Mendelian randomization study to assess the association of DHEA-s (n=9716) with maternal and paternal attained age reported by 389,166 UK Biobank participants, with sensitivity analysis.

**Results:** DHEA-s was unrelated to maternal lifespan using inverse variance weighting, -0.32 years per log transformed mmol/L DHEA-s, 95% confidence interval (CI) -1.06 to 0.42, and was associated with shorter paternal lifespan (-1.46 years, 95% CI -2.12 to -0.81) giving an overall estimate of -1.12 years, 95% CI -1.58 to -0.66. Estimates were similar using sensitivity analysis and as expected for the positive control exposures (the hormones androsterone sulfate and epiandrosterone sulfate) and the positive control outcome (testosterone).

**Conclusion:** Coherent with a growing body of empirical evidence suggesting, consistent with evolutionary biology, that drivers of reproduction trade-off against longevity, this suggests that DHEA-s might be relevant to lifespan, particularly in men. Availability of DHEA as an unregulated supplement might bear consideration.

MR estimates for the associations of genetically predicted log transformed DHEA-s from the UK Household Longitudinal Study with life years by sex (based on maternal and paternal attained age) from the UK Biobank



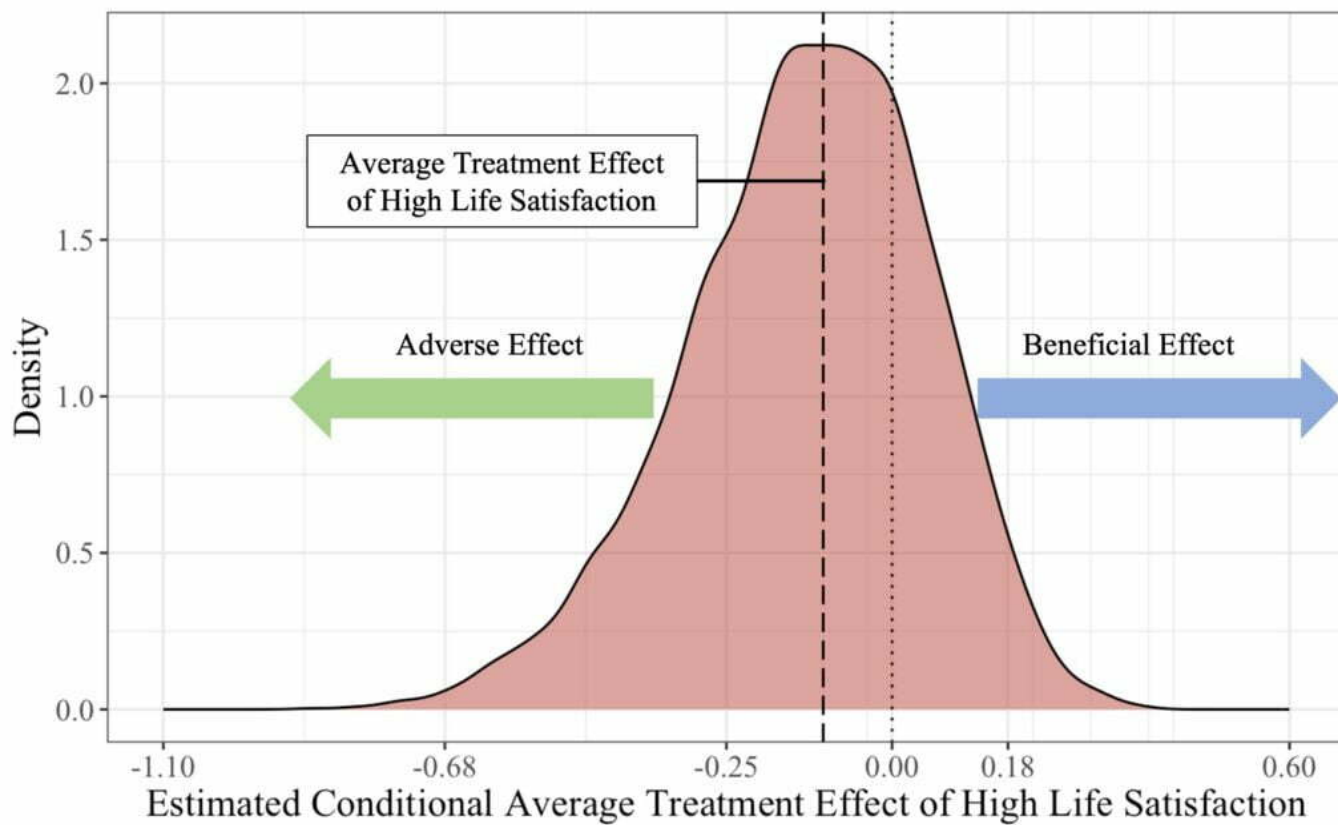
SNP: single nucleotide polymorphism, IVW: inverse variance weighted, WM: weighted median, MRE: MR-Egger, CI: confidence interval, p: p-value, MRE I p: MR-Egger intercept p-value.

**Uncovering heterogeneous associations between life satisfaction and cognitive functioning: a machine-learning approach** Toshiaki Komura\* Toshiaki Komura Koichiro Shiba

**Background:** Although evidence exists for population-average associations between positive psychological well-being and cognitive function, little is known about how the relationship varies across social groups. This study examined heterogeneity in the associations between life satisfaction and cognitive functioning among U.S. older adults.

**Methods:** We analyzed a national sample of U.S. adults aged  $\geq 50$  from the Health Retirement Study ( $n=10,650$ ). We assessed life satisfaction at baseline (2010/ 2012) using the Satisfaction with Life Scale. Cognitive functioning was assessed using a modified version of the Telephone Interview for Cognitive Status score after 4-year follow-up (2014/2016). Higher scores indicate greater cognitive functioning (range: 0-27). We estimated population-average association between life satisfaction and cognitive functioning via doubly-robust targeted maximum likelihood estimation with SuperLearning, adjusting with 46 covariates from the pre-baseline wave (2006/2008). To assess effect heterogeneity, we estimated conditional average effects via the causal forest algorithm.

**Results:** Despite the null evidence for the average association between life satisfaction and cognitive functioning ( $\beta = -0.10$ ; 95%CI: -0.27, 0.06), evidence of large effect heterogeneity (i.e., a widespread distribution of conditional average effects across participants) was observed. We identified subgroups of individuals for whom high life satisfaction was associated with lower subsequent cognitive functioning, and they were characterized by lower socioeconomic status, poor health status, and more negative psychological conditions compared to those who seemed to have benefited from high life satisfaction. Our approach for effect heterogeneity using machine learning algorithms indicates a need for further research to uncover mechanisms through which life satisfaction affects cognitive functioning, as it may have unintended adverse consequences in some contexts.



**Immunosenescence and Global Cognitive Function in 2016 and 2018 in the Health & Retirement Study** Rebecca Stebbins\* Rebecca Stebbins Yuan Zhang Grace A. Noppert Allison E. Aiello

There is mounting evidence that the immune system plays a critical role in cognitive impairment and dementia. While clinical studies have provided support for these associations, population-based evidence remains scarce. Using data on 4,040 participants aged 65 and older from the Health and Retirement Study’s (HRS) 2016 Venous Blood Study and 2016 and 2018 general surveys, we estimated the association between six ratios of adaptive and innate immunosenescence (CD8+:CD4+, Monocyte:Lymphocyte, CD4+ EMRA/Naïve, CD8+ EMRA/Naïve, Memory:Naïve B Cells, and CD56 Low:CD56 High NK Cells) and global cognition measured by the 35-point Telephone Interview for Cognitive Status (TICS) in 2016 and 2018, using linear regression. Models were adjusted for age, sex, race/ethnicity, educational attainment, baseline comorbidities, and ongoing chronic stress. We also investigated effect measure modification by biological sex in sex-stratified models. Despite statistically significant unadjusted associations across all ratio measures, we found no relationship between immunosenescence ratio measures and HRS-TICS score when adjusting for a sufficient set of confounders. Before adjustment, each unit of log-transformed CD8+:CD4+ ratio was associated with 0.58 (95%CI: 0.37,0.79) fewer 2016 HRS-TICS points, but this association was attenuated to null after adjustment (coef.=0.01 (95%CI: -0.16,0.19)). Full results for each ratio measure and model can be seen in the attached Figure 1. Furthermore, no modification by sex was detected. These results do not support the hypothesis of a causal relationship between immunosenescence and accelerated cognitive aging but suggest they may be associated due to common social and biological causes. However, given the limited follow-up time available for investigation, further study is warranted once more data is available.

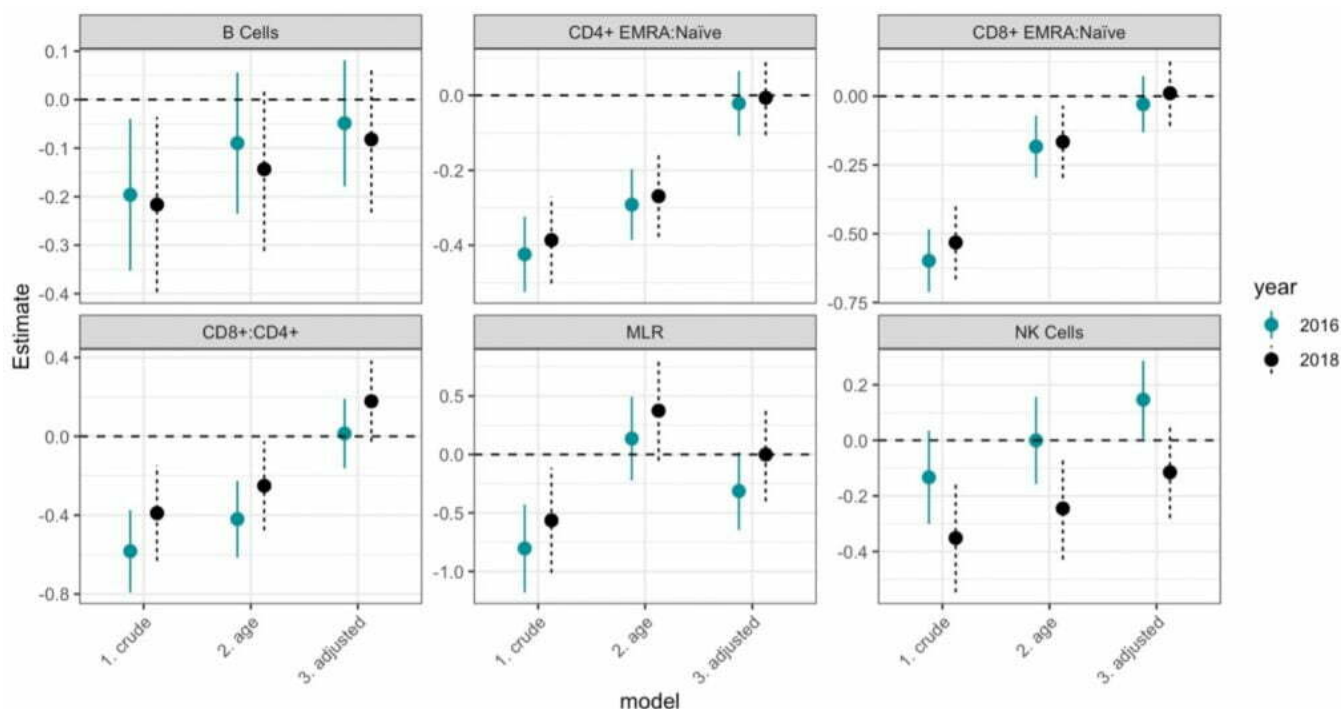


Figure 1. Immune Ratio Measures and Cognitive Performance in the U.S. Health & Retirement Study, N=4,040 (2016) and N=3,165 (2018).



**Changes in Social Participation and Cognitive Disability Following a Natural Disaster: 9-year Follow-up of Survivors of The 2011 Great East Japan Earthquake and Tsunami**

Sakurako Okuzono\* Sakurako Okuzono Koichiro Shiba Aki Yazawa Ichiro Kawachi

Social participation is an established protective factor against the onset of dementia. However, it is not known whether changes in social participation occurring in the aftermath of a natural disaster (e.g., induced by residential displacement) affect cognitive disability among disaster survivors. We conducted a 9-year follow-up study of older adults ( $\geq 65$  years) who survived the 2011 Great East Japan Earthquake to estimate the impacts of different trajectories of social participation on the prevalence of cognitive disability. The baseline survey in 2010 predated the disaster by seven months. Participants completed post-disaster surveys in 2013, 2016, and 2019 ( $n = 3,207$ ). Social participation was repeatedly assessed at each wave as a time-varying exposure. Cognitive disability levels (ranges 0 to 7) in 2019 were assessed via linkage to the national long-term care insurance register. We used cognitive disability levels of 2 as the cut-off of the onset of dementia. We used the doubly robust targeted maximum likelihood estimation to address time-dependent confounding. Sustained higher social participation over three-time points (vs. never) was associated with a lower prevalence of dementia in 2019 (RR=0.47, 95%CI=0.07, 0.87). In addition, social participation in 2010 and 2013 but withholding participation in 2016 (vs. never) was associated with a higher prevalence of mild dementia (social participation: RR=1.81, 95%CI=1.30, 2.32). Interventions to sustain social participation after a disaster may be important to preserve cognitive function among older survivors.

**The association between delayed dementia diagnosis and the risk of mortality in the Health and Retirement Study** Min Hee Kim\* Min Hee Kim Grisell Diaz-Ramirez John Boscardin Katherine Possin M. Maria Glymour

Timely dementia diagnosis enables optimal symptom management, treatment of comorbid conditions, and links to supportive services, which may, in turn, reduce the risk of death from longer preservation of physiological function. Yet few studies test this hypothesis due to methodological challenges (e.g., obtaining a measure of timeliness of dementia diagnosis without inducing immortal time bias).

We quantified the association between delayed dementia diagnosis and the risk of death using the Health and Retirement Study linked with Medicare Claims. The sample included 5,744 participants aged 70 or older, who met survey-based criteria for probable dementia onset, identified through a dementia prediction algorithm, between 2000 and 2018. Delayed diagnosis interval was defined as a time-updated variable, contrasting the time from the date when survey-based criteria for dementia were met until the date of incident clinical diagnosis in Medicare Claims, categorized as <1-11, 12-35, 36-71, 72+ months. We constructed person-month data and applied conditional logistic regression to estimate odds ratios of death as a function of the time-updated delayed diagnostic intervals, adjusting for baseline year, age, sex, comorbidity, observed time since the first presentation of dementia symptoms in survey data, and time-updated diagnosis status.

The baseline mean age was 82.1 years (SD=6.3). 76.7 % of the sample died during the follow-up period. 35.7 % had received a dementia diagnosis within a year of or prior to meeting survey-based criteria, 24.8 % 2 to 3 years, 25.4 % 3 to 6 years, and for 14.1% Medicare diagnosis occurred 6 or more years after meeting survey-based criteria. Results showed that individuals having 2-3, 3-6, and 6+ years of diagnosis delayed had 0.4 (95% CI 0.4-0.5), 0.5 (95% CI 0.5-0.6), and 0.6 (95% CI 0.5-0.7) times the odds of incident mortality, respectively, compared to individuals whose diagnosis is delayed less than a year.

Delayed diagnosis was inversely associated with an increase in mortality risk. We are evaluating to what extent methodological issues (e.g., misclassification of dementia onset in the survey, confounders) derive the current findings.

**Social engagement, multimorbidity, and age-related cognitive decline in older adults from the Rancho Bernardo Study of Healthy Aging** Alexander Ivan B. Posis\* Alexander Ivan Posis Alexander Ivan B. Posis Aladdin H. Shadyab Humberto Parada Jr. John E. Alcaraz William S. Kremen Linda K. McEvoy

Multimorbidity is prevalent among older adults and is associated with increased risk of cognitive decline. Social engagement is associated with lower risk of dementia; however, it is unknown if social engagement modifies the associations between multimorbidity and cognitive decline.

This study used data from the Rancho Bernardo Study of Healthy Aging, a community-based prospective cohort study. Starting in 1992-1996 (baseline), participants completed a battery of cognitive function tests at up to 6 study visits over 23.7 (mean=7.2) years. Multimorbidity was defined as the presence of  $\geq 2$  of 14 common chronic diseases. Social engagement was assessed using items based on the Berkman-Syme Social Network Index. We fit linear mixed-effects models to estimate the associations of multimorbidity and cognitive performance trajectories, adjusted for age, sex, body mass index, education, smoking, and alcohol use. We assessed effect measure modification using social engagement-stratified models and likelihood ratio tests comparing models with and without a 3-way interaction.

Of the 1381 participants (mean age=74.5 years; 60.8% female; 98.8% non-Hispanic White), 41% had multimorbidity at baseline. Multimorbidity was associated with faster declines in Mini-Mental State Examination (MMSE;  $\beta = -0.23$  95% CI -0.38,-0.09), Trail-Making Test Part B ( $\beta = 9.63$  95% CI 5.56,13.71), and Verbal Fluency Test ( $\beta = -0.46$  95% CI -0.75,-0.17) overall. In stratified models, multimorbidity was associated with faster declines in MMSE among those with low ( $\beta = -0.36$  95% CI -0.67,-0.05) vs. medium ( $\beta = -0.20$  95% CI -0.45,0.04) and high ( $\beta = -0.18$  95% CI -0.42,0.07) social engagement ( $P_{\text{interaction}} = 0.015$ ).

Multimorbidity was associated with faster declines in global cognition, executive function, and verbal fluency. Social engagement modified the association between multimorbidity and global cognition suggesting that higher social engagement may mitigate multimorbidity-associated declines in global cognition.

**Prospective study of grandchild caregiving and late life cognitive functioning** Yu-Tien Hsu\*

Yu-Tien Hsu Ichiro Kawachi Jarvis Chen

Involvement in grandchild caregiving may contribute to maintenance of cognitive health for grandparents. However, evidence remains mixed, possibly due to selection into caregiving and uncontrolled confounding. We used data from two cohorts of the Taiwan Longitudinal Study in Aging, a nationally representative sample of adults aged  $\geq 50$  (1989:  $n=4404$  and 2003:  $n=1599$ ). We analyzed participants' caregiving status and cognition in 1996, 1999, 2003, 2007, and 2011, adjusting for baseline and time-varying covariates via marginal structural models with inverse probability of treatment weights. We used inverse probability of censoring weights to account for selection bias and multiple imputations to deal with missingness. We modeled the cumulative and short-term (over two successive waves) associations of caregiving with cognitive function scores measured by the Short Portable Mental Status Questionnaire. We also examined the heterogeneity of associations by educational attainment, urbanicity, gender, and marital status. We found no statistically significant association between cumulative grandchild caregiving on cognitive scores, ranging from 0.21 (95% CI=-0.01-0.52) in the older cohort to 1.54 (95% CI=-1.84-4.92) in the younger cohort. However, in subgroup analyses, grandchild caregiving was associated with higher cognitive scores among participants who were married ( $b=0.23$ , 95% CI=0.02-0.45), male ( $b=2.72$ , 95% CI=0.01-5.43), and middle or high school graduates ( $b=0.37$ , 95% CI=0.30-0.44). By contrast, the association was in the adverse direction for widowed or divorced participants ( $b=-2.87$ , 95% CI=-4.69-1.05), though not significantly so. All estimates of the short-term effects were null. In summary, we found no overall cumulative or short-term associations between grandchild caregiving and cognitive scores, although there was evidence for effect heterogeneity. Grandchild caregiving may benefit men, partnered grandparents, and middle or high school graduates.

**Lifecourse traumatic stress and cognitive decline in a diverse cohort of older adults** Eleanor Hayes-Larson\* Eleanor Hayes-Larson Elizabeth Rose Mayeda M Maria Glymour Rachel A Whitmer Paola Gilsanz Dan M Mungas

The impact of lifecourse traumatic stress on cognitive aging is unknown. We examined this using the Kaiser Healthy Aging and Diverse Life Experiences study and the Study of Healthy Aging in African Americans, harmonized cohorts designed to study cognitive aging in long-term members of Kaiser Permanente Northern California. Childhood measures assessed: parental separation/divorce, parental remarriage, witnessed domestic violence, substance abuse by a family member, parental job loss, parent in jail, serious illness of family member. Adulthood measures included: divorce, spousal death, taking  $\geq 6$  months off work to care for a sick family member, being near an explosion/blast, and being hospitalized for a fall/accident. Confirmatory factor analysis with a one-factor model was applied separately for childhood and adult items, using empirical Bayes modal method to estimate factor scores. We used separate linear mixed effects models to estimate effects of factor scores on domain-specific cognitive decline (Spanish and English Neuropsychological Assessment Scales standardized to baseline), adjusting for time on study, baseline age, sex, race/ethnicity, practice effect, and interactions between time on study and all other variables except the practice effect. Among 352 Asian, 981 Black, 285 Latino, and 409 non-Latino white adults, a 1-factor model for childhood household challenges had adequate fit (CFI=0.936, RMSEA=0.077, factor score range -0.45 to 1.94) and a 1-factor model for adult traumatic and stressful events fit well (CFI=0.906, RMSEA=0.024, factor score range -0.09 to 0.29). Factor scores for childhood household challenges ( $b=-0.026$ , 95% CI -0.053, 0.000) and adult traumatic and stressful experiences ( $b=-0.184$ , 95% CI -0.379, 0.012) were associated with faster annual declines in verbal memory. No associations were observed with executive function. Future work should examine mechanisms through which traumatic stress impacts late-life cognition.

**Retirement and cardiovascular disease: A longitudinal study in 35 countries** Koryu Sato\*

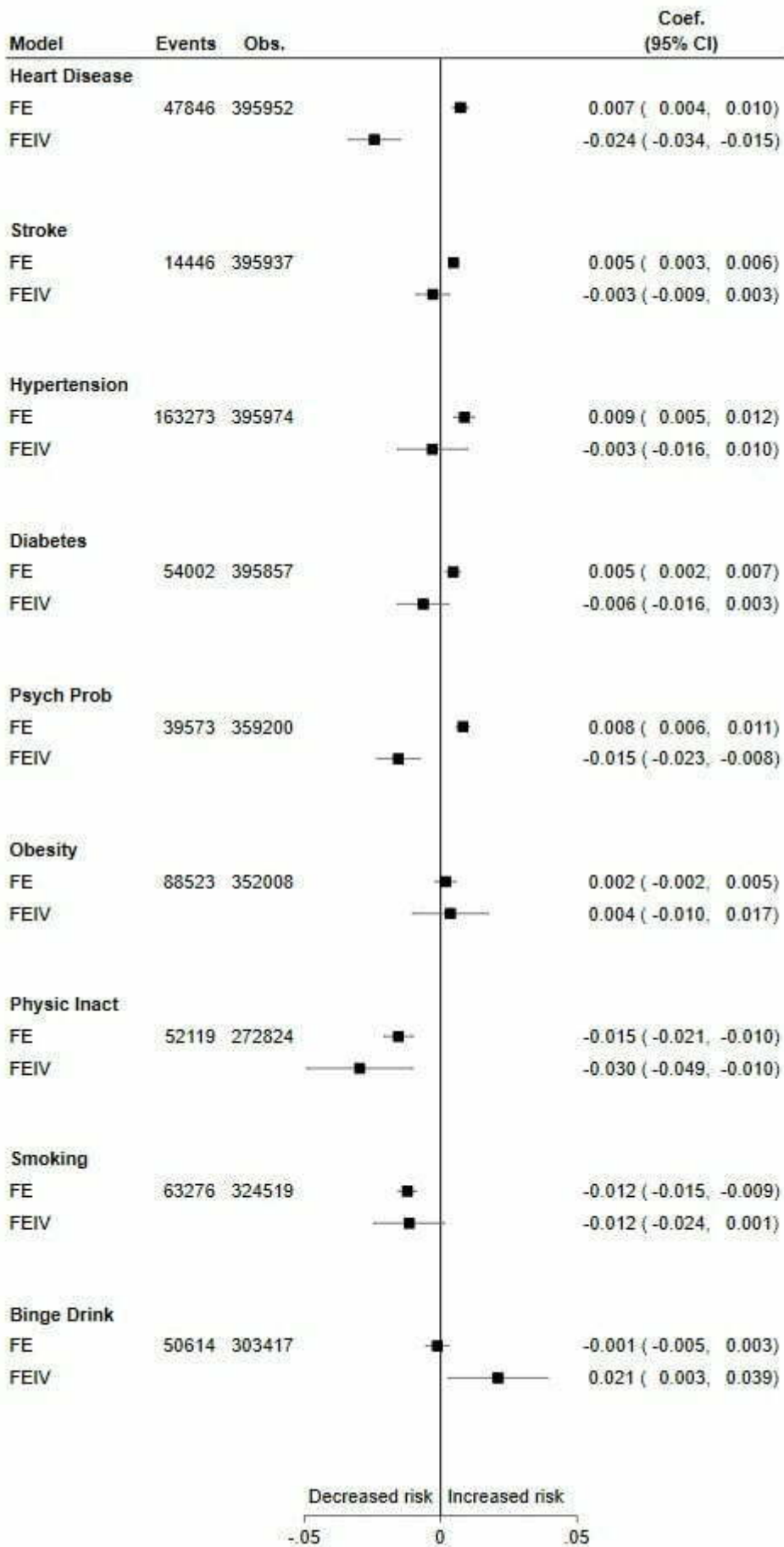
Koryu Sato Haruko Noguchi Kosuke Inoue Ichiro Kawachi Naoki Kondo

**Background:** Many countries have been increasing their state pension age (SPA); nonetheless, there is little consensus on whether retirement affects the risk of cardiovascular disease (CVD). This study examined the associations of retirement with CVD and risk factors.

**Methods:** We used harmonised longitudinal datasets from the Health and Retirement Study and its sister surveys in 35 countries. Data comprised 396 904 observations from 106 927 unique individuals aged 50–70 years, with a mean follow-up period of 6.7 years. Fixed-effects instrumental variable regressions were performed using the SPA as an instrument.

**Results:** We found a 2.4%-point decrease in the risk of heart disease (coefficient = -0.024 [95% confidence interval: -0.034 to -0.015]), a 1.5%-point decrease in psychiatric problems (-0.015 [-0.023 to -0.008]), a 3.0%-point decrease in physical inactivity (-0.030 [-0.049 to -0.010]), and a 2.1%-point increase in binge drinking (0.021 [0.003 to 0.039]) among retirees, compared with workers. In subgroup analyses, people with high educational levels showed associations between retirement and decreased risks of stroke and obesity. People who retired from non-physical labour exhibited reduced risks of heart disease, obesity, physical inactivity, and smoking, whereas those who retired from physical labour indicated an increased risk of obesity.

**Conclusions:** Retirement was associated with a reduced risk of heart disease on average. Some associations of retirement with CVD and risk factors appeared heterogeneous by individual characteristics.



**Money Makes The Survey Go 'Round: Impact of Incentives on Physician Survey**

**Participation** Julia Simard\* Saadiya Hawa Julia F Simard Amadeia Rector Titilola Falasinnu Shalmali Bane Yashaar Chaichian Kayla Kinsler

**Background:**

Online surveys can be effective data collection instruments; however, participation is notoriously low, particularly among professionals such as physicians. Few studies have explored the impact of varying amounts of monetary incentives on survey completion. We conducted a randomized study to assess how different incentive amounts influenced participation among neurologists in the United States.

**Methods:**

We distributed a web-based survey using standardized email text to 21,754 individuals identified by a medical marketing company. Individuals were randomly divided into five equal groups (~4350 per group) and for phase one, each group was assigned to receive either nothing or a gift card for \$10, \$20, \$50, or \$75, which was noted in the email subject and text. After four reminders, we offered each remaining individual a \$75 gift card for phase two to complete the survey. We calculated the proportion who completed the survey, before and after the change in incentives. We used chi-square tests to determine whether the proportion completing the survey varied by the incentive offer and, secondarily, after the amount was changed.

**Results:**

Overall, 2.4% of recipients completed the survey; the proportions increased as the incentive amount increased (1.1%, 2.4%, 2.6%, 2.9%, and 3.3%, for \$0, \$10, \$20, \$50, and \$75, respectively,  $p < 0.0001$ ). In phase two, the survey completion rate for the phase one \$0 arm increased to 3.2%. Those originally offered \$10, \$20, and \$50 who had not yet participated were less likely to participate compared with the former \$0 arm (1.9%, 1.8%, 2.3% respectively,  $p = 0.0003$ ).

**Conclusion:**

Our study suggests that providing monetary incentives can boost survey completion rates among physicians, with a positive correlation between amount and participation.



**Associations between Bike Score and frequency of bicycle ridership among women of reproductive age in the Puget Sound Region of Washington state** Anna L. Harrington\* Anna Harrington Stephen J. Mooney Daniel A. Enquobahrie Anne Lusk Anjum Hajat

## Background

Women and racial minority groups are at higher risk of physical inactivity, which is linked to numerous poor health outcomes. Bicycling is uniquely positioned to foster physical activity and can help mitigate climate change. While few Americans, particularly women, bicycle, prior research suggests that ridership may increase with development of bicycle infrastructure. No research has examined infrastructure-ridership associations among women in the Puget Sound Region of Washington state or how these associations may vary by race/ethnicity.

## Methods

We matched the center of the residential census tract of eligible women of reproductive age (18-54 years-old) who participated in the 2017 or 2019 Puget Sound Regional Council Household Travel Survey (N=3,204) with Redfin's Bike Score, a proxy for infrastructure that measures the "bikeability" of a specific location on a scale of 0-100. We fit a log-linear regression model to investigate the association between Bike Score and bicycle ridership for 15 minutes or more at least once in the past 30 days (versus less than that), adjusted for age and seasonality. We assessed effect modification of the association by race/ethnicity, a proxy for racism, by including interaction terms in models.

## Results

Among study participants, 1,582 (49.38%) lived in regions with Bike Scores less than 70 (the median Bike Score in this study population). The prevalence of having ridden a bicycle recently was 33% higher for each 20 points of Bike Score (aRR=1.33; 95% CI: 1.21, 1.45). None of the interaction terms were statistically significant at alpha-level=0.05. Prevalence was similar among participants of color (aRR=1.35; 95% CI: 1.11, 1.64).

## Conclusion

Bike Score was positively associated with bicycle ridership among women of reproductive age, including reproductive age women of color. Policies supporting the development of bicycle infrastructure may foster an increase in ridership among women of reproductive age.

**LATEBREAKER**

Behavior

**Sedentary behavior associated with dementia, functional disability, and mortality: A cohort study in 90471 older adults** Zhen Du\* Zhen Du Koryu Sato Naoki Kondo Taishi Tsuji Katsunori Kondo

Moderate-to-vigorous physical activity (MVPA) and sedentary behavior (SB) are widely acknowledged contributors to health. For older adults, reducing SB is easier to implement than increasing MVPA. However, evidence on the association between SB and dementia, functional disability, and mortality in older adults is limited.

To examine the associations between SB and dementia, functional disability, and mortality, we conducted this cohort study using data from 23 municipalities from Japan Gerontological Evaluation Study (JAGES) in 2016 and followed up until May 2021. Participants were older adults aged 65 or older who were physically and cognitively independent at baseline. SB (<3 hours per day (h/d), 3-<8 h/d,  $\geq 8$  h/d) was the main explanatory variable of interest. The stratified and joint association of SB and MVPA (0, 0-<1 h/d,  $\geq 1$  h/d) with outcomes were also examined. The incidence of dementia, functional disability, and mortality was ascertained by linking to the public long-term care insurance registry.

Of 90471 participants, 41643 (46.0%) were male, and the median age was 73 (IQR, 69-78). During the median follow-up of 3.4 years, 4135 (4.6%), 4201 (4.6%), and 4,599 (5.1%) participants developed dementia, functional disability, and mortality, respectively. Compared with the reference group (SB<3 h/d), the highest SB ( $\geq 8$  h/d) was associated with higher risks of dementia (hazard ratio [HR], 1.36; 95%CI, 1.22-1.52;  $P$  for trend <0.001), functional disability (HR, 1.32; 95%CI, 1.19-1.48;  $P$  for trend <0.001), and mortality (HR, 1.31; 95%CI, 1.18-1.45;  $P$  for trend <0.001). The joint association showed a trend ( $p$  for trend<0.001) of increasing risks of dementia, functional disability, and mortality with the increase of SB and the decrease of MVPA, where participants who spent the highest SB with no MVPA had the highest risks.

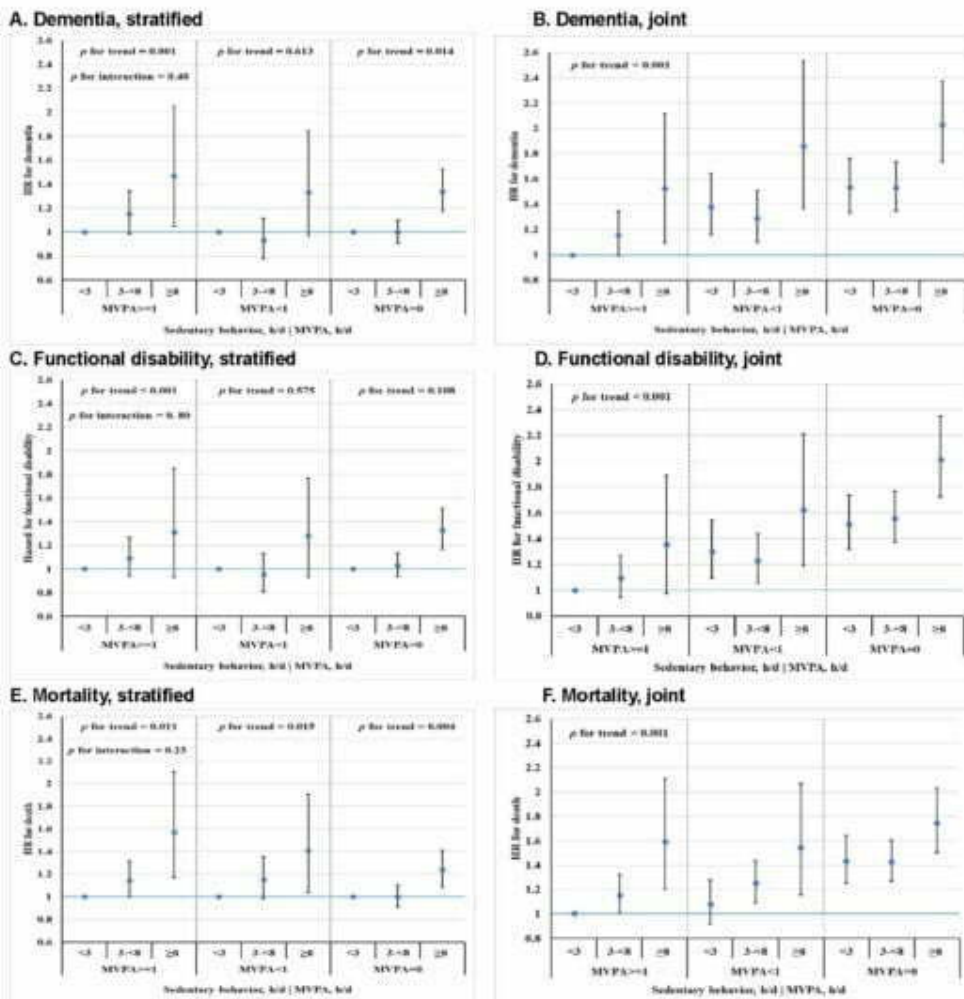
For older adults, reducing SB to less than 8 h/d and/or increasing MVPA may reduce the risks of dementia, functional disability, and mortality.

**Table. Associations between sedentary behavior and dementia, functional disability, and mortality.**

	Dementia		Functional disability		Mortality	
	Model 1	Model 2	Model 1	Model 2	Model 1	Model 2
<3 h/d	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)	1 (Ref)
3-8 h/d	1.07 (1.00-1.15)	1.02 (0.95-1.10)	1.12 (1.04-1.20)	1.03 (0.96-1.11)	1.13 (1.06-1.21)	1.06 (1.00-1.14)
≥8 h/d	1.71 (1.54-1.91)	1.36 (1.22-1.52)	1.83 (1.65-2.03)	1.33 (1.19-1.48)	1.78 (1.61-1.97)	1.31 (1.18-1.45)

Model 1 adjusted for sex and age. Model 2 adjusted for sex, age, marital status, educational attainment, family equivalent income, employment, BMI, comorbidity, self-rated health, alcohol, smoking, frequency of eating meat or fish, frequency of eating fruits and vegetables, and social isolation.

**Figure. Stratified and joint associations of sedentary behavior and moderate-to-vigorous physical activity with dementia, functional disability, and mortality**



MVPA, moderate-to-vigorous intensity of physical activity. A and B, Stratified and joint association for dementia, respectively; C and D, stratified and joint association for functional disability, respectively; and E and F, stratified and joint association for mortality, respectively. Adjusted for sex, age, marital status, educational attainment, family equivalent income, employment, BMI, comorbidity, self-rated health, alcohol, smoking, frequency of eating meat or fish, frequency of eating fruits and vegetables, and social isolation.

**Significant reductions in physical activity among Canadian adults more than 6 months into the COVID-19 pandemic: Results from the INTERACT study** Shelby L. Sturrock\* Shelby L.

Sturrock Dionne Gesink Meghan Winters Yan Kestens Kevin Stanley Rahim Moineddin Sarah Woodruff Daniel Fuller

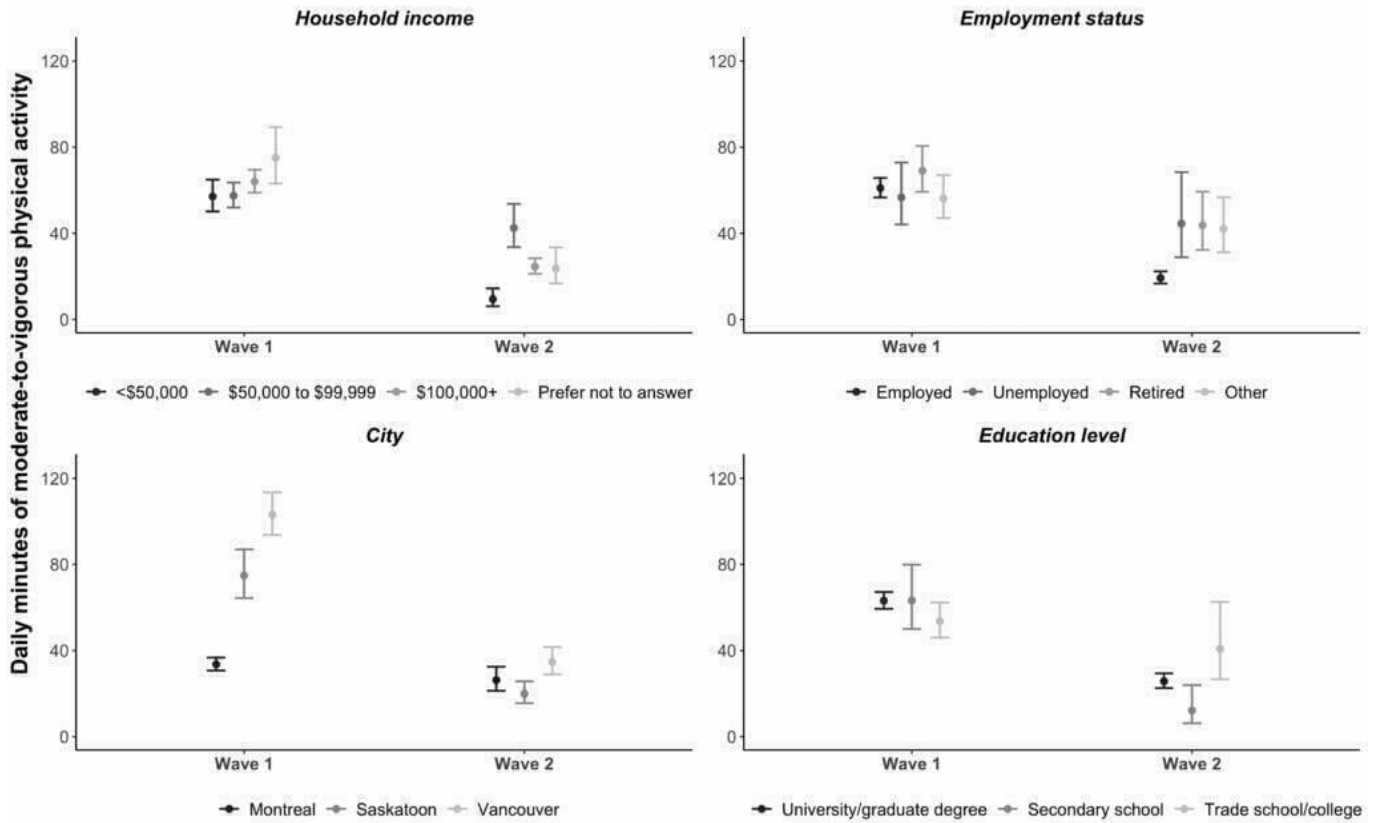
**Background:** Few studies have described physical activity levels more than 6 months into the COVID-19 pandemic. We used data from wave 1 (July 2018-February 2019) and wave 2 (September 2020-February 2021) of the INTERACT cohorts in Montreal, Saskatoon and Vancouver to estimate the effect of (a) the COVID-19 pandemic, and (b) the stringency of COVID-19 restrictions on daily minutes of device-measured moderate-to-vigorous physical activity (MVPA) from September 2020 to February 2021.

**Methods:** The COVID-19 pandemic was operationalized using a binary indicator distinguishing data collected in wave 1 (July 2018-February 2019; before COVID-19) and wave 2 (September 2020-February 2021; during COVID-19) of the INTERACT study. The severity of COVID-19 restrictions was measured using a provincial stringency index calculated by The Institute for Research on Public Policy. Separate mixed effects negative binomial regression models were used to estimate the association between each exposure and daily device-measured minutes of MVPA with a random intercept per participant. Models were run with and without controlling for factors associated with MVPA that were unbalanced across levels of each exposure. Effect modification was assessed via stratification.

**Results:** The pandemic was associated with a 58% reduction in daily MVPA after controlling for city, temperature, precipitation, education, employment status, household income and wear time (adjusted rate ratio = 0.42, 95% CI: 0.37, 0.47). The results were suggestive of effect modification by employment status, household income, education and city. Restriction stringency was not associated with daily MVPA from September 2020 to February 2021 (adjusted rate ratio = 1.01, 95% CI: 0.83, 1.23).

**Conclusion:** This study showed large and statistically significant reductions in MVPA more than 6 months into the pandemic compared to two years prior that remained stable despite increases in COVID-19 restriction stringency during the study period.

**Daily minutes of moderate-to-vigorous physical activity in wave 1 and wave 2 across levels of household income, employment status, level of education and city**



**A quantile regression analysis of physical activity and cognition in a racially/ethnically diverse sample of older adults: Results from the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study**

Annie Pederson\* Annie Pederson Mariana L. Almeida Scott C. Zimmerman Ruijia Chen Sarah F. Ackley Alicia Riley Chloe W. Eng Rachel Whitmer Kristen M. George Rachel L. Peterson Elizabeth Rose Mayeda Paola Gilsanz Dan Mungas M. Maria Glymour

### Introduction

Research on physical activity (PA) and cognitive aging has been in predominantly White samples and focused on mean cognitive outcomes, rather than the distribution of cognition. We used quantile regression to investigate the association of light and heavy PA with level of cognition in a racially/ethnically diverse sample of older adults, considering associations in lower quantiles of cognition where dementia risk is highest.

### Methods

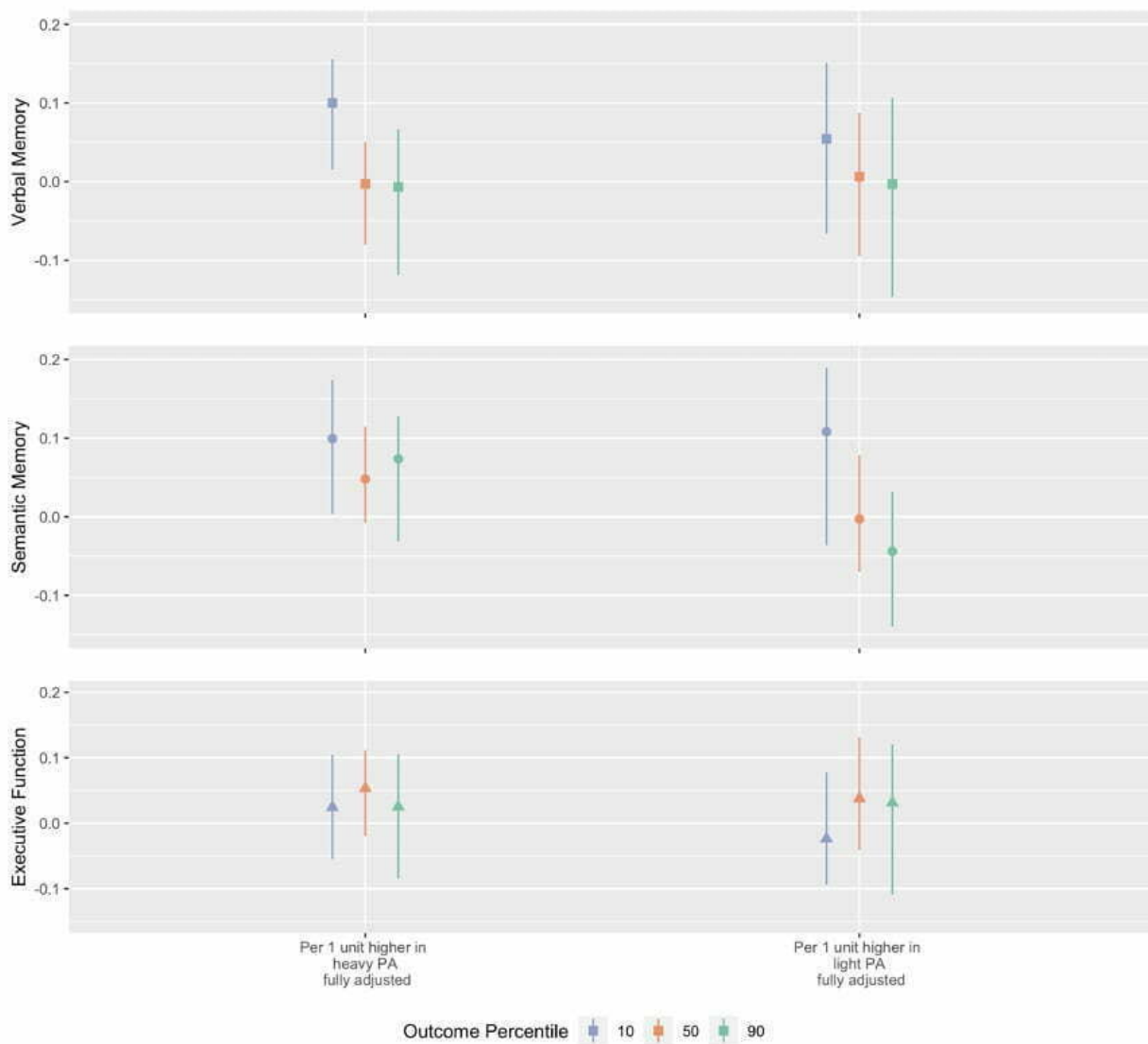
Data from the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study included community-dwelling older adults age 65+ living in Northern California (n=1,441), with approximately equal proportions of Asian, Black, LatinX, and White participants. Frequency of light or heavy PA were each self-reported through three Likert-scale questions, summarized as two continuous variables (heavy PA range 1-5, SD = 0.93; light PA range 1-5, SD = 0.72). Outcomes were z-scored executive function, semantic memory, and verbal episodic memory. We estimated the conditional association of PA (per SD) with the 10<sup>th</sup>-90<sup>th</sup> percentiles of cognitive outcomes.

### Results

Associations of PA with semantic and verbal episodic memory were stronger at low quantiles of cognition than at the median or high quantiles. For example, the 10<sup>th</sup> percentile of verbal episodic memory score was 0.10 SD higher ( $b_{10}=0.10$ ; 95% CI: 0.02, 0.16) for one unit higher in heavy PA, while the median did not vary by frequency of heavy PA ( $b_{50}= -0.00$ ; 95% CI: -0.08, 0.05). Estimates for associations of heavy PA with semantic memory were also larger at low quantiles ( $b_{10}=0.10$ ; 95% CI: 0.00, 0.17) than the median ( $b_{50}=0.05$ ; 95% CI: -0.01, 0.11) or high quantiles. The results were less clear for the outcome domain executive function.

### Discussion

Physical activity is robustly associated with cognitive outcomes in this racially/ethnically diverse sample and may have larger benefits for individuals with low cognitive scores, who are most vulnerable to dementia.



**Figure.** Quantile Regression Model Results for Three Cognitive Domains. Points indicate the effect of the exposure on the outcome for the 10<sup>th</sup>, 50<sup>th</sup>, and 90<sup>th</sup> percentiles for each level of physical activity with fully adjusted covariates. Fully adjusted models include age, gender, education, activities of daily living, self-reported sleep, alcohol use, employment status, and income.

**A novel ML method for temporal evolution of geographic clusters of disease spread**

**patterns** Leigh Metcalf\* Leigh Metcalf Heeralal Janwa Will Casey Shirshendu Chatterjee April Edwards

Longitudinal studies of spread have already shown a geographical correlation along a variety of factors, such as rural and urban. Here, we extend geographical correlation studies by analyzing the modalities COVID-19 outbreak dynamics between the various population levels of counties in the United States. From the cumulative percentage of each population infected up to each time point, our method considers the temporal evolution of clustering results for 3,133 US counties for 800 time steps over the last 2.125 years. We employ machine learning and optimization methods to complete the analysis, the singular value decomposition K-means, and spectral clustering methods. We introduce a novel approach using a shifting window dynamic clustering method and show its result to indicate stable and persistent SARS-CoV-2 outbreak/growth modes. The results of our method reinforce the prior longitudinal studies and imply persistent COVID-19 outbreak/growth modalities (patterns). The most exciting finding is a dynamic feature we term mode reselection events, where counties realign their cluster identity or switch from one rate of SARS-CoV-2 spread to another. The distribution of this dynamic indicates a deeper mathematical growth pattern. To highlight this, we discuss a few case studies and implications. Our findings of a persistent set of three distinct spread patterns are important from a theoretical and practical point of view. Natural descriptive factors the spread of pathogen include transmissibility, population density, and social interactions. The last factor is partially modulated by social behavior and policy that shifted at differing times in different counties, thereby offering causal insights into the trade-offs in these factors that county populations take, a finding that could be useful for policy formation. We further hypothesize that the critical events to mode re-selection are described by and could be predicted by social events such as policy shifts or changing social narratives and behaviors within a population



**Use of Machine Learning for Classification of Death Risk by Covid-19 in the State of Mato Grosso - Brazil** Tiago Almeida de Oliveira\* Tiago Oliveira Maria Fagna Felix de Souza

Several scientific studies consider that individuals with certain comorbidities, as well as biological factors such as age and gender, are at greater risk of death from Covid-19. The use of data from patients' medical records becomes an important tool for obtaining information and applying predictive models capable of contributing to clinical decision-making. In this context, data on biological characteristics and morbidities were collected for this study. To apply the predictive models, a database of 440,153 patients who contracted Covid-19 from March to December 2020 was used. The database was obtained from the website of the state health department of Mato Grosso, in the Midwest region of Brazil. This study aims to predict the risk of death from the Covid-19 disease using machine learning models, considering the distinction between two possible outcomes: discharged patient or death. Five Machine Learning algorithms were used, such as Logistic Regression, Random Forest, XGBoost, LightGBM, and CatBoost. The data was divided into 80% for training and 20% for testing. Cross-validation was performed with 5 folders using the Grid Search method. Additionally, the majority class subsampling technique was used to balance the classes of the outcome variable during model training. The metrics used to evaluate the performance of models were accuracy, precision, sensitivity, specificity, F-score, and ROC curve. The predictors that most influenced the models were age, comorbidity, obesity, sex, and diabetes. The results of the descriptive analysis showed that about 16% of the patients had some type of comorbidity. Less than 2% of the total resulted in deaths, indicating an imbalance in the sample regarding the death outcome. The class imbalance was treated through resampling techniques and returned interesting results. Predictive models showed that all algorithms obtained an area under the ROC curve greater than 0.80. The predictions showed a high rate of true positives and a low rate of false negatives. Thus, this study identifies factors that are good risk predictors of death from Covid-19.

**Assessing and adjusting for potential measurement error inequities in US surveys of health outcomes using machine learning models** Lauren Rossen\* Lauren Rossen Morgan Earp

Measurement equity is critical for the accurate assessment of racial/ethnic disparities in health outcomes. Estimated inequities in the prevalence of a given health outcome can be affected by whether the outcomes are measured or self-reported based on a diagnosis from a health professional. Harmonizing data from several national health surveys, including the National Health and Nutrition Examination Survey (NHANES) which contains both measured and self-reported health information, we explored several machine learning models to assess and adjust for measurement error inequities.

Using data on four health outcomes (e.g., diabetes, hypertension, high cholesterol, and current smoking) from NHANES (2015 through March, 2020), we assessed differences between self-reported and measured outcomes by various sociodemographic characteristics (e.g., age, sex, race/ethnicity, income, health insurance status). We used linear regression trees via the 'rpms' package in R to identify demographic subgroups with larger differences between self-reported and measured health outcomes. We then explored several machine learning models (conditional random forests and Support Vector Machines) to predict measured health outcomes as a function of sociodemographic variables and self-reported health outcomes using NHANES data. We evaluated model accuracy metrics, and the best performing model for each outcome was used to score data from the 2019-2021 National Health Interview Survey (NHIS; a large national household-based survey) and the 2016 and 2019 Research and Development Survey (RANDS; a web-panel survey), which do not include any measured health outcomes. Using this approach, we generated predicted measured health outcomes for the NHIS and RANDS, adjusted for potential measurement error inequities.

Integrating data from several population-based health surveys can leverage the strengths of each data source to facilitate more accurate, timely, and precise estimates of health inequities.

**Provider-level preprocessing and quality assurance can limit the use of cell phone-based mobility data for digital epidemiology: a case study exploring urban greenspace use in Toronto, Canada during the COVID-19 pandemic** Vinyas Harish\* Vinyas Harish Lief Pagalan

Sarah M Mah Muhammad Mamdani Ashleigh Tuite Kamran Khan Laura C. Rosella

**Introduction:**

Urban greenspace (UG) is an indicator of healthy cities. However, our understanding of UG use has relied on resource-intensive surveys and direct observation. Digital datastreams may be an efficient means to study UG at previously unfeasible scales. Here, we describe key considerations for researchers interested in leveraging cell-phone based mobility (CBM) data with the illustrative example of studying UG use during the COVID-19 pandemic.

**Methods:**

We obtained publicly available, weekly, aggregate data on visits to locations corresponding to UG in Toronto, Canada between 01-01-2019 and 12-31-2021 from a CBM data provider. We obtained ground truth UG polygons from the City of Toronto Open Data Portal and area-level demographics from the 2016 Census. We assessed sampling bias, spatial consistency with ground truth data, and temporal stability.

**Findings:**

The CBM data provider only captured 163 of the 1000+ locations reported in the ground truth. Sampling bias decreased with larger geographic units and changed over the study period. Polygons defined by the CBM data provider were often misaligned with those of the City and did not capture full UG areas (0.29% capture rate by area). Capture rates were weakly spatially clustered (Moran's I) but there were no significant associations between capture rate and area-level Census characteristics (Lee test). Temporally, the presence of UG locations in the CBM data varied substantially by week. Provider-level data aggregation prohibited filtering out visitors based on important factors, such as time spent at the location.

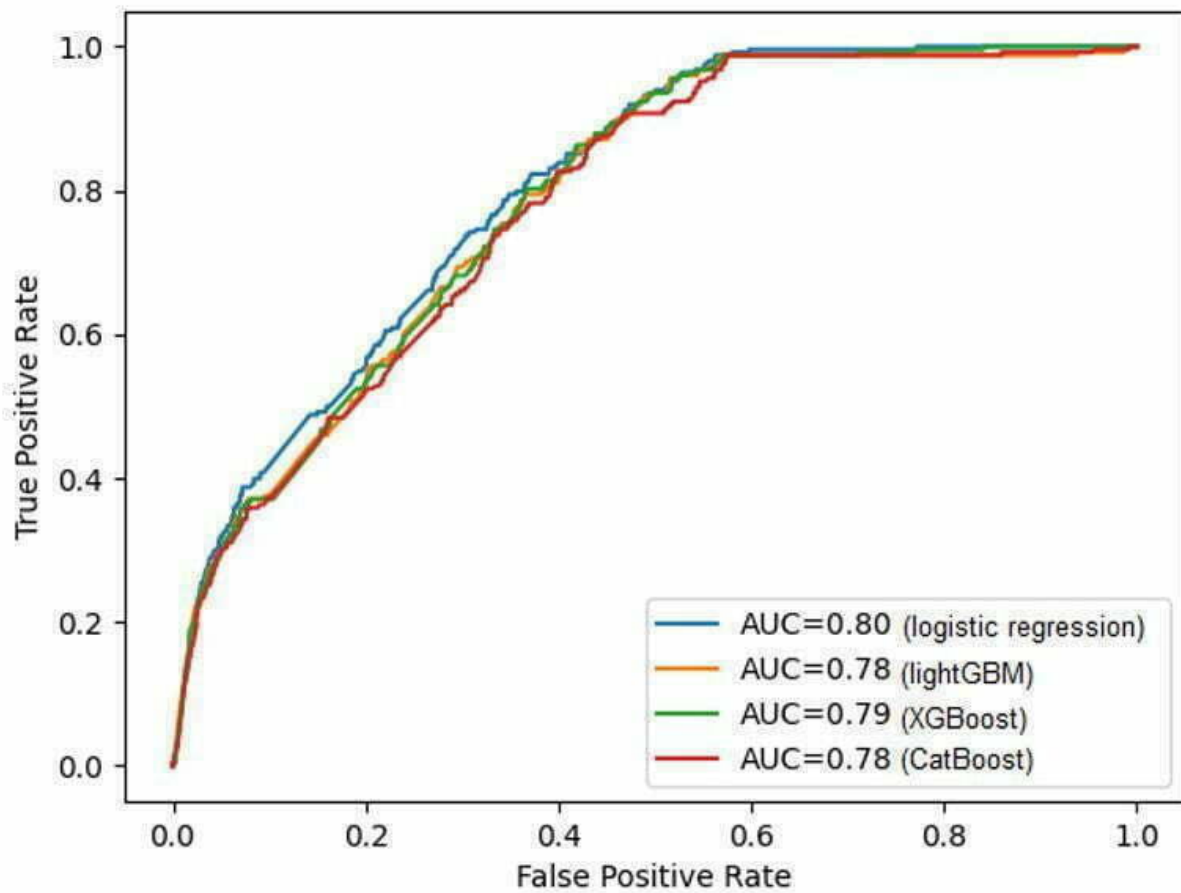
**Conclusions:**

Sampling bias, spatial inconsistencies, temporal variation, and the unavailability of disaggregated measures are likely to confound and limit epidemiological analyses with aggregated CBM data. We encourage researchers to pursue access to more complete and granular data while protecting privacy (e.g., in secure computing environments) for epidemiological research.

**Predicting Alcohol Consumption During Pregnancy Using Machine Learning Techniques: Algorithm Development** Sarah (Soyeon) Oh\* Sarah (Soyeon) Oh Hyewon Jeong Bada Kang Ichiro Kawachi

**Background:** One in 10 women are estimated to consume alcohol during pregnancy, increasing the risk for teratogenic effects on the developing fetus. With improved prediction models, machine learning techniques can be used to identify women who are at high-risk of consuming alcohol during pregnancy. **Objective:** We sought to compare different machine learning algorithms and their predictive performance in identifying women who consume alcohol during their pregnancy. We also aimed to identify which predictors (e.g., pre-pregnancy drinking behavior, exposure to abuse/violence during pregnancy, socioeconomic status etc.) were most influential in generating an accurate model. **Methods:** Data from the Pregnancy Risk Assessment Monitoring System (PRAMS) from 2012-2015 were used to gather information about 17,465 women who had given birth in the last 2-6 months in the United States. 7.82% (n=1,366) reported drinking during pregnancy. Four different machine learning algorithms were trained to predict the risk of alcohol consumption during pregnancy. Model performance was measured by analyzing the area under the receiver operating characteristics curve (AUROC). Feature importance was also analyzed using Shapley Values for the best-performing algorithm. **Results:** Best performance was detected in the logistic regression algorithm which had an AUROC of 0.80, followed by XGBoost which had an AUROC of 0.79. In this model, 12 variables were considered important in pregnancy drinking prediction, with pre-pregnancy drinking behavior, education level, and maternal age scoring highly in overall feature importance. **Conclusions:** Machine learning algorithms were able to predict alcohol consumption risk among pregnant women with a prediction performance similar to that of previous models. Using models like XGBoost in combination with logistic regression may help physicians identify high-risk populations and prevent alcohol-exposure during pregnancies.

**Figure 1. Performance evaluation of ML algorithms for Prediction of Pregnancy Drinking**



**Identifying Predictive Risk Factors for Skin Cancer Development in Solid Organ Transplant Recipients** Cruz Riley\* Cruz Riley Linda D. Tolbert Amandeep K. Sahota Joanie Chung Rebecca Gambatese Annette L. Adams

Recognizing the need for risk-stratification in post-solid organ transplant recipient (SOTR) skin cancer screening, we conducted a retrospective cohort study of all Kaiser Permanente Southern California (KPSC) SOTR's from 2008-2017 who had no known active skin cancer at the transplant date. Incident skin cancers (melanoma and non-melanoma) were identified from the electronic health record (EHR) and KPSC Cancer Registry. Potential predictors of incident skin cancers were identified from the existing literature, which included demographics (age, sex, race/ethnicity) and clinical characteristics (transplant type, evidence of sun damage, human papilloma virus history or clinically evident infection) were also identified from the EHR. Associations between predictors and incident skin cancer (overall and by transplant type) were estimated using logistic regression models. Among the 3168 subjects identified, median age was 56.0 years (IQR 46.0, 63.0), 1907 (60.2%) were male, 952 (30.1%) were White race, and 355 (11.2%) had incident skin cancer. Characteristics most strongly associated with cancer were age 63-80 (OR 3.4, CI 2.4-5.0, compared to ages 18-45 years), male sex (OR 1.7, CI 1.3-2.1), lung transplantation (OR 2.9, CI 1.9-4.4), and sun exposure (OR 2.5, CI 1.9-3.4). All race/ethnicity groups were at a reduced risk compared to White patients. In the multivariable logistic model, the estimates for age, male sex, and race/ethnicity remained unchanged; lung transplantation (aOR 1.8, CI 1.1-2.8) was attenuated but still significant; and sun exposure was no longer a significant predictor of skin cancer development. In Black patients a relatively higher proportion of skin cancers develop in sun protected areas (genital region) compared to all other race ethnicity groups. The identification of these high-risk subgroups of transplant recipients highlights the need for enhanced cancer screening and monitoring protocols to minimize post-transplant cancer morbidity.

## **The Prognostic Role of Cigarette Smoking in Kidney Cancer Survival** Amrit Baral\* Amrit Baral Paulo S. Pinheiro Hannah M Cranford

### **Background**

Cigarette smoking is one of the well-known risk factors for kidney cancer. However, its role as a prognostic factor is unclear. In this population-based study, we analyzed cancer-specific survival outcomes among kidney cancer patients by smoking status at diagnosis in the diverse state of Florida.

### **Methods**

Data on a total of 36,150 primary kidney cancer cases diagnosed during 2005-2018 were obtained from the Florida Cancer Registry for analysis. Five-year cancer-specific survival for current, former, and never smokers was computed. Cox proportional hazard regression was conducted to study the associations between the risk of death due to kidney cancer and potential prognostic factors including smoking status, age, sex, race/ethnicity, socioeconomic status, histology type, stages of cancer, and treatment received.

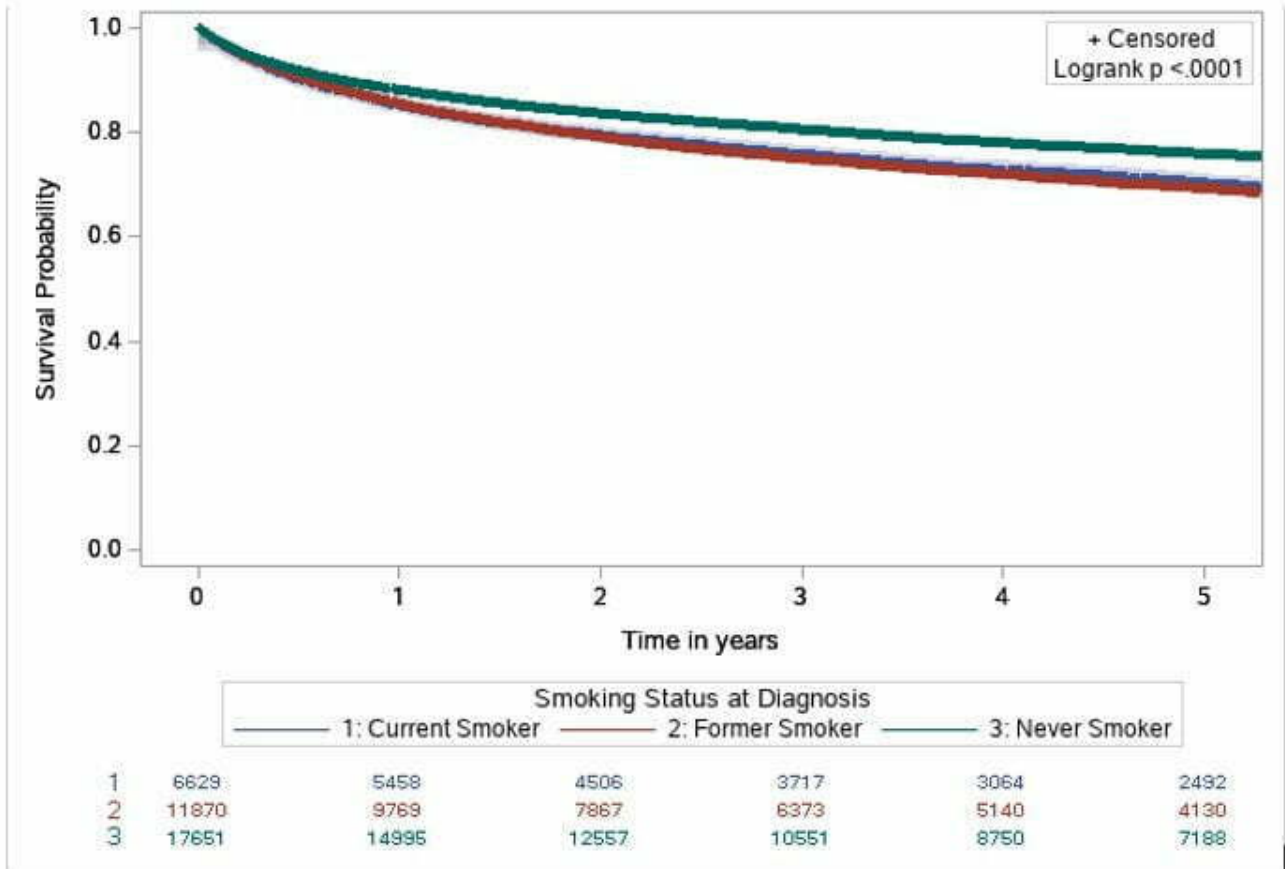
### **Results**

A majority of patients with kidney cancer were either current smokers 6,629 (18.3%) or former smokers 11,870 (32.9%) while 17,651 (48.8%) were never smokers. Ever smokers accounted for 5,659 (56.6 %) of all kidney cancer deaths. Age-standardized five-year survival for current, former, and never smokers was 65.3 (95% CI: 64.1-66.5), 70.6 (95% CI: 69.7-71.5), and 75.3 (95% CI: 74.6-76.0) respectively. In multivariable Cox proportional hazard regression model, current smokers were 30% (HR: 1.30, 95% CI: 1.23-1.40) and former smokers were 14% (HR: 1.14, 95% CI: 1.10-1.20) more likely to die of kidney cancer as compared to never smokers.

### **Discussion**

Our results suggest that smoking at diagnosis was an independent predictor of cancer-specific survival. The risk of kidney cancer death was increased for current and former smokers as compared to never smokers. Clinicians should encourage and implement cigarette smoking cessation interventions targeted at current smokers. Prospective studies are warranted to assess the role of different types of tobacco and smoking cessation on the survival outcomes of kidney cancer patients.

**Figure 1.** Kaplan- Meier estimates of Kidney Cancer Survival by Smoking Status at Diagnosis





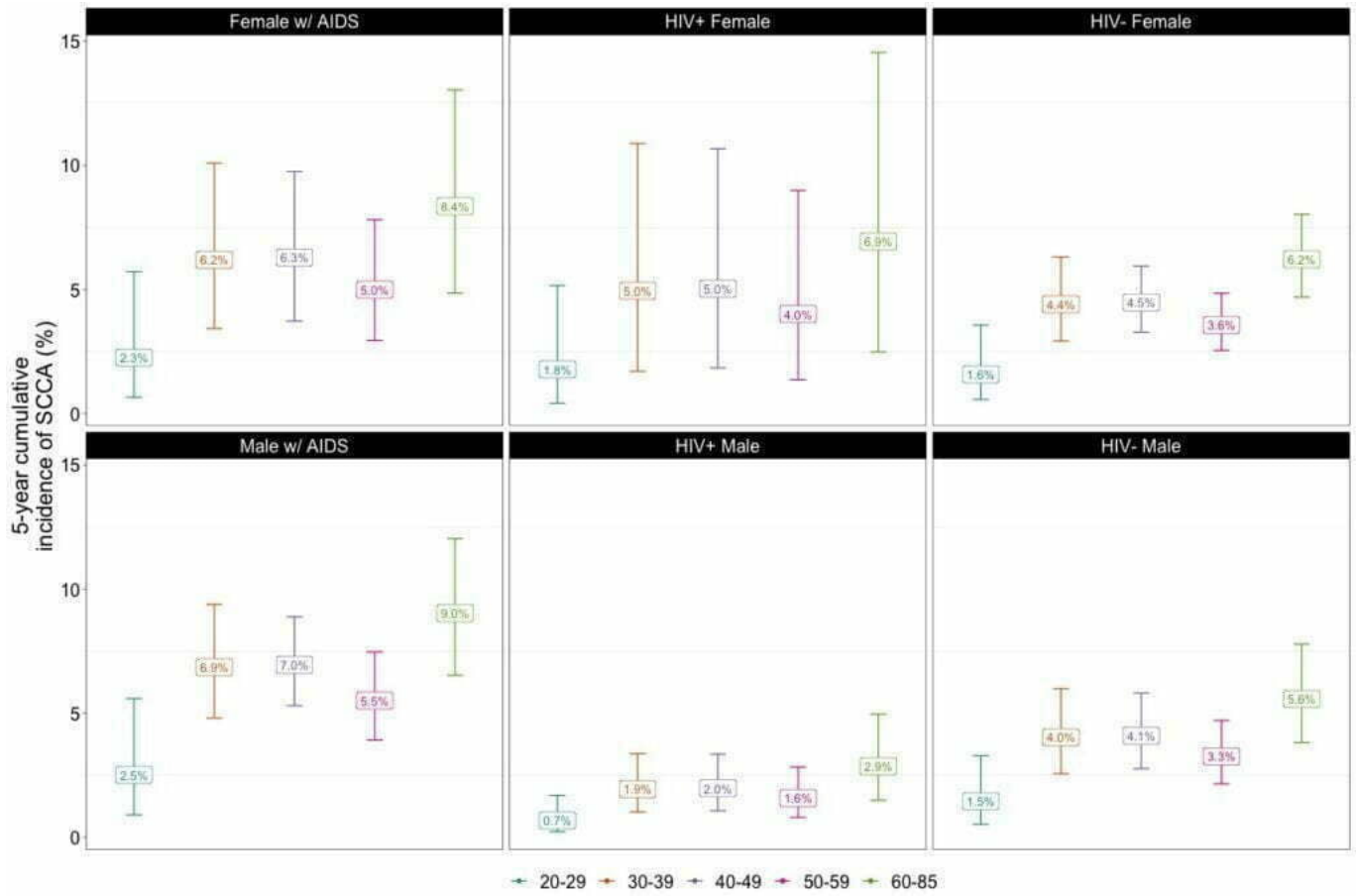
**Incidence of Anal Intraepithelial Neoplasia and Risk of Squamous Cell Carcinoma of the Anus in People with HIV Compared to HIV Uninfected People** Cameron B Haas\* Cameron Haas Eric Engels Megan Clarke Aimée Kreimer Qianlai Luo Ruth Pfeiffer Joel Palefsky Baozhen Qiao Karen S. Pawlish Analise Monterosso Meredith S. Shiels

**Background:** Rates of anal cancer are elevated in people with HIV (PWH), where rates are nearly 20-fold higher compared to the general population. Anal intraepithelial neoplasia grade III (AIN3) is a precursor to squamous cell carcinoma of the anus (SCCA). We aimed to describe trends in AIN3 diagnosis and risk of SCCA following AIN3 by HIV status and sex.

**Methods:** We utilized data from 13 participating regions in the HIV/AIDS Cancer Match (HACM) Study, a population-based linkage between cancer and HIV registries in the United States. We identified individuals with a cancer registry diagnosis of AIN3 and/or SCCA and determined their HIV status. We estimated average annual percentage change (AAPC) of AIN3 over time using Poisson regression within HIV status and sex. We used Fine and Gray method for competing risk of death to estimate the 5-year cumulative incidence of SCCA following AIN3 diagnosis stratified by sex, HIV status and AIDS diagnosis prior to AIN3, and age at AIN3 diagnosis.

**Results:** We observed 4,774 and 4,529 cases of AIN3 during 2000-2019 in people with and without HIV, respectively. Men with HIV had the highest rate of AIN3, among whom men who have sex with men (MSM) accounted for approximately 80% of diagnoses. The AAPC of AIN3 was 15% per year among women with HIV and 13% among men with HIV over the observation period, and 7% for both men and women without HIV. Those with a diagnosis of AIDS prior to AIN3 had a 3-fold increased risk of SCCA following AIN3 compared to those with HIV alone. For females and males with a prior AIDS diagnosis who were 60-years and older at AIN3 diagnosis, the 5-year cumulative incidence of SCCA was a 5.4% and 5.9%, respectively (**Figure**).

**Conclusions:** Rates of AIN3 diagnoses have increased over the last two decades, particularly among MSM with HIV who are at the greatest risk of SCCA. A diagnosis of AIDS was strongly associated with risk of AIN3 diagnosis and shows evidence for greater risk of subsequent SCCA following AIN3 than compared to individuals with HIV only.



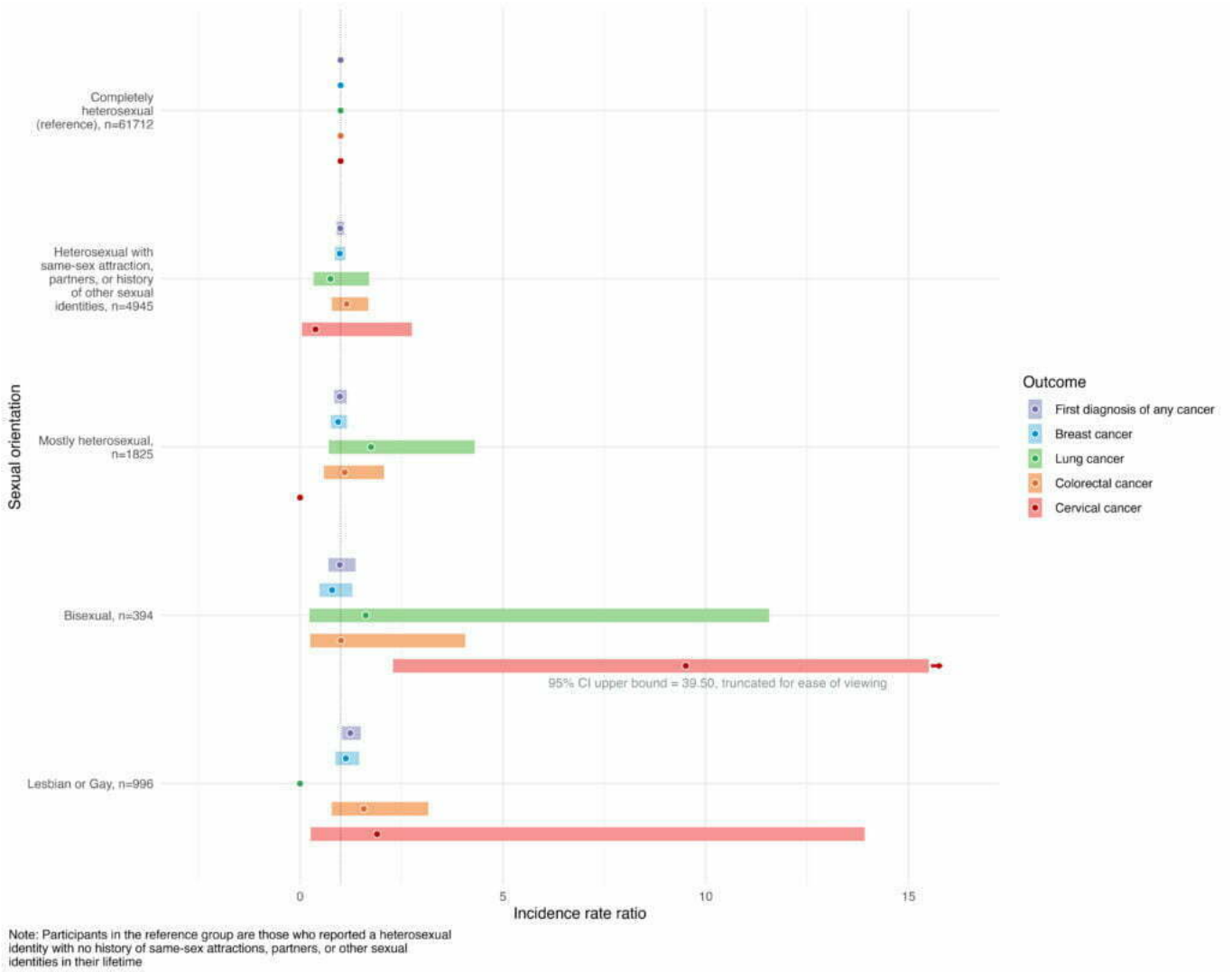
**Disparities in cancer incidence by sexual orientation** Aimee K. Huang\* Aimee Huang Tabot Hoatson Payal Chakraborty Sarah McKetta Kodiak R. S. Soled Ulrike Boehmer Colleen A. Reynolds Alexis Miranda Carl G. Streed Shail Maingi Sebastien Haneuse Jae Hee Kang S. Bryn Austin A. Heather Eliassen Brittany M. Charlton

**Background:** Despite the documented higher prevalence of cancer risk factors among sexual minority populations (e.g., gay, bisexual), little is known about cancer incidence among different sexual orientation (SO) groups. National cancer registries do not include SO data, and existing studies are limited to small samples and methodological challenges (e.g., cross-sectional study designs).

**Methods:** We analyzed data from the Nurses' Health Study II, a longitudinal cohort with 116,429 women across the U.S. We assessed the incidence of any cancer as our primary outcome and conducted sub-analyses at four specific cancer sites with recommended screening tests (breast, lung, colon/rectum, and cervix). We then compared cancer incidence among each of our SO groups to the heterosexual reference group using age-adjusted incidence rate ratios. Participants were excluded from the analyses if no SO data were available.

**Results:** Compared to heterosexual women, lesbian women had elevated cancer rates (aIRR 1.24; CI 1.03-1.50). In the site-specific analyses, bisexual women had elevated cervical cancer rates (aIRR 9.51; CI 2.29-39.47) relative to their heterosexual peers. Additionally, incidence rates at multiple cancer sites were observed to trend higher for all sexual minority subgroups, but those additional findings did not reach statistical significance.

**Conclusions:** Sexual minority women were adversely burdened by cancer relative to their heterosexual peers. National cancer registries should include SO data collection, and sexual minority populations must be included and prioritized in cancer prevention practices to monitor and reduce SO-related cancer disparities.



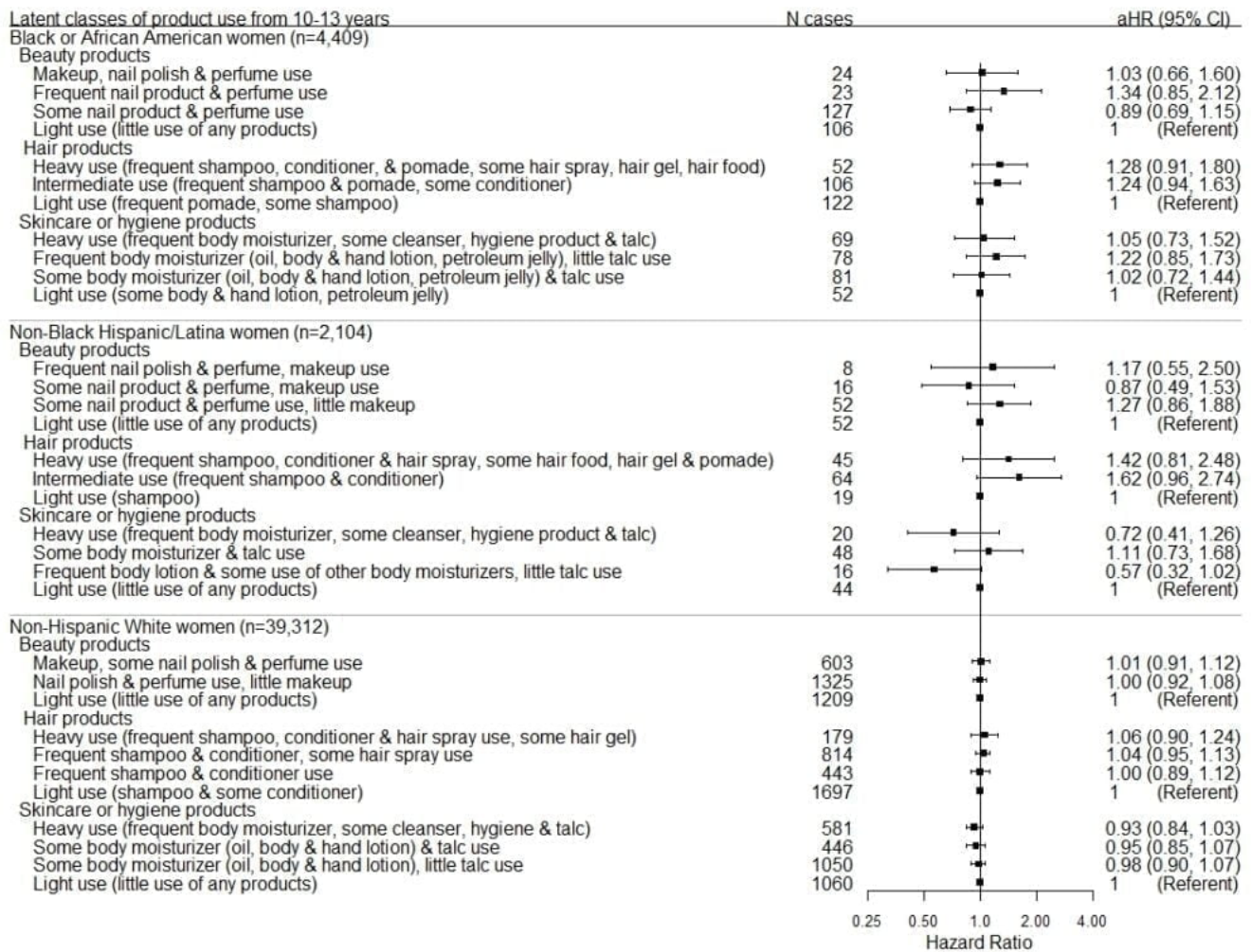
**Personal care product use during puberty and incident breast cancer in U.S. women** Mandy Goldberg\* Mandy Goldberg Che-Jung Chang Kemi Ogunsina Katie M. O'Brien Kyla W. Taylor Alexandra J. White Dale P. Sandler

**Background:** Personal care products (PCPs) are often used daily and contain endocrine-disrupting chemicals that may affect breast cancer (BC) risk. Use frequently starts in adolescence, coinciding with puberty, when the rapidly developing breast may be more susceptible to environmental carcinogens. Because PCP use varies by race/ethnicity, we examined associations of PCP use patterns at ages 10-13 years, when most girls experience pubertal breast development, with incident BC separately in Black, Hispanic/Latina, and non-Hispanic White (NHW) women.

**Methods:** The analytic sample included 4,409 Black women, 2,104 Hispanic women, and 39,312 NHW women ages 35-74 years in the prospective Sister Study (enrolled 2003-2009). At enrollment, participants reported their use of 37 "everyday" PCPs at ages 10-13 (did not use, sometimes used, or frequently used). We used race/ethnicity-specific latent class analysis to identify groups of women with similar patterns of beauty, hair, and skincare or hygiene products use, respectively. We used Cox proportional hazards models with age as the time scale to estimate HRs and 95% CIs for PCP use patterns during puberty and incident BC, adjusting for birth cohort and childhood socioeconomic indicators.

**Results:** During a mean of 10.8 years of follow-up, 280 Black, 128 Hispanic, and 3,137 NHW women were diagnosed with BC. Patterns of adolescent use were not clearly associated with BC risk, though HRs were elevated for heavy hair product use and frequent nail polish and perfume use in Black and Hispanic women compared with light use (Figure). Frequent moisturizer use was positively associated with BC in Black women, while associations were inverse for Hispanic and NHW women.

**Conclusions:** Frequent use of some PCPs (e.g., hair and nail products) during puberty may be associated with incident BC in Hispanic and Black women, who may use products with different chemical properties and are at increased risk of early onset and aggressive BC subtypes.



**Guideline-Concordant Breast Cancer Care by Patient Race-Ethnicity and Facility- and Area-Level Characteristics** Emma Herbach\* Emma Herbach Michaela Curran Ryan M. Carnahan Kai Wang Sarah Nash Ingrid Lizarraga Mary Charlton Brad McDowell

**Purpose.** We examined how adherence to clinical practice guidelines for breast cancer varies across racial-ethnic groups, accounting for individual-, facility-, and area-level factors.

**Methods.** Women diagnosed with invasive breast cancer at 66+ years of age from 2000-2017 were studied using the SEER-Medicare database. Guideline-recommended diagnostic workup, locoregional treatment, systemic therapy, known stage at diagnosis, and oncologist encounters were characterized using SEER and Medicare linked claims data. Mixed-effects multilevel logistic regression models were used to estimate associations between race-ethnicity and guideline-concordance accounting for facility or county of residence as level two groups.

**Results.** Black and American Indian/Alaska Native women were consistently less likely to receive guideline-recommended care than non-Hispanic White women. At the facility-level, Commission on Cancer (CoC) accreditation and increasing breast cancer case volume were significantly associated with higher odds of guideline-concordant care from diagnostics through first-line treatment. Black racial residential segregation) was associated with significantly lower odds of guideline-concordant treatment. Rurality and area socioeconomic position were associated with lower odds of guideline-concordant diagnostics.

**Conclusion.** This is the first study to examine guideline-concordance across the continuum of breast cancer care from diagnosis to treatment initiation. Disparities were present from the diagnostic phase and persisted throughout the clinical course. Facility and area characteristics may serve as facilitators or barriers to guideline-adherent treatment and warrant future investigation as mediators of racial-ethnic disparities in cancer care.

**Cannabis use and communication among cancer survivors** Mimi Ton\* Mimi Ton Jaimee L  
Heffner Salene Jones Rachel C Malen Polly A Newcomb

This study aimed to characterize the prevalence and correlates of cannabis (marijuana) use, reasons for use or non-use, and health care communication among recently diagnosed cancer survivors in a population-based sample within Washington State. Understanding cannabis use and how patients and health care providers communicate about it could contribute to improved survivorship care. We identified individuals diagnosed with invasive cancers in the prior 6-18 months from April 2020 - December 2020 using the Seattle-Puget Sound Surveillance, Epidemiology, and End Results (SEER) cancer registry (n=1515). We ascertained information on demographics, medical history, and substance use, including cannabis through a questionnaire. We used descriptive statistics to describe the prevalence of cannabis use, reasons for use, and communication about cannabis. We also used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) for the association of cannabis use and patient factors. 41% of participants reported post-diagnostic cannabis use and 9% of participants reported probable cannabis use disorder according to the Cannabis Use Disorder Identification Test - Short Form (CUDIT-SF). Over 25% of patients reported being uncomfortable talking about cannabis use with their provider, with 23% reporting that they had discussed cannabis use with a provider. Among post-diagnostic cannabis users, 61% and 44% of patients used edibles and smoking as modes of cannabis use, respectively. Patients' reasons for use included difficulty sleeping (55%), mood, stress, anxiety or depression (44%), pain (42%) and recreational (42%). Cannabis use after diagnosis was associated with younger age, lower educational attainment, former or current cigarette smoking, and consuming more than 2 alcohol-containing drinks per day. In this evaluation of cannabis use in a registry-linked population-based sample of cancer survivors, a large proportion of survivors use cannabis post-diagnosis, with many patients being uncomfortable or not discussing use with their clinician. Patients use cannabis for a variety of reasons, and various demographics and other substance use were associated with use, which may help identify survivors who could benefit from discussions on cannabis use.



**Five-year survival prognosis of young, middle-aged, and elderly adult female invasive breast cancer patients by clinical and lifestyle characteristics** Yu-Tung, Teng\* Yu-Tung Teng  
Jason Liu

**Background:** Female breast cancer is the most common cancer among female adults aged 30-69 in Taiwan, but no studies comprehensively examined how clinical and lifestyle characteristics influence survival in invasive breast cancer patients diagnosed at different ages. We investigated the five-year survival prognosis of young, middle-aged, and elderly adult female invasive breast cancer patients by clinical and lifestyle characteristics.

**Methods:** We explored how clinical and lifestyle characteristics are associated with five-year survival among young (20-39 y/o), middle aged (40-64 y/o), and elderly ( $\geq 65$  y/o) female adult invasive breast cancer patients who was diagnosed between 2002 and 2014 from National Health Insurance Research Database (NHIRD). Chi-squared test was used for comparing clinical and lifestyle characteristics between three age groups, and Poisson Regression was used for evaluating the crude and adjusted risk ratios.

**Results:** Survival risks were significant for almost all clinical characteristics, except for treatment delay. As for lifestyle characteristics, only body mass index was significant. However, in terms of age group stratification, the histological type of infiltrating duct and lobular carcinoma, infiltrating duct mixed with other carcinomas, and others were less identical among the three groups. Chemotherapy and hormone therapy as the first treatment were especially different among young breast cancer patients than among the middle-aged and elderly breast cancer patients. What is more special about lifestyle characteristics is that the survival risk of elderly breast cancer patients with overweight and obese body mass index was significantly increased, and the survival risk of elderly breast cancer patients with casual drinking habits was also significantly increased.

**Conclusion:** According to our findings, the survival risks of histological type, first treatment, body mass index, and drinking were not consistent across age groups. Therefore, future research may need to explore the relationship between these clinical and lifestyle characteristics and survival in more depth.

**Keywords:** female breast cancer; survival; epidemiology

**Physical activity and sleep duration among long-term African American breast cancer survivors** Sarah Nechuta\* Sarah Nechuta Deepika Boopathy Ally Goerge Maureen Sanderson

**Background:** Sleep quality is a major health concern among breast cancer survivors and sleep disturbances can persist many years after diagnosis and initial treatment. Physical activity (PA) has many health benefits including increased quality of life and reduced mortality. Few epidemiologic studies of sleep quality have focused on African American breast cancer survivors and among long-term survivors. We examined the association of PA with sleep duration among long-term African American breast cancer survivors. **Methods:** Women from Tennessee, Georgia, and South Carolina completed a comprehensive survivorship-focused questionnaire (n=323). Validated measures of sleep quality (Pittsburg Sleep Quality Index) and PA, other lifestyle factors, and clinical factors (including cancer treatment) were collected. Adjusted logistic regression models estimated ORs and 95% CIs for the association of shorter sleep duration (<7 hours vs.  $\geq$ 7 hours) and two measures of PA (meeting PA recommendations ( $\geq$ 150 minutes min/week) and recreational PA in min/week categorized in tertiles). Models adjusted for age, clinical factors, and other potential confounders. **Results:** Women were on average 4.2 years post-diagnosis (range:2.5-6.5). Mean age at diagnosis was 54.8 years (range:25-75). About 59% of women had sleep duration <7 hours. In adjusted models, meeting PA recommendations was associated with reduced odds of shorter sleep duration (OR=0.50; 95% CI:0.30-0.85). Higher levels of recreational PA were associated with reduced odds of shorter sleep duration (ORs (95% CIs): 0.56 (0.30-1.06) and 0.44 (0.23-0.86) for 34- <192 min/week and  $\geq$ 192 min/week, respectively). **Conclusions:** Short sleep duration was common among African American breast cancer survivors. Breast cancer survivors with higher levels of PA had reduced odds of shorter sleep duration. Future studies with a larger sample size and longitudinal data among long-term African American breast cancer survivors are needed.

**Establishment of the Michigan Cancer and Research on the Environment Study (MI-CARES) cohort** Lilah Khoja\* Lilah Khoja Maxwell Salvatorre Minh Tung Phung Sara Snyder Shayiza Ahmed Isabella de Sa Anna Graf Manar Aljebori Sailing Jane Tang Burnley Truax Melanie Vukovich Ken Resnicow Justin Colacino Alison Mondul Bhramar Mukherjee Dana Dolinoy Leigh Pearce

The Michigan Cancer and Research on the Environment Study (MI-CARES) is establishing a cohort of over 100,000 Michiganders to examine associations between environmental exposures and cancer risk. Michigan is uniquely positioned for this research due to past and ongoing adverse environmental exposures.

Any Michigan resident aged 25-44 can enroll, allowing us to capture exposures during important windows of susceptibility prior to most cancers' onset. As minority populations are underrepresented in environment and cancer research despite having worse cancer outcomes and being at greater risk of being exposed to environmental hazards, we will enroll equal numbers of Black, Latinx, MENA and White participants.

To democratize participation, remote and paper options for enrollment are available in Arabic, English and Spanish. In addition to a baseline questionnaire, consent for data linkage, and annual follow-up surveys, participants are also asked to provide saliva and blood spot samples via mail. These will be analyzed for environmental exposures such as heavy metals and for intermediate cancer markers. Participant data will be linked to exposure databases through their residential address history and to local and national cancer and vital statistics registries.

MI-CARES has employed a multifaceted community engagement and recruitment strategy, working with community organizations to recruit participants. A stakeholder advisory board with representatives from Metro Detroit, Flint, Lansing, Kalamazoo, Grand Rapids, Bay City-Saginaw-Midland, and northern Michigan is being established to ensure that the communities' needs are considered and met.

Some 2,000 individuals have already enrolled. The challenges and strategies of establishing this contemporary and diverse prospective cohort study will be discussed. MI-CARES is part of the Cohorts for Environmental Exposures and Cancer Risk (CEEER) consortium.

## Longitudinal effects of positive and negative social support on memory aging of middle aged and older cancer survivors: a marginal structural modelling approach

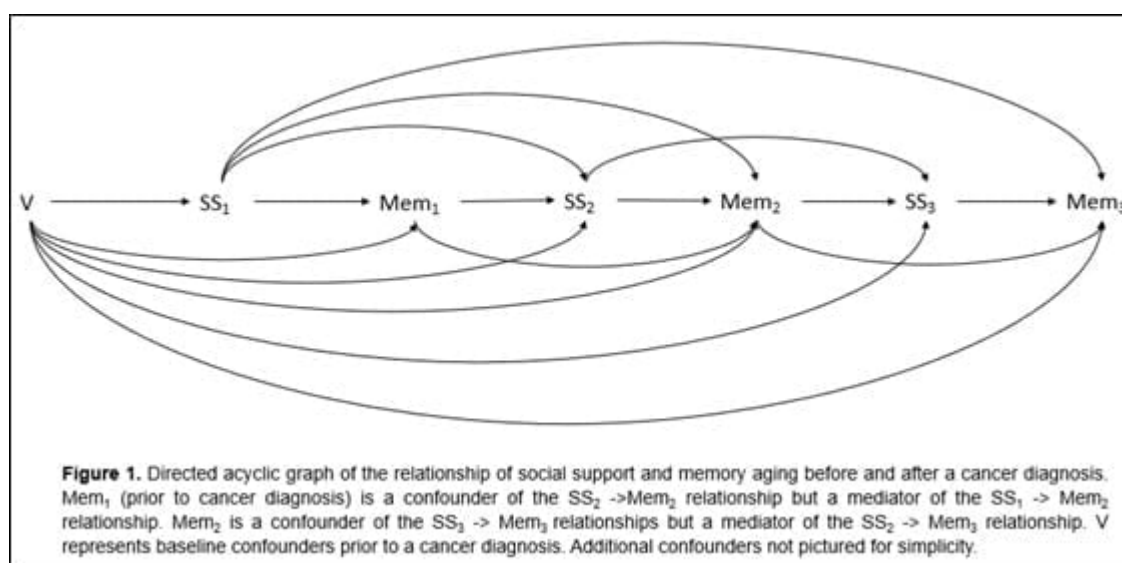
Ashly C. Westrick\* Ashly C Westrick Xuexin Yu Brendan O'Shea Lindsay C. Kobayashi

**Background.** While social support is associated with better cognitive health outcomes in the general population, this relationship is understudied among cancer survivors, who have unique social support needs. We investigated whether positive and negative social support before and after a cancer diagnosis is related to post-diagnosis memory aging among adults aged  $\geq 50$ .

**Method.** Data were from 1,243 cancer survivors in the US Health and Retirement Study (HRS;  $n=621$ ) and English Longitudinal Study of Ageing (ELSA;  $n=622$ ) cohorts from 2006 to 2018. Incident cancer diagnoses and memory function (immediate and delayed word recall) were assessed every two years. Positive and negative social support (high vs. low) was assessed every four years for HRS participants and every two years for ELSA participants. We established three time points relative to cancer diagnosis: pre-diagnosis (the wave prior to cancer diagnosis), time 1 post-diagnosis (the wave when a cancer diagnosis was first reported), and time 2 post-diagnosis (the second wave after a cancer diagnosis). Multivariable-adjusted marginal structural models incorporating inverse probability of treatment and attrition weights estimated the relationship between positive and negative social support and memory function over time, overall

**Results.** Higher vs. lower negative social support was associated with worse memory (-0.49 SD units; 95% CI: -0.84, -0.14) but better memory after a cancer diagnosis (0.47 SD units; 95% CI: 0.04, 0.91) There was no association between positive social support and memory.

**Discussion.** Higher negative social support was associated with better memory immediately after a cancer diagnosis. The long-term impacts of social support on post-diagnosis cognitive health of older cancer survivors should be further explored.



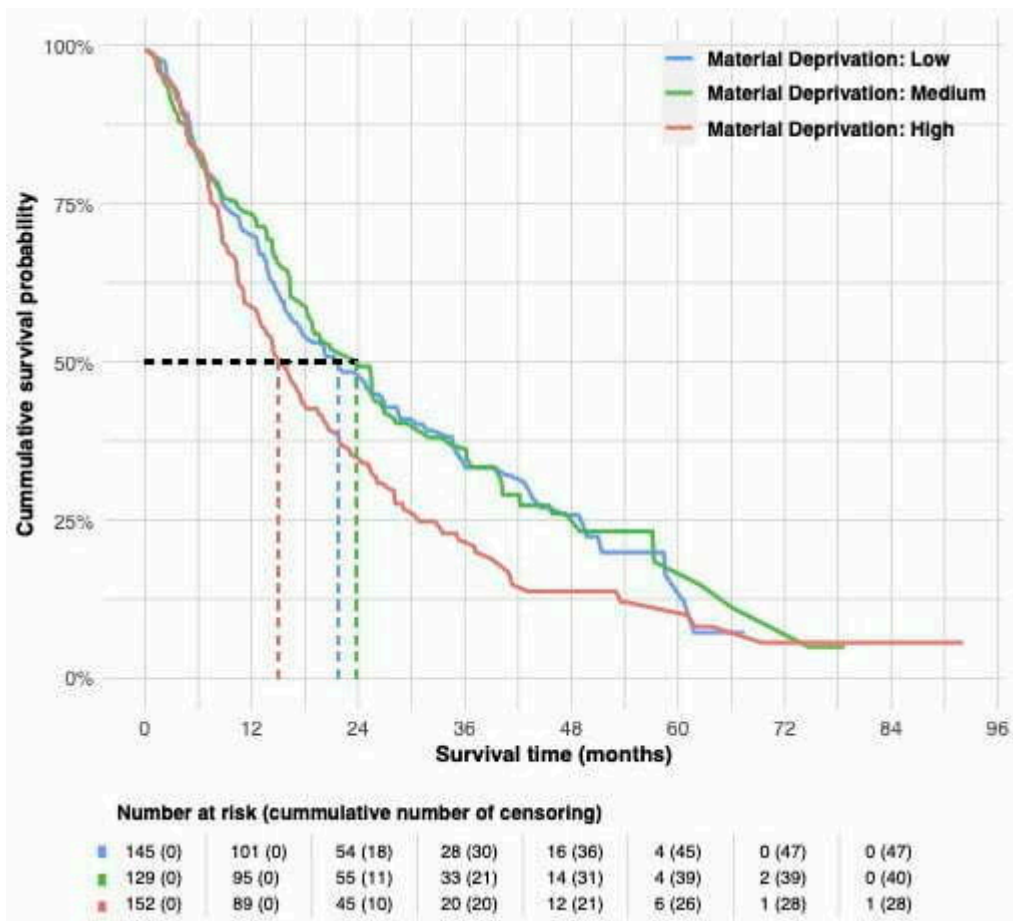
**Inequalities in survival and treatment across social determinants of health in advanced lung cancer patients in Quebec (Canada): a high-resolution population-level analysis** Samia Qureshi\* Samia Qureshi Erin Strumpf Gino Boily Jim Boulanger Élisabeth Pagé

**Background:** Differences in survival across social determinants of health may be weak for advanced lung cancer patients given their poor long-term prognosis. However, this may not apply to patients receiving breakthrough therapies like EGFR tyrosine kinase inhibitors (EGFR-TKI) that prolong survival. This study examined survival and treatment inequalities by social factors in advanced lung cancer patients treated with gefitinib, an EGFR-TKI, as 1<sup>st</sup>-line palliative treatment.

**Methods:** Advanced lung cancer patients receiving 1<sup>st</sup>-line gefitinib from 2001 to 2019 were selected from health administrative databases. We estimated relative measures of the association of neighbourhood-level income, education, and material deprivation and areas of residence characterized by urbanicity and type of health centers with 1) the median overall survival time from treatment to death, 2) the probability of receiving osimertinib as a 2<sup>nd</sup> EGFR-TKI, 3) and the median time from biopsy to receiving 1<sup>st</sup>-line gefitinib. Differences by age and sex were accounted for with regression or propensity score-based methods.

**Results:** Of 457 patients identified, those from materially deprived areas had the shortest median survival time (high/low deprivation, 0.69; 95%CI, 0.47-1.04). The probability of receiving osimertinib was highest for patients from immigrant-dense areas (high/low density, 1.95; 95%CI, 1.26-3.36) or from Montreal (other census metropolitan areas/Montreal: 0.39; 95%CI, 0.16-0.71). The median wait time for gefitinib in regions with health centers peripheral to large centers in Quebec or Montreal was 1.27 times that of regions with university-affiliated centers (95%CI, 1.09-1.54; n=353).

**Conclusion:** The real-world variations we observed in survival and treatment by social factors in advanced lung cancer patients in the current context of breakthrough therapies add to previously limited evidence and support future research on social inequalities across the cancer continuum.



**Diabetes Mellitus and Biliary Tract Cancer Risk: A Pooling Project of 30 Prospective Studies** Ilona Argirion\* Ilona Argirion Jill Koshiol the BiTCaPP Study Group

**Background:** Epidemiological evidence suggests that diabetes mellitus (DM) may be associated with increased risk of several cancers; nevertheless, the relationship with biliary tract cancers (BTCs) remains to be fully elucidated.

**Methods:** Data from thirty prospective studies participating in the Biliary Tract Cancers Pooling Project (BiTCaPP) were harmonized to allow for the investigation of the association between diabetes and BTCs. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated using Cox proportional hazards regression after adjustment for sex, race, education, smoking and body mass index. Sensitivity analyses were conducted to assess the role of geography (Eastern vs. Western cohorts), sex, presence of gallstones, and cholecystectomy on the observed associations. To assess statistical heterogeneity of results between studies, we performed a random-effects meta-analysis using Cochrane  $I^2$ .

**Results:** During 41,946,758 person-years of follow up, 1575 gallbladder cancer (GBC), 1009 intrahepatic bile duct cancer (IHBDC), 1354 extrahepatic bile duct cancer (EHBDC), and 681 ampulla of Vater cancer (AVC) cases occurred. DM was associated with risk of GBC (HR=1.22; 95%CI: 1.01-1.47) and EHBDC (HR=1.24; 95%CI: 1.01-1.51). The association with GBC was particularly pronounced in Western cohorts (HR=1.28; 95%CI: 1.03-1.58) and among males (HR=1.47; 95%CI: 1.06-2.04). We did not find significant heterogeneity between studies. No significant differences were found by cholecystectomy or gallstone status.

**Conclusion:** DM appears to increase the risk of GBC and EHBDC. These findings highlight etiologic heterogeneity across the biliary tract.

**Receipt of chemotherapy by breast cancer stage and prevalent cardiovascular disease in a community setting**

Carolyn Brandt\* Carolyn Brandt Jacqueline Vo Cody Ramin Lene Veiga  
Rochelle Curtis Gina Whelan Clara Bodelon Gretchen Gierach Heather Feigelson Erin Bowles Amy  
Berrington Jennifer Gander Veronique Roger

**Background:** Little is known regarding the association between breast cancer stage, prevalent cardiovascular disease (CVD), and receipt of cardiotoxic chemotherapy treatment (e.g., anthracyclines) in a real-world community setting.

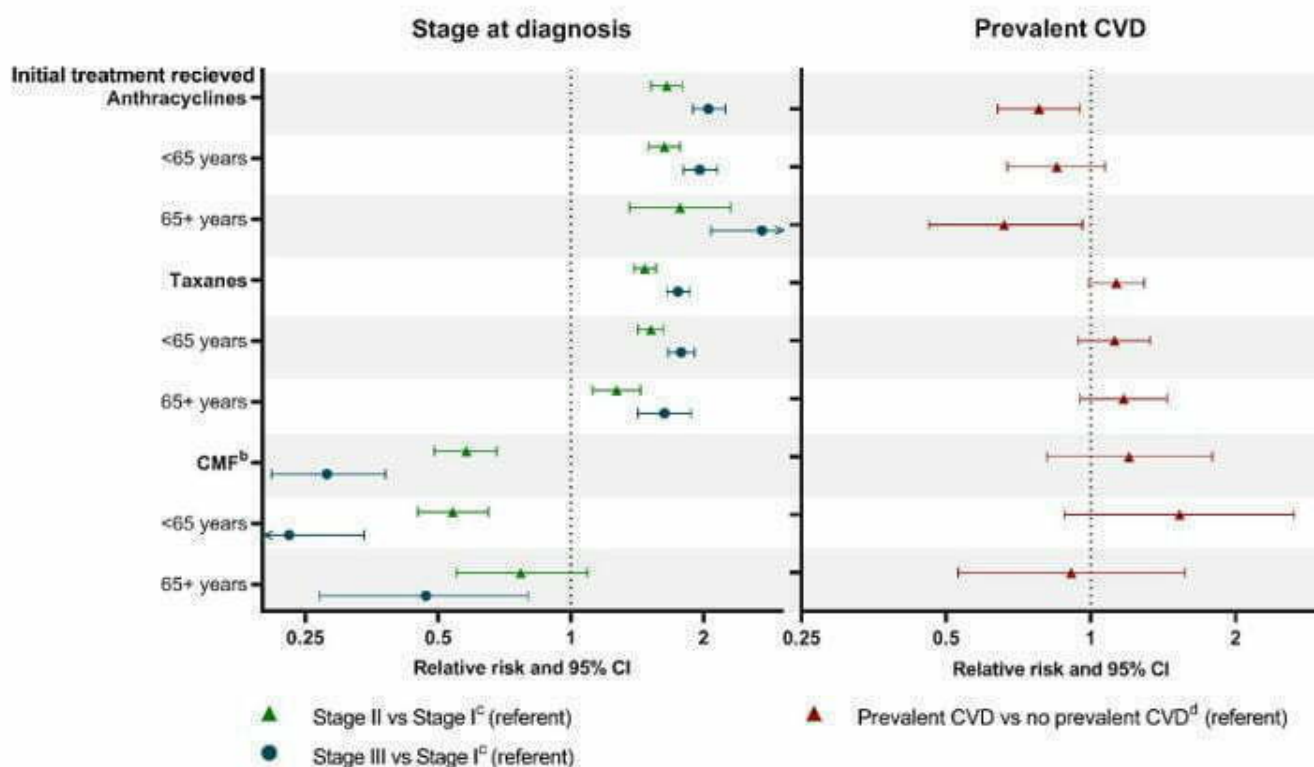
**Methods:** We identified 4,309 women aged 20+ years diagnosed with stage I-III breast cancer who received chemotherapy from two U.S. integrated healthcare systems between 1993-2016 (mean age=54.8 years). Our primary outcomes were chemotherapy type: 1) anthracyclines; 2) taxanes; or 3) cyclophosphamide, methotrexate, 5-fluoracil [CMF]. We used generalized linear models with a log link and Poisson distribution to estimate relative risks (RRs) and 95% CIs for chemotherapy type by stage and prevalent CVD and adjusted for study center, estrogen receptor status, age at diagnosis, and diagnosis year. RRs were further stratified by age at diagnosis (<65/65+ years).

**Results:** Women were primarily diagnosed with early-stage breast cancer (80% stage I/II). CVD prevalence was 2.74%, 3.25%, and 3.54% for stage I-III, respectively. Women with stage II and III breast cancer were more likely to receive anthracyclines (stage II: RR=1.65, 95% CI=1.52-1.79; stage III: RR=2.05, 95% CI=1.89-2.24) and taxanes (stage II: RR=1.47, 95% CI=1.39-1.56; stage III: RR=1.75, 95% CI=1.65-1.86) but less likely to receive CMF (**Figure**) compared to those with stage I breast cancer. Associations were similar when stratified across age. Women with prevalent CVD were less likely to receive anthracyclines (RR=0.78, 95% CI=0.64-0.95) compared to those without prevalent CVD, particularly among older women (65+ years: RR=0.66, 95% CI=0.46-0.96; <65 years: RR=0.85, 95% CI=0.67-1.07), but not significant for other treatment types.

**Conclusion:** Receipt of anthracyclines was higher among advanced stage, but lower among women with prevalent CVD. Further studies are needed to understand treatment outcomes among breast cancer survivors with comorbidities such as CVD in a real-world community setting.



**Figure 1:** Multivariable-adjusted relative risks (RRs) and 95% confidence intervals (CIs) for the association of stage at diagnosis and prevalent CVD with receipt of chemotherapy type, overall and stratified by age at diagnosis (n=4,309)<sup>a</sup>



<sup>a</sup>The analytic population is restricted to women who received chemotherapy. The exposures of interest are stage and prevalent CVD at diagnosis. The outcome of interest is receipt of chemotherapy by type (anthracyclines vs. other, taxanes vs. other, CMF vs. other). RRs (95% CIs) are adjusted for study site (Colorado, Washington), estrogen-receptor status (positive, negative, borderline/unknown), age at breast cancer diagnosis (5-year groups) and year of diagnosis (1993-2000, 2001-2008, 2009-2016). Models examining the association between prevalent CVD and receipt of chemotherapy are also adjusted for breast cancer stage (stage I, stage II, stage III).

<sup>b</sup>CMF: cyclophosphamide, methotrexate, and 5-fluorouracil.

<sup>c</sup>Women were classified as stage I (N=1,095), stage II (N=2,338) or stage III (N=876).

<sup>d</sup>Women with prevalent CVD are defined as having a history of cardiomyopathy/heart failure, ischemic heart disease, or stroke at the time of breast cancer diagnosis (N=137).

**Cancer incidence attributable to alcohol use among adults in the United States, 2008-2019**

Naomi Greene\* Naomi Greene Carolyn Reyes-Guzman Emma Meador Anne-Michelle Noone Nadia Howlader

**Background:** In the United States, 3.0% of all cancer cases (~52,500 cases) were attributable to alcohol in 2020. Alcohol use significantly increased between the late 1990s and 2000s in the US adult population evidenced by several population surveys. Our project extends prior work using single years of data by examining a larger interval of data on alcohol-attributable cancer risk and estimating the proportion of cancer incidence during 2008-2019.

**Methods:** We calculated population attributable fractions (PAFs) using estimated relative risks from a large meta-analysis and estimated annual alcohol prevalence from the National Health Interview Survey (1998-2000 and 2007-2009). Alcohol prevalence data were adjusted to national alcohol sales to account for underreporting of alcohol use in surveys. PAF estimates were combined with cancer registry data to calculate incidence rates attributable to alcohol use, assuming a 10-year latency between alcohol use and cancer incidence.

**Results:** We present preliminary results for three alcohol-associated cancer sites: female breast, colorectal, and oral and pharynx. The largest PAF was observed for oral cavity and pharynx during 2008-2010 (21.7% for men and 22.8% for women) and increased slightly during 2017-2019 (22.4% for men and 23.5% for women). For female breast cancer, the PAF increased to 6.1% in 2017-2019 from 5.3% in 2008-2010. The colorectal cancer PAF was larger during 2017-2019 (8% for men and 2.5% for women) compared with 2008-2010 (7.7% for men and 2.1% for women).

**Conclusions:** Alcohol use contributed substantially to oral cavity and pharynx cancer incidence in US among both men and women, but also led to increases in other alcohol-associated cancers. Future work will explore variance calculations of PAF estimates using simulation methods and additional alcohol-associated cancer sites.

**Leveraging cancer registry data to investigate the impacts of contextual factors on colorectal cancer outcomes: A machine learning approach** Rexford Anson-Dwamena, MPH\*  
Hadiza Galadima Rexford Anson-Dwamena, MPH Ghalib Bello, PhD James Blando, PhD

**Background:** The incidence of colorectal cancer (CRC) is declining among adults in the U.S. However, this decrease is not observed among individuals younger than 50 years of age. There is limited methodological research to accurately assess the cumulative effect and the complex interaction patterns that exist among several potential cancer factors such as demographics, socio-economic, and environmental and occupational exposures to chemical substances. Thus, there is a critical need to aggregate newly generated data and the utility to use innovative analytic methods to accurately delineate complex non-linear relationships that may exist between these factors and their interactions on cancer outcomes. This study aims to use machine learning (ML) methods to examine the contextual predictors of late-stage CRC diagnosis.

**Methods:** Multiple data sources including cancer registry data from Virginia, US Census data, and data from other populations databases were linked to create a 'big' dataset for our research. Gradient boosting machine learning algorithm was leveraged to identify important CRC risk factors. For comparison purposes, a logistic regression with an adaptive lasso penalty was also implemented. Predicted probabilities were then computed and mapped to examine the geographic patterns in late-stage CRC using ArcGIS.

**Results:** Among 4,408 CRC cases, 522 (11.6%) were EOCRC of whom 358 (68.6%) were late stage at diagnosis. The data linkage led to more than 200 covariates. The top features identified by the ML gradient boosting method that are associated with a CRC case diagnosing late stage included demographic characteristics (tobacco smoking, Primary payer information, higher comorbid conditions), living in areas with low education attainment, higher obesity and screening rates, and composed mostly of African American.

**Conclusion:** This study contributed to the scientific innovation of leveraging big health data to innovatively improve our understanding of the impacts of neighborhood characteristics on CRC outcomes to better target interventions, a high-priority public health problem in the US. Finally, the analytics methods developed in this study will serve in CRC risk prediction among individuals younger than 50 years of age.

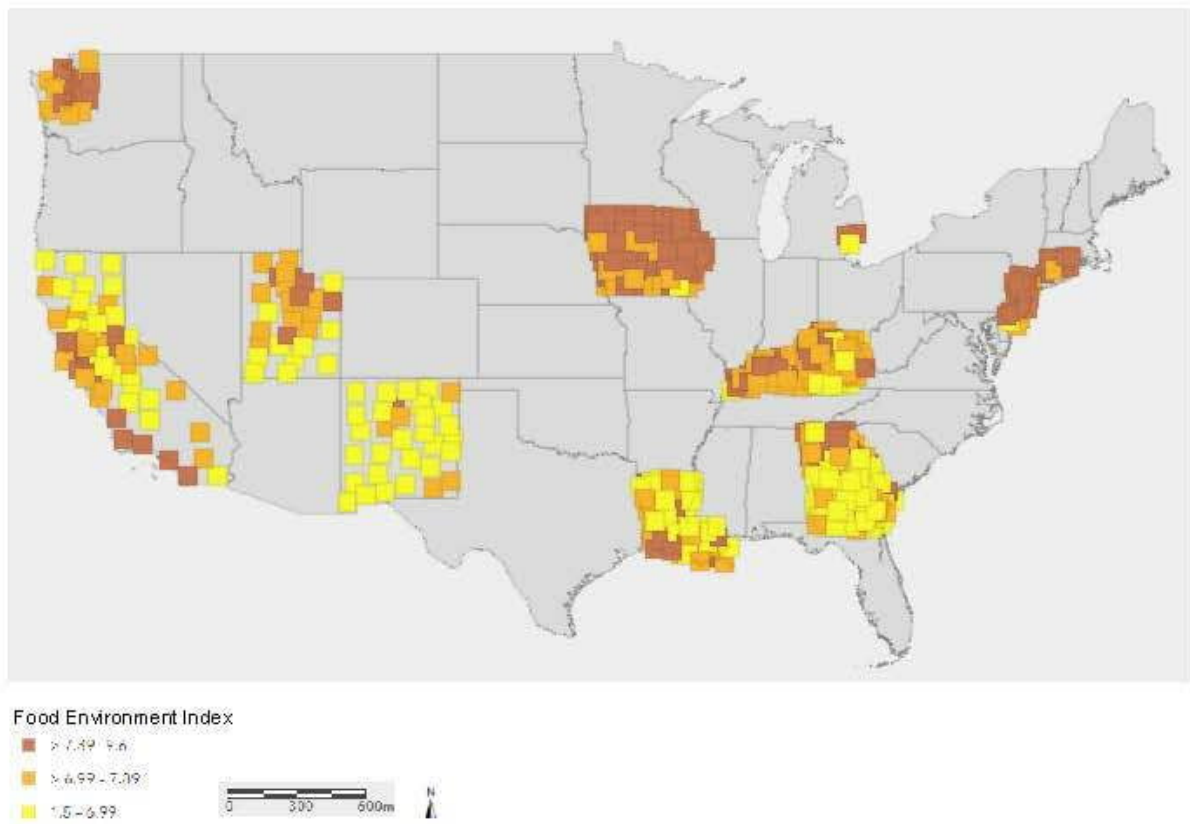
## **Food Environment Index is Inversely Associated with Gastric Cancer Incidence in the United States** Shenghui Wu\* Shenghui Wu Yanning Liu

**Background**— The American Cancer Society estimated that about 26,380 new cases would be diagnosed with gastric cancer (GC) and about 11,090 would die from this type of cancer in 2022. Prior studies have shown that better food access/availability environment was associated with a positive health outcome but did not specifically assess the food environment and risk of GC. Therefore, we conducted the first epidemiologic study prospectively examining the association between the Food Environment Index (FEI) and GC risk in the U.S.

**Methods**— Surveillance, Epidemiology, and End Results provided information on GC incident cases diagnosed between 2000 and 2015 from 16 population-based cancer registries across the U.S. The county-level food environment was assessed using the FEI, an indicator of access to healthy foods (0 is worst, 10 is best). Poisson regression was used to calculate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for the association between FEI and GC risk adjusting for individual-level and county-level covariates. Restricted cubic spline Poisson regression was used to illustrate the association between logarithmic transformed FEI and IRRs of GC adjusting for potential covariates.

**Results**— A total of 87,288 GC cases, diagnosed during 2000-2015, were included in the analysis. Higher levels of FEI were associated with a statistically significant reduced risk for GC (multivariable-adjusted IRR for every score increase=0.50, 95% CI 0.35, 0.70; adjusted IRR for the medium vs. low category=0.87, 95% CI 0.81, 0.94; and adjusted IRR for the high vs. low category=0.89, 95% CI 0.82, 0.95). The cubic spline showed statistically significant inverse association between logarithmic transformed FEI and IRRs of GC.

**Conclusions**— These results suggest that a healthy FE, as measured by FEI, may be a protective factor for GC in the U.S. To reduce the GC incidence, further strategies to improve the food environment at the county level are warranted.



**Figure 1.** Food environmental index across 608 counties in SEER catchment areas in the U.S.

**Assessing the impact of loss to follow-up on racial disparities in a population-based study of cancer survivors** Rebecca Nash\* Rebecca Nash Lauren E. McCullough Deirdre Cronin-Fenton Joellen Schildkraut Kevin C. Ward Timothy L. Lash

**Background:** Recurrence is an intermediate, but understudied, cancer outcome that may provide insight into racial disparities in breast cancer mortality. However, recurrence is not routinely captured in population-based registries largely due to challenges in following patients over time. Recent evidence suggests that current strategies for tracking mobility may be differential by patient factors, including race and ethnicity.

**Methods:** The Cancer Recurrence Information and Surveillance Program (CRISP) cohort was formed by the Georgia Cancer Registry to establish the first population-based surveillance of recurrence among patients diagnosed with one of four common cancers, including female breast cancer. Data sources signaling recurrence are only available for current Georgia residents. Identifying patients who leave Georgia, and are therefore no longer under observation, is critical to accurate accrual of person time. We estimated the expected size of bias due to loss to follow-up in CRISP using mortality data. Unlike recurrence, mortality can be completely identified using the National Death Index. Age-adjusted Cox proportional hazards regression was used to estimate race disparities in breast cancer mortality.

**Results:** CRISP includes 27,453 patients diagnosed with a first primary, nonmetastatic breast cancer during 2013–2017, of which 64% are non-Hispanic White (NHW) and 29% are non-Hispanic Black (NHB). Ignoring emigration from Georgia resulted in misclassification of 4.2% (N=84) of breast cancer deaths, 45% of which were among NHB women. However, the race disparity in breast cancer mortality was similar whether emigration was ignored (NHB vs. NHW HR=1.94, 95% CI: 1.77, 2.13) or complete data were used (HR=1.95, 95% CI: 1.78, 2.13).

**Conclusion:** Given the small proportion of patients who died outside Georgia, loss to follow-up may not substantially bias estimates of race disparities in CRISP. However, the extent of bias should be reassessed with continued follow-up.

### Cancer mortality across rural and urban counties in Virginia Priyadarshini Pattath\*

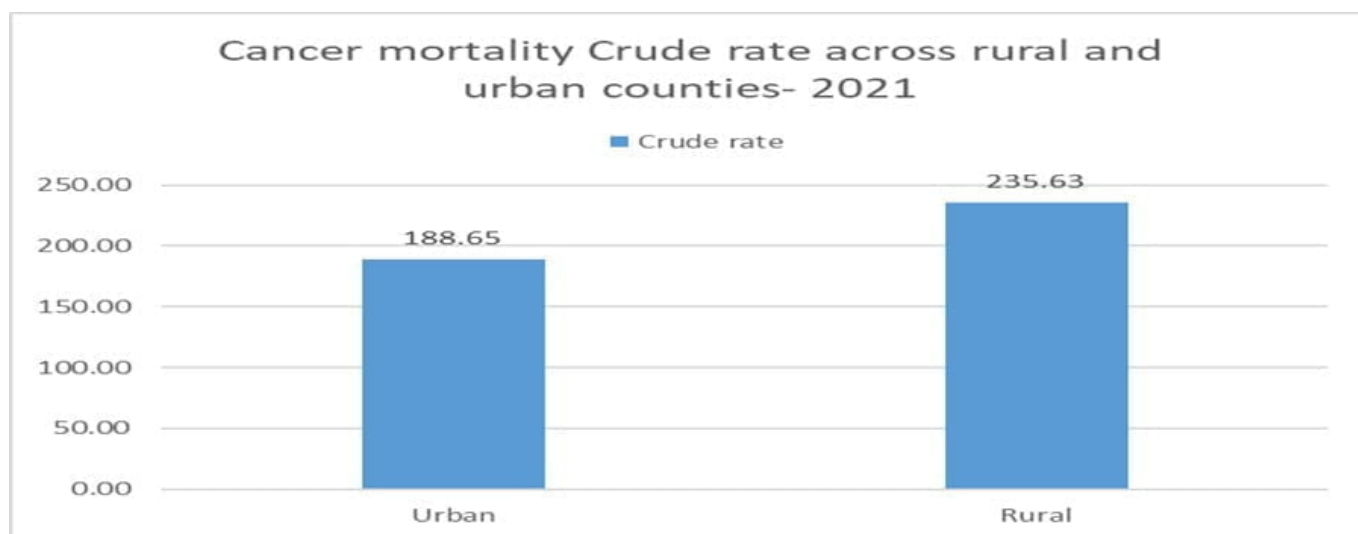
Priyadarshini Pattath Rexford Anson-Dwamena

**Background-** Cancer was the second leading cause of death in the United States in 2021. Residents of rural areas face serious disadvantage related to socioeconomic deprivation, limited access to quality healthcare, and risk factors for cancer relative to urban areas. This study examines county-level differences in cancer mortality by gender, age groups and race/ethnicity across rural and urban counties in Virginia.

**Methods-** County level population was obtained from the 2019 US Census Bureau. Mortality data was obtained from the Virginia department of health, vital statistics for 2021. Neoplasms and insitu neoplasms based on ICD- 10 codes were combined to create the mortality data. Differences in county-level cancer crude mortality rates, across rural and urban counties, using parametric test and non-parametric tests were examined.

**Results-** Rural counties had a significantly higher rate, 235.63 per 100,000 compared to urban counties, 188.65 ( $p < 0.001$ ). When comparing rural-urban differences within gender, there was a significant difference between mortality of males in rural versus urban counties with a large effect (264.51 per 100,000 versus 200.89 per 100,000) ( $p < 0.001$ ). Similar results were found when comparing female mortality rate in rural and urban counties (207.58 versus 177.31 per 100,000). When comparing rural-urban differences within racial and ethnic groups, rural counties had significantly higher cancer mortality rates across White (245.50 versus 192.07 per 100,000,  $p < 0.001$ ), Black (219.23 versus 173.63 per 100,000,  $p < 0.05$ ), and other race groups (105.41 versus 68.08 per 100,000,  $p < 0.05$ ).

**Conclusion-** Rural counties in Virginia had higher rates of cancer deaths than urban counties, and geography can impact prevention, diagnosis, and treatment opportunities. Targeted public health efforts and interventions are needed to close the growing cancer gap between rural and urban counties.



**Post-Diagnostic Alcohol Consumption and Risk of Prostate Cancer Progression** Tanvi Srivastava\* Tanvi Srivastava June M Chan Stacey Kenfield Crystal Langlais Janet Cowan Rebecca E Graff Vivian Liu Jennifer M Broering Peter R Carroll Erin Van Blarigan

The association between post-diagnostic alcohol consumption and the risk of prostate cancer progression remains unclear. We prospectively studied this association in a large cohort of prostate cancer patients. Men diagnosed with prostate cancer actively participating in the Cancer of the Prostate Strategic Urologic Research Endeavor (CaPSURE) cohort study were invited to complete a validated food frequency questionnaire (FFQ) up to twice between 2003-2005 and once between 2015-2017. 1895 patients completed the FFQ and reported a valid number of calories at least once prior to cancer progression. Because only 443 completed more than one survey, we only used each patient's first available FFQ response for these analyses. Exposures were total alcohol (g/day) and types of alcohol (red wine, white wine, beer, liquor; serving frequency). The primary composite outcome included the first record of biochemical recurrence, need for secondary treatment, bone metastases, or death due to prostate cancer confirmed via medical records and death certificates. We used adjusted multivariable Cox proportional hazards models to calculate hazard ratios (HR) and 95% confidence intervals (CI). Among 1,795 men for whom alcohol intake data were available (162 events, median 6.70 years follow-up), we found no statistically significant association between total alcohol and risk of prostate cancer progression. However, red wine consumption was found to be associated with lower risk of prostate cancer progression, with an adjusted HR of 0.34 (95%CI 0.18, 0.67) comparing patients drinking  $\geq 5$  vs. 0 glasses/week (p-trend=0.0007). No other type of alcohol was found to be associated with the risk of prostate cancer progression. While we found no evidence for an association between post-diagnostic consumption of alcohol in general and risk of prostate cancer progression, consumption of at least 5 glasses of red wine per week may be associated with lower risk of prostate cancer progression.



**LATEBREAKER**

Cancer

**Oral Hygiene and Oral Cancer: A Review of Epidemiology Studies** Lauryn Perpall\* Tram Kim Lam Lauryn Perpall

**Background:** Oral hygiene practices may contribute to risk of oral cancer. Oral hygiene practices include regularly brushing teeth, flossing, rinsing the mouth, and attending routine dental checkups. Oral cancer encompasses multiple cancers, including oral cavity, esophageal, pharynx, larynx, head & neck, aerodigestive, and tongue. Understanding the role of oral health and its contribution to cancer risk may inform oral cancer prevention guidelines. We performed a literature review to assess the evidence between oral hygiene practices and oral cancer risk.

**Methods:** We searched PubMed using the following search terms: oral cancer (oral cavity, oropharyngeal, pharynx, larynx, nasopharyngeal, leukoplakia, Head & Neck) AND oral hygiene (brushing, flossing, mouth wash, oral health risk factor, periodontitis). We identified 814 studies; further manual review yielded 47 studies that meet our inclusion criteria.

**Results:** The 47 studies included 42 case-controls, 3 cohorts, and 2 cross sectionals from five different continents with the majority from Asia (61%). The remainders were in Europe (21%), North America (8%), South America (6%), and Africa (4%). The sample size varied ranging from 100 to 2,000+. Most of the studies included 100 to 500 cases (53%). The oral hygiene practices varied among studies with most of the studies investigating toothbrushing frequency (49%), decayed/missing/filled teeth (DMFT, 40%), and dental visit frequency (28%). The remainder of the studies investigated mouthwash use (19%), bad prosthesis/dentures (17%), gum bleeding/periodontitis (13%), recurrent ulceration (6%), flossing (6%), instrument used (toothbrush, finger, stick) (4%), and other hygiene habits (19%). Across all studies, the cancer most studied was oral cavity cancer (51%) followed by pharynx (28%), esophageal (23%), head & neck (13%), larynx (11%), aerodigestive tract (9%), and tongue (4%) cancer.

**Summary:** The current epidemiological evidence, based primarily from case-control studies, is equivocal although there is a suggestive positive association between oral hygiene and oral cancer risk. Less toothbrushing frequency, DMFT index, and dental visit frequency were indicators of oral hygiene. Future studies, using prospective cohort study design and more objective measures of oral health practices, are needed to further elucidate the role of oral hygiene practices and oral cancer risk.

## Oral Hygiene and Oral Cancer: A Review of Epidemiology Studies

Authors: Lauryn Perpall and Tram Kim Lam

Institution: National Cancer Institute/Division of Cancer Control and Population Sciences/Epidemiology and Genomics Research Program/Environmental Epidemiology Branch

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## **Impact of population aging on the cancer incidence burden in South Korea: A projection and decomposition analysis** Hoejun Kwon\* Hoejun Kwon Sanghee Lee Hyunsoon Cho

### **Objective**

Cancer burden is expected to increase in the aging society. Korea has been recognized as having one of the world's highest aging rates. This study aims to analyze the impact of the aging population by quantifying the burden of future cancer incidence.

### **Method**

Based on the population-based cancer incidence case from 2000 to 2019, the future incidence of the most common cancers (gastric cancer, colorectal-anal cancer, liver cancer, pancreatic cancer, lung cancer, skin cancer, breast cancer, prostate cancer, bladder cancer, and thyroid cancer) are projected by 2040 using the age-period-cohort projection model. Changes in the projected trend were decomposed factor into population aging, population growth, and age-standardized incidence rates through decomposition analysis and measured the impact of the aging population. All analysis was performed according to gender.

### **Result**

The projected number of cancer incidences due to population aging increased in all cancer sites, particularly lung, prostate, colorectal, and stomach. From 2019 to 2040, incidences attributable to population aging in the male prostate, lung, and stomach were projected to increase by 147.9%, 106.5%, and 62.7%, respectively, while in women, the increases in lung, colorectal-anal, and stomach cancer were projected by 82.4%, 59.5%, and 53.3% respectively. Incidences due to population growth and changes in the age-standardized rates were projected to decrease for liver cancers, but to increase for thyroid cancer.

### **Conclusion**

Population aging significantly impacted the rapid increase in cancer burden, suggesting an urgent need for appropriate healthcare resource allocations and health policy development focusing on the elderly.

**Investigating red blood cell traits in ischaemic heart disease and lifespan using Mendelian Randomization** Semi Hwang\* Semi Hwang C. Mary Schooling

**BACKGROUND** Red blood cell (RBC) traits have long been through relevant to ischaemic heart disease (IHD). Correspondingly, uncertainty exists about the optimal transfusion threshold in people with cardiovascular disease, with limited evidence from trials. Previous observational studies are inconsistent, did not consider these linked traits together and rarely consider all-cause mortality.

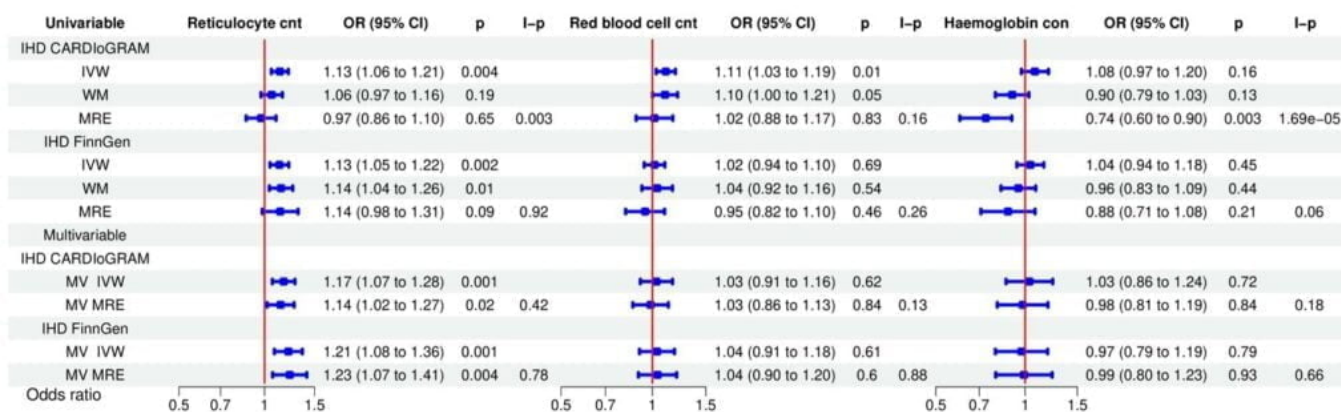
**OBJECTIVES** To assess the role of RBC traits independently and jointly in IHD and lifespan using Mendelian randomization (MR).

**METHODS** Univariable and multivariable MR study using genetic instruments from the UK Biobank applied to genome wide association studies of IHD, i.e., CARDIoGRAMplusC4D 1000 Genomes (cases=60,801, controls=123,504) and FinnGen (cases=31,640, controls=187,152) and of parental lifespan from the UK Biobank (n=389,166).

**RESULTS** In univariable MR, reticulocyte and RBC counts were positively associated with IHD, and all RBC traits considered were associated with lifespan but with evidence of pleiotropic effects. In multivariable MR, considering these three RBC traits together, reticulocyte count was consistently positively associated with IHD in both studies (odds ratio (OR) 1.14, 95% confidence interval (CI) 1.06 to 1.23 and OR 1.14, 95% CI 1.05 to 1.21) and with shorter lifespan (-0.70 years, 95% CI -1.15 to -0.24) with little evidence of pleiotropy. Results were similar including any potential genetic confounding by IHD risk factors.

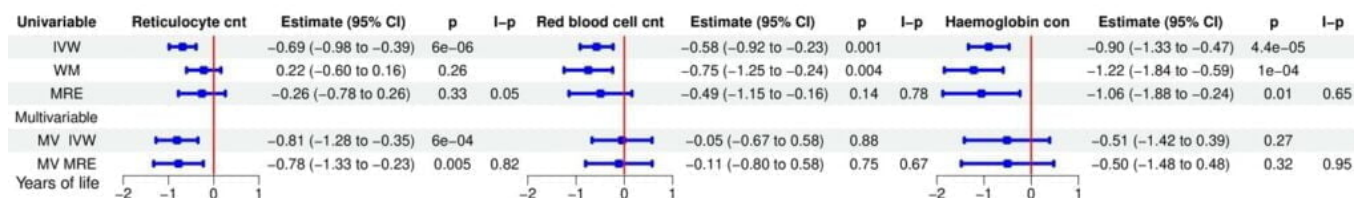
**CONCLUSIONS** Reticulocyte count should be further investigated as an overlooked target of intervention for preventing IHD and reducing all-cause mortality.

**FIGURE 1** Mendelian randomization estimates for effect sizes of reticulocyte count, red blood cell count and haemoglobin concentration on IHD (odds ratio (OR)) from CARDiogram and FinnGen with corresponding multivariable estimates mutually adjusted for other the red blood cell traits, insulin, HbA1c, DBP and BMI



CARDiogram = CARDiogramplusC4D 1000 Genomes; IVW = inverse-variance weighted; WM = weighted median; MRE = MR-Egger; MV = Multivariable; OR = Odds ratio; CI = Confidence interval; p = P value; I-p = MR-Egger intercept P value; cnt = count; con = concentration.

**FIGURE 2** Mendelian randomization estimates for effect sizes of reticulocyte count, red blood cell count and haemoglobin concentration on lifespan (years of life) and corresponding multivariable estimates mutually adjusted for other the red blood cell traits, insulin, HbA1c, DBP and BMI



CARDiogram = CARDiogramplusC4D 1000 Genomes; IVW = inverse-variance weighted; WM = weighted median; MRE = MR-Egger; MV = Multivariable; OR = Odds ratio; CI = Confidence interval; p = P value; I-p = MR-Egger intercept P value; cnt = count; con = concentration.

**Diabetic and hypertensive disorders following early pregnancy loss: a systematic review and meta-analysis** Gizachew Tessema\* Gizachew Tessema Jennifer Dune Damien Foo Sylvester Dodzi Nyadanu Berihun Dachew Gavin Pereira

There is emerging evidence of associations between early pregnancy loss and subsequent risk of development of diabetic and hypertensive disorders. This study conducted a systematic review and meta-analysis of observational studies to identify the effect of early pregnancy loss (spontaneous abortion and induced abortion) on the risk of diabetic and hypertensive disorders in subsequent pregnancies and later life.

Three independent reviewers screened titles and abstracts identified in CINAHL Plus, Ovid/EMBASE, Ovid/MEDLINE, ProQuest, PubMed, Scopus, Web of Science, and Google Scholar from inception until April 2022. Observational studies (cohort, case-control or cross-sectional) were included if the selection criteria were met; exposure is early pregnancy loss and the outcomes are diabetic (gestational diabetes mellitus; type 1 or type 2 diabetes) or hypertensive disorders (pre-eclampsia, eclampsia, gestational hypertension; hypertension). Results were extracted and presented in tabular and narrative forms for all included studies. Random effects meta-analysis was used to compare unadjusted odds ratio (OR) of early pregnancy loss associated with the outcomes of interest. Risk of bias was assessed using the Joanna Briggs Institute Critical Appraisal tool.

Of the 21,940 unique articles identified, 45 met the inclusion criteria and included for the final review. The pooled unadjusted OR of a spontaneous abortion and risk of gestational diabetes mellitus in a subsequent pregnancy was 1.63 (95% CI 0.76 - 3.49) and the OR of a spontaneous abortion of developing diabetes mellitus in later life was 1.09 (95% CI 1.01 - 1.19). The pooled unadjusted OR of developing pre-eclampsia in a subsequent pregnancy was 1.30 (95% CI 0.86 - 1.96) for women who had at least one spontaneous abortion. Our preliminary findings indicate a possible association between early pregnancy loss and subsequent diabetic and hypertensive disorders, particularly for disorders during subsequent.

**Association of Prediabetes and Physical Activity/Sedentary Behavior with All-Cause Mortality and Cardiovascular Events: The Hispanic Community Health Study/Study of Latinos** Sarah Alver\* Sarah Alver Robert Kaplan Yasmin Mossavar-Rahmani Kelly Evenson Linda Gallo Carmen Cuthbertson James Floyd Daniela Sotres-Alvarez Gregory Talavera Jianwen Cai Amber Pirzada Martha Daviglius Frank Penedo Maria Llabre Juan Lin

Previous studies show lower mortality risk with increased physical activity (PA) and decreased sedentary behavior (SB) but have not specifically examined Hispanic/Latinos. In adults with prediabetes (preDM), PA can avert progression to diabetes, but its association with cardiovascular disease (CVD) and mortality is not clearly established. We studied the association of preDM and PA/SB with combined outcome all-cause mortality and adjudicated CVD events (MI, stroke, or heart failure) in 10,065 adults (4957 preDM; 5108 normoglycemia; mean survey-adjusted age 39.8 years; 59.6% female) with baseline 7-day accelerometry-based PA/SB from the Hispanic Community Health Study/Study of Latinos. PA was quantified as meeting/not meeting 2018 PA Guidelines (PAG) for Americans, steps/day above/below 7000, and counts/minute above/below median (CPM). SB compared the lowest vs highest two tertiles. Cox proportional hazard models, adjusted for complex survey design and clinical and socioeconomic factors, were used to estimate hazard ratios (HRs) of the combined outcome for PA measures stratified by glycemic status. During the follow-up period (median (IQR) 6.77 (6.12, 7.52) years), there were 261 events (93 (1.8%), normoglycemia; 168 (3.4%), preDM). In Hispanic/Latinos with normoglycemia, HR (95% CI) for low vs high PA were: 1.99 (1.09, 3.69), PAG; 1.52 (0.86, 2.66), CPM; and 1.88 (0.99, 3.55), steps; HR was 2.5 (1.03, 6.03) for high vs low SB. For individuals with preDM, HRs for PA measures were near 1; for high vs low SB, the HR was 1.37 (0.71, 2.67). In Hispanic/Latinos with preDM, and more significantly in those with normoglycemia, higher SB was associated with greater mortality and CVD events. This highlights the importance of preDM prevention and screening, increased PA, and decreased SB.

**Revisiting the point-source hypothesis of the coronary heart disease epidemic in light of the covid-19 pandemic** George Davey Smith\* George Davey Smith Danny Dorling

The 20<sup>th</sup> century coronary heart disease (CHD) epidemic in many high income countries has been attributed to the cumulative effect of “lifestyle”. However several authorities have suggested a point-source shift in risk combined with changes in cause of death registration fits age and sex specific trends better. The 1889-95 influenza pandemic is a plausible candidate for triggering this shift in risk. In his official report on the 1918 ‘flu pandemic Major Greenwood pointed out that the 1889-95 pandemic led to a substantial permanent upwards shift in respiratory and other morbidity and mortality in the UK. Christopher Andrewes - who identified the influenza virus in 1933 - thought that two diseases were introduced in 1889-95, one of which was influenza of a recognizable type, and another which shifted disease rates upwards and only slowly attenuated as those who lived through the 1889-1917 period died.. Some previous analyses of the rise and fall of CHD mortality fit with this picture. We will present comprehensive analyses of age and sex specific all-cause, and where available cardiovascular and respiratory mortality, from up to 14 countries from 1840 to 2019 and relate these to country specific data on the experience of the 1889-95 pandemic. We will consider when this apparent effect appeared to abate in each country, within which age-sex cohorts and how rapidly. The atypical nature of the 1889-95 pandemic was noted at the time, in particular with regard to long-term neurasthenic symptomatology and the extraordinarily steep mortality curve with age. Phylogenetic dating has suggested that one of the currently circulating seasonal coronaviruses could have entered human populations for the first time around 1890, and represent the second disease mentioned by Andrewes. If this were the case, then the virus would likely have ultimately infected virtually everyone in a state of immunological naivety. We will use UK data on the post-acute outcomes of SARS-CoV-2 infection on those infected prior to vaccination and post-vaccination, and consider the implications of these for the possible long term sequelae of the recent pandemic.



**Adverse Childhood Experiences and Hypertension Risk in Adulthood: Results from Wave V of the Add Health Study.** Fahad Mansuri\* Fahad Mansuri Megan C. Barry Jill Desch Dieu Tran Skai Schwartz Chighaf Bakour

### **Background and objective**

The impact of the clustering of multiple adverse childhood experiences (ACEs) on hypertension in adulthood has not been adequately explored. We examined the association of ACEs with hypertension and assessed sex and race as effect modifiers using data from the National Longitudinal Study of Adolescent to Adult Health (Add Health).

### **Methods**

We used data from Waves I, III, IV, and V of the Add Health study. An ACE score (range: 0-9) variable indicating the total number of ACEs experienced out of the nine ACEs (physical, sexual, and emotional abuse; neglect; parental incarceration, alcoholism, divorce/separation; foster home placement; and exposure to community violence) was created and split into five categories of 0, 1, 2, 3, and 4 or more ACEs. Hypertension was defined as: SBP $\geq$ 130 mm/Hg and/or DBP $\geq$ 90 mm/Hg; taking an antihypertensive medication; and/or self-reported diagnosis of hypertension. The association between ACE score and hypertension was examined using multivariable regression analysis. Interaction terms for race and sex were included in models to examine the effect modification and the models were adjusted for participant's sex; race; age, household income, and parental education at Wave I.

### **Results**

The final sample included 5,157 participants with a mean age of 15 years at Wave I and 37 at Wave V. About 50% of the participants were female and 17% of the participants were African American. The risk of hypertension (Wave V) in participants with 0, 1, 2, 3, and 4 or more ACEs was 37.6%, 39.3%, 44.8%, 42.7% and 41.1% respectively. The adjusted RR (95% CI) of hypertension in the participants with 1, 2, 3, 4 or more ACEs (vs. 0 ACE) was 1.0 (0.9, 1.2), 1.1 (0.9, 1.3), 1.1 (0.9, 1.3), and 0.9 (0.8, 1.2) respectively. Likewise, the adjusted RD (95% CI) of hypertension in the participants with 1, 2, 3, 4 or more ACEs (vs. 0 ACE) was -0.05 (-5.2, 5.1), 4.4 (-1.7, 10.4), 2.8 (-4.8, 10.4), and -1.52 (-9.4, 6.4) respectively. There was no evidence of interaction of sex and race with ACEs score on the multiplicative or additive scales.

### **Conclusion**

Using data from the Add Health study, we found that experiencing higher number of ACEs was not associated higher risk of hypertension in adulthood. We also found no evidence of effect modification of the association between ACEs and hypertension by sex or race.

**Concordant hypertension among middle-aged and older heterosexual couples: analysis of aging cohorts from the USA, England, China, and India** Peiyi Lu\* Peiyi Lu Jithin Sam Varghese  
Peiyi Lu Daesung Choi Chihua Li

## Background

Couples share socio-economic resources and health behaviors. Previous studies based on small and regional samples reported inconsistent results of concordant hypertension between couples. Therefore, we examined how heterosexual couples' hypertension can relate to each other using large national aging cohorts from the USA, England, China, and India.

## Methods

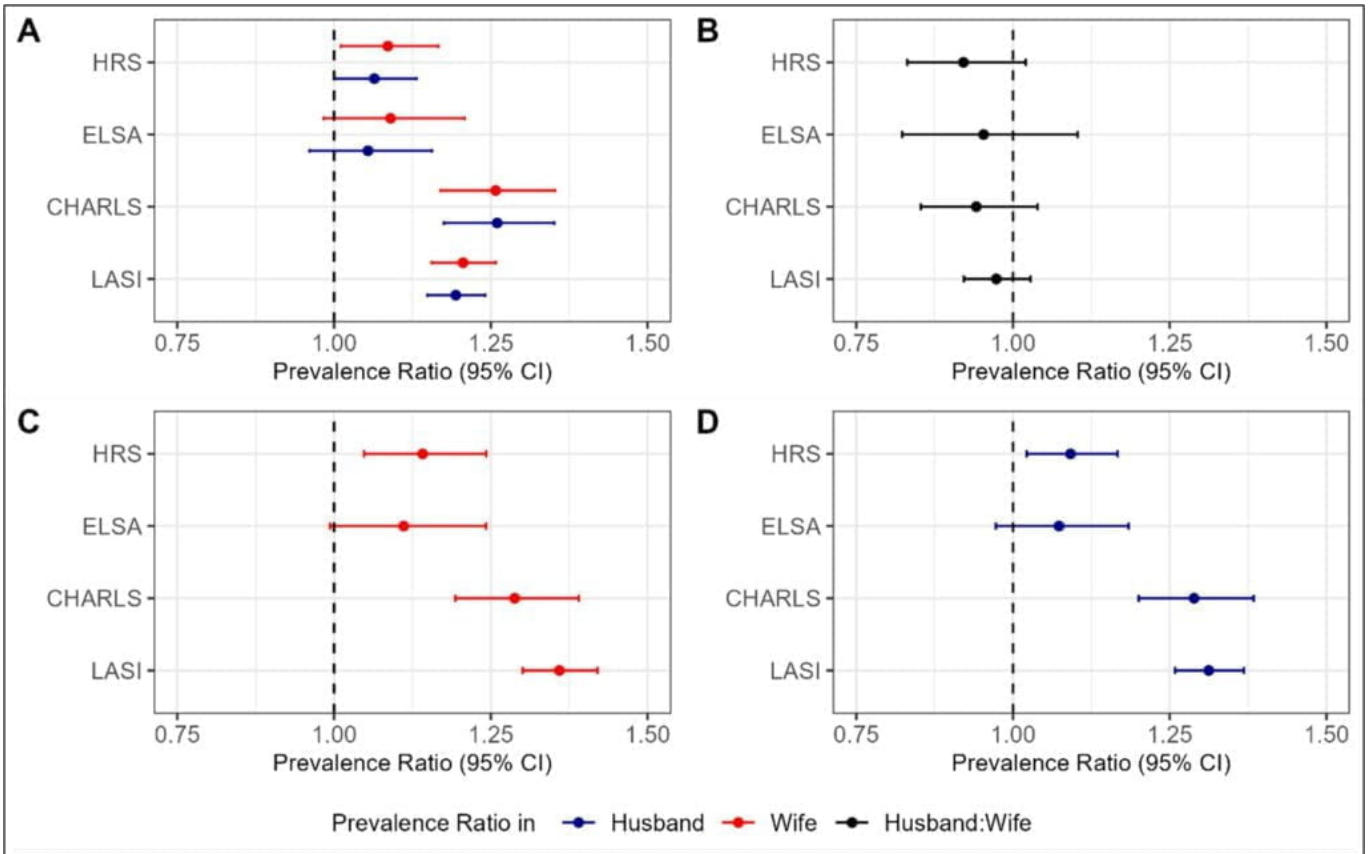
We used dyadic data of couples based on cross-sectional waves of the U.S. Health and Retirement Study (HRS 2016/17, n=3,989), English Longitudinal Study on Ageing (ELSA 2016/17, n=988 for wives and 1019 for husbands), China Health and Retirement Longitudinal Study (CHARLS 2015/16, n=5,399), and Longitudinal Aging Study in India (LASI 2017/19, n=22,389). Modified Poisson regression models were used to examine how husband's hypertension is associated with wife's hypertension and vice versa. We further examined if any gender differences exist for the association of hypertension between couples within countries and any differences exist across countries.

## Results

Couples with concordant hypertension were 37.9% (95% CI: 35.8, 40) in HRS, 47.1% (95% CI: 43.2, 50.9) in ELSA, 20.8% (95% CI: 19.6, 21.9) in CHARLS, and 19.8% (95% CI: 19.0, 20.5) in LASI. Husband's hypertension was positively associated with wife's hypertension in HRS (prevalence ratio, PR=1.09, 95% CI: 1.01, 1.17), ELSA (PR=1.09, 95% CI: 0.98, 1.21), CHARLS (PR=1.26, 95% CI: 1.17, 1.35), and LASI (PR=1.19, 95% CI: 1.15, 1.24). Similarly, wife's hypertension was positively associated with husband's hypertension in HRS (PR=1.06, 95% CI: 1.00, 1.13), ELSA (PR=1.05, 95% CI: 0.96, 1.16), CHARLS (PR=1.26, 95% CI: 1.18, 1.35), and LASI (PR=1.20, 95% CI: 1.12, 1.28). No gender differences in association estimates were observed within each country. While association estimates were comparable between HRS and ELSA, association estimates were larger among CHARLS and LASI compared to HRS.

## Conclusion

Concordance of hypertension between couples were consistently observed across countries. Couple-centered interventions may be a potential shared strategy to improve hypertension diagnosis in these countries.



**Cardiovascular health, risk of depression and anxiety: a prospective cohort study** Xu Gao, Shuzhen Liu\* Xu Gao Shuzhen Liu

**Abstract**

**Background:** Depression and anxiety are the most common mental health disorders. Recent evidence has shown the relationship between cardiovascular system dysfunction and mental health. We aimed to evaluate prospective associations of cardiovascular health (CVH) score redefined in 2022 with risk of incident depression and anxiety in 447,622 UK Biobank participants.

**Methods:** Based on the latest definition of CVH score ("Life's Essential 8"), we calculated the total score (0-800 points) based on eight metrics (0-100 points/metric) including diet, physical activity, smoking, sleep duration, body mass index, blood lipids, blood glucose, and blood pressure. Hospital records and mental health questionnaires were employed to yield the baseline prevalence and incidence of depression and anxiety. To address potential genetic confounding and gene-CVH interactions, we quantified genetic risk for both disorders using polygenic scores derived from genome-wide association studies.

**Results:** At baseline, participants with a lower CVH score more often experienced depression, anxiety, and either disorder. During the follow-up, 17,554 incident cases of either disorder were recorded. Per 100-point decrease in CVH score was significantly associated with an increased risk of incident either disorder (Hazard ratio [HR]=1.149, 95% confidence interval [CI]:1.128-1.170), depression (HR=1.232, 95% CI:1.205-1.260), and anxiety (HR=1.045, 95% CI:1.018-1.072). Sleep duration was the key metric related to the risk of depression/anxiety. A higher genetic risk could significantly enhance the impact of worsened CVH on the incidences of either disorder and depression.

**Conclusions:** Poor CVH is a risk factor for incident mental health disorders in adults and may underscore CVD promotion as a target for risk assessment and intervention of late-life depression/anxiety.

**Association between endocrine disrupting chemicals and metabolic syndrome: a cross-sectional assessment among women in the Multiethnic Cohort Study** Ugonna Ihenacho\*

Ugonna Ihenacho Lynne R. Wilkens Adrian A. Franke Chiuchen Tseng Yuqing Li Meera Sangaramoorthy Mindy Hebert-Derouen Christopher A. Haiman Daniel O. Stram Loïc Le Marchand Iona Cheng Anna H. Wu

Metabolic syndrome (MetS) is associated with a high risk of cardiovascular disease, a leading cause of death among women. MetS is defined as a diagnosis of at least three of the following: high blood pressure, high fasting glucose, high triglycerides, high waist circumference, and/or low high-density lipoprotein cholesterol. Epidemiological studies suggest that endocrine disrupting chemical (EDC) exposure is positively associated with MetS, but the evidence remains inconsistent.

In a cross-sectional study within the Multiethnic Cohort Study, we evaluated the association between EDCs and MetS among 1,728 women with health survey information along with blood and urinary biomarker data. Four classes of EDCs were specified with urinary biomarkers: bisphenol A (BPA), triclosan, parabens, and phthalates. Multivariable logistic regression was used to estimate odds ratios and 95% confidence intervals for the association between tertiles of each EDC and MetS. Models were adjusted for age, body mass index (BMI), race and ethnicity, and breast cancer status. Stratified analysis by BMI (<25, 25-<30,  $\geq 30$  kg/m<sup>2</sup>) were conducted.

MetS was identified in 519 (30.0%) women. We did not detect statistically significant positive associations for BPA, triclosan, parabens and phthalates with MetS. Instead, we observed an inverse association for MetS with total parabens and the ratio of mono(2-ethylhexyl) phthalate to the sum of mono(2-ethyl-5-carboxypentyl) phthalate and mono(2-ethyl-5-hydroxyhexyl) phthalate (MEHP/(MECPP + MEHHP);  $P_{\text{trend}}=0.03$  for each). Among women with BMI <25 kg/m<sup>2</sup> (n=788), the MEHP/(MECPP + MEHHP) ratio and the sum of 10 phthalates + phthalic acid were inversely associated with MetS ( $P_{\text{trend}}=0.03$  for each). We did not observe any statistically significant interactions by BMI.

These findings suggest associations of parabens and specific phthalate metabolites with MetS. Additional analyses are warranted with further investigation of differences in associations by BMI.

**Development of a continuous risk score for the metabolic syndrome spectrum in Taiwanese adolescents** Yu-Ting Chin\* Yu-Ting Chin Pei-Wen Wu Sharon Tsai Wei-Ting Lin Chien-Hung Lee

Metabolic syndrome (MetS) is a clustering of cardiometabolic risk factors that increases the risk of future diabetes and cardiovascular disease. Despite the importance of the diagnosis of MetS for early detection of metabolic disorders in children, the dichotomous nature of MetS appears to limit its use in cardiovascular health, especially in adolescents with low prevalence. In this study, we used the national Nutrition and Health Survey in Taiwan (NAHSIT, n=1925) to investigate heterogeneous contribution of cardiometabolic risk factors to MetS overall and in sex/age subgroups, and develop a group-specific continuous MetS risk score (cMRS) for adolescents using confirmatory factor analysis. We also used the adolescent adipo-cardiovascular axis survey (aAdiCaA, n=3295) conducted in southern Taiwan to validate the applicability of cMRS in determining 4 cardiovascular abnormal factors (CAFs), including high levels of low-density lipoprotein cholesterol, glycated hemoglobin (HbA1c) and HOMA-IR, as well as hyperuricemia. Our findings exhibited that the sex-age-specific model with 5 identified MetS components (RMSEA=0.918, CFI=0.083, SMRM=0.046) fitted better than the model with invariant loadings across groups (RMSEA=0.863, CFI=0.081, SMRM=0.086). The cMRS presented an excellent capability of identifying binary MetS in each subgroup in the NAHSIT data (AU-ROC, 0.935-0.974). The cMRS also revealed a great discriminatory ability in determining binary MetS (AU-ROC, 0.941-0.983) and  $\geq 3$  CAFs (AU-ROC, 0.865-0.957) in the aAdiCaA data. Our study provides a powerful, interpretable new measure for adolescent MetS spectrum that can be used to investigate the continuous association of MetS with other cardiometabolic disorders.

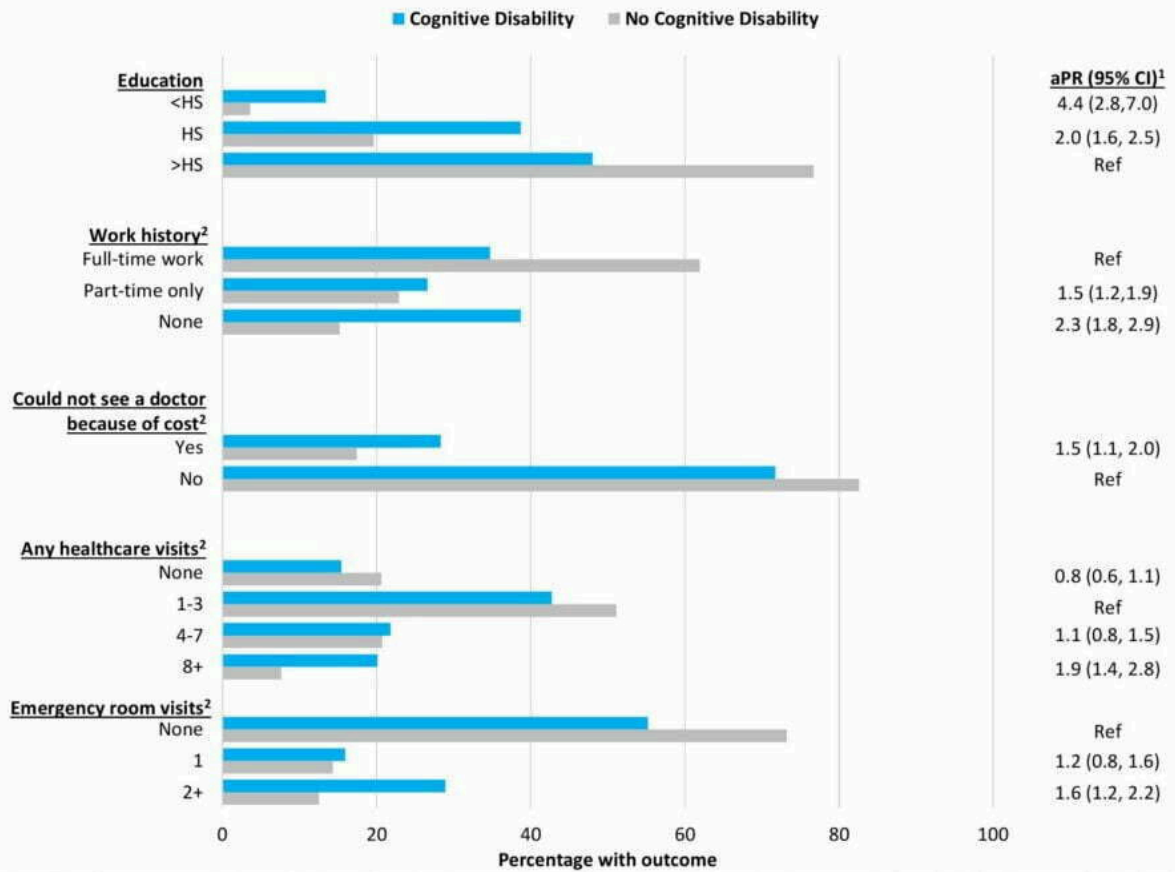
**LATEBREAKER**

Cardiovascular

**Healthcare and socioeconomic outcomes among young adults with congenital heart defects and cognitive disabilities, CH STRONG 2016-2019** Karrie Downing\* Karrie Downing Scott Klewer Wendy Nembhard Anthony Goudie Matthew Oster Sherry Farr

Cognitive disability is common among adults with congenital heart defects (ACHD). We examined socioeconomic outcomes and healthcare access/utilization among ACHD with and without cognitive disabilities. Data were obtained from population-based surveys from the Congenital Heart Survey To Recognize Outcomes, Needs, and well-beinG on 19-38-year-old ACHD without chromosomal anomalies born in Arkansas, Arizona, and Atlanta, GA. Prevalence of cognitive disability among survey respondents was standardized to the 9,312 eligible individuals by site, birth year, sex, maternal race/ethnicity, and CHD severity to reduce non-response bias. We examined education, employment, and healthcare utilization outcomes by presence of cognitive disability. Multivariable Poisson regression models generated adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) for outcomes comparing ACHD with and without cognitive disabilities. Of 1,375 respondents (34% severe CHD, 55% female, 7% Hispanic, 76% White, 27% with non-cardiac birth defects), 26% had a cognitive disability after standardization. ACHD with cognitive disabilities more commonly had <high school education (aPR=4.4, CI: 2.8-7.0), worked part-time (aPR=1.5, CI: 1.2-1.9) or were unemployed (aPR=2.3, 1.8-2.9), identified cost as a barrier to healthcare (aPR=1.5, CI: 1.1-2.0), and had  $\geq 8$  healthcare office visits (aPR=1.9, CI: 1.4-2.8) and  $\geq 2$  emergency room visits (aPR=1.6, CI: 1.2-2.2) in the previous year compared with their ACHD peers (Figure). Among ACHD with cognitive disabilities, 49% received special education, 37% had not seen a cardiologist in >5 years, and 38% ever received disability benefits. ACHD with cognitive disabilities might benefit from educational, employment, and financial resources available to individuals with disabilities, as well as accessible and tailored preventative primary and cardiology care.

Socioeconomic and healthcare outcomes of adults with CHD with and without cognitive disabilities, CH STRONG 2016-2019



aPR=adjusted Prevalence Ratio, CHD = Congenital Heart Defects, CH STRONG = Congenital Heart Survey To Recognize Outcomes, Needs, and well-being, HS= High School, Ref=Reference  
<sup>1</sup>Adjusted for age, site, sex, race/ethnicity, congenital heart defect severity, and having non-cardiac congenital anomalies. Cost and visit models also adjusted for insurance type.  
<sup>2</sup>In the previous year



**LATEBREAKER**

Cardiovascular

**Racial differences in the association between having a health insurance plan and coronary heart disease - results from a multi-year cross-sectional study** Cortez Standing Bear\* Cortez Standing Bear S. Cristina Oancea

**PURPOSE**

Coronary heart disease (CHD) is the leading cause of death for U.S. adults. American Indians/Alaska Natives (AI/AN) have the highest prevalence of no health coverage compared to other racial/ethnic groups in the U.S. This study aimed to assess the association between having a health insurance plan and CHD and determine if race significantly modifies this association.

**METHODS**

Cross-sectional data from the 2018 through 2021 Behavioral Risk Factor Surveillance System (BRFSS) were used in this study. Weighted and adjusted logistic regression models were conducted, and corresponding weighted and adjusted odds ratios (WAOR) and 95% CI were reported on the association between having a health insurance plan and CHD diagnosis. Tests for effect modification and corresponding subgroup analyses were run.

**RESULTS**

Out of the final study sample size (N=912,828), 20,643 identified as AI/AN. Among AI/AN, 1.94% were diagnosed with CHD, and 88.96% had health insurance. Among all racial subgroups, the weighted and adjusted association between having health insurance and being diagnosed with CHD was significant only among AI/AN. Further investigation revealed that the rural-urban status was a significant effect modifier among AI/AN. In urban and rural areas, the WAO of CHD were 53% significantly lower (95% CI: 0.30 - 0.75) and 167% significantly greater (95% CI: 1.17-6.08), respectively, among AI/AN with health insurance compared to those without.

**CONCLUSION**

This study's findings suggest that barriers to accessing healthcare, such as lacking health insurance coverage and living in rural areas, may significantly contribute to CHD among AI/AN. Despite having a health plan, AI/AN who live in rural areas had significantly greater odds of CHD compared to AI/AN who had a health plan in urban areas. The exacerbated odds of CHD for AI/AN in rural areas may reflect inequitable access to primary, secondary, and tertiary care for CHD.

## **Migration and all-cause mortality among adults who have initiated antiretroviral therapy: a target trial emulation study in a population-based cohort in northeastern South Africa**

Rachel Yorlets\* Rachel Yorlets Nina Joyce Hae-Young Kim Joseph W Hogan Maxime Inghels Kobus Herbst Dickman Gareta Frank C Tanser

### **Introduction**

Within-country migrants are one of the few remaining high-HIV-risk groups in South Africa. Migration and HIV is complex: adults need to be healthy to move from rural homes to urban economic opportunities, but inherent lifestyle changes increase HIV acquisition risk and challenge health care engagement. We aimed to address the knowledge gap of long-term effects of out-migration (*i.e.*, moving away from home) in men and women who have started antiretroviral therapy (ART).

### **Methods**

We followed adults aged  $\geq 15$  with HIV who initiated ART (2011-2018) in a population-based longitudinal surveillance system in KwaZulu-Natal. We used a target trial framework to design an emulation study with these observational data. We fit sex-specific marginal structural Cox models with time-varying inverse probability of treatment and censoring weights (to adjust for established predictors of HIV outcomes) to estimate the effect of out-migration on death.

### **Results**

Of the 5052 participants who started ART (2011-2018), 74% were women; mean age was 34. Nearly 9% ( $n=444$ ) died by the end of 2018; 41% of deaths were within six months of ART start. A higher proportion of deaths occurred in men, both overall and from AIDS, per verbal autopsy. On average, in the weighted pseudo-population of men, men who were always away from home after they started ART had a 7% lower hazard of death (HR: 0.93, 95% CI: 0.65-1.35) compared to men who never moved away; women who were always away from home had a 30% lower hazard of death (HR: 0.70, 95% CI: 0.48-1.02) than women who never moved.

### **Conclusion**

Death after ART initiation disproportionately affected men, which aligns with the 'missing men' phenomenon in HIV care. Out-migration may not affect men's probability of death after they start ART, but was slightly protective for women, who may move for different reasons. In both men and women, deaths within six months of ART start suggest that participants started treatment at an advanced stage of HIV.

**Studies of preventive interventions - oversimplifications of underlying causal models** Isaac Núñez\* Isaac Núñez Dalia Stern Martín Lajous

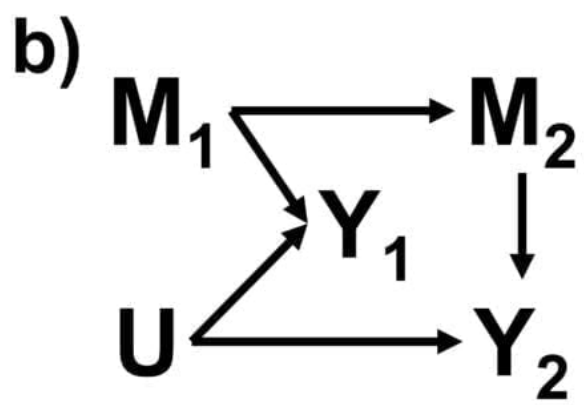
Prevention is central in medicine. Three types of preventive measures are described: primary prevention, secondary prevention, and tertiary prevention. Focusing on the first two, studies often evaluate preventive interventions without accounting for the underlying causal model of different diseases. We consider three scenarios in which the causal models implicitly assumed by stating “primary” and “secondary” prevention may not hold.

In the first scenario, causal models of primary and secondary prevention are different, and thus traditional studies primary and secondary prevention separately are correct.

In the second scenario, the causal model for secondary prevention unknowingly is almost the same as that for primary prevention, but the first event has only a minimal biological effect on new events. Here, using previous disease events as the sole inclusion criterion is inefficient and misses patients that could benefit the intervention.

In the third scenario, the first disease event does not influence posterior events but rather identifies patients with an underlying condition that predisposes them for the event of interest. That is, the causal model of the disease is the same regardless of whether we are evaluating primary or secondary interventions and using only previous events as inclusion criteria results in selection bias.

Let us use a DAG to elucidate this latter scenario. If we have observed (M) and unobserved (U) causes of deep venous thrombosis (Y) then we know that if observed causes are absent, an unobserved cause must be at play (Figure 1a). These events are called unprovoked venous thrombosis and may require anticoagulation for life (secondary prevention). However, it is likely that this represents a failure in identifying patients that would benefit from primary prevention from the start (Figure 1b). Here, U causes both events of thrombosis ( $Y_1$  &  $Y_2$ ) and  $Y_2$  is not affected by  $Y_1$ , which results in a form of M-bias.



**Studying the effectiveness of firearm policies in reducing firearm harms using causal inference** Roni Barak Ventura\* Roni Barak Ventura James Macinko Manuel Ruiz Marín Maurizio Porfiri

Firearms pose a serious public health threat in the U.S., where the number of fatalities by firearms exceeds motor vehicle fatalities. In spite of these unsettling figures, Americans still seek to hold guns for protection of their homes and families. In order to prevent firearm-related harms without limiting citizens' right to bear arms, one must identify the policies that most effectively reduce firearm harms. To this end, we investigate the causal relationships between state firearm laws, firearm ownership, and firearm deaths.

For each US state, we collected the monthly number of firearm background checks registered by the FBI and the monthly numbers of homicides and suicides committed with firearms reported on CDC's Wonder database. We also collated data about firearm-related laws from RAND's State Firearm Law Database, cataloged into 20 different law categories. Considering one US state at a time, we used information-theoretic measures to identify periods of time where a causal link between firearm ownership and firearm deaths appeared or disappeared. To establish the role firearm laws played in the dynamics of these causal links, we applied the synthetic control method.

We identified several laws that significantly reduce firearm deaths. We also pinpointed the specific legal environments that moderate these causal associations. Our findings suggest that certain sets of laws are more effective than others in reducing firearm harms in different states, offering evidence that distinct legislative approaches should be taken as a function of the specific geographic region. This analysis serves as a stepping stone for causal analysis of firearm laws and could provide initial guidance for future legislation to effectively reduce regional firearm harm rates.

**Depicting deterministic variables within directed acyclic graphs (DAGs): An aid for identifying and interpreting causal effects involving tautological associations, compositional data, and composite variables** Peter W G Tennant\* Peter Tennant Laurie Berrie Kellyn F Arnold Georgia D Tomova Mark S Gilthorpe

## Background

Deterministic variables are variables that are fully explained by one or more parent variables. They commonly arise when a variable has been algebraically constructed from one or more parent variables, known as transformed variables and composite variables respectively, and in compositional data, where the 'whole' variable is determined from its 'parts'.

Despite their popularity in health and social science research, deterministic variables are rarely depicted within directed acyclic graphs (DAGs). We discuss how explicitly including deterministic variables within DAGs can help with identifying and interpreting causal effects involving tautological associations, compositional data, and composite variables.

## Methods

We propose a two-step approach to the handling of deterministic variables when identifying and interpreting causal effects. First, a 'full' DAG is drawn that includes all deterministic variables and all determining parents. For clarity, deterministic variables should be depicted with double-outlined nodes and all their incoming arcs should be double-lined. Next, an explicit choice is made whether to focus on the deterministic variable(s) or the determining parents.

## Results

Depicting deterministic variables within DAGs bring several benefits. It is easier to identify and avoid misinterpreting tautological associations, i.e., self-fulfilling associations between variables with shared algebraic parent variables. In compositional data, it is easier to understand the consequences of conditioning on the 'whole' variable, and in turn correctly identify total and relative causal effects. For composite variables, it encourages greater consideration of the target estimand and whether the consistency and exchangeability assumptions can be satisfied.

## Conclusion

DAGs with deterministic variables are a useful aid for planning and/or interpreting analyses involving transformed variables, compositional data, and/or composite variables.

**Validating counterfactual predictions** Christopher Boyer\* Christopher Boyer James Robins  
Andrew Beam Goodarz Danaei

Counterfactual prediction methods may be required when treatment policies differ between model training and deployment settings or when the prediction target is explicitly counterfactual. However, validating counterfactual predictions is challenging as typically one does not observe the full set of potential outcomes for all individuals. We consider methods for validating a prediction model under counterfactual shifts in treatment policy. We discuss how to tailor a model for use in the same population under a counterfactual shift in treatment, how to assess its performance, and how to perform model and tuning parameter selection. We also provide identifiability results for measures of counterfactual performance for a potentially misspecified prediction model based on training and test data from the (factual) source population only. We propose both outcome and weighting estimators of counterfactual performance as well as doubly-robust estimators that can be used with data-adaptive or machine learning algorithms. We illustrate the methods using simulation and apply them to the task of developing a statin-naive risk prediction model for cardiovascular disease.

**Understanding vaccine efficacy in the counterfactual framework** Etsuji Suzuki\* Etsuji Suzuki  
Teppei Yamamoto Eiji Yamamoto

Vaccines are one of the most important concerns in public health today. In vaccine studies, vaccine efficacies are generally measured as 1 minus some measure of relative risk (RR) in the vaccinated group compared with the unvaccinated group. In this presentation, we discuss the concepts of and calculation methods for vaccine efficacy in the counterfactual framework, both with and without stratification by covariates. In this regard, we discuss some measures including preventable fraction, prevented fraction, and preventive excess fraction, and we address issues of study designs. In *Modern Epidemiology*, the preventive excess fraction (population) is explained as a measure that “is also known as the vaccine efficacy” (p. 83). By contrast, in *A Dictionary of Epidemiology*, vaccine efficacy is defined as “[the] proportion of persons in the placebo group of a vaccine trial who under ideal conditions would not have become ill if they had received the vaccine” (p. 287), which may well correspond to the preventable fraction (unexposed). This possible confusion may be caused by the fact that, if exchangeability holds (i.e., the counterfactual outcome and the actual exposure are independent), both the preventable fraction (unexposed) and preventive excess fraction (population) become equivalent to 1 minus associational RR. Vaccine efficacy is typically measured when a study is conducted under ideal conditions (e.g., clinical trials). When vaccine efficacy is estimated in ideal randomized controlled trials, the inconsistent definitions may not make a substantive difference. However, when exchangeability does not hold, the calculation method is invalid irrespective of the definitions. Once vaccine efficacy is clearly defined, one may proceed to estimate it using the appropriate formulae under certain conditions. Given the growing need to assess vaccine efficacy, it is important to have a clearer understanding of the definitions of the relevant measures to avoid confusion.



**A trial emulation analysis of statin use on dementia and death in older adults** Keran W. Chamberlin\* Keran Chamberlin Zhehui Luo Eleanor M. Simonsick Honglei Chen

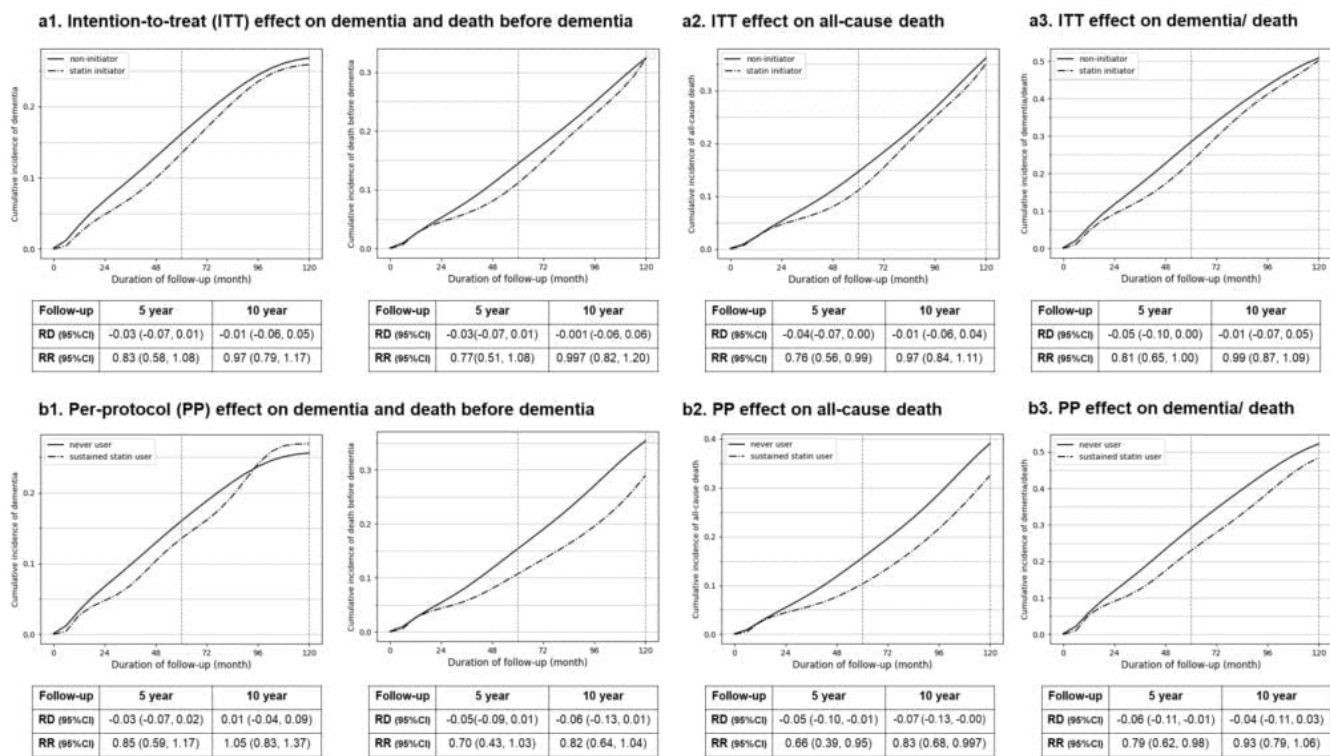
**Background:** The benefit of statin use in old adults beyond cholesterol reduction are largely unknown.

**Objective:** To examine the relationship between statin use in adults aged  $\geq 70$  years and risk reduction of dementia and premature death, using trial emulation analysis.

**Methods:** In the Health, Aging and Body Composition Study ( $n=3,075$ ), we emulated a sequence of target trials every 6 months from April 1997 to June 2003. Eligible subjects were 70-80 years, dementia-free and survived at least 6 months, and never used statins before baseline. Subjects were classified into statin initiators vs. non-initiators and followed until dementia identification, death, last contact, or the end of the 10-y follow-up, whichever came first. We estimated two-type effects of statin use on the cumulative incidence of dementia, all-cause mortality, and the composite outcome of dementia/death: 1) the intention-to-treat (ITT) effect of statin initiation and 2) the per-protocol (PP) effect of sustained statin use. We used inverse-probability-weighting in marginal structural models to account for "treatment-confounder feedback" and loss to follow-up, and bootstrapping with 500 samples to obtain the 95% CIs.

**Results:** The analysis included 2,307 unique subjects and 18,867 person-trials (412 initiators and 18,455 non-initiators), with a mean baseline age of 75 years, 53.6% women, 37.2% black, and a median follow-up of 9.5 years. Compared with non-initiators, initiators had lower risk for all-cause deaths (RD: 0.04) and dementia/death combined (RD: 0.05) for the first 5 years of follow-up, but the difference diminished with longer follow-up. PP analysis showed lasting beneficial effects of sustained statin use for all-cause mortality throughout the follow-up. Both ITT and PP analyses showed lower but non-statistical differences in dementia risk between statin users and nonusers.

**Conclusion:** In adults 70 years or older, statin use modestly reduces mortality, but its effect on dementia was not evident.



**Figure 1. The cumulative incidence plot of different effect types and outcomes. a)** intention-to-treat effect: a1) dementia and death before dementia; a2) all-cause death; a3) dementia/ death; **b)** per-protocol effect: b1) dementia and death before dementia; b2) all-cause death; b3) dementia/ death.

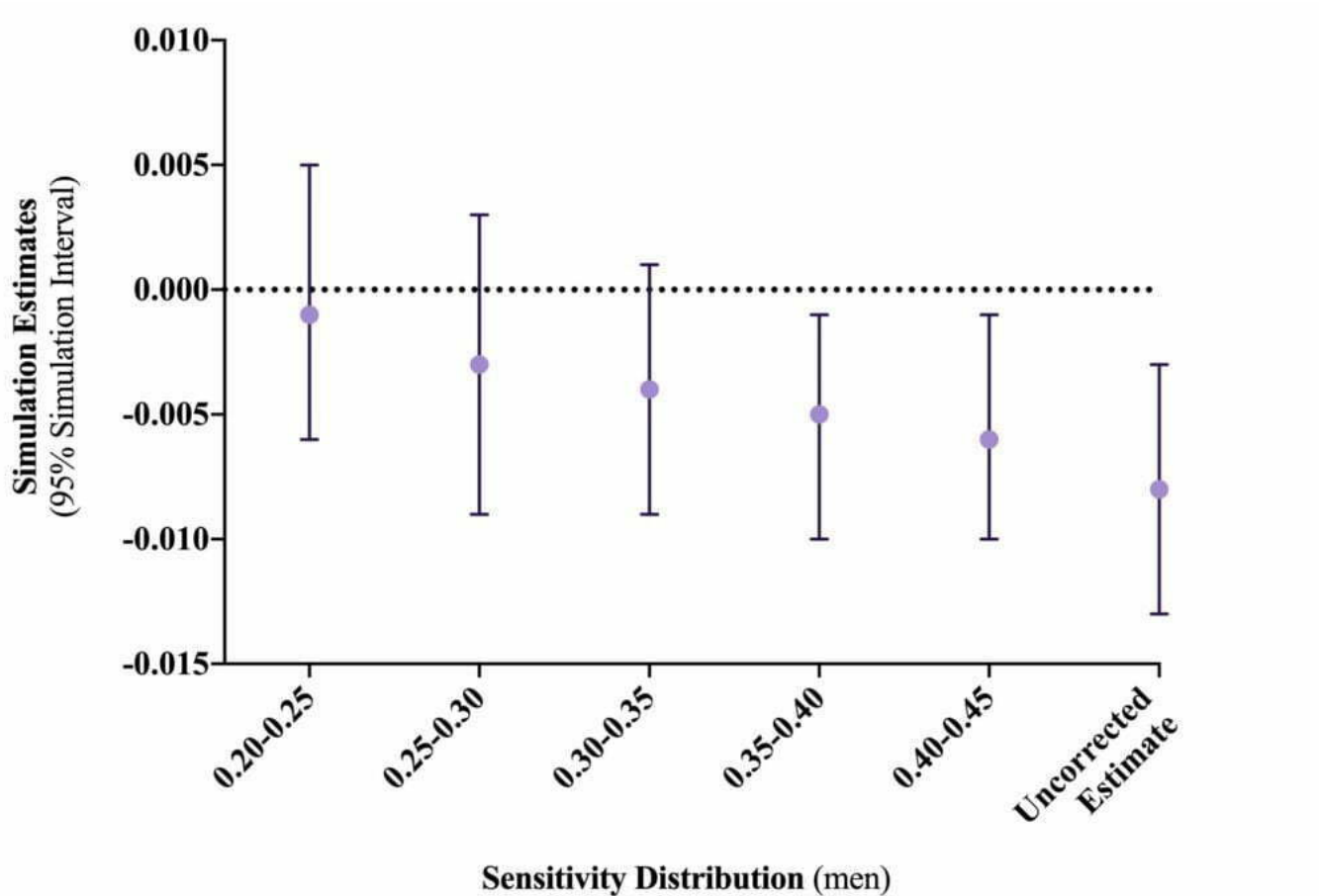
**Could differential under-reporting of loneliness between men and women bias the gender-specific association between loneliness and memory aging? A quantitative probabilistic bias analysis** Xuexin Yu\* Xuexin Yu Laura Zahodne Alden Gross Belinda Needham Kenneth Langa Tsai-Chin Cho Lindsay Kobayashi

**Background:** Loneliness is associated with later-life dementia risk, with conflicting findings on gender as an effect modifier. The causality of this effect modification is difficult to assess, as men may have a lower propensity than women to admit loneliness potentially due to self-perceived “masculinity”, leading to distorted gender-specific estimates. We aimed to estimate the potential magnitude of information bias due to differential loneliness under-reporting by gender in the gender-specific associations between loneliness duration and memory aging.

**Methods:** Data were from respondents aged  $\geq 50$  in the US Health and Retirement Study from 1996-2016 (N=9,032). We conducted quantitative probabilistic bias analyses to simulate various bias-parameter selections and reclassify loneliness status (yes; no) at the record level as measured biennially from 1996-2004. We used sensitivity values of loneliness self-reports of 0.20-0.45 among men and 0.30-0.55 among women, and specificity values of 0.90-1.00, as informed by a validation analysis. We ran mixed-effects linear regression models on the corrected data with a three-way interaction between loneliness duration (0, 1, 2, or  $\geq 3$  time points), years of follow-up (0-12), and gender (men; women) to test gender differences in the association between loneliness duration and memory decline (100 replications).

**Results:** Compared to the uncorrected estimate (-0.008), mean estimates of the three-way interaction attenuated in magnitude, ranging from -0.006 (sensitivity 0.40-0.45 for men and 0.50-0.55 for women) to -0.001 (sensitivity 0.20-0.25 for men and 0.30-0.35 for women; see Figure 1). Approximately 64%, 84%, 96%, and 100% of simulation estimates remained negative while holding sensitivity distribution at 0.20-0.25, 0.25-0.30, 0.30-0.35, and  $>0.35$  among men, respectively.

**Conclusion:** The likelihood of observing gender-specific loneliness-memory relationship reduces as sensitivity values of loneliness self-reports declines.



**Figure 1.** Simulation interval for the three-way interaction between cumulative loneliness over time, years of follow-up, and gender, the US Health and Retirement Study, 1996-2016 (N=9032). For each set of sensitivity distributions, the sensitivity values among women are 0.1 higher than those among men (e.g., 0.20-0.25 among men vs. 0.30-0.35 among women). The sensitivity distributions were chosen based on a validation analysis comparing the single-item measure of loneliness used in this analysis against the 3-item UCLA loneliness scale from the HRS Leave Behind Questionnaire in 2006.

**Burden and impact of post-COVID-19 conditions among adults experiencing sheltered homelessness in King County, WA between September 2020 - April 2022** Sarah Cox\* Sarah Cox Emily M. Scott Julia H. Rogers Eric J. Chow Jessica K. Wasse Marco Carone James P. Hughes Helen Y. Chu

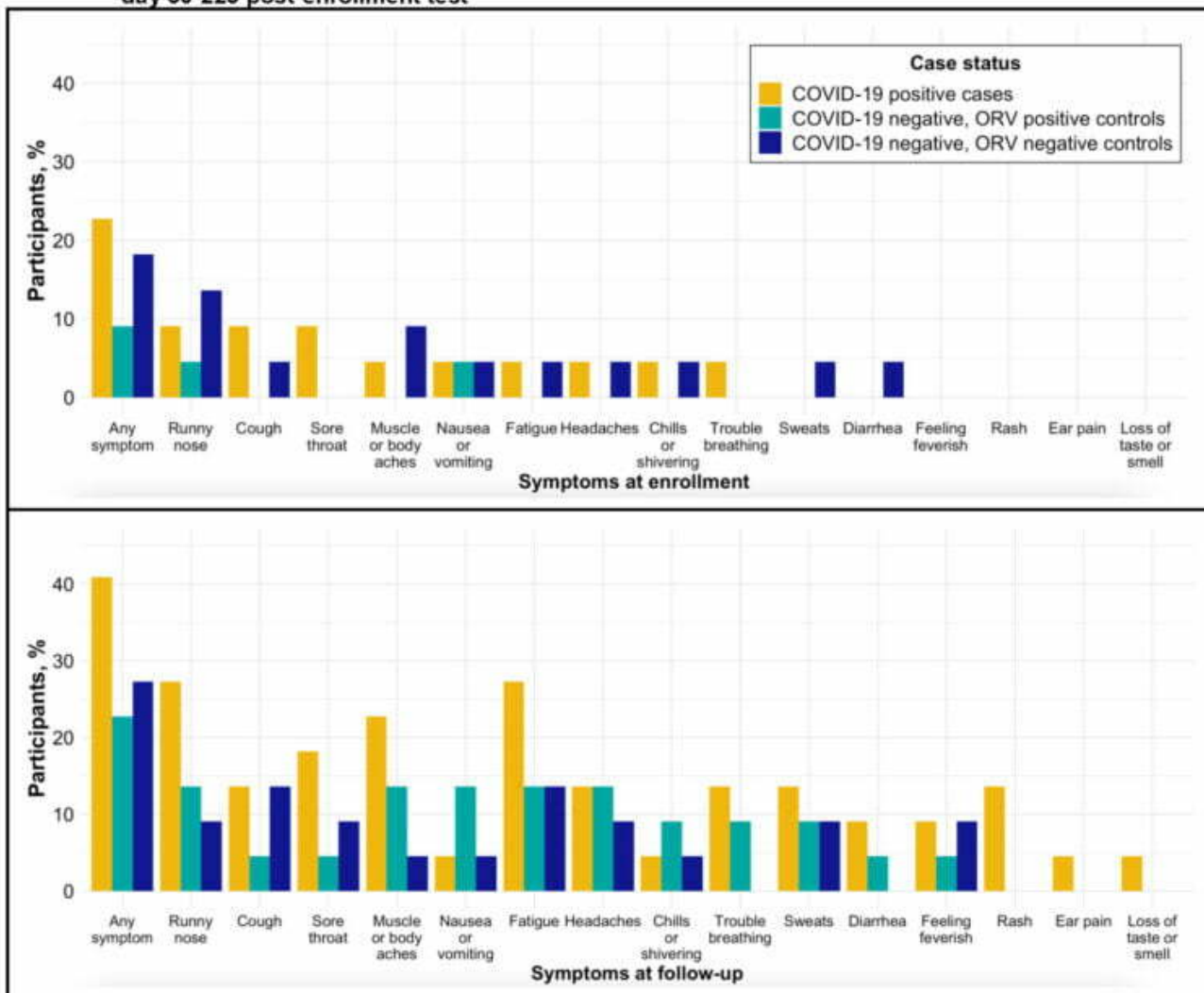
Introduction: People experiencing homelessness (PEH) are at increased risk for COVID-19, but the burden of post-COVID-19 conditions is unknown.

Methods: We conducted a matched prospective cohort study to assess the prevalence, characteristics, and impact of post-COVID-19 conditions among sheltered PEH in Seattle, WA between September 2020-April 2022. Adults  $\geq 18$  years across 9 homeless shelters with active respiratory virus surveillance were eligible to complete in-person baseline surveys and interval follow-up phone surveys. We included a subset of 22 COVID-19 positive cases and 44 COVID-19 negative controls matched on age and sex. Among controls, 22 were positive & 22 were negative for one of 27 other respiratory virus pathogens. To assess the impact of COVID-19 on the risk of symptom presence at follow-up (day 30-225 post-enrollment test), we performed log-linear regression with robust standard errors, adjusting for confounding by shelter site and demographic variables determined *a priori*.

Results: Of 53 eligible COVID-19 cases, 22 (42%) completed  $\geq 1$  follow-up survey. While 5 (23%) cases reported  $\geq 1$  symptom at baseline, this increased to 77% (10/13) between day 30-59 and 33% (4/12) day 90+. The most commonly reported symptoms day 30+ were fatigue (27%) and rhinorrhea (27%), with 8 (36%) reporting symptoms that interfered with or prevented daily activities. Four (33%) symptomatic cases reported receiving medical care outside of a provider at an isolation facility. Of 44 controls, 12 (27%) reported any symptoms day 90+. Risk of any symptoms at follow-up was 5.4 times higher among COVID-19 cases compared to controls (95% CI: 2.7-10.5).

Conclusions: Shelter residents reported a high prevalence of symptoms 30+ days after their SARS-CoV-2 detection, though few accessed medical care for persistent illness. The impact of COVID-19 extends beyond acute illness and may exacerbate existing challenges that marginalized populations face in maintaining their health and wellbeing.

**Figure 1. Symptoms reported by COVID-19 & Other Respiratory Virus (ORV) case status day 30-225 post-enrollment test**



**Racial discrimination in healthcare settings and mental health among adults diagnosed with COVID-19 in Michigan** Soomin Ryu\* Soomin Ryu Jana L. Hirschtick Kristi L. Allgood Robert Orellana Nancy L. Fleischer

**Background:** The COVID-19 pandemic has highlighted existing racial discrimination in accessing and receiving healthcare. Racial and ethnic minoritized populations have been at increased risk of the consequences of healthcare discrimination due to the intersecting stigma of COVID-19 and race.

**Methods:** Using a population-based probability sample of adults with confirmed SARS-CoV-2 infection in Michigan prior to March 1, 2022, we examined how measures of perceived racial discrimination in individuals (1) seeking health care for COVID-19 (n=4,133) and (2) receiving testing/treatment for COVID-19 (n=4,181) were associated with the presence of depressive and anxiety symptoms. We conducted a modified Poisson regression analysis with robust standard errors to estimate associations between each measure of racial discrimination and each mental health outcome separately, adjusting for age, sex, race/ethnicity, marital status, education, income, employment status, health insurance, and pre-existing conditions.

**Results:** Perceived racial discrimination in seeking healthcare for COVID-19 (2.4%) and getting testing/treatment for COVID-19 (3.5%) was uncommon. However, such experiences were associated with increased reporting of depressive symptoms. Adults who experienced racial discrimination in seeking healthcare had 1.73 times higher prevalence of reporting depressive symptoms (95% CI: 1.21-2.48) compared to adults who did not. Moreover, adults who experienced racial discrimination in getting testing/treatment had 1.79 times higher prevalence of reporting depressive symptoms (95% CI: 1.38-2.33) than adults who did not. Neither measure of racial discrimination was associated with anxiety symptoms in adjusted models.

**Conclusion:** This research highlights the need for developing anti-racist discrimination policies, educational programs, and awareness efforts in healthcare settings.

**Impact of the First Year of the COVID-19 on Unmet Healthcare Need Among New York City Adults: A Universal Healthcare Experiment** Madelyn Carlson\* Madelyn Carlson Elizabeth A. Kelvin, PhD, MPH Matthew L. Romo, PharmD, PhD, MPH

**Objectives.** To examine the impact of the first year of the COVID-19 pandemic on unmet healthcare need among New Yorkers and potential differences by race/ethnicity and health insurance.

**Methods.** We used data from the Community Health Survey, collected in 2018, 2019 (pre-COVID-19), and 2020 (first year of the COVID-19 pandemic), were merged to compare unmet healthcare need within the past 12 months during the pandemic versus the two years before the pandemic. Simple and multivariable logistic regression models evaluated change in unmet healthcare need overall and we assessed whether race/ethnicity or health insurance status modified the association.

**Results.** Overall, 12% of New Yorkers (N = 27,660) experienced unmet healthcare during the three-year period. In both univariate and multivariate models, the first year of the pandemic was not associated with unmet healthcare need (OR: 1.04,  $P = 0.548$ ; OR: 1.03,  $P = 0.699$ , respectively). There was no evidence of interaction between the first year of the pandemic and race/ethnicity in predicting unmet healthcare need ( $P$ -values range: 0.081-0.893), but there was significant interaction with health insurance status (interaction  $P = 0.009$ ). After stratifying on health insurance status, those without health insurance had lower odds of unmet healthcare need during the first year of the pandemic compared to the two years before that was of borderline significance (OR=0.72,  $P = 0.051$ ).

**Conclusion.** The proportion of New Yorkers who experienced unmet healthcare need during the first year of the pandemic did not differ significantly from the two years prior, 2018-2019. Federal pandemic relief funding, which offered no-cost COVID-19 testing and care to all Americans, irrespective of health insurance or legal status, may have equalized access to healthcare, improving access for groups historically lacking access such as the uninsured.



**New Criteria for Diagnosing and Controlling an Epidemic Derived from a New Solution to the Complete Kermack and McKendrick Equations** Theodore G Duclos\* Ted Duclos Thomas

We found a closed form solution to the full Kermack and McKendrick integro-differential equations (KMIDE) which we call the KMES. The solution can be used to generate analytical expressions for characterizing and managing an epidemic, e.g., the viral load, final size, effective reproduction number, time to the peak in infections; and can be verified using data from the Covid 19 pandemic.

Since the publication of Kermack and McKendrick's seminal paper in 1927, many authors have utilized Susceptible, Infected, and Recovered (SIR) models to approximately characterize the behavior of epidemics. Use of the SIR approximation implicitly assumes that it adequately characterizes the dynamics of the KMIDE. This assumption is flawed.

A feature of SIR models is the phenomenon, "flattening the curve". In SIR models, strong social measures, such as isolation, project a delay in the peak in new cases, which can lead to severe, economic consequences, and disquiet in political leaders and the affected population. The KMES demonstrates that SIR models are not adequate representations of either the KMIDE or epidemic dynamics. Strong containment measures do not extend the length of an epidemic; but rather, with stronger interventions, they shorten the epidemic by significantly attenuating the peak in cases and moving it to an earlier time. There is simply no need to trade off control against economic hardship.

Using only two parameters, the KMES enables the calculation of the reduction in the number of average infectious contacts required to decelerate and end an epidemic. This calculation only requires information from a short segment of the most recent data on known infections. Expressions for the relative change in contact number required to produce a desired rate of change in new cases will also be shown. So equipped, public health officials can provide ongoing guidance to the populace to achieve case control; and decelerate the epidemic at a rate that is economically tolerable.

**Association between physical activity and subjective stress in university students during the COVID-19 pandemic: 24 h movement behavior and metabolic syndrome (24h-MESYN) study**

Marcus Vinicius Nascimento Ferreira\* Marcus Vinicius Nascimento-Ferreira Evanilson Alves dos Santos Armando Rodrigues de Alencar Santos Antonio Gibran de Almeida Cardoso Maíra Tristão Parra Alaiana Marinho Franco Francisco Leonardo Torres-Leal Heráclito Barbosa de Carvalho Kliver Antonio Marin

**Objective:** To test the association between physical activity and subjective stress in university students during the COVID-19 pandemic.

**Methods:** This is a cross-sectional study that evaluated 195 university students (68.7% females; 44.6% aged between 21 to 25 years; 65.8% enrolled in a health sciences degree; 24.5% enrolled in the 1<sup>st</sup> to 3<sup>rd</sup> semester) aged 17 to 52 years. Data were collected during the first semester of 2021 in the city of Imperatriz, Maranhão, Brazil (Gini Index of 0.56). We collected data online using the Perceived Stress Scale (14-item) and the International Physical Activity Questionnaire (short-version, 8-item). We assessed scores of positive and negative stress dimensions as outcomes (representing perceived self-efficacy and helplessness, respectively), while walking and moderate-to-vigorous physical activity were the independent variables (as minutes/day). The potential confounding variables were biological sex; age; ethnicity; maternal education; degree program (health sciences degree or other undergraduate degree), shift (morning, evening, night or integral), time ( $\leq$  3rd semester or  $>$  3rd semester), number of classes enrolled and, hours of study per day. We assessed the associations using multilevel linear regression models. To retain variable in the multivariate model, we adopted a significance level of 80.0% ( $p \leq 0.20$ ).

**Results:** After adjusting the models for biological sex, age, ethnicity, and degree program time, we observed that higher walking levels ( $\beta = 0.02$  [95% CI 0.001 to 0.03]) were associated with higher scores on the positive dimension of perceived stress.

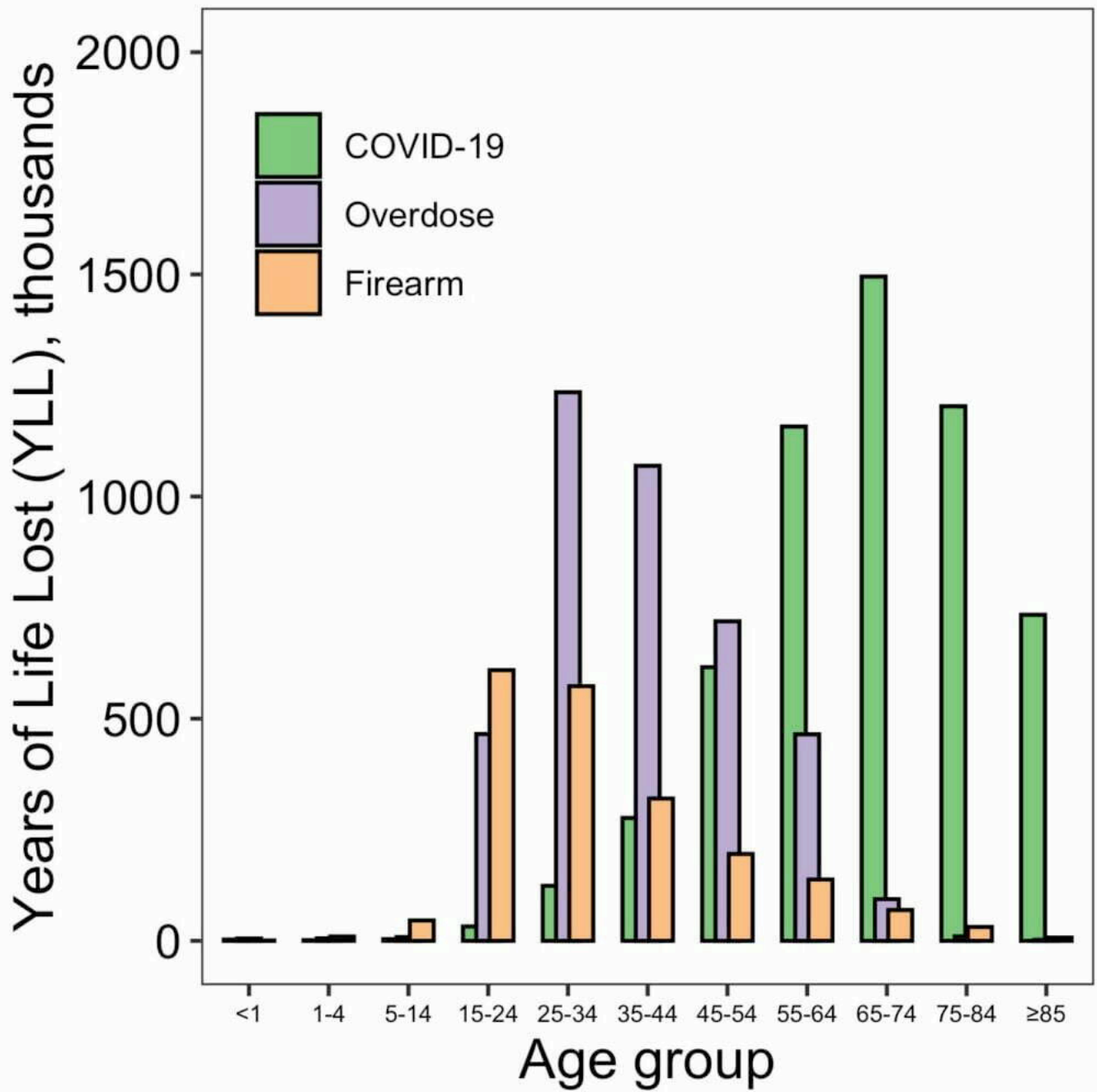
**Conclusion:** Walking was associated with perceived stress. Thus, light physical activity may reduce perceived stress by increasing self-efficacy perception in university students from low-income region during the COVID-19 pandemic.

**Pre-existing conditions associated with post-acute sequelae of COVID-19** Kristen Pogreba-Brown\* Kristen Pogreba-Brown Elizabeth Jacobs Collin Catalfamo Paulina Colombo Sana Khan Erika Authof Felina Cordova-Marks Kacey Ernst Leslie V. Farland

Post-acute sequelae of COVID-19 (PASC) are conditions that occur or remain at least 28 days after SARS-CoV-2 infection. While some risk factors for PASC have been identified, little is known about pre-existing conditions that render one susceptible to developing PASC. Data from participants (n=1,224) in a longitudinal COVID-19 cohort study in Arizona (AZ CoVHORT) were used to investigate comorbid conditions associated with PASC. After adjustment of the models for age, BMI, gender, race, and smoking, the following pre-existing conditions were statistically significantly associated with the development of PASC: asthma (OR=1.54; 95% CI=1.10-2.15); chronic constipation (OR=4.29; 95% CI=1.15-16.00); reflux (OR=1.54; 95% CI=1.01-2.34); rheumatoid arthritis (OR=3.69; 95% CI=1.15-11.82); seasonal allergies (OR=1.56; 95% CI=1.22-1.98); and depression/anxiety (OR=1.72; 95% CI=1.17-2.52). When grouping conditions together, statistically significant associations with PASC were observed for respiratory (OR=1.47; 95% CI=1.06-2.14); gastrointestinal (OR=1.62; 95% CI=1.16-2.26), and autoimmune conditions (OR=4.38; 95% CI=1.59-12.06). After adjustment for severity of acute SARS-CoV-2 infection and depression/anxiety, seasonal allergies (OR=1.48; 95% CI 1.15-1.91) and autoimmune disease (OR=3.78; 95% CI-1.31-10.91) remained significantly associated with risk for PASC. These findings indicate that numerous pre-existing conditions may be associated with an increased risk for the development of PASC. Patients with these conditions should consider taking extra steps to avoid infection.

**Preventable premature mortality across three causes of death in the United States:  
Overdose, firearm injury, and COVID-19** Alexandra Skinner\* Abigail Cartus Alexandria Macmadu  
Josiah Rich Magdalena Cerdá

Firearm injury, overdose mortality, and COVID-19 represent three important causes of preventable and premature mortality in the United States. While these are all public health problems of urgent import, they have vastly different age-specific impacts and mortality rates. In order to contextualize the burden of preventable and premature mortality attributable to each of these three causes, we compared mortality rates and years of life lost (YLL) (as well as years of potential life lost, YPLL) across all three causes using national data (CDC WONDER) from 2020. While COVID-19 mortality rates are the highest in older age groups, particularly age groups  $\geq 65$ , the burden of YLL and YPLL is highest for overdose because overdose disproportionately affects younger and mid-life adults. Both mortality rates and YLL calculations of premature mortality should be evaluated for public health challenges of national import and with age-specific effects.



**Sensitivity and specificity of a saliva antibody-test for the assessment of past SARS-CoV-2 infection in pediatric and adult seroprevalence studies: A Bayesian latent class analysis.**

Joanna Merckx\* Joanna Merckx Nandini Dendukuri Mariska Leeftang Mathieu Roelants Els Duysburgh Isabelle Desombere

**Background** The validity of seroprevalence studies depends on the study population sampling frame and diagnostic accuracy of the test. Saliva tests can replace more invasive serum tests if they are sufficiently accurate and we know their sensitivity and specificity. This study evaluates and compares the diagnostic accuracy of saliva and serum tests for SARS-CoV-2 and their use in sero-epidemiologic studies.

**Methods** We collected paired serum and saliva samples in three prospective seroprevalence studies in Belgian schoolchildren and adults between August 2020 and March 2021. Serum samples were analyzed with a commercial IgA/M/G SARS-CoV-2 RBD-ELISA assay. An in-house adapted assay measured RBD-IgG in saliva. We used Bayesian latent class analysis, not assigning the role of perfect reference standard to either test. We applied the Hui-Walter model making use of the difference in prevalence between PCR positives and negatives using non-informative priors and allowed for conditional dependency.

**Results** In a mixed pediatric (N=129) and adult (N=157) population, the saliva test had a sensitivity of 88.6% (95%CrI 78.9 to 95.3) and a specificity of 94.9% (95%CrI 89.5 to 98.1). Serum sensitivity and specificity were 97.6% (95% CrI 90.5;99.9) and 96.0% (95% CrI 90.1;99.4). The estimated prevalence in this synthetic population was 24.7% (95%CrI 19.3; 29.3) compared to 25.9% (95%CrI 21.1;31.2) and 27.3% (95%CrI 22.4;32.6) using observed saliva or serum positives, respectively. Without correction for its accuracy, observed prevalences of <31% using saliva positives overestimate the population prevalence, and underestimate the prevalence when higher.

**Conclusion** Saliva tests for the assessment of past infection are less accurate compared to serum tests, however provide a less invasive, child friendly alternative with acceptable accuracy to study SARS-CoV-2 in sero-epidemiologic studies. Conditional on correcting for test characteristics their use is favorable above serum tests.

**Domestic violence and loneliness and incidents of suicidal ideation among Japanese perinatal women during COVID-19 pandemic** Midori Matsushima\* Midori Matsushima Naoki Kondo Hiroyuki Yamada Takahiro Tabuchi

Suicide rates elevated during COVID-19 pandemic among Japanese women, yet the reasons are unknown. Particularly, perinatal women are high-risk group as they are more prone to psychosocial issues emerged during the pandemic: domestic violence (DV) and loneliness. Using panel data over two time periods (July-August 2021 and January-February 2022) from a nationwide web survey (n=3101), we aimed to reveal how the new onset of DV and loneliness associated with the new onset of suicidal ideation over the two surveys. In analysis, we used multinomial regression model. Four different groups were set as an outcome variable: the one who never had suicidal ideation for their entire life (*Resilient* group), the one who had been having with suicidal ideation throughout two time periods of the surveys (*Persistent* groups), the one who did not have suicidal ideation in the first survey but newly onset in the second survey (*Onset* group), and the one who had suicidal ideation in the first survey but recovered by the second survey (*Recovered* group). Exposure variables were DV and moderate-to-severe loneliness, and they were created as: never experienced, the one who had been experiencing it throughout two surveys, the one who did not experienced it in the first but newly onset in the second survey, and the one who experienced it in the first but ended by the second survey. By adjusting possible confounders including demographic and economic characteristics, results showed that the new onset of DV raised the risk of becoming the *Onset* (Odds ratio (OR) 3.0 and 95% Confidence Interval (CI)[1.7-5.3]). The new onset of loneliness also raised the risk of new onset of suicidal ideation with OR 9.2 [95% CI (4.5-18.8)]. The one who experienced DV in the first survey but ended by the second survey were more likely to be recovered from having suicidal ideation. Same results were obtained for loneliness. DV and loneliness could be the important targets for the pandemic-related suicide prevention.

**LATEBREAKER**

COVID-19 Pandemic

**Characterizing the socio-spatial distribution of excess mortality in Michigan during the COVID-19 pandemic** Kelly Broen\* Kelly Broen Jon Zelner Krzysztof Sakrejda

Data and analytic challenges associated with measuring the burden of infection and mortality from COVID-19 have been central challenges to effective disease surveillance and resource allocation since the beginning of the pandemic. To assess the scale of the gap between official estimates of SARS-CoV-2 mortality and the true burden of mortality from COVID-19 in Michigan during the period from March 2020 through June 2022, we used fine-scale spatiotemporal information on cause-specific mortality to characterize spatial and sociodemographic variation in excess mortality attributable to respiratory infection. We assess mortality trends across six distinct phases of the COVID-19 pandemic which are defined by variation in lockdown stringency, vaccination coverage, availability of effective antivirals, and viral shifts in infectiousness and case-fatality. We estimated area-specific excess mortality using a hierarchical Bayesian Poisson regression model including sociodemographic covariates at the census tract level. We found that the rate of excess mortality from respiratory infection was greatest during the first phase of the pandemic (March-May 2020), when there were an average of 5.9 excess deaths per expected death (95% CI: 3.0 - 8.7), and lowest during the second phase of the pandemic, (June-August 2020), when there was an average of 4.6 excess deaths per expected death (95% CI: 1.8 - 7.5). Mortality from respiratory infections remains elevated throughout the sixth analyzed pandemic phase (December 2021 - June 2022; 4.6 excess deaths per expected, 95% CI: 2.0 - 7.3). These results demonstrate that the COVID-19 pandemic continues to produce large increases in excess mortality from respiratory infection above the pre-pandemic baseline, and that these deaths are only partially captured by official data.



**LATEBREAKER**

COVID-19 Pandemic

**The relationship of the presence of cancer history and chronic diseases on colorectal cancer screening during COVID-19 pandemic** Meng-Han Tsai\* Meng-Han Tsai Alice Lee

**Purpose:** Our study aimed to examine whether having a history of cancer and chronic diseases is associated with guideline-concordant colorectal cancer (CRC) screening use during the SAR-COV-2 (COVID-19) pandemic.

**Methods:** We used data from the 2020 and 2021 Behavioral Risk Factor Surveillance System in Oregon and West Virginia with available information on CRC screening. Guideline-concordant CRC screening was the outcome of interest. The exposure was having a history of cancer, chronic diseases (i.e., diabetes, coronary heart disease or myocardial infarction, stroke, chronic obstructive pulmonary disease, etc.), or both. Descriptive statistics and multivariable logistic regressions were applied to assess the abovementioned association.

**Results:** Among 10,373 respondents, 74.8% of those with a history of cancer and chronic diseases and 51.8% of those without these conditions had guideline-concordant CRC screening use (p-value <0.05). In multivariable analysis, having a history of both cancer and chronic diseases (OR, 1.44; 95%CI, 1.20-1.72) or having one of the two (OR, 2.23; 95%CI, 1.65-3.01) were positively associated with screening uptake compared to respondents without any history. Regardless of cancer /chronic disease status, older age was associated with greater CRC screening uptake (p-value<0.05). Further, those who have a health care provider were over 2-fold increased odds of receiving CRC screening among respondents with either condition or without any (p-value<0.05).

**Conclusions:** Having a history of cancer and chronic diseases to be strongly associated with guideline-concordant CRC screening use during the COVID-19 pandemic. This suggests that effective implementation of patient centered communication through primary care initiatives may increase adherence to screening recommendations across different cancer/chronic disease status. More data is also needed to examine whether these findings persist in the U.S. after the pandemic.

**LATEBREAKER**

COVID-19 Pandemic

**What role does public health unit engagement in school mental health programs play in adolescent mental health in COVID-19? Results from the COMPASS study 2018-2022** Claire Benny\* Claire Benny Brendan T. Smith Karen A. Patte Scott T. Leatherdale Roman Pabayo

**Introduction.** Public health unit (PHU) engagement in schools can be key to promoting wellness in adolescents and research suggests such engagement during the COVID-19 pandemic benefited the mental health of some sociodemographic groups. We hypothesize that PHU engagement with school mental health programs may be protective of the risk of depression and anxiety in students during the COVID-19 pandemic.

**Methods.** We used longitudinal data from the Cannabis, Obesity, Mental health, Physical activity, Alcohol use, Smoking, and Sedentary behaviour (COMPASS) survey between the 2018/19-2020/21 academic years. Multilevel linear models were used to assess the association between PHU engagement with mental health school programs and depression [10-item Center for Epidemiologic Studies Depression scale Revised (CES-D)] and anxiety scores [7-item Generalized Anxiety Disorder scale (GAD-7)] during COVID-19.

**Results.** The sample included 5,054 students across 77 secondary schools in British Columbia, Alberta, Ontario, and Quebec. Most students were female (60.0%), white (80.5%), and were 14 years of age on average (SD= 1.36). Adjusted models showed that in schools that reported any PHU engagement with mental health services, students had lower depressive (B=-0.22, 95% CI -0.41, -0.03) and anxiety (B=-0.22, 95% CI=-0.40, -0.04) scores in COVID-19. Similarly, in schools that reported solving problems jointly with public health units, students reported a decrease in depressive (-0.09, 95% CI= -0.17, -0.03) and anxiety (B=-0.08, 95% CI=-0.15, -0.02) scores in the pandemic. Other types of PHU involvement in school mental health programs were not statistically significantly associated with student mental health in COVID-19.

**Discussion.** PHU engagement with mental health programming in schools was protective against depression and anxiety risk for students during COVID-19. These findings can inform discussion on the investment in PHUs for improving mental health and pandemic recovery within schools.

**LATEBREAKER**

## COVID-19 Pandemic

**Mortality Rates of SARS-CoV-2 Variants in Turkey** Ayse Ulgen\* Ayse Ulgen Pervin Ozlem Balci Meryem Cetin Sirin Cetin Wentian Li

**Objective:** The aim is to estimate mortality rates caused by different SARS-CoV-2 variants in Turkey. **Methods:** 2578 COVID-19 patients are collected from 2020-2021 from the Tokat State Hospital. Besides 4 samples with multiple variants (three samples with alpha and delta variants, and one sample with alpha and beta variant), there are 269 samples with delta, 542 with alpha, 39 with beta, and 408 without these three variants. The delta variant is determined by the presence of L452R mutation. 39 beta variant samples include 4 that are labeled with the E484K mutation. **Results:** Disease severity distribution is determined by if a patient is outpatient (not-severe) or inpatient (severe). Distribution of COVID-19 inpatients and mortality rates in 2020 and 2021 samples are as follows, respectively: 161 (12.2%) and 163 (12.9%) for inpatients ; and

66 (5%) and 37(2.9%) for mortality rates. This almost 40% reduction in mortality rate from 2020 to 2021 might be explained by the wide availability of vaccine and improvement of treatment of COVID-19 patients. Median age values in the total of 2020 and 2021 samples are as follows, respectively: 47.8 and 44.7 years (p-value<0.001). The age difference between 2020 and 2021 is even more striking for outpatients, respectively: median/mean age 44/44.9 and 38/41.6 years ~ (p-value<0.001). For inpatients, the median/mean distribution for inpatients is as follows respectively; 71/69.0 and 67/65.6 years (p-value=0.04). It is observed that vaccine has an impact on the age distribution in 2021; as older population were vaccinated first and with a higher proportion. For gender differences, while 39.7% of the 2020 COVID-19 patients are male, this percentage is increased to 44.8% in 2021 (p-val=0.0095). This may be due to higher number of male outpatients in 2021 compared to 2020 (opposite trend in inpatients). **Conclusion:** Distribution of SARS-CoV-2 Variants may give a clue about mortality rates of patients and aid in health policy and management.

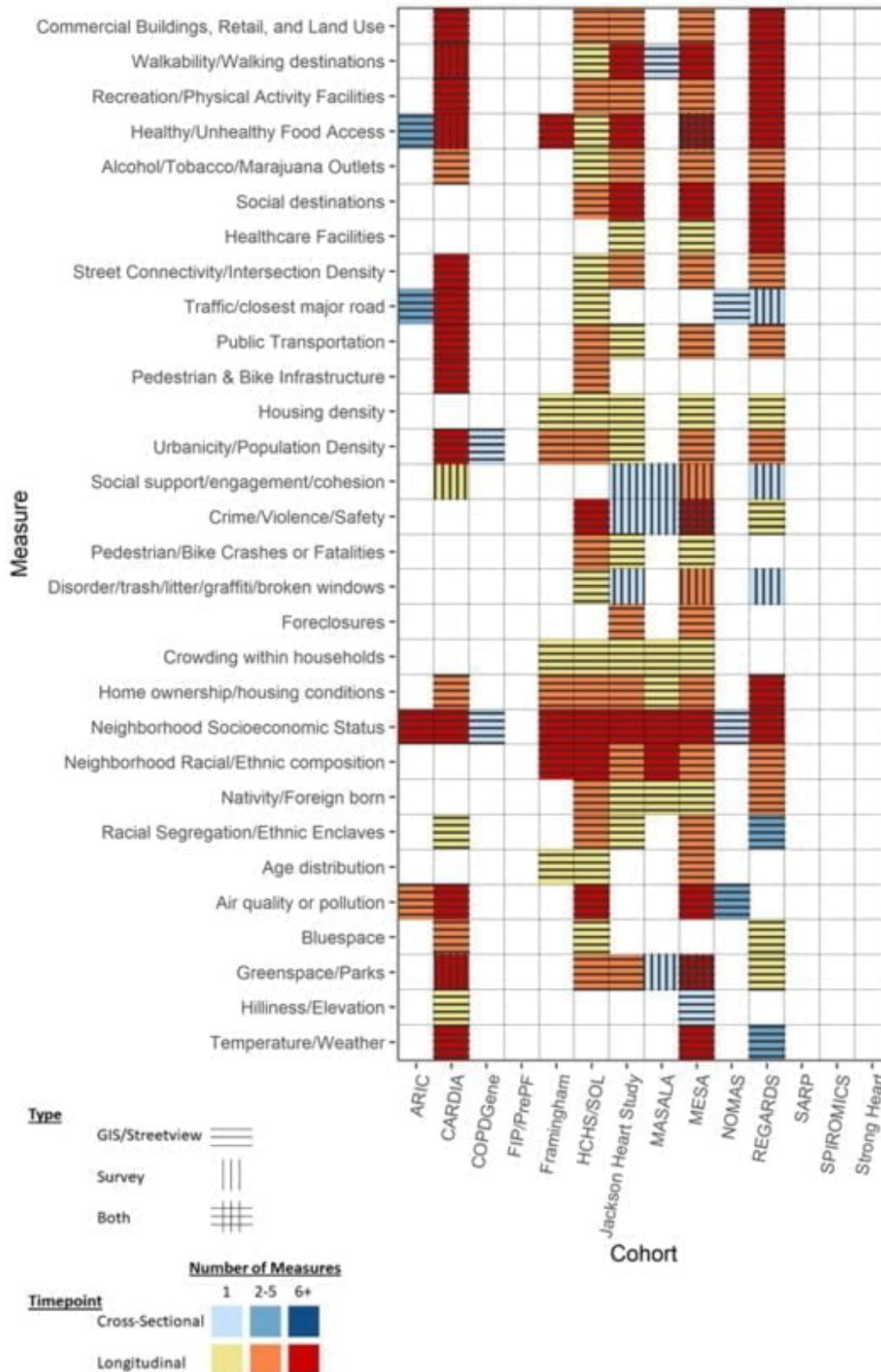
**LATEBREAKER**

COVID-19 Pandemic

**Spatial and neighborhood data in the Collaborative Cohort of Cohorts for COVID-19****Research (C4R)** Jana A Hirsch\* Jana Hirsch Lilah Besser Talea Cornelius Stephen Dickinson  
Stephen Francisco Marcia P. Jimenez Hoda A. Abdel Magid Yvonne L. Michael Elizabeth C. Oeslner

Neighborhood factors may create and reinforce geographic differences in COVID-19 experiences and long-term pandemic impact. These factors include social environments (e.g. employment landscapes), policy implementation (e.g. differences in COVID-19 mitigation mandates), built environment (e.g. housing quality and health care access), and natural environments (e.g. air quality and greenspace). To examine the health impact of neighborhood factors, we need longitudinal datasets of pre-pandemic neighborhood conditions and individual behaviors or health risks. A large, pooled sample with sufficient variability in geographic scope, participant diversity, and area-level neighborhood characteristics is critical to understand the role of context on COVID-19 outcomes. Our primary aim was to evaluate the value of Collaborative Cohort of Cohorts (C4R) for this purpose. C4R is a large geographically, racially/ethnically, and socioeconomically diverse study of 14 pooled cohorts in the US with harmonized data on health outcomes, including vaccination, COVID-19 infection, recovery, death, and more, from over 50,000 participants. We conducted surveys with key data staff for each of the cohorts to assess the spatial scale (e.g., tract, radial buffer, or zip code) and type of neighborhood measures within each cohort. We found that census tracts in which C4R cohort participants have lived covered 28% of the US land area, representing 52% of the US total population. Areas where participants have lived are more dense, urban, affluent, foreign-born, and educated and less car-dependent, employed, and green than the US on average. Ten of the 14 cohorts geocoded participants' addresses to identify their geographic location and collected neighborhood characteristics (Figure 1) - most commonly social environment measures. C4R's combined sample opens numerous opportunities for well-powered research on the influence of neighborhood characteristics on COVID-19 outcomes across various geographies.

**Figure 1:** Summary of neighborhood data timing (shown by color), availability (shown by color intensity), and type (shown by pattern) in the C4R Cohorts. Four cohorts (FIP/PrePF, SARP, SPIROMICS, and SHS) indicated they have not collected, processed, or linked any neighborhood geospatial data for their participants (blank columns).



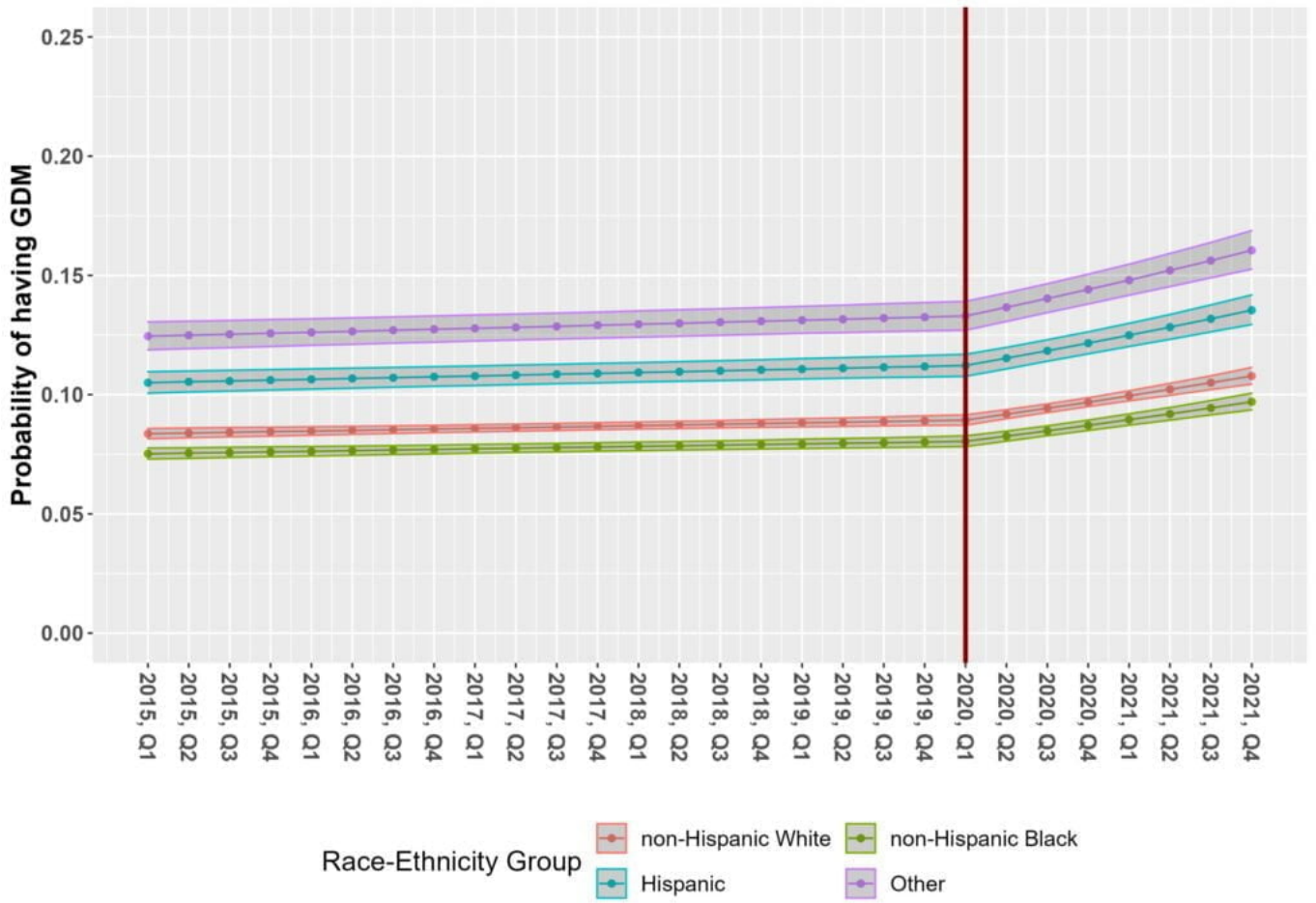
**Increasing prevalence of diagnosed gestational diabetes in South Carolina: 2015-2021** Kelly J Hunt\* Kelly Hunt Chun-Che Wen Brain Neelon Dulaney A. Wilson Julio Mateus John Pearce Kalyan Chundru Sarah Simpson Jeffrey E. Korte Hermes Florez Angela M. Malek

**Introduction:** The objective of our study was to examine the prevalence of gestational diabetes (GDM) prior to and during the COVID-19 pandemic in South Carolina.

**Methods:** The study included 194,841 non-Hispanic White (NHW), 108,195 non-Hispanic black (NHB), 25,560 Hispanic and 16,346 other race-ethnic group livebirths from 2015 through 2021. Maternal hospital and emergency department discharge codes were linked to birth certificate data. GDM was defined by ICD-9-CM (i.e., 6488), ICD-10-CM (i.e., O244, O249) or indication of GDM on the birth certificate without evidence of diabetes outside pregnancy in the 3 years prior.

**Results:** While the prevalence of reported GDM was increasing prior to the pandemic, its rate of increase accelerated at the onset of the pandemic. The relative risk for GDM prevalence associated with a one-year increase in time was 1.01(95% CI: 1.01, 1.02) prior to the pandemic and 1.11(95% CI 1.09, 1.14) after the pandemic started. Moreover, while there were race-ethnic differences in the prevalence of GDM, increasing trends were similar across all race-ethnic groups both before and after the onset of the pandemic [See Figure, p-values for the interaction between time and race-ethnic group were non-significant (pre,  $p=0.0904$ ; post,  $p=0.1613$ )]. Adjusting for socio-demographic factors including maternal age, education level, Medicaid eligibility, use of WIC services, and rural versus urban residence attenuated trends only slightly. By the fourth quarter of 2021, the prevalence of reported GDM was 10.8% in NHW, 9.7% in NHB, 13.5% in Hispanics and 16.1% in the other race-ethnic group.

**Discussion:** An increasing prevalence of diagnosed GDM was reported during the COVID-19 pandemic. GDM prevalence is impacted by screening, diagnostic, and reporting practices across different data sources, as well as by actual changes in prevalence. One potential explanation for observed results is changes in the GDM diagnostic procedure resulting from the pandemic.



**Racial differences in nursing home mortality before and during the COVID-19 pandemic**

Michelle A. DeVost\* Michelle A. DeVost Yea-Hung Chen Ruijia Chen Marie-Laure Charpignon Alicia R. Riley Mathew V. Kiang Aayush Khadka Scott Zimmerman Whitney Wells Jingxuan Wang Erin Ferguson Kendra D. Sims Sarah F. Ackley M. Maria Glymour

**Background**

Studies of racial disparities in nursing home (NH) mortality during the COVID-19 pandemic have focused on the racial composition of NH populations as predictive of COVID-specific NH mortality. Trends in differences by race in all-cause mortality in NHs in the pandemic era are less well understood. We investigated the relationship between race and all-cause NH mortality over time to evaluate whether racial differences in the probability of dying in a NH changed during the pandemic.

**Methods**

Using California state mortality data from 2016-2021, we characterized differences in the likelihood of NH residence at death between Black (n=134,212) and White (n=1,004,969) decedents. We used logistic regression models to estimate ORs and 95% CIs for associations between race and NH death by year and overall, controlling for decedent age and sex.

**Results**

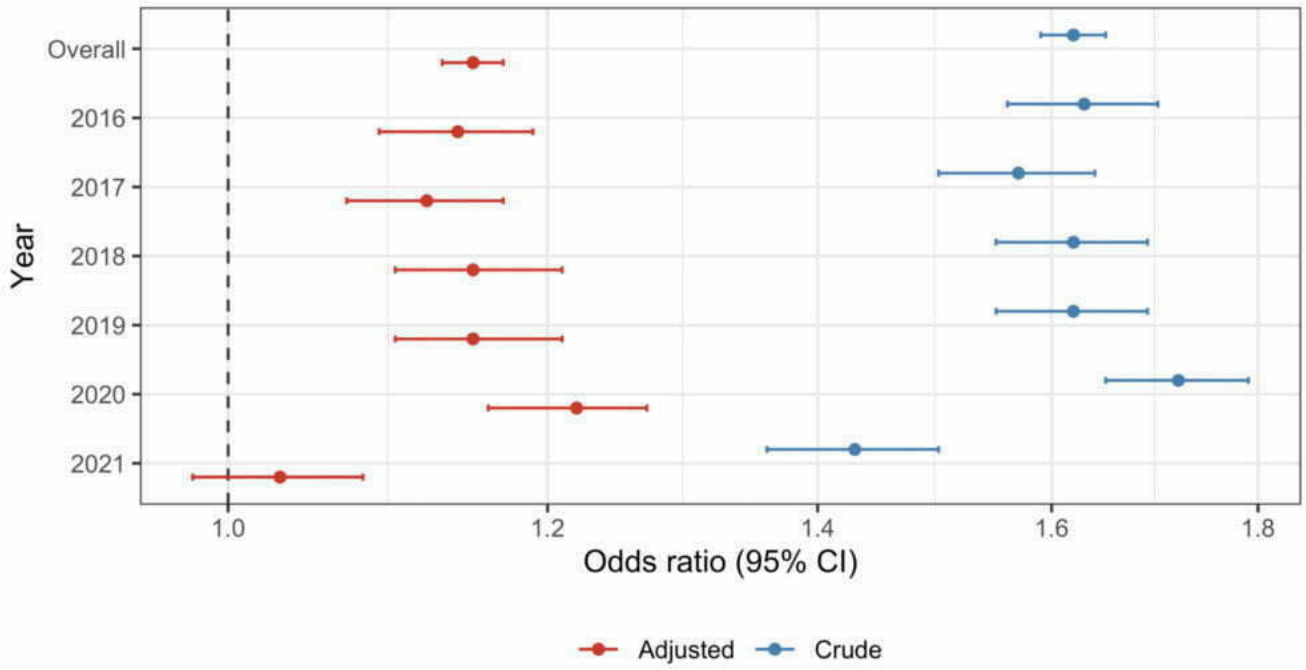
Of the 1,139,181 deaths in this analysis, 16% occurred in NHs. Overall, 16% of White and 11% of Black decedents died in NHs. The mean (SD) age of NH decedents was 84.0 (11.2) overall, 84.5 (10.8) for White, and 77.5 (13.1) for Black NH decedents. For non-NH decedents, the mean (SD) age was 74.1 (17.0) overall, 75.2 (16.4) for White, and 66.4 (19.1) for Black individuals. The OR (95% CI) for dying in a NH was 1.15 (1.13, 1.17) for White compared to Black decedents overall. Yearly estimates for 2016-2019 reflected the overall estimate, but the OR (95% CI) in 2020 was 1.22 (1.16, 1.27) and 1.03 (0.98, 1.08) in 2021.

**Discussion**

The ORs in 2020 and 2021 compared to those for 2016-2019 suggest that the COVID-19 pandemic affected racial differences in the likelihood of dying in a NH. The oldest NH residents may have been most likely to die in 2020, when the OR was highest for White compared to Black NH deaths. The lower OR in 2021 may be due to a disproportionate decline in White NH resident mortality or to White NH residents being more likely to move out of NHs at end of life compared to Black NH residents.



**Figure 1.** Odds ratios and 95% confidence intervals for dying in a nursing home among White decedents (n=1,004,969) compared to Black decedents (n=134,212) overall and by year, 2016-2021.

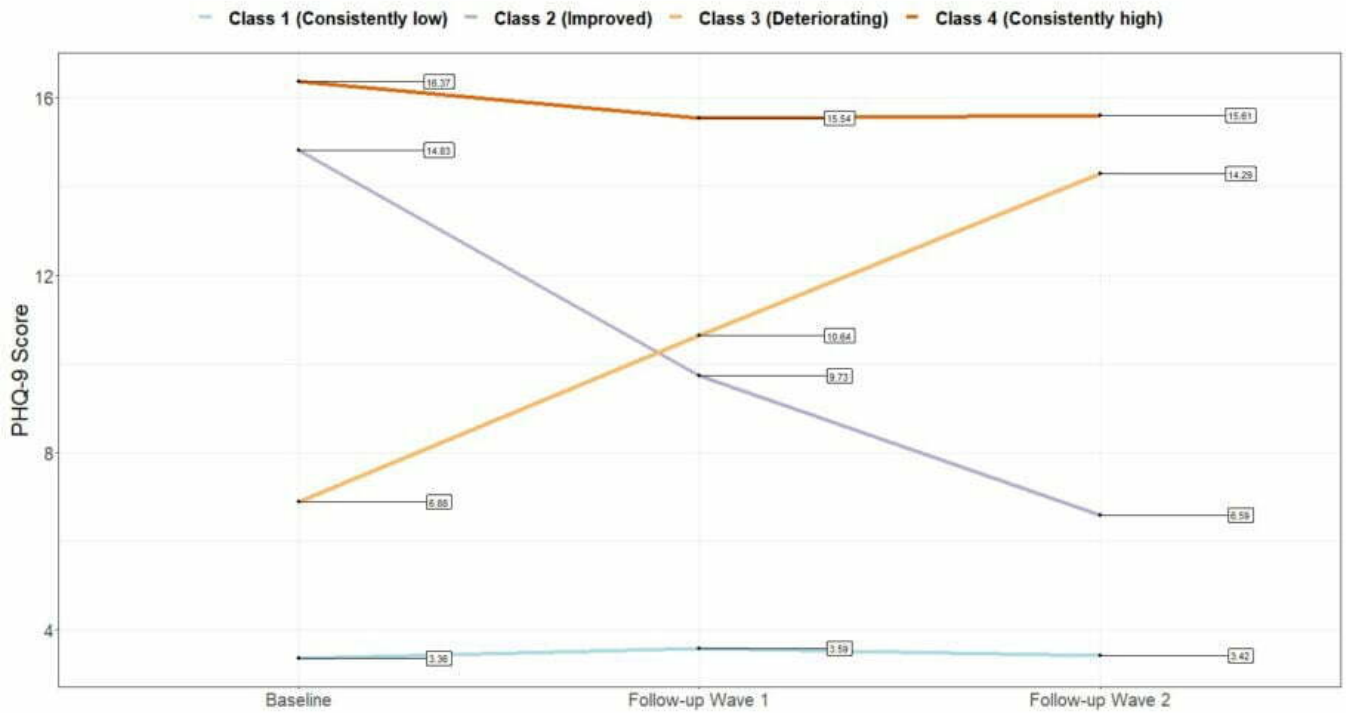


**Symptom trajectories of depression in the Icelandic population during the COVID-19 pandemic** Yue Wang\* Yue Wang Fenfen Ge Thor Aspelund Unnur Anna Valdimarsdóttir

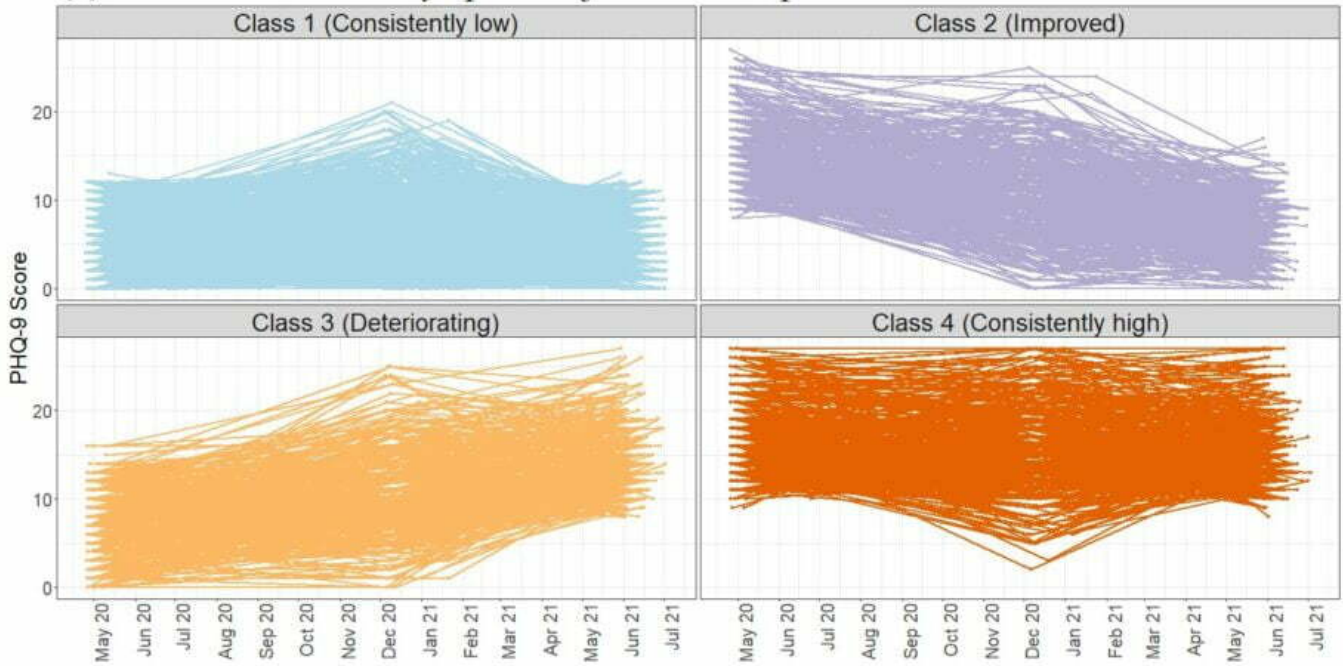
**Background** Changes in depressive symptom during the COVID-19 pandemic have been described across populations, but data are still scarce on the role of pandemic-specific factors on varying trajectories of depression in the general population. We aim to identify determinants of varying trajectories of depression in the Icelandic population during the COVID-19 pandemic. **Methods** We used data from the Icelandic COVID-19 National Resilience Cohort of 8307 individuals 18 years or older with three consecutive response data on depressive symptoms across the pandemic period (April 2020 - July 2021). We assessed 40 candidate features including demographic, lifestyle, physical and psychological health, and pandemic-specific factors. We used a latent growth mixture model to identify varying trajectories of depression, and performed both logistic regression and X-GBoost model to identify determinants of unfavorable trajectory vs. favorable trajectory.

**Results** We identified 4 distinct trajectories during the median 13 months of follow-up with most individuals showing consistently low (83.2%) or improved (5.4%) symptom of depression, while 11.4% participants showed unfavorable trajectories (i.e., deteriorating or consistently high symptom). Both logistic regression model and X-GBoost model showed good performance in distinguishing unfavorable trajectories from favorable trajectories (C statistics 0.81-0.85). Risk factors identified of unfavorable trajectories were younger age, pre-pandemic existing psychiatric disorders and financial difficulties, while identified protective factors were increased family support, regular exercise and frequent in-person social contact. **Conclusions** These data suggest that the vast majority of the Icelandic population maintained favorable mental health during the COVID-19 pandemic and that social support may be a key factor against unfavorable trajectories of depression.

(a) Observed mean PHQ-9 score for 4 distinct symptom trajectories of depression



(b) Observed individual symptom trajectories of depression



## **Prediction of the Effective reproduction number from a novel Spatiotemporal Model of Epidemic Spread and Validation Using COVID-19 Data: An Interdisciplinary Approach**

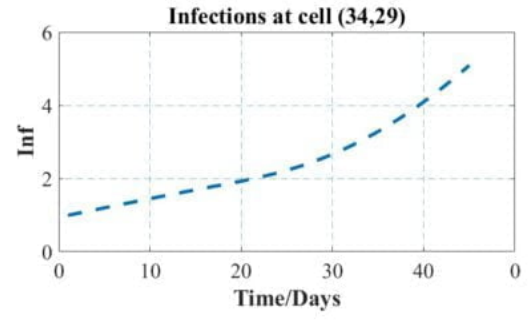
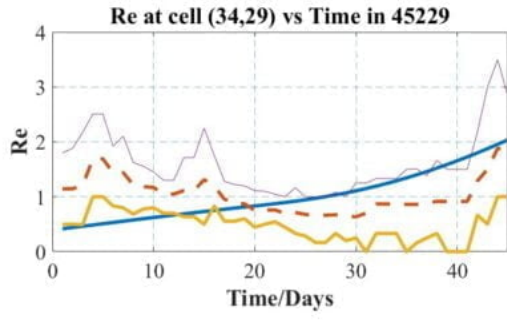
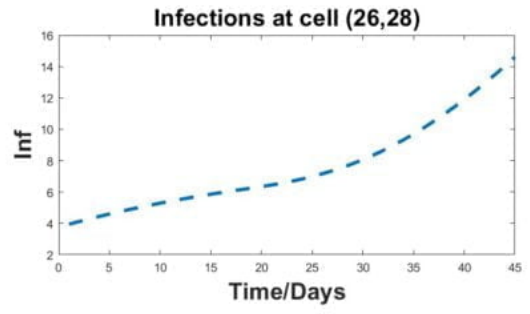
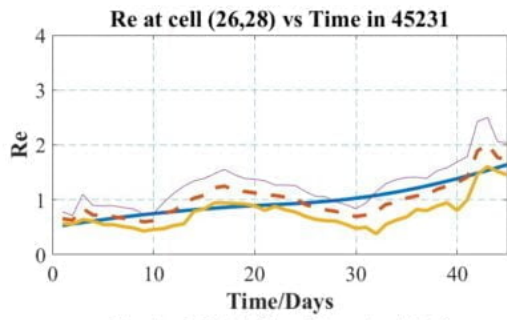
Shelley Ehrlich\* Shelley Ehrlich Deepak Antony David Chunyan Liu Subramanian Ramakrishnan Manish Kumar

**Introduction:** The Covid-19 pandemic has highlighted the importance of forecasting infection spread patterns for timely implementation of preventive measures. The basic and effective reproductive numbers ( $R_0$ ,  $R_e$ ) are widely used as quantitative metrics for estimating the rate of spread, despite well documented limitations of currently used methods of computing  $R_0$  and  $R_e$ . We propose a new way of calculating  $R_e$ , accounting for spatiotemporal dynamics of disease spread based on a partial differential equation (PDE) based Susceptible-Latent-Infected-Recovered (SLIR) compartmental epidemic model, validated in our previous studies. Our novel PDE model effectively accounts for spatiotemporal dynamics driven by human behavior, pathogen transmission characteristics and uncertainties therein. Furthermore, computation of  $R_e$  from PDE models that account for latency along with validation using real life data remains largely unexplored in the literature.

**Methods:** The  $R_e$  is typically calculated using the spectral radius of the next generation matrix from the infected compartments in ODE-based compartmental models. A numerical framework for solving the proposed PDE allows us to predict values of S, L, I, and R values for different time periods of the infection chronology. Using this information, we adapt the ODE-based calculation methodology for our PDE model in order to obtain  $R_e$ . We then validate our method using Covid-19 data from three hotspot zipcodes identified within Hamilton County, Ohio from the initial period of the pandemic, by comparing  $R_e$  derived from the retrospective Wallinga-Teunis (WT) method.

**Results:** The  $R_e$  values from PDE models were in good agreement with WT method values (see Figure), noting our method is predictive.

**Conclusion:** Our method provides a valid alternative to the standard methods used to compute  $R_0$  and  $R_e$ , and also inherits the advantages of PDE models. We will continue to validate the method, using larger spatiotemporal Covid-19 datasets.



**The COVID-19 Pandemic, Anxiety, and Depression in Canadian Healthcare Workers** Andem Effiong\* Andem Effiong Ugochukwu Odimba Michael Oluwalana

Healthcare workers commonly report anxiety and depression symptoms. Yet the evidence is sparse on the impacts of the COVID-19 pandemic on anxiety and depression symptoms specific to the personal health and work-life of Canadian healthcare workers. This study aimed to understand the pandemic's impact on Canadian healthcare workers' anxiety and depression symptom severity scores. We used information obtained from participants (n = 8 478) in the survey of healthcare workers' experiences during the pandemic collected between September 2 and November 12, 2021, for analysis. The Generalized Anxiety Disorder-2 and Patient Health Questionnaire-2 were used to screen for anxiety and depression. A generalized estimating equations procedure with a negative binomial distribution was used to assess both symptoms' incidence rate ratio (IRR). Stress was the exposure variable, with adjustments made for various covariates, e.g., age, sex, and aerosol-generating medical procedures (AGMPs). The reference groups were 18 - 34 for age, female for sex, and did not perform or assist with AGMPs for AGMPs. The adjusted IRRs (aIRRs) for depression were 1.10 [1.05 - 1.15] for those aged 45 years and above and 1.03 [0.99 - 1.07] for those aged 35 - 44 years compared to the reference group; 1.06 [1.01 - 1.12] for males versus females; 0.92 [0.89 - 0.96] for those who performed or assisted with AGMPs versus those who did not. For anxiety, the aIRRs were 1.14 [1.09 - 1.20] for those aged 55 years and above, 1.11 [1.06 - 1.17] for 45 - 54 years, 1.03 [0.98 - 1.08] for 35 - 44 years compared to the reference group; 1.09 [1.03 - 1.15] for males versus females; and 0.95 [0.91 - 0.99] for those who performed or assisted with AGMPs versus those who did not. Anxiety and depression symptom severity scores are potential risk factors for health and work-life balance during the COVID-19 pandemic. The prioritization of tailor-made anxiety and depression interventions for healthcare workers is imperative.

**Comparative risk of adverse events following BNT162b2 and mRNA-1273 mRNA vaccination in 6.4 million US older adults: A difference in safety or early effectiveness?**

Daniel Harris\* Daniel Harris Kaleen Kayes Preeti Chachlani Andrew Zullo Vincent Mor Stefan Gravenstein

**Background:** Head-to-head safety comparisons of mRNA vaccines for SARS-CoV-2 are needed for decision making; however, current studies lack generalizability and are too small to capture rare adverse events over a short and clinically relevant period. Also, it is important to situate potential differences in safety within the context of differential early effectiveness, whereby a more effective vaccine may appear safer due to the prevention of COVID-19 disease misclassified as safety events. We aimed to compare the risk of potential adverse events and COVID-19 between mRNA vaccines within a month of vaccination.

**Methods:** Using novel linked commercial pharmacy and Medicare data, we conducted a retrospective cohort study of US community-dwelling Medicare fee-for-service beneficiaries  $\geq 66$  years who received BNT162b2 or mRNA-1273 as their first vaccine dose between December 2020 and July 2021. We measured the risk of diagnosed COVID-19 and 13 serious adverse events (e.g., pulmonary embolism) in the 28-days following vaccination. We estimated RRs and RDs with 95% CIs adjusting for sociodemographic and clinical characteristics, prior health services use, month of vaccination, region, and prior COVID-19 using generalized linear models.

**Results:** In total, 6,388,196 persons received BNT162b2 or mRNA-1273 (median age=75 years; 59% female). The risk of all outcomes was low in both vaccine groups. Persons who received mRNA-1273 had a lower risk of pulmonary embolism (RR=0.96; 95%CI=0.93-1.00; RD=9; 95%CI=1-16 events per 100,000 persons) and diagnosed COVID-19 (RR=0.86; 95%CI=0.84-0.87; RD=82; 95%CI=71-94 event per 100,000 persons) compared to those who received BNT162b2.

**Conclusions:** Even shortly after vaccination, mRNA-1273 (vs BNT162b2) had a lower risk of serious adverse events, possibly via greater early effectiveness and reduction of SARS-CoV-2 sequelae. The reduced risk of serious health outcomes observed with mRNA-1273 may be meaningful at the population level.

**Perceived Stress as a Risk Factor for the Development of Post-Acute Sequelae of COVID-19**

Sana Khan\* Sana Khan Katherine D. Ellingson John M. Ruiz Kelly M. Heslin Felina M. Cordova-Marks Elizabeth T. Jacobs Kristen Pogreba-Brown

**Objective:** Stress impacts physical health through immune dysfunction and increased frequency of illness. The COVID-19 pandemic has resulted a vast number of infections and long-term effects are still being assessed. The etiology of post-acute sequelae of COVID-19 (PASC) have not yet been well characterized. The aim of this study was to determine if perceived stress around the time of acute infection predicted the development of post-acute sequelae COVID-19 (PASC), and if receipt of COVID-19 vaccine modified this relationship.

**Methods:** This analysis used a subset of participants from The Arizona CoVHORT who had a baseline survey with a completed Perceived Stress Scale-10 survey within a month of testing positive for SARS-CoV-2 and who completed a follow-up symptom survey after six-weeks. PASC was defined as the presence of symptoms at least six-weeks after initially testing positive. This analysis used log-binomial regression models to determine if perceived stress at the time of infection was a risk factor for PASC, after adjusting for age and co-morbid conditions.

**Results:** In the sample of 279 participants, those with moderate or high stress had an elevated risk of PASC compared to those with low stress (aRR: 1.8 (95% CI: 1.2 - 2.5) and (aRR: 2.1 (95% CI: 1.5 - 3.0), respectively. After stratifying by vaccination status at the time of infection, this relationship remained significant among unvaccinated participants (moderate stress aRR: 1.7 (95% CI: 1.2 - 2.5); high stress aRR: 2.1 (95% CI: 1.5 - 3.0)) but was attenuated among those with at least 1-dose COVID-19 mRNA vaccines (moderate stress aRR: 1.0 (95% CI: 0.6 - 1.7; high stress aRR: 0.5 (95% CI: 0.08 - 3.4)).

**Conclusions:** Those with moderate to high stress had an increased risk of developing PASC, indicating that stress at the time of infection is a risk factor for PASC. Future public health campaigns focused on reducing the incidence of PASC should focus on stress reduction and encouraging vaccination uptake.



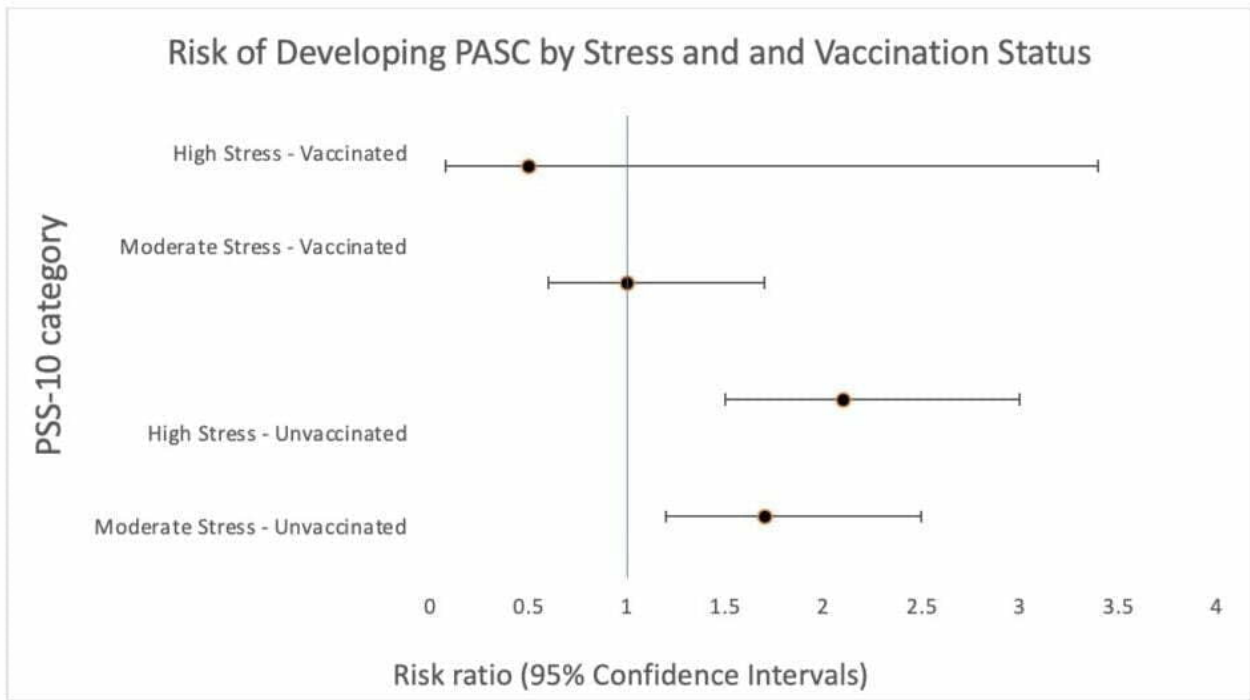


Figure 1: Adjusted Risk Ratio by Vaccination Status

**Serologic correlates of protection of COVID-19 vaccination** Nancy H. L. Leung\* Nancy H. L. Leung Samuel M. S. Cheng Leo L. H. Luk Leo C. H. Tsang Kelvin K. H. Kwan Sara Chaothai Karl C. K. Chan John K. C. Li Dennis K. M. Ip Gabriel M. Leung J. S. Malik Peiris Benjamin J. Cowling

**Background:** Among many immunological markers elicited by COVID-19 vaccination, neutralizing antibodies are considered as the correlate of protection (CoP) against infection to predict vaccine efficacy. However, we recently showed that in a randomized trial of homologous and heterologous inactivated and mRNA third-dose COVID-19 vaccination in adults (the Cobovax study), the risk of infection was similar across all study arms despite significant differences in the neutralizing antibody responses. One hypothesis is that prior vaccination and infection history may affect the role of individual immunological markers to protection.

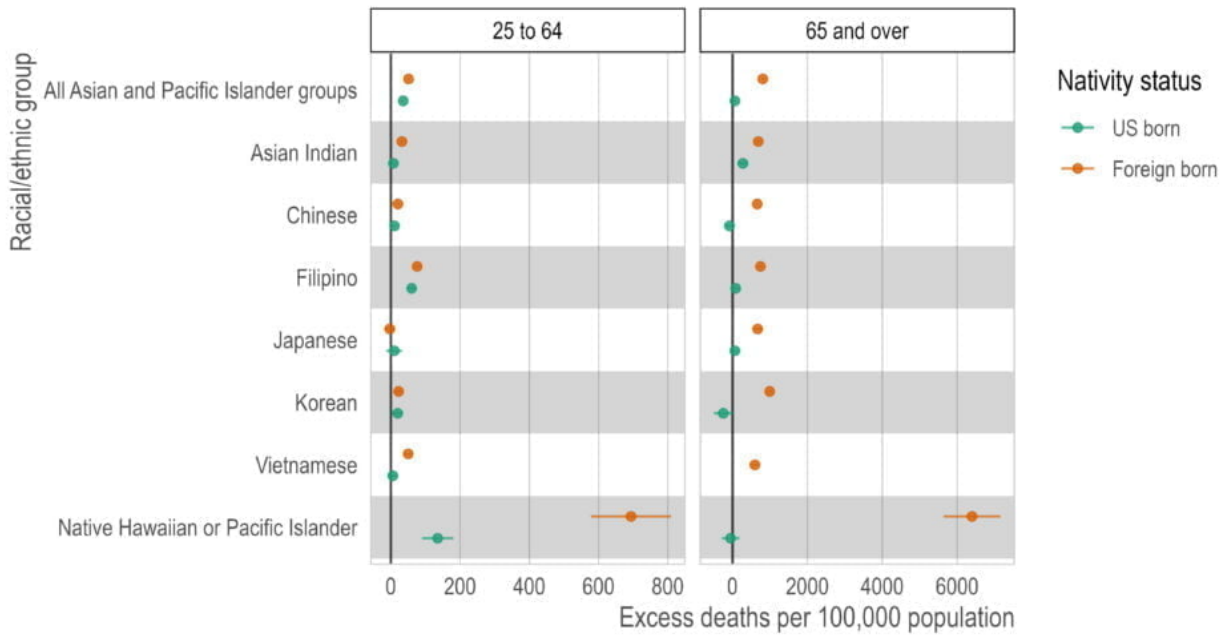
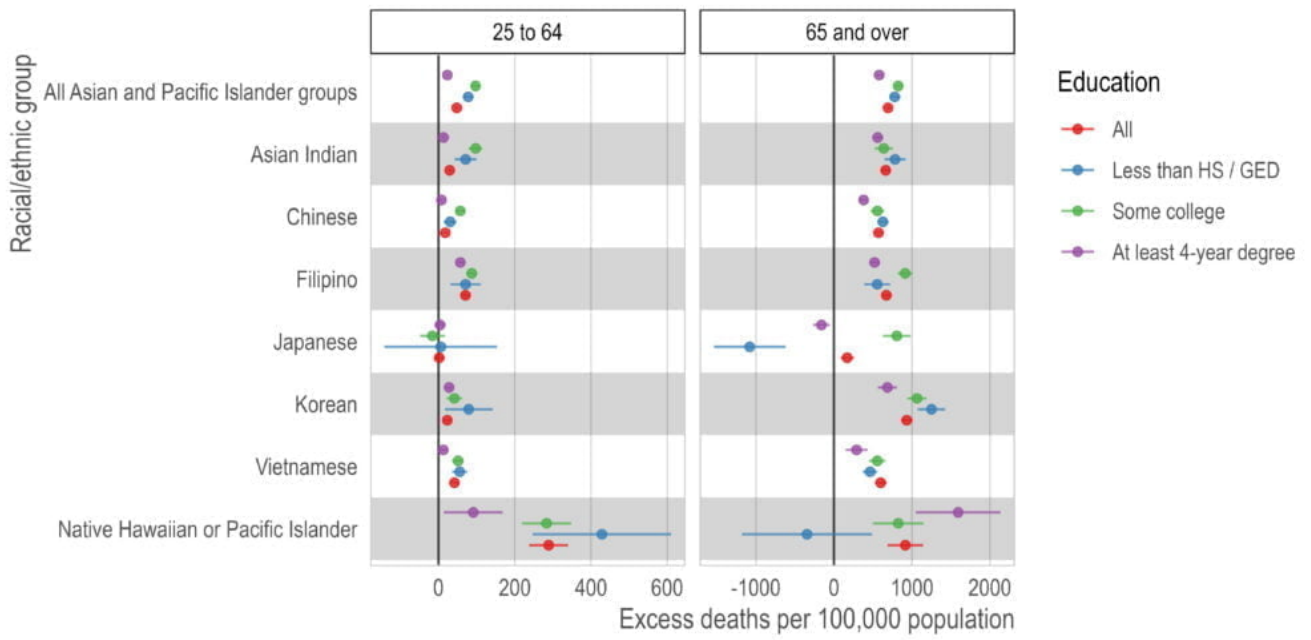
**Methods:** We are conducting several on-going longitudinal cohorts and vaccine trials of COVID-19 vaccination in Hong Kong, altogether include >3,000 participants with diverse vaccination and infection history. SARS-CoV-2 infections are identified by self-reported questionnaires or self-administered COVID-19 rapid antigen tests. We selected a subset of participants from all studies and tested post-vaccination (day 30) sera to measure various serologic markers including antibodies against the SARS-CoV-2 Spike and Nucleocapsid proteins, and surrogate neutralisation test and plaque reduction neutralisation test.

**Results:** In the Cobovax trial where participants were adults who did not have SARS-CoV-2 infection prior to enrolment, we identified 58 (15%) infections from 378 participants within 4-6 months after third-dose vaccination. Significant difference in post-vaccination neutralizing antibodies against Omicron BA.2 between infected and non-infected individuals were only observed in participants who received third-dose inactivated vaccine after primary two-dose mRNA vaccine series, but not in participants in other study arms.

**Conclusions:** We are expanding laboratory testing to additional serologic markers parallelly done in the same individuals, and to additional individuals with different vaccination and infection history. We will also explore the relative contribution of different serologic markers to protection.

**Excess Deaths Due to the Covid-19 Pandemic Among Asian American, Native Hawaiian and Pacific Islander Subgroups by Age, Education, and Nativity** Ruijia Chen\* Ruijia Chen Supriya Misra Yea-Hung Chen Andrew C. Stokes Alicia R. Riley Mathew V. Kiang

The COVID-19 pandemic has resulted in well-documented disparities in death across racialized groups. However, despite being the fastest-growing minoritized group in the US, Asian Americans (AsA) and Native Hawaiians or Pacific Islanders (NHPI) have been inconsistently included in research on COVID-19 inequities—often treated as a uniform group, analyzed as “Other”, or excluded altogether. We use national death certificate data to quantify excess deaths among disaggregated AsA/NHPI subgroups (i.e., Asian Indian, Chinese, Filipino, Japanese, Korean, Vietnamese, and Native Hawaiian or Pacific Islander). We fit overdispersed Poisson models stratified by subgroup and sociodemographic characteristics such as age, educational attainment, and nativity status. Our preliminary results suggest there were 20,701 (95% CI: 19,585 to 21,816) excess deaths among Asian Americans between March and December 2020 in the US, corresponding to 741 (95% CI: 706 to 777) per 100,000 population. Within nearly all subgroups, there was a nonlinear educational gradient with the highest excess deaths among those with some college, followed by those with less than a high school diploma, and the lowest excess mortality among those with a four-year degree. Unexpectedly, for Japanese, those with a less than high school/GED degree had the lowest excess deaths rate (-1080 (95% CI: -1538, -622)). In general, the NHPI subgroup experienced the highest excess mortality with over 6000 excess deaths per 100,000 among older foreign-born NHPI. We observed a clear contrast in excess deaths between foreign-born and US-born AsA/NHPI adults in the older age group, with foreign-born AsA/NHPI older adults having a much higher number of excess deaths than native-born older adults for all subgroups. These results highlight the importance of disaggregating by AsA/NHPI subgroup and nativity status in analyses of mortality disparities and can inform targeting of resources to subgroups most impacted by the pandemic.



**A Bayesian and GEE examination of religion, negative emotional symptoms, peritraumatic distress, and satisfaction with life** Andem Effiong\* Andem Effiong

This study aimed to understand the effects of religion and negative emotional symptoms on peritraumatic distress and satisfaction with life during the COVID-19 pandemic.

Evidence from the COVID-19 Psychological and Behavior Impact Survey collected during wave 1 of the pandemic was applied. A total of 447 Canadians categorized into four age groups (0 -24 years, 25 - 44 years, 45 - 64 years, and 65+) were included in the analysis. Depression, anxiety, stress, peritraumatic distress, and satisfaction with life were measured using the Depression, Anxiety, Stress Scale 21, the COVID-19 Peritraumatic Distress Inventory, and the Satisfaction with Life Scale. Bayesian multivariate regression with Gibbs sampling and Markov Chain Monte Carlo simulations were used to determine the clinical significance of religion, anxiety, stress, and sleep quality on peritraumatic distress. A Generalized Estimating Equations (GEE) population-averaged model was used to estimate the clinical significance of religion on life satisfaction after adjusting for peritraumatic distress and other sociodemographic, cognitive, behavioral, and negative emotional symptomatic covariates and exposures.

Self-identifying as “religious” instead of “none/other” was in some instances associated with a lower or higher risk of peritraumatic distress ((RRR = 1.05 [0.71 - 1.52] for Buddhism; (RRR = 0.92 [0.83 - 1.01] for Christianity; and (RRR = 0.88 [0.76 - 1.03])) for Islam. Life satisfaction yielded similar estimates. The IRRs for “lower” satisfaction with life were: 0.99 [0.91 - 1.08] for Christianity, 0.95 [0.84 - 1.07] for Islam, and 0.80 [0.62 - 1.04] for Buddhism.

Religion can be a protective factor for mental health. Nonetheless, it can also be a risk factor for adverse mental health. Practitioners, clinicians, researchers, policymakers, and decision-makers should make more concerted efforts to draw upon the more positive aspects of religion in their encounters with other stakeholders.

**Changes in cognition and function among long-term care residents before and during the COVID-19 pandemic** Colleen Webber\* Colleen Webber Kruti Patel Christina Milani Daniel Myran Luke Turcotte Amit Arya Kevin Brown Andrew Costa Stacey Fisher Dawn Guthrie Paul Hebert John Hirdes Sarina Isenberg Wenshan Li Daniel Kobewka Reem Mulla Annie Robitaille Paula Rochon Rachel Savage Peter Tanuseputro

**Objectives:** There are concerns that public health restrictions introduced in long-term care (LTC) homes to limit the spread of COVID-19 have contributed to declines in residents' health. This study evaluated changes in LTC resident function and cognition before and during the COVID-19 pandemic and explored whether outcomes differed according to home-level COVID-19 burden.

**Methods:** This retrospective cohort study used health administrative data. The study population included older adults in LTC in Ontario, Canada on March 17, 2020 (COVID-19 group) and March 17, 2018 (pre-COVID-19 group). Cognition and activities of daily living (ADLs) were measured using LTC assessment data, with a maximum of 21 months of follow-up. Home-level COVID-19 burden was measured as the number of COVID-19 cases per 100 beds. We compared declines in cognition and function between groups, as well as within the COVID-19 group across quintiles of COVID-19 infection burden.

**Results:** The study included 138,488 LTC residents (COVID-19=69,672, pre-COVID-19=68,816). The proportion of residents with ADL decline was similar between the groups (42.1% in the COVID-19 group and 42.0% in the pre-COVID-19 group). The proportion of residents with cognitive decline was higher in the pre-COVID-19 than COVID-19 group, at 34.2% and 32.0%, respectively. The proportion of residents experiencing cognitive or functional decline was lower in homes with a higher COVID-19 burden. However, the proportion of residents who died during follow-up was higher in the COVID-19 group, as well as in homes with higher COVID-19 outbreak burden. Further analyses will compare these outcomes between groups, while accounting for the competing effect of death.

**Conclusion:** While LTC residents have been hard-hit by the COVID-19 pandemic, with high levels of infection and deaths, these preliminary results suggest that LTC residents during the pandemic have not experienced large declines in cognition and function.

**Disparities in COVID-19 vaccination by race and ethnicity and workplace COVID-19 policies**

Celeste J. Romano\* Celeste Romano Erika Meza Kristina W. Lai Katherine Lamba Esther Lim Megha L. Mehrotra David P. Bui Ximena P. Vergara Joshua Quint

**Objective:** To characterize COVID-19 vaccination by race and ethnicity and COVID-19 workplace policies and assess the dual effect of these social determinants on vaccination.

**Methods:** CalScope, a population-based serosurvey, recruited from seven California counties, October 2021–February 2022. Employed survey respondents reported employer COVID-19 policies and their COVID-19 vaccination status ( $\geq 1$  dose vs none). Disparities in vaccination were calculated at the intersection of race and ethnicity and relevant policies using saturated weighted linear regression models, with weights for the inverse probability of jointly belonging to a particular racial and ethnic and workplace policy category, conditional on age and sex. Non-Hispanic White individuals served as the referent racial and ethnic group because of their position as beneficiaries of structural racism.

**Results:** Among 3662 working adults captured in CalScope, 91.9% were vaccinated. Vaccination status varied by race and ethnicity (American Indian and Alaska Native: 89.4%, Asian: 97.3%, Black: 89.6%, Hispanic: 89.0%, Multiracial: 91.5%, Native Hawaiian and Pacific Islander: 100.0%, Non-Hispanic White: 91.8%). Black, Hispanic, Multiracial, and Non-Hispanic White participants without an employer COVID-19 vaccine mandate had vaccination rates 18.6% (95% CI: -27.5, -9.6), 11.1% (95% CI: -15.1, -7.2), 10.2% (95% CI: -14.3, -6.2), and 11.5% (95% CI: -13.7, -9.4) lower, respectively, than their counterparts with an employer COVID-19 vaccine mandate, but disparities in vaccination did not persist among marginalized racial and ethnic groups with an employer vaccine mandate relative to Non-Hispanic White individuals with a mandate. Policies prohibiting working in-person with COVID-19 symptoms and providing paid time off for vaccination were not associated with vaccination coverage.

**Conclusions:** Employer COVID-19 vaccine mandates may increase vaccination coverage and reduce racial and ethnic disparities in vaccination.

**The impact of the first two years of the COVID-19 pandemic on heavy and binge drinking among U.S. adults** Jacqueline Ryder\* Jacqueline Ryder Jacqueline Ryder Elizabeth A. Kelvin Katarzyna Wyka

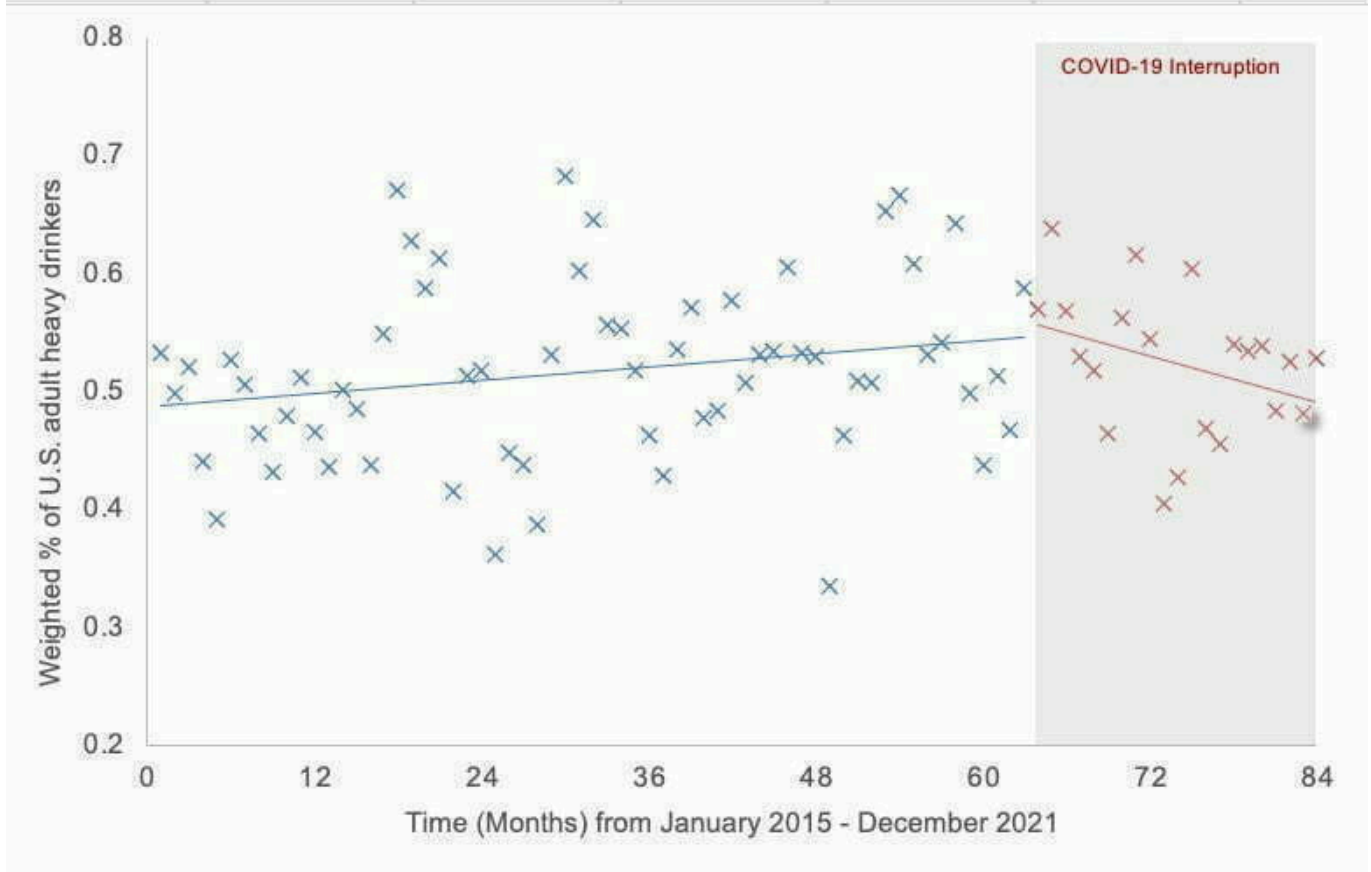
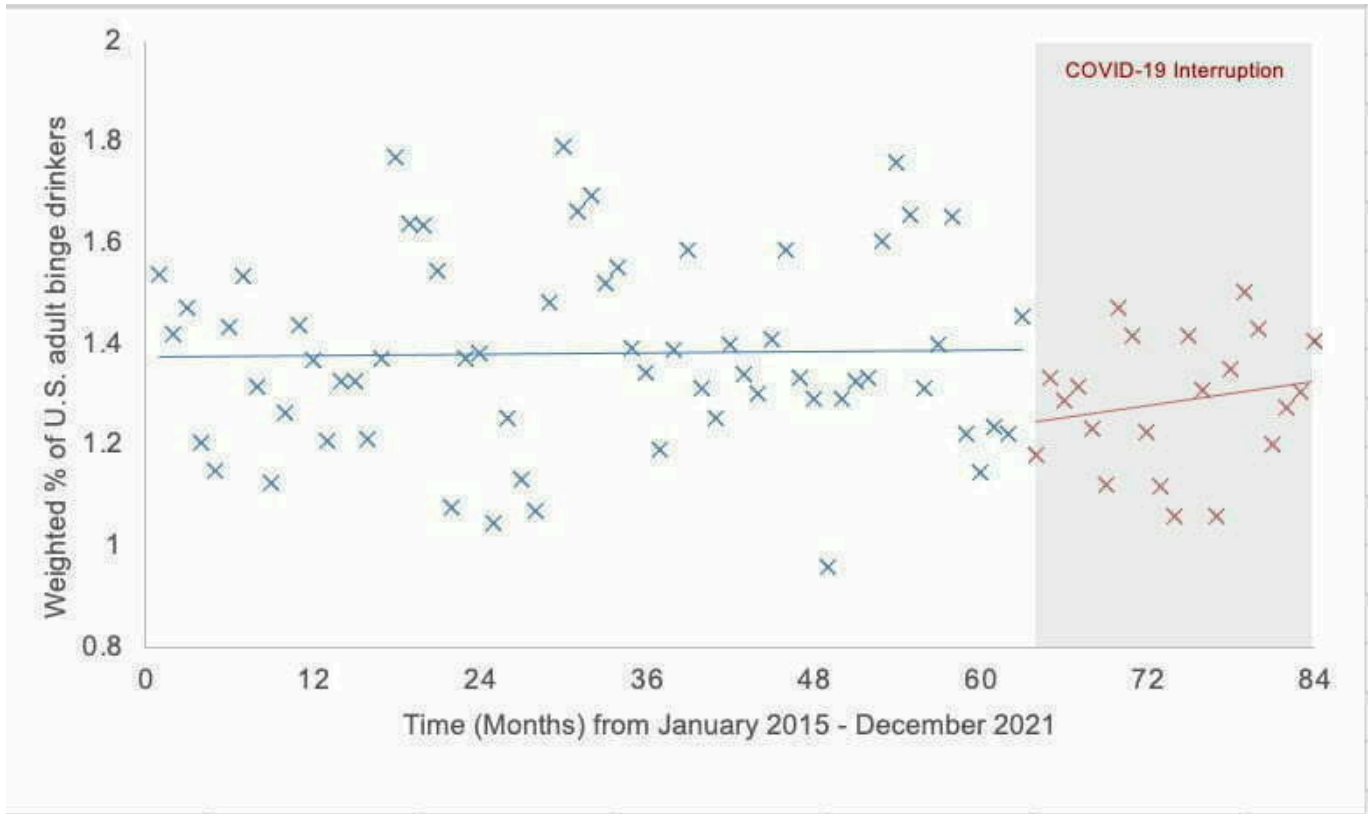
**Background:** The COVID-19 pandemic in the United States led to state-imposed changes in alcohol sales policies, including allowing alcoholic beverages for take-out and home delivery, along with restrictions that altered work, family and social life. Previous research suggests that alcohol use increased in certain segments of the U.S. population during the early months of the pandemic. However, less is known about how consumption patterns changed over time in the U.S., such as the immediate impact of the pandemic versus subsequent patterns over time as the pandemic became entrenched. We assessed changes in binge and heavy drinking among U.S. adults over time by comparing pre- versus post-pandemic patterns.

**Methods:** Adult binge and heavy drinking data was obtained from the 2015 - 2021 Behavioral Risk Factor Surveillance System (BRFSS) survey. We calculated weighted monthly prevalence estimates for each outcome pre-pandemic (January 2015 - March 2020) and post-pandemic (April 2020 - December 2021). We conducted an interrupted time series analysis to assess the pandemic effect on binge and heavy drinking separately, adjusting for monthly autocorrelation.

**Results:** There was an immediate drop in binge drinking at the start of the pandemic that was of borderline significance (coef= -0.2, p= 0.055), but no significant change was observed in the binge drinking trend over time (coef= 0.0, p= 0.482). For heavy drinking, the COVID-19 pandemic was not associated with a significant change in the level at the start of the pandemic (coef= 0.0, p= 0.963) or in the trend over time (coef= -0.0, p=0.150).

**Conclusion:** Binge and heavy drinking patterns remained mostly stable among Americans during the pandemic. However, from these methods, we are unable to differentiate between the pandemic impact versus those brought on by changes in alcohol sales policies. These may have had opposite effects, resulting in null results.





**COVID-19 Knowledge, Attitudes, and Practices during Delta and Omicron waves in two border provinces in Thailand** Natalie R. Wodniak\* Natalie Wodniak Saithip Bhengsri Pongpun Sawatwong Nuttagarn Chuenchom Tanaphat Lertwitayakumjorn Barameht Piralam Samkan Chaoprasert Anupong Sujariyakul Beth Skaggs Emily Bloss James D. Heffelfinger

During the COVID-19 (CV19) pandemic, Knowledge, Attitudes, and Practices (KAP) surveys have been used to assess perceptions and behaviors in populations of interest. We collected KAP data during a surveillance project on febrile patients presenting to six hospitals in two Thailand provinces, Nakhon Phanom (NP), bordering Laos, and Tak, bordering Myanmar, to assess geographic and temporal differences during the pandemic. Chi-square tests were performed to compare KAP between provinces and between the CV19 Delta wave (July-December 2021) and the Omicron wave (January-April 2022), when more Thais had been vaccinated, illness was less severe, and mitigation policies were loosening. In addition, multivariable logistic regression was performed to assess factors associated with preventive measures during each wave.

Knowledge of the main symptoms and transmission of CV19 was higher in NP than in Tak (63% vs. 44%,  $p < 0.01$ ). Fear was more common during the Delta than the Omicron wave (73% vs. 54%,  $p < 0.01$ ) in both provinces. Compliance with recommended preventive measures of physical distancing, mask-wearing, and handwashing was higher in NP than Tak (63% vs. 55%,  $p = 0.03$ ) and during Delta vs. Omicron wave (67% vs. 55%,  $p < 0.01$ ).

The practice of preventive measures during the Delta wave was higher among females (aOR [95% CI]: 1.9 [1.3-2.7]), age  $\geq 25$  (2.1 [1.3-3.4]), Thai ethnicity (4.1 [1.7-10.1]), and those with secondary school or higher education (1.6 [1.0-2.5]). During the Omicron wave, preventive practices were associated with NP province (1.8 [1.1-2.9]), receipt of any CV19 vaccine doses (3.1 [1.5-6.1]), and fear towards CV19 (0.5 [0.3-0.7]).

Demographic, geographic, and temporal differences in CV19 perceptions and behaviors were observed in patients attending hospitals in two border provinces in Thailand. Results can inform targeted public health strategies and messaging to populations in which CV19 preventive practices were less common.

**Demographic Differences in Sleep Deprivation and Diabetes in The U.S.: Behavioral Risk Factor Surveillance System 2013-2020** Sina Kianersi\* Sina Kianersi Tianyi Huang

**Objectives:** To estimate population trends of sleep deprivation and diabetes over time, and evaluate heterogeneity in the association of sleep deprivation with diabetes by gender and race and ethnicity.

**Methods:** We used multiple cross-sectional datasets collected in 2013-2020 in Behavioral Risk Factor Surveillance System, an annual telephone-based survey among a representative sample of U.S. adults (N=1,960,473). Complex survey methods accounting for the sampling design were used to calculate the weighted age-standardized prevalence estimates. Sleep deprivation was defined as self-reported sleep duration <7 hours. Diabetes was assessed by self-reported diagnoses. Weighted Poisson regression was used to examine the association between sleep deprivation and diabetes by gender and race and ethnicity, controlling for age, body mass index, and lifestyle factors.

**Results:** Prevalence of sleep deprivation decreased from 36.1% in 2013 to 33.7% in 2020 ( $p<.0001$ ), with the highest prevalence consistently observed in Black men. Diabetes prevalence slightly increased from 9.5% in 2013 to 10.1% in 2020 ( $p<.0001$ ). Black women had the highest diabetes prevalence. The association between sleep deprivation and diabetes was slightly stronger in women [PR (95% CI): 1.15 (1.12, 1.18)], compared to men [1.13 (1.10, 1.16),  $p$ -interaction=0.006]. When examining the association by race and ethnicity ( $p$ -interaction<0.0001), sleep deprivation was associated with prevalent diabetes in American Indians [1.20 (1.08, 1.33)], Whites [1.17 (1.15, 1.19)], Hispanics [1.12 (1.06, 1.18)] and Asians [1.13 (0.99, 1.29)], but not in Blacks [1.00 (0.96, 1.04)].

**Conclusion:**

Despite the highest burden of sleep deprivation and diabetes in Black men and women from 2013 to 2020, associations between these two were only observed in other racial and ethnic groups. Additional studies are needed to understand the reasons underlying these observations and potential implications for targeted public health interventions.

**Finite mixture model-based community profiles characterized by distinct social, natural, physical activity, and food environments and their relation to type 2 diabetes in Pennsylvania**

Katherine A. Moon\* Katherine A. Moon Melissa N. Poulsen Annemarie G. Hirsch  
Jonathan Pollak Brian S. Schwartz

Understanding geographic disparities in type 2 diabetes (T2D) onset requires approaches that recognize the multidimensional nature of communities. Most studies of the contextual effects on health evaluate single features or use administrative boundaries. We hypothesized that categorizing communities holistically using social, natural, physical activity (PA), and food environment data could better identify communities at risk of T2D. In a case control study in the Geisinger electronic health record, we identified persons with new onset T2D from 2008 to 2016 (n=15,888). Controls without T2D were frequency matched by age, sex and year (n=79,435, 65,084 unique persons). We defined T2D with encounter diagnoses, medication orders and laboratory test results. We used finite mixture models to create distinct community profiles based on 17 variables measuring socioeconomic status, green and blue space, land use, PA resources (parks and fitness facilities), and food outlets (grocery, fast food, and convenience). We estimated odds ratios (OR) of T2D with 95% confidence intervals (CI) using logistic generalized estimating equation models, with robust standard errors, adjusted for sociodemographic variables. We identified four community profiles in 1413 communities in central and northeastern Pennsylvania: 40% in Class 4, 28% in Class 3, 17% in Class 2, and 15% in Class 1. Cities were mostly Class 3, boroughs were mostly Class 1 or 3, and townships were mostly Class 2 or 4. These patterns suggest that these profiles capture heterogeneity in community features not captured by administrative boundaries in townships and boroughs. Class 3 ("Urban") communities had the highest density, lowest SES, low greenness, but high PA and food resources. Class 4 ("Rural") communities had low density, high SES, high greenness, and low PA and food resources. Compared to Class 2, Class 1 had higher SES, greenness, and parks, but differed in fitness and food outlets. Compared to Class 4 ("Rural"), Class 3 ("Urban") communities had higher odds of T2D (OR: 1.16, 95% CI: 1.09, 1.23). Despite different patterns of adverse and protective features, the odds of T2D were similar in Class 1 (OR: 0.99, 95% CI: 0.92, 1.06) and in Class 2 (OR: 0.94, 95% CI: 0.89, 1.00). These findings could help identify patterns of community features that protect against T2D.

**Effectiveness of Land Use Regression Modeling to Assess the Disparities of Environmental Noise in a New England City** Nina Franzen Lee\* Nina Franzen Lee Erica Walker

**Background:** Urban sound is complex and known to harm health through consistent activation of the nervous system. The complexity of sound sources, the wide range of health effects from different sound metrics (low frequency vs. A-weighted), and the limitation of resources necessitate high-quality models to predict noise exposure for individuals in a diverse city setting and suggest interventions. **Aim:** To identify the effectiveness of prediction models for the typically measured A-weighted and understudied low frequency sound and characterize environmental health disparities at every parcel in Providence, RI. **Methods:** In total, a representative sample of 715 short-term sound measurements were collected across Providence from Sep-Dec 2022, during the day and night and on all days of the week. Land-use regression models were created for A-weighted and low frequency sound using these measurements. Land-use and social characteristics of parcel centroids and average weather conditions of samples were used in these models to predict and map estimated sound for all ~44k parcel centroids at all time points. We tested differences of sound by social and health classes across all parcels. **Results:** Models were successful at predicting sound levels with minimal covariates, with  $R^2$  of 0.42 and 0.29 for A-weighted and low frequency models respectively, and low testing error with average difference between predicted and actual decibels (dB) of 1.896 dBA for modeled A-weighted sound and 4.5 dB for modeled low frequency sound. There was a significant difference of both sound metrics between parcels of high and low income as defined as above or below median income as well as parcels of high and low physical health. **Conclusion:** Modeled sound across all frequencies from short-term measurements can identify at-risk addresses for frequency-specific noise-related health disparities and be used with individual health data to determine the influence of urban noise on health.

**Indoor air pollution and cardiovascular health of adults in biomass fuel-using households of Bangladesh: A cross-sectional study.**

Mohammad Shahriar\* Mohammad Shahriar Mahbub Eunos Shyfuiddin Ahmed Muhammad Ashique Haider Chowdhury Shirmin Bintay Kader Bilkis A Begum Rabab-Al-Shams Golam Sarwar Dewan S Alam Faruque Parvez Rubhana Raqib Mohammad Yunus Habibul Ahsan

*Background:* Indoor Air Pollution (IAP) has been linked to an array of adverse health hazards, including cardiovascular mortality and morbidity. We assessed whether IAP is associated with cardiovascular (hemodynamic) parameters as part of the Bangladesh Global Environmental and Occupational Health (GEO Health) project.

*Methods:* We assessed cardiovascular parameters-Systolic Blood Pressure (SBP), Diastolic Blood Pressure (DBP), and Heart rate (HR) using a standard cuff sphygmomanometer (Omron); Mean Arterial Pressure (MAP) and Pulse Pressure (PP) using the standard formula and endothelial dysfunction using a fingertip peripheral arterial tonometry device (EndoPAT). The exposures to particles with an aerodynamic diameter  $< 2.5\mu\text{m}$  (PM<sub>2.5</sub>) and Black Carbon (BC) from biomass fuel were measured for 24 hours using a personal monitor, RTI MicroPEM (RTI International, NC), among healthy, non-smoking women (n=400) and men (n=200). A multiple linear regression model adjusted for potential confounders was used to examine the association between HAP exposures and hemodynamic outcomes.

*Results:* The average 24-hour PM<sub>2.5</sub> concentration was 167.7  $\mu\text{g}\cdot\text{m}^{-3}$  for females and 98.0  $\mu\text{g}\cdot\text{m}^{-3}$  for males. The average 24-hour concentration of BC was 14.1  $\mu\text{g}\cdot\text{m}^{-3}$  for females and 10.3  $\mu\text{g}\cdot\text{m}^{-3}$  for males. In the adjusted multivariable regression model, a 1% increase in BC resulted in a 1.6 mm of Hg reduction in MAP (95% CI: -3.24, -.03 mm of Hg, P=0.04), 2.8 mm of Hg increase in PP (95% CI: 1.55, 4.22 mm of Hg, P=0.00) and 2.6 mm of Hg reduction in DBP (95% CI: -4.09, -1.10 mm of Hg, P=0.00). No association was observed between BC and SBP, as well as BC and HR. PM<sub>2.5</sub> was not associated with any of the hemodynamic parameters, even after adjusting for age, cooking duration, household income, and Body mass index (BMI). Also, none of the exposures were associated with endothelial dysfunction.

*Conclusion:* This population-based study provides evidence that exposure to IAP (BC) is linked with central hemodynamic parameters, especially MAP and PP, both of which have negative implications for cardiovascular health when they become high and low.

### Association between use of hair products and DNA methylation-based metrics of biological age in the Sister Study

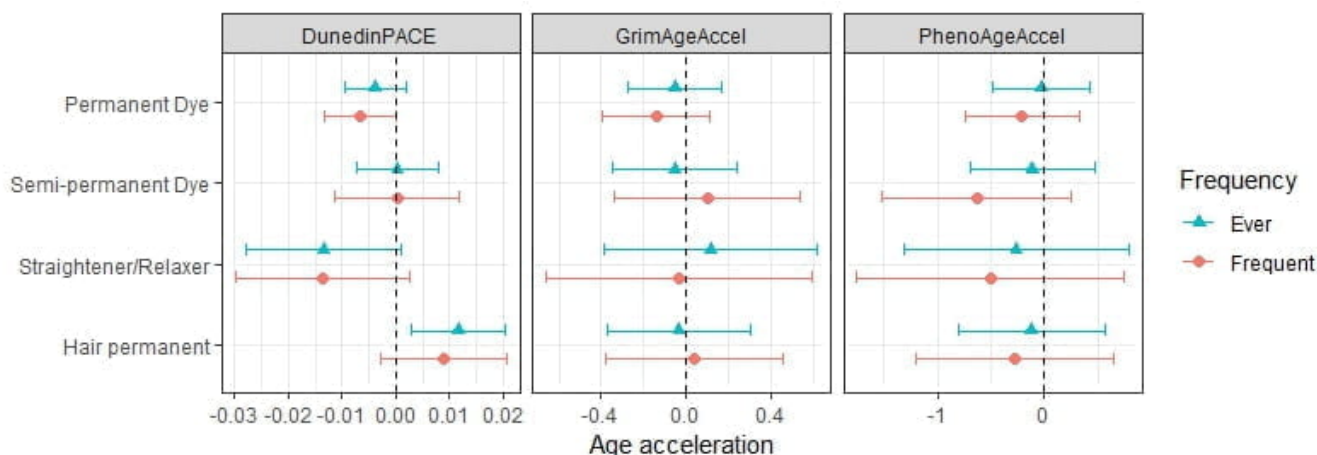
Che-Jung Chang\* Che-Jung Chang Katie M. O'Brien Zongli Xu Jacob K. Kresovich Jamaji C. Nwanaji-Enwerem Symielle A. Gaston Chandra L Jackson Dale P. Sandler Jack A. Taylor Alexandra J. White

**Background.** Use of hair products, a potential source of chemical exposure, has been associated with age-related diseases such as cancer. However, to our knowledge, no prior study has examined the associations between hair products and DNA methylation (DNAm)-based metrics of biological aging.

**Methods.** This cross-sectional study was conducted in a stratified random sample of Black (n=675) and non-Hispanic White (NHW) women (n=3,728) in the Sister Study. Participants self-reported their frequency of use of hair products (permanent dyes, semi-permanent dyes, straighteners/relaxers, and hair permanents) in the 12 months prior to enrollment (2003-2009). Blood DNAm was measured using either Illumina's HumanMethylation450 or MethylationEPIC arrays. DNAm age acceleration was measured by GrimAgeAccel and PhenoAgeAccel, and DNAm aging rates were measured by DunedinPACE. We examined associations between use of hair products and the three biological age metrics using linear regression adjusting for sampling weights, methylation arrays, race, socioeconomic status, BMI, smoking status, and physical activity.

**Results.** As measured by DunedinPACE, use of hair permanents was associated with faster biological aging (ever vs never,  $\beta=0.012$ , 95%CI: 0.003-0.021; >2 times vs never,  $\beta=0.009$ , 95%CI: -0.003, 0.021), whereas use of permanent dyes and straighteners/relaxers were associated with slower biological aging (permanent dyes: ever vs never,  $\beta=-0.004$ , 95%CI: -0.010, 0.002, >4 times vs never,  $\beta=-0.007$ , 95% CI: -0.013, 0.000; straighteners/relaxers: ever vs never,  $\beta=-0.013$ , 95% CI: -0.028, 0.001, >4 times vs never,  $\beta=-0.014$ , 95% CI: -0.030, 0.003). We did not observe consistent associations between hair products and GrimAgeAccel or PhenoAgeAccel or heterogeneity by race.

**Conclusion.** Hair product use may contribute to DNA methylation-based biological aging among women in the US.



**Parental preconception exposure to per- and polyfluoroalkyl substances in relation to birthweight** Yu Zhang\* Yu Zhang Vicente Mustieles Leah Martin Yang Sun Alexandra Hillcoat Zainab Bibi Nicole Torres Ayanna Coburn-Sanderson Irene Souter John C. Petrozza Yi-Xin Wang Carmen Messerlian

## Background

Although prenatal per- and polyfluoroalkyl substances (PFAS) exposure has been associated with lower birthweight, the influence of preconception PFAS exposure in either parent is absent.

## Methods

This study included 312 mothers and 145 fathers with a singleton live birth from a prospective preconception cohort of subfertile couples seeking fertility treatment at a clinic in Massachusetts, USA. Six PFAS compounds were quantified in baseline serum samples. Birthweight was obtained from delivery records and low birthweight (LBW) was defined as < 2500 grams. We utilized linear regression, logistic regression, and quantile-based g computation to examine the associations between maternal or paternal serum PFAS concentrations (log-2 transformed single compound concentration or quartiles of the total mixture) and birthweight and LBW, adjusting for confounders.

## Results

The mean (SD) age was 34.5 (3.8) years for mothers and 36.6 (5.1) years for fathers. Most of the participants were white, non-smokers, and nulliparous. Maternal preconception serum concentrations of perfluorooctane sulfonate (PFOS) (-161.4 g, 95% CI: -268.3, -54.6), perfluorohexane sulfonate (PFHxS) (-94.3 g, 95% CI: -180.4, -8.1), and the total PFAS mixture (-96.9 g, 95% CI: -195.8, 2.0) were inversely associated with birthweight. Maternal preconception serum PFOS concentration was associated with an increased risk of LBW (OR: 1.87, 95% CI: 1.09, 3.21). In contrast, paternal preconception serum concentrations of PFOS (144.5 g, 95% CI: -10.0, 299.0) and PFHxS (111.5 g, 95% CI: -16.9, 240.0) were positively associated with birthweight.

## Conclusion

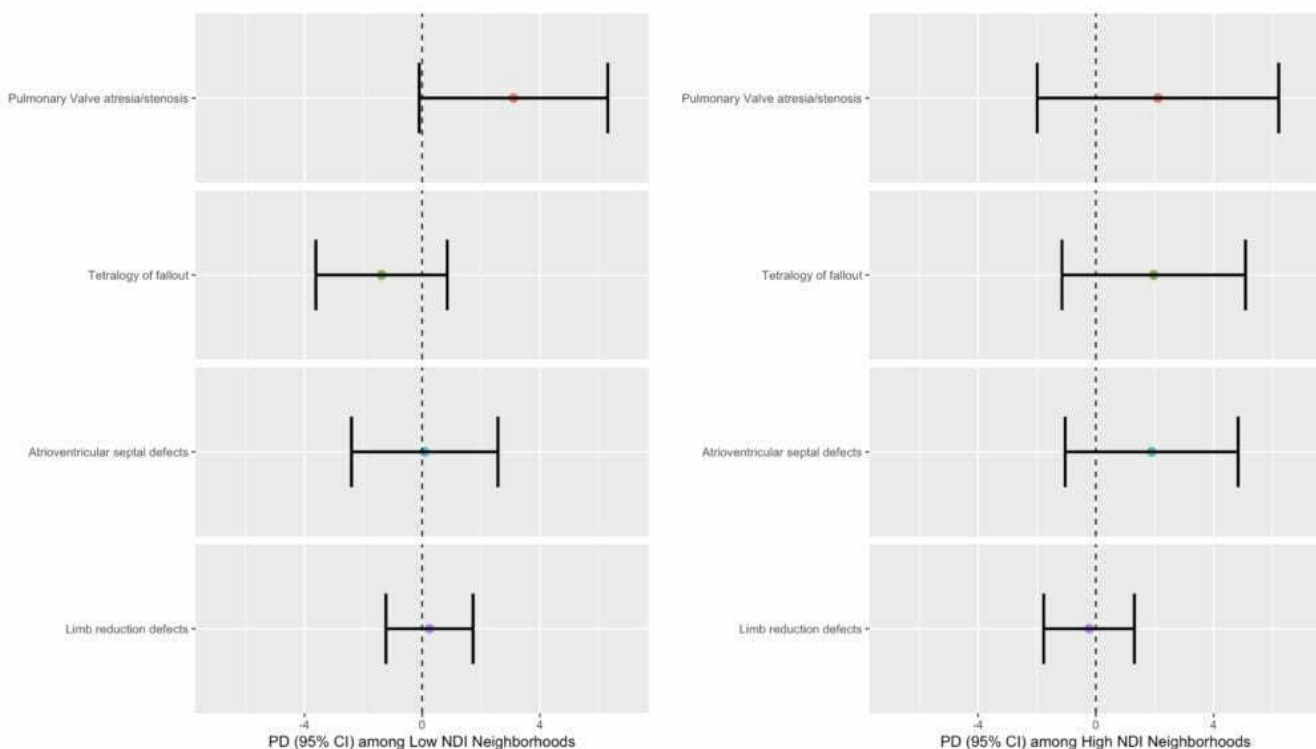
In this prospective cohort of subfertile couples, maternal preconception exposure to PFOS, PFHxS, and the total PFAS mixture was associated with lower birthweight, while opposite associations were found with birthweight for paternal preconception PFOS and PFHxS exposure. Future studies with larger sample sizes are needed to validate these findings.



**Effect measure modification of the association between air pollution and birth defects by neighborhood deprivation, North Carolina 2011-2015** Kristen Cowan\* Kristen Cowan Monica P. Jimenez Lynne C. Messer Alison K. Krajewski Thomas J Luben Kristen M. Rappazzo

About 3% of babies born in North Carolina (NC) are diagnosed with a birth defect. The objective of this study was to evaluate whether associations between gestational exposure to fine particulate matter (PM2.5) during trimester 1 and birth defects were modified by neighborhood deprivation in a NC birth cohort from 2011-2015. Modeled daily PM2.5 concentrations from EPA’s Community Multiscale Air Quality (CMAQ) model were aggregated to census tract, and linked to residential address at delivery, and then averaged across the first trimester to estimate exposure. The Neighborhood Deprivation Index (NDI) was created using principal component analysis with census variables representing income/poverty, education, employment, housing, and occupation; with NDI dichotomized into high and low deprivation at the median. Linear binomial regression models were used to estimate prevalence differences (PDs) per 10,000 births stratified by high or low NDI categories, adjusted for gestational education. Of the 566,799 births, 3.12% had at least one birth defect, 479 had pulmonary valve atresia/stenosis, 245 had tetralogy of Fallot (TOF), 299 had atrioventricular septal defects, 80 had lower limb reduction defects and 213 had gastroschisis. The daily median PM2.5 concentration during trimester 1 was 9.45 µg/m3 among those in low NDI neighborhoods and 9.36 µg/m3 among those in high NDI neighborhoods. The adjusted PDs for PM2.5 and birth defects were not significant for the birth defects examined in this population and the estimates were similar between high and low NDI groups except for TOF which had a negative PD estimate for those in low NDI neighborhoods and a positive PD for those on high NDI neighborhoods. While power is limited, the potential separation of effects may suggest increased birth defects in high deprivation areas, which warrants further study with larger case numbers.

**Prevalence Differences and 95% CI for the association between a 5 unit increase in PM2.5 and Birth Defect prevalence adjusted for education**



**Cross-sectional and prospective associations of early childhood metal exposures with cognitive function: findings from the Project Viva cohort**

Ruwan Thilakaratne\* Ruwan Thilakaratne Pi-I D. Lin Sheryl L. Rifas-Shiman Julio Landero Robert O. Wright Marie-France Hivert Emily Oken Andres Cardenas

The brain develops rapidly in early childhood and is sensitive to environmental factors, but the short- and long-term impacts of exposure to heavy metals and other trace elements on cognitive ability are not well-understood, particularly while accounting for co-exposure confounding. We aimed to address this gap using data from children in Project Viva, a pre-birth cohort in Boston, Massachusetts. We measured erythrocyte concentrations of 9 non-essential metals (As, Ba, Cd, Co, Cs, Hg, Pb, Sn, and Sr) and 6 essential metals (Cu, Mg, Mn, Mo, Se, and Zn) in early childhood blood samples (mean age: 3.0 years). Children completed cognitive tests at the same visit, measuring visual-motor ability (Wide Range Assessment of Visual-Motor Abilities (WRAVMA)) and receptive vocabulary (Peabody Picture Vocabulary Test, 3<sup>rd</sup> edition (PPVT-III)). Children also completed cognitive tests at the mid-childhood visit (mean age: 7.8 years). We used multivariable linear regression to estimate the mean difference in test score associated with a doubling of metal concentration, adjusting for confounders and metal co-exposure. Among 349 children included in the analyses (college-educated mothers: 74%), a doubling of Pb concentration was associated with lower WRAVMA score (-2.48 points, 95% CI: -4.01, -0.95) and lower PPVT-III score (-1.42 points, 95% CI: -3.26, 0.41). A doubling of Mg was associated with higher WRAVMA score (9.27 points, 95% CI: 2.87, 15.66) and higher PPVT-III score (6.91 points, 95% CI: -0.92, 14.74). Metal concentrations were not significantly associated with mid-childhood cognition. After accounting for metal co-exposure, we observed cross-sectional associations of Pb and Mg with early childhood cognition that did not persist into mid-childhood. As erythrocyte metal concentrations represent recent (~3 months) exposure, these results suggest potentially acute or reversible effects of early life metal exposure on cognition.

**Transgenerational Effects of Arsenic Exposure among Mother-Daughter pairs on Obesity**

Shelbie Stahr\* Shelbie Stahr Lora Rogers Gail Runnells Edgar Ellis Susan Kadlubar Jun Ying Ping-Ching Hsu L. Joseph Su

**Purpose.** Exposure to high levels of arsenic (As) is known to cause cancer, heart disease, and diabetes, all of which have obesity as a risk factor. However, little is known on its association with obesity in human studies. Arkansas has high environmental levels of As with low population mobility resulting in prolonged lifetime exposure across generations. There is a gap in the literature regarding the long-term effects of As exposure and the consequences of said exposure in offspring. This study aims to examine the relationship between As exposure and the risk of obesity in mother-daughter pairs. **Methods.** A cross-sectional sample of 709 mother-daughter pairs (total N=1,418) from the Arkansas Rural Community Health Study were recruited between 2007 and 2013 with detail survey and saliva samples collected. Inductively coupled plasma-mass spectrometry was used to detect salivary As concentrations. Multivariable logistic regression models were performed to determine the odds ratio (OR) and 95% confidence intervals of the association between As levels and obesity status among mother-daughter pairs while adjusting for the age difference between mothers and daughters, mothers ethnicity, daughters age and geographic location. **Results.** This study found that obese mothers had increased odds of having an obese daughter (OR 4.08; 95%CI 2.12-7.88), and mothers with high As levels were more likely to have a daughter with high As levels (OR 5.48; 95%CI 3.06-9.83). Lastly, when observing the effect of both mothers obesity and As levels on daughters obesity, obese mothers with low As have increased odds of having obese daughters, compared to non-obese mothers with low As (OR 4.39; 95%CI 1.38-14.01). **Conclusion.** This study suggests that environmental As affects the odds of obesity across generations, although the exact mechanism is unknown. Continued investigation is necessary to determine the location of As on the causal pathway of obesity.

**PAH Biomarkers of Air Pollution, Adverse Pregnancy Outcomes and Placental Weight in a Los Angeles Birth Cohort** Sanjali Mitra\* Sanjali Mitra Qi Meng Irish Del Rosario Michael Jerrett Peggy S. Sullivan Sherin U. Devaskar Carla Janzen Beate Ritz

Numerous studies have shown the association of air pollution with adverse birth outcomes, such as, reduced birth weight, preterm birth and preeclampsia. The mechanisms of these associations are yet to be delineated. Polycyclic aromatic hydrocarbons (PAHs) are found in air pollution from traffic and industries. They are endocrine disrupting chemicals that form adducts with DNA in the human placenta. The placenta not only exchanges fetal waste and supports fetal growth with nutrients but also produces and metabolizes growth-regulating hormones. We studied the association between biomarkers of PAH exposure in pregnant women and placental weight at birth as well as ischemic placental diseases (IPD). IPD includes preeclampsia, preterm birth and intra-uterine growth restriction.

A prospective cohort study, PARENTs, recruited pregnant women between 2016 and 2019 from antenatal clinics at the University of California, Los Angeles. For 159 participants, PAH metabolites were measured in the urine during pregnancy. Placentas were collected and weighed at birth. IPD was assessed using medical records and study exams. Multiple linear and logistic regression was used to analyze the data.

Increases in PAH metabolites were associated with a decrease in placental weight and higher odds of IPD. We estimated a 12.2g decrease (95% CI: - 23.30, -1.09) and a 7.6g decrease (95% CI: -14.0, -1.09) in placental weight, per IQR increase in average level of 4-hydroxyphenanthrene (PHEN4) and 1- hydroxypyrene (PYR1) measured during pregnancy, respectively. Each per IQR increase in 3-hydroxyphenanthrene (PHEN3) measured in the first trimester increased the odds of IPD 1.97-fold (95% CI: 1.03, 3.79).

Metabolic products of PAHs in pregnant women are linked to poor birth outcomes and placental weight. Our results can inform public health policies aimed at reducing the impacts of air pollution.

**An evidence mapping approach to support hazard identification for polychlorinated biphenyl (PCB) mixture exposure and developmental endpoints** Krista Christensen\* Krista Christensen Rachel Shaffer Catheryne Chiang John Meeker Geniece Lehmann

Systematic evidence maps (SEMs) facilitate the organization and review of complex databases. SEMs can be helpful in identifying when epidemiological data may be sufficient to determine associations between exposures and health effects, and where animal or other data can address research gaps in the human database. We used SEM methods to survey human and animal studies on polychlorinated biphenyls (PCBs) exposure and developmental effects and determine if the database is likely to support human health hazard identification. We developed a Population, Exposures, Comparators, and Outcomes (PECO) statement to direct the literature search (through Sept 2021), screening, and categorization. Data were extracted into literature inventory tables. To identify outcomes promising for human health hazard identification, we considered: database size, study design, biological significance of the outcome, and exposure characterization. We identified >300 studies evaluating PCB exposures and developmental effects. Most human studies focused on birth weight or other aspects of fetal growth. Body size in early life also had an abundance of animal data. Similarly, human studies of pregnancy loss are supplemented by many animal studies that assessed offspring viability. Birth defects were investigated in few human studies and tended to have few cases, but 24 studies investigated PCBs and structural alterations in animals. Database strength is high for birth weight and other indicators of size and growth in early life. The strength of the human evidence for other developmental effects is limited by few studies, small sample sizes or case numbers, and variations in study design. However, animal studies can provide additional information for evaluating potential hazards of PCB exposure. *Disclaimer: The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the U.S. EPA*

**Assessing the Effect of Decreased Tailpipe Emissions on Adverse Birth Outcomes: A 20-Year Retrospective Accountability Study** Mary D. Willis\* Mary Willis Elaine L. Hill Lena Harris Andrew Larkin Beate Ritz Perry Hystad

Background: Billions of dollars have been spent to reduce the toxicity of tailpipe emissions via federal regulations over the past three decades, but the benefits for population health are unclear. We hypothesized that the magnitude of association between adverse birth outcomes and indicators of traffic related air pollution (TRAP) exposure would decrease over time, paralleling regulatory improvements in tailpipe emissions.

Methods: Using geocoded vital statistics data (n=7.2 million, Texas, 1996-2016), we linked maternal residence at delivery to TRAP exposure measures: 1) distance to the nearest major road (i.e., highway or expressway), 2) annual vehicle miles traveled (VMT, a measure of traffic volume) within 500 meters, and 3) outdoor nitrogen dioxide (NO<sub>2</sub>) concentrations. We implemented linear and logistic regression models to examine associations with term birth weight, term low birth weight (<2,500 g), preterm birth (<37 weeks), and very preterm birth (<32 weeks.)

Results: TRAP exposures were consistently associated with adverse birth outcomes; however, results were mixed on whether associations reduced over the 20-year period. The strongest decreases were observed for highway proximity (e.g., estimates for term birth weight were -13.0 g (95% CI: -17.7, -8.3) in 1996 versus -7.3 g (95% CI: -11.4, -3.2) in 2016). For VMT, decreased associations were only observed for very preterm birth (e.g., odds ratios for >20,000 VMT compared to <1500 were 1.15 (95% CI: 0.97, 1.37) in 1996 versus 1.08 (95% CI: 0.96, 1.20) in 2016). The impact of a 1-unit increase in NO<sub>2</sub> concentrations on birth outcomes were also consistent across the 20-year period.

Conclusion: We observed some evidence of improvements in birth outcomes associated with reductions in tailpipe emissions over a 20-year period in Texas; however, results varied by TRAP exposure metric and adverse birth outcome and were much smaller than the 70% reduction in TRAP levels observed over this period.

**Does hypertension mediate the effect of long-term air pollution exposure on dementia?**

Tanya Libby\* Tanya Libby Sindana Ilango Cindy Leary Erin Semmens Claire Adam Annette Fitzpatrick Anjum Hajar Joel Kaufman

Growing evidence links air pollution exposure to risk of dementia, although the underlying mechanisms remain unclear. We hypothesize that hypertension may partially mediate the effect of air pollution on dementia.

We have previously documented an association between air pollution and dementia in the Ginkgo Evaluation of Memory Study (GEMS), a clinical trial of 3,046 adults  $\geq 75$  years across four U.S. sites who were evaluated for dementia every 6 months from 2000 - 2008. We used causal mediation analysis to decompose the total effect of air pollution on dementia into its natural direct and indirect effect through hypertension. Hypertension was defined as systolic blood pressure (BP)  $\geq 140$  mmHg, diastolic BP  $\geq 90$  mmHg, or use of an antihypertensive. Exposure to air pollution 20 years before enrollment was assigned using estimates from fine-scale spatial-temporal air pollutant models for  $\text{NO}_2$  and  $\text{PM}_{2.5}$ . We used logistic regression models for hypertension and Cox proportional hazard models for time to dementia for each interquartile range (IQR) increase in pollutant, adjusting for age, sex, education, smoking, secondhand smoke, and neighborhood deprivation index (NDI). We ran separate models for all-cause dementia, Alzheimer's disease (AD), and vascular dementia with or without AD (VaD).

At enrollment, 69% of participants had hypertension; during follow-up, 12% developed all-cause dementia (AD=212; VaD=97).  $\text{NO}_2$  and  $\text{PM}_{2.5}$  were associated with 1.04 (0.90, 1.19) and 0.96 (0.85, 1.07) times the odds of hypertension per IQR increase, respectively. Hypertension was significantly associated with VaD (HR 2.32 [1.47, 3.67]) but not AD or all-cause dementia. We did not observe mediation through hypertension for the effect of either pollutant on dementia outcomes.

There was no evidence that hypertension mediated the effect of air pollution on dementia outcomes for either pollutant. This may be due to the minimal effect of air pollution on hypertension in this cohort of older adults.

**LATEBREAKER**

Environment/Climate Change

**Chronic Kidney Disease (CKD) in Chile: changes in the period 2010-2021** SANDRA CORTES\*

Sandra Cortés Jenny Ruedlinger Standen LUIS CELIS Claudia Foerster

**Background:** The climatic variability characteristic of the Anthropocene is expressed in the occurrence of events such as heat waves, changes in precipitation, or droughts. These events have already been reported in Latin America, among other regions. International agencies are promoting research into the links between these events and damage to respiratory, cardiovascular, and renal health.

**Aim:** To identify changes in the presentation of CKD and describe temporal and geographic trends in hospital admissions for CKD in Chile during the period 2010-2021.

**Methods:** An ecological study of hospital discharge data of patients diagnosed with CKD was conducted using ICD10 codes: N18.1 (CKD stage 1), N18.2 (CKD stage 2-mild), N18.3 (CKD stage 3-moderate), N18.4 (CKD stage 4-severe), N18.5 (CKD stage 5-very severe), N18.6 (end-stage CKD), and N18.9 (CKD unspecified). Rates per 100,000 population (100,000 inhabitants) are calculated using official estimates of the population at risk during the period 2010-2021.

**Results:** A total of 113,762 hospital admissions for CKD were reported under the N18 code. The rate per 100,000 population showed a decreasing trend from 61.54 in 2010 to 37.66 in 2021. From the age of 30, the average rate of hospital discharges between 2010 and 2021 at the national level was 20.29 per 100,000 inhabitants; this figure increased more than sevenfold from the age of 60 (average rate 160.16 per 100,000 inhab. in the same period studied). However, stage 5 CKD, in particular, has shown a sustained increase (7.85 per 100,000 inhab. in 2010 and 20.13 per 100,000 inhab. in 2021). On the other hand, unspecified CKD has shown a significant decrease (53.13 per 100,000 inhab. in 2010 and 16.53 per 100,000 inhab. in 2021). Moderate and severe CKD, with lower rates, show significant increases in the period (N18.3 from 0.14 to 0.95 per 100,000 inhab; N18.4 from 0.39 to 1.93 per 100,000 inhab. respectively).

The highest rates of discharges were concentrated in the central-southern zone of Chile, an area with a temperate rainy and dry climate and a predominance of agro-forestry activities.

CKD is a pathology whose evolution in severity should be monitored, considering the different meteorological scenarios that occur throughout Chile and the productive characteristics of each region with their consequent exposures. Particular attention should be paid to the younger and working people to prevent the progression to more severe and terminal stages.



**Phthalates and Replacements Associated with Fetal Growth in the Human Placenta and Phthalates Study** Danielle Stevens\* Danielle Stevens Emma Rosen Erin McNell Elena Sinkovskaya Anna Przybylska George Saade Alfred Abuhamad Kelly Ferguson

**Background:** Pregnant persons are commonly exposed to endocrine-disrupting chemicals such as phthalates and increasingly to potentially harmful chemicals introduced to replace phthalates, referred to as “regrettable substitutions”. Exposure to these chemicals may perturb fetal growth, potentiating adverse consequences for the infant.

**Objective:** Investigate longitudinal associations between phthalate and replacement biomarkers in pregnancy and fetal growth.

**Methods:** We analyzed data from 295 participants in the Human Placenta and Phthalates Study, a prospective pregnancy cohort of predominantly Black Americans with recruitment 2017-2020. Participants provided up to eight urine samples, which were used to quantify average concentrations of phthalate and replacement biomarkers in early, mid, and late pregnancy. Outcomes were fetal ultrasound biometry z-scores (head and abdominal circumferences, femur length, estimated fetal weight) in early, mid, and late pregnancy. Time-varying g-computation was used to estimate the difference, on average, in longitudinal fetal growth for a one-interquartile range (IQR) increase in phthalate and replacement biomarkers. Models were then extended to examine periods of susceptibility.

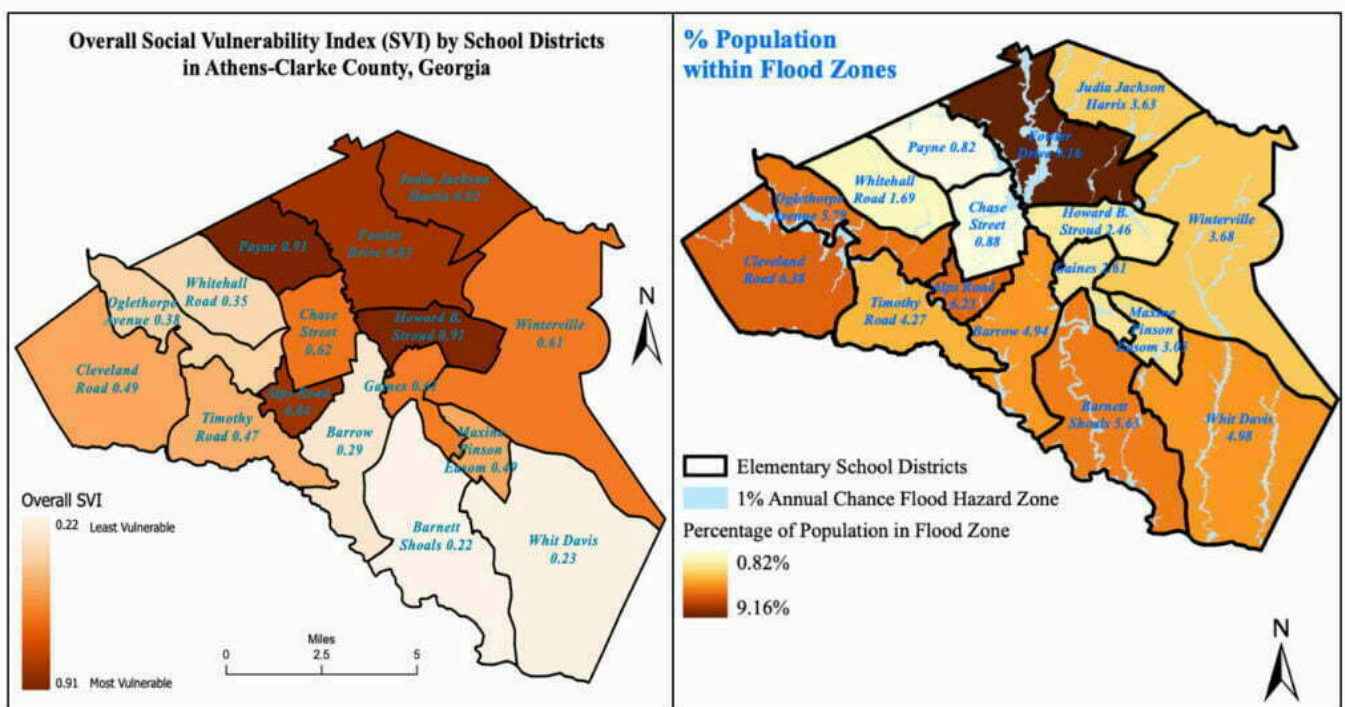
**Results:** Gestational phthalate and replacement biomarkers were imprecisely inversely associated with fetal head circumference ( $\beta$ : -0.19 [95% confidence interval: -0.4, 0.03]), abdominal circumference (-0.17 [-0.43, 0.08]), and estimated fetal weight (-0.17 [-0.63, 0.29]), but not femur length (-0.01 [-0.05, 0.03]). For abdominal circumference, late pregnancy appeared to be a period of increased susceptibility (early: 0.11 [-0.13, 0.35], mid: -0.2 [-0.43, 0.03], late: -0.51 [-0.87, -0.15]) to exposure. The association was mainly driven by phthalates, with no associations observed for replacements.

**Conclusions:** In a modern, diverse cohort with well-characterized, longitudinal exposure and outcome assessment, phthalates were inversely associated with fetal growth.

**The Use of Geospatial Methods to Determine Social and Climatological Risk of Communities in Athens-Clarke County, Georgia** Christopher P. Carr\* Christopher Carr Yasemin Inceoglu Koyun Jun Tu Allan D. Tate

Hurricanes, floods, and other climatological events will continue to affect more geographic areas and populations in the U.S with greater frequency and intensity. When exposed to these events, racially minoritized populations experience worse health outcomes relative to racial majority populations. This is referred to as the extreme weather-climate gap. The application of geospatial methods to determine where the most at-risk populations live is key to addressing this gap. Classification of geospatial, social and natural hazard vulnerability to climatological disasters is needed for intervention development; however, data are frequently not in shared formats and structures. For example, CDC’s Social Vulnerability Index (SVI) is at the census tract level, US Census data is at the census block level, and school attendance zones (SAZs) are the practical administrative unit for local government. Computing spatial vulnerability requires new methods for SAZ linkage. Areal interpolation is one suitable method and was used to assess the social and climatological vulnerability of SAZs. This process involved calculating SVI for each SAZ from CDC SVI data at the census tract level and the SAZ population from U.S. Census data at the census block level. Estimating the population under flood risk for each SAZ was conducted using the flood zone layer from FEMA’s Flood Insurance Rate database to clip the layer of population by census block of the SAZs. Figure 1 shows the calculated SVI and percentage of population residing in a 1% annual chance flood hazard zone for each SAZ and shows Fowler Drive is one of the most socially vulnerable and has the largest population living in a flood zone (9.16%). The current methodological study explores applications of geospatial methods for disaster prevention and intervention across multiple spatial scales for building climate resilience.

Figure 1: Social Vulnerability and Percent of Population within Flood Zones, Athens-Clarke County, Georgia



**Toxic and essential metals associated with gestational age in the ELGAN cohort** Eric Brown, Jr.\* Eric Brown, Jr. Rebecca Fry T. Micheal O'Shea Amaree Gardner

Prenatal exposure to individual toxic metals is associated with adverse neonatal outcomes, specifically reduced gestational age, but few studies have investigated whether such outcomes are associated with metal mixtures. This study evaluated the association between umbilical cord metal concentrations and gestational age. Data were collected from 294 children from the Extremely Low Gestational Age Newborn (ELGAN) cohort, a multi-center cohort study. Umbilical cords were collected and analyzed for levels of 11 metals: Arsenic (As), Manganese (Mn), Cadmium (Cd), Lead (Pb), Mercury (Hg), Copper (Cu), Antimony (Sb), Strontium (Sr), Selenium (Se), Barium (Ba), and Zinc (Zn). Metal co-exposures were modeled in three groups: total measured metals (As, Mn, Cd, Pb, Hg, Cu, Sb, Sr, Se, Ba, and Zn), toxic metals (Pb, As, Mn, Cd, Hg, Sr, Sb, Hg, Ba), and essential metals (Cu, Zn, Se). Additional metal mixtures analyses were performed using quantile g-based computation including the same groupings of total metals, toxic metals, and essential metals. All models controlled for maternal education, insurance status, maternal age, maternal body mass index, and maternal smoking status. In the co-adjustment models, cord levels of Sr ( $\beta$ : -2.25,  $p = 0.04$ ) and Se ( $\beta$ : -6.93,  $p = 0.03$ ) were significantly associated with decreased gestational age. In the metal mixtures analysis, a combined total metal mixture was related to gestational age with an estimated reduction of 2.75 gestational days ( $p=0.01$ ). Levels of Pb, Sb, Cu, and As were associated with increased gestational age (mean difference: +1.85 days), while Ba, Mn, Se, Cd, Hg, Zn, and Sr are associated with 4.61 gestational day reduction. In summary, prenatal metal exposure is associated with altered gestational age in preterm infants, highlighting the need for exposure monitoring programs for metal mixtures in pregnant women.

**Urinary arsenic and incident cognitive impairment: the REGARDS Trace Element Study**

Meghan Angley\* Meghan Angley Yijia Zhang Liping Lu Shai Bejerano Ka Kahe

**Objective:** Arsenic exposure can impair cognitive function. Most studies examining this association include populations with high arsenic exposure and few examine individual arsenic species. We investigated the associations between cognitive impairment and total arsenic, inorganic arsenic and two arsenic metabolites in a population with low to moderate arsenic exposure.

**Methods:** We used data from the Reasons for Geographic and Racial Differences in Stroke (REGARDS) Trace Element Study, a U.S. study of Black and White individuals  $\geq 45$  years at baseline. Total urinary arsenic (As) was measured in 2,666 participants while concentrations of inorganic arsenic (iAs), monomethylarsonic acid (MMA) and dimethylarsinic acid (DMA) were measured in a subset of participants ( $n=325$ ) using inductively coupled plasma mass spectrometry. All measurements were normalized by urinary creatinine and log-transformed. The Six-Item Screener (SIS), a test of global cognitive functioning, was administered annually. Participants were impaired on the SIS if they scored  $\leq 5$  on at least 2 assessments and  $\leq 4$  on at least 1 assessment (out of 6). Associations between As, iAs, MMA and DMA and incident impairment were assessed using logistic regression.

**Results:** After exclusions for impairment at baseline, 2,101 individuals with a median As concentration of 8.1 (IQR: 4.6 - 16.8)  $\mu\text{g/g}$  creatinine were included. Over 10 years of follow-up, 195 individuals developed impairment. After adjustment for confounders, As (OR: 0.96 [95% CI: 0.79, 1.17]), iAs (OR: 1.24 [95% CI: 0.77, 1.89]) and DMA (OR: 0.87 [95% CI: 0.44, 1.73]) were not associated with impairment. MMA was associated with a 2-fold increase in odds of incident impairment (OR: 2.59 [95% CI: 1.02, 6.59]).

**Conclusions:** MMA, an arsenic metabolite, but not As or iAs, was associated with impairment. This suggests that individual arsenic metabolites, particularly MMA, may be predictors of cognitive functioning even at a relatively low levels of exposure.

**Associations between urinary o-toluidine and depressive symptoms in NHANES 2013-2014**

Giehae Choi\* Giehae Choi

**Introduction:** O-toluidine is a widespread, high production volume carcinogen used in dyes, pigments, rubber, and photographic agents. Evidence from high-exposure, occupational settings suggests that the central nervous system is another target organ. Research is needed on low-level exposures that are relevant to those in the general U.S. population.

**Methods:** Associations between o-toluidine and mental health were explored cross-sectionally using NHANES 2013-2014. Urinary o-toluidine concentrations were creatinine standardized after substituting values below the limit of detection (LOD) with LOD/ $\sqrt{2}$ . Patient Health Questionnaire-9 on anhedonia, depressed mood, sleep disturbance, fatigue, appetite changes, low self-esteem, concentration problems, psychomotor disturbances, and suicidal ideation (0-3 scale) was used to identify participants with clinically significant depressive symptoms (summed score  $\geq 10$ ). The odds ratios (ORs) and corresponding confidence intervals (CI) per interquartile range increase in o-toluidine were estimated with generalized linear models using quasibinomial link. Crude, adjusted (age, education, sex, and country of origin), and sex-stratified analyses were conducted.

**Results:** Of the 2,100 individuals with complete data, o-toluidine was detectable in 87.3% and clinically significant depressive symptoms were present in 10.6%. The ORs of clinically significant depressive symptoms associated with 956 pg/mL increase in o-toluidine was 1.08 in the crude model [CI: 0.99, 1.19] and 1.16 in the adjusted model [1.03, 1.29]. ORs were greater in males (1.19 [1.00, 1.41]) than in females (1.04 [1.04, 1.36]), however, CIs overlapped.

**Conclusion:** Higher levels of urinary o-toluidine were associated with greater odds of clinically significant depressive symptoms. Findings suggest the need for further investigations using longitudinal study designs.

**Interaction between epigenetic age acceleration and demographic factors on blood lipid levels in the Health and Retirement Study** Lisha Lin\* Lisha Lin Jenna Kiryakos Farah Ammous Scott M. Ratliff Erin B. Ware Jessica D. Faul Sharon L.R. Kardia Kira Birditt Jennifer A. Smith

Understanding the relationship between the epigenome and lipid levels can help guide prevention and treatment efforts of dyslipidemia, a major risk factor for cardiovascular disease. We used weighted linear regression models to cross-sectionally investigate the associations between measures of epigenetic age acceleration estimated from whole blood DNA methylation and blood lipids (total cholesterol (TC), LDL-C, HDL-C, and triglycerides (TG)) in 3,813 participants (mean age=70 years) from the Health and Retirement Study. After adjusting for age, race/ethnicity, gender, fasting status, lipid-lowering medication use, body mass index, smoking, and education, GrimAge acceleration and DunedinPoA38 acceleration were associated with all lipid measures ( $p < 0.05$ ), except for DunedinPoA38 and TG. These associations were stronger in participants who fasted prior to blood draw and those not taking lipid-lowering medication. Further adjustment for white blood cell proportions did not attenuate the associations. We next added interaction terms between epigenetic age acceleration and demographic factors (age, gender, or education). A 1-year increase in GrimAge acceleration had a stronger association with decreased TC in older vs. younger participants (1.11 vs. 0.34 mg/dL at the 75<sup>th</sup> vs. 25<sup>th</sup> age percentile, mean=77 vs. 62 years) and with increased TG in younger vs. older participants (2.23 vs. 1.01 mg/dL). PhenoAge acceleration and GrimAge acceleration were both associated with a larger decrease in HDL-C in females than in males (0.23 vs. 0.06 mg/dL and 0.74 vs. 0.28 mg/dL, respectively). For those with a high school degree vs. those without, a 1-year increase in HannumAge acceleration was associated with a 0.01 vs. 0.51 mg/dL decrease in HDL-C. The inverse associations between epigenetic aging and TC may be due to survival bias. In conclusion, epigenetic profiles may increase our understanding of the relationship between biological aging and cardiovascular disease risk factors.

**LATEBREAKER**

Genetics

**Polygenic risk for major depression, attention deficit hyperactivity disorder, neuroticism, and schizophrenia are associated with childhood and adulthood indicators of socioeconomic status.** Andrew Ratanatharathorn\* Andrew Ratanatharathorn Lori B. Chibnik Karestan C. Koenen Natalie Slopen Marc G. Weisskopf Andrea L. Roberts

**Background:** Research has suggested that low socioeconomic status is a risk factor for later mental illness. We tested whether this association is due in part to gene-environment correlations.

**Methods:** Using polygenic risk scores for six psychiatric disorders - attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), bipolar disorder (BPD), major depressive disorder (MDD), neuroticism, and schizophrenia - and a combined measure of overall genetic risk for mental illness, we tested whether women's genetic risk for mental illness was associated with indicators of childhood SES (maternal and paternal education and occupation) as well as adult SES (marital status, income, social standing, and community measures).

**Results:** Participants in the highest quintile of genetic risk for ADHD, MDD, neuroticism, schizophrenia, and combined genetic risk were at higher risk of having parents with lower education attainment (OR range: 1.15 to 1.38) compared to participants in the lowest quintile of genetic risk. Participants in the highest versus lowest quintile of genetic risk for ADHD and overall genetic risk were more likely to have married, while those in the highest quintile for MDD, schizophrenia, and overall genetic risk, versus those in the lowest quintile, were more likely to have been divorced or separated. Participants in the highest quintile of genetic risk for BPD were less likely to be in a lower income quartile, while in the highest quintile of genetic risk for ASD, neuroticism, and overall genetic risk were more likely to be in a lower quartile of community social standing and, except for ASD, US social standing.

**Conclusion:** Associations between SES and mental illness may be confounded in part by genetic risk for mental illness. These results indicate that interventions on childhood and adult SES may have less effect than predicted on later mental illness especially for individuals with high genetic risk.

**Human milk oligosaccharides and enteric infection risk in Nicaraguan children** Rebecca Rubinstein\* Rebecca Rubinstein Roberto Herrera Christian Toval Nadja Vielot Lester Gutiérrez Yaoska Reyes Fredman González Omar Zepeda Filemón Bucardo Sylvia Becker-Dreps Samuel Vilchez

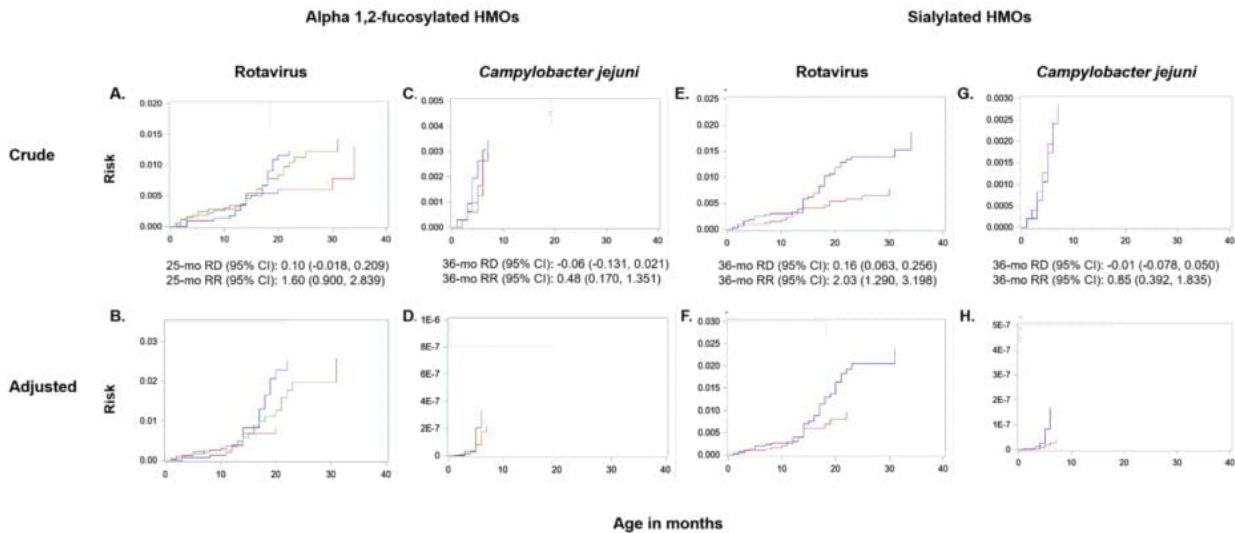
**Background:** Diarrhea is the third-leading cause of death in children under 5 worldwide, claiming 525,000 lives annually. Children who survive may develop malnutrition, stunting, and cognitive delays. Most of the leading infectious causes of diarrhea are not vaccine-preventable. Human milk oligosaccharides (HMOs) in breastmilk are a modifiable risk factor for enteric infections, as they can be added to formula.

**Methods:** We examined how the 36-month risk of rotavirus and *Campylobacter jejuni* infections differed by concentrations of alpha 1,2-fucosylated and sialylated HMOs in a Nicaraguan birth cohort. Eligible children were breastfed for at least 2 months. HMO composition at 1-month post-partum was measured using fluorescent high-and-ultra-high-pressure liquid chromatography. Children were surveilled weekly for diarrhea, and stool pathogens were detected using polymerase chain reaction. We stratified Kaplan-Meier curves by expression of alpha 1,2-fucosylated oligosaccharides in children and adjusted for child sex, Cesarean delivery, poverty, and weekly breastfeeding frequency.

**Results:** In 286 children, children consuming the highest concentrations of alpha 1,2-fucosylated and sialylated HMOs had the highest risk of rotavirus. Similar patterns were observed in crude but not adjusted models of *C. jejuni* incidence (Fig. 1). These trends persisted in children stratified by expression of intestinal oligosaccharides, and after removing breastfeeding from the model to avoid conditioning on a potential mediator. *C. jejuni* infections also occurred earlier than rotavirus.

**Conclusions:** Our findings support prior studies on rotavirus, *C. jejuni* and HMOs, suggesting that alpha 1,2-fucosylated and sialylated HMOs may reduce rotavirus vaccine immunogenicity yet protect against *C. jejuni* by serving as decoy receptors that prevent these pathogens from attaching to the gut. Future studies should investigate additional HMOs and outcomes and confirm these findings in randomized trials.





**Figure 1. 36-month cumulative risk of rotavirus and *Campylobacter jejuni* infections in 286 Nicaraguan children by concentrations of alpha 1,2-fucosylated and sialylated HMOs in breastmilk.** Alpha 1,2-fucosylated HMOs were stratified into thirds. Red strata represent mothers producing the bottom 33% of HMOs, blue strata represent mothers producing the middle 33% of HMOs, and green strata represent mothers producing the top 33% of HMOs. Sialylated HMOs were stratified into halves. Red strata represent mothers producing the bottom 50% of HMOs, and blue strata represent mothers producing the top 50% of HMOs. Crude RD and RR were calculated for the risk of rotavirus and *Campylobacter* infections comparing the top 33% and bottom 33% strata of alpha 1,2-fucosylated HMOs and the top 50% and bottom 50% of sialylated HMOs. A,C,E,G represent crude models, and B,D,F,H represent adjusted models.

**Early life grandmother caregiving trajectories and child development in rural Pakistan**

Esther Chung\* Esther Chung Linda Adair Stephanie Martin Brian Pence Sean Sylvia Siham Sikander  
Joanna Maselko

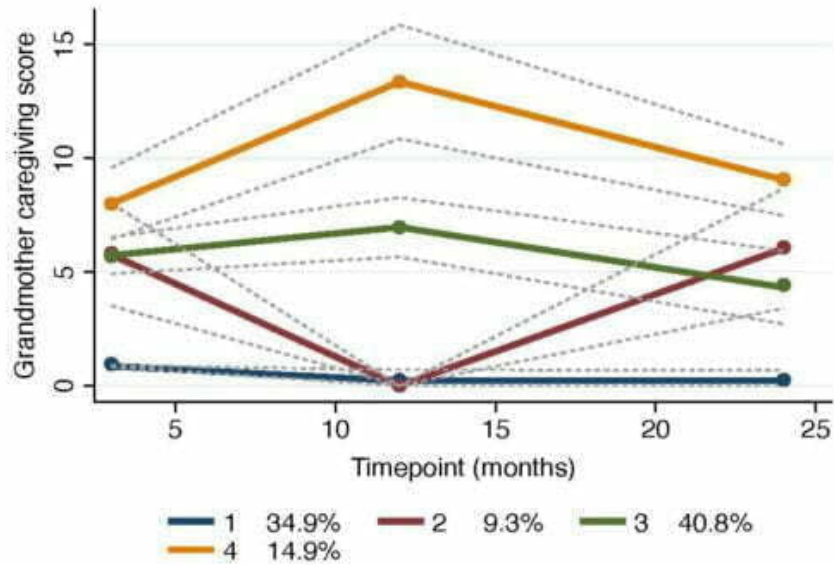
**Background:** Most child health interventions target mothers, however, across many contexts, grandmothers are key decision-makers on maternal and child health issues. This study sought to characterize trajectories of grandmother childcare from infancy to 2 years and examine associations between these trajectories and child development at 6 years.

**Methods:** We used data from 959 families participating in a birth cohort in rural Pakistan. Maternally reported grandmother caregiving was measured at 3 months, 1, and 2 years using a 24-hour recall of childcare activities. Child outcomes at 6 years included cognitive and socioemotional development. We identified groups of children who shared common grandmother caregiving trajectories using group-based trajectory modeling. We estimated weighted multivariable generalized linear models of the relationships between grandmother caregiving trajectory membership and child outcomes.

**Results:** We found four distinct grandmother childcare trajectories across the first 2 years of life: (1) Consistently Low (34.9%), (2) Medium-Low-Medium (9.3%), (3) Medium (40.8%), and (4) Consistently High (14.9%). Children with grandmothers in the Consistently High trajectory group had better inhibitory control scores compared to those in the Consistently Low group. No meaningful differences were found between trajectories with vocabulary or working memory skills. Those with grandmothers in the Medium-Low-Medium group had more behavioral problems and less prosocial behaviors. No differences with anxiety scores were observed.

**Discussion:** Overall, we found dynamic grandmother caregiving patterns across the first 2 years of life. Children whose grandmothers provided consistently high levels of caregiving during this period had better inhibitory control. Importantly, children with inconsistent grandmother caregiving exhibited worse behavioral problems. Capturing caregiving patterns over time is key and stability may be especially important in early life.

**Figure 1. Grandmother caregiving trajectories among families in rural Pakistan, Bachpan Cohort (n=959).**



The solid lines show predicted mean grandmother caregiving scores and the dotted lines are 95% confidence limits. The groups were labeled as (1) Consistently Low, (2) Medium-Low-Medium, (3) Medium, and (4) Consistently High. The size of each group (%) were estimated by the model and were slightly different from the actual size in subsequent analyses.

**Assessing the impact of substance use treatment for preventing criminal justice system contact in Chile** Andrés González-Santa Cruz\* Andrés González-Santa Cruz Mariel Mateo-Pinones Álvaro Castillo-Carniglia

**Background.** Extensive research has shown that reducing substance abuse through effective treatment leads to a reduction in criminal activity. However, evidence from Latin America is largely unknown. We analyse Chile as a case study and examine the impact of SUT outcome (completion, late drop-out at  $\geq 90$  days in treatment or early drop-out at  $< 90$  days) on the prevention of contact with the criminal justice system in different periods.

**Methods.** We used a deterministic linkage process (using encrypted Chilean national IDs) to merge electronic records of individuals in publicly funded Chilean SUT programs with the Prosecutor's Office data at the national level between 2010-2019. Incidence rates were used to determine the extent to which treatment was associated with time until committing an offense that led to a contact with the criminal justice system or to imprisonment after baseline treatment.

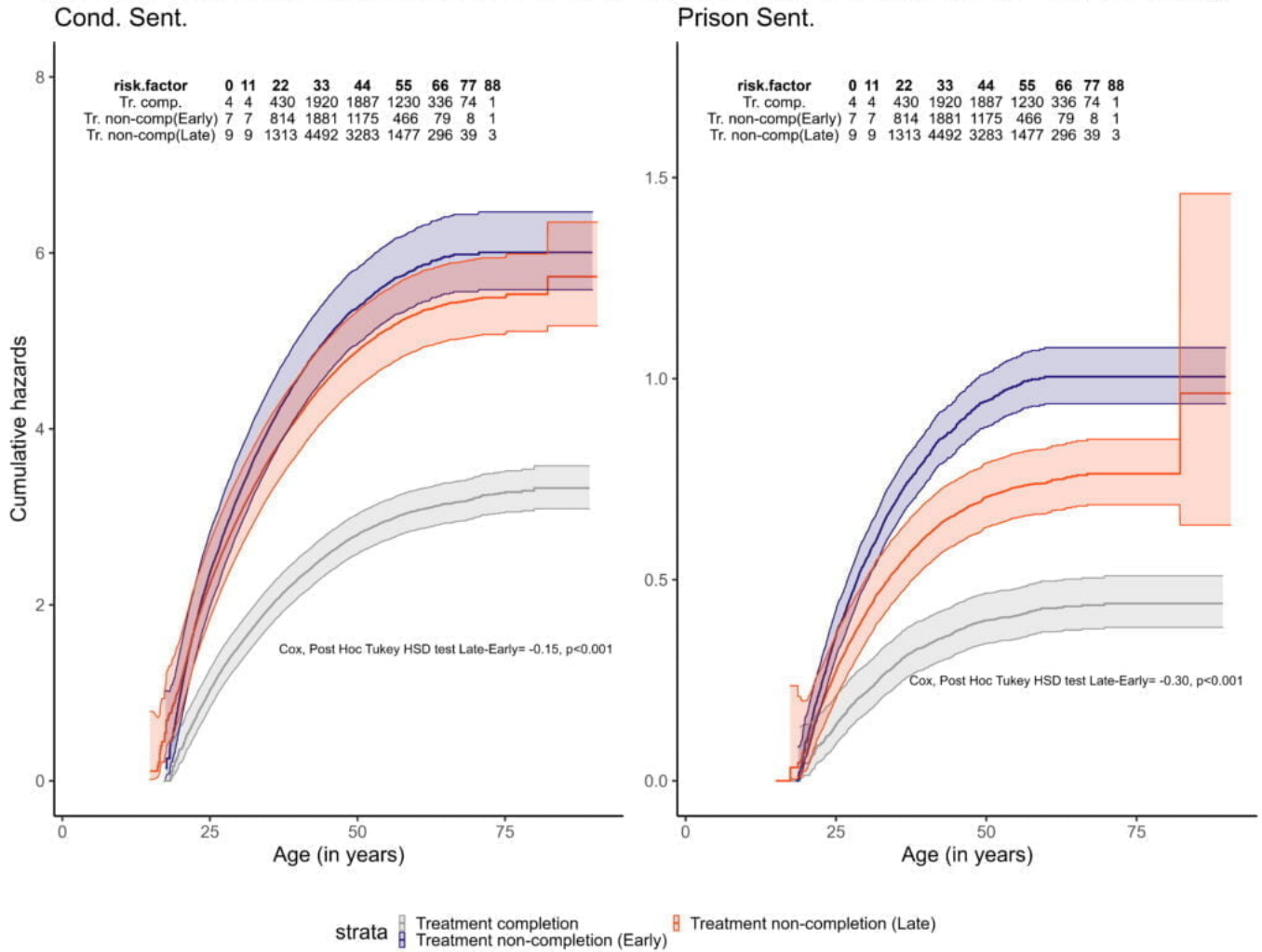
**Results.** Of the 85,048 SENDA patients, 70,863(83%) were matched with the Prosecutor's Office database. Of the sample, 22,287(31%) had at least a contact with the criminal justice system, while 5,144(7%) for imprisonment.

Compared to early drop-out, those completing SUT took longer to contact the criminal justice system (IRR= 2.18 95% CI 2.09, 2.27) and to an offence leading to imprisonment (IRR=2.90 95% CI 2.64, 3.18).

Compared to late drop-out, those completing SUT took longer (IRR=1.73 95% CI 1.67, 1.80) to contact the criminal justice system and to an offence leading to imprisonment (IRR=1.93 95% CI 1.77, 2.10). The difference was lower when we compared those who received some treatment with the least exposed to SUT for some period (early vs. late drop-out) regarding the time to contact the criminal justice system (IRR=1.26 95% CI 1.22, 1.30) and imprisonment (IRR=1.50 95% CI 1.41, 1.61) (Figure 1).

**Conclusion:** Further research is needed to account for staggered entry to follow-up and confounders of the association.

Figure 1: Nelson-Aalen Cumulative Hazards of Offense from baseline treatment outcome (Staggered entry)



**Menstrual Hygiene Management and School Attendance Among Schoolgirls in a Peri-Urban Region of Nigeria: “We Secretly Hide Them”** Madeline Tomlinson\* Madeline Tomlinson  
Natalie DuPre Anne Wallis Richard Baumgartner Friday Okonofua Muriel Harris

Girls in low-income settings face challenges preventing attainment of adequate menstrual hygiene management (MHM), which can lead to poor health, educational, and social outcomes. This study aimed to investigate the MHM factors associated with school attendance to identify MHM improvements in a peri-urban region of Edo State, Nigeria.

Mixed methods were conducted among consenting girls aged 11-19 years old in 3 secondary schools in Edo State. In-depth interviews with students, a questionnaire, and an assessment of school MHM facilities. MHM was defined as access to sanitary materials, changing space, disposal, and water sources. Inductive thematic analysis was used to assess the qualitative interviews (N=60). Among 539 menstruating schoolgirls, descriptive statistics and multivariable logistic regression estimated the association between individual MHM factors, physical symptoms, knowledge of menstruation and school days missed in the past 3 months.

The median age of menarche was 12.9 years (SD=1.3 years). Across the interviews and questionnaires, girls reported physical pain, anxiety, and a lack of MHM facilities at school, among other issues. 74 (13.7%) girls reported missing at least one day of school due to menstruation. Missing school was associated with inconsistent access to water at school (OR 1.75 (0.81, 3.78)), although not significantly. In addition, physical symptoms (headache OR 1.90 (1.10, 3.28); stomach pains OR 1.43 (0.71, 2.91); and back pain OR 1.52 (0.83, 2.75)), and never learning about menstruation (OR 2.71 (1.03, 7.14)) were associated with missing school due to menstruation.

Among this Nigerian schoolgirl population, a lack of water access at school, delayed MHM education, and painful symptoms increased the odds of missed school days. This study highlights the need for an intervention that addresses the structural challenges (e.g., access to sanitation, disposal, and changing facilities), pain management, and menstrual education.

**The Physical and Mental Health of Sexual and/or Gender Minority Parents** Diana M. Tordoff\*  
Diana Tordoff Ava Snow Brent Monseur Mitchell R. Lunn Annesa Flentje Micah E. Lubensky Zubin  
Dastur Deb Kaysen Stephanie Leonard Juno Obedin-Maliver

**Background:** An estimated 3 million sexual and/or gender minority (SGM) adults in the US are parents. The number of SGM parents is expected to increase as younger SGM cohorts desire parenthood at nearly twice the rate of older generations. However, little is known about the health and wellbeing of SGM parents.

**Methods:** We conducted a cross-sectional analysis with 2018-2020 data from The PRIDE Study, a national online cohort of SGM adults. We used Poisson regression to compare physical and mental health outcomes of SGM people who are parents to those who are not parents, adjusted for age. Outcomes included self-reported diagnosis history and standardized assessment tools for current mental health symptoms (*e.g.*, PHQ-9 for depression, GAD-7 for anxiety, and PCL-5 for post-traumatic stress [PTSD]).

**Results:** Among the 9625 SGM participants, 1460 (15%) were parents. Parents were significantly older than non-parents (median age of 45 v 28 years). Compared to non-parents, parents were more likely to have been diagnosed with pelvic inflammatory disease (aPR 1.80 95%CI: 1.25-2.61) or to have ever smoked (aPR 1.18 95%CI: 1.07-1.30) and were less likely to be living with HIV (aPR 0.37 95%CI: 0.24-0.57). Parenthood was also associated with adverse depression (aPR 1.19 95%CI: 1.06-1.34), anxiety (aPR 1.26 95%CI: 1.10-1.45), and PTSD symptoms (aPR 1.28 95%CI: 1.11-1.47). Notably, a higher proportion of young parents age <30 reported adverse mental health symptoms compared to older parents age 30-39 and 40, including moderate to severe depression (54%, 37%, and 21%, respectively), anxiety (50%, 30%, 14%), and PTSD symptoms (45%, 27%, 16%; all p-values<0.001). There was no association between parenthood and alcohol use, substance use, diabetes, or hypertension.

**Conclusion:** SGM parents reported poorer mental health symptoms compared to SGM non-parents. SGM parenthood is likely associated with unique minority stressors that influence their mental and physical health.

**Mexican Americans agree to participate in stroke research more than non-Hispanic whites**

Chen Chen\* Chen Chen Xu Shi Madeline Kwicklis Madelyn Malvitz Erin Case Lynda D Lisabeth Lewis B Morgenstern

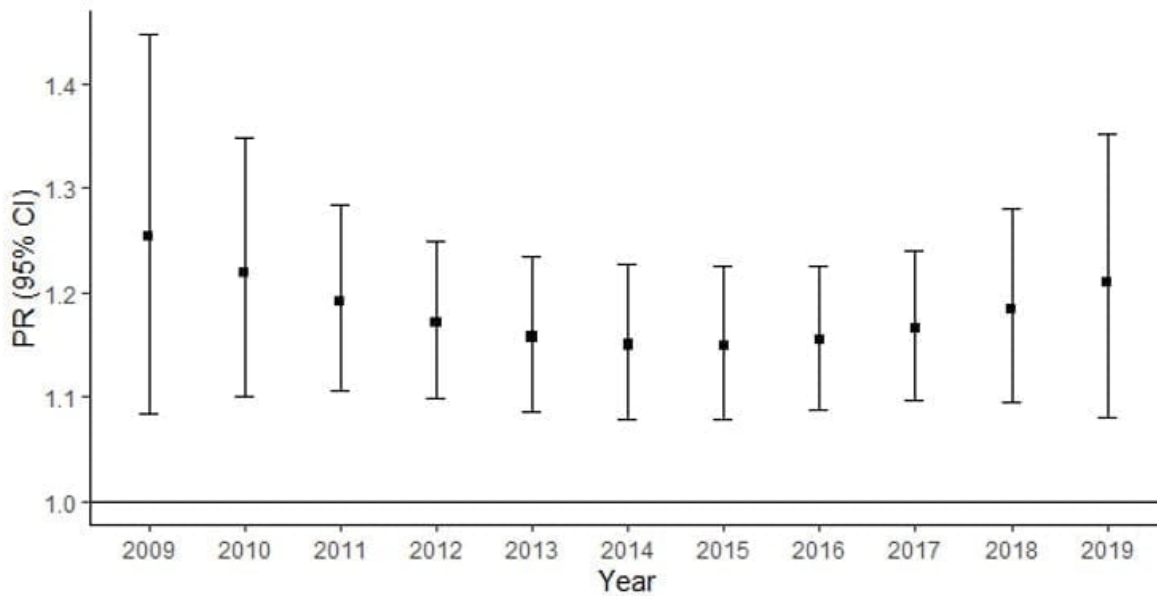
**Introduction:** The National Institutes of Health advocates for improved participation of minorities in clinical research. However, prior research focused almost exclusively on ethnic differences in participation in clinical trials, especially on differences between Black Americans and non-Hispanic whites (NHW). Limited data exist for Mexican American (MA) participation in observational clinical research. We examined differences between MA and NHW participation in a community-based stroke cohort study.

**Methods:** Data were from the Brain Attack Surveillance in Corpus Christi Project, 2009-2020 in Texas, USA. Patients with validated strokes are approached and invited to participate in a structured baseline interview. We included all patients with first-ever strokes. We defined participation as completing baseline interview by patient or proxy. We used modified Poisson models adjusting for prespecified potential confounders to estimate prevalence ratios (PR) of participation comparing MA with NHW. We further stratified the analysis by sex to examine potential effect modification in the ethnic differences in participation by sex. Finally, we included an interaction between year and ethnicity in the unstratified final model to examine ethnic specific trends in participation in the total population.

**Results:** Among 3,594 first ever stroke patients (57.7% MA), baseline participation was 77.0% in MA and 64.2% in NHW (PR 1.20; 95% CI, 1.14-1.25). The ethnic difference remained after multivariable adjustment (1.19; 1.13-1.25). The PR of participation was 1.20 (1.11-1.30) and 1.18 (1.10, 1.27) in women and men respectively. Participation increased over time for both ethnic groups ( $P_{trend} < 0.0001$ ), but remained significantly different throughout the 11-year time period (**Figure**).

**Conclusion:** MAs were persistently more likely to participate in this observational clinical study, which questions the commonly held view of lower participation in minority groups drawn from clinical trials.





**Figure Year-specific ethnic differences in participation over time**

Figure shows the participation prevalence ratio comparing MAs to NHWs in each year. Prevalence ratios were adjusted for age, sex, health insurance status, stroke severity, disease histories of hypertension, high cholesterol, diabetes, atrial fibrillation, coronary artery disease, comorbidity score, smoking status, binge drinking status, and neighborhood socioeconomic status indicators. Functional forms of calendar year, age, and stroke severity required quadratic terms.

**Examining Fairness of the Premature Mortality Population Risk Tool (PreMPoRT):****Development, Validation, and Calibration Across Equity Stratifiers** Laura C. Rosella\* Meghan O'Neill Mackenzie Hurst Lief Palagan Lori Diemert Kathy Kornas Stacey Fisher Andy Hong Douglas G. Manuel Laura C. Rosella

**Introduction:** Population risk models that perform poorly among equity deserving groups can exacerbate health inequities. Premature mortality (death prior to age 75) is an important indicator of population health that is largely preventable through targeted policies and interventions. We sought to evaluate subgroup performance of a prediction model for premature mortality.

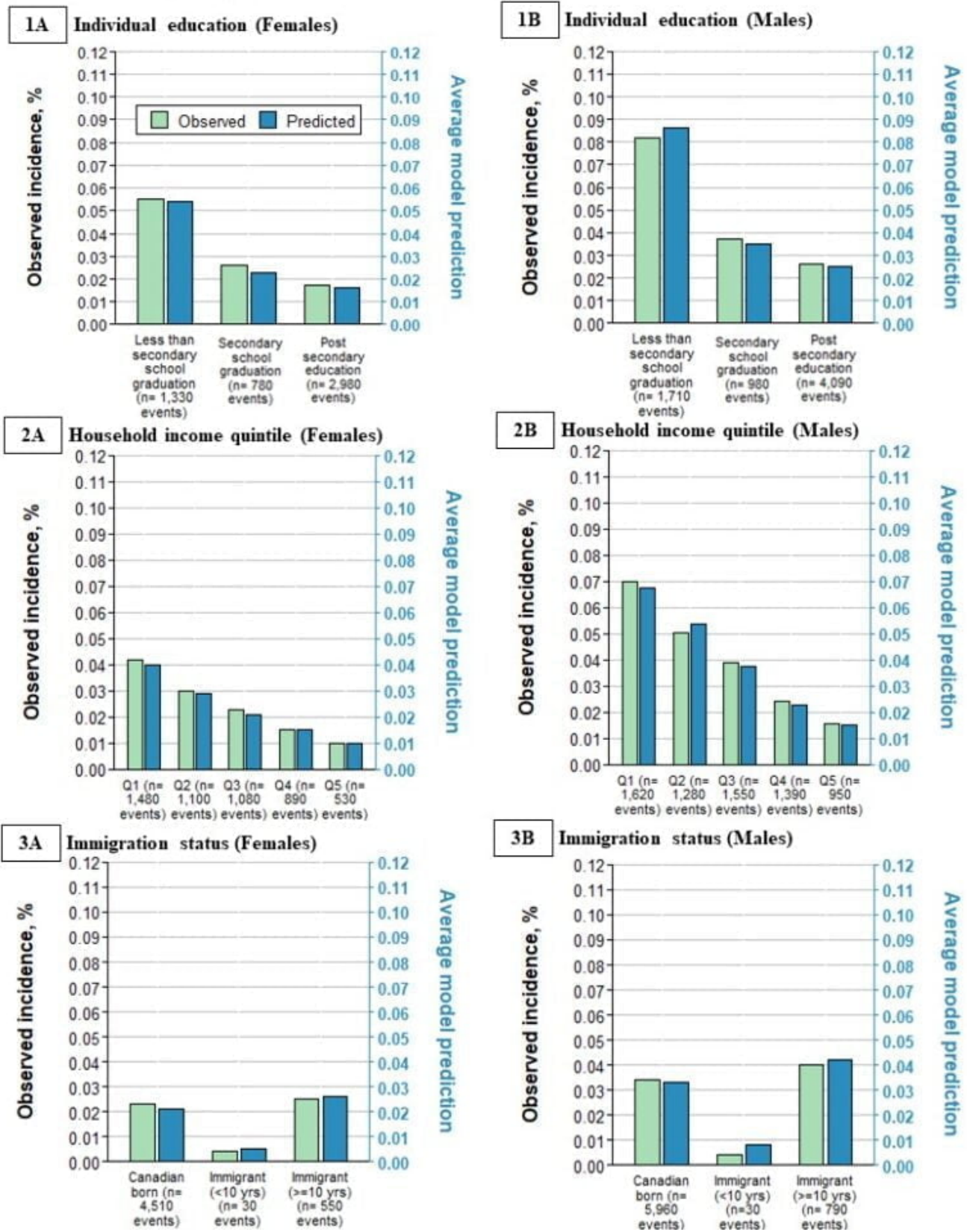
**Objective:** Using the Premature Mortality Risk Prediction Tool (PreMPoRT) we describe model development, validation, and assess calibration across important equity stratifiers.

**Methods:** Sex-specific Weibull survival models were developed to predict the 5-year incidence of premature mortality in the Canadian adult population. PreMPoRT was developed using 6 cycles of the Canadian Community Health Survey (CCHS) linked to the Canadian Vital Statistics Database from 2000-2017 for mortality outcomes. PreMPoRT was internally validated using a 70%/30% split set approach and externally validated using 3 hold-out CCHS cycles (2007-2012). Predictors included demographic, socioeconomic, health behaviours, and chronic conditions. We evaluated model calibration across equity stratifiers.

**Results:** The incidence of premature mortality was 1.40% and 2.05% for females and males, respectively, with an average follow-up time of 4.78 years. In the external validation, the models achieved c-statistics of 0.86 and 0.85 for females and males, which suggests the predictive performance of the model is strong. The model also demonstrated good calibration across equity stratifiers (Panel Figure 1). There was slight over-prediction among those with less than secondary school graduation among males (1B). Generally, there was modest under-prediction for those in lower income quintiles (2A and 2B) and slight over-prediction for immigrants (3A and 3B).

**Conclusion:** The results suggest that PreMPoRT is well calibrated across equity stratifiers and can be used to inform population-wide strategies for premature mortality prevention.

**Panel Figure 1.** Model evaluation on equity stratifies. For household income quintiles, Q1 corresponds to the lowest income and Q5 corresponds to the highest income. The number of events refers to the number of premature deaths by category.



**Modifiable risk factors for Alzheimer's disease and related dementias among Middle Eastern and North African adults** Tiffany Kindratt\* Tiffany Kindratt Kristine J. Ajrouch Florence J. Dallo Laura B. Zahodne

Modifiable risk factors across the life course play a role in the development of Alzheimer's disease and related dementias (ADRD). Studies have identified racial/ethnic disparities in ADRD risk factors. There remains a gap in the literature on the epidemiology of ADRD risk among Middle Eastern and North African (MENA) Americans, largely due to their classification as White in US national health surveys. Our aim was to estimate ADRD risk among foreign-born MENA adults compared to US-born Whites after adjusting for age and sex. We linked 2000-2017 National Health Interview Survey and 2001-2018 Medical Expenditure Panel Survey data (N=108,695; age $\geq$ 18 years). Risk factors for ADRD identified using a life course model were evaluated (yes or no) including less than ninth grade education, hearing loss, hypertension, obesity, smoking, depressive symptoms, marital status, physical inactivity, diabetes, and alcohol use. The total population attributable fraction of these risk factors for dementia is 40%. Bivariate analysis and multivariable logistic regression were conducted. Compared to US-born Whites, foreign-born MENA adults had higher odds of reporting lower education (OR=1.93; 95%CI=1.17-3.21) and depressive symptoms (OR=1.28; 95%CI=1.06-1.56). Foreign-born MENA adults had lower odds of hearing loss (OR=0.42; 95%CI=0.28-0.64), hypertension (95%CI=0.67; 95%CI=0.56-0.81), obesity (OR=0.79; 95%CI=0.63-0.98), current smoking (OR=0.60; 95%CI=0.46-0.77), and alcohol use (OR=0.42; 95%CI=0.31-0.56) than US-born Whites. Findings provide the first comprehensive look at modifiable risk for ADRD among foreign-born MENA adults and reveal evidence for both risk and resilience in this group. Without a racial/ethnic identifier for MENA individuals nationally, ADRD risk factors among US-born MENA adults cannot be examined. More research is needed to explore these risk factors by life stage (early/midlife/late) to further determine ADRD risk and prevention strategies for MENA Americans.

**Racial and ethnic disparities in recovery of everyday activities among survivors of respiratory failure** Kaitlyn Parrotte\* Kaitlyn Parrotte Mari Armstrong-Hough Luz Mercado Sherry Wu Naiyue Liang Yiwen Chen

Survivors of respiratory failure experience poor physical function and quality of life persisting five years after discharge. Racial and ethnic disparities in survival of respiratory failure are well documented; however, little is known about social determinants of recovery of physical function. Thus, we evaluated the association between race/ethnicity and level of function among survivors of respiratory failure. We identified participants enrolled in the National Institutes of Health All of Us Research Program who self-reported having experienced respiratory failure or had a code indicating respiratory failure in their electronic health record. Function was measured via a self-reported five-point Likert scale, which asked "To what extent are you able to carry out your everyday physical activities such as walking, climbing stairs, carrying groceries, or moving a chair". Unadjusted and adjusted ordinal logistic regression models were used to evaluate associations between race/ethnicity and function of survivors. Compared to non-Hispanic White survivors, Non-Hispanic Black (OR=0.76, CI=0.68-0.83) and Hispanic (OR=0.75, CI=0.68-0.83) survivors had lower odds of reporting higher function, adjusting for age and sex at birth. In analyses adjusting for education, health insurance coverage and marital status, non-Hispanic Black (OR=0.90, CI=0.82-1.00) and Hispanic (OR=0.91, CI=0.82-1.01) survivors were not significantly less likely to report higher function than non-Hispanic white survivors. In adjusted analyses, survivors with at least a high school diploma or GED reported higher levels of functional capacity (OR=1.34, CI=1.19-1.51). We found that non-Hispanic Black and Hispanic survivors of respiratory failure report lower levels of ability to carry out everyday activities after surviving respiratory failure. These differences may be explained by patterns in other social determinants of health such as education, health insurance coverage, and marital status.

**Trajectories of contacts to the healthcare system in adolescence and young adulthood** Lau Caspar Thygesen\* Sanne Pagh Møller Andrea Willson

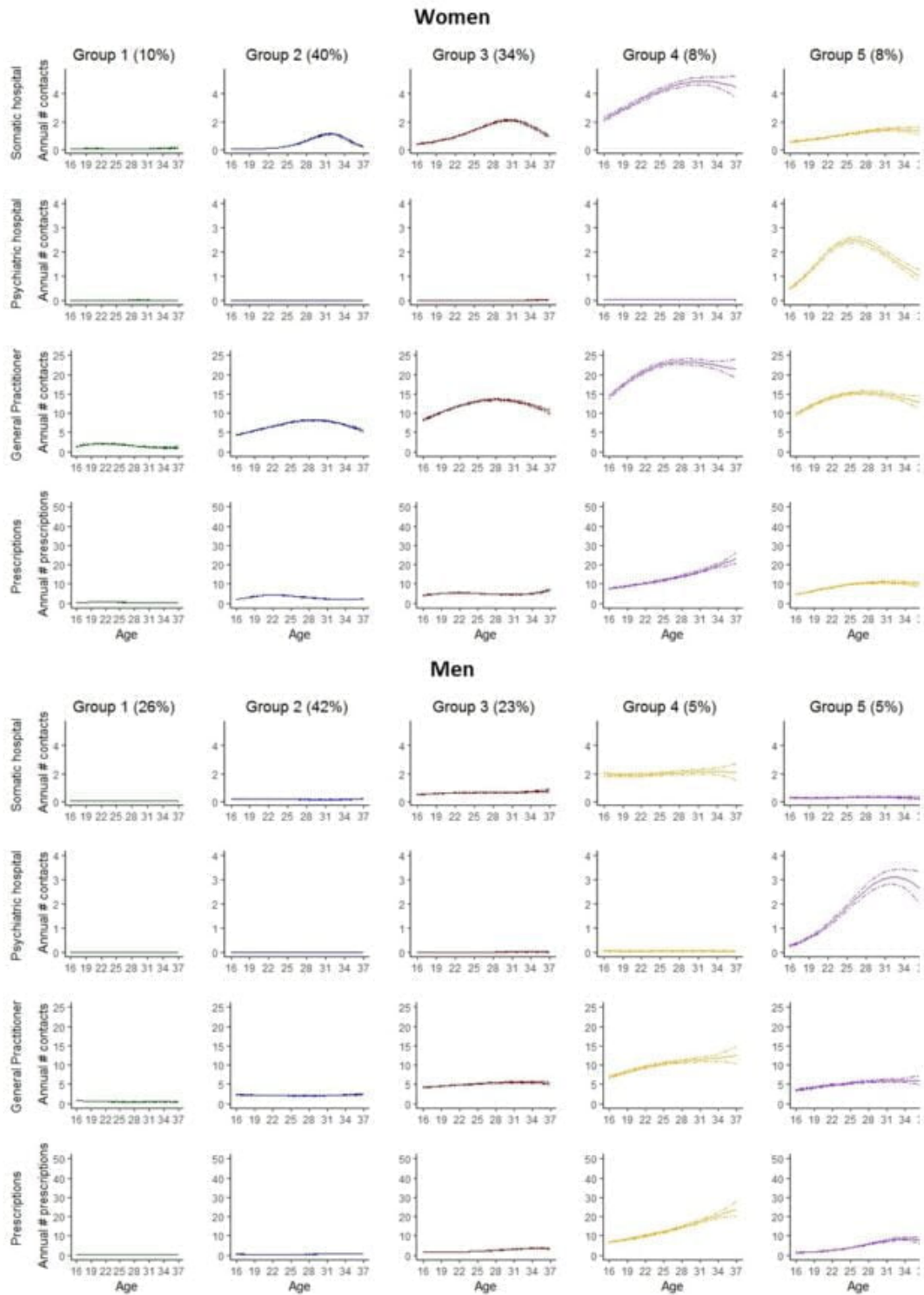
**Background:** Understanding of the healthcare utilization of different populations can be useful for both prevention and prioritization of healthcare resources. Populations following different trajectories of contacts to the healthcare system across dimensions of somatic hospitals, psychiatric hospitals, general practitioners, and redeemed prescriptions have not been previously described. This study aims to identify these populations and to describe their sociodemographic characteristics.

**Methods:** A cohort of individuals born 1980-2003 in Denmark were linked to national health registers. The annual number of contacts to somatic hospitals, psychiatric hospitals, general practitioners, and redeemed prescriptions were counted for each year between 16 and 37 years of age. Trajectories of contacts to the four dimensions of the healthcare system were identified using group-based multi-trajectory modeling. Analyses were made separately for women and men.

**Results:** Five trajectory groups were identified. Similar groups were identified for women and men but with differences in group sizes and in trajectory shapes with a higher number of contacts in women compared to men. One group had low healthcare utilization (10% in women; 26% in men), one had a high number of contacts to psychiatric hospitals (8% in women; 5% in men), one had a medium number of contacts to somatic hospitals (34% in women; 23% in men), and one had a high number of contacts to somatic hospitals (8% in women; 5% in men). The largest group mainly had contacts to the general practitioner (40% in women; 42% in men). Short parental education and unemployment was most frequent in the high and low utilization groups.

**Conclusion:** Annual information on contacts to somatic hospitals, psychiatric hospitals, general practitioners, and redeemed prescriptions was utilized to identify groups following distinct trajectories of contacts to the healthcare system. The groups differed on several sociodemographic characteristics.

Identified trajectories of contacts to the healthcare system among women and men.



**Social Determinants of Health Characteristics of Kidney Transplant Candidates Waiting from January 1, 2020 to December 31, 2020** Jesse Howell\* Jesse Howell Tatenda Mupfudze Trenece Wilson Anne Zehner Kelley Poff Alejandro Diez Paulo N. Martins

**Purpose:** The Organ Procurement and Transplantation Network (OPTN) monitors organ allocation policies in the U.S. to determine their impact. Monitoring is limited to data collected by the OPTN which contains limited information on social determinants of health (SDoH), restricting the ability to assess the effect of OPTN policies on equity in access to transplantation. The OPTN Minority Affairs Committee was interested in analyzing additional data to evaluate various SDoH stratifications to fill this gap. This abstract summarizes those results.

**Methods:** Adult kidney candidates ever waiting on the OPTN Waiting List in 2020 were linked by person-level address to a SDoH source provided by LexisNexis (LN). The OPTN-LN dataset was then linked to the Area Health Resources File (AHRF) and Robert Wood Johnson County Health Rankings by Census tract or county. The linkages allowed for use of additional variables on economic stability, health and healthcare, neighborhood and built environment, and social and community context.

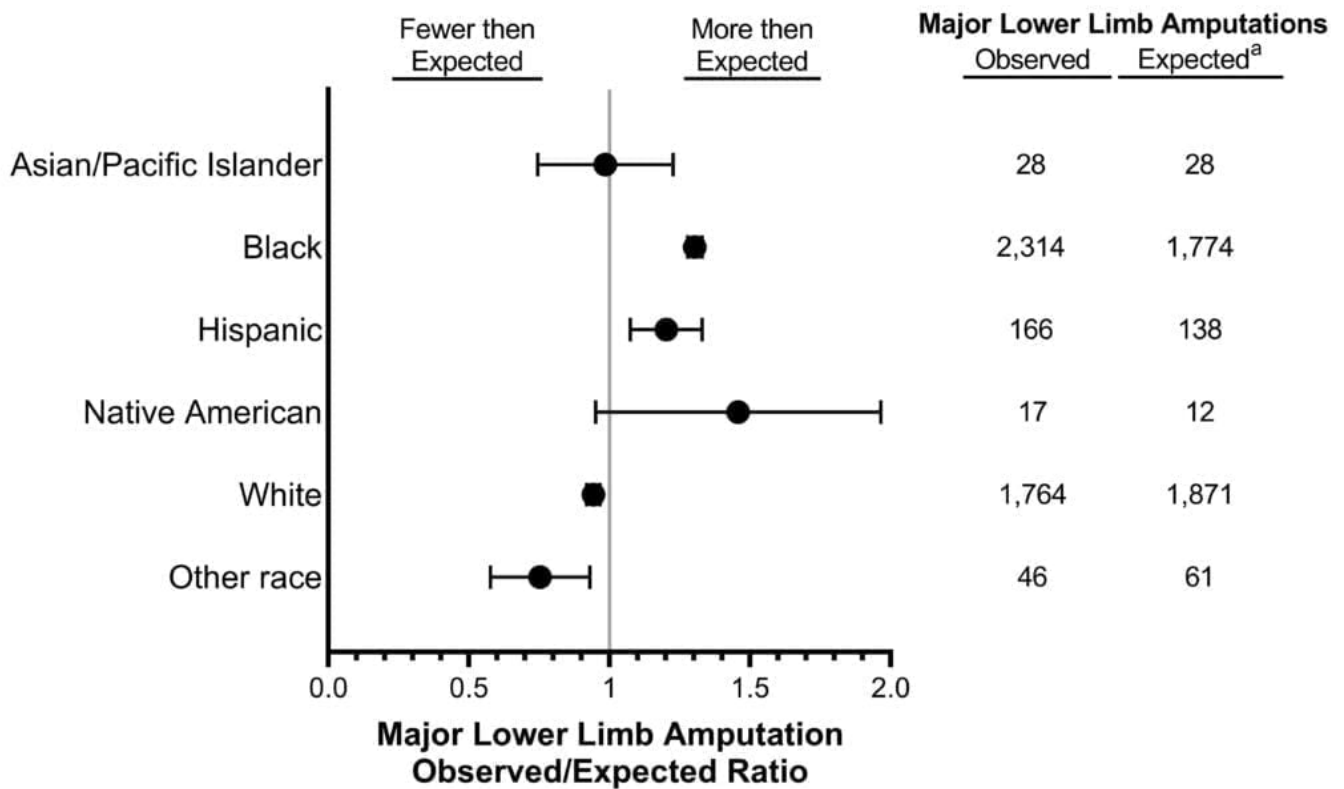
**Results:** A total of 110,611 kidney candidates were analyzed. About half the cohort (49.7%) had a history of a derogatory public record, including felonies, liens, bankruptcies, or evictions. A majority of candidates (88.2%) lived in a partial county primary care shortage area as defined by the AHRF. A third of candidates (33.0%) had an estimate annual income of \$31k-\$50k. The median neighborhood property value was \$183,177. Less than half of candidates (42.6%) had a voter registration record.

**Conclusion:** This was an early step in using third-party data to add SDoH measures to OPTN policy monitoring. With this linked data, the OPTN can assess how policies are impacting access to transplantation across SDoH stratifications that have not previously been explored. Next steps include reviewing additional cohorts of kidney candidates to analyze changes across policies, expanding analysis to additional organs, and connecting to additional data sources.



**A Novel Approach to Quantifying Health Disparities with Predictive Modeling using Racial-Ethnic Amputation Disparities as an Exemplar** Paula Strassle\* Paula Strassle Jamie Ko Corey Kalbaugh Katharine McGinigle Samantha Minc Anna Nápoles

Health disparities (HD) are health differences that adversely affect disadvantaged populations, like racial-ethnic minorities. Common methods to assess HD compare outcomes across race-ethnicity using non-Hispanic White as reference; however, this approach 1) assumes non-Hispanic White populations are the gold standard and 2) doesn't account for expected differences in outcome risk due to clinical differences and HD in upstream risk factors. To address these issues, we developed a novel approach using predictive modeling where outcome incidence is compared within each racial-ethnic group. We used major lower limb amputation (MLLA) in patients with peripheral artery disease (PAD), which has well-documented racial-ethnic disparities, as an example. PAD hospitalizations among adults  $\geq 40$  years old from 2016-2019 were identified using the Georgia State Inpatient Database, an all-payer database of all community hospital admissions in the state. We used multivariable logistic regression, adjusting for demographics and clinical characteristics (e.g., history of foot infection, chronic medical conditions) to predict the probability of MLLA using all hospitalizations; race-ethnicity was not included. Predicted probabilities within each racial-ethnic group were summed to estimate the expected number of MLLA. Observed to expected (O/E) ratios were then calculated and bootstrapping ( $n=200$ ) was used to calculate 95% CIs. Overall, 100,404 hospitalizations and 3,884 MLLAs (3.9%) were included. Even after accounting for clinical differences, an excess of MLLAs were observed among Black (O/E ratio 1.30, 95% CI 1.28-1.33) and Hispanic patients (O/E ratio 1.20, 95% CI 1.05-1.31); no excess was seen in White patients (O/E ratio 0.94, 95% CI 0.92-0.97), Fig. This approach to quantifying HD is easy to implement and interpret, can be applied to any disadvantaged population (e.g., rural patients), including assessing intersectionality, and can be tailored to address outcome-specific risks.



<sup>a</sup> Expected values rounded for interpretation purposes; Predictive model used to estimate expected number of amputations included: age, sex, admission type, emergency department services, transfer status, diagnoses present on admission (superficial infection, deep infection, gangrene, corn or callus, foot deformity, chronic limb ischemia, osteoporosis, hypertension, hypercholesteremia, coronary artery disease, revascularization complication), diagnoses present on hospitalization records in the past 365 days (superficial infection, deep infection, gangrene, corn or callus, foot deformity, chronic limb ischemia, osteoporosis, hypertension, hypercholesteremia, coronary artery disease, revascularization complication), procedures in past 365 days (lower limb revascularization, minor lower limb amputation, major lower limb amputation), number of hospitalizations in past 365 days, number of PAD-related hospitalizations in past 365 days, chronic conditions (Charlson comorbidity index components)

**The alcohol harm paradox: The joint effects of socioeconomic position and heavy drinking on 100% alcohol-attributable hospitalizations and death in Canada, 2000-2017** Brendan Smith\* Brendan Smith Christine Warren Alessandra Andreacchi Erin Hobin

**Background:** The alcohol harm paradox, where at similar levels of alcohol use individuals with low socioeconomic position (SEP) experience increased alcohol-attributable harm compared to those with higher SEP, has not been quantified in Canada. Our objective was to estimate the association between SEP and 100% alcohol-attributable harm and whether it varies by heavy drinking.

**Methods:** We conducted a cohort study among current and former alcohol consumers aged 15-64 from Canadian Community Health Surveys (CCHS, 2000-08) linked to hospitalization and mortality records through 2017. SEP was measured using equivalized household income quintiles. The association between income and incident 100% alcohol-attributable harm (hospitalization or death) was estimated using Fine and Gray subdistribution hazard models, with non-alcohol mortality as a competing risk. We estimated the interaction between dichotomized income (quintiles 1-3 (low) vs. 4-5 (high)) and heavy drinking (consuming  $\geq 5$  standard drinks in an occasion  $\geq$  once a month in the past year) on alcohol-attributable harm. Canadian population weighted and bootstrapped models were adjusted for age, sex, marital status, immigration, rurality, province and cycle.

**Results:** An inverse gradient was observed between income and alcohol-attributable harm, which was 3.4 (95%CI:2.8,4.1) times greater for the lowest compared to the highest income quintile. Among non-heavy drinkers, low compared to high income was associated with alcohol-attributable harm (HR=1.9, 95%CI:1.6,2.3). Similarly, relative to high income non-heavy drinkers, the risk of alcohol-attributable harm was higher among low income heavy drinkers (HR=6.8, 95%CI:5.7,8.1) than high income heavy drinkers (HR=3.8, 95%CI:3.2,4.4).

**Conclusions:** The alcohol harm paradox exists in Canada, where heavy drinking cannot fully explain the inverse gradient between SEP and 100% alcohol-attributable harm. Research is required to explore other potential mechanisms of this association.

**Racial/Ethnic Differences in the Concordance and Agreement of Self-Reported and Actigraphy-Measured Sleep Duration in Adolescents** Kaylin M. White\* Kaylin M. White Laura Ward Ryan Saelee Orfeu M. Buxton Lauren Hale Anne-Marie Chang Dayna A. Johnson

Epidemiologic studies often use self-reported sleep duration to assess sleep disparities. Data among adults suggest racial/ethnic differences in measurement error for self-reported sleep duration; however, evaluations in adolescents are lacking. Therefore, we examined differences in subjective and objective sleep duration for Black, Hispanic, and White adolescents (N=634) enrolled in the Fragile Families and Child Wellbeing Study. Linear regression models were fit to estimate the concordance between subjective and objective sleep duration by race/ethnicity. The agreement between self-reported and actigraphy-assessed sleep duration was calculated with simple Kappa and weighted Kappa statistics. The sample was 54.0% female and 51.4% Black, 30.4% Hispanic, and 18.1% White; the mean (SD) age was 15.4 (0.5) years. The mean sleep duration was 8.5 (1.2) hours for self-report and 7.8 (1.0) hours for actigraphy. Sleep duration was then categorized as short (<8 hours), recommended (8 - 10 hours), and long (>10 hours). Prevalence of actigraphy-measured short sleep was 66.9%, 48.7%, and 55.7% for Black, Hispanic, and White adolescents, respectively. Overall, there was no observed difference between self-reported and actigraphy-measured sleep duration in minutes after adjusting for covariates (7.91 min [95% CI: -12.0, 27.9]). The concordance between self-reported and actigraphy-measured sleep duration was 48% ( $\kappa_w = 0.16$ , 95% CI: 0.03, 0.20), 53% ( $\kappa_w = 0.13$ , 95% CI: 0.02, 0.23), and 50% ( $\kappa_w = 0.10$ , 95% CI: = -0.04, 0.23) for Black, Hispanic, and White adolescents, respectively. Slight agreement was observed across each group, indicating that minimal bias was observed in self-reported sleep duration in this cohort of adolescents.

**Multilevel Associations Between Genetic Ancestry, Neighborhood Socioeconomic Status, Tumor Subtypes, and Cause-specific Mortality in Black Breast Cancer Survivors** Hari Iyer\*

Hari Iyer Nur Zeinomar Angela Omilian Kitaw Demissie Chi-Chen Hong Song Yao Christine Ambrosone Elisa Bandera Bo Qin

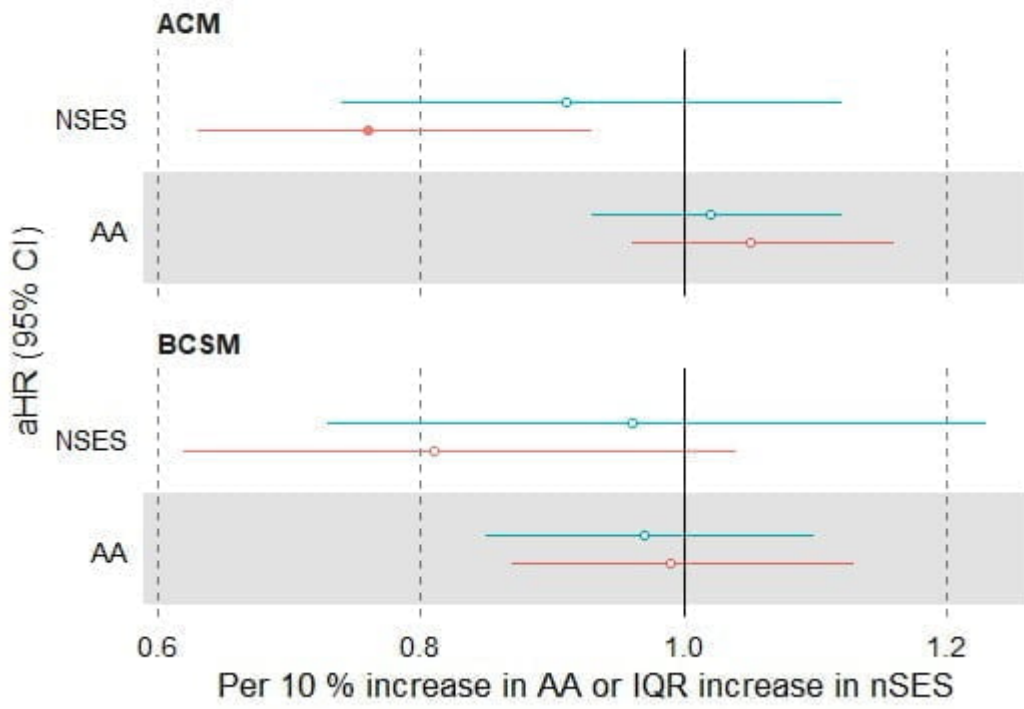
**Background:** Black-White disparities in breast cancer (BrCa) survival arise from genetic and environmental causes, which may exert influence at different stages of BrCa initiation and progression. We sought to clarify associations between genetic ancestry, social environments, aggressive BrCa tumor subtypes, and mortality in a cohort of Black women with BrCa.

**Methods:** Data were obtained from 1575 self-identified Black women interviewed between 2006 and 2020 in New Jersey. A neighborhood socioeconomic status (nSES) summary index composed of Census tract measures (education, income, wealth, employment status, and occupation) was linked to residential addresses at diagnosis. Percentage African ancestry was estimated using the ADMIXTURE program. We fit sequentially adjusted (age adjusted: age, interview year; fully adjusted: + individual SES, lifestyles, comorbidities) logistic regression models to estimate associations with tumor subtypes (Estrogen Receptor-negative (ER-) vs ER+; Triple Negative Breast Cancer (TNBC) vs Luminal), and Cox models for associations with all-cause (ACM) and breast cancer-specific mortality (BCSM). Due to similarities in results from age and fully adjusted models, we present results from fully adjusted models unless otherwise specified.

**Results:** Participants had a median age of 55 years, 18% had TNBC, and 29% had ER- tumors. There were 215 ACM and 120 BCSM events over 7,191 person-years of follow-up. A 10% increase in African ancestry was associated with higher odds of ER- (aOR: 1.08, 95% CI: 0.98, 1.18) and TNBC (aOR: 1.16, 95% CI: 1.02, 1.31) tumors, but not with ACM or BCSM. Higher nSES was associated with lower ACM (aHR for IQR: 0.76, 95% CI: 0.63, 0.93) and BCSM (aHR: 0.81, 95% CI: 0.62, 1.04) in age adjusted models, but associations were attenuated in fully adjusted models.

**Conclusions:** Findings from this study of Black BrCa survivors suggest that African ancestry may influence risk of aggressive BrCa tumors but not mortality. Compared to genetic ancestry, social environments may be more important determinants of BrCa survival.

# Associations with mortality



**Characterizing disinvestment in urban and rural neighborhoods of Jackson, MS** Dustin Fry\*

Dustin Fry Sharrelle Barber Stephen J. Mooney Jessica Whitley

Neighborhood disinvestment—a result of structural racism—is geographically and racially patterned and has been associated with poor health outcomes. Associations between disinvestment and disease may be direct (such as inadequate water infrastructure exposing residents to noxious contaminants) or indirect, such as residents internalizing signs of institutional neglect through stress pathways. Emerging techniques, such as virtual audits of Google Street View imagery, enable observed measures of neighborhood disinvestment to be obtained across neighborhoods of diverse social and built-environmental characteristics. We developed and validated a scale measuring visual indicators of disinvestment for Jackson, MS.

270 street segments sampled from the Jackson, MS metropolitan area were virtually audited using an instrument assessing aspects of neighborhood disinvestment. The tool also included an assessment of the urban or rural character of the street segment and a five-level ordinal indicator of the auditor's perception of the level of investment on the street segment. Factor analysis was used to develop a disinvestment scale from audit items and this scale was compared with the overall investment variable on both urban and rural segments.

The disinvestment scale was strongly and negatively associated with perceived investment ( $r=-0.82$ ,  $p<0.001$ ). The disinvestment scale indicated higher levels of disinvestment on rural segments ( $p<0.001$ ) but perceived investment was not associated with urbanicity ( $p=0.147$ ). This discrepancy was not readily explained by other variables in the data, although the presence of trees was negatively associated with perceived investment ( $p<0.001$ ) but not associated with the disinvestment scale ( $p=0.321$ ) and more trees were indicated on rural segments ( $p<0.001$ ). Auditors may be conditioning their expectations of investment based on the urban or rural character of the street segment.

**Factors associated with HPV vaccination uptake among U.S. females aged 9-26** Sophie Feng\* Sophie Feng Jessica Currier Amanda Bruegl Jessica Buck DiSilvestro Lu Zhang

**Background:** The CDC recommends Human Papillomavirus (HPV) vaccination for most individuals aged 9-26, which prevents infection from HPV strains associated with cervical cancer. While the importance of vaccination is known, the vaccination rate in the US ranges from 40-58%. The objective of this study was to identify social and health factors contributing to HPV vaccination.

**Methods:** Female participants aged 9-26 years in the recent 2017-2020 National Health and Nutrition Examination Survey were analyzed (data up to March 2020 were used to exclude confounding effects from the COVID-19 pandemic). The outcome variables were initiation and completion of the HPV vaccine series. Exposure variables included race, poverty, general health condition, insurance status, food security, and BMI. Chi-square test, T-test, and survey logistic regression were performed.

**Results:** We identified 1,667 participants, representing 35 million female residents in the US, among whom 45% received at least one HPV vaccine dose. After adjusting for covariates, individuals who self-reported "fair" health had a lower vaccination uptake (at least 1 dose) compared to those who reported "excellent" health (aOR: 0.41, 95% CI: 0.25-0.67). Individuals without insurance had a lower vaccination uptake than those with insurance (aOR: 0.47, 95% CI: 0.30-0.78). Individuals with higher BMI had a higher uptake than those with lower BMI (aOR: 1.00, 95% CI: 1.00-1.04). Additionally, Mexican American (aOR: 0.25, CI: 0.13-0.50) and non-Hispanic Black (aOR: 0.49, CI: 0.30-0.82) individuals were less likely to complete the vaccine series than Whites.

**Conclusion:** Individuals without health insurance, with worse general health, or lower BMI were less likely to be vaccinated. Targeted interventions to increase vaccine access to uninsured and underinsured individuals, those with poorer health, and those with lower BMI are needed, as well as efforts to ensure marginalized individuals can complete the vaccine series.



**LATEBREAKER**

Health Disparities

**Impact of COVID-19 vaccination on adult immunization capture: demographic trends within Oregon's ALERT-IIS** Corey Pierce\* Corey Pierce Vivian Larson

**Introduction:** Immunization Information Systems (IIS) are valuable repositories for the capture of vaccine history and hold importance for patients, clinicians, pharmacists, schools, and public health agencies. While IIS vaccine capture has been reported in adolescents, reported knowledge base for adult capture is limited. Upon exiting adolescence, many adults fail to stay up-to-date absent school attendance requirements. Along with migration between different states, and fragmented medical insurance coverage, IIS participation in adults is difficult to gauge. Little has been reported regarding differences in adult capture between sex, race, and age groups. The COVID-19 pandemic presents a rare window into vaccine capture, as a surge of people opted to vaccinate against COVID-19 in 2021. This study compares new participants to Oregon's IIS in 2021 relative to typical years (2017-2019).

**Methods:** Data was used from Oregon's ALERT-IIS to investigate adult immunization capture. Primary analysis looked at proportions of new ALERT-IIS participants by year of entry, with demographic groups that garner proportional increases in 2021 suggesting under-representation in typical years. Persons with vaccine records dated at age 18 or greater were included in the ALERT-IIS data extract (on March 10, 2022). Comparisons were made between years of entry into ALERT-IIS, and groupings based on *Sex*, *Age*, and *Race/Ethnicity*.

**Results:** We observed a 320% increase in new adult participants in 2021 compared with previous years (n = 521,582). New participants in 2021 were 54.1% *male* (+16% proportional increase vs typical year). *LatinX* participants increased dramatically in 2021 (+74%), along with large increases in *Black* and *Asian* race (+46% and +24%). Younger adult participation (18-49 years old) increased in 2021 (+7%). For *Race* stratified by *Age*, the largest proportional increases in 2021 were; 18-49 *LatinX* (+71%), 50-64 *LatinX* (+69%), 50-64 *Asian* (+60%) and 65+ *Black* (+43%).

**Conclusion:** Unprecedented high vaccine participation in 2021 allowed for measurement versus typical years. The observed proportional increases in IIS participation in 2021 found notable increases in younger adults (18-49 years old), *males*, and *LatinX*, *Black*, and *Asian* racial/ethnic groups. The surge in participation from these sub-groups suggests they are under-represented in typical IIS capture years. With equity in mind, these groups may warrant efforts to increase routine vaccination in typical years.

**Racial and Ethnic Disparities in Glaucoma Surgical Outcomes Persist after Accounting for Mediating Effects of Socioeconomic Status** Ken Kitayama\* Ken Kitayama Yusuke Tsugawa Fei Yu Victoria L. Tseng Akihiro Nishi Elizabeth Rose Mayeda Anne L. Coleman

Little is known about differences in glaucoma surgical outcomes over different racial/ethnic groups of patients and whether socioeconomic status (SES) can explain such differences. Therefore, we conducted a retrospective cohort study using a 20% random sample of 2016-2018 national fee-for-service Medicare beneficiaries with a claim for incisional glaucoma surgery (trabeculectomy, tube shunt, or EX-PRESS shunt). Follow-up extended through 2019. Inclusion criteria were age 65+, residence in the US, and no missing on eye laterality. The exposure of interest was patient race/ethnicity: Non-Latino White, Black, Latinx, Asian, or Other. SES was considered as a potential mediator, which was dichotomized to low/non-low based on dual-eligibility for Medicaid. Time to failure event (the primary outcome of interest) was defined as revision of index surgery or reoperation. Time-to-event was modeled using Cox proportional hazards with age and sex as covariates. Causal mediation analysis was used to estimate the total effect (TE) of the entire racial/ethnic disparity and the controlled direct effect (CDE) for the remaining disparity after fixing SES to non-low. Among 13,420 beneficiaries in the final sample (non-Latinx White: 68.4% [reference group], Black: 18.9%, Asian: 3.3%, Latinx: 7.2%, Other: 2.3%), 15.5% (n=2,075) were low SES and 21.0% (n=2,817) had a failure event. The TE estimates suggested a greater risk of failure in two groups: Asian (HR: 1.31, 95% CI: 1.08-1.58) and Latinx (HR: 1.19, 95% CI: 1.04-1.36). The CDE estimates showed persistent differences after fixing SES to non-low in Asian (HR: 1.30, 95% CI: 1.01-1.66) and Latinx (HR: 1.21, 95% CI: 1.01-1.45) beneficiaries. The results indicate that there is an increased risk of glaucoma surgical failure in Asian and Latino patients, which persists after excluding the SES-mediated path, suggesting other mechanisms need to be explored to explain racial/ethnic disparities in glaucoma surgery.

**Rural-urban disparities in long COVID** Colleen L. MacCallum-Bridges\* Colleen MacCallum-Bridges Jana L. Hirschtick Kristi L. Allgood Robert Orellana Nancy L. Fleischer

**Background:** Long COVID is a post-viral condition that affects roughly 7% of US adults and often leads to functional impairment and disability. Risk factors for long COVID include age, sex, acute COVID-19 severity, vaccination status, and SARS-CoV-2 variant. Due to differences in the distribution of some of these risk factors, COVID-19 cases from rural areas may be at an increased risk for developing long COVID.

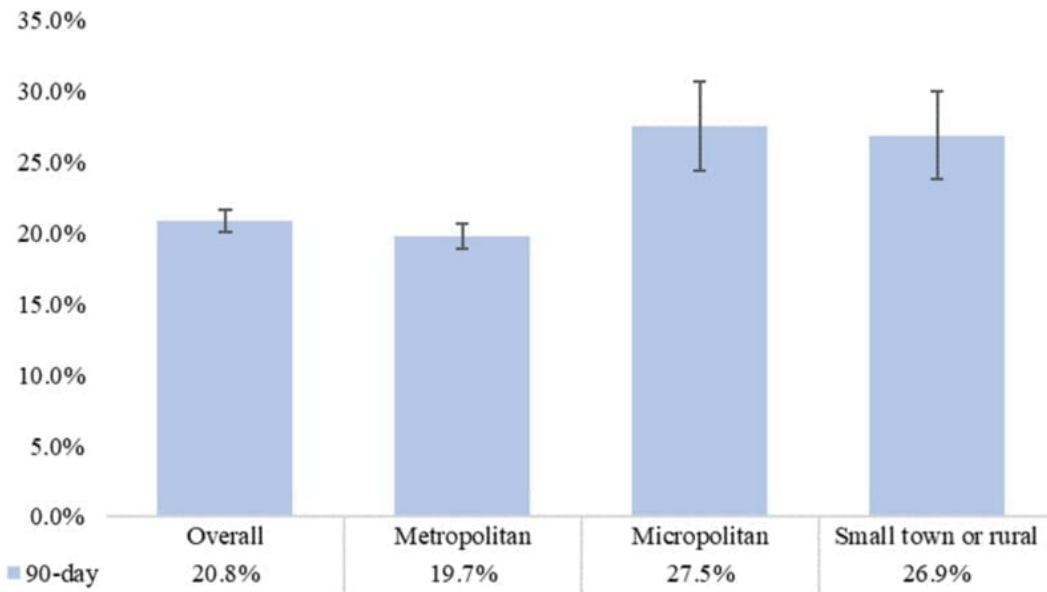
**Objective:** Assess whether a rural-urban disparity in prevalence of long COVID exists among COVID-19 cases, and if so, evaluate whether accounting for known risk factors reduces or eliminates this disparity.

**Methods:** We used data from the Michigan COVID-19 Recovery Surveillance Study of adults with SARS-CoV-2 infection prior to August 2021 (n=2,670). We defined long COVID as the presence of symptoms  $\geq 90$  days after COVID-19 onset and residential rurality/urbanicity as metropolitan, micropolitan, or small town/rural based on Rural-Urban Commuting Area codes. We estimated rural-urban disparities in long COVID using Poisson regression to produce prevalence ratios (PR). Then, we adjusted our model for known risk factors - i.e., age, sex, acute COVID-19 severity (hospitalization status), vaccination status, and timing of infection (a proxy for variant) - to assess whether this attenuated the estimated disparities.

**Results:** When compared to cases from metropolitan areas, the unadjusted prevalence of long COVID was higher among cases from micropolitan [PR=1.31 (95%CI: 1.03,1.67)] and small town or rural areas [PR=1.37 (95%CI: 1.06,1.78)]. Adjustment for known risk factors did not reduce these disparities.

**Conclusion:** Long COVID was more common among cases from non-metropolitan areas and differences in the distribution of known risk factors did not appear to explain these disparities. Additional work is needed to determine the causes of these disparities, and to identify public health or public policy interventions that can reduce burden of and disparities in long COVID.

Adjusted prevalence of 90-day long COVID, overall and by rurality/urbanicity\* based on MI CReSS analytic sample (n=2,670)



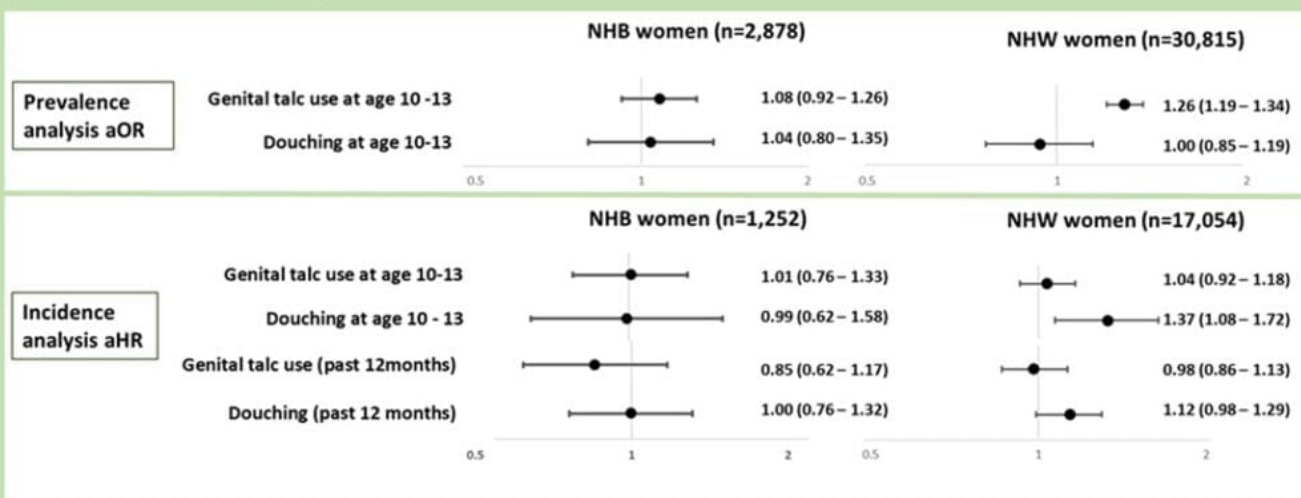
MI CReSS = Michigan COVID-19 Recovery Surveillance Study

\*Rurality/urbanicity is based on USDA Rural-Urban Commuting Area codes, available at the Census tract level

**The association of genital talc use and douching in early adolescence or adulthood with prevalent and incident uterine fibroids** Kemi Ogunsina\* Kemi Ogunsina Dale P. Sandler John D. Murphy Quaker E. Harmon Aimee A D'Aloisio Katie M. O'brien

**Background:** Genital talc use and douching may involve exposure to chemicals linked to certain gynecologic cancers. However, it is unclear if they impact fibroid risk. **Objective:** Evaluate the impact of genital talc and douche use on prevalent and incident fibroids among Black and Non-Hispanic White (NHW) women. **Study design:** Data were from the Sister Study (2003-2021), a prospective cohort of 50,884 U.S. women ages 35-74 years at enrollment. Participants were asked if they ever had a fibroid diagnosis and at what age, and if they used genital talc and/or douched between ages 10-13 years or in the past 12 months. Multivariable and polytomous logistic regression was used to compute adjusted OR and 95% CI for having vs. not having fibroids before age 50 among women 50 to 74 years old at enrollment. For incidence analysis, we used Cox regression to estimate adjusted HR and 95% CI for incident fibroids among women with an intact uterus and no prevalent fibroids, following women from age at enrollment to age at fibroid diagnosis, censoring at hysterectomy, end-of-follow-up, or at age 60. **Results:** Genital talc use at 10-13 years was positively associated with fibroids at enrollment (aOR:1.26, CI: 1.19-1.34) among NHW women, but not Black women (1.08, 0.92-1.26). Douching at 10-13 years was not associated with prevalent fibroids in either group (1.00, 0.85-1.19 for NHW and 1.04, 0.80-1.35 for Black women). In the prospective analysis, we followed participants for an average of 7.3 years (maximum 16.7 years). Fibroids were associated with douching at 10-13 years (aHR:1.37, 1.08-1.72) and moderately associated with use at enrollment (1.12, 0.98-1.29) among NHW women but not among Black women (0.99, 0.62-1.58 and 1.00, 0.76-1.32). **Conclusion:** Genital talc use in early adolescence and douching in early adolescence or adulthood are associated with fibroids among NHW women, but other unknown factors account for the excess fibroid risk among Black women.

Figure : Adjusted odd ratios (aOR) and hazard ratios (aHR) for fibroids among women who use genital talc and douche in the prevalence and incidence analysis.



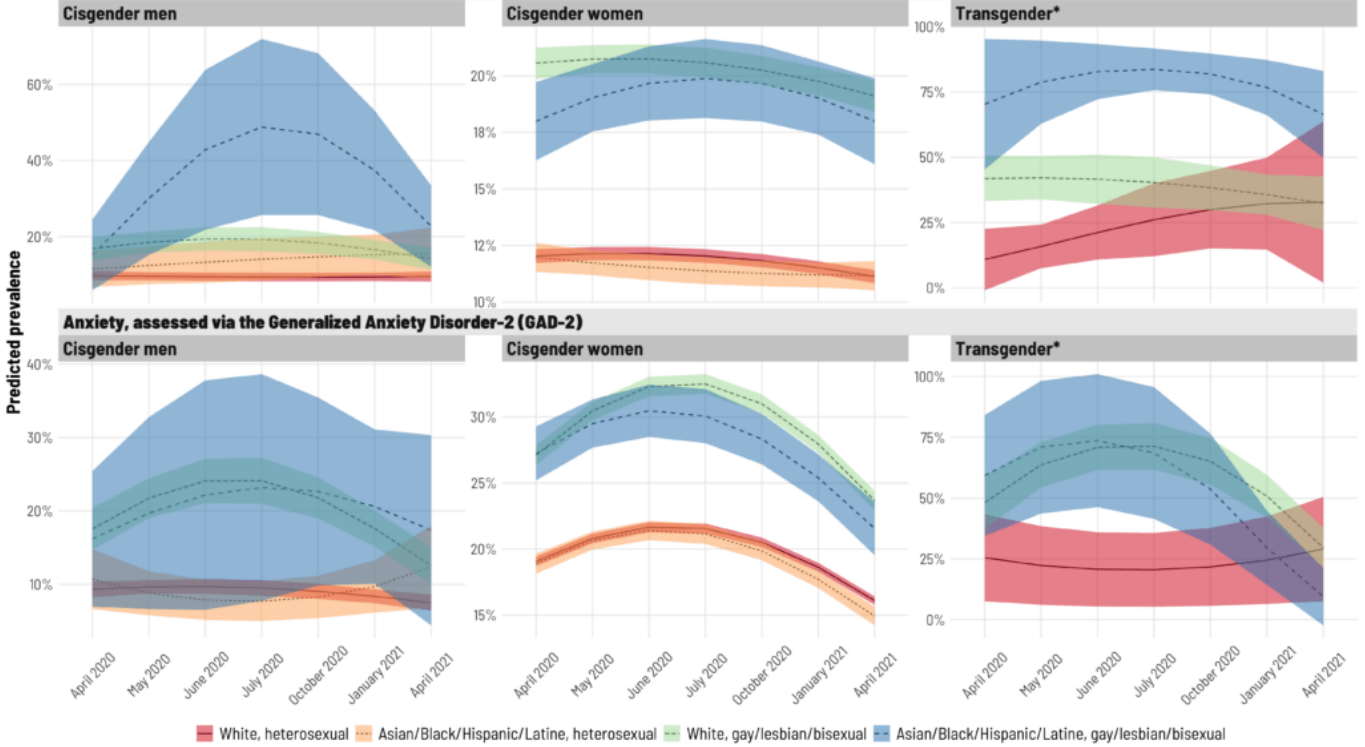
**Mental distress during the COVID-19 pandemic at the intersection of gender, race/ethnicity, and sexual orientation: A longitudinal intersectional Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA)** Ariel Beccia\* Ariel Beccia Jonggyu Baek Dougie Zubizarreta Brittany M. Charlton Jaime E. Hart S. Bryn Austin

The COVID-19 pandemic and its sociopolitical sequelae are worsening mental health inequities, yet few studies have used an intersectional lens to assess whether compounding forms of structural disadvantage exacerbate risk for multiply marginalized populations. We thus leveraged novel data and methods to examine longitudinal trajectories in COVID-19-related mental distress at the intersection of gender, race/ethnicity, and sexual orientation. Participants were 53,368 US adults from Nurses' Health Studies 2 and 3 and the Growing Up Today Study who completed 7 monthly/quarterly surveys from April 2020–April 2021. Informed by advances in quantitative intersectionality, we conducted a Multilevel Analysis of Individual Heterogeneity & Discriminatory Accuracy that we adapted for longitudinal settings. First, we sorted participants into “intersectional strata” defined by combining gender (cisgender man, cisgender woman, transgender), race/ethnicity (Asian/Black/Hispanic/Latine, White), and sexual orientation (gay/lesbian/bisexual, heterosexual) categories. We then fit multilevel logistic models with random effects for participants and strata to estimate stratum-specific prevalence trajectories of depression (Patient Health Questionnaire-2 score  $\geq 3$ ) and anxiety (Generalized Anxiety Disorder-2 score  $\geq 3$ ). IPW accounted for loss-to-follow-up. In April 2020, 13% of participants reported depression and 21% reported anxiety; levels fluctuated over time and differentially by strata. While 95% credible intervals were often wide, multiply marginalized strata (e.g., sexual minorities of color) had the highest prevalence of mental distress across the study period and some experienced widening inequities (e.g., from 1.5 to 2 times higher prevalence) relative to singly/non-marginalized strata. Our findings reveal a complex social patterning of COVID-19-related mental distress that non-intersectional analyses may have obscured. Future work should identify drivers of the observed inequities.

# Intersectional inequities in mental distress during the first year of the COVID-19 pandemic

Findings from the COVID-19 Sub-Study of the Nurses' Health Studies 2 and 3 and the Growing Up Today Study (N = 53,368)

## Depression, assessed via the Patient Health Questionnaire-2 (PHQ-2)



\*Includes transgender men, transgender women, and another/unlisted gender identity participants. Shaded regions represent 95% credible intervals. Estimates for strata with n<10 are suppressed. Figure made in R using code adapted from [www.andrewheiss.com](http://www.andrewheiss.com).

**Enhancing Unemployment Insurance Data for policy research and public health practice**

Olivia Peterson\* Sarah Andrea Mya Froese Anjum Hajat

**Background:** More generous unemployment insurance (UI) - in terms of dollar amount and duration - is associated with reductions in the prevalence of poverty as well as improved subjective well-being and mental health, making UI generosity a target to improve population health. The existence of publicly available easy to use data on UI generosity parameters has facilitated research in this area. UI accessibility is a comparatively less studied potential policy target; evaluations have been limited to proxy measures like UI reciprocity rate due to the absence of easy to use publicly available data.

**Objective:** To create a database of annual state-level UI accessibility policy indicators and to examine how UI accessibility differs between states and within states over time.

**Methods:** State-level UI law data were abstracted in duplicate from the US Department of Labor's annual documentation (1992-2020). Abstracted parameters included: timing of base period and the existence of extended base periods for disability, minimum required earnings, minimum hours and weeks worked. Abstractor discrepancies were resolved by a third reviewer. We subsequently examined annual trends in changes in UI accessibility.

**Results:** A total of 13 UI accessibility parameters were abstracted for all US states. On average, states in the Pacific region started with - and maintained the most accessible UI policies while states in the South Atlantic started with the least accessible UI policies. In general, an increasing number of states have adopted more accessible base periods, while patterns in required minimum wages during the base period have been more variable.

**Conclusion:** An initial set of publicly available UI accessibility data will facilitate policy research and public health practice. Additional abstraction efforts are warranted to assess data from before 1992 or after 2020 and to examine other aspects of UI accessibility (e.g., active work search requirements, nature of employment relationship).



**LATEBREAKER**

Health Services/Policy

**Evaluating the impact of integrating new services into a child health and nutrition program in rural Madagascar** Caitlin Hemlock\* Caitlin Hemlock Emanuela Galasso Ann M. Weber Christian Tsirery Mathilde Col Maria Dieci Lisy Ratsifandrihamanana Lia C.H. Fernald

**Background:** In low-resource settings, adding components to integrated health services for children may compete for caregiver time. We analyzed how offering a new early childhood development (ECD) program affected children's attendance at health and nutrition sessions in rural Madagascar and examined whether adding play materials increased ECD program attendance.

**Methods:** We conducted a three-arm cluster RCT in 75 sites from 2021-22. The intervention consisted of offering two cycles of 12 ECD stimulation sessions over 6 months to eligible children (6-30 months); 50 treatment sites were cross-randomized to receive toyboxes in Cycle 2. Variables associated with takeup were analyzed using random intercept models. We analyzed treatment effects on monthly attendance in nutrition sessions using differences-in-differences (DiD) due to baseline imbalance between groups. We also used DiD to analyze attendance at ECD sessions in T+ compared to T and the whether children not signed up in Cycle 1 signed up for Cycle 2. We conducted analyses intention-to-treat using ordinary least squares regression with standard errors clustered by site.

**Results:** We analyzed data for 9408 age-eligible children; 30% and 32% of whom signed up in Cycle 1 and 2. Younger children from wealthier households already attending nutrition sessions were more likely to sign up. There was no effect of T or T+ on nutrition session attendance. Toyboxes had no effect on ECD session attendance but did encourage children in the oldest cohort who did not attend any sessions in Cycle 1 to attend in Cycle 2 (0.06; 95% CI: 0-0.11). Children from larger sites were less likely to attend the ECD program due to enrollment limits, but were also less likely to attend nutrition sessions.

**Conclusions:** Integration of new services did not crowd out participation in existing services but should target children not already captured by the system. Equitable coverage in more populated areas is needed to reach all children.

**National Utilization Patterns of Hormone Replacement Therapy and Gender-Affirming Surgery by Insurance and by State among Transgender Individuals** Adan Z. Becerra\* Adan Becerra Grace M. Sassana-Khadka Yolana L. Pollak Morgan R. Sturgis Brielle Weinstein Amir H. Dorafshar Loren S. Schechter

Transgender people experience barriers to access to health care, often caused by structural factors. The objective was to evaluate how insurance plans and states affect utilization patterns of hormone replacement therapy (HRT) and gender-affirming surgery (GAS) among transgender people. We executed a retrospective cohort study using PearlDiver-Mariner, a national all-payer claims database. We identified individuals with gender dysphoria in 2010-2020 and calculated the percent of these individuals who received HRT and/or underwent GAS. Rates of HRT and GAS utilization were stratified by insurance and state. Adjusted analyses employed multivariable logistic regression. We identified 78,169 transgender individuals with an insurance distribution as follows: 60,275 (77%) commercial, 12,383 (16%) Medicaid, and 5,511 (7%) Medicare. Across all states, rates of HRT and GAS utilization were highest among those with commercial insurance and were lowest among those with Medicare. In adjusted analyses, individuals covered by Medicaid and those covered by Medicare had 9% (OR=0.91,95% CI 0.87,0.95) and 25% (OR=0.75,95% CI 0.71,0.80) lower relative odds of HRT use, respectively, compared to those covered by commercial insurance. Similarly, individuals covered by Medicaid and those covered by Medicare had 22% (OR=0.78,95% CI 0.73,0.83) and 31% (OR=0.69,95% CI 0.63,0.75) lower relative odds of undergoing GAS, respectively, compared to those covered by commercial insurance. However, these differences varied by state. For example, in Illinois, differences in HRT use by insurance (38% commercial, 37% Medicaid, 33% Medicare) were smaller than other states such as Idaho (35% commercial, 15% Medicaid, 23% Medicare). Utilization patterns of HRT and GAS among transgender people were affected by insurance. While those with commercial insurance utilized more gender-affirming care, individual states were able to mitigate these patterns. Future studies will analyze individual state policies.

**Changes in, and factors associated with, parental intention to vaccinate their daughters with human papillomavirus (HPV) vaccine in Korea: a nationwide cross-sectional survey 2016 and 2020** Yejin Ha\* Yejin Ha Kyeongmin Lee Jae Kwan Jun Mina Suh Kui Son Choi

**Purpose:** In 2016, South Korea introduced bivalent and quadrivalent Human Papillomavirus (HPV) vaccines for girls aged 12 as a National Immunization Program. We aimed to compare and identify characteristics and factors associated with parental intention to vaccinate their daughters under the age of 12 in 2016 and 2020.

**Methods:** Data were obtained from the Korean National Cancer Screening Survey for 2016 and 2020, a nationwide, cross-sectional survey that used nationally representative random sampling. A total of 3,510 parents who had a daughter < 12 years were included in this analysis. The changes in parental intention rate were calculated by subtracting the rate in 2020 from the rate in 2016. Chi-squared test and logistic regression analysis were performed to identify factors associated with parental intentions to vaccinate their daughters.

**Results:** The respondents who are willing to vaccinate their daughters significantly increased from 33.4% in 2016 to 58.9% in 2020 (25.5%p increase). The proportion of fathers who responded positive intention towards HPV vaccination largely increased by 31.5%p, and female participants showed a 20.9%p increase since 2016. The results from logistic regression analysis showed that parents who have a strong intention to vaccinate their daughters are more likely to be younger, more educated, aware of the free vaccination program, and have previous experience of HPV vaccination and cervical cancer screening within 2 years, compared to those who do not intend to vaccinate their daughters. Mothers with previous experience of HPV vaccination (adjusted odd ratio [aOR], 7.35; 95% confidence interval [CI], 2.57 to 21.04) was the strongest predictor of positive intention to vaccinate.

**Conclusion:** To raise the HPV vaccination rate, strong recommendation and education for parents as well as young generation are necessary; it will ultimately reduce the cervical cancer burden.

**Use of medical imaging among immigrants to Ontario, Canada** Giancarlo Di Giuseppe\*

Giancarlo Di Giuseppe Priscila Pequeno Rinku Sutradhar Marilyn L. Kwan Diana Miglioretti Rebecca Smith-Bindman Jason D. Pole

**Background:** Medical imaging is an integral part of health care. The association between immigration status and the utilization of medical imaging remains unexplored.

**Methods:** A retrospective study of 1,848,222 immigrants to Ontario, Canada between April 1, 1995 and December 31, 2016 was performed. Immigrants were matched 1:1 to non-immigrants on age, sex, index year, and postal code. Utilization of computed tomography (CT), magnetic resonance imaging (MRI), radiography, and ultrasonography were captured. Incidence rate differences (RD) per 1,000 person-years comparing immigrants to non-immigrants were calculated. Multivariable relative rates (RR) were calculated using a recurrent event framework and adjusted for time-varying socioeconomic status, comorbidity score, and visits to a physician. Estimates were stratified by age at immigration: children and adolescents ( $\leq 19$  years); young adults (20-39); adults (40-59); and older adults ( $\geq 60$ ).

**Results:** Use of CT, MRI, and radiography were lower for immigrants across all age groups, with the largest reduction in imaging seen in the oldest adults. The longer the time since immigration, the larger the gap in imaging use. Older adult immigrants had the largest gap in imaging utilization, which included an RD of -422 for radiography exams (95%CI: -426, -418) within five years of immigration which increased to -1,046 (95%CI: -1,096, -996) after 20 years. In multivariable analysis, the RR of imaging was approximately 20-30% lower for immigrants: ranging from 0.77 to 0.88 and 0.72 to 0.80 for CT and MRI imaging, respectively. Radiography RRs ranged from 0.84 to 0.90. All age groups except older adults had higher rates of ultrasonography, with young adults (RR, 1.21; 95%CI: 1.21, 1.21) having the highest usage.

**Conclusions:** Immigrants underwent less CT, MRI, and radiography but more ultrasonography. Future research should evaluate whether lower utilization is due to barriers in healthcare access or health-seeking behaviours.

**Ethnic structure of residence and preventive health services use of US immigrant children**

Ye Ji Kim\* Ye Ji Kim Michael R. Kramer Melvin D. Livingston E. Kathleen Adams Jennifer A. Lucas Shakira F. Suglia John D. Heintzman

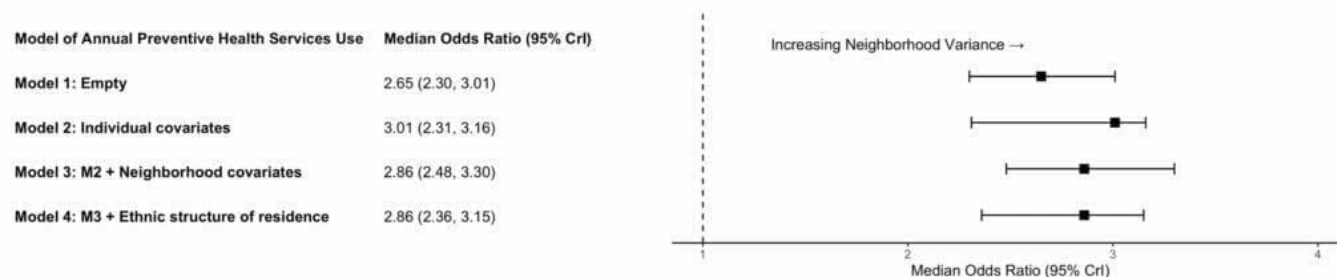
Ethnic enclaves and ethnoburbs can serve as a vehicle for health resources among immigrant families. In this study, we estimate the relationship between ethnic structure of residence with the odds of annual preventive health services use over time among immigrant children. We also estimate the variation of health services use between neighborhoods.

**Method** We used electronic health record-based data from the Foreign-Born Latinos Cardiovascular Screening study. The analytic sample was restricted to foreign-born children (ages 9–18 years) with at least one visit to the study clinics between 2012–2020 (N = 6,524). We used American Community Survey 2012–2016 estimates of percent ethnicity, percent families in poverty, and population density to define four ethnic structures of residence: ethnic enclave, low-income ethnoburb, high-income ethnoburb, and other. We defined preventive services use as binary measurement of annual use of any of the three markers of preventive services including body mass index, blood pressure, and well-child visits. We used generalized linear mixed models and tested for differences by insurance type. Median odds ratios (MOR) and 95% credible intervals (CrI) were calculated to estimate the variation between neighborhood clusters.

**Results** Majority of our study sample lived in ethnic enclaves (62%). Second, there was no evidence of an association between the ethnic structure of residence and use of preventive health services. Neighborhood level income inequality and unemployment rates explained much of the variance in children’s use of preventive services between neighborhoods [Model adjusting for Gini index and unemployment rate; MOR (95% CrI) = 2.86 (2.48, 3.30) vs. Model without these variables: MOR (95% CrI) = 3.01 (2.31, 3.16)].

**Conclusion** The findings from this study support the need to understand neighborhood level area deprivation and income inequality to reduce neighborhood disparities in use of health services among immigrant children.

**Figure.** Forest plot of median odds ratios and 95% credible intervals (CrI) of sequential, generalized linear mixed models of preventive health services use among immigrant children, 2012–2020 (N = 6,524)

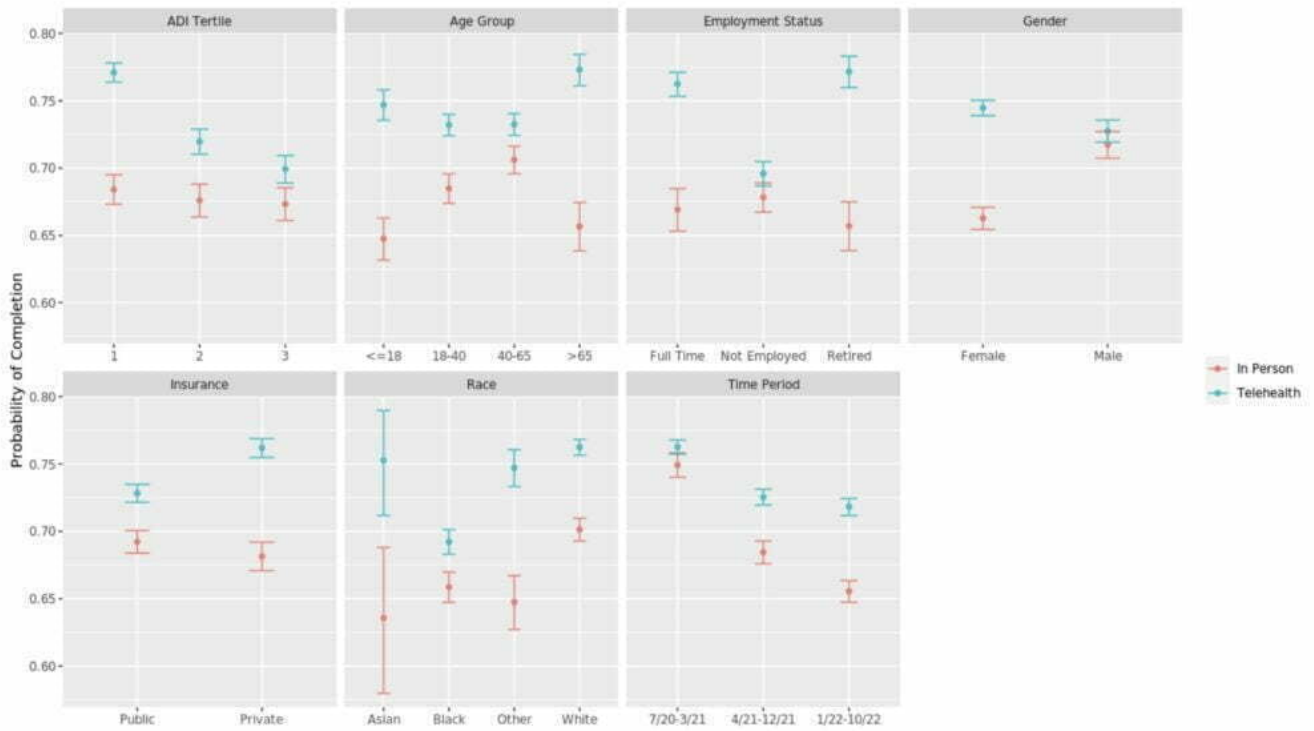


Note: Individual covariates included child’s sex, age at first encounter, race/ ethnicity, insurance type, household FPL, preferred language at visit. Neighborhood covariates included Gini index and unemployment rate at the tract level.

**Trends in telehealth and in-person psychiatric care from 2017-2022 among patients with depression in a large US academic medical system** Catherine Ettman\* Catherine Ettman Carly Lupton Brantner Elizabeth A. Stuart Peter P. Zandi

We aimed to assess the differences in completion rates between telehealth and in-person outpatient appointments in a large Department of Psychiatry among patients with depression. Using a longitudinal cohort study of patients with depression using electronic health records (EHR) from Johns Hopkins Medicine from November 2017 through October 2022, we examined appointment completions by telehealth or in-person care over time. We used multivariable logistic regression with random effects for patient IDs to assess how completion rates varied by telehealth versus in-person care and whether associations differed across patient characteristics. Our participants included patients  $\geq 10$  years old with a depression diagnosis in the Department of Psychiatry between November 2017 - October 2022 who had at least one scheduled outpatient appointment (Analytic sample: 257,347 appointments across 7,825 patients). With almost no telehealth appointments conducted before the COVID-19 pandemic, telehealth was the modal form of care in the Department of Psychiatry from April 2020 through October 2022, with the total number of telehealth and in-person appointments nearly converging over time. In analyses using logistic regression models with random effects for patient IDs, appointments had 1.30 (95%CI: 1.27, 1.34) times the odds of being completed if conducted over telehealth relative to in person from July 2020 through October 2022. The association remained significant after adjusting for patient characteristics (aOR: 1.19 95%CI 1.16, 1.22). Telehealth appointments had a higher completion than in-person appointments in the Department of Psychiatry across almost all patient characteristics. As in-person operations resume following the COVID-19 pandemic, it may be beneficial to maintain options for care via telehealth to optimize delivery of care and patient outcomes.

**Figure 1. Relationships between probability of completion and telehealth visits, across patient characteristics**



Note: Probability of appointment completion in the Department of Psychiatry between July 2020 – October 2022 based on seven separate models (N=257,347 appointments). Models adjusted for random effects for patient ID. Data: Johns Hopkins Medicine electronic health records (EHR) for patients with depression.

**Exploring inequalities in primary care continuity and avoidable hospitalizations for older adults living in Quebec, Canada.** Giovanna Busa\* Giovanna Busa Isabelle Vedel Isabelle Dufour Amélie Quesnel-Vallée

**Background and objectives:** Canadian guidelines recommend that older adults receive primary care continuity (PCC) as it can enable better preventative care leading to less potentially avoidable hospitalizations. Yet, there is a growing difficulty of accessing primary care especially for disadvantaged groups. Our study aims to (1) measure the risk of potentially avoidable hospitalization in community-dwelling older adults with high versus low PCC and (2) to measure the influence of predisposing and enabling factors on this relationship. **Approach:** TorSaDE cohort which links patient-reported socio-demographic information from survey data (Canadian Community Health Survey 2007, 2009, 2011, or 2013) with Québec provincial health administrative data. **Index:** Participants must have completed the survey, be 67+ years old, living in a community dwelling in Québec, and had in the previous year  $\geq 2$  primary care visits. **Exposure:** High or low PCC as defined by a dichotomized-Usual Provider Continuity Index 1 year preceding index. **Outcome:** Number of potentially avoidable hospitalization as defined by ambulatory care sensitive conditions measured 1 year following index. **Expected results:** Inverse probability of treatment weighting will be used to adjust for confounding. We will compare the number of avoidable hospitalizations based on high versus low PCC. Results will be presented as RR, RD, numbers needed to treat to prevent one avoidable hospitalization, and stratified by predisposing and enabling factors, if interactions exist. Individuals with high PCC will have a lower risk of hospitalizations than those with low PCC. The strength of association will differ based on predisposing and enabling factors. **Conclusion:** Increasing continuity with a primary care physician might be an avenue to reduce potentially avoidable hospitalizations in community dwelling older adults on a population-wide level. But policies must adopt equitable approaches to avoid increasing health disparities.



**Multimodal Analgesia Use and Variation Over Time** Laura A. Graham, PhD, MPH\* Laura A. Graham Sherry M. Wren, MD, FACS Seshadri C. Mudumbai, MD, MS Michelle C. Odden, PhD

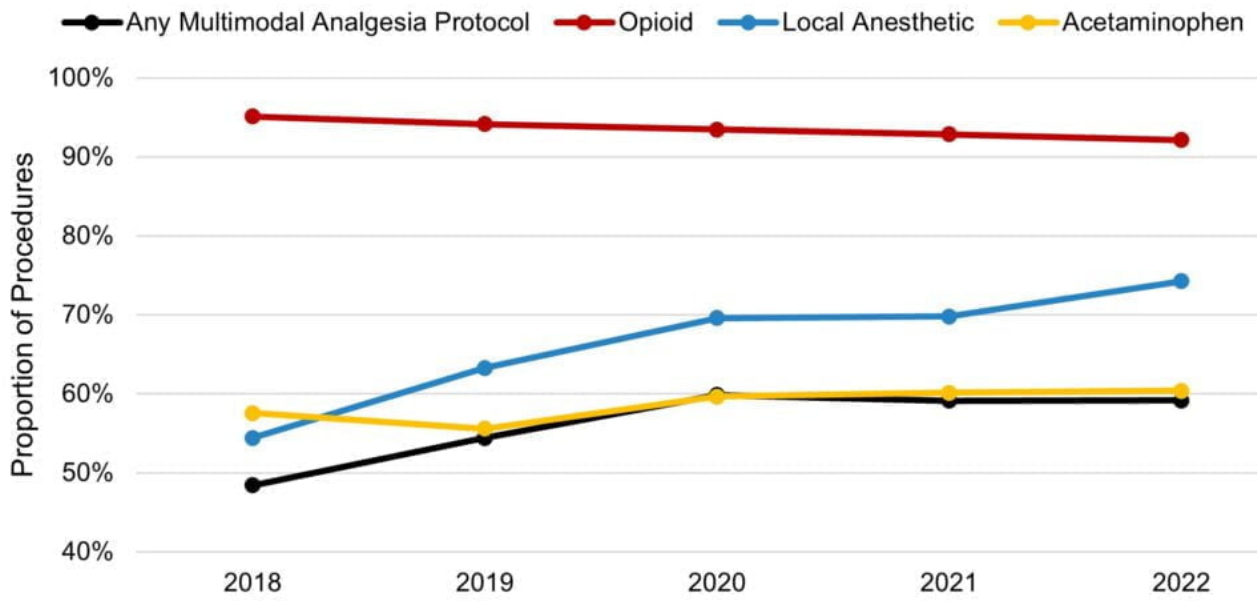
Opioids are the most common form of pain management used during surgery. Multimodal analgesia (MMA) seeks to reduce surgery-related opioid needs by adding non-opioid pain medications in combination with opioids. Many pain medication combinations can be used in an MMA protocol, and there is no guidance on which protocols are most effective in high-risk populations. The goal of this study was to describe the use and variation of MMA protocols over the past 5 years at a single hospital.

Our study population includes all patients undergoing surgery with general anesthesia at a single hospital between 1/1/2018 and 3/31/2022. Intraoperative pain medications were obtained from the hospital's perioperative information management system. MMA was defined as an opioid plus at least one other non-opioid analgesic. Chi-square tests and ANOVA were used to describe MMA use over time.

We identified 8,788 procedures among 6,622 patients. 93.8% of cases received at least one opioid intraoperative, and 13.8% received a peripheral nerve block or epidural. Overall, 55.5% of cases involved at least some form of MMA. The most common non-opioid analgesics were local anesthetics (64.6%), acetaminophen (58.2%), N-methyl-D-aspartate antagonists (24.7%), and alpha-2-adrenergic agonists (14.1%). The most common MMA protocol included opioids, acetaminophen, and local anesthetics (17.5% of cases), followed by opioids plus only a local anesthetic (11.6%). MMA use increased from 47.3% in 2018 to 61.2% in 2022 ( $p < 0.01$ ) and varied significantly by specialty ( $F = 83.0$ ,  $p < 0.01$ ) and anesthesiologist (interquartile range = 48.7-71.4%,  $F = 3.7$ ,  $p < 0.01$ ) even after adjusting for the use of a peripheral nerve block or epidural.

MMA protocols are becoming more common, but there is wide variation and little guidance on the most effective protocols. Future studies should focus on identifying the most effective MMA protocols for specific patient populations to guide the adoption of MMA into routine practice safely.

## Intraoperative Pain Medication Use Over Time



**Disruptions and inequalities in access to oral healthcare during the first year of the COVID-19 pandemic in Chile** Doris Duran\* Doris Duran Josefina Aubert Madeleine Urzua Carlos Zaror Maria Jose Monsalves Cristobal Cuadrado

The COVID-19 pandemic and the control measures in place challenged healthcare delivery globally. Quantifying the impact on oral healthcare has yet to be studied, especially in Latin America. We aimed to assess the extent of oral healthcare disruptions in Chile and to examine changes in inequalities in access to oral care during 2020.

**Methods:** Household telephone survey for adults (18+) living in urban areas. Probabilistic random sampling was performed using the census sampling frame. Weights were used for the probability of selection and non-response. We collected sociodemographic information, history of chronic conditions, and healthcare access details during 2020. In addition, we estimated the absolute and relative differences using rate differences and ratios for sex and health insurance (SES proxy) and the slope indexes of inequality for education.

**Results:** The total sample was 1,261. The average age was 45(SD:18.5), and 51.6% were women. 29.4% reported complete secondary education. 53.9% lived outside the metropolitan area, and 75.6% had public health insurance. In addition, 35.1% reported at least one postponed healthcare visit, with oral healthcare being the second most frequently postponed (9.8%). 68.1% of those who postponed oral care also postponed some other healthcare visit, and 39.9% reported more than high school education. For disparities, women postponed oral care 64% more than men (Rate Ratio (RR) 1.64, CI 95% 0.96; 2.33). People with public health insurance postponed oral care 35 times more than those privately insured (RR 1.35 CI 95% 0.73; 1.98). No disparities were observed for educational level.

**Conclusion:** Disruptions were frequent in our study, with oral care in second place. Regardless of health insurance and educational level, dental care was frequently postponed. Disparities were marked for women, which can be explained by the disproportionate differences in caregiving responsibilities with men reported in the literature during the pandemic.

**Intimate partner violence and HIV care engagement among peripartum women living with HIV in Lilongwe, Malawi** Madelyn Frey\* Madelyn Frey Wiza Kumwenda Shaphil Wallie Sophie Lazar Denzel Matiya Angela Bengtson

Intimate partner violence (IPV) may be a barrier to HIV care engagement, which is critical to the health of women living with HIV (WLHIV). There is little known about this relationship during the perinatal period. This study aimed to describe the prevalence and predictors of IPV and investigate its relationship with HIV care engagement among WLHIV enrolled during antenatal care (baseline). Physical, emotional and sexual IPV were measured using the WHO Violence Against Women validated questionnaire at baseline. Care engagement outcomes, including viral suppression (<1000 copies/mL) and HIV visit attendance (no missed visits), were measured at 9-months postpartum. We used log binomial models to explore predictors of IPV at baseline and associations between IPV and care engagement, adjusted for education, alcohol use, status disclosure, income, social support and planned pregnancy. Among 399 women enrolled, 272 (68%) were included in the analysis. Nearly one-third (30.75%) reported IPV. Emotional IPV was the most common IPV type reported, with 25% of all participants reporting emotional IPV, followed by physical IPV (14.03%) and sexual IPV (9.85%). In unadjusted models, women with probable common mental disorder (CMD) were more likely to report IPV (PR 2.6; 95% CI 1.88, 3.37), while women with higher levels of social support were less likely to report IPV (PR 0.62; 95% CI 0.42, 0.91). In an adjusted model, those with IPV had 1.13 (95% CI 0.59, 2.17) times the risk of unsuppressed viral load and 0.95 (95% CI 0.83, 1.09) times the risk of missing at least one HIV care visit by 9-months postpartum, compared to those with no IPV. In this cohort of WLHIV, increased social support correlated with a lower IPV prevalence, while CMD correlated with a higher IPV prevalence. IPV was not associated with postpartum disengagement from HIV care. Our findings underscore the importance of IPV screening during antenatal care to link women to resources to address and prevent IPV.

**Elevated mortality due to HPV-associated cancers among cis men diagnosed with HIV in San Francisco, USA** Jason S. Melo\* Jason Melo Sharon Pipkin Vani Nimbale Ling C. Hsu

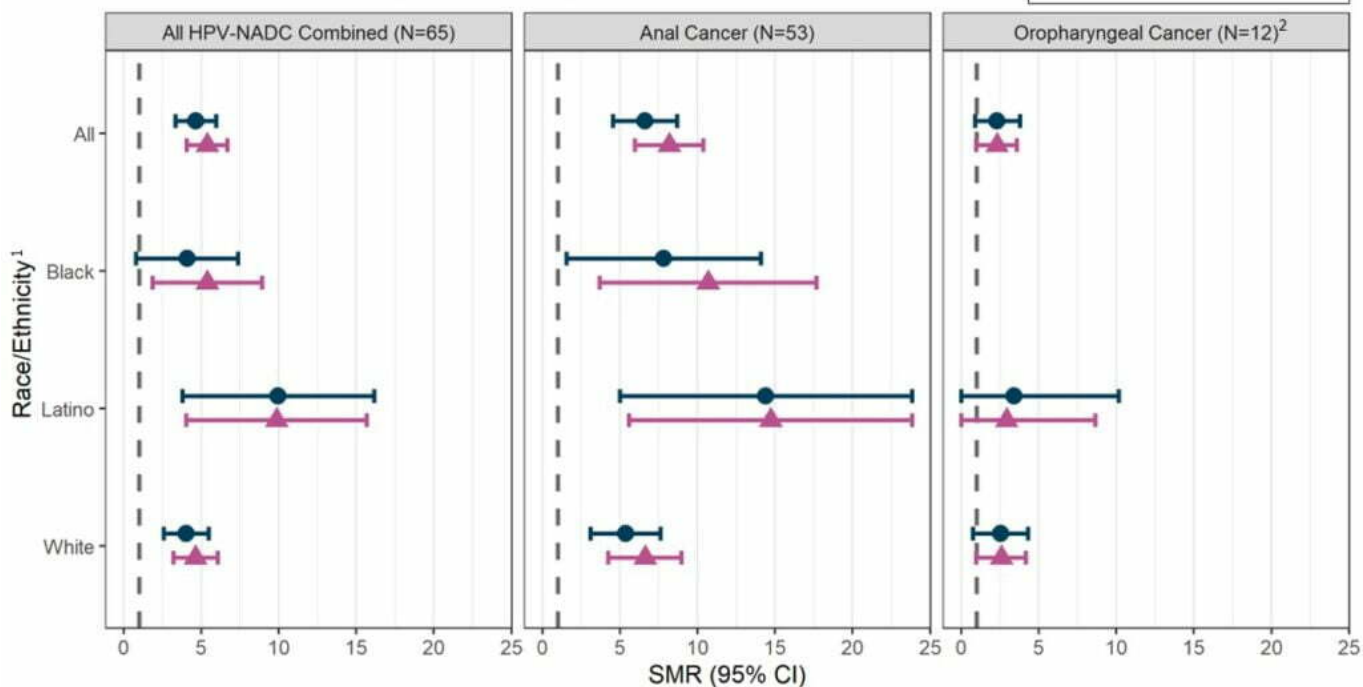
**Background:** In the antiretroviral therapy era, non-AIDS-defining cancer (NADC) has contributed an increasing proportion of deaths among people with HIV (PWH) in San Francisco (SF). Potentially preventable NADC include carcinomas of the anus, oropharynx, and penis, with an estimated 63-91% of cases due to human papillomavirus (HPV) infection. Among SF PWH, most HPV-associated NADC (HPV-NADC) decedents are cis men. We compared cause-specific mortality among this demographic to the general population.

**Methods:** Cis men in the SF HIV case registry who died at age  $\geq 15$  years in 2011-2020 were included. Underlying and multiple cause of death (UCOD; MCODE) were extracted from the National Death Index. Chi-squared tests compared HPV-NADC and non-HPV-NADC decedents by clinical and demographic characteristics. We calculated 10-year age standardized mortality ratios (SMR) for cumulative and specific HPV-NADC, using the distribution of SF PWH as of 12/31/2015 for the midpoint population and United States men as the reference. We measured both aggregate and race/ethnicity stratified SMRs.

**Results:** A total 2159 decedents were included, representing 97% of 2011-2020 deaths. HPV-NADC contributed 65 deaths (53 anal cancer; 12 oropharyngeal cancer). HPV-NADC decedents were more likely than others to have a CD4 count  $< 200$  cells/ $\mu$ L preceding death ( $p < 0.05$ ). Among all cis men, significantly elevated UCODE SMRs were observed for combined HPV-NADC [4.67, 95%CI (3.36-5.98)] and anal cancer [6.62, 95%CI (4.54-8.70)] (Figure 1). Findings were comparable across MCODE and race/ethnicity-specific analyses, though point estimates were higher among Blacks and Latinos compared to Whites (Figure 1).

**Conclusions:** Elevated SMRs emphasize HPV-NADC as a target for cancer prevention, screening, and treatment among PWH. Improvement areas include expanded HPV vaccination among cis men and HPV-NADC screening programs for at-risk populations (e.g., men who have sex with men), especially among Blacks and Latinos.

**Figure 1.** 10-year age standardized mortality ratios (SMR) for HPV-associated non-AIDS-defining cancer (HPV-NADC) deaths among cis men with HIV, stratified by race/ethnicity and cancer type, 2011-2020, San Francisco, USA



<sup>1</sup>The All measures include cis men of all race/ethnicity categories, including Other/Unknown.

<sup>2</sup>No deaths attributed to oropharyngeal cancer were reported among Black cis men. The SMR and 95% confidence interval are not calculated.

**Mediation of condomless anal sex on the relation of HIV PrEP and bacterial sexually transmitted infections among in an online sample of gay, bisexual, and men who have sex with men**

Nguyen K. Tran\* Nguyen Tran Neal D. Goldstein David J. Brennan Jason A. Roy Esther Chernak Seth L. Welles

**Background:** Increasing rates of bacterial sexually transmitted infections (STI) among gay, bisexual, and men who have sex with men (GBM) in Canada has been attributed to risk compensation, a theory that assumes individual behavioral change in response to an external stimulus to maintain a “risk equilibrium”. In the context of HIV pre-exposure prophylaxis (PrEP), this theory may inaccurately imply increased condomless anal sex due to lower perceived HIV risk among GBM using PrEP. Thus, we evaluated the association of PrEP uptake and bacterial STI and quantified how condomless anal sex mediated this association.

**Methods:** We abstracted data from the iCruise Study, an online longitudinal diary survey of GBM in Ontario, Canada. PrEP uptake was based on a self-reported measure from the baseline survey. Condomless anal sex was defined as never using condoms during anal sex with any cisgender man during weeks 1-3 of follow-up. Bacterial STI was quantified as any self-reported new chlamydia, gonorrhea, and syphilis diagnoses or treatment over weeks 4-12 of follow-up. We calculated risk ratios using Poisson models with robust standard errors and used g-computation to quantify the total effect, natural direct and indirect effect, and proportion mediated, bootstrapping to acquire confidence intervals.

**Results:** Of 535 GBM, 53 (9.9%) reported PrEP uptake at baseline, 186 (34.8%) reported condomless anal sex between weeks 1-3, and 34 (6.4%) reported a bacterial STI between weeks 4-12. While GBM taking PrEP had twice the risk of bacterial STI, this effect was not statistically significant (aRR: 2.22; 95% CI: 0.83, 4.94). The natural direct and indirect effect were also non-significant, and the proportion mediated was 7% of the total effect.

**Conclusions:** Findings suggest that condomless anal sex did not mediate the relation between baseline PrEP uptake and bacterial STI. Different mechanisms, such as increased STI testing, may better explain the increased incidence of bacterial STI among GBM using PrEP in the sample.

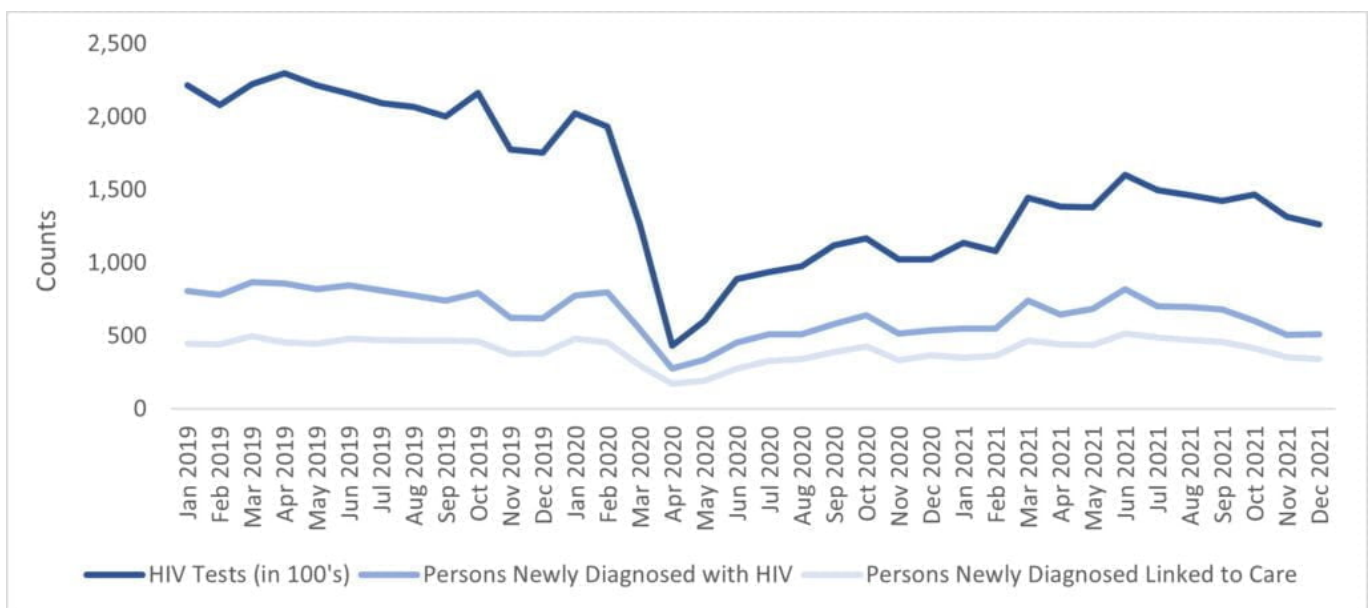
**Changes in CDC-Funded HIV Testing Services Outcomes During the COVID-19 Pandemic, 2019-2021** Deesha Patel\* Deesha Patel Weston Williams Carolyn Wright Guoshen Wang Nicoline Collins Tanesha Joshua

*Background:* CDC funds U.S. health departments and community-based organizations to conduct HIV prevention services, many of which reported interruptions during the COVID-19 pandemic. We assessed changes in CDC-funded HIV testing services outcomes from 2019 to 2020 and 2021.

*Methods:* Using data from the National HIV Prevention Program Monitoring & Evaluation system, we analyzed CDC-funded HIV tests (i.e., tests), persons newly diagnosed with HIV and positivity, and linkage to HIV medical care within 30 days of diagnosis (i.e., linkage). Percent changes from 2019 to 2020 and 2021 were calculated; Chi-square analyses were conducted to statistically analyze differences in test counts. Robust Poisson regression provided PRs with 95% CIs to compare prevalence of positivity and linkage between 2019 and later years. Analyses were adjusted for multiple testing using Bonferroni correction.

*Results:* Compared to 2019 (n=2,504,239), there was a 46.5% reduction in test counts in 2020 (n=1,339,052) and a 34.3% reduction in 2021 (n=1,645,556) (both p<0.001); reductions were observed among all subgroups in both years (all p<0.001). Despite these reductions and thus fewer persons being identified with newly diagnosed HIV (2019: n=9,346; 2020: n=6,486; 2021: n=7,694), positivity was greater in 2020 (0.5%; PR=1.30, 95% CI: 1.05-1.61) and 2021 (0.5%; PR=1.25, 95% CI: 1.03-1.53) versus 2019 (0.4%). Positivity was greater among 12 subgroups in 2020 and six subgroups in 2021 (all p<0.05). Linkage did not significantly differ from 2019 (71.3%) to 2020 (76.2%; PR=1.07, 95% CI: 0.96-1.19) or 2021 (80.2%; PR=1.12, 95% 0.98-1.29) overall or by subgroups (all p>0.05).

*Conclusion:* Although improved from 2020, CDC-funded HIV testing in 2021 did not revert to 2019 levels. CDC and recipients should further scale up HIV testing to cover for these missed tests and thereby identify more persons with HIV. Further assessment should examine 2022 data to capture the potential impact of mpox with COVID-19.





**Weather-related risk factors for Legionnaires' Disease and Pontiac Fever** Timothy J. Wade\*

Timothy Wade Carly Herbert

Background: Legionellosis is a respiratory infection caused by *Legionella pneumophila* bacteria that are found in water and soil. Infection may cause severe pneumonia (Legionnaires' Disease) and milder illness (Pontiac Fever) and is a particular concern for the elderly. *Legionella* can colonize water systems and may result in human exposure by inhalation of aerosolized bacteria. The incubation period ranges from 2-14 days. Previous studies have suggested that precipitation and humidity may be associated with an increased risk of Legionellosis. Methods: We used records from the Centers for Medicare and Medicaid Services for the years 1999-2018 to identify hospitalizations for Legionnaires' Disease (ICD 9/10 codes 428.4/A481) and Pontiac Fever (ICD 9 code A482) among the Medicare-eligible population. Antecedent weather (precipitation, temperature, relative humidity) was obtained from the PRISM Climate Group (<https://prism.oregonstate.edu/>) using the case's zip code of residence. We used a time-stratified bi-directional case-crossover design stratifying by month and year and matching on day-of-week, with +/- 14 days between case and control days. Lags of up to 20 days were considered for daily precipitation, relative humidity and maximum temperature. Data were analyzed using conditional logistic regression. Results: Over the study period 37,883 Legionellosis cases were identified. After correction for false-discovery, increases in precipitation at lags 8-12 and 17 and relative humidity at lags 9, 11 and 13 were associated with increases in Legionellosis hospitalization. The strongest association was for precipitation at day 10 lag (OR=1.22, 95% CI 1.18-1.26 per inch). Conclusion: Wet and humid weather may be favorable to the survival of *Legionella*. Among the Medicare-eligible population, increases in precipitation and humidity were associated with hospitalization for Legionellosis at lags consistent with the incubation period for infection.

**Modeling the use of influenza antivirals as prophylaxis during outbreaks in long-term care facilities** Sinead E. Morris\* Sinead Morris Casey M. Zipfel Prabasaj Paul Rachel B. Slayton Matthew Biggerstaff

Influenza antivirals can protect against influenza virus infection when administered as prophylaxis, and reduce symptoms and virus shedding in subsequent infections. Prophylaxis is recommended during outbreaks in long-term care facilities (LTCFs) where residents are at greater risk of infection and developing severe disease. CDC guidance recommends prophylaxis be initiated among LTCF residents once two or more cases are identified in the facility within 72 hours and be continued for at least 14 days and until 7 days after symptom onset of the last case. However, not all LTCFs fully adhere to this guidance: one study found prophylaxis was administered for 14 days or less in 50/74 LTCF outbreaks (68%) from 2017-2019. It is thus unclear how antivirals currently impact influenza outbreaks in LTCFs, and whether this impact could be improved. We develop a mathematical model of influenza transmission in a LTCF with 100 residents and 100 healthcare personnel (HCP). We allow residents and HCP to initiate and stop prophylaxis with different uptake and adherence rates, and approximate resident turnover by distinguishing between short- and long-stay residents who enter and leave the facility at different rates. With this model, we estimate that administering prophylaxis according to CDC guidance reduces resident cases by 16% and hospitalizations by 45% compared with no prophylaxis. When prophylaxis is administered for 14 days or less, cases are only reduced by a maximum of 1% and hospitalizations by 27%, demonstrating the importance of following CDC guidance. We also show that increasing prophylaxis uptake among HCP only improves the impact of antivirals if HCP adherence levels are high. Similarly, high uptake and adherence must be maintained among residents for prophylaxis to successfully mitigate influenza outbreaks. Thus, we find that CDC guidance can substantially reduce the impact of influenza outbreaks in LTCFs, if prophylaxis uptake and adherence among residents is high.

**Hepatitis B and C in Individuals with a History of Antipsychotic Medication Use: A****Population-Based Evaluation** Alison Simmons\* Alison Simmons Amnah Awan Sharara Shakik Hailey Banack David Fisman

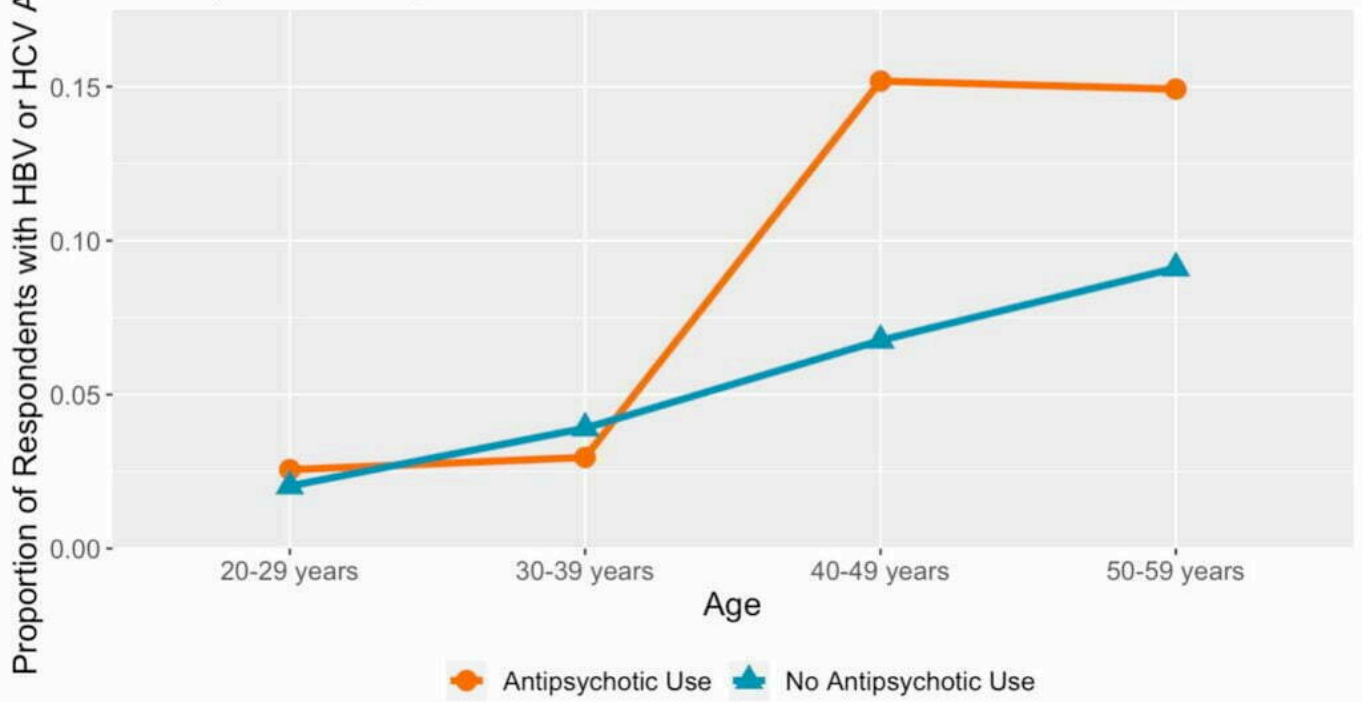
**Background:** A better understanding of links between mental illness and risk of bloodborne infectious disease could inform preventive and therapeutic strategies in individuals with mental illness.

**Methods:** We performed a cross-sectional study using the National Health and Nutrition Examination Survey (NHANES) to estimate the seroprevalence of hepatitis B and C in individuals with and without a prior prescription for antipsychotic medications, and to determine whether differences in seroprevalence could be explained by differential distribution in known infection risk factors. Multivariable logistic regression models were used to examine the association between receipt of antipsychotic medication and HBV and HCV seropositivity.

**Results:** Those who had HBV antibody had 1.64 (95% CI: 0.89, 3.02) times the odds and those with HCV antibody had 3.48 (95% CI: 1.71, 7.09) times the odds of having a prescription for at least one antipsychotic medication compared to those who did not have HBV or HCV antibodies, respectively. While prior antipsychotic receipt was a potent risk marker for HCV seropositivity, risk was explained by adjusting for known bloodborne infection risk factors including age, sex, race, immigrant status, marital status, education, income, history of a blood transfusion, harmful alcohol use, injection drug use, history of a sexually transmitted infection, and number of lifetime sex partners (adjusted ORs 1.00 [95% CI: 0.50, 2.03] and 1.40 [95% CI: 0.44, 4.48] for HBV and HCV, respectively).

**Interpretation:** Prior receipt of antipsychotic medications is a strong predictor of HCV (and to a lesser extent HBV) seropositivity, though we cannot draw causal inferences from these results. Treatment with antipsychotic medications should be considered as additional risk markers for individuals who may benefit from targeted prevention, screening, and harm reduction interventions for HCV.

Population Weighted Seroprevalence of Hepatitis B Virus (HBV) or Hepatitis C Virus (HCV) by Age Group Among Respondents to the National Health and Nutrition Examination Surveys Between 2005 and 2014 (n = 16,960)



**Utilization of mid-upper arm circumference and triceps skin fold thickness in determining body composition measurements as an alternative nutritional assessment to body mass index among tuberculosis index cases and their household contacts in Tamil Nadu, India.**

Chelsie Cintron\* Chelsie Cintron Meagan Karoly Prakash Babu Narasimhan Subitha  
Lakshminarayanan Pranay Sinha

India holds a quarter of the global TB burden with 2.9 million cases in 2021. Undernutrition is the leading risk factor for TB in India. Undernourished individuals have a blunted innate and adaptive response to TB resulting in increased risk of TB progression and unfavorable outcomes despite therapy. This critical risk factor is widespread in India as 16% of the population has a body mass index (BMI) less than  $18.5\text{kg/m}^2$ . It is common practice to use BMI to inform nutritional status among persons with TB. However, BMI cannot provide nuanced data regarding body composition. Measurements, like mid-upper arm circumference (MUAC) in combination with the triceps skinfold thickness (TSF) can provide additional detail inexpensively. Using our data on TB index cases (IC) and their household contacts (HHC) from Tamil Nadu, India, we assessed the association of BMI, MUAC and triceps skinfold thickness (TSF) (as a measure of body fat) using Pearson correlation and t-test. There is a strong, positive correlation between BMI and MUAC among HHC and IC, respectively ( $r=0.86$ ;  $r=0.60$ ,  $p < 0.001$ ). Using MUAC upper limit cutoff of 25cm, 19% of HHC are undernourished compared to 21% via BMI while 100% and 98% of IC are undernourished. TSF and MUAC values were used to calculate arm muscle (AMA) and arm fat (AFA) areas. Among the undernourished, compared to HHC, IC have lower mean AMA ( $407,926\text{mm}^2$ ;  $91,606\text{mm}^2$ ) and AFA ( $14,926\text{mm}^2$ ;  $9,003\text{mm}^2$ ). The stark differences in muscle composition may speak to anabolic block, where TB infection impacts how nutritional intake is processed, and may inform protein composition of nutritional interventions. Further, reduced AFA potentially suggests overall sub-acute or chronic energy deficits and emphasizes the importance of required nutritional support for rehabilitation and improving treatment outcomes of TB patients. Our findings suggest a potential role for MUAC and TSF in determining body composition and guiding nutritional support for IC and their HHC.

**Epidemiological trends of Dengue fever 2021-2022 in Hajjah Yemen** Rima Alusfi\* Abdullah Gafer**Background :**

Dengue Fever (DF) is a significant health problem in Yemen, especially in the coastal areas. Yemen is one of the poorest countries in the world and the absence of a mosquito control system facilitates the dengue prevalent in the warmest area at a different rate. Also, numerous factors attributed to the increase of suspected cases of Dengue Fever among study areas. A significant increase in dengue cases was observed at the end of 2019 this Dengue outbreak has affected 174 of 333 total districts (54%) in 22 of 23 governorates of the country. This analysis aims to assess the trend and magnitude of Dengue fever for the 2 last years in Hajjah governorate , Yemen

**Method:**

The analysis carried using CDC guidelines for surveillance analysis during September -November 2020. The data was taken as a soft copy from the Electronic Integrated Diseases Early Warning System(eIDEWS )program in Hajjah, Yemen. Microsoft Excel 2013 was used to analyze the data. Frequencies and Numbers were used.

**Results:**

The incidence rate of confirmed dengue fever cases increased in 2022(125/100,000) compared with 21/100,000 in 2021. The attack rate in 2022(12.8/10000) increased compared with 2021(2.1/10000). Regarding the seasonality, the peak of transmission of confirmed dengue fever cases was high in (November - April). In 2022, the number of suspected cases was 3103 compared to 512 suspected cases in 2021: The Suspected cases of dengue fever in 2022 increased by 83.0% compared with 17.0 % in 2021. Abs district had the highest incidence rate (391/100,000) followed by Shers district (396/100,000) in 2022.

**Conclusion:** Incidence rate increase in 2022. Strengthening Dengue fever surveillance with appropriate season-based bed net use is required, and control activities should be continued and scaled up. Supervise the elimination of breeding places and application of vector control measures.

**Modeling ICU's MRSA Acquisitions with Different Staffing Levels and Finite Direct Care****Tasks** Stephanie Johnson\* Stephanie Johnson Matthew Mietchen Eric Lofgren

Background: Models are a cost-effective way to evaluate specific areas and interventions pertaining to hospital infection acquisitions, such as staffing levels. Increasing the number of nurses and doctors in an intensive care unit impacts rates of HAI transmission by reducing the number of patient interactions (e.g. contact rate) per provider and allows for greater segmentation of the patient population. The way compartmental models are often formulated assumes a never-ending series of tasks for healthcare workers to perform. Our previous models have assumed a baseline ratio of 1:3 nurses to patients and kept the number of tasks equal across staffing ratios. We wanted to understand how a finite number of tasks across staffing levels, using this baseline number, affected HAI, particularly Methicillin-resistant *S. aureus* (MRSA), acquisitions.

Methods: We used a stochastic mathematical model to study the impact that changes in staffing and tasks have on MRSA acquisitions. For a 15-bed ICU, we vary the number of intensivists on staff from one to three, and within those scenarios, set the Nurse:Patient ratio at 1:1, 1:1.5, 1:2.5, 1:3, 1:5 and 1:7.5, representing staffing levels from the extreme ends to more moderate values in line with critical care society guidelines and advisory statements. Each model was simulated 1000 times. The outcome of each scenario is the median number of hospital-associated MRSA acquisitions in one year from those 1000 simulations.

Results: Comparing the single-intensivist, 1:3 Nurse:Patient ratio as the baseline with 45 MRSA acquisitions per year to the two additional intensivist models, adding a second intensivist had a rate ratio of 0.89, and adding a third had a RR of 0.73, showing modest impact with just intensivists.

Increasing the number of nurses from five to six (moving from a 1:3 to 1:2.5 Nurse:Patient Ratio) had a RR of 0.77, suggesting a small change in nurse staffing levels has a larger impact on acquisition rates, due to the higher overall level of contact between nurses and patients. MRSA acquisition rates continued to be directionally impacted with large changes in staffing ratios; 1:1 Nurse:Patient ratio (RR = 0.17) compared to 1:7.5 Nurse:Patient ratio (RR = 4.66). Comparing the infinite to finite models, the ratios with more nurses had lower acquisitions, ranging from 20% to 50% decreases. Ratios with less nurses in the ICU had 100-400% increase in the number of acquisitions. All results were statistically significant.

Conclusion: These results suggest that as staffing levels go up the number of direct care tasks decreases per staff member, resulting in a direct impact on MRSA acquisition rates. Appropriate staffing should be considered in infection control guidelines, and the cost of staffing be weighed against its impact on infection prevention as well as other areas of patient care. This study only considers the impact of changes in contact patterns emerging from different staffing levels - further insights may exist when considering improved patient care, reduced errors from fatigue, increased time for hand hygiene, etc. that also accompany increased staffing levels.

**LATEBREAKER**

Infectious Disease

**Timeliness and completion rates of routine pediatric immunizations and the impact of the COVID-19 pandemic in the Military Health System, 2010-2019** Monica Burrell\* Monica Burrell Celeste J. Romano Anna T. Bukowinski Clinton Hall Gia R. Gumbs Nanda Ramchandrar Ava Marie S. Conlin

**Objective:** To assess pediatric immunization rates from birth to age 2 and the impact of the COVID-19 pandemic on pediatric immunization among military beneficiaries.

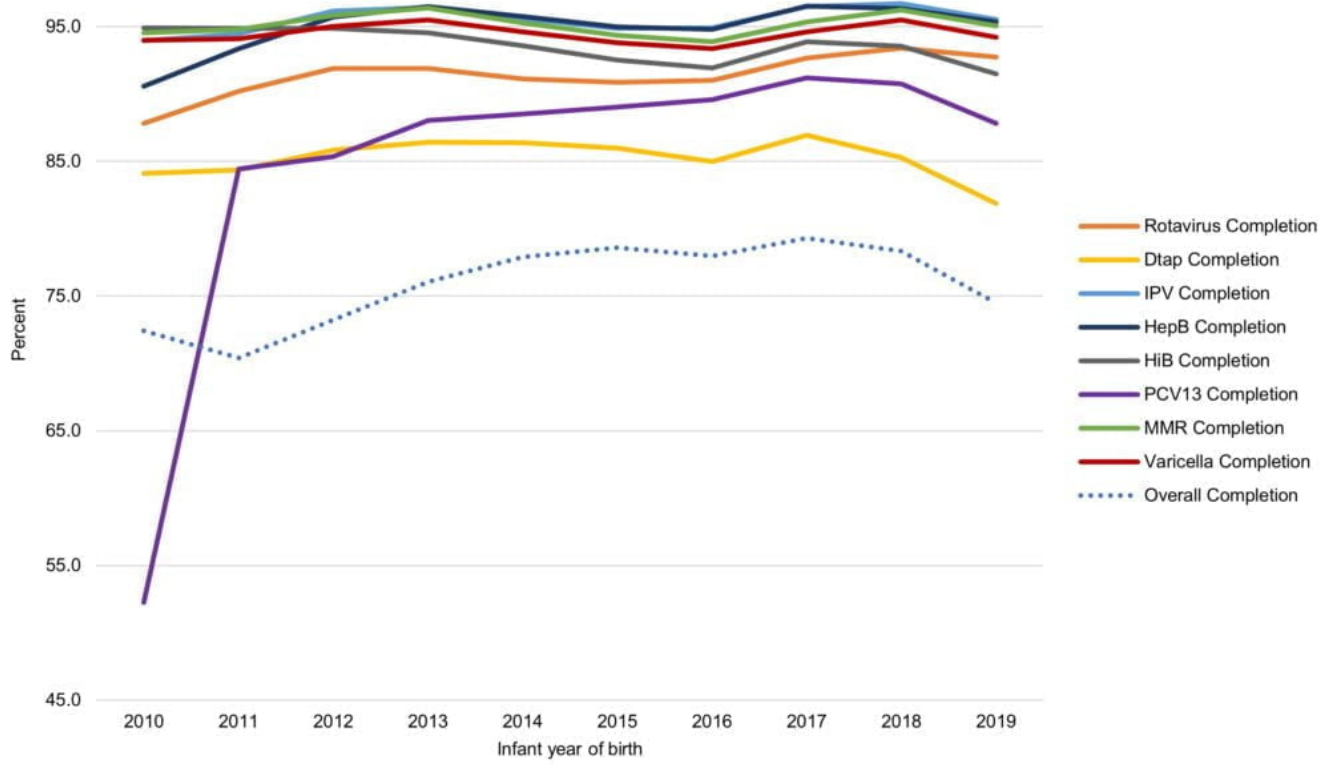
**Methods:** Department of Defense Birth and Infant Health Research program data were used to identify infants born at military treatment facilities (MTFs), 2010-2019, with visibility in medical encounter data through age 2. Using MTF immunization records and outpatient medical encounter records, completion of the combined series of diphtheria, tetanus, and acellular-pertussis (DTap); inactivated polio virus; measles, mumps, and rubella; rotavirus; Hepatitis B; *Haemophilus influenzae* type b; varicella; and pneumococcal conjugate vaccine (PCV13) was assessed as a 4:3:1:2:3:3:1:4 dose metric. Timeliness was assessed by applying the Advisory Committee on Immunization Practices pediatric vaccination schedule. Temporal trends were assessed to determine the impact of the COVID-19 pandemic on vaccine timeliness and completion rates.

**Results:** Of 304,034 included infants, 90.7% received at least one dose of each vaccine and 75.8% completed the 4:3:1:2:3:3:1:4 metric by age 2, though only 45.7% had no delay. Overall coverage increased from 72.4% in 2010 to 79.3% in 2017, but completion decreased while delays increased for those born in 2018-2019, therefore impacted by pandemic-related disruption to care. The fourth doses of DTap and PCV13 and the second dose of rotavirus were the leading contributors to full series incompleteness.

**Conclusions:** Vaccine series completion appeared high, but disparities were evident for DTap and PCV13, which both have recommended doses in the second year of life. Ensuring that infants return for a second annual well-child visit can help limit undervaccination across full and individual series. Initial data suggests the COVID-19 pandemic had a negative impact on timeliness and completion rates, warranting continued research and efforts to restore coverage rates to or above pre-pandemic levels.



Percent of infants born to active duty service members who complete vaccine recommendations, by vaccine series and overall, Department of Defense Birth and Infant Health Research program data, 2010–2019

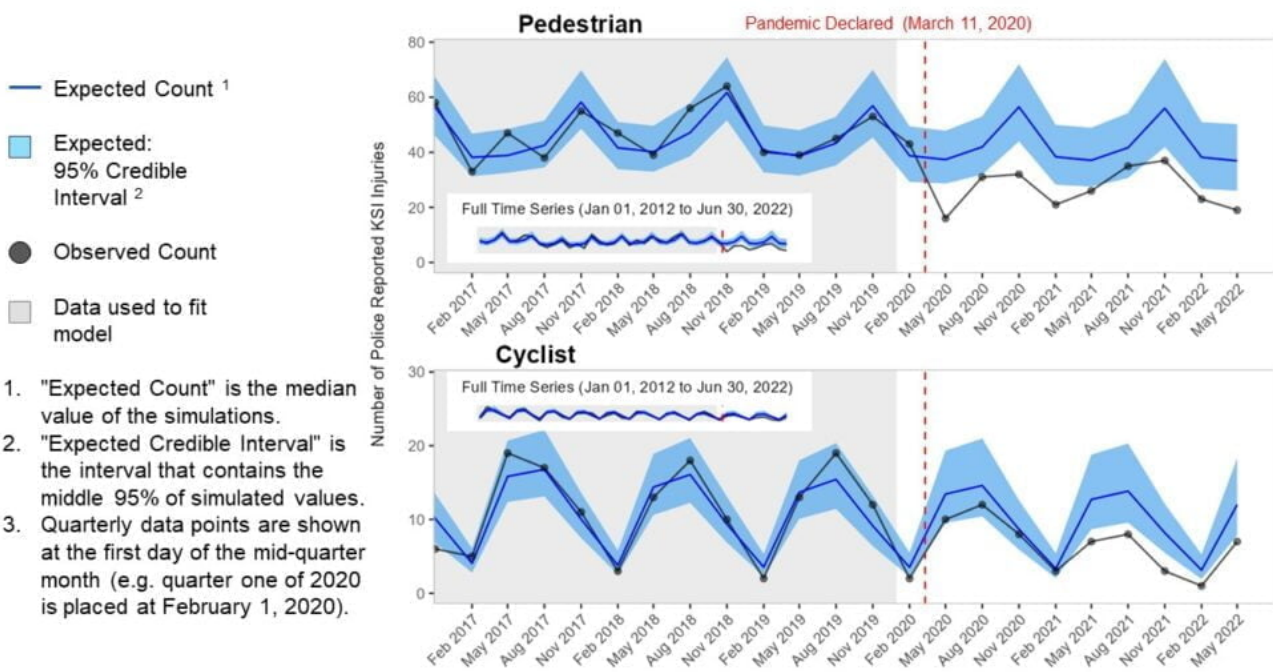


### COVID-19 Pandemic and Vulnerable Road User Injury Trends: An Interrupted Time Series

**Analysis** Brice Batomen\* Brice Batomen Jeremy Lewis Andrew Howard Natasha Saunders Marie-Soleil Cloutier Alison Macpherson Anne Harris Meghan Winters Brent Hagel Sarah Richmond Ian Pike Colin Macarthur Tate Hubkarao Linda Rothman

The COVID-19 pandemic led to changes in road traffic volumes and transportation modes, which may have influenced road traffic safety for vulnerable road users (pedestrians and cyclists) in cities across the world. In Toronto, Canada, work from home policies and interventions such as cycle tracks and quiet streets were implemented to support walking and cycling during social distancing periods. Understanding trends in road traffic injuries involving vulnerable road users resulting from these changes could help inform future road safety interventions. We examined the trends of killed or severely injured (KSI) pedestrians and cyclists in traffic collisions before and during the pandemic using data provided by the City of Toronto Transportation Services. We used an interrupted time series design, with KSI pedestrians and cyclists counts aggregated quarterly. We fit a negative binomial regression using a Bayesian modelling approach, to data prior to the pandemic (January 2012 to December 2019) that included a secular time trend, quarterly indicator variables for seasonality, and autoregressive terms. This model was then used to estimate expected counts of KSI pedestrians and cyclists during the pandemic (April 2020, to June 2022), and the differences between observed and expected KSI counts with 95% credible intervals. Pre-pandemic, the median quarterly number of KSI was 45 pedestrians and 13 cyclists. On average, we estimate that there were 16 (95% CI: 6, 28) fewer KSI pedestrians per quarter during the pandemic, compared to what would have been expected based on pre-pandemic trends. For cyclists, we estimate a quarterly reduction of 3 collisions (95% CI: 1, 7). These observed reductions shortly followed the pandemic onset and were sustained throughout the pandemic period. These reductions are likely due to changes in road traffic volumes and travel modes, along with the impact of transportation interventions initiated by the City of Toronto in response to the pandemic.

### Quarterly Observed and Expected KSI (Police-Reported)



**25 Year Trends in Occupational Homicides: 1992-2017** Chelsea Martin\* Chelsea Martin  
Shabbar Ranapurwala Maryalice Nocera John Cantrell Elizabeth McClure Amelia Martin Stephen  
Marshall David Richardson

**Background:** Determining victim-perpetrator relationships, as well as the occupation and industry of decedents, is crucial to inform and evaluate occupational homicide prevention strategies. In this study, we examine occupational homicide rates in North Carolina (NC) by victim-perpetrator relationship, industry, and victim characteristics between 1992 to 2017.

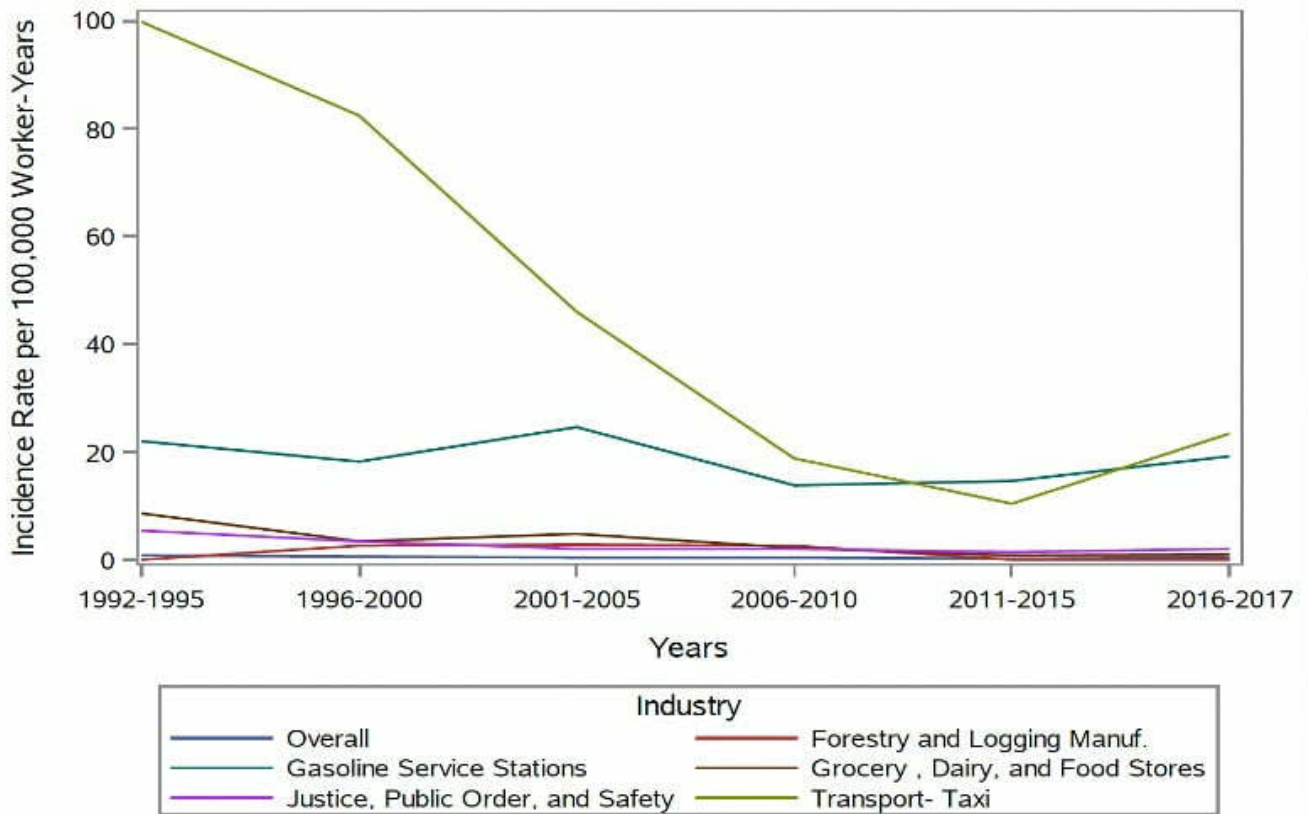
**Design:** Cohort Study

**Methods:** Occupational homicides were identified from records of the NC Office of the Chief Medical Examiner system and the NC death certificate from January 1, 1992 to December 31, 2017. Information abstracted included sex, age, race, ethnicity, education, class of worker, manner of death, victim-perpetrator relationship, and industry. Crude, age and sex standardized homicide rates were calculated as the number of homicides at work divided by an estimate of the NC population employed in the particular industry. Rate ratios and 95% CIs were calculated for the specified industry compared to all industries. Temporal trends were calculated overall and by industry.

**Results:** 456 homicides over 111,573,049 worker-years (w-y) were captured. Most victims were male (322, 83%), 35-44 years of age (124, 27%), non-Hispanic white (287, 63%), high-school educated or less (273, 60%), and privately employed (261, 57%). Occupational homicide rates decreased from 0.82 per 100,000 w-y for the period 1992-1995 to 0.21 per 100,000 w-y for the period 2011-2015, but increased to 0.32 per 100,000 w-y in the period 2016-2017. Most occurred during robberies by unknown perpetrators (252, 55%). Taxi drivers experienced an occupational homicide rate (crude: 39.7 per 100,000 w-y; standardized: 50.2 per 100,000 w-y) that was 98 times (95% CI: 65.1, 146.4) the overall rate of occupational homicide in NC; however, this rate declined markedly over the study period. Gasoline service station workers (18.5 per 100,000 w-y) also experienced among the highest homicide rates of any occupation; in contrast to taxi drivers, there was minimal evidence of reduction in occupational homicide rates for gasoline service station workers.

**Conclusion:** Our findings identify industries and worker demographics that experienced the highest occupational homicide fatality rate. Targeted and tailored mitigation strategies among vulnerable industries is recommended.

### Temporal Trends of Intentional Occupational Injuries: Homicide Rates by Top Five Industries



**Historical redlining and current racial disparities in sports and recreation-related injury hospitalizations in the United States** Oluwatosin Ogunmayowa\* Oluwatosin Ogunmayowa Alicia Lozano Alexandra Hanlon Freddy Paige Natalie Cook Charlotte Baker

Approximately 9 million people are injured annually from sports and recreation in the U.S., more than a third seek treatment in the emergency department, and several thousands are hospitalized for more severe injuries. In this study, we examined the association between historical redlining, a government-sanctioned racial discriminatory practice of the 1930s, and present-day sports and recreational injury (SRI) hospitalization in the U.S. We obtained 2011 SRI hospitalization data in the U.S. from the National Inpatient Sample (NIS) database, linked it to 1930s Home Owners' Loan Corporation (HOLC) redlining maps, and assigned U.S. hospitals to one of three HOLC grades (A+B - best/still desirable, C - definitely declining, and D - hazardous/redlined). Generalized linear mixed models, accounting for sample weight, stratified sampling, and patients clustered within hospitals, were used to examine these relationships. We found no association between HOLC grade and the risk of hospitalization for SRI in Black, Hispanic, and White patients after adjusting for confounders; however, HOLC grade was associated with length of hospital stay and total charges per discharge. Black patients who were hospitalized for SRI in historically redlined neighborhoods had 38% longer length of stay compared to those hospitalized in neighborhoods graded A+B. In contrast, White and Hispanic patients who were hospitalized for SRI in historically redlined neighborhoods had 8% and 9% shorter length of stay, respectively, compared to those hospitalized in neighborhoods graded A+B. Total hospital charges per discharge were 29% and 12% lower for Black and Hispanic patients hospitalized in redlined neighborhoods compared to those hospitalized in neighborhoods graded A+B, but no difference was observed among White patients. This study indicates that redlining, an indicator of structural racism, has a lasting impact on the length of stay and cost of hospitalization for SRI in the U.S.

**Impact of two statewide policies in North Carolina on opioid prescribing among surgery and injury pain patients: a controlled interrupted time-series study, 2014-2019** Theo G. Beltran\* Theo Beltran Brian W. Pence Naoko Fulcher Stephen W. Marshall Maryalice Nocera Courtney N. Maierhofer Bethany L. DiPrete Nabarun Dasgupta Li-Tzy Wu David A. Edwards Timothy S. Carey Paul Chelminski Juan Hincapie-Castillo Scott K. Proescholdbell Joacy G. Mathias Whitney R. Robinson Shabbar I. Ranapurwala

### **Background:**

Implementation of opioid prescribing limitation policies have been enacted across the United States and their impacts on racially minoritized populations are not well known. We quantified the impact of two state-level policies in North Carolina (NC) on opioid prescribing among injury and surgical pain patients by race and ethnicity.

### **Methods:**

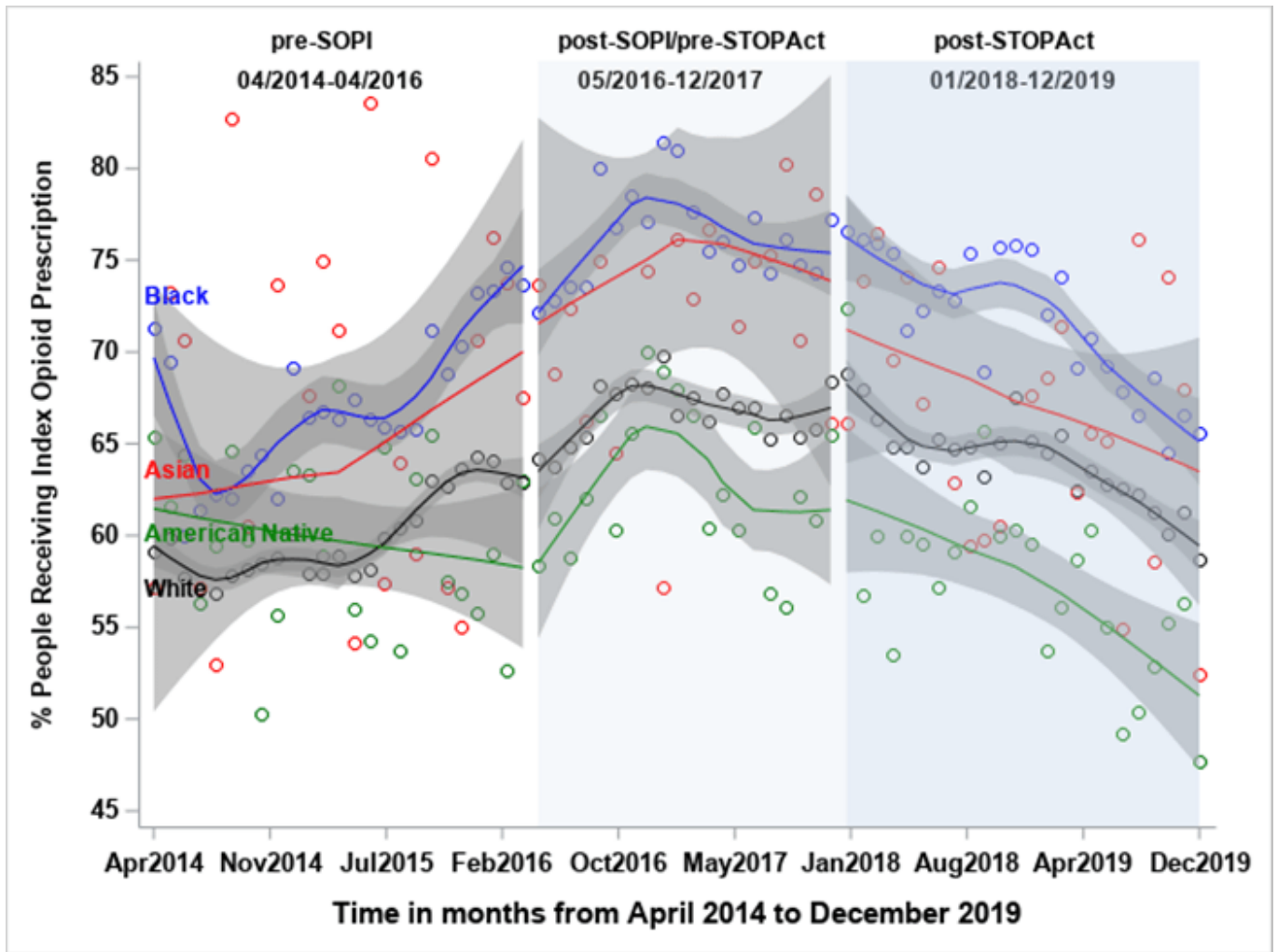
We conducted a controlled interrupted time series study using electronic health records from two large healthcare systems, in patients >11 years of age who received injury care and surgery from April 2014 to December 2019. The policy interventions were: NC safe opioid prescribing investigative initiative (SOPI, May 2016) and NC law mandating opioid days' supply prescribing limits (STOP Act, January 2018). Study outcomes included, 1) proportion and rate of patients receiving an index and subsequent opioid prescription (Rx), 2) days' supply and morphine milligrams equivalent (MME) for dispensed index and subsequent Rx.

### **Results:**

Of the 621,997 surgical and 864,061 injury patients, 69.4% and 19.7%, respectively, received an index opioid Rx. Implementation of SOPI and STOP Act were followed by sustained declines in the proportion of patients receiving an index opioid Rx among post-surgical pain patients (SOPI: -2.7% per year [-4.6, -0.9]; STOP: -4.1 [-5.9, -2.2]), with no change among injury patients. There was a sustained decline in subsequent opioid Rx rate among post-surgical and injury patients after SOPI, but not after STOP act. Index and subsequent days' supply of opioid Rx had sustained declines after SOPI, with immediate and sustained declines after STOP act among post-surgical patients. There was no policy impact on MME. The policy impact was larger among black Americans.

### **Conclusions and Relevance:**

Policies limiting opioid Rx were associated with reductions for post-surgical pain patients. Racial disparities in the effects of these policies may reflect implicit and explicit bias in pain management practices.



**Trends in Suicides by Drug Overdose Involving Psychostimulants with Abuse Potential, United States, 2010-2021** Jing Wang\* Jing Wang Kristin Holland Laura Welder Deborah Stone

The rates of drug overdose deaths involving psychostimulants (e.g., methamphetamine) has sharply risen 317% from 2013 to 2019 and 50% from 2019 to 2021. These shifts likely stem from factors related to increased supply, potency, and composition of methamphetamine in recent years. Methamphetamine use is also associated with increased risk of suicide and its being more accessible may also impact suicide deaths. To inform suicide prevention efforts, we aimed to examine national trends in suicides involving psychostimulants stratified by co-involvement of opioids from 2010-2021.

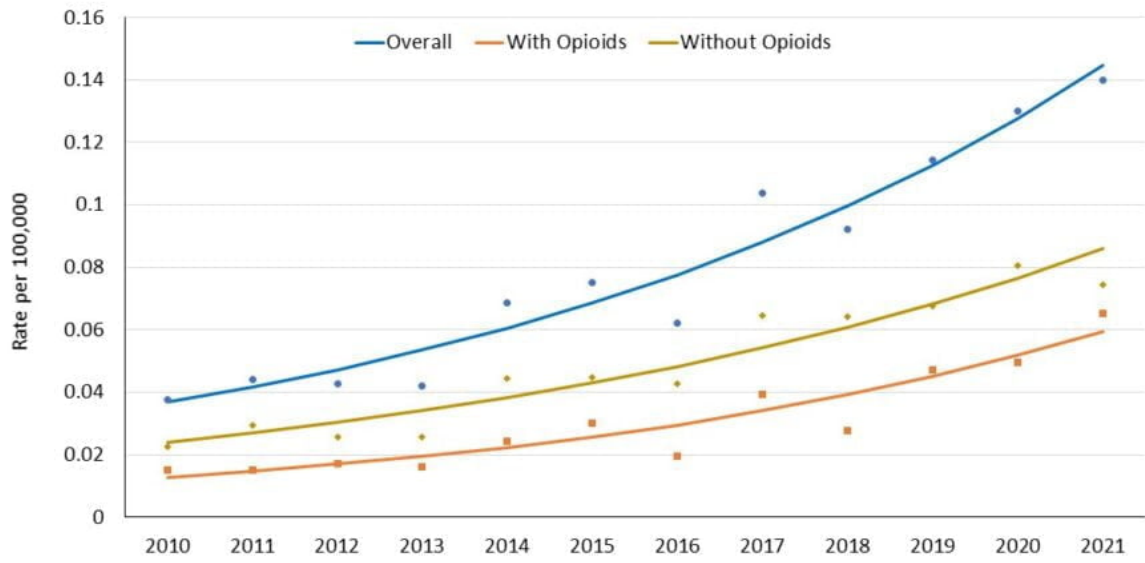
Suicides by drug overdose of persons ages 10 years and older were defined by International Classification of Diseases, 10th Revision (ICD-10) code X60-64 and identified using National Vital Statistics System mortality multiple cause-of-death data, which was final for 2010-2020 and provisional for 2021. Deaths involving poisoning by psychostimulants were defined by ICD-10 code T43.6; opioids co-involvement was defined by ICD-10 codes T40.0 to T40.4, and T40.6. Trends in the annual rate of suicides involving psychostimulants stratified by co-involvement of opioids were examined using Joinpoint regression for overall and by age groups (age 10-44 years, 45 years or older), sex, and race/ethnicity (non-Hispanic White, non-White).

Suicides by drug overdose involving psychostimulants tripled from 97 deaths in 2010 to 342 estimated deaths in 2021. From 2010-2021, the rates of suicide by drug overdose involving psychostimulants increased 11.8% per year from 0.036 per 100,000 in 2010 to 0.12 per 100,000 in 2021 ( $p < 0.001$ ). The rates increased similarly for those with and without co-involvement of opioids (figure). Rapid increases in suicides by drug overdose involving psychostimulants were observed for all subgroups analyzed.

Suicides by drug overdose involving psychostimulants remained relatively uncommon. However, rapidly increasing trends warrant ongoing monitoring and response.



### Rates of suicides by drug overdose involving psychostimulants, United States, 2010-2021



**Impacts of environmental exposures and community characteristics on school violence in Minnesota school children: a cross-sectional study** Austin Rau\* Austin Rau Jesse Berman Andy Ryan Alyson Harding Marizen Ramirez Lynette Renner

Schools, a place where children spend a large portion of their waking hours, are community settings where violence and aggressive behaviors can occur. While previous research studied effects of the environment on academic performance and absenteeism in school children, far fewer works explored the effects of the environment on school violence. We completed a cross sectional study of 2,681 schools in Minnesota using data through Minnesota-Linking Information for Kids (Minn-LInK), a comprehensive linked system of individual level administrative data from the Minnesota Departments of Education, Human Services and Corrections including enrollment characteristics of all K-12 schoolchildren and discipline data from MDE's Disciplinary Incident Reporting System (DIRS). A cohort of ~900,000 K-12 children from Minn-LInK were obtained and followed from 2008 - 2019 for discipline infractions (overall, violent and weapons related). Discipline incidents were aggregated to annual counts at the school level and linked to environmental exposure (air pollution, social vulnerability, and greenspace) data. We analyzed a cross section of data from 2008 - 2012 and estimated IRRs and IRDs using random effects negative binomial regression models. Our preliminary results suggest higher overall DIRS rates associated with greater air pollution and social vulnerability and lower overall DIRS rates associated with more greenspace. Crude IRRs and IRDs compared the overall DIRS rates per 100,000 students in the 4th to 1<sup>st</sup> quartiles of environmental exposures: carbon monoxide IRR 2.50, 95% CI (2.11, 2.98), IRD 2.77, 95% CI (2.16, 3.38); social vulnerability IRR 2.49, 95% CI (2.09, 2.96), IRD 2.71, 95% CI (2.11, 3.32); greenspace IRR 0.34, 95% CI (0.28, 0.40), IRD -3.33, 95% CI (-3.98, -2.68). The results of this work can support policy efforts to improve environmental conditions around schools and future work to evaluate how early life exposures may affect long-term aggressive behavior.

**Examining the impact of offense severity on racial/ethnic differences in criminal charge conviction rates: A 12-year longitudinal cohort of Minnesota youth** Andrew Ryan\* Andrew Ryan Marizen Ramirez Lynette M Renner Alyson Harding Austin Rau Jesse Berman

**Introduction:** Although the frequency of arrests for violent crimes among youth has decreased in recent years, youth of color are still overrepresented in the justice system for crimes involving firearms and other weapons. Using a longitudinal study of children and youth in Minnesota, we compared criminal charge conviction rates among racial/ethnic groups.

**Methods:** Our cohort included all public school students (N=933,663) in Minnesota in 2008 and followed them for 12 years, focusing on involvement in the justice system. Using Minnesota-Linking Information for Kids (Minn-LInK), data from the Minnesota Department of Education were linked with data from the State Court Administrator's Office. Charge conviction rates (# convicted charges/# charges) were calculated for total charges and for weapon-related violence charges among several race/ethnicity groups, including American Indian or Alaskan Native, Asian or Pacific Islander, Hispanic, Black not of Hispanic origin (Black), and White not of Hispanic origin (White). Rate ratios were estimated using negative binomial regression.

**Results:** Cohort members had 2.1 million total charges and 13,838 weapon-related violence charges from 2008 to 2019. Most of the total charges (89%) were for misdemeanor or lower severity offenses and >99% of the weapon-related violence charges were for felony offenses. Overall conviction rates were lower among American Indian (RR 0.854, 95% CL 0.845-0.863) and Black (RR 0.817, 95% CL 0.812-0.823) compared to White participants. In contrast, conviction rates for the high-severity weapon-related violence charge events were higher among American Indian (RR 1.17, 95% CL 1.06-1.28) and Black (RR 1.39, 95% CL 1.31-1.48) compared to White participants.

**Conclusion:** Differences in charge conviction rates among race/ethnic groups varied by severity of the offenses. Future work must examine the potential causes of these disparities, both before and after entry into the justice system.

**Trajectories of intimate partner violence in relation to stress among young women in South Africa: an HPTN 068 study** Nicole K. Kelly\* Nicole K. Kelly Marie C.D. Stoner Nivedita L. Bhushan F. Xavier Gomez-Olive Allison E. Aiello L. Danielle Wagner Nisha Gottfredson Kathleen Kahn Audrey E. Pettifor

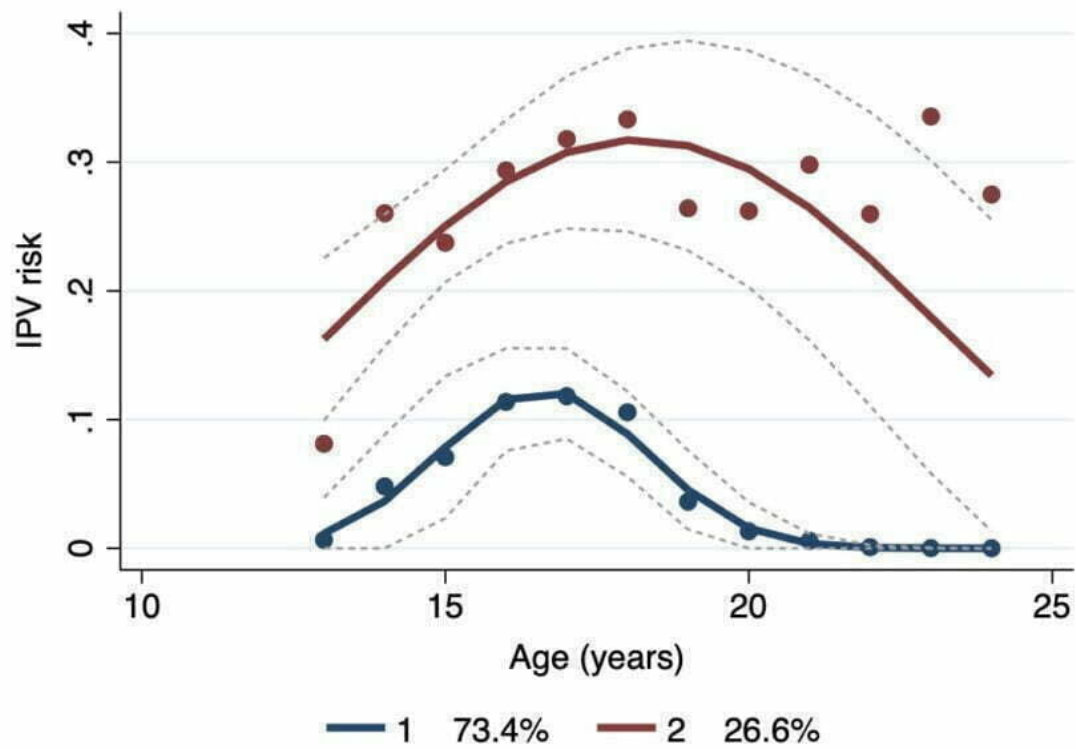
**Background:** Intimate partner violence (IPV) is associated with poor health (e.g., HIV, depression) among adolescent girls and young women (AGYW). In addition, cross-sectional data, primarily from high income countries, has shown that violence impairs the physiological stress response and adversely affects health. Building off prior work, we aimed to identify IPV trajectories among South African AGYW and determine whether high, sustained IPV trajectories were associated with stress.

**Methods:** We used data from 2,183 AGYW ages 13-24 in the HIV Prevention Trials Network 068 study in South Africa. Physical IPV was measured at 5 visits in 2011-2017, and stress was captured in 2018-2019. Stress measures included the Cohen Perceived Stress Scale (low vs. moderate/high) and stress biomarkers (C-reactive protein (CRP), cytomegalovirus (CMV), and herpes simplex virus type-1 (HSV-1)). Biomarkers were operationalized ordinally (CMV and HSV-1: 0=seronegative, 1=low antibodies, 2=medium, 3=high; CRP: quartiles). Group-based trajectory modeling was used to identify IPV trajectories. Ordinal logistic regression was used to estimate the association between trajectory group and the stress measures.

**Results:** A 2-group quadratic trajectory model was identified. In the lower risk group, IPV risk increased from ages 13-17 before declining to 0 by age 21. In the higher risk group, IPV risk increased from ages 13-18 before slowly decreasing during ages 19-24, although this trend was imprecise and may reflect a leveling of risk. Belonging to the higher risk group was associated with an increased odds of elevated CRP (OR: 1.39, 95% CI: 1.09,1.77).

**Conclusions:** In a cohort of South African AGYW, 2 IPV trajectories were identified. Belonging to the higher risk group was associated with elevated CRP but not with other stress measures. High, sustained IPV risk during adolescence may impact biological stress and affect health. Biological stress should be targeted with IPV prevention interventions.

**Figure 1.** Trajectories of physical intimate partner violence (IPV) among adolescent girls and young women (ages 13-24) in rural South Africa



**Is masculinity protective against anxiety in men?** Nikk Leavitt\* Nikk Leavitt Peter Kellett  
Cheryl Currie Richard Larouche

**Background:** Masculinity has been associated with poor mental health outcomes in adult men and is colloquially referred to as toxic. Masculinity is traditionally measured using the Male Role Norms Inventory which examines behaviors that may be common in men, but that are themselves associated with poor mental health regardless of gender (e.g., aggressiveness). The purpose of this study was to examine if masculinity is associated with generalized anxiety among men using this inventory vs. a man's personal definition of it.

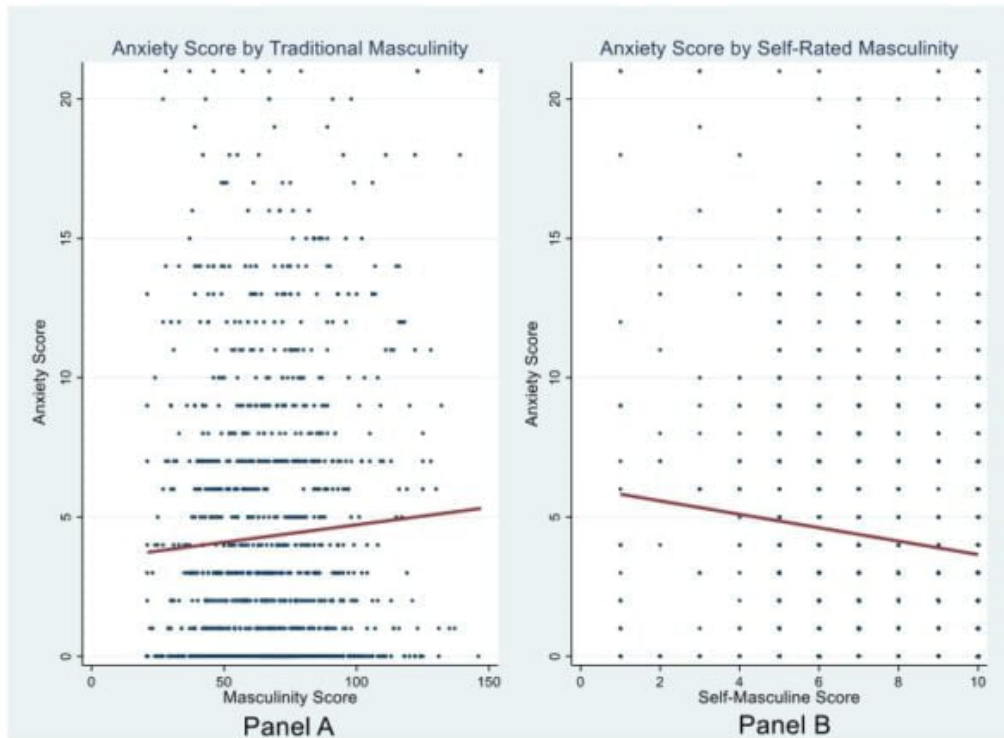
**Method:** An online survey collected data from 1,200 men aged 18-65 across Canada in July 2022. Masculinity was measured using: 1) the Male Role Norms Inventory Short Form and 2) by asking men to self-define what being masculine means. Men were then asked to rate the extent they perceived themselves to be masculine on a scale of 1 to 10 based on their definition of the construct. Generalized anxiety disorder was measured using the GAD-7. Multiple linear regression was used to examine associations between each masculinity score and anxiety score adjusting for confounders.

**Results:** Masculinity score measured using the Inventory was positively associated with increased anxiety scores among men ( $\beta = 0.02$ ,  $p < 0.01$ ) (see Panel A). Masculinity subscales most strongly correlated with higher anxiety were Restrictive Emotionality ( $\beta = 0.29$ ,  $p < 0.01$ ) and Dominance ( $\beta = 0.30$ ,  $p < 0.01$ ). When traditional masculinity was replaced by a man's self-rated masculinity score in the model, the reverse association was found, with increasing masculinity resulting in a significantly reduced anxiety score ( $\beta = -0.13$ ,  $p = 0.04$ ) (see Panel B).

**Discussion:** These findings highlight the need to revisit the ways in which masculinity is defined and operationalized in research to better understand its impacts on men's mental health. The findings also highlight the importance of allowing participants to self-define gender-based constructs given they are fluid and socially constructed.

**Figure 1**

Traditional masculinity score is associated with increased anxiety while self-rated masculinity score is associated with decreased anxiety among men aged 18-65.



**Estimating Joint Effect of Adverse Childhood Experiences and Asthma on Subsequent Depressive Symptoms: A Marginal Structural Modeling Approach** Yuta Takemura\* Yuta Takemura Koryu Sato Naoki Kondo Kosuke Inoue

**Introduction:** Despite the mounting evidence showing the relationship of adverse childhood experiences (ACEs) with increased risk of depression, it is unclear whether the long-term mental health burden of ACEs is increased by stress-related chronic diseases like asthma—one of the major early-stage comorbidities affected by ACEs. We thus examined the joint association of ACEs and asthma with subsequent depressive symptoms among US adults.

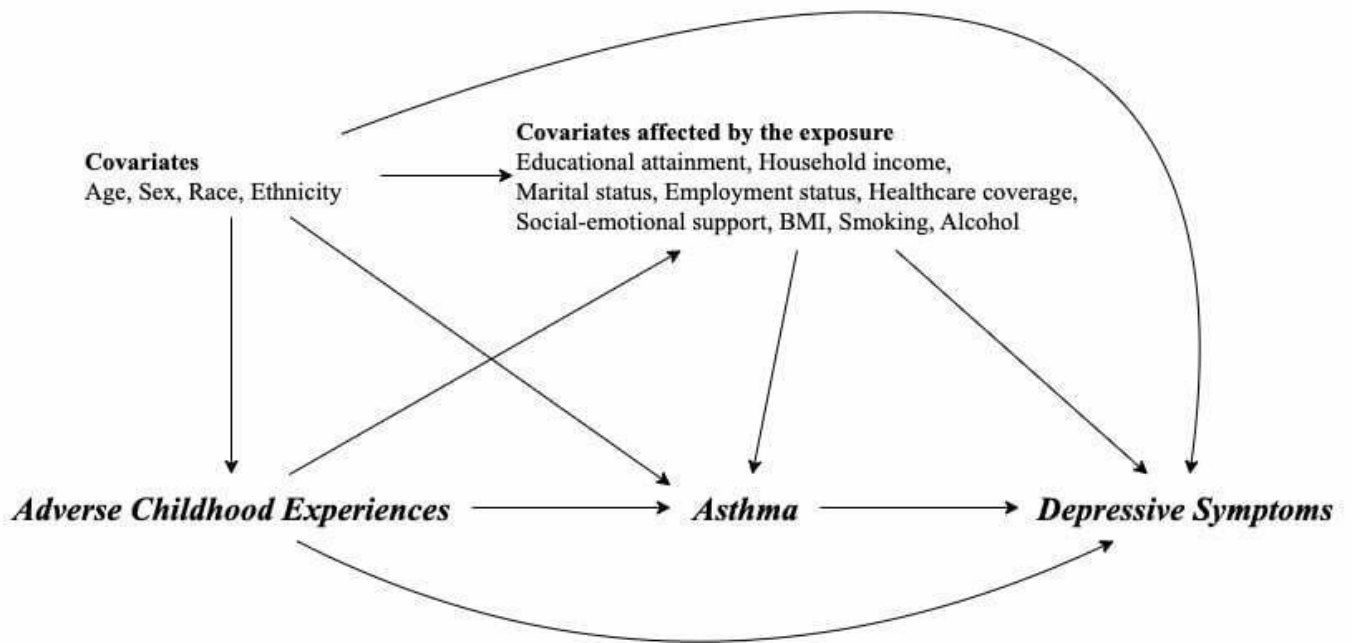
**Method:** This study used data from BRFSS 2010, including 21,544 participants over 18 years old from four states where participants were questioned about adverse childhood experiences (Hawaii, Nevada, Vermont, and Wisconsin). We utilized logistic regression models to calculate the adjusted odds ratio (aOR) for elevated depressive symptoms (evaluated by PHQ-8) according to ACEs and asthma, with marginal structural models to take account of time-varying confounders. The relative excess risk due to interaction (RERI) was calculated to evaluate additive interaction between ACEs and asthma.

**Result:** Among 21,544 participants (mean age, 56.4 years; women, 59.5%), 11,257 (52.3%) showed one or more ACEs, 3,219 (14.9%) reported past history of asthma, and 856 (4.0%) showed elevated depressive symptoms. ACEs and asthma were associated with elevated depressive symptoms (ACEs, aOR[95% CI] = 3.63[3.05-4.36]; asthma, aOR[95% CI] = 1.95[1.29-2.87]), respectively. After adjustment for time-varying confounders, we found an additive interaction between ACEs and asthma for elevated depressive symptoms (RERI [95% CI] = +1.71[0.63-2.78]).

**Conclusion:** The risk of elevated depressive symptoms due to ACEs was increased by the presence of asthma. Our findings suggest that prevention and early treatment for asthma might be effective to mitigate the potential burden of ACEs on mental health, which should be the subject of future research.



**Figure 1.** Directed acyclic graph illustrating proposed causal structure from adverse childhood experiences, through asthma, to depressive symptoms.



**Childbirth as a Risk Factor of Suicide Ideation in South Korean Women** Kayden Jeong\*

Kayden Jeong

**Background**

**Suicide rates are rising especially among women in Korea. As in most developed countries, Korean women are educated that they have equal opportunities to pursue any profession regardless of sex. However, they are still expected to cater the traditional gender role. In many cases, when Korean women become pregnant, they stay at home solely with their babies, disconnected from previous social relationships, which could negatively impact their self-efficacy and social belongingness. According to Interpersonal Suicide Theory, Korean women in this situation would experience greater suicide ideation due to higher feelings of burdensomeness and less belongingness.**

**Method**

**We investigated the effect of childbirths on the suicide ideation of Korean women by conducting cohort-longitudinal study with samples obtained for 14 years. We selected 962 individuals who had childbirths and 12,177 who had not, and compared the incidence of suicide ideation.**

**Results**

Relative risk for having suicide ideation is significantly higher in the group with childbirths for ages < 40 years old. This means < 40 years old women are 129% more likely to have suicide ideation after childbirth than 40+ years old women. The results shows that there is a positive relationship between childbirth and suicide ideation among younger women. This suggests that younger women may experience a larger shift in their gender role before and after childbirth.

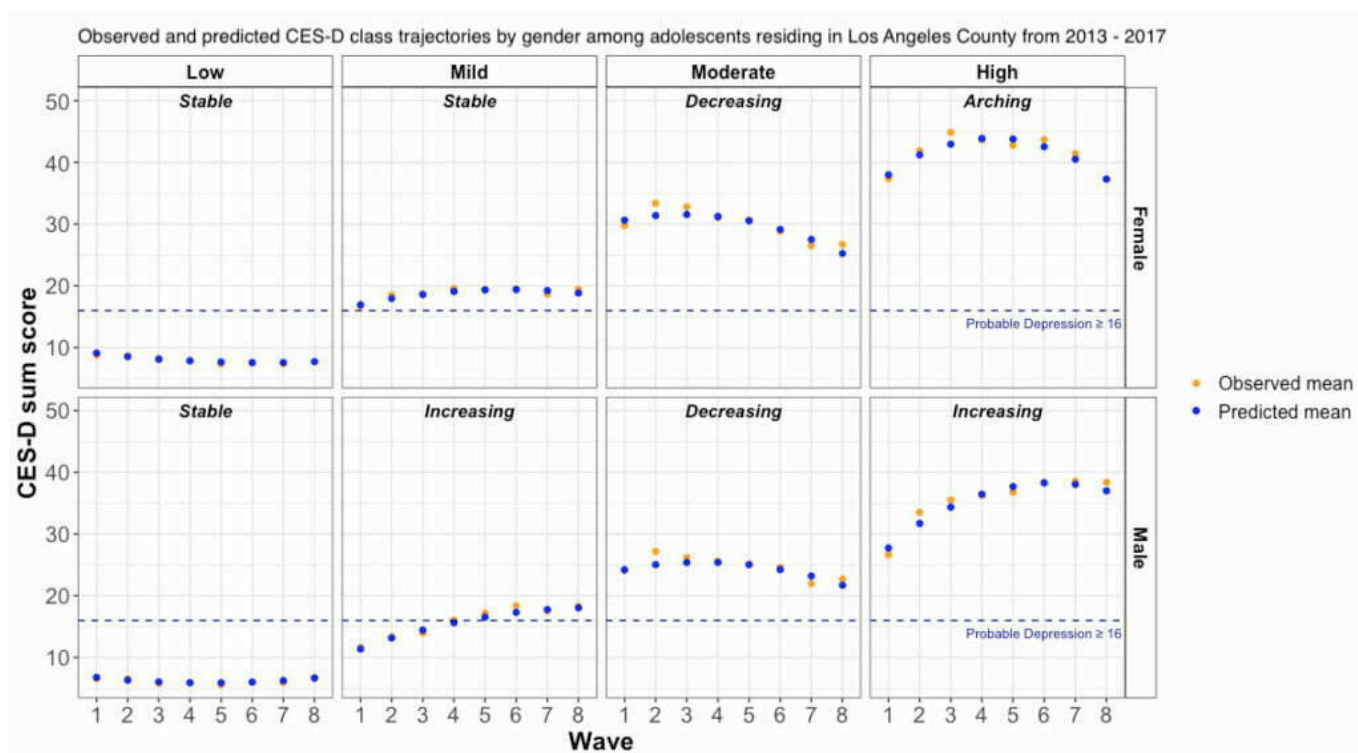
**Discussion**

Future study needs to investigate the mechanisms how childbirths affect suicide ideation in women. To find a stronger evidence for causal relationship, it's desirable to study the relationship between the number of childbirths and suicide ideation.

**Differentiation of depression trajectories among adolescents living in Los Angeles County**

**from 2013 to 2017** Catherine Gimbrone\* Catherine Gimbrone Megan C. Finsaas Kira E. Riehm Ahuva Jacobowitz Nadav L. Sprague Samuel E. Packard Adam M. Leventhal Andrew G. Rundle Katherine M. Keyes

Over the past decade, marked increases in mental health disorders have been observed among US adolescents, with cross-sectional data indicating that secular trends are more evident among girls than boys. There has been little investigation into recent longitudinal patterns in adolescent mental health, which would expand our understanding of symptom trajectories within these secular trends. We sought to address this gap using data from the Health and Happiness Cohort, a longitudinal 8-wave study of high school students residing in Los Angeles County from 2013 to 2017 (N = 3,393). A multigroup latent class growth analysis by gender was used to differentiate trajectories in depressive symptoms scores measured with the Center for Epidemiological Studies Depression (CES-D) (Range: 0 - 60). A four-class solution with quadratic terms provided the best model fit. Classes encompassed low, mild, moderate, and high trajectories, with further demarcation by gender. Trajectories among female adolescents included low-stable (N = 633), mild-stable (N = 764), moderate-decreasing (N = 309), and high-arching (N = 107). Those among male adolescents included low-stable (N = 777), mild-increasing (N = 538), moderate-stable (N = 202), and high-increasing (N = 63). Notably, estimated CES-D scores consistently exceeded or crossed the threshold for probable depression ( $\geq 16$ ) among over half of all adolescents, with female adolescents experiencing higher average scores compared to male adolescents in parallel classes and male adolescents experiencing larger increases in CES-D scores over time. Our four class solution aligned with prior findings of depression trajectories among adolescents, suggesting that recent secular trends have not been motivated by changes in overall longitudinal trends. Nonetheless, our findings highlight that a large subset of adolescents may be vulnerable to developing clinical depression over the course of high school and experiencing increased symptom severity.



**Using Behavioral Health Demand to Prioritize Areas for Improving Telehealth Capacity**

Shinobu Watanabe-Galloway\* Shinobu Watanabe-Galloway Kendra Ratnapradipa Josiane Kabayundo  
Ronnie Horner

**Background:** COVID-19 accelerated the use of telemedicine for behavioral health care, which has potential to increase access to underserved patient populations including rural residents. However, internet service availability at speeds necessary to deliver telemedicine remains limited in rural communities. State and federal policies are being proposed to expand broadband access but resources are limited, necessitating some type of prioritization for the effort. **Objective:** To examine the impact of prioritization based on demand for services vis-à-vis adequacy of current broadband access. **Methods:** Data sources were Federal Communications Commission Fixed Broadband Deployment, 2021 Behavioral Risk Factor Surveillance and 2021 Nebraska Health Profession Tracking Services. The smallest possible analytic unit was health department district (contiguous counties). We used 4 behavioral health conditions: binge drinking, marijuana use, depression diagnosis and 30-day distress. Behavioral health providers were categorized as: prescriber (psychiatrist, advanced practice registered nurse, physician assistant), non-prescriber (psychologist, licensed independent mental health practitioner), and licensed alcohol and drug counselor (LADC). We calculated median percentage of district residents with adequate broadband speed (100/10 Mbps), and demand as the ratio of individuals with a given behavioral problem to available providers. **Results:** Demand range varied: binge drinking (LADC: 270.7-2176.6), marijuana use (LADC: 42.4-931.1), depression (Prescriber: 567.1-5084.0; Non-prescriber: 77.6-328.4), and distress (Prescriber: 322.3-2359.0; Non-prescriber: 62.0-213.5). Twelve of 19 districts (63%) had adequate broadband access. Priority areas for broadband build-out include 1 district for binge drinking and 2 districts for depression or psychological wellness. **Conclusions:** Demand for behavioral health services is a useful metric for prioritizing areas for receipt of broadband resources.

**Neighborhood Racial Residential Segregation and Mental Health during Pregnancy** Sylvia E Badon\* Sylvia Badon Wendy T Dyer Alex Asera Huyun Dong Tess Baker Kiarri N Kershaw Charles P Quesenberry Kelly C Young-Wolff Mibhali Bhalala Kathryn Erickson-Ridout Lyndsay A Avalos

**Background:** Research suggests the social, physical, and socioeconomic contexts of residing in segregated neighborhoods may negatively impact mental health. This study assessed the influence of racial residential segregation on prenatal mental health among Asian/Pacific Islander, Black, and Hispanic individuals.

**Methods:** We used data for 125,341 pregnancies in the Kaiser Permanente Northern California healthcare system (2014-2019). Race and ethnicity (self-reported in clinical care), address, and prenatal depression and anxiety diagnoses were extracted from electronic health records. We used the local Getis-Ord  $G_i^*$  statistic in each race and ethnicity group as a measure of neighborhood racial residential segregation [low (<0), medium (0-1.96), high (>1.96)] and regression models stratified by race and ethnicity to estimate associations.

**Results:** Depression and anxiety diagnoses were highest in Black (18%) and Hispanic (13-14%) groups, and lower in Asian/Pacific Islanders (6-7%). Asian/Pacific Islander (40% vs 32%) and Black individuals (43% vs 23%) were more likely to live in neighborhoods with high vs low segregation, while Hispanic individuals were equally likely (35% vs 34%). In Black individuals, high segregation was associated with greater odds of depression (aOR=1.25; 95%CI: 1.10,1.42) and anxiety (aOR=1.14; 95%CI: 1.00,1.29) during pregnancy. In Asian/Pacific Islander and Hispanic individuals, high segregation was associated with lower odds of depression (aOR=0.76; 95%CI: 0.70,0.84 and aOR=0.88; 95%CI: 0.82,0.94, respectively) and anxiety (aOR=0.81; 95%CI: 0.74,0.88 and aOR=0.88; 95%CI: 0.82,0.93, respectively) during pregnancy.

**Conclusion:** Racial residential segregation was associated with worse prenatal mental health for Black individuals, but better mental health for Asian/Pacific Islander and Hispanic individuals. These findings suggest policies reducing segregation and its impact may improve mental health outcomes in pregnant Black individuals.

**Stress Variability Typologies Using Ecological Momentary Assessment and Associations with Individual and Family Wellbeing in a Diverse Community-Based Sample: Results from the Family Matters Study** Émilie Ellis\* Émilie Ellis Allan Tate Andrea Trejo Anna Hochgraf Alicia Kunin-Batson Jerica Berge

Background: Chronic and acute stress are linked to biopsychosocial health yet little is known about stress variability. The current study characterized groups of stress variability in a diverse, community-based sample of parents to identify stress typologies and to explore associations with individual and family wellbeing.

Methods: Ecological momentary assessment (EMA) self-report data from the Family Matters Study (n=631 adults) was used to operationalize participant stress level and variability (i.e., daily mean and diurnal slope of stress, average between-survey change, standard deviation of survey-stress change, and volatility of daily change variability over a one-week EMA period). Latent class analysis was used to group participants based on stress characteristics. Using baseline survey data, multinomial logistic regression was used to identify predictors of class membership and cross-sectional associations with wellbeing.

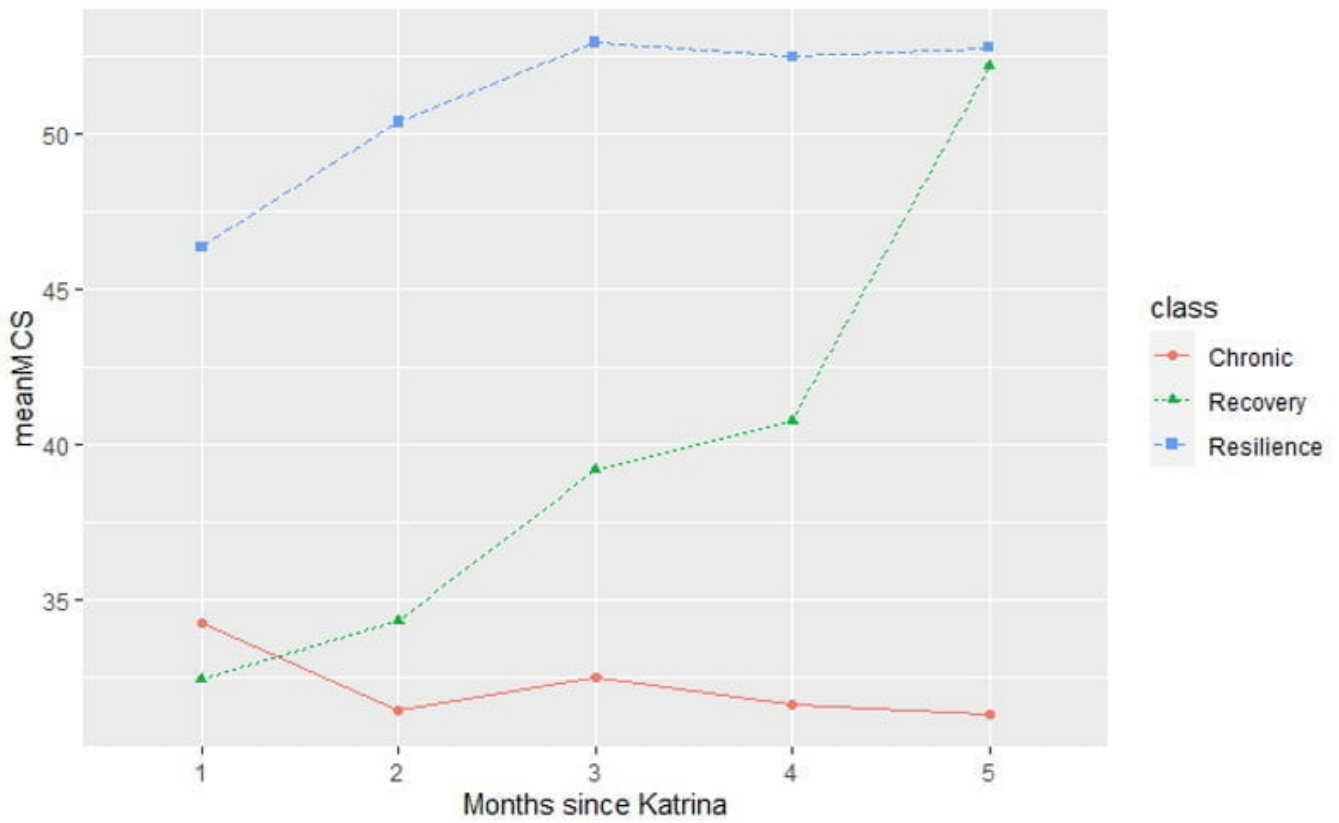
Results: A 3-class model best fit the data (entropy = 0.821) and demonstrated qualitatively distinct classes (low, medium, and high stress variability). Using the low stress variability group as a reference, higher anxiety (=1.55), overall baseline stress (=1.25), and lower family functioning (=1.96) predicted membership in the medium stress variability class. Higher number of recent stressful events (=1.24), anxiety (=2.34), and overall stress (=1.35) predicted membership in the high stress variability group versus the reference group. Coping, self-esteem, and resilience did not predict class membership. Mean levels of pain, energy, depression, and adverse childhood experiences were correlated with typologies, but effect sizes were small ( $r^2$  range = 0.01-0.07).

Conclusion: High stress variability had strong links with elevated anxiety and recent stressful events. Future research should prospectively examine stress variability on biopsychosocial health to develop interventions that buffer against momentary stress on wellbeing.

**Predictors of mental health trajectories among adult survivors ten years after Hurricane Katrina, 2005-2015** Angela-Maithy Nguyen\* Angela-Maithy Nguyen David Abramson

There are long-term mental health impacts among those who experience disasters. While the incidence and prevalence rates of post-traumatic stress disorder are well-documented, the current literature recognizes the heterogeneity of responses to trauma. Our objective was to identify the post-disaster mental health trajectories among survivors of Hurricane Katrina (Katrina), a tropical cyclone that made landfall along the United States Gulf Coast on August 29, 2005. Our study used longitudinal data from The Gulf Coast Child and Family Health Study, a representative cohort (N=1,075) of households directly impacted by Katrina. We conducted latent growth mixture modeling to identify distinct trajectories from mental component summary scores. Three latent classes were observed and classified as “Resilience”, “Recovery”, and “Chronic” groups. The majority of participants (52.4%) were classified in the Resilience group, a relatively sharper increase in mental health in the immediate aftermath, followed by a stable and near flat line in its trajectory. We then examined a range of predictors associated with each identified trajectory class. Age, gender, pre-disaster household income, employment change, residential mobility, post-disaster financial resources, and mental health needs were significant predictors of mental health trajectories. Those who became unemployed after Katrina were less likely to be in the Resilience group compared to the Chronic group [adjusted odds ratio (aOR): 0.56, 95% confidence interval (CI): 0.32, 0.98]. Compared to the 18-34-year-old group, those 66 years and older had more than twice the odds of being in the Resilience group compared to the Chronic Group (aOR: 2.69, 95%CI: 1.25, 5.79). In addition to informing approaches to examining post-disaster mental health, our findings underscore the need for future research to elucidate the mechanisms of trajectories related to resilience and recovery, particularly across different survivor cohorts.

**Trajectories of mental health component scores over time among Hurricane Katrina survivors from the Gulf Coast Family and Child Health Study, 2005-2015 (N=1,075)**



MCS: Mental Component Summary Score

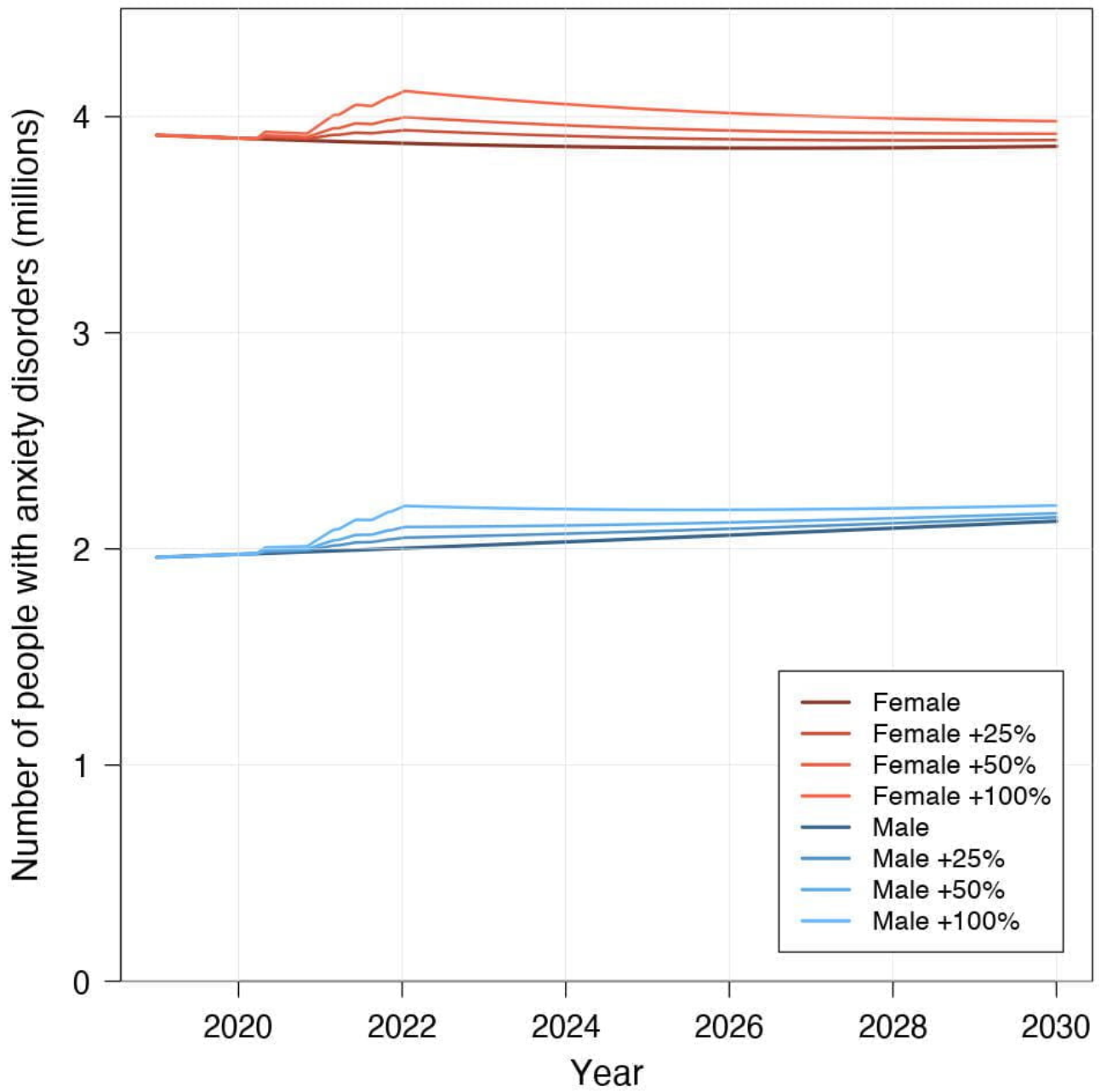


**Estimation of additional anxiety disorder burden during and beyond the COVID-19 pandemic in Germany using the illness-death model** Chisato Ito\* Chisato Ito Tobias Kurth Bernhard Baune Ralph Brinks

The COVID-19 pandemic has exacerbated the burden of anxiety disorders globally. However, to what extent this additional disease burden may persist over time is unknown. We aimed to estimate the anxiety disorder burden of the pandemic by projecting the number of people with the disease in Germany from 2019 to 2030 with varying levels of incidence increase during the pandemic using the illness-death model.

We first ran a baseline projection assuming no anxiety disorder incidence increase during the pandemic. The number of men and women with the disease were estimated up to 2030 using the population projection estimates of the Federal Statistical Office and models for sex and age-specific prevalence, incidence, remission, and mortality fitted to the Global Burden of Disease Study 2019 data, and by repeatedly applying the recursion formula that relates the above transition probabilities in the illness-death model. We then modelled a function to simulate spikes in anxiety disorder incidence following the pandemic wave peaks and durations, based on the German COVID-19 incidence data. We set the incidence to peak at +25, +50, +100%, then to attenuate from one wave to another, assuming the level of uncertainty and fear related to the pandemic would be the highest at the onset. The addition of this model to the application of the recursion formula generated the projections under varying peak incidence assumptions.

Our baseline projection estimates 3,862,333 women and 2,128,410 men with anxiety disorders in Germany in 2030. A 25% incidence increase during the pandemic would lead to an additional 29,215 (+0.8%) cases in women and 18,212 (+0.9%) cases in men in 2030. A 100% incidence spike during the pandemic would result in an additional 116,526 (+3.0%) cases in women and 72,682 (+3.4%) cases in men in 2030. The results indicate that any additional burden of anxiety disorders due to increased incidence during the pandemic would persist far beyond the pandemic.



**Sexual and Gender Minority status, race/ethnicity, and risk of Depression and Anxiety in the Household Pulse Survey** Cody Ingle\* Cody Ingle Dr. Andrew Williams

*Background.* Sexual and Gender Minorities(SGM) have historically reported approximately twice the rate of depression and anxiety compared to non-SGM. Intersectionality of SGM and race is important, as those who experience multiple layers of discrimination may have increased rates of depression and anxiety. We examined risk of anxiety and depression among SGM, stratified by race/ethnicity, using the Household Pulse Survey(HPS).

*Methods.* Data for 918,892 individuals were drawn from HPS. Individuals with PHQ-2 scores  $\geq 3$  were identified as having depression symptoms. Those with GAD-2 scores  $\geq 3$  were identified as having anxiety symptoms. Sexual orientation(Gay/Lesbian, Straight, Bisexual, Something Else, or I don't know), gender identity(Cisgender Male, Cisgender Female, Transgender/other identity) and race/ethnicity(Hispanic, non-Hispanic White, non-Hispanic Black, non-Hispanic Asian, Other) were self-reported. Logistic regression(adjusted for education, job loss, age, and income; weighted for survey design) estimated odds ratios and 95% confidence intervals for depression and anxiety among sexual minority individuals compared to straight individuals and transgender individuals compared to cisgender males, overall and stratified by race/ethnicity.

*Results.* Overall, odds of depression(OR:2.30 95%CI:1.98,2.67) and anxiety(OR:2.41 95%CI:2.23,2.61). were greater among transgender individuals compared to cisgender individuals. Compared to straight individuals, bisexuals had the highest odds of depression(OR:2.84 95%CI:2.76,2.92) and anxiety(OR:3.07 95%CI:2.83,3.33). Stratified by race/ethnicity, non-Hispanic White SGM had highest risk of poor mental health, yet risk of poor mental health was elevated for SGM in all racial/ethnic groups.

*Discussion.* Overall, our observations align with prior literature on mental health outcomes among SGM individuals. Race/ethnicity-specific results were unexpected, yet may be driven by differences in self-report of depression and anxiety.

**Structural racism as a determinant of adolescent mental health in the United States**

Katherine M. Keyes\* Paris B. Adkins-Jackson Victoria Joseph

**Background:** Depressive symptoms rapidly increased among US adolescents in the past decade, with consequences especially apparent among youth racialized as Black. Structural racism is a pervasive and persistent form of systemic inequity and the root cause of US health disparities. Measurement remains a challenge and associations for youth mental health are untested. The present study assesses theory-informed indicators of state-level structural racism and associations with youth mental health.

**Methods:** 15 downstream indicators of state-level structural racism from publicly available sources (2015-2019), were evaluated encompassing inequities in socioeconomic factors, civic representation, incarceration, health-related racism. Indicators were linked with composites of loneliness, self-esteem, self-derogation, and depressive symptoms (25<sup>th</sup> percentile) from 12<sup>th</sup> grade respondents of Monitoring the Future (2015-2019, N=41,258), an annual nationally-representative survey.

**Results:** Signals of associations emerged whereby Black students in states with high structural racism in incarceration (OR=1.20, 95% C.I. 0.86-1.66) and maternal mortality (OR=1.25, 95% C.I. 0.99, 1.56) have increased odds of high depressive symptoms compared with Black students in states with lower structural racism. Black students in states with high neighborhood segregation have 1.22 (95% C.I. 1.01-1.48) and 1.19 (95% C.I. 0.95-1.49) increased odds of high self-derogation and depressive symptoms, respectively. Odds ratios ranged from 1.02-1.12 for white students, indicative of specificity of associations.

**Conclusion:** Adolescents currently racialized as Black in the US face worse mental health when living in states with higher levels of health-related racism, family disruption and separation due to incarceration, and siloed housing through segregation. The historical impact of structural racism are pernicious and emerge as poor mental health during adolescence with potentially long-lasting consequences.

**The Association Between Top/sub Drop and Lifetime Suicide Attempts Among Kinksters in the United States in 2016** Teresa Filipowicz\* Teresa Filipowicz Sydney Browder Anna Randall Richard Sprott

**Background:** Kink is an umbrella term to describe a variety of non-traditional sexual and erotic acts. People who practice kink, or kinksters, are susceptible to unique mental health experiences, such as Top/sub drop—a detached or depressive state after an intense experience as a Dominant or submissive. Kink-related stigma and other factors, such as Top/sub drop, may contribute to an increased mental health burden among kinksters, a population with increased experiences of suicide attempts. This analysis estimated the association between Top/sub drop and lifetime suicide attempts and assessed modification by gender identity.

**Methods:** We cross-sectionally surveyed American, adult, self-identified kinksters in 2016. The primary exposure was experiences of Top/sub drop, asked via 2 binary questions, and the primary outcome was a lifetime binary, self-report of past suicide attempt; gender identity was a potential modifier. Modification on the multiplicative scale was assessed via stratum-specific estimates and a likelihood ratio test comparing models with and without an interaction term. The log-binomial model adjusted for age, race, past mental health treatment, and childhood trauma score.

**Results:** Among 990 kinksters, the prevalence of lifetime suicide attempt was 24.2%, far higher than a 2018 U.S. prevalence estimate of 0.5%. The prevalence ratio comparing kinksters with prior Top/sub drop experiences to those without prior Top/sub drop experiences was 1.38 (95% CI: 1.12, 1.72). Gender identity did not modify this relationship on the multiplicative scale (likelihood ratio test p-value=0.98).

**Conclusions:** Top/sub drop conferred a prevalence of lifetime suicide attempt .38 times that of kinksters without Top/sub drop experiences, after adjusting for known confounders. Gender identity did not modify this association. Increased mental health support after Top/sub drop may be a potential area of intervention to reduce the prevalence of suicide attempt among kinksters.

**Multiple exposures to natural hazards and anxiety and depression symptoms among young adults: evidence from Ethiopia, India, Peru, and Vietnam** Ilan Cerna-Turoff\* Ilan Cerna-Turoff Waveley Qiu Joan A. Casey Katherine Keyes Kara E. Rudolph Daniel Malinsky

Young adults may be at increased risk of poor mental health after exposure to natural hazards. This study sought to understand the effect of early life, recent, and repeat exposures to natural hazards on anxiety and depression symptoms among young adults.

We analyzed data from the Young Lives study (2002-2020) on 9441 participants from Ethiopia, India, Peru, and Vietnam. Anxiety and depression symptoms were measured, using psychometrically validated scales. We estimated differences in anxiety and depression scores between young adults with one of three natural hazard exposure patterns (early, recent, or repeat) and their unexposed peers, adjusting for selected individual- and community-level covariates. We applied targeted maximum likelihood estimation (TMLE) with an ensemble of machine learning algorithms for analysis. Sensitivity analyses identified possible biases by age cohort, missingness in recent exposures, and missingness in Peru's outcome measures.

Any pattern of natural hazard exposure tended to lead to higher anxiety and depression symptoms among young adults, in contrast to never being exposed, in three of the four countries (Ethiopia, India, and Vietnam). These higher anxiety scores among exposed young adults ranged from 0.03 points [95% CI: 0.01, 0.05] higher in Vietnam to 1.09 points [95% CI: 0.85, 1.34] higher in Ethiopia after recent exposures. For depression, scores ranged from 0.31 points [95% CI: 0.22, 0.40] higher after recent exposure in India to 1.40 points [95% CI: 0.99, 1.82] higher after early life exposure in Ethiopia. The findings were largely consistent across sensitivity analyses.

Young adults exposed to natural hazards at any time point are vulnerable to poor mental health. Climate change will continue to drive increases in natural hazards, disproportionately affecting low- and middle-income countries where most young people live, and to exacerbate inequalities in global mental health.

**LATEBREAKER**

Mental Health

**Early Life Participation in Cognitively Stimulating Activities and Risk of Depression, Anxiety in Late Life** Xinye Qiu\* Xinye Qiu Andrea L. Roberts Kaleigh McAlaine Luwei Quan Joseph Mangano Marc G. Weisskopf

Much less is known about associations between early-life positive experiences, such as participation in cognitively stimulating activities, and late-life mental health. We investigated whether greater engagement in cognitively stimulating activities, such as reading, writing and playing cognitive games in early life was associated with lower risk of late-life psychiatric symptoms. Former participants of the St. Louis Baby Tooth Survey were re-contacted to collect information on their current depression/anxiety symptoms and early-life cognitive activities over 2021-2022. A total of 2187 individuals (mean age 63 yrs.) were included based on completeness in response. A composite activity score was created by averaging the frequency of self-reported participation in common cognitive activities during early life (age 6, 12, 18), each rated on a 1 (least frequent) – 5 (most frequent) point scale. Outcomes of interest were risk of major depressive disorder (depression) and generalized anxiety disorder (anxiety) measured by 9-items Patient Health Questionnaire and 7-items Generalized Anxiety Disorder Screener. We used logistic regression to estimate OR and 95% CIs of outcome risk associated with frequency of early-life activity. Each 1 point increase of early-life activity score was associated with an OR of 0.54 (95% CI: 0.38- 0.77) for late-life depression and an OR of 0.94 (95% CI: 0.61-1.43) for late-life anxiety, adjusting for age, sex, race, parental education, childhood family structure and socioeconomic status. In stratified analyses, the protective association for depression was stronger in those with lower vs. higher childhood socioeconomic level, but the differences did not reach statistical significance. Associations were similar by sex. Activities at age 6 and 18, but not 12, were significantly associated with depression. More frequent participation in cognitively stimulating activities during early life was associated with reduced risk of late-life depression.

**LATEBREAKER**

Methods/Statistics

**Accounting for outcome misclassification under outcome dependent sampling** Ning Zhang\*  
Ning Zhang Jessie K. Edwards Grace E. Mulholland Paul N. Zivich Stephen R. Cole

In case-control (CC) studies, approaches correcting outcome misclassification by applying source population (or validation study) sensitivity and specificity can give biased results. This bias is due to differing sampling fractions between cases and non-cases, which alters population sensitivity and specificity.

We present a “fusion” M-estimator that accounts for outcome misclassification and properly estimates the standard error (SE) in this setting. We examined its finite sample properties through simulation. We simulated scenarios with varied odds ratios (OR), prevalence of a binary outcome and a binary exposure, sample sizes, sampling fractions, population sensitivity and specificity. In each iteration, we generated a source population, and sampled one CC study based on the misclassified outcome and one validation sample. To estimate CC OR, we considered three estimators: (a) a naïve estimator which ignores misclassification; (b) a proposed fusion M-estimator; (c) an intermediate estimator which uses untransported sensitivity and specificity. We evaluated estimators by several metrics, including bias, empirical SE, model-based SE, and coverage probability. We will also illustrate this approach to estimate the association between type of employment and HIV prevalence in a population in East Africa.

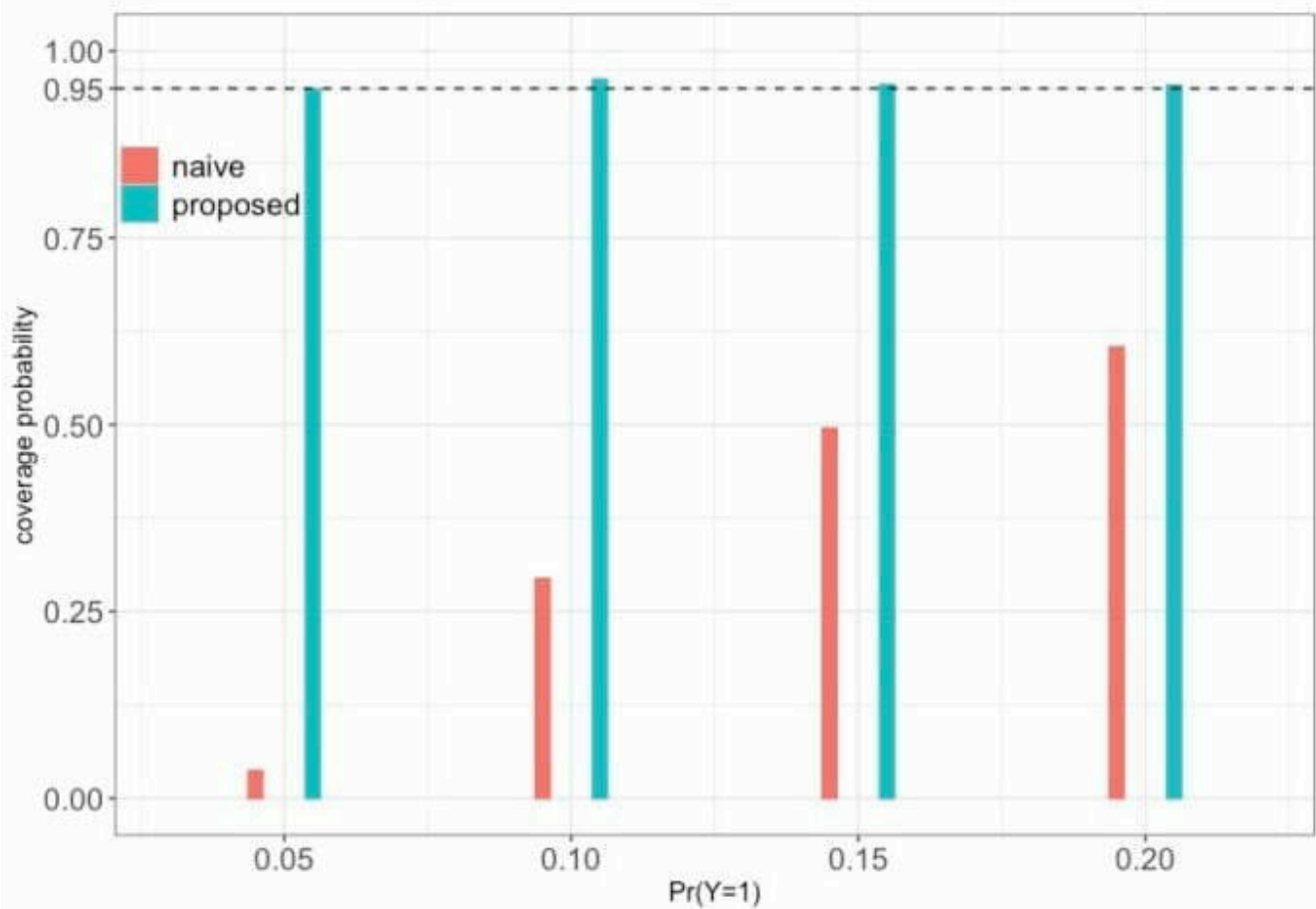
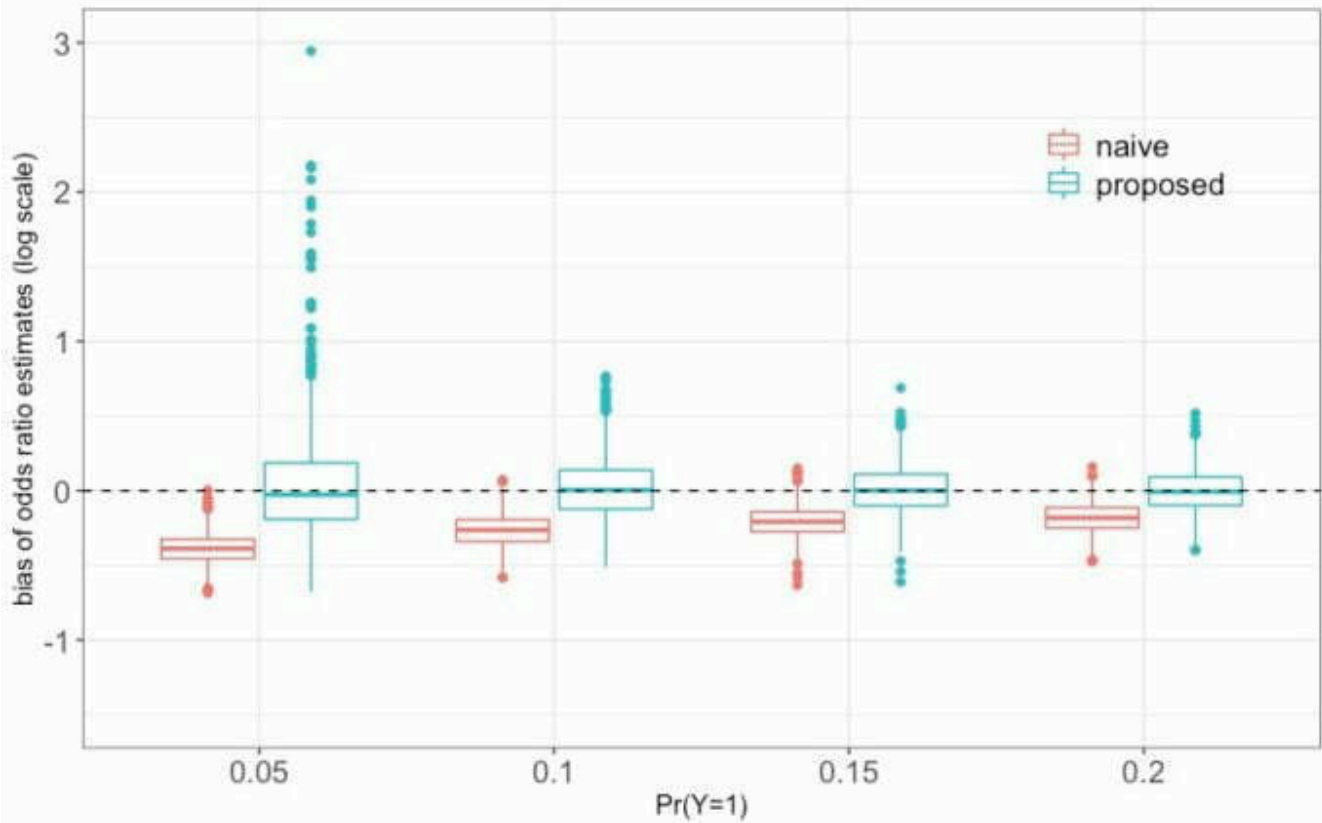
For a rare disease (5%), the naïve estimator was biased with low coverage (<10%); for a common disease (20%), the naïve estimator was still biased but had higher coverage probability (40%-60%). In all scenarios, the proposed M-estimator had negligible bias, and appropriately reflected uncertainty across information sources with nominal coverage probability (95%).

When a sampling mechanism is outcome dependent, obtaining unbiased point estimates and SEs in the presence of outcome misclassification requires accounting for both the sampling fractions and any relevant uncertainty.



### Bias (top figure) and coverage (bottom figure) of naive and proposed estimators

Source population=10,000, true OR=2, sensitivity=0.8, specificity=0.95,  $\Pr(X=1)=0.25$ , case-control study sample=2,000, validation study=1,000, simulated 1,000 times.



**LATEBREAKER**

Methods/Statistics

**Survey sampling methods for partial verification bias in diagnostic evaluation studies**

Katherine Thomas\* Katherine Thomas Allison Meisner

**Introduction:** In studies of diagnostic accuracy of a test versus a given reference standard from a random sample of reference positive and reference negative patients, estimation of sensitivity and specificity is unbiased. However, partial verification bias occurs if selection of patients for reference testing is differential, for instance if likelihood of verification depends on an alternative, but related, reference test.

**Methods:** We discuss design of diagnostic accuracy studies with multiple reference standards where one reference standard is not fully verified and likelihood of verification depends on the result of a different reference standard. We consider standard survey sampling techniques to correct the bias by adjusting for the known sampling fractions. We apply this to the evaluation of a test for SARS-CoV-2 against reference standards of polymerase chain reaction (PCR) and viral culture, where culture has scientific interest unique from PCR, but is more difficult to obtain.

**Results:** Among 257 participants given both the investigational test and the PCR reference standard, all 32 with available specimen from the 40 PCR-positive participants and a random sample of 20 of the 217 PCR-negative participants were tested by culture. Naïve analysis of the resulting 52 participants yielded sensitivity of 90.9% and specificity of 64.1% for the investigational test against culture. Recognizing that selection for verification by culture was based on PCR status, survey sampling techniques with inverse sampling weights of 40/32 and 217/20 for PCR-positive and -negative participants, respectively, were used and resulted in corrected sensitivity of 90.9% and specificity of 92.7% and appropriate standard errors.

**Conclusion:** In the case of partial verification bias from simple stratified sampling, naïve estimation of sensitivity and specificity will generally be biased. Standard survey sampling methods are a readily available solution in standard statistical software.

**Validity of Complete Case Analysis Depends on the Target and Analytic Population** Michael Webster-Clark\* Michael Webster-Clark Jess Edwards Rachael Ross

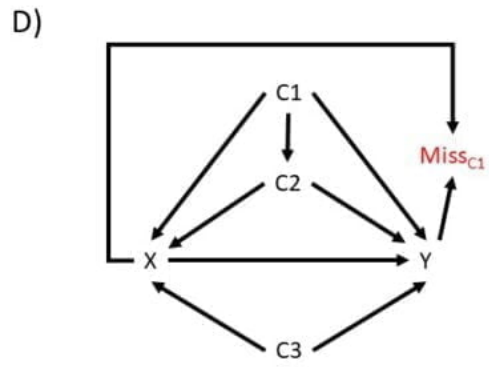
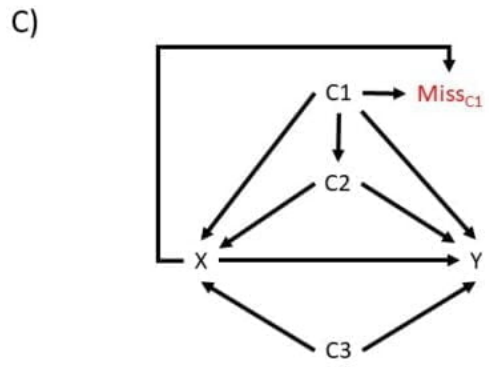
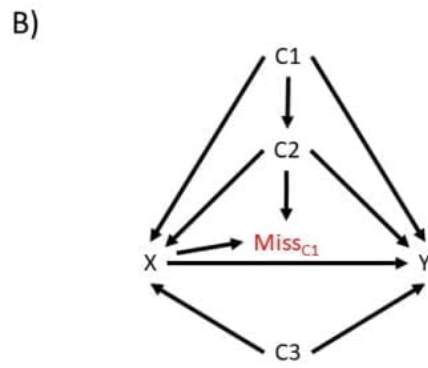
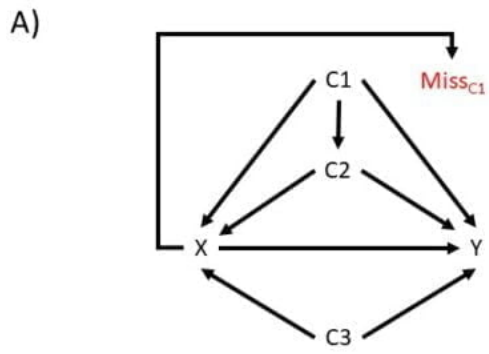
Missing data is a pernicious problem in epidemiologic research. Research on the validity of complete case analysis for missing data has focused on estimating the average treatment effect (ATE) in the whole population. However, other target populations are often of substantive interest (e.g., the average treatment effect in the treated (ATT) or external target populations). In such cases, the validity of complete case analysis may depend on whether missingness is within the target or analytic populations (for the ATT, for example, the untreated are a part of the analytic, but not target, population).

We sought to assess bias in complete case analysis when covariate data is missing in the analytic population but not in the target population.

We simulated 2000 replicates of a 20000-person study of the effect of a binary treatment  $X$  on a binary outcome  $Y$  and 3 confounders  $C1-C3$  that were also modifiers of the risk difference (RD). We induced missingness in  $C1$  only among the untreated under 4 scenarios A) completely randomly (MCAR); B) randomly based on  $C2$  and  $C3$  (MAR); C) randomly based on  $C1$  (MNAR); or D) randomly based on  $Y$  (MAR). **Figure 1** shows DAGs for each scenario. We estimated the ATE and ATT using weighting and averaged results across the replicates. We conducted a parallel simulation transporting trial results to a target population in the presence of missing covariate data in the trial.

The true ATE RD was 0.170 and the true ATT RD was 0.206. In the complete case analysis, ATE estimates were always biased (Scenario A: 0.175, B: 0.164; C: 0.163; D: 0.218). In contrast the estimated ATT was unbiased except when  $Y$  caused missingness (0.256). The parallel simulation generalizing and transporting trial results had similar bias patterns.

In the presence of missing covariate data, complete case analysis is unbiased when missing covariate data are only present outside the target population unless missingness is independently associated with the outcome.





## Assessing the impact of COVID-19 lockdown on air quality in two counties of New York City using interrupted time series analysis Raoul KAMADJEU\* Raoul KAMADJEU

### Assessing the impact of COVID-19 lockdown on air quality in two counties of New York City using interrupted time series analysis

**Raoul KAMADJEU, PhD Student. CUNY/SPH/ Department of Epidemiology and Biostatistics**

**Background:** Nitrogen Dioxide (NO<sub>2</sub>) is one of the pollutants released into the environment, primarily through the burning of fuel from internal combustion engines, power plants. Breathing air with a high concentration of NO<sub>2</sub> can be detrimental to the health of the respiratory system, particularly in children and the elderly. **Research question:** Was COVID-19 lockdown associated with a decrease in greenhouse gas and improvement in ambient air quality in NYC? In this analysis, we assess the impact of COVID-19 lockdown on air quality as measured by NO<sub>2</sub> air maximum daily concentration using publicly available US EPA monitoring data from two counties of NYC (Bronx and Queens).

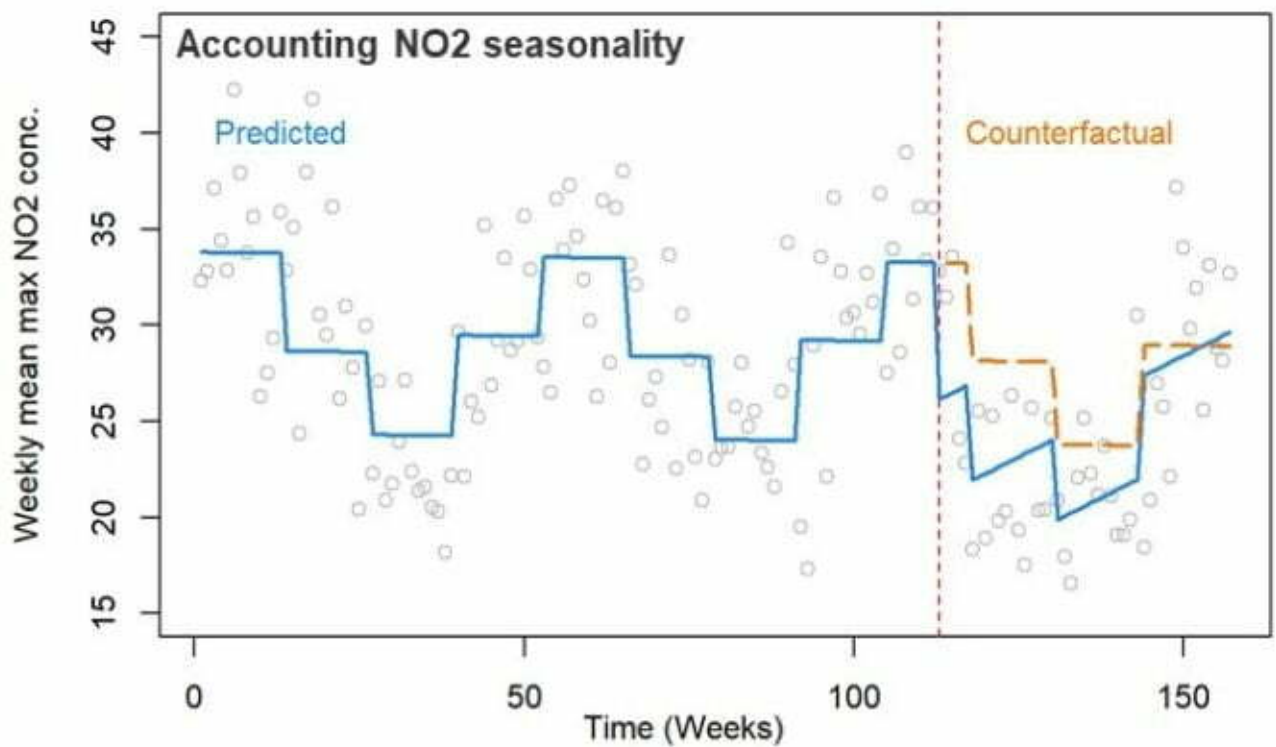
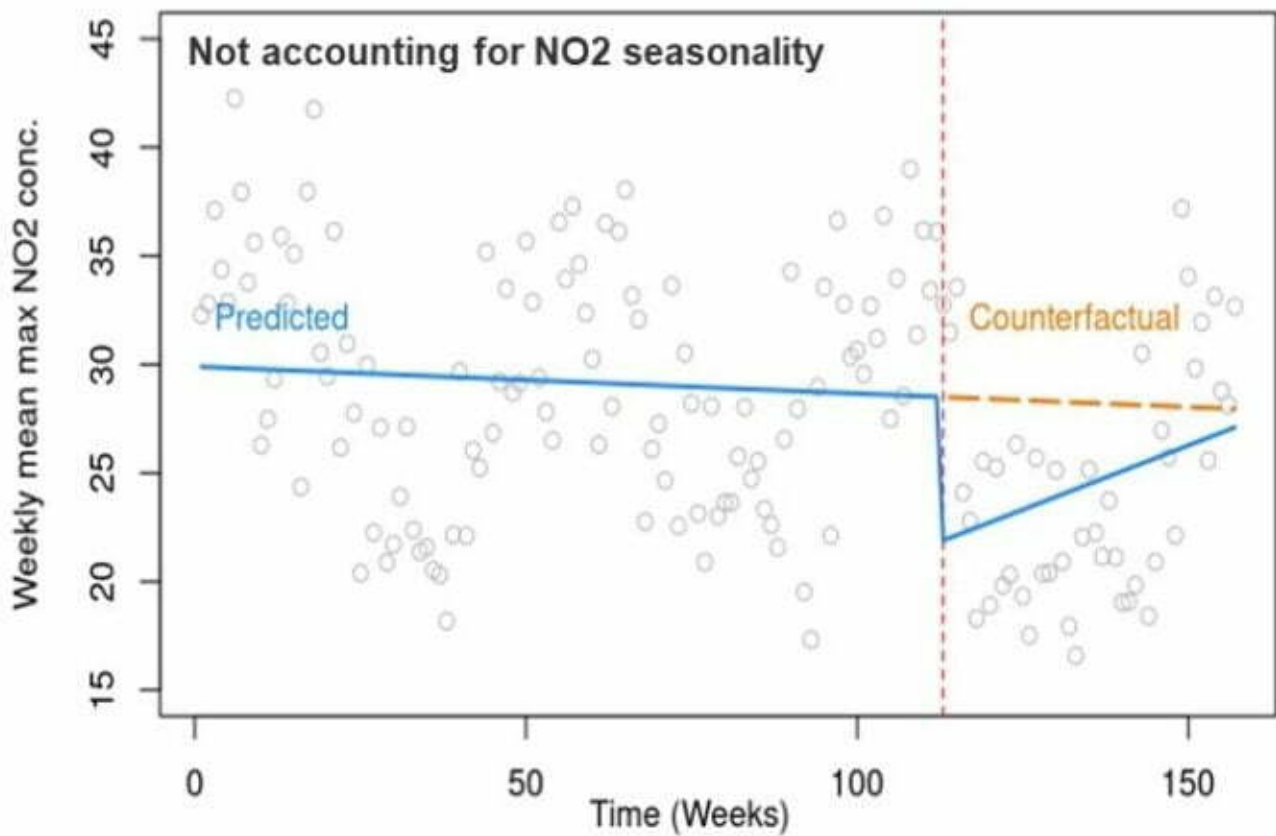
**Methodology:** We downloaded daily data, from 1st January 2018 to 31 Dec 2020, from monitoring sensors located in the two NYC counties of Bronx and Queens. We used interrupted time series (ITS) analysis to assess the impact of COVID-19 lockdown on mean Daily NO<sub>2</sub> concentration. We define the date of intervention as 20 March, corresponding to the date the executive order declaring state-wide stay-at-home, and closure of non-essential businesses went into effect. In summary, our analysis identified two periods: pre-COVID-19 lockdown period: from 1 Jan 2018 to 19 March 2020 and the post COVID-19 lockdown period: from 20 March 2020 to 31 Dec 2020. Our main outcome was the change in maximum daily NO<sub>2</sub> concentration, in part-per-billion (PPB). We modelled NO<sub>2</sub> concentration, accounting for the seasonal release of NO<sub>2</sub>.

We summarize our data into weekly lags, for each week the mean NO<sub>2</sub> max daily concentration was calculated. **Time variable (TIME):** as the count of weeks, from the beginning to the end of the entire series. The entire series spanned over a total of 157 weeks. **Treatment/intervention variable (TX):** dichotomous variable, with value 0 for pre-COVID-19 lockdown (Before Week 8 of March 2020) and 1 for post COVID-19 lockdown (after Week 8 of March 2020). **Time since intervention variable (TIME\_SINCE):** a variable identifying the time (in weeks) since the intervention: 0: for all pre-lockdown period; and incremental weeks from 1, after lockdown. We accounted for the seasonality in NO<sub>2</sub> concentration over time using a dummy seasonal variable.

**Results:** Our analysis demonstrated that, the COVID-19 lockdown and stay-at-home orders were followed by a drastic decrease in NO<sub>2</sub> mean weekly concentration (Beta = -7.264914, p < 0.0000, Beta = -7.264914, p < 0.0000). The decrease was, however, short-lived since the trend in NO<sub>2</sub> concentration accelerated rapidly, on average by 0.177 PPB per week post lockdown (Beta = 0.177, p < 0.001) towards their pre-COVID levels. The changes in NO<sub>2</sub> remained within the set national ambient air quality standards of nitrogen oxides set by the EPA.

**Conclusion:** Our analysis corroborates findings in other locations demonstrating the improvement in air quality associated with COVID-19 lockdowns. This analysis is a practical use-case of modeling time series data using ITS analysis, with review trends, seasonality, and autocorrelation.

# Modelling Nitrogen Dioxide in 2 counties of NY City



**Weighting approaches for external validity: a clarification** Daniel Westreich\* Daniel Westreich

Existing literature proposes a taxonomy of external validity, separating *generalizability* and *transportability*. In previous work we described a method for calculating inverse odds of sampling weights (IOSW; Westreich et al. 2017) for transportability; here, we clarify a subtle point on this method compared with inverse probability of sampling weights (IPSW; Cole & Stuart, 2010): namely, that an odds-weights approach is usually necessary for transportability, but is sometimes necessary for a generalizability approach as well.

One way to consider the issue of when to use inverse probability vs. inverse odds weighting is in terms of the relationship between the data for the study sample and for the target population, and in particular whether a study initially involves two *separate* datasets for study and population, or instead involves a *single* dataset with a variable indicating “in the study.”

Most transportability scenarios will involve two separate datasets at the outset: one for the study and one for the target population. The method proceeds by concatenating the two into a single dataset. In such a situation we estimate and use IOSW to map the individuals originating in the study sample to those in the target population.

Generalizability scenarios can involve a single dataset from the outset: a target population with the members of the study sample marked with an indicator variable, allowing the use of IPSW to weight the study sample back to the whole population. But generalizability may also rely on two separate datasets: for example, the study sample, and an enumeration of the target population that *lacks* an indicator for those who were in the study. In such a latter case, we proceed as with transportability, by concatenating the two datasets and using IOSW.

The question of IPSW vs. IOSW is one more influenced by how the data are structured, rather than the more-causal taxonomy of generalizability vs. transportability.



**Automated, reproducible generation of results tables: bridging the rift between epidemiologists and their data** Konrad H.\* Konrad H. Stopsack

Tables are the key format in which epidemiologists present their results. Many results tables in applied studies merely show point estimates and confidence intervals, or even  $p$ -values, from regression models: a “growing rift between epidemiologists and their data” (Rothman). “Actual,” descriptive data, such as counts stratified by exposure and a main confounder or effect modifier, are often lacking. Most analysis results stem from statistical software packages that, in principle, allow for reproducible reporting. However, most result tables are presumably being created by reading off results from the printout of statistical software and manually entering them into a word processor, a laborious and inevitably error-prone process. Some existing R packages for table generation return all parameters from a regression model (the “table 2 fallacy”). This presentation introduces a new R package, *rifftable*, that creates presentation-ready results tables for epidemiologists in an automated, reproducible fashion. The user provides the final analytical dataset and specifies the design of the table, with rows and/or columns defined by exposure(s), effect modifier(s), and estimands as desired, allowing to show descriptors and inferential estimates in one table. Built-in functions handle binary, continuous, and survival outcomes as well as stratified and joint models. Descriptors such as prevalence, risk based on binary or survival outcomes, various counts, sums, averages, and quantiles are built in, as are point estimates and confidence intervals from regression-based estimators, including linear, Poisson, Cox, and quantile regression models, regression-based estimates of risk ratios, risk differences, and mean ratios, and others. Estimates are rounded to the desired level of precision. In addition, any other estimators can be used by supplying custom functions. Presentation-ready results tables from *rifftable* help bridge the rift between epidemiologists and their data, one table at a time.

```

library(rifftable)

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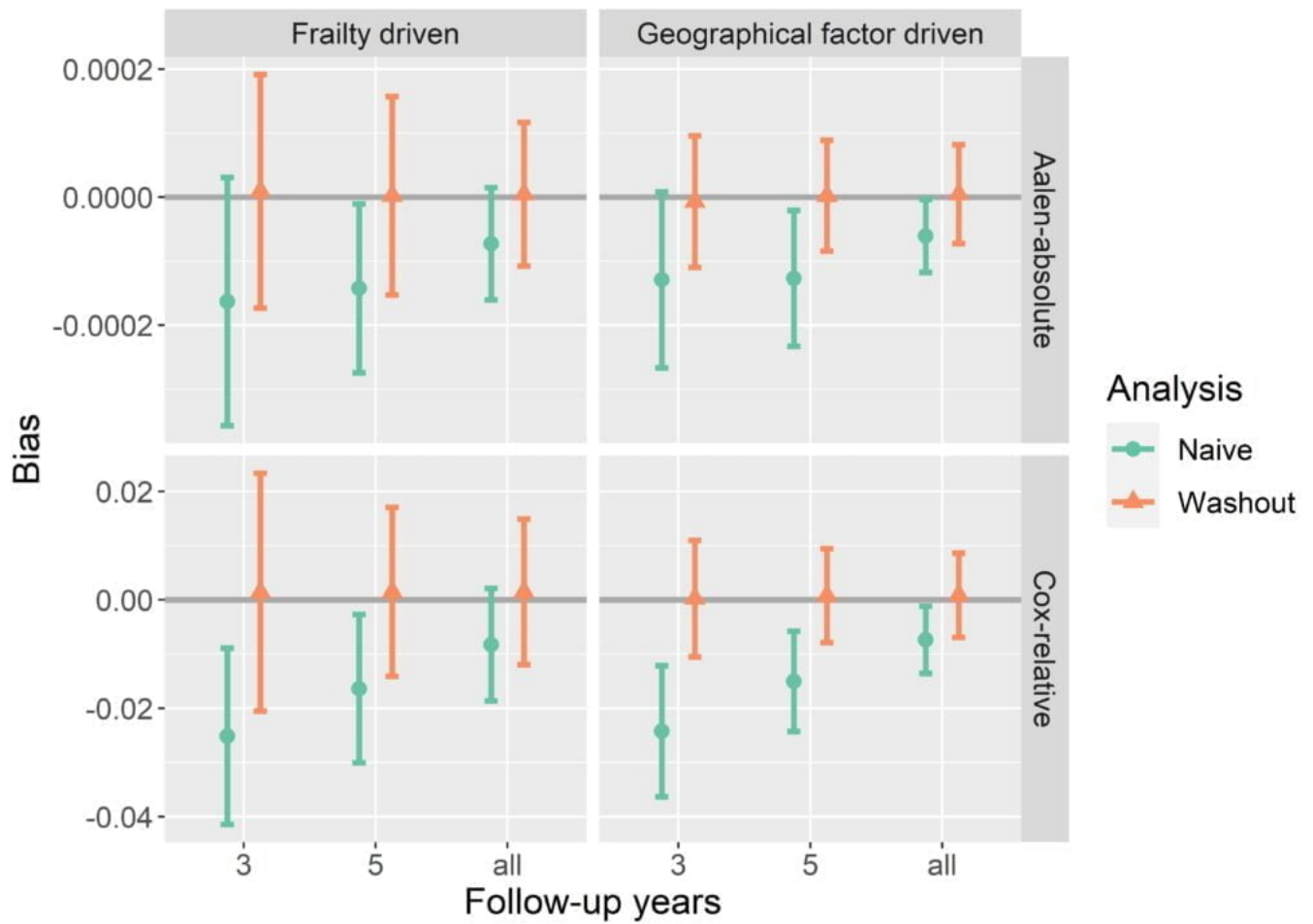
```

Stage	Stage I	Stage II	Stage III
Overall			
- Deaths/N	7/67	26/96	21/29
- Risk	0.10	0.27	0.72
- Risk ratio (95% CI)	1 (reference)	2.59 (1.20-5.62)	6.93 (3.32-14.47)
- Risk difference (95% CI)	0 (reference)	0.17 (0.05 to 0.28)	0.62 (0.44 to 0.80)
Low hormone receptor			
- Deaths/N (Risk)	2/12 (0.17)	9/22 (0.41)	12/14 (0.86)
- Risk difference (95% CI)	0 (reference)	0.24 (-0.05 to 0.54)	0.69 (0.41 to 0.97)
High hormone receptor			
- Deaths/N (Risk)	5/55 (0.09)	17/74 (0.23)	9/15 (0.60)
- Risk difference (95% CI)	0 (reference)	0.14 (0.02 to 0.26)	0.51 (0.25 to 0.77)

**Differential participation, a potential cause of spurious associations in observational cohort studies in environmental epidemiology** Chen Chen\* Chen Chen Hong Chen Jay Kaufman Tarik Benmarhnia

An important discrepancy between the target population and the study population may occur due to differential participation in cohorts studying the etiologic effects of long-term environmental exposures, potentially leading to biased or even reversed estimates. While differential participation bias has been discussed previously, literature on differential participation in observational cohorts of environmental epidemiology is limited. In this paper, we describe the potential for differential participation in cohorts studying environmental health. Such cohorts are prone to differential participation because only those who survived until the start of follow-up and were healthy enough before enrollment could participate, and many environmental exposures are prevalent in the target population and connected to participation via geographical factors or frailty. The relatively modest effect sizes of environmental exposures also make reversed associations more likely. We use causal graphs to propose two example mechanisms through which differential participation can occur in studies of long-term environmental exposures. To illustrate the magnitude of resulting bias, we use a real-life example, the Canadian Community Health Survey cohort. We show that the bias due to differential participation is not negligible. In addition, we show that implementing a simple washout period may reduce the bias and recover more valid results if the effect of interest is constant over time. Furthermore, we model this bias by implementing simulation scenarios to confirm the plausibility of the two mechanisms and the utility of the washout method. Since the impact of differential participation can be difficult to diagnose with traditional analytical approaches for time-to-event outcomes such as the Cox proportional hazard model, we encourage researchers to systematically investigate the presence of time-varying effect estimates and potential spurious patterns (especially in initial periods in the setting of differential participation) by using methods that can produce time-varying effect estimates so that simple corrections like washout techniques can be implemented to recover less biased effect estimates.

# Simulation



**Hypothetical limits on workplace exposure for reducing non-Hodgkin lymphoma incidence: An illustrative application of the hazard-extended iterative conditional expectation parametric g-formula** Kevin T. Chen\* Kevin Chen Ellen A. Eisen Sally Picciotto

**Background:** Non-Hodgkin lymphoma (NHL) incidence has increased significantly since 1960 and was recently linked to workplace exposure to soluble metalworking fluids (MWF) in a standard survival analysis of the United Auto Workers-General Motors (UAW-GM) cohort. Here, we investigate the causal effects of hypothetical limits on soluble MWF exposure in relation to NHL risk using an iterative conditional expectation (ICE) parametric g-formula estimator. Despite their advantages, ICE g-formula estimators are applied far less often in epidemiology than their non-ICE counterparts.

**Methods:** We estimated counterfactual risk of NHL between 1985 and 2004 in the UAW-GM cohort of autoworkers at three Michigan plants ( $n = 34,734$ ) under hypothetical limits on average annual exposure to soluble MWF. We applied the hazard-extended ICE parametric g-formula, which like the canonical non-ICE parametric g-formula, adjusts for time-varying confounding affected by past exposure. Unlike the canonical parametric g-formula, ICE g-formula estimators do not require modeling the joint distribution of confounders, treatments, and outcomes over time.

**Results:** During follow-up, 231 NHL cases occurred. Stronger hypothetical limits on soluble MWF exposure resulted in monotonic reductions in NHL risk estimates. Capping average annual exposure at  $0.5 \text{ mg/m}^3$ , the NIOSH recommended exposure limit, would have prevented 44 (95% CI: 92, -6) cases. Capping at  $0.25 \text{ mg/m}^3$  would have prevented 52 (95% CI: 107, -4) cases. Finally, capping at  $0.05 \text{ mg/m}^3$  would have prevented 71 (95% CI: 128, 10) cases.

**Conclusion:** Stronger limits on soluble MWF exposure would have prevented more cases of NHL in the UAW-GM cohort. Our application demonstrates the utility of an ICE g-formula estimator for estimating the effect of realistic stochastic exposure interventions on a survival outcome. Greater availability of worked examples and software would facilitate wider application of ICE g-formula estimators.

**The Impact of Differential Exposure Misclassification in a Study of Maternal Genitourinary Infections and the Risk of Gastroschisis** Rashida S. Smith-Webb\* Rashida S. Smith-Webb Martha M. Werler Mahsa M. Yazdy Matthew P. Fox

**Background:** Maternal genitourinary infections (GUIs) have been shown to increase the risk for gastroschisis, a severe abdominal wall defect. However, retrospective assessment of GUIs might be prone to reporting inaccuracies potentially resulting in recall bias. We conducted quantitative bias analyses to quantify the direction and magnitude of the potential impact of differential exposure misclassification in a study of maternal GUIs and the risk of gastroschisis.

**Methods:** Using data from two external validation studies which compared self-reported GUIs to medical records and serology tests, we parameterized sensitivity as 50% among controls, and based on expert judgement, specificity as 96% among controls. Assuming that cases more accurately recalled their exposures than controls, we modeled the difference in sensitivity for cases as 10% and 15% greater than controls whereas specificity was 2% greater than controls. We conducted summary-level probabilistic bias analyses (PBA), using 1,000,000 Monte Carlo simulations and used a beta distribution to model probability density functions for the selected bias parameters. To account for greater uncertainty in the chosen values, we divided the bias parameters by 1.2 to widen the distribution.

**Results:** The conventional OR for maternal report of any GUI in the first trimester compared to no GUI on the risk of gastroschisis was 1.80 (95% CI: 1.30, 2.40) adjusted for maternal age. After adjusting for differential misclassification of GUIs, assuming a 10% and 15% difference in sensitivity and 2% difference in specificity, the OR was 1.95 (95% Simulation Interval [SI]: 1.27, 3.04) and 1.67 (95% SI: 1.10, 2.55), respectively.

**Conclusion:** Our findings suggest that adjusting for differential exposure misclassification does not lead to changes in the interpretation for the impact of GUIs on gastroschisis, assuming specificity is high, and sensitivity is 50% among controls and 60% or 65% among cases.

**Moving Beyond Risk Ratios: An Analysis of Quantitative Measures of Health Disparities** Zoe Jocelyn Haskell-Craig\* Zoe Haskell-Craig

Addressing racial and ethnic disparities in health has become a top priority for public health practitioners. A critical part of this work is the ability to quantify differences in disease prevalence between different racial/ethnic groups and to assess these trends over time and in response to various interventions. Six quantitative measures have been developed for unordered groups, and their use has been demonstrated in case studies focused on chronic diseases. However, to date, few researchers have examined how these measures respond to data patterns commonly found in infectious disease prevalence. In this analysis, I examine racial/ethnic trends in the incidence of 14 infectious diseases from 1995 to 2019, including HIV, tuberculosis, and rocky mountain spotted fever, using data available from the Centers for Disease Control and Prevention (CDC). Moreover, I include simulations alongside real-world datasets as a novel approach to isolate and interpret the effect of different data patterns. I identify the response of each quantitative measure to small (or zero) case numbers, large differences in population size between racial/ethnic groups, high variability in yearly incidence, and absolute versus relative changes in case counts. This research provides a framework for choosing which health disparity measures to report. Based on my findings, researchers should apply caution when using the range ratio or index of disparity when the lowest burden of disease is in a demographically small group. I recommend that as a best practice, researchers should always plot health data by group, include at least one measure that incorporates data from all groups, and include at least one absolute and one relative measure. These case studies also demonstrate the benefit of using a population-weighted health disparity measure.

**The impact of different imputation methods on predictive model performance for premature mortality using census survey data.** Mackenzie Hurst\* Mackenzie Hurst Meghan Lief Lori Laura

**Introduction:** Missing data techniques are commonly used to address bias and calculate accurate standard errors of estimates. However, it is less understood how these techniques effect the predictive accuracy of prediction models for population health outcomes.

**Objective:** We aimed to show the impact of different missing data techniques on the performance measures of a prediction model for premature mortality.

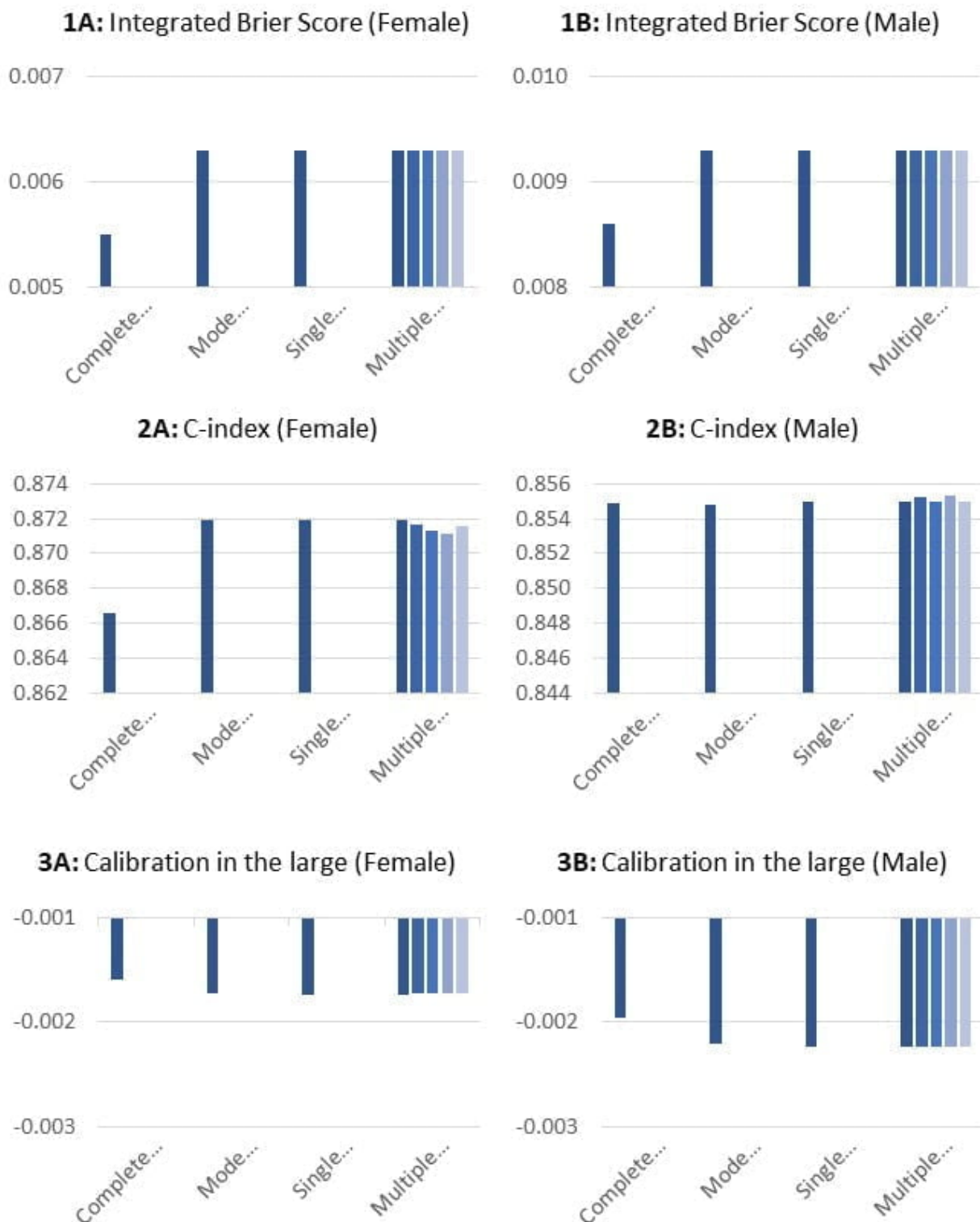
**Methods:** Sex-specific Weibull survival models were developed to predict the 5-year incidence of premature mortality in the Canadian adult population by linking the Canadian Community Health Survey (CCHS) to the Canadian Vital Statistics Database from 2000-2017. These models were run four times using complete case, mode imputation, single imputation and multiple imputation to compare performance measures across each imputation method. These measures include: Nagelkerke R<sup>2</sup>, integrated brier score, c-index, discrimination slope, calibration in the large, and calibration slope.

**Results:** The missing rate in the predictors ranged from 0.03%-10.86%. Figure 1 shows three performance measures for each imputation method. The integrated brier score for the female model was 0.0055 for complete case, and 0.0063 for mode and multiple imputation (1A), with similar results for the male model with 0.0086 and 0.0093, respectively (1B). The female model gave a c-index of 0.8666, 0.8719 and 0.8711-0.8719 for complete, mode and multiple imputation, respectively (2A), with the male model giving 0.8549, 0.8548 and 0.8550-0.8553 (2B). Finally, calibration in the large for complete, mode and multiple imputation was -0.00159, -0.00173 and -0.00174 - -0.00172 for the female model and -0.00196, -0.00221 and -0.00224 - -0.00223 for the male model.

**Conclusion:** Given the level of missingness in this data, mode imputation provides similar performance measures to that of multiple imputation. This simpler imputation approach can be used in similar contexts without biasing the predictive accuracy.



**Figure 1.** Integrated brier score, c-index, and calibration in the large values for each imputation method, separated for each sex-specific Weibull model.



**Epidemiological considerations for the spatial analysis of hyperlocal community**

**interventions: The case of New York City overdose prevention centers** Victoria Jent\* Victoria Jent Bennett Allen Brent Gibson Brandi Moore William C. Goedel Khadija Israel Alexandra B. Collins Brandon D. L. Marshall Magdalena Cerdá

In 2021, New York City (NYC) allowed the opening of the nation's first-ever city-sanctioned overdose prevention centers (OPCs). Peer-reviewed studies from other countries suggest an association between OPCs and improved neighborhood-level outcomes, including overdose fatalities, public drug use and syringe litter, and the risk of bacterial and viral infections. However, the impact of sanctioned OPCs on public health in the United States is not unclear.

Identifying and defining meaningful neighborhood catchment areas is important to accurately assess the magnitude of the intervention's impact. Prior studies in other countries used 500m buffers surrounding OPCs to define catchment areas. However, boundaries based on spatial distance, such as 500m buffers, or those based on administrative definitions, such as census tracts, do not necessarily reflect the spatial boundaries of the population served by hyperlocal interventions. How researchers define these areas affects modelling outcomes and the ability to assess if changes occurred because of an intervention or simply by chance.

We use three guiding questions to define the spatial scope of study catchment areas in our study: (1) who provides the intervention services and who uses these services?; (2) does the outcome cluster spatially within the community and if so what are the clustering boundaries?; and (3) is there local expert knowledge that can guide the definition of a catchment area? Herein, we illustrate how researchers can partner with local service providers to define and map the community catchment area for the intervention and comparison sites. We further assess the extent to which intervention effects on outcomes of interest vary by catchment area definition approaches. Our study insights will inform OPC evaluations, but also provide broader insights into the application of geospatial methods in other types of hyperlocal intervention evaluations.

**Estimating post-treatment tuberculosis recurrence after multidrug-resistant tuberculosis treatment among patients with and without HIV: the impact of assumptions about death and loss to follow-up** Sara Sauer\* Sara Sauer Carole Mitnick Molly Franke

**Background:** Evaluation of regimens for multidrug-/rifampicin-resistant tuberculosis (MDR/RR-TB) requires quantification of tuberculosis recurrence risk following successful treatment. Analyses of recurrence require assumptions about patients who die or become lost during post-treatment follow-up.

**Methods:** We analyzed 1,855 patients enrolled in the endTB observational study who successfully completed a longer MDR/RR-TB regimen containing bedaquiline (BDQ) and/or delamanid (DLM) between 2015 and 2018 in 11 countries. We estimated the six-month risk of post-treatment TB recurrence overall and by HIV status using logistic regression models, under three different assumptions about post-treatment deaths: i) deaths were not due to recurrent TB and patients who died would not have developed recurrent TB had they lived (i.e., deaths were counted as non-cases), ii) the risk of recurrence among people who died was similar to those who did not die (i.e., deaths were censored) and iii) deaths were due to recurrent TB (i.e., deaths were included as a composite outcome of recurrent TB or death). We used inverse-probability-weighting to account for potential selection bias due to post-treatment loss-to-follow-up (LTFU).

**Results:** Twelve individuals experienced recurrent TB, 14 died, and 619 were LTFU post treatment. Recurrence occurred among an estimated 9.9 per 1000 individuals (95%CI: 5.5,17.7) when deaths were treated as non-cases and 10.1 per 1000 (95%CI: 5.6,18.0) when deaths were censored. The estimated frequency of recurrence or death was 20.8 per 1000 (95%CI: 14.0, 30.7). Corresponding risk ratios comparing patients with and without HIV were 1.12 (95%CI: 0.2, 6.12); 1.10 (95%CI: 0.20, 6.08); and 0.91 (95%CI: 0.26, 3.15). Ignoring potential selection bias due to LTFU had a small but apparent impact on estimates.

**Conclusion:** The six-month frequencies of recurrent TB were low, substantiating the effectiveness of longer MDR-TB regimens containing BDQ and/or DLM. We found no significant difference in the risk of recurrence by HIV status; however, a larger sample is needed to yield more conclusive findings. Valid estimation of post-treatment recurrence will be enhanced by explicit assumptions about post-treatment deaths and methods that appropriately account for potential bias due to post-treatment LTFU.

**Might underestimating smoking: misclassification, effects, and residual confounding be prolonging the tobacco and “it seems like everything causes cancer” epidemics? Quantifying aggregate covert, forgotten, passive, irregular, ... smoking effects ignored by standard cohort study queries about ever smoking** Bruce Leistikow\* Bruce Leistikow

**Background.** Tobacco smoke exposure (smoking) is pervasive, deadly, and routinely misclassified in RR for ever regular (or similar) versus “never” smoking that includes forgotten, covert, passive,... smoking. That underestimates smoking RR and confounding. And that prolongs the tobacco, cancer, ... epidemics. So I estimated the lung cancer (CaL) RR of smoke-free nations per Global Burden Of Disease Study (GBD) estimates versus the truly unexposed.

**Methods.** CaL United States (US) year 2000 age standardized mortality rates (ASMRs) per 100,000 came from published rates. Given consensus that smoking epidemics ~drove CaL epidemics, I followed, then extrapolated, the CaL ASMR trends back to estimate the average 1900 ~pre-smoking ASMR and its sensitivity range (SR) across Americans and English males. I then compared those ASMRs to health focused groups’ and GBD “smoke-free” recent CaL ASMRs.

**Results.** The CaL ASMR rises for Englishmen 1910-1945 and the US 1930-1945 fit exponential curves (R-squareds 0.95-0.99) and back extrapolate to a mean ASMR of 0.6 in 1900 with a conservative SR of 0.1 to 4 (~the ASMRs of English males in 1920, US females in 1940...). Those ASMRs are quite compatible with the published CaL ASMRs of 5-10 across both recent cohort “never” smokers and healthy US areas with 5-10% current and ~30% “ever” adult cigarette smoking. In contrast, the GBD shows smoke free CaL ASMRs averaging 12.9 for the gender-nations cited above. It appears that the GBD overlooked 95% (SR 69-99%) of the relative and 34% (SR 24-35%) of the absolute 2019 CaL ASMR risks of smoking in those gender-nations.

**Conclusions.** GBD and like cohort studies likely greatly underestimate their smoking: mismeasurement, effects, and confounding. That feeds spurious associations, “everything causes cancer” appearances, confusion, smoking, and industry profits. By disclosing their “never” smoker CaL age-specific and ASMRs, cohort studies may aid both estimation of smoking mismeasurement and humanity.

**Extending Mean Risk Stratification - Rejection Criteria and Simulated Power Calculation for Multilevel Clinical Tests** Brian Befano\* Brian Befano Mark Schiffman Stephen Schwartz Didem Egemen

**Introduction:**

Comparing the effectiveness of two clinical tests should go beyond standard measures of test performance such as positive predictive value (PPV) or area under the curve (AUC). While a difference in PPV compared to pre-test risk is critical to individual patients and clinicians, test effectiveness at a population level is further dependent on the prevalence of each test stratum. This statistical concept is formalized as Mean Risk Stratification (MRS), calculated as the prevalence-weighted average change in pre-test risk of disease for each test stratum. Prior work developed the statistical methods for binary outcomes, this research extends the approach to test results with more than 2 levels, e.g. HPV genotyping assays, mammograms.

**Methods:**

We conducted a power calculation by simulating 10,000 samples of varying size to compare two tests with different underlying MRS. To generate each sample, a binomial random number generator was used with realistic prevalence for each test stratum, based on existing literature, and each stratum's risk was modified to create MRS differences ranging from 1% to 6%. To compare two tests within the same population, the ratio of the MRS is used and the variance of the log of that ratio is a function of the variance of each tests AUC, the AUC value, and a covariance term accounting for lack of test independence. This variance is asymptotically normal, allowing for a z-score based rejection criteria.

**Conclusions:**

Assessing the effectiveness of new tests requires comparing how much information each test yields at a population level. Formally, this is summarized as the average ability to modify pre-test risk of disease. This research extends MRS from binary tests to a multilevel tests, derives the variance calculation to compare MRS, and provides an example of power calculations that could be used to inform a proposed study.

## Power Calculation – 10,000 iteration simulation

- Proportion of iterations with Mean Risk Stratification (MRS) difference between HPV screenfire alone and HPV Screenfire + AVE is statistically greater than 0%, calculation for 1-sided test at alpha level of 0.05

Sample Size	MRS difference					
	1%	2%	3%	4%	5%	6%
1000	19.02%	23.82%	28.97%	34.60%	40.60%	47.06%
2000	36.99%	45.45%	54.28%	62.85%	71.62%	79.95%
3000	50.17%	61.26%	70.83%	79.73%	87.67%	93.57%
4000	62.64%	74.19%	83.45%	90.69%	95.52%	98.18%
5000	73.19%	83.17%	90.88%	95.38%	98.07%	99.52%
6000	80.53%	88.97%	94.80%	98.09%	99.42%	99.89%
7000	85.98%	93.15%	97.25%	99.20%	99.82%	99.99%
8000	90.49%	95.85%	98.65%	99.62%	99.94%	99.99%
9000	92.75%	97.45%	99.19%	99.83%	99.98%	100.00%
10000	94.81%	98.38%	99.57%	99.91%	99.99%	100.00%

Assumes HPV prevalence (type specific and overall (7.4% among ages 25+) from Demarco typing paper in KPNC

Assumes risk from unpublished Zambia paper (Didem)

Simulation with 10,000 iterations

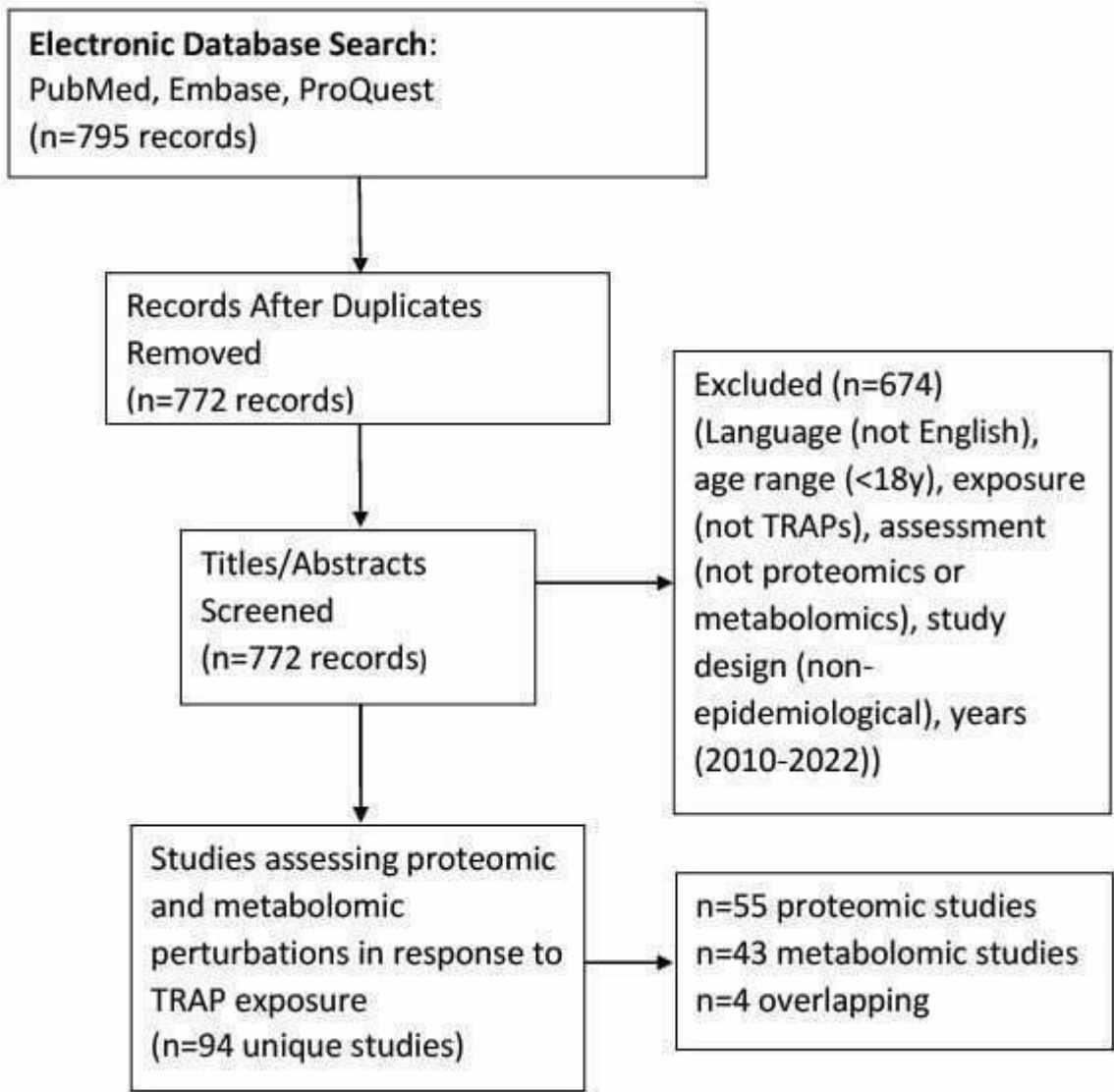
**A systematic review of evidence on multi-omic correlates of traffic-related air pollution and cardiorespiratory outcomes** Cameron Casella\* Laura Corlin Cameron Casella Frances Kiles Catherine Urquhart Kipruto Kirwa

**Background:** Most studies of the biological pathways through which exposure to traffic-related air pollution (TRAP) affect cardiorespiratory health consider only a single type of 'omic' biomarker. We synthesized evidence from across the 'omics' literature to provide comprehensive, multidimensional insights into the biological networks underlying the association.

**Methods:** Systematic review of epidemiological articles from 2010-2022 describing associations among TRAP exposures and proteomic and/or metabolomic profiles in adults, identified using PubMed, Embase, and ProQuest.

**Results:** We identified 55 articles relating TRAP exposure to protein biomarkers (12 with >10 biomarkers within a single study) and 38 relating to metabolite biomarkers (6 included proteomics and metabolomics within a single study), representing 16 countries. Overall, 47% of studies had  $n > 100$ , 21% were randomized crossover studies, and 18% were cohort studies. TRAP exposure was associated with proteomic markers of inflammation, coagulation, endothelial function, immune responses, oxidative stress, and protein degradation. TRAP-associated metabolic pathways involved oxidative stress, inflammation, energy production, endothelial function, immune activation, coagulation, and stress signaling.

**Discussion:** Multi-omic synthesis of evidence on TRAP-related proteomic and metabolomic perturbations enriches our understanding of the pathogenesis of sub-clinical and clinical cardiorespiratory disease, enabling us to diagram the complex underlying pathways. Our review suggests specific biological pathways that should be investigated as part of an integrated multi-omics approach. Multi-omic perspectives can provide a better understanding of the interrelationships among biomolecules associated with disease pathogenesis.





**LATEBREAKER**

Molecular

**Socioeconomic disadvantage is associated with metabolite peaks linked to greater chronic disease risk: the Coronary Artery Risk Development in Young Adults (CARDIA) Study**

Brooke S. Staley\* Brooke Staley Annie Green Howard Autumn G. Hullings Mohanraj Krishnan Allison E. Aiello Katie Meyer Kari E. North Kiarri N. Kershaw Susan C. J. Sumner Cora E. Lewis Penny Gordon-Larsen Christy L. Avery

**Background:** Biological pathways linking socioeconomic disadvantage (SED) to greater chronic disease risk, including cardiometabolic disease (CMD), remain largely unclear. To better identify and characterize these pathways, we performed an untargeted metabolomics study in the population-based CARDIA study (Year 20).

**Methods:** Our exposure was a SED composite score of five indicators: education, income, financial hardship, employment, and wealth. Each indicator was dichotomized as high or low and summed (range 0-5). The score was dichotomized as advantaged (>3, ref.) vs. disadvantaged ( $\leq 3$ ). The outcome variables were untargeted plasma metabolite peaks obtained from ultra-performance liquid chromatography-mass spectrometry. Linear regression models adjusted for self-reported sex and race, age, batch, and field center were used to identify significant associations (false discovery rate < 0.05). Functional analysis (MetaboAnalystR - Mummichog v2) was used to identify pathways with higher metabolic activity than expected by chance.

**Results:** Data on 3,356 participants (aged 37-55; 56% female; 46% Black) were examined; 35% (n=1,165) were characterized as disadvantaged. Of the 7,522 metabolite peaks, nearly 40% (2,999) were significantly associated with SED. For example, disadvantage was associated with lower levels of docosahexaenoate (unsaturated fatty acid biosynthesis) and 25-, 27- and 7 $\alpha$ -Hydroxycholesterols (cholesterol metabolism), and higher levels of deoxycholic acid (bile acid pathways) and glycochenodeoxycholate (cholesterol metabolism). Mummichog analyses yielded bile acid biosynthesis and sialic acid metabolism as enriched pathways (p < 0.05). These pathways provided support for the regression results and have been associated with greater risk of CMD.

**Conclusion:** SED is associated with many metabolic pathways, some of which have been associated with CMD. Metabolic differences may reflect disparities in health behaviors, stress, or environmental exposures.

**Data-Driven Discovery of Optimal Treatment Rules for Intensive Blood Pressure Control and Prevention of Mild Cognitive Impairment and Dementia in the SPRINT-MIND Trial**

Neal Jawadekar\* Neal Jawadekar Katrina Kezios Maya Pandit Kara Rudolph Adina Zeki Al Hazzouri

Evidence that antihypertensive use in older age is protective against dementia is inconsistent, which may be partially explained by differences in participants' characteristics (e.g. age, sex, race/ethnicity, comorbidities). Identifying population subgroups who could most benefit from antihypertensive use may prove useful for dementia prevention efforts. We used data from the Systolic Blood Pressure Intervention Trial (SPRINT-MIND; 2010-2015), a US-based RCT of 9361 adults with hypertension randomized to intensive blood pressure (BP) control (systolic BP (SBP) target <120 mmHg) or standard BP control (SBP target <140 mmHg). We combined mild cognitive impairment (MCI) and probable dementia into a singular outcome and used an honest causal forest (HCF) to identify covariates with the highest Variable Importance Factor (VIF; an indicator of heterogeneous treatment effects between intensive BP control and MCI/dementia). Next, we learned optimal treatment rules using these 20 covariates with k-fold cross validation and the doubly robust policy tree, before estimating the expected reduction in dementia/MCI cases that could result from implementing such rules. A total of 8,541 participants with non-missing outcome data were included in the HCF analysis; among them, average age at baseline was 67, 65% were male, 66% were White, with 7 median years of education. Of 148 covariates in the HCF, we selected the 20 with the highest VIF. 7,854 participants with complete information on this subset of 20 covariates were then included in the policy trees for learning optimal treatment rules. The resulting treatment rules yielded expected absolute risk reductions ranging from -0.16% to -2.03%, averaging to an overall expected risk reduction of -1.09%, or about 85/725 cases prevented under these rules (**Table 1**). In conclusion, we used policy trees to help identify subgroups of the population represented by optimal treatment rules to reduce the burden of MCI/dementia.

**Table 1:** Expected Risk of Dementia/MCI for each policy rule identified by Policy Trees

Fold Number	Policy Rule	Expected Risk in Test	Actual Risk in Test	Risk Reduction
1		8.20%	9.55%	-1.35%
2		8.79%	9.42%	-0.63%
3		8.25%	9.55%	-1.30%
4		9.28%	9.36%	-0.16%
5		9.05%	11.08%	-2.03%
Average (OVERALL)		8.70%	9.79% (725 / 7354)	-1.09%

**Footnote:**

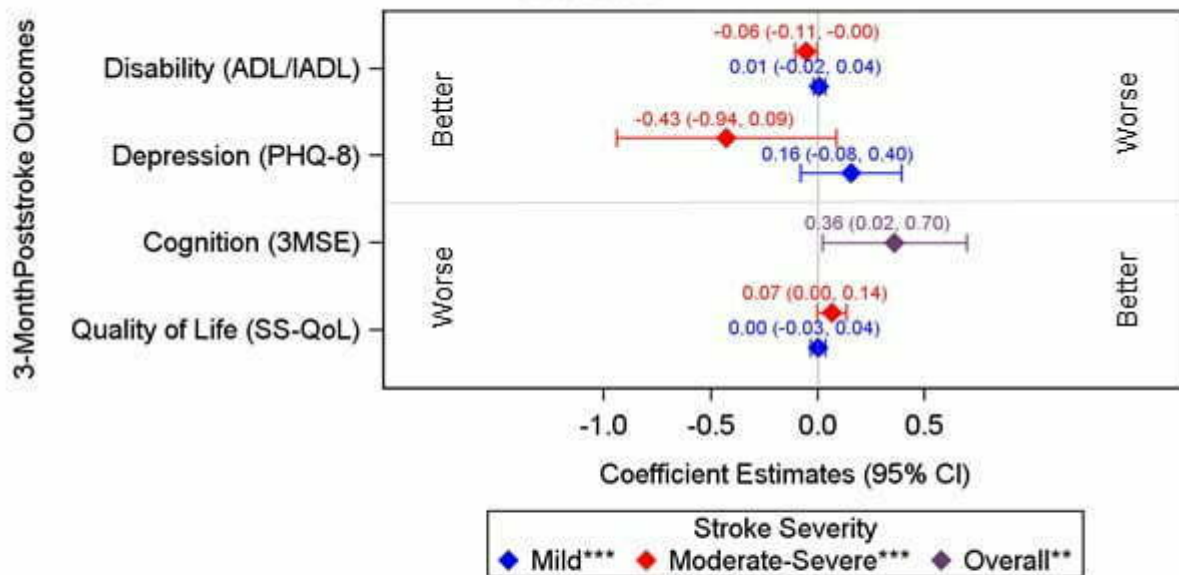
An optimal treatment rule is a decision rule that recommends treatment to individuals based on the values of specific covariates, with the goal of minimizing the mean outcome. Here, "Expected Risk" refers to the risk of dementia/MCI that would be expected if that particular subsample were to be treated based on that particular rule. Meanwhile, "Actual Risk" is the observed percentage of individuals in that subsample who got dementia/MCI during follow-up. Expected risk reduction was estimated using 5-fold cross-validation, using 5 folds (and 5 corresponding policy rules). The average expected risk reduction is simply the result of averaging the estimates across those 5 folds.

Other covariates tested in the policy trees but not depicted here include: Digit Symbol Test (0-135), Derived Montreal Cognitive Assessment (MOCA) Score, Logical Memory II (0-14) score, Participant Age at Randomization, Estimated Glomerular Filtration Rate (eGFR), High Density Lipoprotein (HDL, mg/dL), Standing Diastolic BP, Average of 3 seated systolic blood pressures, Standing diastolic blood pressure at 1 minute, Standing heart rate at 1 min, and Response to: "Have you had problems with your work or other daily activities as a result of any emotional problems? Didn't do work or other activities as carefully as usual"

**Street connectivity and post-stroke outcomes among a population-based cohort** Leanna Delhey\* Leanna Delhey Xu Shi Lewis Morgenstern Devin L Brown Melinda A Smith Erin Case Lynda Lisabeth

**Objective:** Assess associations between street connectivity and outcomes post-stroke. **Methods:** We used data from a population-based cohort in south Texas (Brain Attack Surveillance in Corpus Christi [BASIC] project) and the National Neighborhood Data Archive. We included Non-Hispanic White and Mexican American (MA) persons with first-time stroke (2009-2020). We summarized 9 measures of street connectivity (e.g., median block length, intersection density) by census tract into principal components (PC) that explain most of the information via PC analysis. Outcomes at 3-months included disability (activities of daily living (ADL)/instrumental ADL (IADL)), cognition (Modified Mini-mental State Exam (MSE)), depressive symptoms (Patient Health Questionnaire-8 (PHQ8)), and quality of life (abbreviated Stroke-Specific Quality of Life scale (SSQOL)). Lower score is better for the ADL/IADL (range 1-4) and PHQ8 (range 0-5) and higher is better for the MSE (range 0-100) and SSQOL (range 0-5). We conducted inverse probability weighting, multiple imputation, and fit adjusted linear mixed models. Stroke severity (NIH Stroke Scale,  $\leq 5$ : mild,  $> 5$ : moderate-severe) was assessed as an effect modifier. **Results:** Survivors were 45-95 years old (median=64), primarily male (53.4%) and MA (62.6%). The 1st and 2nd PCs (PC1 and PC2) explained 91% of the information in street connectivity; PC1 primarily reflected measures evaluating street or intersection density and PC2 primarily reflected block length. PC1 was not associated with outcomes. Stroke severity modified the association of PC2 with ADL/IADL, SSQOL, and PHQ8 ( $p=0.037$ ,  $p=0.092$ ,  $p=0.044$  respectively). See figure 1 for these associations and the overall association with MSE. **Conclusions:** Among stroke survivors, greater street connectivity was associated with better cognition. Among moderate-severe stroke survivors, it was associated with less disability and better quality of life. Future research should consider likely mechanisms.

**Figure 1. Association of Principal Component 2\* with 90-Day Poststroke Outcomes**



\*Principal Component 2 is a measure of street connectivity (higher value indicates greater connectivity), this measure primarily reflects block length.

\*\*Adjusted for demographics (age, sex, race/ethnicity), individual socioeconomic status (education, health insurance), pre-stroke health (comorbidities, function, cognition, depression, smoking), interpersonal factors (marital status, social support), neighborhood socioeconomic status (neighborhood disadvantage, neighborhood affluence), and stroke severity.

\*\*\*Results by stroke severity are additionally adjusted for interaction between principal component 2 and stroke severity.

**Prenatal dietary patterns and infant weight trajectories from the 3rd trimester to 2 years of age**

Nan Ji\* Nan Ji Luis E. Maldonado Mark Johnson Sandrah P. Eckel William J. Gauderman Thomas A. Chavez Dema Faham Brendan H. Grubbs Deborah Lerner Rima Habre Shohreh F. Farzan Theresa M. Bastain Carrie V. Breton

**Background/Aims:** Although maternal diet during pregnancy has been associated with fetal and newborn development, few diet studies have evaluated in utero growth measures and postnatal weight trajectories along a continuum. This study aims to (1) assess associations between prenatal dietary patterns and weight trajectories from the 3rd trimester through 2 years of age; and (2) determine whether these associations vary by gestational complications (diabetic and/or hypertensive disorders).

**Methods:** Fetal weights during the 3rd trimester were abstracted from maternal ultrasound records for the women participating in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES)—a pregnancy cohort of predominantly low-income Hispanic/Latina women in Los Angeles. Infant weight measures were abstracted from medical records. Two maternal dietary patterns previously identified in MADRES participants were examined in relation to weight trajectories using piecewise linear spline models (N=398). The first dietary pattern included a higher intake of vegetables, oils, and fruits (VOF). The second dietary pattern included a higher intake of solid fats, refined grains, and cheese (SRC).

**Results:** In the whole population and those without gestational complications, both VOF and SRC were associated with decreased growth from the 3<sup>rd</sup> trimester to age 3 months. For women with gestational complications, comparing to the lowest quartiles, the growth rate from the 3<sup>rd</sup> trimester to age 3 months was significantly decreased in children of mothers in the 4<sup>th</sup> quartile of VOF pattern scores, but significantly increased in children of mothers in the 3<sup>rd</sup> quartile of SRC pattern, with relative changes in growth of 0.66% [95%CI 0.48%, 0.92%] and 1.50% [95%CI 1.07%, 2.10%], respectively.

**Conclusion:** Both dietary patterns during pregnancy could impact infant weight gain trajectories, with a stronger impact on early infancy. These associations vary by gestational complications.

**Girls', but not boys', iron intake and iron status at childhood were associated with the risk of anxiety disorder at late adolescence and young adulthood** Hsin-Jen Chen\* Hsin-Jen Chen Jung Chu

**Objectives:** Brain development involves iron. Iron intake and iron status at childhood may affect children's future mental health at adulthood. This study examined the association between iron status and iron intake with the risk of anxiety disorder diagnosis.

**Methods:** Nutritional data of a national representative sample of schoolchildren (6-12 year-old, n=2028) in the Nutrition and Health Survey in Taiwan in 2000-2001 were used. Iron intake was assessed using a 1-day dietary recall assisted by caregiver. Iron status, plasma ferritin level, was collected in a physical exam. Child's data collected in the survey were individually linked to medical claims in the National Health Insurance Database between 2007 and 2018. Children were treated as at risk since the 15<sup>th</sup> birthday in life. Sex-stratified Cox proportional hazard models were applied to examine the association between the nutritional status and incidence of anxiety disorders diagnosis. Incidence of anxiety disorder diagnosis was defined as the date when a child had a medical claim that contained ICD-9-CM or ICD-10 code for anxiety disorder.

**Results:** There were 194 cases of incident anxiety disorder diagnosis during 10 years of follow-up on average. Compared to girls of lower ferritin tertile group, girls of middle and upper tertile groups had lower risk of anxiety disorder: HR = 0.62 (CI: 0.43-0.88) and 0.38 (CI: 0.18-0.81), respectively, after adjusting for demographics, socioeconomic status, total energy intake and body mass index at childhood. On the contrary, girls' iron intake was associated with higher risk of anxiety disorder: HR = 1.86 (CI: 0.77-4.50) comparing middle to low tertile and HR = 2.17 (CI: 1.19-3.97) comparing high to low tertile. These findings were not statistically significant in boys.

**Conclusion:** Although iron status, i.e. ferritin level, is a protective factor for anxiety disorder, iron intake was associated with a higher risk of anxiety disorder. This phenomenon was only observed in girls.

**Red meat consumption and the risk of cardiovascular diseases and diabetes: A systematic review and meta-analysis of observational studies and randomized controlled trials** Jie V Zhao\* Jie V Zhao Wenming Shi Xin Huang C Mary Schooling

**Background:** Observational studies show inconsistent associations of red meat consumption with cardiovascular disease (CVD) and diabetes. Red meat consumption also varies by sex, whether associations vary by sex remains unclear.

**Methods and Results:** We conducted a systematic review and meta-analysis to summarize the evidence concerning the associations of unprocessed and processed red meat consumption with CVD and its subtypes (coronary heart disease (CHD), stroke, heart failure), type 2 diabetes (T2DM), and gestational diabetes mellitus (GDM), and to assess differences by sex and region. Two researchers independently searched PubMed, Web of Science, Embase, and the Cochrane Library for observational studies and randomized controlled trials (RCTs) published before July 2022. A total of 43 observational studies (N=4,462,810, 2,752,274, 61.7% women) for CVD and 27 observational studies (N=1,760,774, 1,133,843, 64.4% women) for diabetes were included. Red meat consumption was positively associated with risk of CVD [hazard ratio (HR) 1.11, 95% confidence interval (CI) 1.05 to 1.16 for unprocessed red meat (per 100g/d increment); HR 1.26, 95% CI 1.18 to 1.35) for processed red meat (per 50g/d increment)], CHD, stroke and heart failure. Unprocessed red meat was associated with higher risk of CVD in men (HR 1.28, 95% CI 1.10 to 1.49) but not women (HR 1.06, 95% CI 0.92 to 1.23), although the difference was not significant. The associations with CVD and T2DM were larger in western countries. Both unprocessed and processed red meat consumption were related to higher risk of T2DM, and unprocessed red meat consumption to risk of GDM.

**Conclusions:** Our study suggests that unprocessed and processed red meat consumption are both associated with higher risk of CVD and diabetes, with a difference by region but not by sex. These findings highlight the need for a better understanding of the mechanisms to facilitate improving cardiometabolic health.



**Sugar intake and type 2 diabetes risk: A prospective study and a meta-analysis** Rieko

Kanehara\* Rieko Kanehara Mayo Hirabayashi Atsushi Goto Manami Inoue Norie Sawada

**Background:** Evidence on the association between sugar (mono- and disaccharides) intake and type 2 diabetes (T2D) risk in Asian populations is currently insufficient. We aimed to investigate the association between sugar intake and T2D risk in middle-aged Japanese adults.

**Methods:** Participants comprised 27,797 men and 36,880 women aged 45-75 y with no history of diabetes and critical illness before the survey in 1995-1999 in the Japan Public Health Center-based Prospective Study. We calculated the intake (% energy/d) of sugar (total sugar, total fructose, and each sugar subtype) using a validated 147-item food frequency questionnaire. T2D onset during the five-year follow-up period was defined by self-report, the validity of which was confirmed. ORs and their 95% CIs, adjusted for potential confounders were estimated using multi-valuable logistic regression with categorical and cubic spline models. The lowest quartile and its median intake were used as reference. Furthermore, we searched the literature for previous studies and carried out a meta-analysis on an association between total sugar intake and T2D risk.

**Results:** During the follow-up, 690 men and 500 women were identified as new T2D cases. In women, the quartiles of total sugar or total fructose intakes were not significantly associated with T2D risk; however, the spline curves showed an increased T2D risk at extremely high intake levels (ORs [95% CI]: 1.88 [1.07-3.31] at 30% energy/d for total sugar and 1.87 [1.10-3.16] at 14% energy/d for total fructose). In men, sugar intakes were not associated with T2D risk. The meta-analysis including these results suggested an inverse association between total sugar intake and T2D risk.

**Conclusions:** The intakes of total sugar and total fructose at standard level were not associated with an increased T2D risk among Japanese adults and in the meta-analysis. However, for extremely high intake, a possible increased risk cannot be excluded among Japanese women.

**LATEBREAKER**

Nutrition/Obesity

**Impact of dietary inflammatory index on mortality in Korean adults: a population-based prospective cohort study** Dahyun Park\* Dahyun Park Garam Jo Min-Jeong Shin**Objectives**

The Dietary Inflammation Index (DII) has been found to be associated with morbidity and mortality. However, the association between DII and mortality was not investigated in Koreans. Therefore, the purpose of this study was to explore whether DII affects mortality risk among Korean adults using a population-based prospective cohort study.

**Methods**

This analysis included 33,627 subjects aged 19-79 who participated in the Korean Health and Nutrition Examination Survey 2007-2015. Subjects who were cancer or cardiovascular disease (CVD) patients or pregnant women at baseline were excluded. These subjects were followed up for mortality through December 31, 2019 (mean follow-up: 5.5 years). The DII score was calculated based on baseline dietary intake using 24-hours dietary recall. Risk of mortality was assessed using a Cox proportional hazard model after adjusting for age, sex, income, smoking status, obesity, and diabetes status.

**Results**

In Korean healthy adults, DII score was significantly associated with increased risk of all-cause mortality (Hazard ratio (HR) 3<sup>rd</sup> tertile vs 1<sup>st</sup> tertile: 1.41; 95% confidence interval (CI) 1.09-1.84; p-value = 0.010). This association was also significant for both men (HR: 1.74; 95% CI: 1.20-2.51; p-value = 0.003) and women (HR: 1.65; 95% CI: 1.01-2.71; p-value = 0.046). For CVD death, DII score was associated with higher risk, but not significant (HR: 1.21; 95% CI: 0.74-1.96; p-value: 0.453). On the other hand, total and men with the highest tertile of DII score had higher risk of cancer mortality, but not women.

**Conclusions**

The results indicate that inflammatory diet appears to significant increase risk of all-cause and cancer mortality in Korean adults. Our results support the hypothesis that a pro-inflammatory diet is associated with mortality risk, but also suggests a slightly different association by cause of death in Koreans.

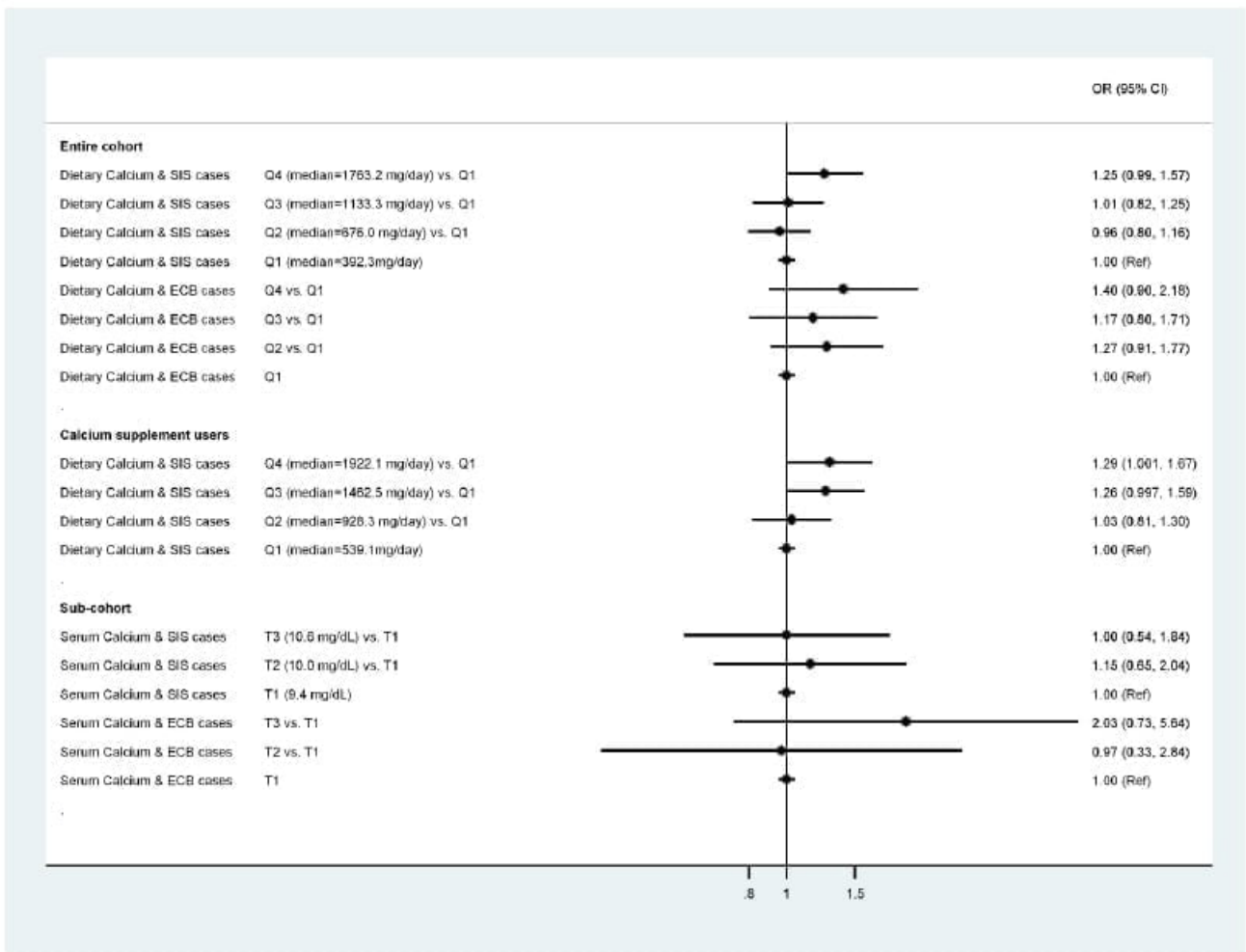
**Serum and dietary calcium in relation to the risk of cognitive impairment: the REGARDS study** Liping Lu\* Liping Lu Yijia Zhang Meghan Angley Ka Kahe

**Background** Previous studies regarding the associations between calcium (Ca) and cognitive impairment are inconclusive. We aimed to examine serum Ca level and dietary Ca intake in relation to the risk of cognitive impairment.

**Methods** We used data from the REasons for Geographic and Racial Differences in Stroke (REGARDS) study (n=30,239) for examining dietary Ca and a random sub-cohort (n=2,666) for serum Ca. At baseline (2003-2007), serum Ca concentration was measured via inductively coupled mass spectrometry and dietary Ca intake (from food and supplements) was assessed by the Block 98 food frequency questionnaire. Global cognitive impairment was determined every year by the Six Item Screener (SIS) and domain-based cognitive impairment was assessed every other year through the Enhanced Cognitive Battery (ECB) during an average 10-year follow-up. Multivariable-adjusted logistic regression models were used to examine the associations of serum (tertiles) and dietary (quartiles) Ca with the odds of cognitive impairment in participants free of stroke and cognitive impairment at baseline. The association of Ca intake with cognitive impairment was further examined separately in Ca supplement users and non-users.

**Results** In the entire cohort, a total of 1,424 SIS cases and 386 ECB cases were identified. Dietary Ca intake was marginally associated with the global cognitive impairment [quartile (Q) 4 vs Q1: OR=1.25, 95% CI=0.99-1.57]. The observed association was strengthened and became statistically significant in Ca supplement users [Q4 vs Q1: OR (95% CI) =1.29 (1.001-1.67)]. No association was found between dietary Ca intake and ECB impairment. In the sub-cohort, a total of 184 SIS cases and 48 ECB cases were determined. No association was observed between serum Ca concentration and cognitive impairment.

**Conclusion** Findings from this US cohort suggest that individuals with higher Ca intakes especially in supplement users may be at higher risk for global cognitive impairment.



**Figure 1 Associations (ORs and 95% CIs) of baseline dietary Ca intake and serum Ca concentration with cognitive impairment**

Abbreviation: Ca, calcium; CI, confidence interval; ECB, Enhanced Cognitive Battery; OR, odds ratio; Q, quartile; SIS, Six-item Screener; T, tertile.

**Forty Years of Struggle in North Carolina: Workplace segregation and fatal occupational injury rates** Elizabeth S McClure\* Elizabeth McClure Amelia T Martin Shabbar I Ranapurwala Maryalice Nocera John Cantrell Stephen Marshall David B Richardson

North Carolina's workforce has a legacy of racial and ethnic segregation and persistent disparities in fatal occupational injuries, with Black men historically experiencing the highest rates. Over the past 20 years, the Hispanic workforce in North Carolina has grown, and rates of occupational fatal injury have increased among Hispanic men. We assessed the role of workplace segregation in shaping disparities in fatal occupational injury from 1992-2017 in North Carolina, adding to an analysis from 1977-1991. We calculated observed rates of occupational fatal injury within categories of occupation, industry, race, age, and sex; and we estimated expected number of fatalities among Black and Hispanic male workers had they experienced the mortality rates of White male workers, within age strata. The ratio of the observed to expected deaths represents the standardized rate ratio (SRR). Hispanic males experienced over twice the number of deaths they would have expected under White male mortality rates (SRR: 2.11, 95% CI: 1.86-2.40). The Hispanic-White and Black-White disparities were widest in the 35-54 age group, with Hispanic males having 3.54 (95% CI: 2.95-4.26) times the mortality expected under White mortality reference rates and Black males experiencing 1.41 (95% CI: 1.24-1.60) times the expected mortality. Hispanic workers were highly segregated into the construction industry, working 32% of their worker-years in construction. Fatal injury in the construction industry among Hispanic males aged 35-54 years was over 4-fold that observed among White males. These results suggest that if Hispanic and Black workers experienced the workplace safety of their White counterparts, their rates of fatal injury would be substantially reduced. Workforce segregation reflects pervasive structural discrimination, which contributes to mortality disparities. Root causes, like the distribution of employment opportunity, must be addressed to eliminate these disparities.

**Safety climate and injury: An assessment of the Fire service Organizational Culture of Safety (FOCUS 2.0) survey sample** Ashley Geczik\* Ashley Geczik Jin Lee Madison Raposa  
Christian Resick Joseph Allen Andrea Davis Jennifer Taylor

**Background:** Safety climate is a known upstream predictor of safety outcomes. The Fire service Organizational Culture of Safety (FOCUS) survey measures the industry-specific safety climate of the US fire and rescue service resulting in cross-sectional data. FOCUS safety climate is expressed by two factors, Management Commitment to Safety and Supervisor Support for Safety. FOCUS has been administered in 516 fire departments, with 179 assessing with FOCUS 2.0.

**Methods:** The FOCUS 2.0 survey sample was obtained using convenience sampling of US fire departments in 2019-2020. Our final sample included 16,876 individuals nested within 170 fire departments. We reported the individual level characteristics and stratified by fire department organization type (career, volunteer). Multilevel logistic regression models were used to investigate the associations between FOCUS safety climate and injury status (yes/no). We adjusted for age, years of experience, sex (male, female), and officer status (non-officer, officer, leadership).

**Results:** In our sample 3,105 individuals (18.4%) reported they had experienced an injury in the last 12 months prior to completing the survey. We observed that 18.7% of individuals from career departments reported an injury, whereas only 7.4% of individuals from volunteer departments reported an injury. We observed a mean Management Commitment score of 65.1 and a mean Supervisor Support score of 82.8 for the total population. Overall, a higher Supervisor Support score was associated with 2% lower odds of injury reported in the last 12 months (OR=0.98 [95% CI: 0.97-0.99]).

**Conclusion:** Our findings implied that members perceive that their supervisors are more focused on their safety than management leadership. This finding suggests that Supervisor Support may be an important driver in injury prevention for the US fire and rescue service. Further investigations into the associations between Supervisor Support and specific injury outcomes is warranted.

**The association between the incidence of postmenopausal breast cancer and occupational exposure to selected organic solvents, Montréal** Sydney Westra\* Sydney Westra Mark S. Goldberg France Labrèche Jill Baumgartner Vikki Ho

**Background:** Breast cancer is the most diagnosed cancer among women and accepted risk factors only explain 25% to 47% of cases. Organic solvents are used widely in the workplace. A hypothesis from the 1990s postulated that exposure to organic solvents may increase the risk of developing breast cancer, yet there is insufficient data to confirm this hypothesis. We sought to determine whether past occupational exposures to organic solvents known to exert mammary toxicity were associated with the incidence of invasive breast cancer in postmenopausal women in Montréal.

**Methods:** From a population-based case-control study (2008 to 2011), using in-depth interviews we elicited information on risk factors and lifetime occupational histories. A team of industrial hygienists and chemists translated each detailed job description into specific chemical and physical exposures. We selected six individual solvents and four solvent groups. We assessed indices of past exposures to the selected solvents and the risk of developing postmenopausal breast cancer using unconditional logistic regression. Indices of exposure included any previous exposure, frequency in hours per week, duration in years, and average cumulative concentration with concentration on a scale of 1 ("low"), 2 ("medium"), 3 ("high") weighted by hours per week exposed.

**Results:** We enrolled 695 cases and 608 controls. We found increased ORs for average cumulative concentration of exposure to mononuclear aromatic hydrocarbons (OR: 1.52, 95%CI: 1.04, 2.28), chlorinated alkanes (OR: 2.42, 95%CI: 1.23, 5.68), toluene (OR: 1.59, 95%CI: 1.02, 2.59) and the group of organic solvents with reactive metabolites (OR: 1.53, 95%CI: 1.08, 2.24). Positive associations were found across all exposure metrics and were higher among women who had estrogen positive/progesterone negative tumours.

**Conclusion:** Our results suggest that occupational exposure to certain organic solvents may increase the risk of incident postmenopausal breast cancer.

**Association Between Exposure to Violence, Job Stress and Depressive Symptoms Among Platform Workers in Korea** Min-seok Kim\* Min-seok Kim Jin-ha

There is a lack of study about occupational health related to platform workers in Korea. We aim to explore the occupational exposure to violence and job stress which is related to depressive symptoms in platform workers. Total of 962 people participated in the study, including 528 platform workers and 434 general workers, using a self-report questionnaire.. Depressive symptoms were evaluated by the Patient Health Questionnaire-9 when the score was greater than or equal to 10 points, which means moderate depressive symptoms. The exposure to occupational violence and job stress are measured with self-reported questionnaires. The odds ratio with 95% confidence interval (OR(95%CI)) was calculated by multivariable logistic regression adjusted for age, gender, working hours, education level and number of chronic diseases. The platform worker more frequently exposed to violence such as verbal, physical, sexual, humiliating treatment, blasphemy experience. In platform workers, the OR (95% CI) of depressive symptoms were 2.55 (<12, 1.40-4.66) for verbal violence, 5.54 (2.05-14.95) for sexual harassment, 3.87 (2.10-7.14) for humiliating treatment, 2.38 (1.05-5.39) for physical violence. Also, platform workers are more exposed to job stress similar to exposure to violence than general workers. In platform workers, the OR of depressive symptoms were 3.14 (1.80-5.48) for less than 3 meals per day, 3.34 (1.16-9.62) for too tired to do house work and 4.71 (2.30-9.65) for worry about work even not working. Platform workers experience various violence and job stress during work, and those factors are related to depressive symptoms. Policy researchers and related ministries should further develop and improve the 'health management' program for platform workers, a new form of work.



**The effect modification of employment status on the association of health service participation and mortality with any cause** Byungyoon Yun\* Byungyoon Yun Juyeon Oh Jin-Ha Yoon

**Background:** Although biennial health service has been implemented by Korean government as a preventive measure for various diseases, the association of health service participation and mortality remains controversial. This study aims to assess the association of mortality risk with health service participation.

**Methods:** This is a retrospective nationwide cohort study using data from the National Health Insurance Service in Korea. Working age individuals aged 20 to 59 in January 2007 were included in this study and followed up until December 2021. Health service participation was defined as individuals who participation in health services in previous two years. Adjusted Hazard ratios (HRs) and 95% confidence interval (CIs) of mortality with any cause by health service participation were estimated using Cox proportional hazard models, adjusting for age, sex, income level, region, disability status, employment status (either self-employed or employee), and chronic disease status. Subgroup analysis stratified by employment status was further performed.

**Results:** Among 13,960,557 participants (median 15-year follow-up, mean age 40.2 [SD 9.3], female 31.45%), death occurred in 426,062 participants (141,090 for participation vs. 284,972 for non-participation). The proportion of health service participation in employee were significantly higher than that in self-employed (62.46% vs 15.73%;  $p < 0.001$ ). Adjusted HR (95% CI) of mortality with any cause by health service participation was 0.78 (0.78-0.79). In subgroup analysis, health service participation in self-employed group has stronger association with decreased risk of mortality with any cause, compared with that in employee group (adjusted HR (95% CI): 0.64 (0.63-0.65) vs. 0.86 (0.86-0.87), respectively).

**Conclusion:** This study highlighted the significant association between health service participation and decreased risk of mortality with any cause and employment status might be an effect modifier.

**LATEBREAKER**

Occupational

**Impact of shiftwork on retinal vessel diameters** Luenda Charles\* Luenda Charles Ja K. Gu Desta Fekedulegn Penelope Allison John Violanti

**Objective:** There is ample evidence of the adverse effect of shiftwork on the macrovascular system but not as much on the microvascular system. Our aim was to investigate the impact of shiftwork on changes in central retinal arteriolar equivalent (CRAE), a measure of retinal arteriolar width, and central retinal venular equivalents (CRVE), a measure of retinal venular width.

**Methods:** Participants were 146 officers (71.2% men) from the Buffalo Cardio-Metabolic Occupational Police Stress study. Shiftwork data (day, afternoon, night) were obtained from City of Buffalo, NY payroll records. Retinal vessel diameters were measured using a standardized protocol. ANOVA and ANCOVA were used to compare mean change in CRAE and CRVE over a five-year period from the 1st follow-up exam (2011-2014) to the 2nd follow-up exam (2015-2019) across shiftwork categories.

**Results:** Shiftwork adversely affected CRAE and CRVE but in unexpected directions. Officers who worked  $\geq 70\%$  on day shift had a significantly larger decrease in the mean CRAE ( $-5.01 \mu\text{m}$ ) compared to those who worked  $< 70\%$  ( $-0.59 \mu\text{m}$ ) after multivariable adjustment ( $p=0.021$ ) and was only significant among men ( $p=0.027$ ). CRVE increased for officers on afternoon shift ( $2.96 \mu\text{m}$ ) but declined in those on day and night shifts after multivariable adjustment ( $p=0.043$ ). CRVE also increased for officers who worked  $\geq 70\%$  day ( $3.88 \mu\text{m}$ ) but declined in those who worked  $< 70\%$  ( $-1.55 \mu\text{m}$ );  $p=0.007$ . This increase was only significant among women ( $\geq 70\%$  day= $4.56 \mu\text{m}$ ;  $< 70\%$  day= $-2.54 \mu\text{m}$ ;  $p=0.025$ ).

**Conclusion:** Shiftwork adversely affected the diameters of the retinal arterioles and venules; the effect was observed among day and afternoon shift officers and differed by sex. Men on day shift had narrower (i.e., worse) arterioles and women on day and afternoon shifts had wider (i.e., worse) venules over the two periods. These results should be interpreted with caution due to small sample sizes. Future research is warranted to understand these results.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Respectful Maternity Care Collaborative: Identifying a Research Agenda for Black Birthing Research with Birth Equity Stakeholders** Afua Nyame-Mireku\* Afua Nyame-Mireku LaTasha Snell Gatling Zainab Jah Susan Perez Yasmine Griffiths Carmen Green

**Research Objective:** Black birthing people are often excluded from lead or partnering roles in research despite often being included as subjects. This causes a missed opportunity for Black birthing people to develop research topics that are important to them. The National Birth Equity Collaborative (NBEC) established the Respectful Maternity Care Collaborative (RMCC), a formalized partnership of stakeholders where Black birthing people initiate, design, and lead research initiatives. The RMCC developed a research agenda on Black maternal health based on the knowledge and experiences of Black birthing people and stakeholders.

**Study Design:** From February 2022 to April 2022, NBEC distributed *The Future of Black Birthing Research*, a survey on eradication strategies for Black maternal health disparities, to NBEC staff, birth equity stakeholders, and the general public via social media and email. The qualitative survey results were thematically analyzed to identify research priorities. In October 2022 and January 2023, NBEC hosted virtual convenings of Black birthing people and stakeholders to prioritize the survey themes and develop a research agenda that addresses the Black maternal health crisis.

**Principal Findings:** Ten research priorities were identified (1 = Highest priority, 10 = Lowest Priority): 1) Systemic Change, 2) Full Spectrum Perinatal Care Integration, 3) Culturally Safe Care, 4) Personal Decision-Making, 5) Birth worker and Healthcare Professional Pipeline 6) Investing and Funding, 7) Listening and Supporting Black Birthing People and their Villages, 8) Availability and Access to Respectful and Quality Perinatal Care, 9) Accessible and Respectful Education and Resources, and 10) Professional Development.

**Conclusions:** Developing a birth equity research infrastructure elevates the knowledge and experiences of Black birthing people and stakeholders in priorities for research and policies.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Maternal history of sexually transmitted infections and child's pubertal timing** Sara Aghaee\*  
Sara Aghaee Julianna Deardorff Ai Kubo

**Introduction:** Earlier puberty is associated with higher risk of adverse health outcomes in adulthood. Studies have found that maternal and intrauterine exposures may predict pubertal timing. Animal models suggest that prenatal immune response to infections can alter puberty in offspring, however comparable human studies are scarce. Sexually transmitted infections (STIs) may be of particular importance due to their ability to interact with hormonal pathways that may influence sexual development. Thus, we explore associations between maternal STIs and child's pubertal timing. **Methods:** This prospective cohort study included 77,975 boys (53%) and girls who were born at a Kaiser Permanente Northern California facility in 2003-11. Mothers reported history of STIs at routine prenatal checkups. Pubertal onset was measured using clinician-assessed sexual maturity ratings (SMRs), defined as the age at transition from SMR 1 to SMR 2+ for breast development (thelarche) in girls, testicular enlargement (gonadarche) in boys, and pubic hair development (pubarche) in both. Early menarche (<12 years) was assessed in girls. SMRs were collected through September 2022. Adjusted Weibull and logistic regression models were used. **Results:** Girls whose mom had chlamydia had a slightly elevated risk of earlier thelarche (HR=1.07, 95%CI=1.01-1.14) and menarche (OR=1.13, 95%CI=1.01-1.26) compared to girls whose mom never had chlamydia. Boys also had higher risk of earlier gonadarche (1.07, 1.01-1.14) and pubarche (1.08, 1.01-1.15). Girls whose mom had hepatitis had 28% higher odds of experiencing earlier menarche (1.28, 1.06-1.56). Among girls whose mom had hepatitis, White girls specifically had an increased risk of earlier thelarche (1.62, 1.21-2.16). Girls whose mom had syphilis or HIV had up to twice the risk of earlier puberty although results were not statistically significant. **Conclusion:** Our results suggest that maternal infections may have longer lasting impacts on child outcomes.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Paired Maternal and Cord Blood DNA methylation Signatures** Sahra Mohazzab-Hosseinian\*  
Sahra Mohazzab-Hosseinian Carrie Breton Joseph Wiemels Erika Garcia Crystal Marconett

**Background and Aims**

Pregnancy is a period of rapid biological change for mother and child. Changes in maternal prenatal biology (e.g., DNA methylation) may influence fetal outcomes. This study aimed to characterize the effect of differences in prenatal whole blood DNA methylation (DNAm) on cord blood DNAm signatures.

**Methods**

This analysis was conducted in the Maternal and Developmental Risk Factors from Environmental Stressors (MADRES) pregnancy cohort, composed of low-income Hispanic women in Los Angeles. Maternal whole blood samples were collected during early and late pregnancy, and cord blood samples were collected at birth. Difference in methylation z-score was calculated per probe for each mother. Infant DNAm was regressed onto 4,155 CpGs displaying intra-individual differences in pregnancy using adjusted linear models for infant cell type. Interaction by maternal pre-pregnancy BMI, dietary folate, and gestational weight gain was investigated.

**Results**

Among the 4,155 CpGs tested, we found evidence of 134 prenatal CpGs influencing neonatal DNAm signatures. Several imprinting genes were implicated, including neonatal *HOXA2* signatures. Maternal pre-pregnancy BMI modified the effect of difference in methylation z-score in neonatal CpGs.

**Conclusion**

There is evidence that changes in prenatal DNA methylation may influence neonatal DNA methylation signatures.

**Using Latent Class Analysis to understand developmental outcomes and profiles of****comorbid birth defects** Dorothy J. Mandell\* Dorothy Mandell Rachel Allred Mimi T. Le Mark A. Canfield

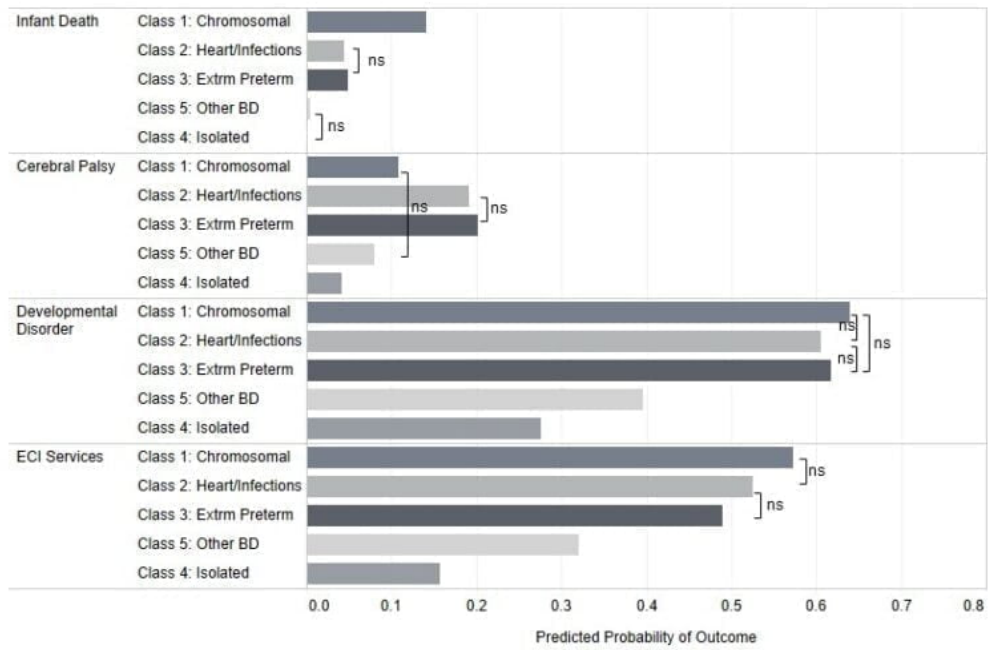
A common statistical and clinical problem with birth defects is understanding the impact of comorbidities on later developmental outcomes. Birth defects are commonly not isolated and co-occur with other illnesses that complicate prognosis. Analyses often exclude or control for comorbidities or use clinical judgement to group them. These three approaches lead to widely varying results. This study offers an approach to assess the impact of comorbid conditions on developmental outcomes using infants born with microcephalus as an example.

**Methods:** Data were from a linked birth-death-Birth Defects Registry (BDR)-Medicaid dataset in Texas, covering 6 years of births. Those with verified microcephalus and Medicaid claims were included (N=2516). Recorded birth defects were coded into 12 birth defect categories and the presence of chromosomal anomalies or prenatal infection were coded. Birth weight and clinical gestational age were also identified. Outcome variables (death, Cerebral Palsy, developmental disorder, or receiving early childhood intervention) were coded from death and Medicaid data. Latent Class Analysis was conducted then regressed onto the outcomes data using the DCAT procedure in MPlus.

**Results:** This modelling resulted in 5 distinct latent classes of microcephalus: isolated, chromosomal defects, heart defects, extremely preterm, and other brain/head anomalies. The chromosomal class had the highest predicted probability of two outcomes: death (.14) and developmental disorders (.64). In contrast, the isolated class had the lowest predicted probability of experiencing any of the four outcomes.

**Conclusion:** These results show that meaningful profiles of comorbid defects can be statistically identified and be used to differentiate developmental outcomes. This approach can be used to better understand the relationship between combinations of comorbidities and outcomes.

Predicted probability of each developmental outcome by comorbid class of microcephalus



Notes  
 ECI = Early Childhood Intervention Services  
 Brackets indicate differences between classes that were not significantly (ns) different at the p < .03 level

**Metal co-exposures in relation to serum lipid levels during childhood in the Rhea mother-child cohort in Greece** Gyeyoon Yim\* Gyeyoon Yim Katerina Margetaki Megan E. Romano Shohreh F. Farzan Maria Kippler Marina Vafeiadi Leda Chatzi Caitlin G. Howe

### Background

Growing evidence suggests that cardiovascular disease, the leading cause of mortality worldwide, develops over the lifetime, often beginning in childhood. Exposure to metals may contribute to dysregulation of lipid levels during childhood. However, previous epidemiologic studies have mainly focused on evaluating the impacts of single metal exposures on lipid levels in adults.

### Objectives

To investigate the joint and individual associations of metal mixture exposures with lipid levels during childhood.

### Methods

The current cross-sectional study included 297 mother-child pairs from the Rhea Cohort Study in Heraklion, Greece. Seven metals (cadmium, cobalt, mercury, manganese, molybdenum, lead, and selenium) were measured in child blood at 4 years of age. Serum lipid measures included total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). To determine the joint and individual impacts of child metal exposures (log-transformed) on lipid levels, Bayesian kernel machine regression (BKMR) was employed as a multi-pollutant approach. Models were adjusted for maternal education and child sex, secondhand smoke exposure, and fish consumption.

### Results

BKMR identified a positive association between the metal mixture and both TC and LDL. Of the seven metals, selenium (median 90.6 [IQR=83.6, 96.7] µg/L) was assigned the highest posterior inclusion criteria for both TC (0.89) and LDL (0.85). A difference in LDL of 4.76 mg/dL (95% CI=-0.12, 9.64) was observed when blood selenium was set to its 75th versus 25th percentile, holding all other metals at their median values.

### Conclusion

Higher blood selenium concentrations during childhood may increase LDL. Given that selenium is an essential element which may have benefits in small quantities, additional studies in populations that span a wider range of selenium intake are needed to elucidate the full dose-response relationship between this element and child lipid levels.



**Relationships between Maternal, Offspring, and Pregnancy Factors and Extracellular Vesicle and Particle miRNAs in Prenatal Maternal Plasma and Postpartum Human Milk: A Pilot Study**

Caitlin G Howe\* Caitlin Howe Meghan E Muse David A Armstrong Diane Gilbert-Diamond Jiang Gui Anne G Hoen Thomas J Palys Brock C Christensen Margaret R Karagas

**Introduction:** MicroRNAs (miRNAs) carried by extracellular vesicles and particles (EVPs) in maternal circulation during pregnancy and in breast milk postpartum are hypothesized to facilitate maternal-offspring communication and contribute to developmental programming. However, the factors that influence them remain largely unknown.

**Methods:** EVP miRNAs were extracted from maternal plasma samples collected at approximately 24-28 weeks gestation and paired breast milk samples collected at approximately 6 weeks postpartum from 54 participants in the New Hampshire Birth Cohort Study. 798 miRNAs were profiled using the Nanostring nCounter platform. Associations between maternal, offspring, and pregnancy factors and maternal EVP miRNA levels were investigated using covariate-adjusted robust linear regression models.

**Results:** 142 miRNAs were detectable in  $\geq 60\%$  of plasma samples, and 200 miRNAs were detectable in  $\geq 60\%$  of milk samples; 92 miRNAs were common between the two sample types. Shared detectable miRNAs in plasma and breast milk were poorly correlated with each other ( $|r| < 0.25$ ). Total milk EVP miRNA counts were significantly ( $P = 0.018$ ) lower among mothers with a BMI  $> 25 \text{ kg/m}^2$  compared with mothers with a BMI between 18 and  $25 \text{ kg/m}^2$  prior to pregnancy. Infant age at breast milk collection was inversely associated ( $FDR < 0.05$ ) with two miRNAs (miR-146a-5p and miR-130b-3p) in breast milk EVPs. Maternal pre-pregnancy BMI and gestational age at sample collection were not significantly associated with plasma EVP miRNA levels. Other factors investigated, including maternal parity, education, gestational weight gain, delivery mode, infant sex, and gestational age at delivery, were not significantly associated with maternal EVP miRNAs in either sample type.

**Conclusions:** MiRNA levels in breast milk EVPs may be influenced by pre-pregnancy weight status and infant age. Additional research is needed to investigate possible implications for offspring health.

**Season of Conception Effects on Risk of Cerebral Palsy in California** Haoran, Zhuo\* Haoran  
Zhuo Beate, Ritz Zeyan, Liew

Cerebral palsy (CP) is the most prevalent neuro-motor disability in children, while most cases have an unknown etiology. The detection of seasonal variation could help indicate etiological roles of seasonally varied factors. We examined the seasonal variation of CP occurrence in a study cohort consisted of over 4 million children born in California in 2007-2015 identified in the California birth records. CP diagnoses were identified from recipients of California Department of Developmental Services. We derived the month/season of conception as major exposure from the date of birth and gestational age from birth records. Odds ratio (OR) and 95% confidence interval (CI) were estimated for CP, controlling for long-term trend of incidence change, maternal individual-level sociodemographic characteristics, community-level social vulnerability, and child's sex. To investigate the potential spatial variation, we further stratified the study population by geographical locations of birth (Northern, Central, Southern regions) and percentile of social vulnerability index. Heterogeneity of seasonal trend of CP sub-phenotypes and between sex were also investigated. In addition, sibling-comparison design was utilized to triangulate our findings. We identified 4,651 CP cases in this cohort. Children who were conceived in winter (Jan-March; OR=1.13, 95% CI: 1.03-1.23) and spring (April-June; OR=1.11, 95% CI: 1.02, 1.21) had higher odds of CP compared to summer conceptions (July-Sept). The occurrence of CP peaked in February (e.g., 11.40 cases per 10,000) while had trough in July (e.g., 9.55 cases per 10,000). The seasonality associations were slightly stronger in northern and central regions, high vulnerability neighborhoods (SVI  $\geq$  90<sup>th</sup>), and overall spastic subtypes. The results using the sibling-comparison are similar, but precision is much lower. Seasonally varied environmental factors should be examined in etiological research of CP.

**Asthma as an effect modifier of the association between adverse birth outcomes and neurodevelopmental disabilities** Jenil Patel\* Jenil Patel Omobola Oluwafemi Sneha Manoharan Sarah Messiah Luyu Xie

The role of childhood asthma on the relationship between adverse birth outcomes and neurodevelopmental disabilities (NDDs) in adolescence has not been clearly described in the context of racial/ethnic disparities. The objective of this study was to examine the role of asthma as an effect modifier of the association between adverse birth outcomes and NDDs with an emphasis on race/ethnicity.

Data were collected through the National Survey of Children's Health. The study included 131,774 children aged 0-17 years. Study exposures comprised of adverse birth outcomes including preterm birth and low birth weight. Weighted prevalence estimates and odds ratios with 95% confidence intervals among children with and without adverse birth outcomes were calculated for NDDs including attention-deficit/hyperactivity disorder, autism spectrum disorder, cerebral palsy, seizure, and several other including behavior problems. Adjusted odds ratios were stratified by asthma status and separate interactions were assessed for each outcome.

Of 131,774 participants, 10,227 were born low birth weight (9.12%; 95% CI: 8.77%-9.49%), 14,058 were born preterm (11.35%; 95% CI: 10.94%-11.76%), and 16,166 participants had asthma (11.97%; 95% CI: 11.58%-12.37%). There were 68,100 males (51.11%), 63,674 females (48.89%), 102,061 non-Hispanic whites (NHW) (66.92%), 8,672 non-Hispanic blacks (NHB) (13.97%), and 21,041 participants (19.11%) categorized as Other. NHB children with adverse birth outcomes had higher prevalence of several NDDs compared to NHW children.

These results suggest that US children with adverse birth outcomes have higher prevalence of NDDs and NHB children with adverse birth outcomes have higher prevalence of NDDs compared to NHW children. These findings support screening for NDDs in pediatric health care settings among patients with adverse birth outcomes, particularly among those from ethnic minority backgrounds.

**Contextualizing relationship quality between mother and father of the baby during pregnancy: A latent class analysis** Rosemary Adaji\* Rosemary Adaji Carmen Giurgescu Dawn Misra

**Background:** Understanding of contextual variables is pertinent to interpreting findings linking socio-environmental correlates of health outcomes, including birth outcomes. For example, in the psychosocial domain of pregnancy, constructs such as relationship quality are multidimensional. However, analytical approaches in many studies mainly focus on one or two proxy indicators independently (e.g., social support). Such an approach is inadequate, especially when correlation among these indicators is likely high. This study aims to identify a construct of mother of the baby with the father of the baby (FOB) relationship quality during pregnancy using multiple self-reported relationship indicators among Black women.

**Methods:** This is a secondary data analysis from a subsample of 404 Black pregnant women who participated in the Biosocial Impacts on Black Births study, a prospective cohort study. Participants completed questionnaires at 19-29 weeks' gestation including six measures of woman's relationship with the FOB: 1) contact with FOB, 2) FOB involvement, 3) overall relationship, 4) change in relationship prior to pregnancy to during pregnancy, 5) social support from FOB, and 6) conflict with FOB. Latent class analysis was used to identify and classify the relationship construct.

**Results:** We identified three classes of mother-FOB relationship quality: good, conflictual, and no relationship. Good relationship comprised 50% of responses, while conflictual, and no relationship comprised 29% and 21%, respectively. Class names were assigned based on theoretical knowledge of how mother-father relationships have been defined in previous literature.

**Conclusion:** Characterizing complex constructs using methods like latent class analysis could help identify subgroups of women or individuals who are at increased risk of adverse health outcomes or who could benefit from specific public health interventions based on their shared characteristics.

**Maternal mental health indicators and gestational weight gain in the 3D prospective cohort study** Isabelle Hardy\* Isabelle Hardy Catherine Allard Felix Camirand-Lemyre Jean R. Séguin Catherine Herba Negar Tabatabaei Isabelle Marc Lise Dubois Jean-Patrice Baillargeon William D. Fraser

**Background:**

Certain maternal mental health indicators (MMHI) may be associated with gestational weight gain (GWG).

**Study Design:**

We analyzed data from 2204 pregnant women in the 3D prospective cohort. MMHI were assessed with validated tools in the first trimester (psychiatric history, perceived stress, depressive symptoms, pregnancy-related anxiety, and the quality of marital relations) and at the second study visit (20 weeks) (anxiety, adverse life events, optimism, self-esteem, workplace stress, attachment style and food insecurity). Multiple imputation of missing data was performed. We used 2009 IOM guidelines to categorize average weekly GWG after 20 weeks as insufficient, adequate, or excessive. Associations between each MMHI and GWG categories were assessed using multivariable multinomial logistic regression adjusted for BMI, age, gestational age (GA) at visit 2, GA at delivery, income, education, prematurity, gestational diabetes, preeclampsia and parity. For each model, interactions of body mass index (BMI), parity, ethnicity, income, and newborn sex were assessed and retained for stratification if significant at the level of  $p < 0.1$ . Results are presented as standardized OR (sOR) with [95% CI], and  $p$  for interaction= $\pi$ .

**Results:**

Among participants with a prepregnancy BMI  $< 18.5$ , risk factors for excessive GWG were perceived stress (sOR=2.44 [1.24;4.8],  $\pi$  BMI=0.05) and depressive symptoms (sOR=2.58 [1.07;6.20],  $\pi$  BMI=0.06). Among modest-income women (20 000-39 999\$), disagreement with the statement "my work is repetitive" was a risk factor for excessive GWG (sOR=1.83 [1.04;3.22],  $\pi$  income=0.06); but among high-income women ( $> 80 000$ \$), it was protective against insufficient GWG (sOR=0.72 [0.56;0.94]) as well as excessive GWG (sOR=0.72 [0.58;0.89]). We did not observe any appreciable associations between the other MMHI and GWG.

**Conclusion:**

In the 3D cohort, some MMHI were associated with increased odds of excessive GWG among underweight and modest income women.

**Maternal Acetaminophen Use and Adolescent Behavioral Problems: Discrepancies by****Reporter** Rashida S. Smith-Webb\* Rashida S. Smith-Webb Ruby Barnard-Mayers Martha M. Werler Samantha E. Parker

**Background:** Acetaminophen is commonly used for pain and fever during pregnancy. Research suggests an association between maternal acetaminophen use and poor neurodevelopmental outcomes among offspring. However, studies often rely on maternal report of exposure and outcomes, which is subject to dependent misclassification. We examined the association between maternal acetaminophen use and behavioral problems during adolescence by parent, teacher, and the child.

**Methods:** We conducted a follow-up study of children born between 1996-2002. Exposure to acetaminophen was assessed via a standardized maternal interview after delivery. Behavioral assessments were conducted during adolescence (ages 11-17) using the Child Behavior Checklist (CBCL), Teacher Report Form (TRF), and Youth Self Report (YSR). Outcomes included internalizing (e.g., anxious) and externalizing (e.g., aggressive behavior) behavioral problems. We used linear regression models to calculate adjusted mean differences (MD) and 95% CI in T-scores. We also calculated weighted MD to account for lost to follow-up.

**Results:** Among 230 mothers, 66% reported acetaminophen use while pregnant. Acetaminophen use was generally not associated with behavioral problems by any reporter. Adjusted effect sizes varied across reporters. For instance, the MD for anxious/depressed was 1.5 (95% CI: -0.2, 3.2), 0.9 (95% CI: -0.8, 2.6), and -0.5 (95% CI: -2.2, 1.3) for parent, teacher, and self-report, respectively. Weighted results revealed a downward bias of MD based on maternal reported scores whereas those from teacher and youth reports were changed little. For example, the MD for anxious/depressed decreased to 0.9 for parent report but was unchanged for teacher report.

**Conclusions:** Prenatal acetaminophen use was not associated with behavioral problems during adolescence. Given the discrepancies by reporter and the influence of selection bias evident in maternal reporting, multi-informant assessments are indicated.

**Does domestic violence legislation improve infant health? A difference-in-differences analysis using longitudinal data from 56 countries** Robin Richardson\* Robin Richardson Anna Tarik

Intimate partner violence poses a substantial risk to infant health. In this analysis, we evaluated the effect of domestic violence (DV) legislation on one indicator of poor infant health: small birth size. We linked national-level domestic violence policy information with individual-level birth size data, which was collected in population-based, repeated cross-sectional surveys that included data from 3,587,299 mothers between the years 1990 to 2020 from 56 low- and middle-income countries. Small birth size was captured with a question asking women who had a live birth in the past five years their perceptions of baby size at birth, and we aggregated responses to the country-level to estimate yearly prevalence. We evaluated the effect of adoption of DV legislation on small birth size using a difference-in-differences study design that allowed staggered treatment adoption, controlled for time-varying country-level factors (i.e., gross domestic product, literacy rate, index of women's legal rights), estimated variances that accounted for country-level clustering, and accounted for potential selection bias of policy adoption using stabilized inverse probability weights. Over the study period, 30 countries adopted domestic violence legislation (treatment countries) and 26 did not (control countries). In adjusted models, adoption of DV legislation corresponded to reductions in the proportion of births that had small birth size (average treatment effect among treated (ATT) = -0.107, 95% CI: -0.110, -0.104), suggesting that policies confronting DV may have important implications for child health. Additional work will explore heterogeneity by sociodemographic factors (e.g., household wealth) and will explore temporal timing of policy adoption and child health through lagged effects.

**Longitudinal Comparison of Two DNA Methylation Smoking Signature Scores Across Children at Risk for Type 1 Diabetes** Lauren Vanderlinden\* Lauren Vanderlinden Randi K Johnson Patrick Carry Teresa Buckner Fran Dong Katerina Kechris Jill M Norris

Smoke exposure *in utero* and in early childhood remains a high public health concern. Development of a strong biomarker of smoke exposure is essential for research due to maternal underreporting of cigarette smoking. While numerous groups have proposed and validated a smoke exposure signature from DNA methylation (DNAm) CpG sites measured cross-sectionally, less is known about their stability over time. We compared two smoking signatures, developed by Reese (et al 2017, developed to measure *in utero* smoke exposure) and McCartney (et al 2018, developed to measure packyears of smoke exposure in adults) in 423 children from the prospective Diabetes Autoimmunity Study in the Young (DAISY) cohort. We measured DNAm longitudinally on one to five pre-disease samples (from cord blood or peripheral whole blood, age range birth-22 years) using either Illumina's 450K or EPIC platform and calculated the Reese and McCartney smoking signature score for each sample (n=1,116). The smoking signatures were significantly correlated (Pearson  $\rho=0.55$ , p-value=1.0e-92) despite only having a single DNAm CpG site in common. To assess the repeatability of each signature throughout childhood, we calculated the intraclass coefficient (ICC) of a linear mixed regression model with the smoking signature as the outcome, age and Illumina platform as fixed effects and a random slope and intercept for each subject. The Reese signature resulted in an ICC of 0.75 (95% credible interval: 0.70-0.80) and the McCartney an ICC of 0.39 (95% credible interval: 0.31-0.47), indicating Reese is a more repeatable biomarker over time in our population. In order to investigate whether the differences in repeatability of the biomarker over time between the two signatures is due to differences in response to changes in exposure, we are currently assessing self-reported smoke exposure status in our cohort in order to establish consistency of exposure over time.



**Increasing Preterm Delivery Trends in South Carolina** Kalyan Chundru\* Kalyan Chundru  
Jeffrey E. Korte Chun-Che Wen Brian Neelon Dulaney A. Wilson Julio Mateus John Pearce Sarah  
Simpson Hermes Florez Kelly J. Hunt Angela M. Malek

**Introduction:** With preterm delivery (PTD) trends rising in the U.S. and the multitude of complications for neonates, we aimed to assess the early impact of the COVID-19 pandemic and change in trends in PTD in South Carolina (SC).

**Methods:** Our study used 2015-2021 SC vital records data for singletons (n=338,784) born to non-Hispanic White (NHW), non-Hispanic Black (NHB) and Hispanic women. PTD was defined on the birth certificate as delivery <37 weeks gestation. Generalized estimating equation modified Poisson regression was used to assess the pandemic's impact on PTD. A fixed changepoint at the first quarter (Q1) of 2020 was fitted to test the change in slope of PTD trends.

**Results:** In SC, the overall PTD rate rose (9.09% to 10.26%) from 2015 to 2021, with the largest differences observed for NHB women compared to NHW and Hispanic women. The relative risk (RR) for PTD with a one quarter increase in time was 1.0055 (95% CI: 1.004-1.006). PTD increased steadily throughout the study period, with no time-race interaction before (p=0.35) or after (p=0.30) the changepoint. Adjusting for demographic factors (race-ethnicity, maternal age, education, Medicaid eligibility, urban vs. rural residence and use of Women, Infants and Children [WIC] services) attenuated PTD trends in this population (Figure 1). The RR for the prevalence of PTD with a one quarter increase in time was 1.003 (95% CI: 1.002-1.004). The prevalence of PTD for an average NHB woman was highest in the first quarter of 2021 (RR=0.115, 95% CI: 0.112-0.118] and in the last quarter of 2021 (RR=0.125, 95%: CI 0.122-0.128) compared to an average NHW or Hispanic woman in SC (Table1).

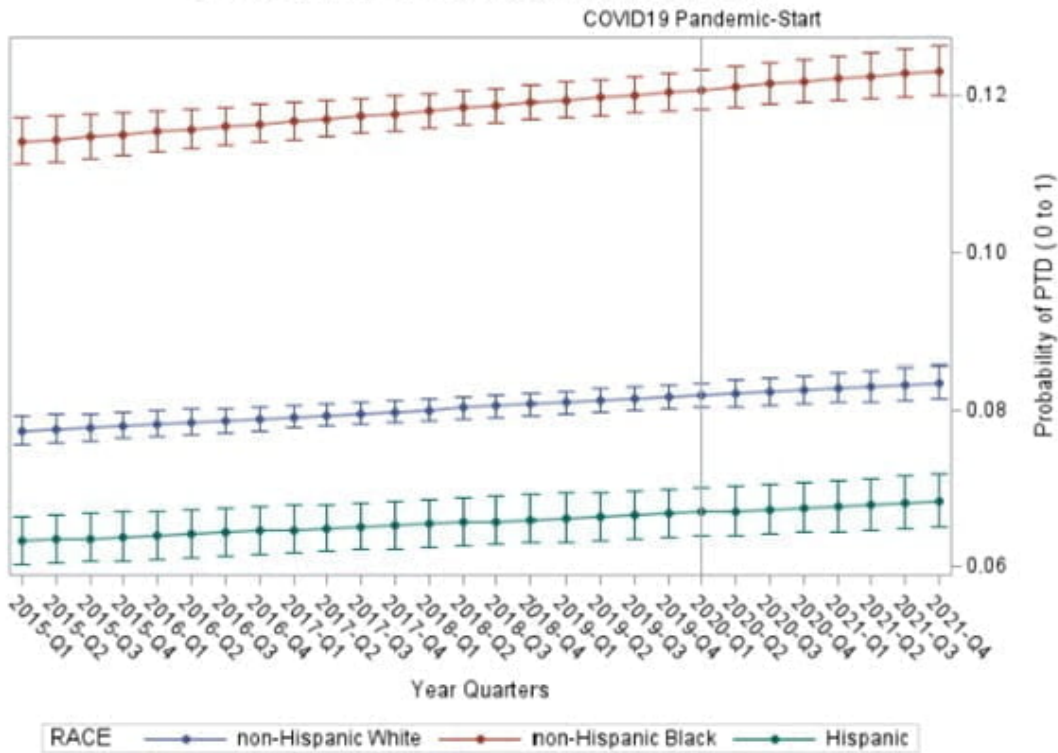
**Conclusion:** Although we did not observe a significant change in PTD trends before vs. after the pandemic's early phase, the steady rise in PTD and racial-ethnic group differences is concerning. Women delaying childbearing and clinical risk factors may be contributing to current PTD trends in this population.

**Table 1:** Prevalence of PTD for an average woman in SC.

Ethnicity-Race	1st Quarter of 2015			4th Quarter of 2021		
	Estimate	95%CI	p value	Estimate	95% CI	p value
Non-Hispanic Black	0.115	(0.112, 0.118)	<.0001	0.125	(0.122, 0.128)	<.0001
Non-Hispanic White	0.078	(0.076, 0.080)	<.0001	0.085	(0.083, 0.087)	<.0001
Hispanic	0.061	(0.058, 0.064)	<.0001	0.066	(0.063, 0.070)	<.0001

Demographic Factors	Relative Risk (RR) of PTD	95% CI	p value
One Year Increase in Women's Age	1.030	(1.028, 1.032)	<.0001
Non-Hispanic Black	1.471	(1.435, 1.508)	<.0001
Hispanic	0.782	(0.761, 0.818)	<.0001
Education: High school	0.865	(0.836, 0.895)	<.0001
Education: Some College Education (No Degree)	0.789	(0.761, 0.818)	<.0001
Education: College Graduate	0.618	(0.594, 0.644)	<.0001
Medicaid Access	1.231	(1.199, 1.265)	<.0001
WIC Services	0.908	(0.886, 0.931)	<.0001
Rural	1.006	(0.982, 1.030)	0.6044

**South Carolina- Preterm Birth Trends 2015-2021**



**Figure 1:** Probability of PTD per Quarter in SC by Race-Ethnicity

**Housing characteristics, in-home environmental exposures, and lung function in a safety net population of children with asthma** Matthew Bozigar\* Matthew Bozigar Catherine Connolly Kimberly Vermeer Luis Carvalho Robyn Cohen Julianne Dugas Jonathan Levy Patricia Fabian

**Objective:** The health effects of in-home environmental exposures (IHEEs) including asthma triggers are challenging to examine in large populations. We investigated the influence of housing and IHEEs on lung function among children with asthma visiting a safety net hospital.

**Methods:** We merged clinical lung function data from electronic health records (EHRs) for 1,070 children from Boston Medical Center to publicly available geospatial data on housing and census tract characteristics and previously predicted probabilities of IHEEs - indoor cockroach and rodent presence. We fit two Bayesian hierarchical models of percent predicted forced expiratory volume in one second (FEV<sub>1</sub>%) with and without IHEEs as latent variables to identify confounders.

**Results:** The study population had a mean age of 10.2 years, was 58% male, and 75% identified as Black. In fully adjusted models, we found 6.4% lower FEV<sub>1</sub>% (95% confidence interval, CI: -9.3%, -3.5%) from a one-unit increase in the log odds of the probability of cockroach presence, and no significant association with rodents (point estimate: -0.1, 95% CI: -3.5%, 3.4%). Living in public housing, housing built before 1950 and after 1980, were associated with 5.1% (95% CI: 1.6%, 8.6%), 5.8% (3.7%, 7.9%), and 2.7% (95% CI 0.0%, 0.6%) higher FEV<sub>1</sub>%, respectively. Living in a Black residentially segregated census tract was associated with 3.9% lower FEV<sub>1</sub>% (95% CI: -6.4%, -1.4%).

**Discussion:** In this safety net population of children with asthma, cockroach allergen presence predicted from EHRs and geospatial housing and neighborhood characteristics such as housing age and racial residential segregation were associated with differential lung function. Our unique approach provided evidence that IHEEs confounded the relationship between housing, neighborhood characteristics, and lung function. Observational environmental epidemiological studies can articulate the health effects of underlying and modifiable indoor environmental exposures.

**Upward mobility is associated with preterm birth but not low birthweight** Julia M Porth\* Julia M Porth Bobby K Cheon

**Background:** Changes in socioeconomic status (SES) between adolescence and adulthood, termed SES mobility, may influence perinatal health via changes in resources available to engage in healthy behaviors, stress, and psychological strain due to changing status. This analysis examined relationships between SES mobility and women's experiences of delivering a child who is preterm (PTB) or has a low birthweight (LBW). **Methods:** Data came from the National Longitudinal Study of Adolescent to Adult Health. SES was defined as a combination of education, occupation, and income, assessed among parents (when participants were aged 12-19) and later in adult participants (aged 24-32). SES mobility was the difference between parent and adult SES quintile, categorized as short-range (adult SES 1 quintile higher/lower than parent SES) and long-range (adult SES 2-4 quintiles higher/lower than parent SES). Those who did not experience SES mobility were categorized as having high SES immobility or low SES immobility. Relationships were assessed using logistic regressions accounting for complex survey design and clustering of births by mother. **Results:** Samples included 1,041 births from 672 mothers (PTB) and 1,013 births from 655 mothers (LBW). Compared to high SES immobility, upward mobility was associated with higher odds of PTB (OR: 2.77 [95% CI: 1.26, 6.08]), results which seem to be largely driven by short-range upward mobility (OR: 2.78 [1.28, 6.03]). Odds of PTB were higher among downwardly mobile participants though the 95% CI contained the null (OR: 1.82 [0.82, 4.03]). Neither upward nor downward mobility were associated with odds of LBW. **Conclusions:** Contrary to previous studies using more geographically restricted samples, results of the present study suggest upward mobility may be associated with increased odds of PTB. Future research should seek to clarify specific groups in which upward SES mobility can be harmful to perinatal health.

**Examining the sex differential in childhood stuttering in the United States** Kathleen Bainbridge\* Kathleen Bainbridge Danita Byrd-Clark

Examining the sex differential in childhood stuttering in the United States

Kathleen E Bainbridge<sup>1</sup> and Danita Byrd-Clark<sup>2</sup>

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**Background**

Heritability estimates suggest that 80% of the variance in childhood stuttering is attributable to genetic contributions. The greater prevalence of persistent stuttering among males, however, is hypothesized to result from non-inherited causes.

**Objective**

To identify non-genetic factors that might explain the sex differential in childhood stuttering.

**Methods**

We used nationally-representative data collected between 1999-2004 as part of the National Health and Nutrition Examination Survey (NHANES) to compute sex-specific prevalence estimates of stuttering of 8223 children aged 4-15 years whose parents reported they had stuttered/stammered during the past twelve months. Prevalence estimates were further stratified by socio-demographic characteristics, (age, race/ethnicity, head-of-household education level, and income-to-poverty ratio), maternal and neo-natal characteristics (birthweight, maternal age, specialized newborn care, and maternal report of smoking while pregnant), extent of social contact (household size, attended daycare/preschool) and serum level of toxins (cadmium, lead) and serum cotinine, a marker of tobacco smoke exposure. We used multiple logistic regression models to 1) identify factors independently associated with stuttering and 2) determine whether adjusting for these factors eliminated the sex differential for stuttering.

**Results**

We observed a more than doubling of the odds of stuttering among males compared to females [OR=2.8 (2.0, 4.1)] after adjusting for other significant factors. In addition to young age, non-Hispanic Black or Mexican-American race/ethnicity, and low income-to-poverty ratio, having

received specialized newborn care [OR=2.0 (1.2, 3.3)] and having a serum cotinine level greater than the limit of detection [OR=1.5 (1.0, 2.1)] were associated with childhood stuttering.

## **Conclusions**

We did not identify environmental factors which explain the greater prevalence of stuttering among male children compared to female children. We observed a variety of socio-demographic factors associated with childhood stuttering that may indicate markers of risk.

**Effectiveness of mRNA COVID-19 vaccination during pregnancy by circulating viral variant**

Ousseny Zerbo\* Ousseny Zerbo G. Thomas Ray Bruce Fireman Evan Layefsky Kristin Goddard Pat Ross Mara Greenberg Nicola P. Klein

**Objective:** To evaluate mRNA COVID-19 vaccine effectiveness (VE) during pregnancy.

**Methods:** This retrospective cohort study included pregnant persons who delivered between December 15, 2020, and September 30, 2022, and were members of Kaiser Permanente Northern California. The primary outcome was hospitalization for COVID-19; The secondary outcome was PCR-confirmed SARS-CoV-2 infection. The exposure was receipt of an mRNA vaccine during pregnancy. VE was estimated by SARS-CoV-2 variant period (pre-Delta, Delta, Omicron variant and sub-variants) and by time since vaccination using Poisson regression for the primary outcome and Cox regression for the secondary outcome adjusted for socio-demographics and calendar time.

**Results:** Of 57,688 pregnant persons in the study, 28% were vaccinated during pregnancy.

During days 14- <150 post-vaccination, 2-dose VE against hospitalization for COVID was 100% (95% confidence interval [CI] -6%, 100%), 100% (CI 88%,100%), 51% (CI -64%, 98%) and 100% (CI -90%, 100%) during the pre-Delta, Delta, Omicron, and Omicron sub-variant periods, respectively. Two-dose VE against SARS-CoV-2 infection during days 14 - <150, was 86% (CI 70%, 93%) during pre-Delta, 78% (CI 72%, 83%) during Delta, 14% (CI -5%, 30%) during Omicron and -16% (CI -60%, 43%) during omicron sub-variant periods. VE for  $\geq 150$  days was 68% (CI 52, 78), 10% (CI: -17%, 33%) and -33% (CI: -65%, 24%) during Delta, Omicron and Omicron sub-variant periods, respectively.

**Conclusion:** mRNA COVID-19 vaccination during pregnancy is effective against hospitalization for COVID and SARS-CoV-2 infection. VE waned over time since vaccination and decreased over calendar time, especially with the emergence of Omicron variants. New vaccines matching circulating strain may be necessary to prevent infection.

**Gabapentinoids and the risk of severe exacerbations in patients with chronic obstructive pulmonary disease** Alvi Rahman\* Alvi Rahman Sophie Dell’Aniello Erica E.M. Moodie Madeleine Durand Janie Coulombe Jean-François Boivin Pierre Ernst Christel Renoux

**Background:** Gabapentinoid drug use has recently surged and case reports of associated respiratory adverse events prompted North American and European health agencies to warn of severe breathing problems, including in patients with chronic obstructive pulmonary disease (COPD). However, no supporting evidence is available from large population-based studies. Hence, we assessed whether gabapentinoid use was associated with severe exacerbations in patients with COPD.

**Methods:** We conducted a population-based cohort study using computerized healthcare databases from the Régie de l’assurance maladie du Québec. Within a base cohort of patients with COPD between 1994 and 2015, aged  $\geq 55$ , those initiating gabapentinoids were matched 1:1 on age, sex, calendar year, and time-conditional propensity score to non-users from the same time-based exposure set. We used Cox regression to estimate HRs for severe COPD exacerbation (defined as hospitalization for COPD) associated with gabapentinoid use, compared with non-use. We also assessed the risk of respiratory failure as a secondary outcome.

**Results:** The cohort included 23,061 gabapentinoid initiators matched to 23,061 non-users (56.5% female; mean [SD] age, 74.6 [8.4] years). Overall, 6,232 severe COPD exacerbations occurred during 72,349 person-years of follow-up (incidence rate 8.6, 95% CI 8.4-8.8 per 100 person-years). Gabapentinoid use was associated with an increased risk of severe COPD exacerbation (HR 1.47, 95% CI 1.38-1.57), compared with non-use. The association was numerically higher for gabapentin (HR 1.61, 95% CI 1.45-1.78) than for pregabalin (HR 1.43, 95% CI 1.33-1.53). Gabapentinoids were also associated with an increased risk of respiratory failure (HR 1.47, 95% CI 1.33-1.62).

**Conclusions:** In patients with COPD, the use of gabapentinoids was associated with an increased risk of severe COPD exacerbation, highlighting the importance of risk-benefit assessment when prescribing gabapentinoids to patients with COPD.



**A multiprovincial analysis of the incidence of myocarditis or pericarditis after mRNA vaccination by varying dosing intervals, compared to the incidence after SARS-CoV-2 infection: a Canadian Immunization Research Network (CIRN) study.** Zaeema Naveed\*

Zaeema Naveed Cherry Chu Mina Tadrous Areti-Angeliki Veroniki Julia Li Isabelle Rouleau Yossi Febriani Andrew Calzavara Sarah Buchan Sharifa Nasreen Kevin Schwartz James Wilton Chi Yon Seo Nisha Thampi Sarah Wilson Monika Naus Gaston de Serres Naveed Z. Janjua Jeffery C. Kwong

**Objective:** To compare the risk of myocarditis/pericarditis after COVID-19 mRNA vaccination versus confirmed SARS-CoV-2 infection, and to assess if the risk of myocarditis/pericarditis varies by vaccine dosing interval.

**Methods:** We conducted a population-based retrospective cohort study using linked provincial databases in Quebec, Ontario, and British Columbia. We included individuals aged  $\geq 12$  years who received an mRNA vaccine as the second dose (vaccination cohort) or those who tested positive for SARS-CoV-2 by RT-PCR (infection cohort). The primary outcome was an incident hospitalization or emergency department visit with a diagnosis of myocarditis or pericarditis within 21 days of an exposure. We calculated age and sex-stratified incidence ratios (IRs) of myocarditis/pericarditis following mRNA vaccination versus SARS-CoV-2 infection. We also calculated post-vaccination incidence of myocarditis/pericarditis by vaccine type and dosing intervals. Province-specific estimates were pooled in a one-stage meta-analysis using the Poisson likelihood within provinces and allowing for random-effects on the province-specific effects.

**Results:** We observed 692 and 161 myocarditis/pericarditis cases within 21 days following 18,860,817 mRNA vaccinations and 860,335 SARS-CoV-2 infections, respectively. The overall incidence of myocarditis/pericarditis was lower following vaccination than infection ( $IR_{\text{BNT162b2/SARS-CoV-2}}=0.14$ ; 95%CI:0.07-0.29;  $IR_{\text{mRNA-1273/SARS-CoV-2}}=0.28$ ; 95%CI:0.20-0.39). The overall incidence of myocarditis/pericarditis was lower with longer dosing intervals;  $IR_{31-55 \text{ days}/15-30 \text{ days}}$  was 0.43 (95%CI:0.30-0.61) for BNT162b2 and 0.63 (95%CI:0.44-0.90) for mRNA-1273, and  $IR_{\geq 56 \text{ days}/15-30 \text{ days}}$  was 0.28 (95%CI:0.19-0.41) for BNT162b2 and 0.26 (95%CI:0.18-0.38) for mRNA-1273. Irrespective of the vaccine schedule, the adjusted incidence of myocarditis/pericarditis was lower for individuals with longer dosing intervals.

**Conclusion:** The risk of myocarditis/pericarditis is lower after mRNA vaccination than after SARS-CoV-2 infection and is lower with longer intervals between primary doses of mRNA vaccines than shorter intervals.

**Does Incarceration Effect all Black Men Equally? Heterogeneity of Effect Among US-born African American and US- and Foreign-born Caribbean Black Men with History of Incarceration** Adiba Hassan\* Adiba Hassan Vickie Mays Taylor Reed Shane DeGrace Susan Cochran

**Introduction:** Black men are disproportionately affected by the justice system, but trajectory of their lives after incarceration is understudied. To focus away from Black-white dichotomy and capture within-race heterogeneity, we explore the effect of incarceration history on economic hardship, material/resource disadvantage, and relationship strain among Black men by race, nativity, and ethnicity.

**Methods:** Using cross-sectional data from the National Survey of American Life, we included 1,914 Black men (67% US-born African American, 24% foreign-born Caribbean, and 9% US-born Caribbean) aged  $\geq 18$  years. Principal factor was used to reduce from 9 variables to 3 factors encompassing economic hardship (employment, job security, and poverty), material/resource disadvantage (food shortage, financial insecurity, life dissatisfaction, and material hardship), and relationship strain (closeness with family/ friends). Composite scales for factors were created using mean response to items and dichotomized at 50<sup>th</sup> percentile. Effect of incarceration history on each factor was assessed using age- and region-adjusted logistic regression weighted for sampling design, and tested for effect measure modification by race, nativity, and ethnicity.

**Results:** Black men reporting incarceration histories experienced higher odds of subsequent: 1) Economic hardship (OR:1.51, 95% CI 1.15-1.98), 2) Material/resource disadvantage (OR:1.94, 95% CI 1.47-2.56), and 3) Relationship strain (OR:1.54, 95% CI 1.19-1.98), compared with men without incarceration histories. Race, nativity, and ethnicity modified this relationship, namely, foreign-born Caribbean men were less likely to report incarceration histories and had lower odds (OR:0.32, 95% CI 0.15-0.71) of economic hardship compared with US-born African American men.

**Conclusion:** Incarceration has varying long-term consequences among Black men limiting upward mobility and exacerbating life hardship, with US-born African American at highest disadvantage.

**LATEBREAKER**

Policing/Incarceration

**Quantifying the true population-wide tuberculosis burden attributable to incarceration in Brazil** Yiran Liu\* Yiran Liu Yasmine Mabene Sergio Camelo Jeremy Goldhaber-Fiebert Julio Croda Jason Andrews

In South America, tuberculosis (TB) incidence is 27 times higher in prisons than in the general population. In Brazil, where incarceration rates have increased by over 500% since 1990, standard methods for calculating the population attributable fraction (PAF) of incarceration yield estimates of 8.9-11.5%. However, these likely underestimate the true effects of incarceration on population TB incidence due to not accounting for prison-acquired infections that progress to disease and generate secondary infections outside prisons. Furthermore, policy guidance for addressing TB in prisons focuses on biomedical interventions, overlooking potentially impactful interventions to reduce exposure to incarceration. Using a dynamic compartmental transmission model, we quantified the true population-wide excess TB burden in Brazil attributable to the historical rise in incarceration and estimated the effect of interventions to reduce incarceration exposure on population-wide TB incidence. We used newly available, unpublished data on incarceration and TB over time in Brazil to parameterize and calibrate the model. We estimate that the observed national TB incidence today is 47.8% (95% CrI, 35.2-62.3) higher than that expected without the historical rise in incarceration. Looking forward in time, compared to a base case scenario of continual growth in incarceration rates, we predict that national TB incidence in Brazil could be reduced by 25.7% (95% CrI, 19.6-33.0) in ten years with policies that reverse the historical growth in incarceration rates to the levels in 1990. Our findings reveal the substantial excess TB burden attributable to incarceration, which has been under-recognized by crude PAF estimates that do not account for the dynamic nature of incarceration and the interconnectedness between prisons and the community. Ultimately, these results highlight the urgent need for multifactorial interventions for TB control, including those that reduce incarceration exposure.

**The effect of mandatory arrest laws for intimate partner violence on women's incarceration: A difference-in-differences analysis** Sandhya Kajeepeta\* Sandhya Kajeepeta

Intimate partner violence (IPV) is estimated to impact about one in four U.S. women in their lifetime and represents 15% of all violent crime. Total violent crime rates have steadily declined across the country, but rates of IPV victimization have fallen at far slower rates and the incidence of intimate partner homicide has been increasing in recent years. These alarming trends suggest that current strategies for IPV prevention are insufficient and may even be counterproductive. Since the 1970s, the U.S. has developed and maintained a police-centric response to IPV—a response that relies on arrest as its primary tool through practices and policies including mandatory arrest laws. Existing evidence suggests that mandatory arrest laws are ineffective in preventing or reducing IPV and have perversely led to increased women's arrest rates. However, no studies to date have examined the effect of mandatory arrest laws on women's jail or prison incarceration rates. There are also likely profound racialized disparities in the effect of mandatory arrest laws on women's criminalization because of the ways in which policing, and the criminal legal system more broadly, disproportionately harms Black communities and other communities of color. However, such racialized disparities are underexplored. This study fills these gaps in the literature by presenting a difference-in-differences analysis estimating the effect of state-level changes in mandatory arrest legislation for IPV on women's jail and prison incarceration rates from 1980-2020 in the U.S. We also fit models with race-specific rates of women's incarceration to assess if there are differences by racialized group. Mandatory arrest laws remain hotly debated, but the debate currently lacks evidence on the relationship between such laws and women's incarceration, which this study provides.

**The consequences of maternal and paternal incarceration: Racial differences in adolescent externalizing behaviors** Shadiya L. Moss\* Shadiya Moss

**Aim:** Parental incarceration is a common lifecourse event in the U.S., with estimates suggesting that 2.7 million children/adolescents have a parent incarcerated in their lifetime. Children of incarcerated parents experience various negative health consequences throughout the lifecourse, including externalizing behaviors. However, evidence has been mixed. This study estimated the relationship between parental incarceration and adolescent externalizing behaviors, and effect modification by race.

**Methods:** Respondents included 14-19 year-olds (N=4,898) from the longitudinal cohort study Fragile Families and Child Wellbeing Study (1998 to 2017). Measures of parental incarceration were used to construct binary lifetime maternal and paternal incarceration variables. Youth reported past-year externalizing behaviors using the Child Behavior Checklist. Race was classified as non-Latine white and non-Latine Black. Negative binomial regression models were adjusted for parental socioeconomic status, parental depression and alcohol use, youth physical abuse, and externalizing behaviors in childhood.

**Results:** Adolescents of mothers who were incarcerated in their lifetime had an increased incidence rate of past-year externalizing behaviors (incidence rate ratio [IRR]=1.14, 95% CI=1.02-1.28). Exposure to lifetime maternal incarceration was associated with an increased incidence rate of past-year externalizing behaviors (IRR=1.31, 95% CI= 1.12-1.53) among non-Latine Black adolescents, and a decreased incidence rate of past-year externalizing behaviors (IRR=0.93, 95% CI= 0.69-1.26) among non-Latine white adolescents. Adolescents of fathers who were incarcerated in their lifetime had an increased incidence rate of past-year externalizing behaviors (IRR=1.25, 95%CI=1.16-1.36). Exposure to lifetime paternal incarceration was associated with an increased incidence rate of past-year externalizing behaviors among both non-Latine Black and white adolescents'.

**Conclusion:** Evidence from the current study shows that both maternal and paternal incarceration are associated with increases in adolescent externalizing behaviors. Racial differences may be important from a clinical and public health perspective, as the direction of the associations were different by race.

**Female orgasm frequency and time to pregnancy in pregnancy planners** Julia Bond\* Julia Bond Katharine O White Amelia K Wesselink Lauren A Wise

**Introduction:** The evolutionary origin of the female orgasm has been a subject of intense scientific debate. One hypothesis is that female orgasm facilitates conception, though no research has directly evaluated the relationship between female orgasm and time to conception.

**Methods:** We used data from Pregnancy Study Online (PRESTO), a North American preconception cohort study of pregnancy planners (2013-2022). Self-identified female participants completed questionnaires at enrollment and were followed up every eight weeks for pregnancy status. Beginning in March 2021, we invited female PRESTO participants to complete an optional survey related to sexual health that included a question about orgasm frequency during sexual intercourse in the past 4 weeks. Participants in our analysis were residents of the United States or Canada, aged 21-45, attempting pregnancy without the use of fertility treatment, in a relationship with a male partner, had <2 menstrual cycles of pregnancy attempts at enrollment, and completed the sexual health questionnaire within 2 months of enrollment (N=575). We used fully conditional specification methods to impute missing data on exposures and covariates. We used proportional probabilities regression to calculate fecundability ratios (FRs) and 95% confidence intervals (CIs) comparing orgasm frequency and time to pregnancy, adjusting for prespecified confounders.

**Results:** Twelve percent of the sample reported that they rarely or never orgasmed, 13% reported <half the time, 16% reported half the time, 23% reported >half the time, and 37% reported almost always or always with corresponding FRs and 95% CIs, compared to those who reported never/rarely orgasming, of 0.88 (0.61, 1.25), 0.81 (0.58, 1.14), 0.88 (0.64, 1.20), and 1.07 (0.80, 1.42), respectively, after adjustment for confounders.

**Conclusions:** There was no consistent pattern between orgasm frequency and time to pregnancy.

**Association between serum 25-hydroxyvitamin D and antimüllerian hormone** Anita

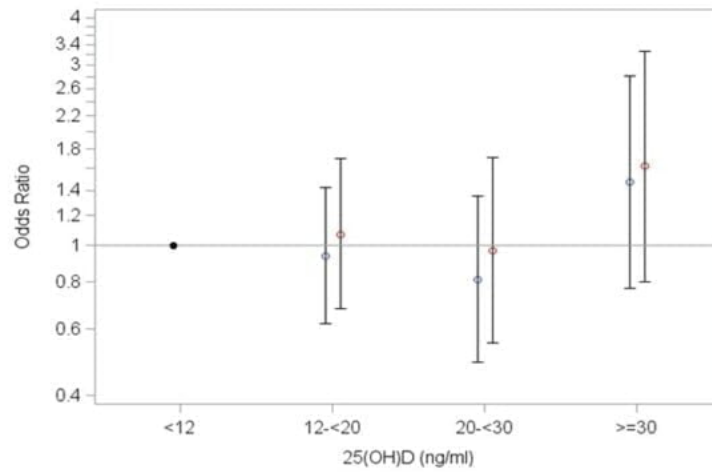
Subramanian\* Anita Subramanian Quaker E. Harmon Lia A. Bernardi Mercedes R. Carnethon Donna D. Baird Erica E. Marsh Anne Marie Z. Jukic

**Background:** Vitamin D has been associated with fertility and reproductive outcomes. Antimüllerian hormone (AMH) is considered a marker of ovarian reserve. The objective of this study was to examine the association between 25-hydroxyvitamin D [25(OH)D] concentration and ovarian reserve as measured by AMH.

**Methods:** Cross-sectional analysis of African American participants living in the Detroit, Michigan area, ages 23-35 years, using enrollment data from prospective cohort study designed to assess fibroid development. Participants (N=1591) included those without polycystic ovarian syndrome, pregnancy, and non-missing AMH or 25(OH)D measures at baseline. Linear regression was used to examine the associations between categorical 25(OH)D (ng/ml: <12, 12-<20, 20-<30, ≥30) and continuous natural log transformed AMH. Logistic regression was used to estimate the odds ratio for high or low AMH.

**Results:** Participants had a mean age of 29 years (standard deviation: 3.0 years). The 25(OH)D levels were low in this population with 29% of participants having levels less than 12 ng/ml, 41% with levels from 12-<20 ng/ml, 22% with levels from 20-<30 ng/ml, and 8% with levels ≥30 ng/ml. In models adjusted for age, BMI, hormonal contraceptive use, smoking and exercise, compared to 25(OH)D levels <12 ng/ml, AMH was 11% higher (95% CI: -0.07, 0.28) for 25(OH)D levels ≥30 ng/ml. Those with 25(OH)D ≥30 ng/ml, had higher odds of high AMH (>7.8 ng/ml, based on the 90<sup>th</sup> percentile) (OR [95% CI]: 1.47 [0.77, 2.81]). Exclusion of participants with irregular cycles and very high AMH, which might indicate undiagnosed PCOS, did not alter the association.

**Conclusion:** Higher 25(OH)D was imprecisely associated with higher AMH. To further explore this association, studies should examine populations with higher 25(OH)D levels and AMH measured at multiple time points to determine if long-term changes in 25(OH)D impact AMH levels.



Association between 25(OH)D and high AMH. The blue circles represent the odds ratio from the model which included all AMH values. The red circles represent the odds ratio from the model which excluded participants with irregular cycles and very high AMH values.



**Height, fertility and lifespan in men and women: an exploration from an evolutionary biology perspective using Mendelian randomization** C Mary Schooling\* C Mary Schooling Man Ki Kwok

**Background:** Identification of optimal early life conditions to promote health and longevity are crucial to population health, but difficult to discern observationally because of the timescale involved. Insights from evolutionary biology suggest an interplay between growth, reproduction, metabolism and longevity, possibly sex-specifically, such that optimal early life conditions might promote fertility instead of longevity, within the constraints of metabolism. To address these questions, we examined the associations of height and basal metabolic rate (BMR) with sex-specific fertility and lifespan using Mendelian Randomization (MR).

**Methods:** We used univariable and multivariable MR with sensitivity analysis taking advantage of summary statistics from the largest available publicly available suitable genome-wide association studies, i.e., the GIANT consortium of up to 0.25 million people for height and the UK Biobank of 0.5 million people for fertility, BMR and lifespan.

**Results:** BMR promoted fertility in men (0.05 children per standard deviation BMR, 95% confidence interval (CI) 0.03 to 0.07) but not women (-0.04, -0.07 to 0.003). Height was inversely associated with lifespan in women (-0.52 years per standard deviation of height, 95% CI -0.81 to -0.23) but not men (0.03, 95% CI -0.25 to 0.30) (p-value for interaction 0.007). Height also reduced fertility in women (-0.03, 95% CI -0.05 to -0.02) but not men (0.01, 95% CI -0.001 to 0.02). After allowing for BMR, height was positively associated with longevity in men and unrelated to fertility in men or women.

**Conclusions:** In men, BMR more than height appeared to underlie a trade-off promoting fertility at the expense of longevity. No such trade-off was evident in women. Optimal childhood conditions for longevity may differ by sex and might involve smaller size and/or slower metabolism, possibly at the expense of sex-specific effects on fertility.

**Early life trauma and adverse pregnancy outcomes in the Sister Study cohort** Sharonda M. Lovett\* Sharonda M. Lovett Jennifer M.P. Woo Dale P. Sandler

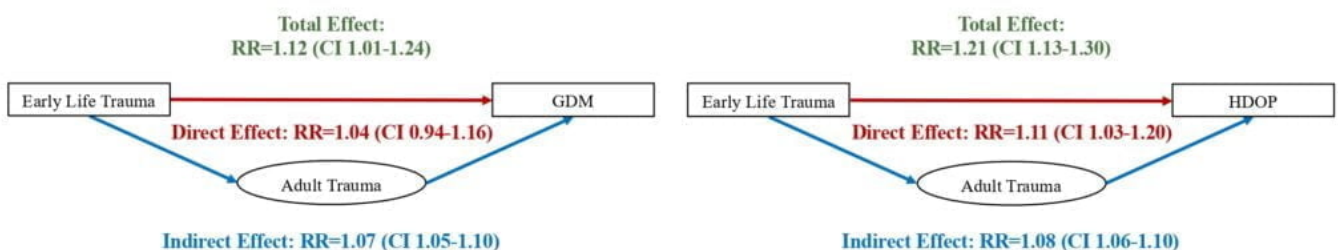
**Background:** Early life trauma (ELT) is hypothesized to increase risk for adverse pregnancy outcomes via pathways related to biological embedding of stress; however epidemiologic findings are mixed.

**Methods:** The Sister Study is a prospective cohort of U.S. women aged 35-74 years. ELT (<18 years) was assessed with an adapted Brief Betrayal Trauma Survey using conventional measures (e.g., binary measure, substantive domains) and a five-class latent variable of co-occurring traumas. Adverse pregnancy outcomes at baseline and diagnoses of gestational diabetes mellitus (GDM) or hypertensive disorder of pregnancy (HDOP: pre-eclampsia/toxemia or eclampsia) in pregnancies lasting ≥20 weeks were self-reported. We used log-binomial regression to estimate relative risks (RR) and 95% CIs among 34,879 parous women. Models were adjusted for age, race and ethnicity, and childhood socioeconomic position. We also investigated mediation by adult trauma.

**Results:** Across an average of 3 pregnancies per participant (range: 1-20), 4% reported GDM and 8% reported HDOP. Relative to no ELT, the RR associated with having any ELT was 1.12 (CI 1.01-1.24) for GDM and 1.21 (CI 1.13-1.30) for HDOP. Elevated risk of adverse pregnancy outcomes was observed for most domains of ELT. RR were highest for physical trauma (GDM RR=1.42, CI 1.18-1.71; HDOP RR=1.66, CI 1.47-1.88). In contrast, experiencing a major accident was not associated with risk of GDM (RR=0.95, CI 0.71-1.27), but risk of HDOP was elevated (RR=1.12, CI 0.93-1.36). The RRs for GDM and HDOP associated with high ELT in the latent class analysis were 2.00 (CI 1.49-2.68) and 2.02 (CI 1.64-2.48), respectively, compared to low ELT. Adult trauma mediated approximately 63% of the total effect between ELT-GDM and 45% of the total effect between ELT-HDOP.

**Conclusions:** Women reporting any ELT had increased risk of GDM and HDOP. Our findings add to growing evidence that ELT, independent of adult trauma, is associated with adverse pregnancy outcomes.

**Figure 1.** Model diagrams of the association between early life trauma (<18 years) with gestational diabetes mellitus (GDM) or hypertensive disorder of pregnancy (HDOP) via the direct effect and indirect effect of adult trauma while adjusting for age, race and ethnicity, and childhood socioeconomic position



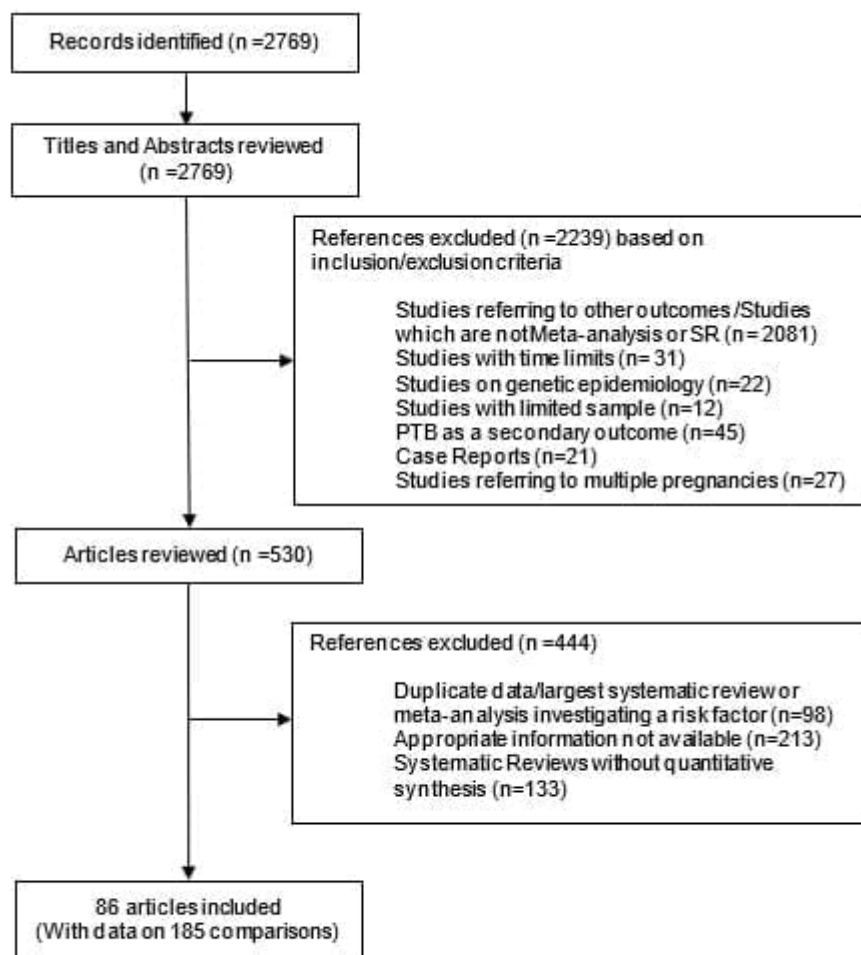
**Risk factors for preterm labor: an umbrella review of meta-analyses of observational****studies** Stefania Papatheodorou\* Stefania Papatheodorou Ioannis Mitrogiannis Vangelis Evangelou George Markydimas

**Background/Objective:** Preterm birth (PTB) defined as delivery before 37 gestational weeks, is a leading cause of neonatal and infant morbidity and mortality. We performed an umbrella review to summarize the evidence from meta-analyses of observational studies on risk factors associated with PTB, evaluate whether there are indications of biases in this literature, and identify which of the previously reported associations are supported by convincing evidence.

**Methods:** We searched PubMed and Google Scholar from inception to February 2021, to identify those meta-analyses examining associations between risk factors and PTB. For each meta-analysis, we estimated the summary effect size, the 95% confidence interval, the 95% prediction interval, the between-study heterogeneity, evidence of small-study effects, and evidence of excess-significance bias.

**Results:** Eighty-six eligible meta-analyses were identified, which included 1636 primary studies providing data on 185 associations, covering a wide range of comorbid diseases, obstetric and medical history, drugs, exposure to environmental agents, infections, and vaccines. 108 (58%) associations had nominally statistically significant findings at  $P < 0.05$ , while 36 (19%) were significant at  $P < 10^{-6}$ . 106 (57,3%) associations had large or very large heterogeneity. Evidence for small-study effects and excess significance bias was found in 48 (25,9%) and 15 (8,1%) associations, respectively. Seven risk factors provided robust evidence: amphetamine exposure, fetuses with isolated single umbilical artery, maternal personality disorder, sleep breathing disorders, prior termination of pregnancy with vacuum aspiration, low gestational weight gain, and interpregnancy interval following miscarriage less than six months.

**Conclusions:** A large proportion of meta-analyses of risk factors for PTB have caveats that threaten their validity. Some robust risk factors are not routinely screened for in clinical practice, such as maternal mental health and sleep breathing disorders. Incorporating screening programs including robust risk factors for PTB will promote the development and training of prediction models, in a way that offers new perspectives on both risk stratification and prevention of PTB.



**Figure 1.** Flow Diagram for the selection of included studies

**Assisted reproduction in Canada: mapping the policy landscape and exploring potential effects** Nichole Austin\* Nichole Austin

**Background:** Canadian coverage for assisted reproduction (ART) varies by province, ranging from nonexistent to complete. As treatment costs for procedures like in-vitro fertilization easily exceed \$10,000, provincial coverage may have a direct effect on the sociodemographic composition of the patient pool (and by extension, treatment outcomes); however, the impact of coverage remains largely unexplored in the Canadian context. In this analysis, we present new data on shifts in provincial coverage over time; we then use these data to estimate the relationship between coverage and selected population-level reproductive outcomes. We focus specifically on Quebec, which shifted from full coverage (2010) to restricted coverage (2015) and back again (2021).

**Data and Methods:** We merged our novel coverage dataset with publicly-available data on fertility and births from Statistics Canada (2000-2021). We identified two population-level indicators that could plausibly be influenced by changes to ART coverage: age-specific fertility rates (ASFRs) and multiple births. We used a controlled interrupted time series (CITS) design to assess coverage-induced changes in these outcomes in Quebec.

**Results:** Quebec's implementation of full ART coverage was associated with a notable and robust shift in the 40-44 ASFR (RD: .37, 95% CI: .10, .64), but no change in ASFRs among younger age groups, and no change in multiple births. Restricted coverage in 2015 was not associated with any changes in ASFRs or multiples compared to the preceding period.

**Conclusion:** Quebec's comprehensive ART coverage may have contributed to a meaningful increase in 40+ ASFRs. Notably, while declines in multiple births are commonly linked to the implementation of ART coverage, our analysis suggests that these declines may be attributable to other factors. As only a subset of the population accesses fertility treatment, individual-level data are required to better understand the effects of coverage.

**Pregnancy preferences among people living in US-Mexico border states: A longitudinal analysis** Isabel Muñoz\* Isabel Muñoz Elizabeth Gonzalez Miriam Parra Corinne Rocca

**Background:** Accurate measurement of pregnancy intentions is essential for understanding and addressing unintended pregnancy risk. Research has been hampered by crude and retrospective measurement.

**Methods:** We conducted a one-year longitudinal study among individuals aged 15-34 years with the capacity for pregnancy, seeking care from 23 health facilities in US-Mexico border states (2019-2023, n=2,010). Participants completed a new validated measure of feelings around pregnancy and childbearing (Desire to Avoid Pregnancy [DAP] scale, range 0-4, 4=higher preference to avoid pregnancy) at baseline and quarterly. We fit a random effects regression model, including a priori identified sociodemographic and health variables, to identify factors that shape prospective pregnancy preferences. We described the degree of quarterly change in pregnancy preferences and fit a random effects multivariate model to identify predictors.

**Results:** At baseline, the mean DAP score was 2.35 (SD:1.10) on the 0-4 scale. Importance of religion and relationship status and quality were among the predictors most strongly associated with desire to avoid pregnancy (very important vs. no religion, coeff=-0.36 [-0.46,-0.26]; no main partner vs. good relationship with cohabitating partner, coeff=0.29 [0.24,0.35]). Between quarterly surveys, 5% of DAP scores increased by one point or more, and 4% decreased by that amount. The strongest predictor of a subsequent quarterly change in DAP score in either direction was being in a poor quality romantic relationship (vs. good romantic relationship, OR: 2.21 [1.43,3.40]).

**Conclusions:** When measured prospectively with a valid instrument, people hold ranges of feelings about a potential pregnancy that can change over short periods of time, particularly according to relationship characteristics. Understanding the time varying and complex nature of pregnancy preferences is crucial when reporting on the risk of unintended pregnancies.

**Investigation of intrauterine exposures and adenomyosis risk using a population-based case-control study employing two control groups** Mandy S. Hall\* Mandy S. Hall Holly R. Harris Sawsan As-Sanie Kristen Upson

Adenomyosis is characterized by the presence of endometrial tissue within the myometrium. As the gold standard for diagnosis requires hysterectomy, control selection for a case-control study is challenging. Adenomyosis risk may increase with disruption during fetal development. Yet, few studies have investigated this critical developmental window. We investigated intrauterine exposure to indicators of maternal stress including age, stillbirth history, and participant birth order and maternal cigarette smoking on adenomyosis risk. Among enrollees ages 18-59 of an integrated healthcare system in Washington, cases (n=386) had incident, pathology-confirmed adenomyosis diagnosed between 2001-2006. Two control groups were employed: hysterectomy controls (n=233) and randomly selected age-matched enrollees with an intact uterus ("population controls", n=323). A family history questionnaire was mailed to collect data on early-life factors. We estimated ORs and 95% CIs using logistic regression, adjusting for age, reference year, maternal smoking, birthweight, and first-born status. Comparing cases to population controls, participants whose mothers were ages  $\leq 19$  (vs. ages 25-29) at participant's birth had 80% increased adenomyosis risk (OR 1.8, 95% CI: 0.9, 3.5). Participants who were the fourth or later live birth (vs. first-born) had 40% increased adenomyosis risk (OR 1.4, 95% CI: 0.8, 2.3). In analyses using hysterectomy controls, these associations were attenuated. However, maternal stillbirth history before the participant's birth was associated with twice the risk of adenomyosis (OR 2.1, 95% CI: 1.1, 3.8). Among never-smoking participants, we observed intrauterine exposure to cigarette smoking was associated with 30-40% increased adenomyosis risk (hysterectomy controls: OR 1.3, 95% CI: 0.7, 2.2; population controls: OR 1.4, 95% CI: 0.9, 2.3). Our findings suggest an altered intrauterine milieu may increase adenomyosis risk in adulthood and warrant further investigation.

**LATEBREAKER**

Reproductive

**Average Treatment Effect of Endometriosis on Miscarriage** Amanuel Gebremedhin\* Amanuel Gebremedhin Gizachew Tessema Gavin Pereira

**Background:** Endometriosis is a chronic condition where endometrial-like tissue grows outside the uterus, leading to inflammation, pain, and subfertility. Although there has been a growing interest in the potential association between endometriosis and miscarriage, the findings to date are inconclusive.

**Objective:** To estimate the causal association between endometriosis and a miscarriage.

**Study design:** A population-based retrospective cohort study was conducted among 468,778 eligible women who contributed 912,747 singleton livebirths between 1980 and 2015 in Western Australia. We used probabilistically linked perinatal and hospital separation data from the Midwives Notification System and Hospital Morbidity Data Collection databases. Our exposure of interest (Endometriosis) and all the outcomes were ascertained using ICD-9/10 codes. We used a doubly robust estimator to estimate the effect (*average treatment effect*) of endometriosis on miscarriage.

**Results:** There were 19,476 singleton livebirths among 8,874 women diagnosed with endometriosis. Using a doubly robust estimator, we found pregnancies in women with endometriosis to be associated with an increased risk of miscarriage (relative risk, 2.16, 95% confidence interval, 1.63 – 2.86). The observed association persisted when stratified by the use of Medically Assisted Reproduction (MAR), with a slightly elevated risk among pregnancies conceived spontaneously. MAR does not modify but mediates the association between endometriosis and miscarriage. Our causal mediation analyses suggest that 34% of the effect of endometriosis on miscarriage was mediated through MAR.

**Conclusion:** In this large population-based cohort, endometriosis is associated with an increased risk of miscarriage, and the effect is mediated through MAR. The study paves the way for future research on mechanisms underlying the relationship between endometriosis and miscarriage.



**Trends of sex ratio at birth and its associations with sociodemographic factors among Asian American subgroups in the U.S. from 2016 to 2021** Hyelee Kim\* Hyelee Kim Bennett Leventhal Yeojin Julie Kim Patty Lee Nadia Diamond-Smith

### Objective

Using the Natality Data of the US National Vital Statistics System, this study describes the male-to-female sex ratio at birth (SRB) and investigates its association with sociodemographic factors and birth order among Asian American (AA) subgroups from 2016 to 2021.

### Methods

AAs were defined as mothers or fathers whose ancestors were from Asian countries, including but not limited to Asian Indian, Chinese, Filipino, Vietnamese, Korean, and Japanese (top size groups). Within each AA, we estimated changes in SRBs by year and birth order and then performed the multivariable logistic regression for female birth, adjusting for maternal variables (age, education, and nativity), marital status, birth order, and supplemental food program participation.

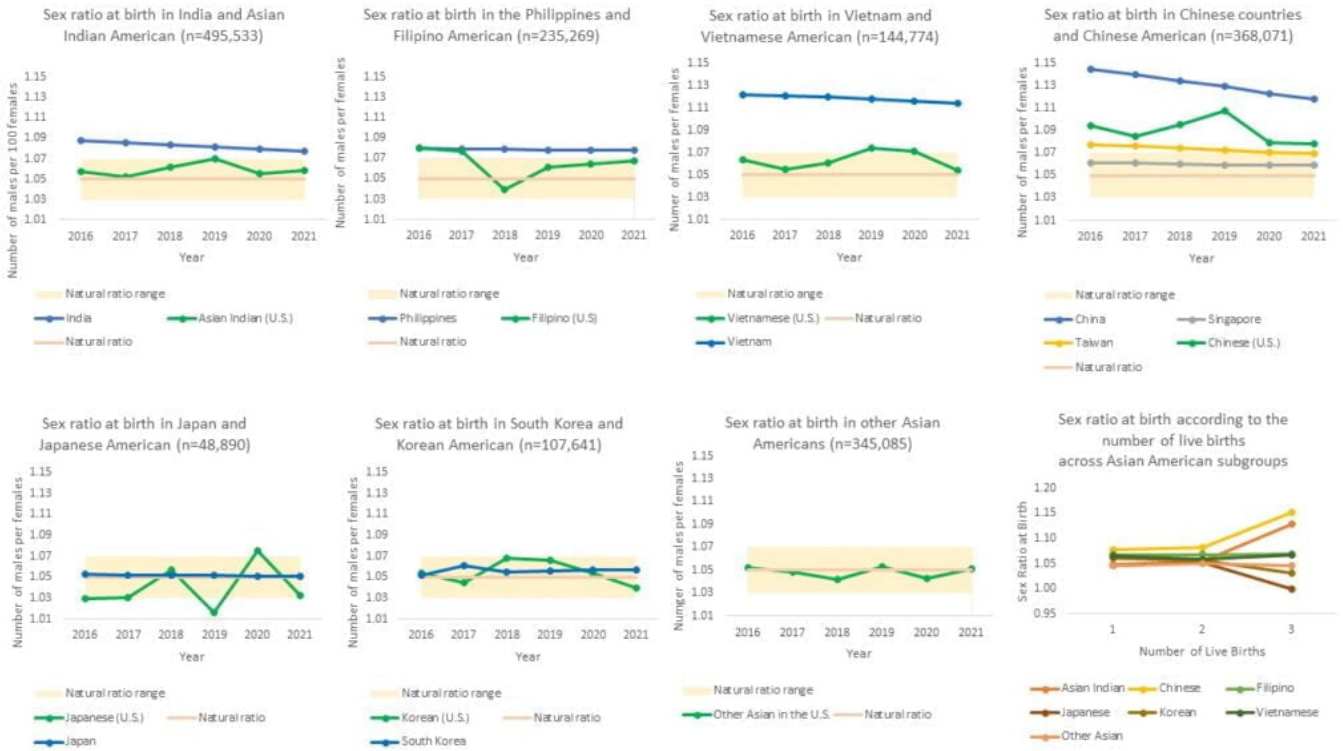
### Results

The mean SRB for all 1,668,875 AAs was 1.06. SRBs per AA were lower than those in Asian countries or fluctuated around the natural ratio (1.05). However, stratified by birth order, some AA groups' SBR became away from the natural ratio in the 3rd birth.

In the adjusted analysis, unmarried AAs had greater odds of female birth than did the married among Asian Indians (aOR 1.03; 95% CI 1.00-1.06) but lower odds in Koreans (aOR 0.95; 95% CI 0.90-0.99) and Chinese (aOR 0.98; 95% CI 0.97-1.00). The 3<sup>rd</sup> child had lower odds of female birth than the first child in Asian Indians (aOR 0.93; 95% CI 0.91-0.95) and Chinese (aOR 0.94; 95% CI 0.91-0.96). Foreign-born mothers had lower odds of female birth than US-borns in Asian Indians (aOR 0.97; 95% CI 0.95-0.98) and Chinese (aOR 0.95; 95% CI 0.94-0.97). Mothers with high school degrees had greater female SRBs than did Filipino mothers with a college degree (aOR 1.02; 95% CI 1.00-1.04) but lower odds in Japanese (aOR 0.95; 95% CI 0.90-1.00).

### Conclusion

Amongst AAs, different subgroups have heterogeneous SRBs. These findings suggest a need to ensure equity and full access to reproductive health care as well as long-term plans to address gender inequality and empower women.



**Blood lead concentrations and uterine fibroid incidence: A prospective study** Kristen Upson\*  
Kristen Upson Mandy S. Hall Quaker E. Harmon Robert O. Wright Lauren A. Wise Ganesa Wegienka  
Ruth J. Geller Amelia K. Wesselink Birgit Claus Henn Janet E. Hall Erik J. Tokar Donna D. Baird

Toxic metal lead exhibits mutagenic and hormonal properties that may contribute to the development of uterine fibroids (smooth muscle neoplasms). Prior human studies of lead and fibroids have yielded discrepant results. However, none were prospective, screened for fibroids by ultrasound, or accounted for progestin-only injectable contraceptive use and recent birth, factors associated with increased blood lead concentrations and decreased fibroid incidence. We investigated the association between blood lead concentrations and fibroid incidence in the Study of Environment, Lifestyle & Fibroids, a prospective cohort study of 1,693 Black women ages 23-35 years in the Detroit, Michigan area. Participants underwent transvaginal ultrasound at baseline and every 20 months for 5 years to detect fibroids  $\geq 0.5$ cm in diameter. Baseline whole blood lead concentrations were measured using inductively coupled plasma-mass spectrometry-triple quadrupole. Among 1,215 fibroid-free participants, we conducted Cox regression to estimate adjusted hazard ratios (aHRs) and 95% CIs for the association between quartiles of lead and fibroid incidence, adjusting for time-varying factors of parity, years since last birth, years since last depot medroxyprogesterone acetate (DMPA) use, body mass index, smoking, education, and blood cadmium concentrations. Median blood lead concentration was 0.47  $\mu\text{g}/\text{dl}$  (IQR: 0.36-0.65). Select blood lead quartiles (Q2 and Q3) were associated with decreased fibroid incidence (vs. Q1) (Q2: aHR 0.87, 95%CI: 0.63-1.19; Q3: aHR 0.68, 95%CI: 0.48-0.97; Q4: aHR 0.94, 95%CI: 0.65-1.35). Sensitivity analyses excluding smokers, DMPA use in past 2 years, and birth in past 3 years, and restricting follow-up to the first 20-month visit yielded similar results. Our data suggest a possible non-linear association between blood lead concentrations and fibroid incidence. This work is a vital first step in a larger research program to evaluate metal mixtures and fibroid incidence.

**Racial disparities and metals exposure among children living near coal-fired power plants are associated with asthma** Oludesola Ogunesan\* Oludesola Ogunesan Kristina Zierold Lonnie Sears John Myers

**Background:** Asthma is a public health issue affecting millions of children around the world. Previous studies indicate an association between metal exposure and decreased pulmonary function and asthma in children. Asthma pathogenesis in children indicates the key role of metal exposure as a type 2 inflammatory response to childhood exposure. The purpose of this study was to assess asthma in children living near coal-fired power plants.

**Methods:** This study was a community-based study in Kentucky with children aged 6-14 years living near two coal-fired power plants. Nail samples were collected and analyzed using inductively coupled plasma mass spectrometry (ICP-MS). Medical history of asthma was defined as a parent report of having medical breathing problems. Logistic regression and the Wilcoxon test were used to evaluate the relationship between metal(loid)s, race, and asthma.

**Results:** The prevalence of asthma was 74% in black children and 26% in white children. Our result shows that children who have asthma have a significantly higher body burden of cadmium (OR=2.1; 95%CL = 1.2-3.9) and arsenic (OR=1.8; 95%CL = 1.0-3.2) compared to children who do not have asthma. Non-white children are 4.5 times more likely to have cadmium (95%CL = 2.3-8.2;  $p < 0.0001$ ) and 4.0 times more likely to have arsenic (95%CL = 2.2-7.3;  $p < 0.0001$ ) in their nails compared to white children.

**Conclusions:** Findings suggest that exposure to metals is associated with asthma in children, especially among non-white children. Given the significant health burden caused by childhood exposure to metals, regulations to prevent these concerns are essential and required to be recognized as a public health goal to improve children's health.

**Association between age at first respiratory syncytial virus infection and child asthma**

**inception: prospective birth cohort study** Akihiro Shiroshita\* Akihiro Shiroshita Tebeb Gebretsadik Christian Rosas-Salazar William Dupont Larry Anderson Tina V. Hartert

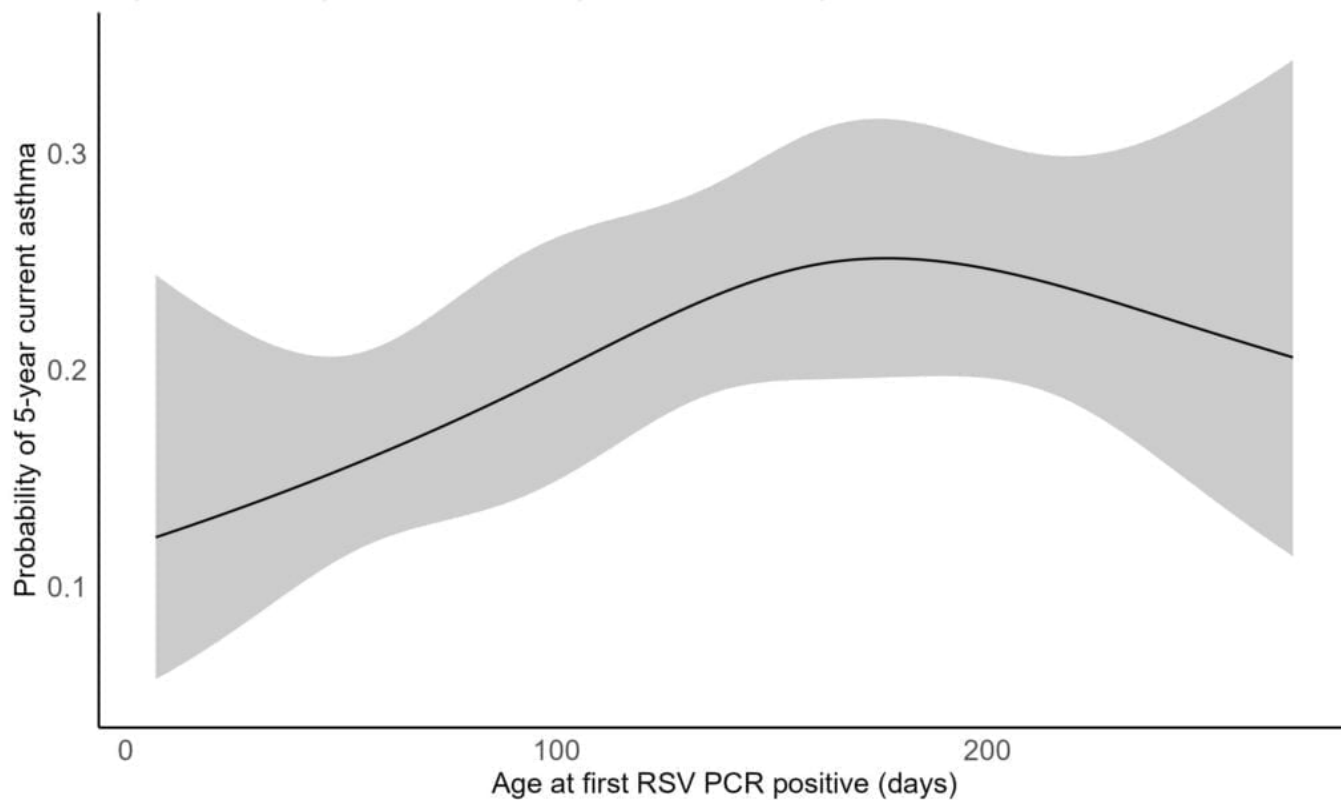
**Introduction:** No studies have determined if there is an age during infancy when RSV infection confers the greatest risk for subsequent childhood asthma.

**Methods:** Our study is a prospective population-based birth cohort study. Term, healthy infants in the middle Tennessee region, the United States were enrolled from 2012 through 2013. First RSV infection was determined during each infant's first year of life by biweekly active and passive surveillance, and RSV infection during the first year of life was determined by RSV PCR or serology. Our exposure of interest was the infant's age at first RSV infection. The date of infection was a positive nasal RSV PCR. For infants who were defined only by RSV serology at the 1-year follow-up visit, we imputed the date of the first RSV infection by random draw during each RSV season. The primary outcome was 5-year current asthma. We assessed the association of 5-year current asthma and infant's age at first RSV infection using restricted cubic spline with 4-knots using multivariable logistic regression.

**Results:** A total of 1,946 children were enrolled in the INSPIRE cohort and among them, 944 infants were infected with RSV during their first year of life; 361/944 (38%) were detected by nasal PCR and 582/944 (62%) were detected only by RSV serology. At the five-year follow-up, 274/944 (29.3%) of the infants had missing data in 5-year current asthma, and 139/670 (20.7%) of the infants with RSV infection during the first year of life had asthma. The fitted logistic regression curve demonstrated a non-linear association between age and asthma with a peak during mid-infancy of the first RSV infection but did not reach statistical significance.

**Conclusions:** First infection with RSV during mid-infancy may be associated with a higher risk of subsequent childhood asthma compared with infection during early infancy. However, for the identification of a narrow age susceptibility band with precision, a larger study population is needed.

Imputed model (Restricted cubic spline with 4 knots)



**LATEBREAKER**

Respiratory

**Patterns of healthcare utilization for RSV, influenza, pneumonia among children under age 6**

Djeneba Audrey Djibo\* Djeneba Audrey Djibo Charlalynn Harris Jennifer Pigoga Cheryl N. McMahill-Walraven

**Background:** Respiratory syncytial virus (RSV), influenza viruses, and acquired pneumonia represent a large public health burden as these generate an extensive number of healthcare visits and lead to thousands of deaths yearly. Recently, the COVID-19 pandemic may have influenced the previously observed seasonality and severity of health outcomes related to RSV, pneumonia, and influenza.

**Methods:** Children  $\leq 5$  years old with healthcare visits and diagnoses of RSV, influenza, or pneumonia among research-eligible enrollees of a large U.S. commercial health plan from January 2020 to December 2022 were included in this study. Rates and percent change of diagnoses and visits per 100,000 eligible enrolled children were calculated by calendar month and compared using ANOVA.

**Results:** The peak rates of children diagnosed were 2815.2, 544.5, and 147.8 per 100,000 for influenza, pneumonia, and RSV, respectively, during the study period. The largest monthly increases in diagnosis rate were seen in May 2021 (201%) and October 2022 (195%) for RSV, December 2021 (261%) and October 2022 (286%) for influenza, and May 2021 (88%) and October 2022 (71%) for pneumonia. There was a statistically significant increase in the rate of young children diagnosed with RSV ( $p=0.02$ ) or influenza ( $p=0.009$ ) in October to December of 2022, compared to the same months in 2021.

**Conclusions:** While the overall healthcare utilization due to influenza and pneumonia maintained historical seasonality, there were clear surges in RSV-related visits and diagnoses in the second quarter of 2021 and the last quarter of 2022. RSV infections have historically peaked in the December to February months pre-COVID-19 pandemic. Primary prevention tools such as vaccination are not currently available for RSV among the young pediatric population; therefore, the burden and seasonality will likely continue to be strongly influenced by other public health stressors.

**An Online Directory of Food Environment Data Sources: The Food Environment Electronic Database Directory** Edwin McCulley\* Edwin McCulley Sarah Boise Aldo Crossa Analee Etheredge Gina Lovasi Felicia Bayer

The food environment can promote or impede the health of communities; therefore, measuring it is critical to understanding how it impacts population health. The complexity of the food environment is reflected in ongoing challenges surrounding how researchers define and measure it across data sources. Additionally, many food environment data sources can be linked to health data allowing for observational studies which can identify important policy levers and inform evidence-based action strategies to improve health. Building on a strategic partnership with the New York City Department of Health and Mental Hygiene, and with support from the Mid-Atlantic Regional Public Health Training Center, we developed and launched the Food Environment Electronic Database Directory (FEED), a web-based tool for up-to-date information on food environment data sources. We identified data sources based on recent literature and experience within our academic and practice-based institutions, independently reviewed each source, and extracted source details and information related to the food environment. In addition to basic information regarding access permissions and spatiotemporal details, each source is annotated with strengths and limitations, is mapped to food environment constructs, and includes relevant publications. FEED launched in 2022, with plans to update the tool annually. FEED is currently available at [www.foodenvironmentdirectory.com](http://www.foodenvironmentdirectory.com). FEED can be used to guide researchers and local health departments in the selection of data sources and the operationalization of food environment measures. FEED also provides public health researchers with the information that they need to make evidence-based decisions surrounding the food environment, its measurement, and population health.



**LATEBREAKER**

## Screening

**Psychometric Properties of the Arabic Version of the Pittsburgh Sleep Quality Index in Hemodialysis Patients** Ahmed Albatineh\* Ahmed Albatineh Abdullah Al-Taiar Reem Al-Sabah Bashar Zogheib

The Pittsburgh Sleep Quality Index (PSQI) is widely used in screening for self-reported sleep disturbances in clinical groups or healthy populations. The literature lacks rigorous psychometric evaluation of the Arabic Pittsburgh Sleep Quality Index (A-PSQI) in hemodialysis (HD) patients. This study aims to estimate reliability, extract, and test the underlying factor structure of the A-PSQI in HD patients, and determine its suitability for this clinical group. In a sample of 461 HD patients (287 males, 62.3%) recruited from all health districts in Kuwait., inter-components, between A-PSQI components, and its global score correlations were estimated. Component analysis was conducted to identify inconsistent components with the rest. Cronbach's  $\alpha$  and McDonald's  $\omega$  estimated reliability. Stability and convergent validity were assessed. Construct validity was explored by exploratory factor analysis (EFA). Confirmatory factor analysis (CFA) was conducted to test factor structure. Results indicated that patients had a median (Interquartile Range) age of 54 (22) years. The A-PSQI had a mean (SD) score of 7.1 (3.65). The Cronbach  $\alpha = .634$  and McDonald  $\omega = 0.62$  indicated moderate reliability. EFA resulted in two factors highly correlated (0.83,  $PV < 0.001$ ) with A-PSQI global score indicating two distinct constructs. CFA provided weak evidence supporting the one-factor model, but the two-factor model (explained 51.8% of total variance) without the "use of sleep medication" item, which has the smallest corrected-item total correlation, showed a good fit with the smallest AIC. Conclusion The A-PSQI seems moderately reliable to screen for sleep disorders in HD patients. Future research on scoring in the two-factor model is warranted. It can help clinicians better understand sleep disturbance and improve the instrument's sensitivity.

**Sense and Sensibility: Reasons Behind Cervical Screening Non-attendance** Anna Altova\*

Anna Altova Michala Lustigova Ivana Kulhanova

Cervical screening is a crucial tool for reducing cervical cancer burden, but uptake is still insufficient in many countries with implemented screening programmes. To investigate the reasons behind cervical screening non-attendance, we conducted a mixed-methods study, combining two data sources. First, we analysed data from a representative survey (N=902) to determine the reasons behind cervical screening non-attendance among Czech women. Second, we conducted semi-structured interviews with nine women who do not attend the screening, to build a typology of reasons behind non-attendance. In our survey sample, 35.5% of women were considered non-attendees. Their most common reasons for non-attendance were 'not experiencing any symptoms' (37.5%), 'fear of cancer diagnosis' (23.8%), and 'fear of examination procedure' (20.9%). Using binary logistic regression, we found no differences between women who declared the most common reasons based on their age, education, and marital status. Furthermore, preliminary results from the qualitative part of the research indicate that there could be several basic underlying causes of screening non-attendance: negative previous experience with healthcare and/or healthcare professionals; poor health literacy; traditional barriers (e.g., lack of time, lack of finances) and possibly personal traits (laziness, lack of interest in health). To improve cancer prevention, it is essential to identify barriers to screening attendance. Since most of the women have mentioned negative previous healthcare experiences in the interview, it is of great importance to invest in proper medical professionals' training to mitigate such experiences. Although this study is limited to one European country, we believe that perceptions about screening are similar globally and may be even more pronounced in countries with less-developed healthcare, opening opportunities for future research.

**Neighborhood green spaces and child physical and mental health outcomes: An exploratory geospatial analysis among racially and ethnically diverse children** Junia de Brito\* Junia de Brito Allan Tate Christine Prissel Angela Fertig Mark Pereira Jerica Berge

**Background:** Emerging evidence suggests that neighborhood green space exposure is an important structural determinant of children's physical and mental health. However, evidence is limited among children living in socioeconomically disadvantaged households. We explored the relationship between neighborhood green space access on children's physical activity (PA), sedentary behavior (SB), BMI percentile, cortisol levels (chronic stress), and emotional health.

**Methods:** The analytic sample included cross-sectional baseline data from the *Family Matters* study, a longitudinal cohort of 1307 racially/ethnically diverse families with children (aged  $7 \pm 1.5$  yrs) from Minneapolis-St. Paul, MN. Participant addresses were matched to corresponding US 2010 Census Tracts ( $n=367$ ). The presence of any park within each census tract was obtained using the National Neighborhood Data Archive to indicate green space access. Parents self-reported child's PA, SB, and emotional health. Children's BMI percentile were retrieved from electronic medical records. Hair cortisol levels were measured in a subsample of 260 children ( $n=150$  census tract). Random effects linear regressions were adjusted by the index of concentration at the extremes, child age, sex, race and ethnicity, and household income.

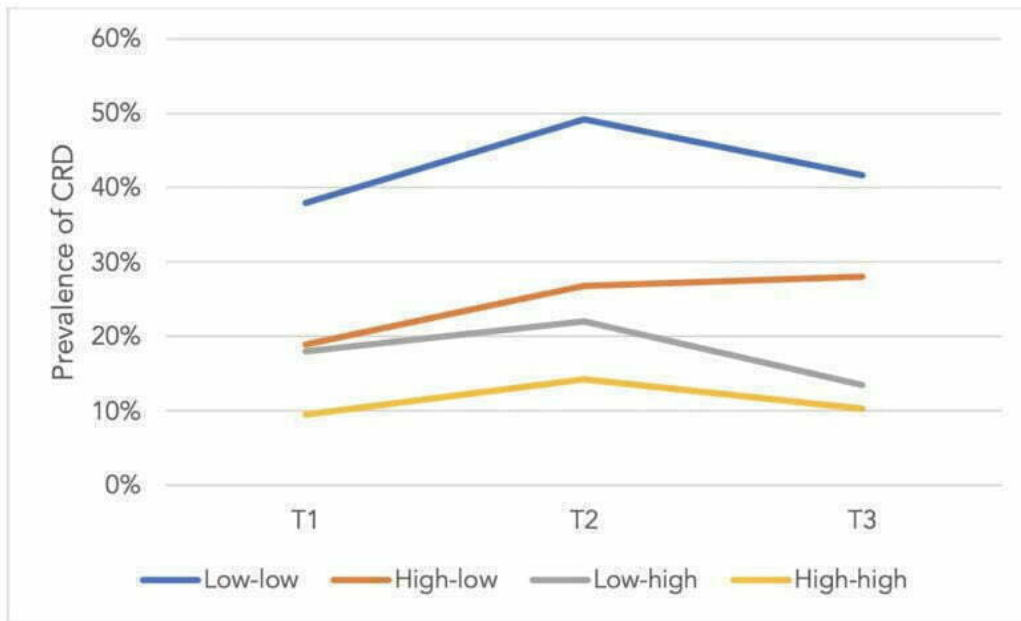
**Results:** Findings indicated 3% of the sample lived in a census tract without any parks, 76% with 1-5 parks, 14% with 6-10 parks, and 6% with  $\geq 11$  parks. Adjusted analysis revealed that green space access was associated with vigorous-intensity PA (0.81 hours/week; 95% CI 0.1, 1.5) and cortisol (-141 pg/mg; 95% CI -261, -22) in children. We found no evidence of association with the remaining outcomes.

**Conclusions:** Green space access was positively associated with 49 min/week of vigorous-intensity PA and decreased hair cortisol levels in children. Future work should include smartphone location tracking, momentary assessments, and examine participants' perceived benefits/barriers of green space access and use.

**Depression during the COVID-19 pandemic: the experience of Four Americas** Catherine Ettman\* Catherine Ettman Gregory H. Cohen Salma M. Abdalla Brian C. Castrucci Rachel H. Bork Sandro Galea

The prevalence of depression in U.S. adults during the COVID-19 pandemic has been high overall and particularly high among persons with fewer assets. Building on previous work on assets and mental health, we document the burden of depression in groups based on income and savings during the first two years of the COVID-19 pandemic. Using a nationally representative, longitudinal panel study of U.S. adults (N=1183) collected in April-May 2020 (T1), April-May 2021 (T2), and April-May 2022 (T3), we estimated the adjusted odds of reporting Clinically Relevant Depression (CRD)—defined as a score of  $\geq 10$  on the Patient Health Questionnaire-9 (PHQ-9)—at any time during the COVID-19 pandemic using generalized estimating equations (GEE). The prevalence of CRD was consistently high in Spring 2020, Spring 2021, and Spring 2022 with 26.8% of U.S. adults reporting CRD in Spring 2022. We found that there were four distinct “Americas” that experienced different CRD trajectories over the COVID-19 pandemic, grouped by income ( $\geq \$65,000$ ) and savings ( $\geq \$20,000$ ) categories. Low income-low savings (low-low) America had the highest level of CRD across time, reporting 4.9 times the odds (95% CI 3.32, 7.21) of CRD at any time relative to high income-high savings (high-high) America. The prevalence of CRD across T1, T2, and T3 was 41% for low-low America, 24% for high-low America, 19% for low-high America, and 12% for high-high America. Four Americas defined by income and savings groupings experienced different depression trajectories over the course of the COVID-19 pandemic. Persons with low income and low savings reported 4.9 times the odds of clinically relevant depression as persons with high income and high savings over the course of the pandemic. While discussions on equity often focus on income, incorporating savings may provide insights into population experiences and mental health.

Figure 1. Weighted prevalence of Clinically Relevant Depression (CRD) by the Four Americas across time.



Note: T1: April - May 2020; T2: April - May 2021; T3: April - May 2022. The Four Americas: "low-low" represents low income with low savings, "high-low" represents high income with low savings, "low-high" represents low income with high savings, and "high-high" represents high income with high savings. Low income was defined as below \$65,000 and low savings was defined as below \$20,000. T1 used T1 weights, T2 used T2 weights, T3 used T3 weights. CRD defined by PHQ-9 score  $\geq 10$ .

**Adverse childhood experiences and risk of spontaneous abortion** Sharonda M. Lovett\*

Sharonda M. Lovett Renée Boynton-Jarrett Yael I. Nillni Amelia K. Wesselink Ruth J. Geller Mary D. Willis Elizabeth E. Hatch Kenneth J. Rothman Lauren A. Wise

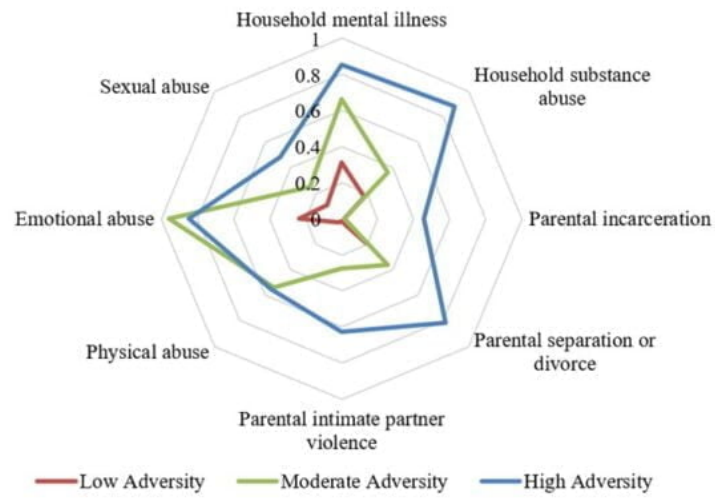
**Background:** Adverse childhood experiences (ACEs) are associated with incidence of spontaneous abortion (SAB, pregnancy loss <20 weeks' gestation), but no prior study has investigated different patterns of adversity. We prospectively evaluated the association between ACEs and SAB using a three-class latent measure.

**Methods:** We analyzed data from Pregnancy Study Online (PRESTO), a preconception study of North American couples aged 21-45 years. On the psychosocial supplemental questionnaire, participants reported experiences of ACEs (instrument adapted from Behavioral Risk Factor Surveillance System) and childhood social support (modified Berkman-Syme Social Network Index; high social support: score  $\geq 4$ ). Over follow-up, participants reported pregnancies and SABs. We conducted latent class analysis to identify subgroups of participants by different patterns of adversity. We fit multivariable-adjusted Cox models to estimate hazard ratios (HR) and 95% CIs, using gestational weeks as the time scale. Models were adjusted for age, race/ethnicity, and childhood socioeconomic position.

**Results:** Among 5,059 participants, 56% experienced  $\geq 2$  ACEs and 23% reported SAB. Using latent class measures, we observed a higher SAB risk among participants reporting high adversity (HR=1.14, CI 0.94-1.38) and moderate adversity (HR=1.08, CI 0.93-1.25) compared with low adversity. HRs for moderate adversity were attenuated among participants who reported high childhood social support (HR=0.84, CI 0.58-1.23), but not high adversity (HR=1.13, CI 0.71-1.82) vs. low adversity. High adversity was more strongly associated with SAB risk among younger participants (aged <30 years: HR=1.34, CI 1.00-1.80;  $\geq 30$  years: HR=0.97, CI 0.75-1.26).

**Conclusions:** Greater exposure to ACEs was associated with a slightly higher incidence of SAB. Associations were stronger among younger participants, for whom adverse experiences are more recent, and were attenuated among those reporting high childhood social support.

**Figure 1.** Radar plot of adverse childhood experiences (3 clusters) among PRESTO participants who completed the psychosocial supplemental questionnaire, June 2013 - September 2022



**Note:** Figure illustrates different patterns of adversity based on posterior probabilities of latent class membership across eight domains of adverse childhood experiences.

**The Effect of Collateral Consequence Policies on Mental Health among Adults with****Criminal Records** Kaitlyn Berry\* Kaitlyn Berry John Robert Warren Christopher Uggen Darin J. Erickson Nancy E. Sherwood Rachel Widome

**Introduction:** Approximately 64 million adults in the US have some form of a criminal record. This population has worse mental health than the general population. Additionally, people with criminal records face substantial barriers due to policies that limit access to resources such as employment and public assistance. However, little is known about the link between these policies and mental health among people with criminal records.

**Methods:** We linked family-level survey data from the Future of Families and Child Wellbeing Study to state-level policy data compiled by Legal Action Center in their 2009 *After Incarceration: Roadblocks to Reentry* report. We considered adults to have a criminal record if they reported having ever been booked/charged with a crime, convicted, or incarcerated (n=1,520). Participants were classified as living in states with low, moderately low, moderately high, or high barriers for people with criminal records (**Figure 1**). Using mixed effects logistic regression, we assessed the association between state-level policy barriers and major depression among adults with criminal records. This model included random effects for state and family unit and adjusted for sex, race, age, state incarceration rates, state poverty rates, and a measure of where states' policies tend to fall on the political spectrum.

**Results:** Depression was more common among adults who had been booked/charged (23%), convicted (26%), and incarcerated (24%) than among adults without a criminal record (14%). However, similar prevalence of depression was observed among adults with criminal records living in states with low [26% (95% CI: 21-32%)], moderately low [20% (14-25%)], moderately high [23% (18-28%)], and high [24% (19-29%)] barriers for people with criminal records.

**Conclusion:** We did not find evidence that living in a state with more policy barriers for people with criminal records increased risk of depression for adults with criminal records.





**Associations between area-level income inequality and health-related school absenteeism: Evidence from the COMPASS study** Stephen Hunter\* Stephen Hunter Carla Hilario Karen A. Patte Scott T. Leatherdale Roman Pabayo

**Background:** Income inequality is theorized to impact health. However, evidence among adolescents is limited. This study examined the association between income inequality and health-related school absenteeism in adolescents.

**Methods:** Data for this investigation are from adolescents (n= 74,501) attending secondary schools (n=136) who participated in the 2018-19 wave of the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking, and Sedentary behaviour (COMPASS) study. Chronic- (missing  $\geq 3$  days of school in the previous four weeks) and problematic- (missing  $\geq 11$  days of school in the previous four weeks) health-related school absenteeism was self-reported. Income inequality was assessed via the Gini coefficient at the census division level. Multilevel modelling was used to assess the relationship between income inequality and the likelihood of health-related absenteeism. Race and gender were tested as effect modifiers.

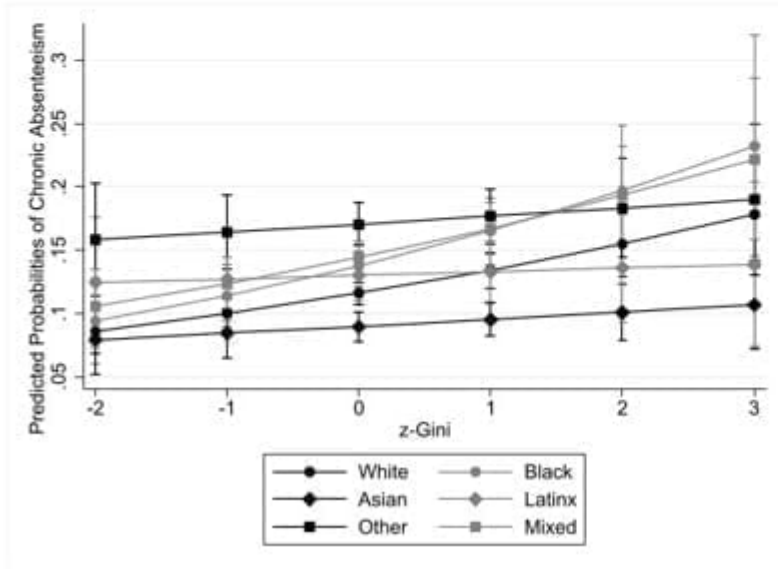
**Results:** A SD-unit increase in Gini Coefficient was associated with a higher likelihood of chronic- and problematic- health-related school absenteeism (Chronic: OR = 1.17, 95% CI: 1.06, 1.29; Problematic: OR = 1.27, 95% CI: 1.09 to 1.47). Increased predicted probabilities were observed among students who identified as either White, Black, or Mixed, while protective associations were observed among students who identified as Asian or Other. No associations were modified by gender.

**Conclusion:** Income inequality demonstrated unfavourable associations with health-related school absenteeism. which appeared to be modified by racial identity. Interventions targeting health-related school absenteeism in areas with higher income inequality should consider the varying impacts for different racialized groups.

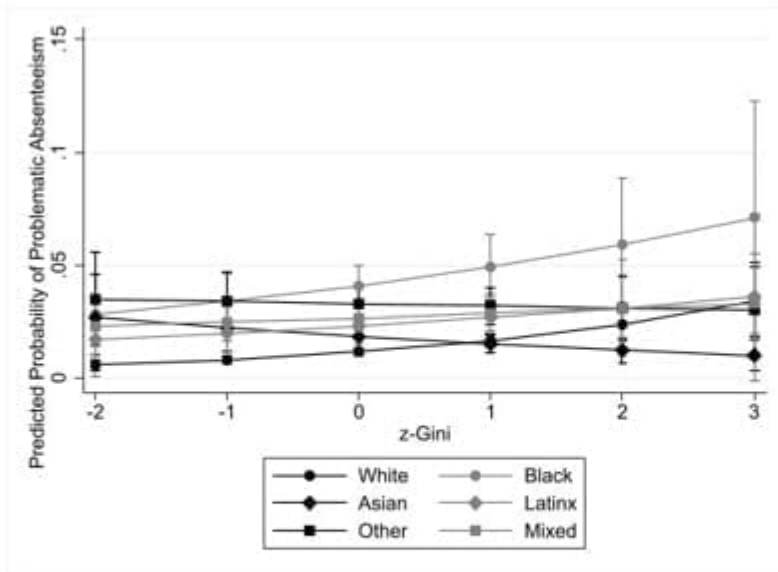
Figure

Predicted probabilities of health-related school absenteeism from income inequality by racial identity (COMPASS 2018-19)

A)



B)



Note: Predicted probabilities are modelled across the range of z-Gini coefficients by student racial identity for A) Chronic health-related school absenteeism and B) Problematic health-related school absenteeism

**Intersectional Suicide Deaths in the United States from 2000-2020** Jonathan Platt\* Jonathan Platt John Pamplin Amanda Sursely Katherine Keyes

Utilizing an intersectional framework, this project estimated trends in the spatiotemporal distribution of all US suicide deaths from 2000-2020 across race, sex, education.

Data from the US National Vital Statistics System included all ICD-10 coded suicide cases. Intersectional groups were defined by race: (American Indian/Alaska Native (AI/AN), Asian/Pacific Islander (A/PI), Black, White); sex (male, female), and education (<college degree, ≥college degree). Spatiotemporal clusters were identified using the SaTScan space-time statistic, based on lower- and higher-than-expected suicide rates (cold and hot clusters) in a prespecified area (150 km) and time interval (12 months).

From 2000-2020, suicide rates increased from between 37% among AI/AN (95% CI: 1.22, 1.55) to 81% among A/PI (95% CI: 1.65, 2.01) groups. Increases were greater among men across all racial groups, but differed by education; risks were greater among A/PI with ≥college degree, while risks were greater among those with <college degree for all other racial groups. Over time, the likelihood of detecting cluster increased over time with considerable differences in the number of clusters in each racial group (4 among AI/AN to 72 among White individuals). Among Black individuals, 27 total clusters were identified, and hot clusters were concentrated in Southeastern and mid-Atlantic counties.

Intersectional patterns highlight opportunities to center historically marginalized groups and tailor individual- and population-level prevention efforts to the appropriate geographic and cultural context. A successful public health suicide prevention agenda must dismantle social inequities to reverse the harmful impact of intertwined power structures on health. This project demonstrates the feasibility of uniting the appropriate theoretical and methods needed to translate intersectionality theory into a quantitative research framework with fidelity.

## **The deaths of despair phenomenon in Canada: Is it occurring, and among whom?** Calvin Yip\* Calvin Yip Arjumand Siddiqi

### **Background**

Most high-income countries experienced an unprecedented decline or stagnation in life expectancy in the 21st century, even prior to the COVID-19 pandemic. The decline in life expectancy in the U.S. has been attributed to increases in mortality from drug poisoning, alcohol abuse, and suicide (i.e., “deaths of despair”), but it remains unclear as to whether the same phenomenon is occurring in Canada. While deaths of despair are associated with a lack of social support, no studies have examined patterns in these deaths by marital status, a key indicator of social support. We assessed whether Canada is experiencing a “deaths of despair” phenomenon, and whether patterns in these deaths differ by age, sex, province, and marital status.

### **Methods**

The incidence of mortality from drug poisoning, alcohol abuse, and suicide between 2001 and 2017 in Canada was calculated for all adults overall and separately by age, sex, marital status, and province. Population estimates were derived from Statistics Canada survey data, while death counts came from the Canadian Vital Statistics Death Database.

### **Results**

Between 2001 and 2017, the incidence of mortality from drug poisoning per 100,000 increased by 246% (from 4.3 to 14.9) in the overall population, while mortality from alcohol abuse increased by 21% (from 13.2 to 16.0) and mortality from suicide decreased by 9% (from 15.2 to 13.9). During this period, notably large increases in mortality from drug poisoning per 100,000 were observed among men (5.9 to 22.6) and single (never married) individuals (9.2 to 38.1), while the largest absolute increase was observed among single men (12.7 to 56.8).

### **Conclusion**

These results suggest that stagnating life expectancy in Canada may not be driven by the deaths of despair phenomenon as a whole, but rather mostly by mortality from drug poisoning specifically. They also suggest that risk mitigation strategies for drug poisoning should consider marital status and social support.

**Role of individual deprivation and area-based deprivation on suicidal behaviours: evidence from the UK Biobank Study** Kwanghyun Kim\* Kwanghyun Kim Doo Woong Lee Sun Jae Jung

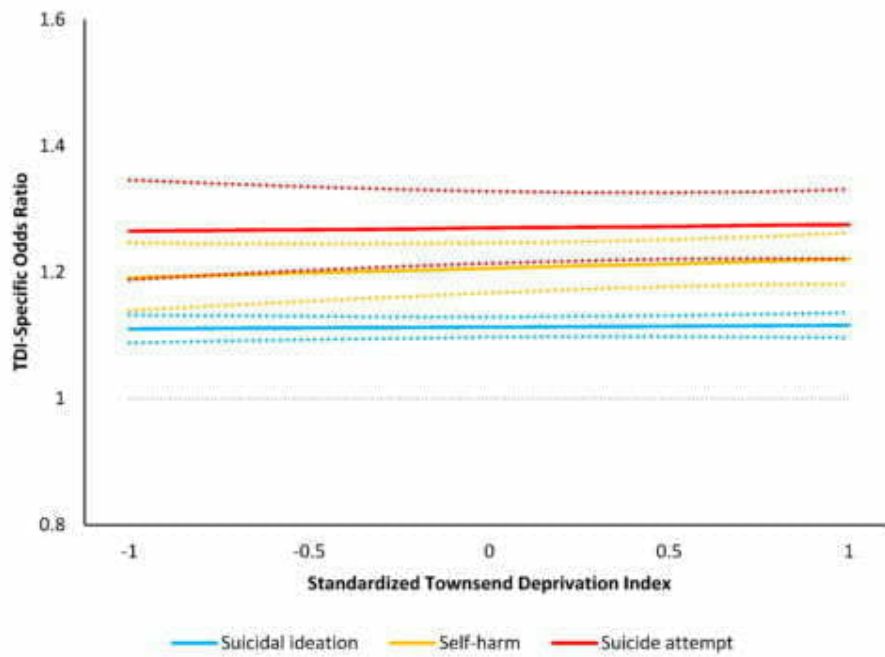
**Introduction:** We tested how individual deprivation and community-level deprivation affects suicidal behaviour of community members.

**Methods:** We used data from 350,884 participants of UK Biobank for constructing individual deprivation index. Objective poverty was defined as having household income before tax of less than £18,000. We included sex, ethnic background, type of accommodation, housing tenure type, number of vehicles, educational qualifications, employment status, and overall subjective health rating as predictors of objective poverty. Logistic models to predict objective poverty was developed to construct individual deprivation index. Townsend Deprivation Index (TDI) was selected as a representative variable for community level deprivation. Association between individual deprivation index, TDI, and suicidal behaviours (suicidal ideation, self-harm, suicide attempt) was tested by applying multivariate logistic regression to participants who had completed online mental health questionnaire assessment (N = 119,585). Linear and nonlinear interaction analysis was conducted to test the effect modification.

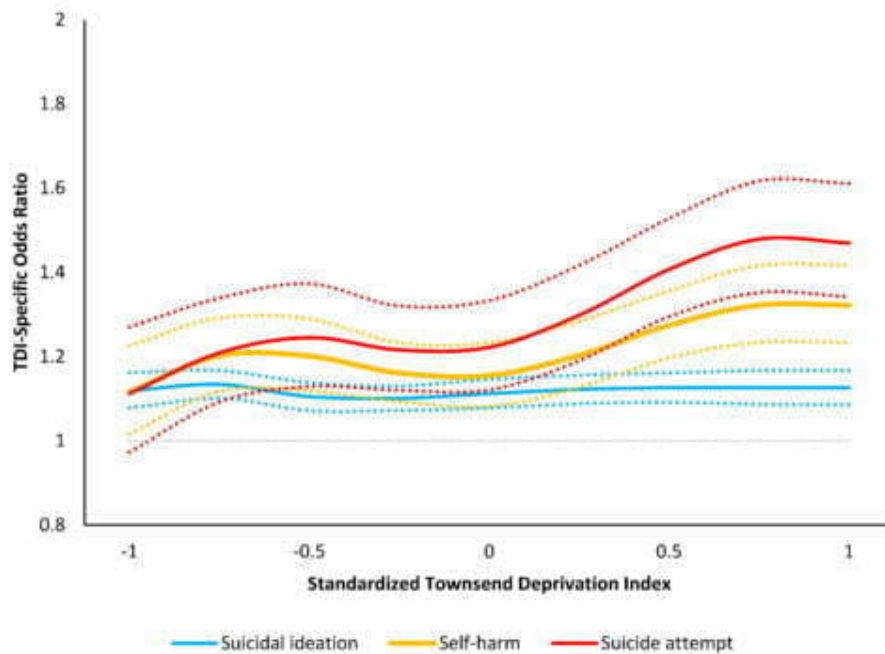
**Results:** Logistic regression model for predicting absolute deprivation presented high quality of prediction (AUC = 0.840). Associations between individual deprivation index and suicidal behaviours were stronger than associations between TDI and suicidal behaviours. Positive interaction between individual deprivation index and TDI was detected: TDI-specific odds ratios of individual deprivation index on suicidal behaviours gradually increased as TDI increased.

**Conclusion:** We were able to construct an individual deprivation index that could be widely used to measure comprehensive individual-level deprivation. Effect of individual-level deprivation on suicidal behaviours was stronger than those of community-level deprivation. Individual-level deprivation and community-level deprivation had synergistic effect on suicidal behaviours.

### A. Linear interaction model



### B. Polynomial interaction model



**Spillover Effects of Residential Socioeconomic Spatial Social Polarization and High Blood Pressure among VA Nursing Home Residents** Hoda S. Abdel Magid\* Hoda Abdel Magid Yongmei Li Laura Graham Michelle Odden

Spatial social polarization (SSP) - the process by which a population within an area diverges across socioeconomic characteristics- has been associated with hypertension. SSP indices measure the extent to which a population is distributed at extremes of privilege and deprivation. The VA nursing home represents an environment where spatially-oriented disparities are expected to be attenuated due to the fact that Veterans have equal access to care. We examined the association between SSP measured at residents' home addresses prior to admission with blood pressure outcomes in the first four weeks after admission. We evaluated the use of the index of concentration (ICE) of extremes to measure SSP across four socioeconomic domains including race/ethnicity, income, home ownership, and joint race/ethnicity with income at the tract level using 2010 census data. SSP was dichotomized as the first (most polarized and disadvantaged) quintile vs. the 2<sup>nd</sup> -5<sup>th</sup> quintiles. The analytic sample included 41,972 long-term care residents aged  $\geq 65$  years admitted from 2006-2019. Systolic and diastolic blood pressure were averaged over the first four weeks of the residents' stay and we defined high blood pressure as average  $\geq 140$  mmHg systolic or  $\geq 90$  mmHg diastolic. Multilevel mixed-effects regression models were adjusted for age, sex, race/ethnicity, diabetes, heart failure, kidney disease, and metastatic cancer. We found Veterans who had resided in the most polarized and disadvantaged quintile (Q1) had a 1.10 (95% 1.01, 1.19) relative risk of high blood pressure compared to those in Q 2-5 for the ICE jointly measuring race/ethnicity and income. We found similar results for systolic blood pressure. ICE measures for race/ethnicity, income, and home ownership alone were not associated with high blood pressure. In summary, SSP that jointly measures economic and racial/ethnic polarization, may have a spillover effect on health disparities even in a healthcare setting with equal access.



**Evaluating the impact of access to universal early childhood education on mental distress during adolescence in high-income countries** Arijit Nandi\* Arijit Nandi Efe Atabay Ilona Vincent Jasleen Arneja Sarah Windle Sam Harper

Randomized evaluations of small-scale, means-tested, early childhood education and care (ECEC) programs suggest that ECEC programs have the potential to improve health outcomes over the life-course. However, few studies have assessed the impact of large-scale, universal ECEC programs, including those implemented by many high-income countries over the past two decades. In this study we used a difference-in-differences design applied to data from the Health Behaviour in School-aged Children (HBSC) study, a repeated, cross-sectional, school-based survey, to estimate the impact of introducing free ECEC on indicators of mental distress during adolescence among children exposed to ECEC during their preschool years.

After merging the 2002, 2006, 2010, 2014, and 2018 HBSC waves, our sample included 345,662 9-17-year-old youth from 15 European countries, including 11 treated countries that introduced free ECEC and 4 control countries that did not. We used linear probability models to estimate the effect of any free access to ECEC, measured on the prevalence difference (PD) scale, with fixed effects for country and birth cohort to account for unobserved time-invariant confounders that varied across countries and shared temporal across countries.

Over the study period, 16.4%, 23.6%, 21.6%, and 20.7% of adolescents reported feeling low, irritability or bad temper, feeling nervous, or difficulty sleeping at least once per week over the past 6 months, respectively. We found little evidence of any impact of free access to ECEC on the probability of feeling low (PD=0.1, 95%CI=-1.6, 1.9), irritability or bad temper (PD=0.6, 95%CI=-2.0, 3.2), feeling nervous (PD=0.8, 95%CI=-2.3, 3.9), or difficulty sleeping (PD=0.1, 95%CI=-1.2, 1.3), with effect estimates that were small in comparison to variation across age group and gender. In ancillary analyses, we assess the effect of continuous years of free ECEC access and account for potentially heterogeneous treatment effects.

**Life and Death Among the Most Vulnerable Americans: An Examination of Public Burials**

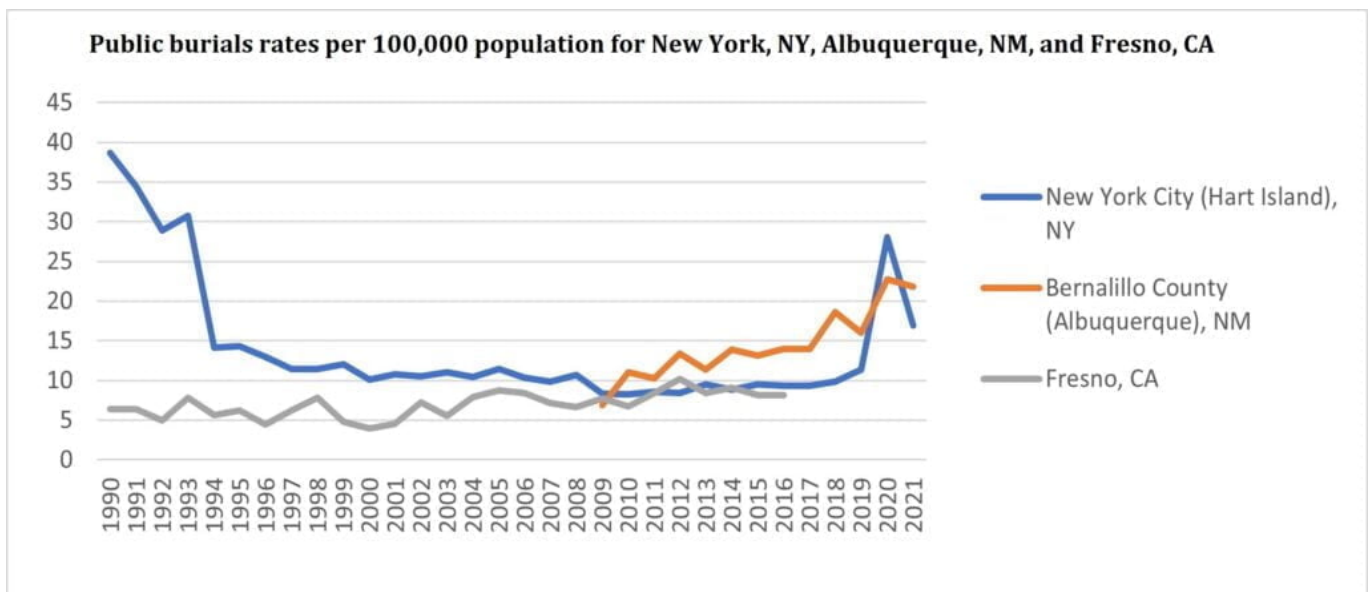
Jennifer Brite\* Jennifer Brite Jennifer Laird Deborah Balk Frank Heiland

**Background:** A public burial is defined as any disposition of a decedent by the government and generally occurs when next of kin do not exist or are unable or unwilling to pay for burial. Increasing loneliness and its effect on morbidity and mortality has been well documented in Western societies. However, very little is known about the demographic and social predictors of public burial due to the lack of a centralized dataset. This research examines a novel outcome of social isolation, public burial, and examines a vulnerable population that is difficult to capture in epidemiological surveys.

**Method:** Data were obtained in a pilot study via a combination of web scraping of publicly available websites and contacting localities directly.

**Results:** Demographic and burial data from 90,559 decedents has been collected from eight jurisdictions throughout the United States, as well as also The National Missing and Unidentified Persons System (NamUs), a clearinghouse for missing person data that includes information for some unclaimed decedents, and Dignity Memorial, a charity for unclaimed veterans. Decedents on Hart Island, New York City, were the oldest (median age=62) while those in Fresno, CA, and Yakima County, WA were younger (median age=47 and 58 respectively). In addition, in the jurisdictions that provided sex, the overwhelming number burials occurred among men. Only data source provided race/ethnicity data, NamUS, in which Whites and Blacks comprised 38.9% and 21.7% of unclaimed deaths respectively. Time trends deaths by year were examined since 1990 due to concerns about underreporting in early time periods. Overall, public burials decline until the mid-2010’s, when the trend appears to reverse with a notable increase in 2020, most likely due to the first wave of the COVID-19 pandemic.

**Conclusion:** Public burial remains understudied but appears to be increasing and to be more common among men and racial minorities.



**Does Treatment of Early Maternal Thyroidal Insufficiency [EMTI] prevent its Adverse Developmental Effects?** Isabella Boroje\* Isabella Boroje Steven H. Lamm

**Background:** L-Thyroxine treatment is currently recommended for both 1<sup>st</sup> trimester overt [OT] (High TSH; low fT4) and subclinical [SCH] (High TSH; normal fT4) hypothyroidism with little literature specifically relevant to support this.

**Material and Methods:** Study designs examining the association between early maternal thyroidal values and subsequent IQ include historical prospective and retrospective outcome studies and, now, randomized clinical trials. A minimal data set should include gestational age of maternal blood sample, TSH and fT4 levels, treatment age, and age at IQ tests. Ideally, absence of anti-thyroidal antibodies and iodine sufficiency should be reported. The historical and recent literature has been examined.

**Results: Hypothyroxinemia:** Though early 1<sup>st</sup> trimester studies showed adverse IQ effects only if hypothyroxinemia extended into later trimesters, randomized clinical trials of hypothyroxinemia diagnosed and treated in the 2<sup>nd</sup> trimester found no effect from treatment. **Hypothyroidism:** Subclinical hypothyroidism (SCH) identified at the end of the 1<sup>st</sup> trimester was associated with lower IQ at 6 months but not at 24 months. A major 2<sup>nd</sup> trimester hypothyroidism study found IQ deficits at age 7-8 but did not distinguish between OV and SCH and the cases were 70 % TPO (+). Randomized clinical trials [RCT] of treatment of 2<sup>nd</sup> trimester SCH found no IQ effects at 5 years or at 9.5 years. However, adverse behavioral difficulties were found among those who had been over-treated prenatally. None of these studies dealt with 1<sup>st</sup> trimester treatment.

Chen (2022) presented a new methodology to study the effect of 1<sup>st</sup> trimester treatment of SCH in mothers TPO(-). Following early SCH diagnosis (age 6.5 weeks), the patient was offered the option of being treated or not. Treated and matched untreated patients in a variety of diagnostic categories were followed-up, and their children had developmental testing at two years of age.

Adverse effects were observed only for those SCH mothers with 1<sup>st</sup> trimester TSH of 4-10 mIU/L and who chose to decline treatment.

**Conclusions:** The question is whether the decision on L-thyroxine treatment of 1<sup>st</sup> trimester hypothyroidism should be based on RCTs of 2<sup>nd</sup> trimester hypothyroidism or on 1<sup>st</sup> trimester hypothyroidism cases where mothers chose to be treated or not.

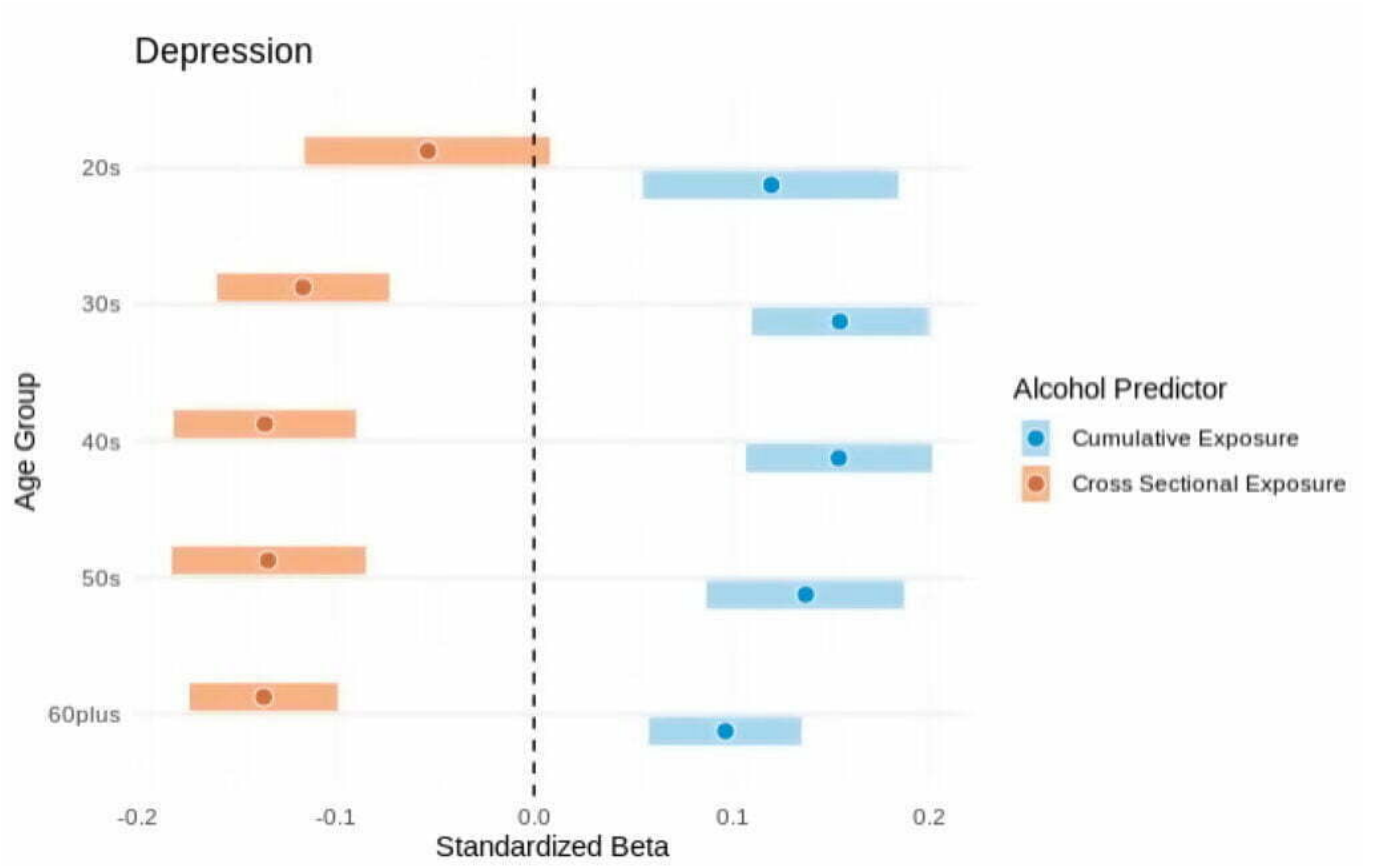
## **Evaluating Cumulative versus Cross-Sectional Alcohol Exposure Ascertainment in Disease Risk Models** Alexandra Reynoso\* Alexandra Reynoso Stella

**Background:** The majority of studies to date have investigated the role of alcohol consumption and disease using cross-sectional exposure measurements, which may be vulnerable to reverse causation. This study aims to compare disease association findings yielded by cross-sectional versus cumulative alcohol exposure assessment.

**Methods:** Self-reported cross-sectional and lifetime alcohol consumption data was captured via surveys from 23andMe, Inc. research participants (N>35,000). The cumulative exposure variable aggregated the self-reported amount of alcoholic drinks consumed in each participant's decade of adult life. We fit age-stratified models using the two alcohol variables as predictors and the following outcomes: non-alcoholic liver disease, high blood pressure, depression, pancreatitis, and tobacco use. All regression models adjusted for age, sex, and genetic ancestry.

**Results:** Depression (Figure), pancreatitis, and high blood pressure were positively associated with cumulative alcohol use and negatively associated with cross-sectional alcohol use in most age groups. For example, in pancreatitis models including participants 40-49 years of age, the standardized regression coefficients were -0.06 for the cross-sectional variable (95% CI: -0.122 to -0.007) and 0.083 (95% CI: 0.025 to 0.141) for the cumulative one. In tobacco use models, the cumulative exposure variable consistently yielded stronger positive associations. Finally, in models of non-alcoholic liver disease used as a negative control, we observed a negative association for both alcohol phenotypes, but it was attenuated with the cumulative alcohol variable.

**Conclusion:** This analysis found substantial differences between cross-sectional and cumulative exposure variables in disease risk models, possibly due to the latter's decreased susceptibility to reverse causation. Our findings underscore the importance of utilizing cumulative exposure variables to model disease risk.



**Challenges ahead for HCV elimination in the evolving epidemics of methamphetamine and opioid use: Trends in direct-acting antiviral medications in the US South** George Pro\* George Pro Corey Hayes Mofan Gu Jonathan Bona

### Introduction

Methamphetamine and opioid use disorders (MUD/ODU) and injection drug use are increasing in the US, paralleled by a surge in hepatitis C virus (HCV). This trend is worrisome in Arkansas, a poor rural state representative of the US South. Direct-acting antiviral treatment (DAA) cures HCV but only a third of those in need receive it. The World Health Organization has set HCV elimination by 2030 as a goal, targeting 80% treated with DAA. Methamphetamine and opioid use are not contraindications for DAA, but evidence around alcohol use disorder (AUD) as a contraindication is mixed. Better understanding differences in DAA receipt may inform resource allocation and intervention design.

### Methods

We used the Arkansas All Payer Claims Database to identify individuals with HCV who also had MUD, OUD, and/or AUD (2016-2020; N=4,892). We used multiple logistic regression to model DAA receipt. We included an interaction between year and disorder type and adjusted our model for covariates. We derived the probability of DAA receipt over time and by disorder type based on our model.

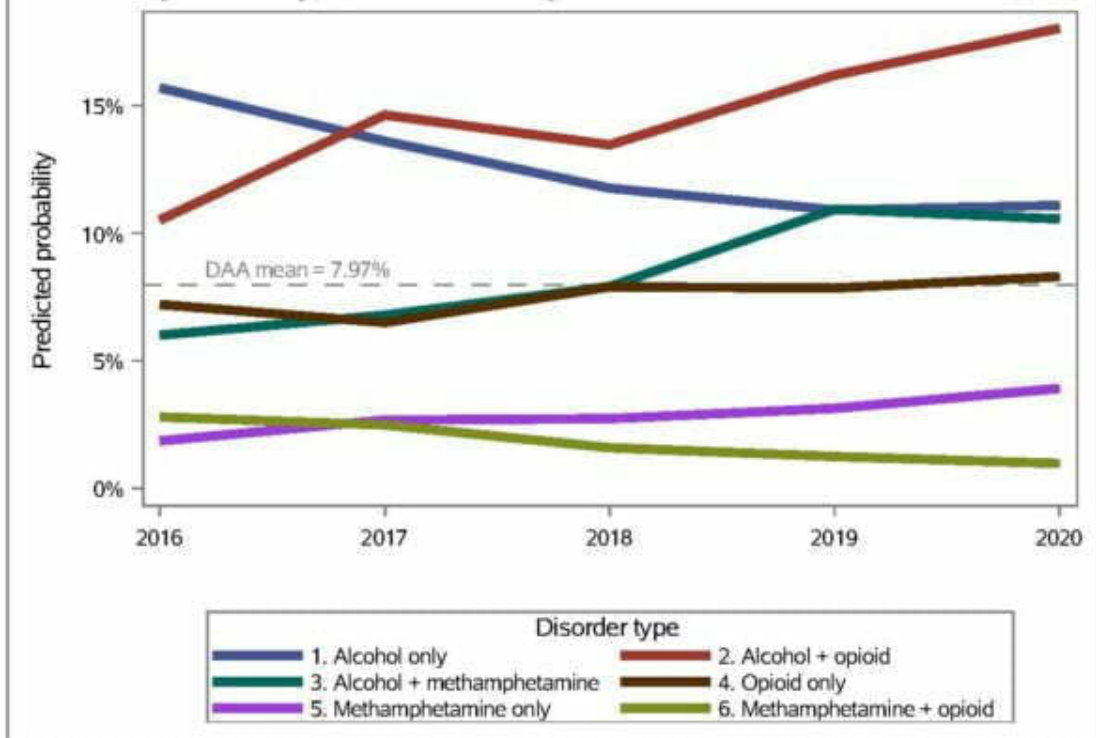
### Results

Only 8% of our sample received DAA. DAA receipt decreased over time (10% in 2016; 6% in 2020). Only 2% of those with combined MUD+OUD received DAA, compared to 13% of those with AUD only. The change in DAA over time varied significantly within groups ( $p=0.06$ ,  $F=2.26$ ; Figure 1). The fastest increase was observed among people with AUD+OUD, while the fastest decrease was observed among those with AUD only.

### Conclusion

DAA was low across all groups, suggesting a sizeable gap between clinical need and service delivery in Arkansas. Despite major medical and public health organizations recommending universal DAA coverage for people who use methamphetamine, those with MUD had markedly low probability of receiving DAA. These trends pose substantial challenges for HCV elimination efforts. The juxtaposition of stigmatized drug use and normalized alcohol use should be considered in new DAA interventions.

**Figure 1: Predicted probability of DAA receipt among individuals with HCV, over time and by disorder type (Arkansas All Payer Claims Dataset, 2016-2020, N=4,892)**



*Note: Model adjusted for HCV severity, age, gender, insurance status, and county-level indicators of rurality, provider shortage, and race/ethnicity*

**Prevalence and predictors of waterpipe/shisha smoking among youth in Senegal: Global Youth Tobacco Survey, 2020** Bai Cham\* Bai Cham Scott R. Weaver Candace K Jones Lucy Popova Nerline Jacques

## Introduction

Shisha smoking has become more prevalent especially among youth. Notwithstanding the health risk associated with shisha smoking, there are few studies on shisha smoking in West Africa and none in Senegal. Our study assessed the prevalence and predictors of shisha smoking among youth aged 13-15 years in Senegal.

## Methods

We used the 2020 Global Youth Tobacco Survey (GYTS) Senegal data, which covered a sample of 4,320 youth, aged 11-17+ years. However, because GYTS is designed to be representative of the national population of students aged 13-15 years, we restricted our analysis to this age cohort. We calculated the weighted prevalence (with 95% confidence intervals) of ever and current (past 30 days) smoking of shisha. We conducted multivariable logistic regression analysis to identify factors associated with ever and current shisha use among youth.

## Results

The prevalence of ever and current shisha smoking was 9.8% (95% CI:7.7-12.3) and 2.2% (95% CI:1.5-3.1), respectively. Among the 3.4% of youth who currently smoke cigarettes, more than half ever tried shisha smoking (50.5%, 95% CI:36.9-63.9) and 26.6% (95% CI:15.4-42.0) currently smoked shisha. In fully adjusted models, higher school grade (adjusted odds ratio [AOR]=2.5, 95% CI: 1.3-5.2), male gender (AOR=2.2, 95% CI:1.5-3.1), higher pocket money (AOR=2.9, 95% CI:1.6-5.2), current cigarette smoking (AOR=8.4, 95% CI:4.0-17.7), having close friends who smoke (AOR= 2.6, 95% CI:1.0-6.7), use of smokeless tobacco (AOR=9.5, 95% CI:4.7-19.4), and exposure to second-hand smoke (AOR=1.9, 95% CI:1.2-2.8) were significantly associated with ever shisha smoking. Likewise, higher pocket money, current cigarette smoking, exposure to second-hand smoke, and having parents who smoke were significantly associated with current shisha smoking.

## Conclusion

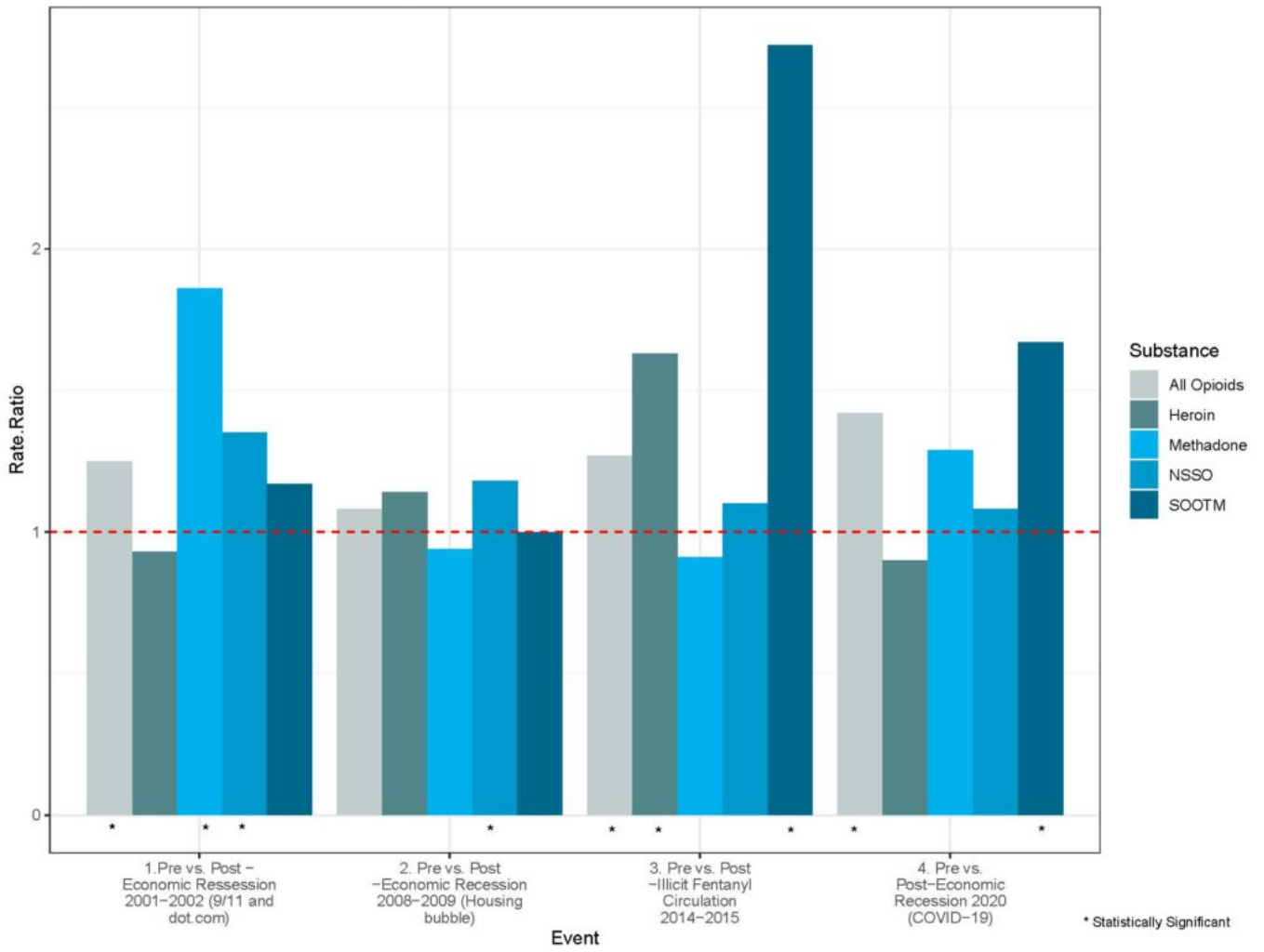
Our findings suggest youths in Senegal have access to shisha, despite laws prohibiting the importation, distribution, and sale of shisha in the country. Further enforcement of this law might help reduce youths' access to shisha and reduce prevalence of shisha smoking in Senegal.



**Opioid deaths following national recessions** Elizabeth Best\* Elizabeth Best Tony Cappello Alex Riordan

As opioid overdose deaths (OOD) continue to rise in the United States (U.S.), epidemiological evaluation is warranted to evaluate potential root causes influencing this ongoing public health problem, particularly when experiencing social distress or crisis. This study evaluated trends in OODs prior to and during three recessions/crises in 2001-2002, 2008-2009, and 2020. All available U.S. mortality data on OODs were ascertained from the CDC's WONDER system from 1999 to 2021. Point comparisons were conducted around the three recessions, by averaging the number of deaths and calculating the average death rate (per 100,000) for two years pre- event and comparing to data from two years post- event. Differences in the number of deaths, rate differences, and RR with 95% CIs were calculated to quantify the magnitude of change around these events; analyses were stratified by opioid type, including heroin, natural and semisynthetic opioids (NSSO), methadone, and synthetic opioids other than methadone (SOOTM) (*see Figure 1*). The number of deaths due to all opioids combined was statistically significantly increased following the 2001-2002 and 2020 recessions/crises; however, the increase before and after the 2008-2009 recession was not statistically significant. Methadone and NSSO deaths were statistically significantly increased following the 2001 recession, while SOOTM deaths were statistically significantly increased post the 2020 recession, which is consistent with the rise in fentanyl overdose deaths after 2013. In fact, the magnitude of the SOOTM overdose death rate when comparing 2012-2013 to 2014-2015 was approximately 2x greater than any of the overdose death rates in the three studied recessions regardless of opioid type. These results support the structural analysis that social distress is a likely upstream root cause and/or influence of opioid abuse. Furthermore, the introduction and use of illicit fentanyl appears to increase this effect.

Figure 1. Comparison Among U.S. Opioid Death Rates



**Differences in access to medications for opioid use disorder across racial/ethnic groups: a county level analysis in New York State** Ariadne Rivera Aguirre\* Ariadne Rivera-Aguirre Noa Krawczyk Magdalena Cerdá Julian Santaella-Tenorio

**Introduction:** The opioid overdose epidemic continues to be a major public health problem in the U.S. Among people with opioid use disorder (OUD), treatment initiation/retention with medication for opioid use disorder (MOUD) is associated with better health outcomes. However, uptake of MOUD is low and may differ by race/ethnicity.

**Aim:** To evaluate differences in use of MOUD among people receiving treatment for OUD across racial/ethnic groups in metro/micropolitan areas in New York State (NYS).

**Methods:** We used NYS data (2017-2020) from the Treatment Episode Data Set on Admissions (TEDS-A), a national data system of admissions to publicly-funded substance use treatment facilities. We examined race/ethnicity differences in receipt of MOUD as part of care in logistic regression models. We included interaction terms to explore whether racial/ethnic differences in MOUD access vary across metro/micropolitan areas and time. We adjusted models by service setting (rehab/residential, ambulatory), treatment referral source, other substance use, employment status, and arrest history.

**Results:** Between 2017 and 2020, 92,043 individuals were admitted to substance use treatment facilities for OUD. While use of MOUD as part of care increased over time (56.9% in 2017 vs 70.4% in 2020), among those admitted to treatment across study years, only 55.4% received MOUD. Compared to Non-Hispanic white clients, Non-Hispanic Black clients were less likely to receive MOUD (OR=0.67; 95%CI:0.63-0.71%). Interactions between race/ethnicity and metro/micropolitan areas revealed that Non-Hispanic Black clients in metropolitan areas have lower odds of receiving MOUD (OR=0.53; 95%CI: 0.48-0.6) than Non-Hispanic white clients in micropolitan areas.

**Conclusion:** Differential access to MOUD treatment prevails across racial/ethnic and geographic groups in NY State. Addressing sources of inequalities in access to MOUD among those who have been diagnosed with OUD remains a key goal to prevent opioid overdoses.

**Opioid Misuse Incidence and Cigarette Smoking Status in the United States, 2015-2020**

Maria Parker\* Maria Parker Raul Cruz Joanna Streck Andrea Weinberger

**Aims:** The prevalence of opioid misuse is more than two times higher for persons with versus without cigarette smoking, but it is unknown whether the incidence of opioid misuse varies by smoking status. We estimated the incidence of opioid misuse for persons with current, former, and lifetime smoking versus never smoking.

**Methods:** Data came from the 2015-2020 National Surveys on Drug Use and Health, cross-sectional surveys of US civilians aged 12+. Weighted incidence of opioid misuse and average time between cigarette initiation and opioid misuse initiation were calculated annually by smoking status (i.e., current, former, lifetime/ever, never). Logistic regression models tested time trends in incidence by smoking status.

**Results:** Overall, 0.75% persons initiated opioid misuse per year. The incidence of opioid misuse was 1.35% for current smokers, 0.54% for former smokers, and 0.67% for never smokers. For persons who both smoked and misused opioids (2.32%), 94.71% smoked prior to opioid misuse. The average time between smoking followed by incident opioid misuse was 9.9 years and 3.4 years for those who first misused opioids followed by smoking. Former smokers were less likely (OR=0.79; 95% CI: 0.66, 0.96) and current smokers were 1.98 more likely to misuse opioids than never smokers (95% 1.78, 2.20). There was a decrease in the incidence of opioid misuse over time (OR=0.90; 95% CI: 0.87, 0.93), which did not differ by smoking status.

**Conclusions:** The incidence of opioid misuse decreased from 2015-2020. Compared to persons who never smoked cigarettes, those who currently smoked were more likely and those who formerly smoked were less likely to initiate opioid misuse. As the overwhelming majority of individuals smoked cigarettes before misusing opioids, efforts focused on preventing the incidence of opioid misuse among those with smoking may help decrease the number of persons who misuse opioids in the US over time.

**Correlates and time trends in naloxone access among a community-based cohort of sex workers in Metro Vancouver (2017-2021)** Sarah Moreheart\* Sarah Moreheart Kate Andrea Emma Christie Charlie Shira

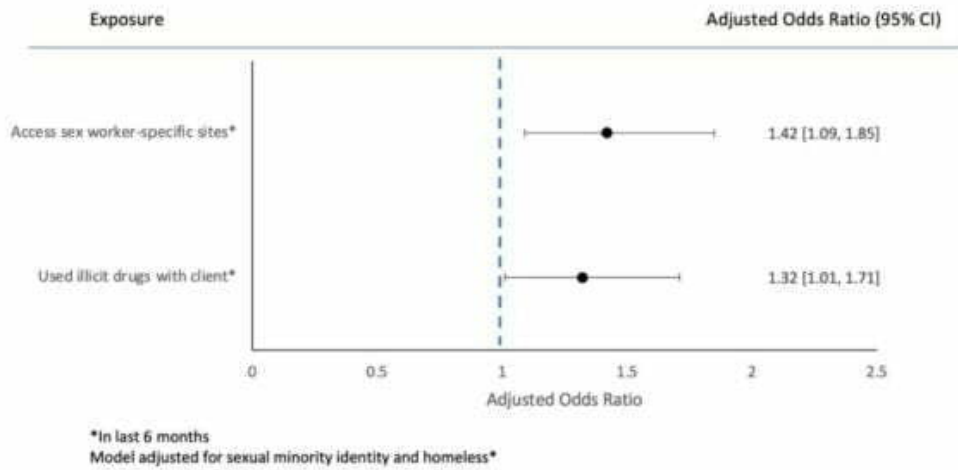
**Background:** While women sex workers who use drugs face a disproportionately high burden of overdose, we know very little about access to overdose prevention services. In the context of an ongoing toxic drug poisoning crisis intensified by COVID-related disruptions, access to naloxone for overdose reversal is a life-saving intervention for women sex workers impacted by overlapping criminalization and stigma of both sex work and drug use. We examined correlates and time trends in naloxone access amongst sex workers who use drugs over 4-years (2017-2021).

**Methods:** Data were from a prospective, community-based cohort of women sex workers in Vancouver (AESHA) from 2017-2021. Bivariate and multivariable logistic regression with generalized estimating equations (GEE) modelled correlates of naloxone access (i.e., currently owning a naloxone kit) in the last 6 months. Time series analysis assessed annual trends in naloxone access.

**Results:** Among 446 sex workers who use drugs, 73.5% (n=328) reported owning a naloxone kit at any follow-up visit during the 4-year study period. Time series analysis demonstrated increasing trends in naloxone ownership, with annual proportions increasing 1.85% (95%CI 1.40-2.29%) every 6 months, on average. In multivariable GEE analysis adjusted for demographic factors, accessing sex worker-specific services (AOR 1.42, 95%CI: 1.09-1.85) and using drugs with clients (AOR 1.32, 95%CI: 1.01-1.71) were associated with enhanced naloxone access.

**Conclusion:** The majority of sex workers who use drugs reported naloxone access, and this was most likely among those accessing sex worker-specific services (e.g., drop-in spaces, outreach) and in the context of occupational overdose risk. Scale-up of sex worker-led and specific support services that include naloxone distribution and training, alongside other overdose prevention services, is recommended.

Figure 1: Adjusted Odds Ratios and 95% Confidence Intervals for the associations with naloxone kit ownership amongst a cohort of sex workers who use drugs in Metro Vancouver 2017-2021 (n=446)



**Experiences of Discrimination and Treatment Outcomes Among Pregnant and Postpartum People with Opioid Use Disorder** Nichole Nidey\* Nichole Nidey Angel Ehrenschwender Stephanie Merhar Emily DeFranco Jennifer McAllister Christine Wilder Aaron Murnan Mishka Terplan

## OBJECTIVE

Experiences of discrimination among pregnant and postpartum people with opioid use disorder (OUD) are common and likely affect utilization of medication for OUD (MOUD), which is associated with reduced risk of overdose and death. The objective of our study was to examine experiences of discrimination among pregnant and postpartum people with OUD by healthcare setting (prenatal care and substance use disorder (SUD) treatment) and estimate its effect on the risk of not using MOUD treatment as prescribed, MOUD discontinuation, return to substance use, and overdose.

## STUDY DESIGN

Patient-stakeholders co-designed survey questions to measure self-reported outcomes related to MOUD treatment utilization, return to use, and overdose. A modified Healthcare Discrimination Scale (HDS) was used to measure discrimination during pregnancy. The effect of discrimination experienced by healthcare setting on postpartum MOUD utilization, return to use, and overdose was estimated using log-binomial models to calculate the relative risk (RR) of each outcome.

## RESULTS

Among the 100 participants enrolled in the study, 57 reported experiencing discrimination, 56 within prenatal care and 33 within SUD treatment settings. Discrimination within prenatal care (RR 2.6, 95% CI 1.06-6.40) and SUD treatment (RR 3.26, CI 1.59-6.70) were associated with increased risk of not using MOUD as prescribed. Discrimination within SUD treatment settings was associated with greater than two-fold increased risk of MOUD discontinuation and return to use (**Table 1**).

## CONCLUSION

Experiences of discrimination were common, especially within prenatal care settings, and discrimination was associated with poor MOUD treatment outcomes and risk of return to use. Institutional policies, provider-focused trainings, and accountability practices are needed to address discrimination within healthcare settings to improve outcomes for pregnant and postpartum people with OUD.

Table 1: Effect of Prenatal Discrimination on Postpartum Outcomes

	Prenatal/Obstetric Care Setting Discrimination RR(CI)	Substance Use Treatment Setting Discrimination RR(CI)
Not using MOUD as prescribed	<b>2.6 (1.06, 6.40) *</b>	<b>3.26 (1.59, 6.70) *</b>
Discontinuation of MOUD	2.17 (0.86, 5.46)	<b>2.56 (1.19, 5.54) *</b>
Return to use	1.14 (0.55, 2.37)	<b>2.36 (1.18, 4.73) *</b>
Overdose	1.44 (0.47, 4.46)	2.10 (0.74, 5.98)

\***BOLD** indicates p-value < 0.05, MOUD = medication for opioid use disorder; Any Discrimination = discrimination endorsed in prenatal/obstetric care and/or substance use treatment setting



**Medication for opioid use disorder and non-fatal overdose among pregnant and postpartum people with opioid use disorder** Erin Rogers\* Erin Rogers Ashley Naimi

Opioid overdose is estimated to contribute to between 11-25% of pregnancy-associated deaths in the United States. To reduce overdose risk among pregnant people, medication for opioid use disorder (i.e., methadone or buprenorphine) is considered standard of care. However, only 50-66% of pregnant people with an opioid use disorder are receiving these treatments and among those who do, only a fraction receive a dose high enough to achieve the full therapeutic effect.

Using insurance claims collected from the Merative® MarketScan® Commercial Claims and Encounters data system between January 1<sup>st</sup>, 2009 and December 31<sup>st</sup>, 2019, we will create a prospective cohort of pregnant people diagnosed with an opioid use disorder. The estimated sample size is 7,000 pregnant people with ~15% prescribed to buprenorphine. Study entry will begin at the last menstrual period and follow up will continue until first overdose (outcome), loss of insurance or prescription drug coverage (right censored), or at 12-months postpartum (administratively censored). Prescription drug claims will be used to ascertain buprenorphine uptake, measured at baseline and every 3-months.

Using parametric g-computation, we will estimate the risk difference of overdose among those who fill buprenorphine consistently compared to those who are not prescribed. We will control for the following covariates at baseline: age, relationship to primary insurer, and at baseline and every 3 months: HIV status, prescription medication for comorbidities, mental health diagnoses and treatment, and co-occurring substance use disorders. 95% confidence intervals will be estimated using bootstrapping.

This is the first study to use large insurance claims data to compare risk estimates of overdose among pregnant and postpartum people by buprenorphine status and is strengthened using parametric g-computation, which has strong performance in the context of time-varying confounding. Because we are limited to availability of data provided by MarketScan, we are aware of unmeasured confounding. The greatest unmeasured confounder of concern is race. To account for this known limitation, we will conduct a sensitivity analysis to represent the potential range of risk estimates when accounting for black-white disparities in buprenorphine uptake and overdose.

**How should we study substance abuse treatment careers? A 9-year longitudinal approach using latent class growth analysis and state sequence analysis**

Ignacio Bórquez\* Ignacio Bórquez Magdalena Cerda Andrés González-Santa Cruz Ignacio Madero-Cabib Álvaro Castillo-Carniglia

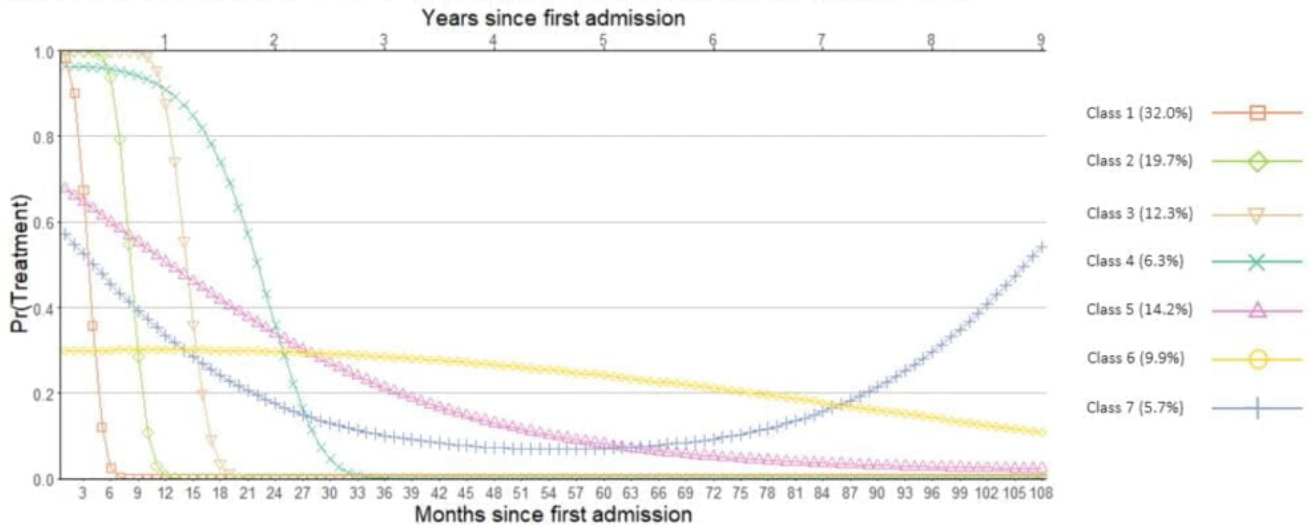
**Aim:** Longitudinal studies have revealed that substance use treatment usage is recurrent among patients; the characteristics of those treatment trajectories have received less attention. The purpose of the article is to disentangle heterogeneity in treatment careers by comparing two longitudinal approaches.

**Methods:** We used a registry-based retrospective cohort design (N = 6,266) of people entering treatment programs at the national level during 2010 and followed them for 9 years. We obtained data from the National Drug and Alcohol Service in Chile. We used latent class growth analysis (LCGA) and state sequence analysis (SSA) to estimate distinctive treatment careers. Further, we explore baseline characteristics associated with them.

**Results:** In the LCGA a 7-class solution fitted best the data, whereas in the SSA we chose an 8-cluster solution. Both approaches managed to characterize heterogeneity in patterns of the length of stay between entry and first discharge, as well as in recurrence patterns of treatment usage over time. Nonetheless, because it enables us to describe the qualitative nature of healthcare provision (i.e., outpatient or inpatient) and multiple possible discharge motives (i.e., early dropout or referral), SSA allows us to examine a more complex picture of the treatment trajectories. Being treated in inpatient (OR = 1.81; 95% CI = 1.40, 2.34) programs (versus outpatient low intensity) was associated with membership in longer treatment trajectory groups when compared to the Early dropout group. Being a woman was associated with recurrence when comparing the early dropout groups (OR = 1.43; 95% CI = 1.15, 1.78). Finally, presenting a cocaine paste polysubstance use pattern (versus alcohol use pattern) decreased the odds of recurrence (OR = 0.73; 95% CI = 0.54, 0.97) when comparing both early dropout groups.

**Conclusion:** Treatment careers are not just heterogeneous in length and recurrence over time, they also vary as qualitative processes that were better described by state sequence analysis.

**Figure 1:** Trajectories of substance abuse treatment usage since first admission, 7 class solution (N=6,266)



**Note:** Class 1 = Early dropout (32%); Class 2 = Less than a year in treatment (19.7%); Class 3 = Year-long episode, no recurrence (12.3%); Class 4 = Long first treatment, immediate recurrence (6.3%); Class 5 = Recurrent and decreasing (14.2%); Class 6 = Early dropout with recurrence (9.9%); Class 7 = Recurrent after long between treatments periods (5.7%)

**Interaction between Tobacco 21 laws and taxation policies on cigarette smoking in US****youth** James H. Buszkiewicz\* James Buszkiewicz Yanmei Xie Annie Cohen David C. Colston Megan E. Patrick Nancy L. Fleischer

**Background:** The majority of US adults who smoke cigarettes daily begin before age 18. Previous research has shown that the implementation of Tobacco 21 (T21) laws and higher state taxes were, separately, associated with lower prevalent youth tobacco use.

**Methods:** We used national, repeated cross-sectional data from the 2014-2020 Monitoring the Future study to examine the associations between county-level T21 coverage (100% vs. <100%) and state-level cigarette taxes on 30-day cigarette smoking, daily and first cigarette initiation, and 5-year smoking intentions in US youth. We implemented weighted, grade-stratified, modified Poisson regression models to test for interactions between county T21 coverage and state taxes on each outcome. We also examined sociodemographic disparities across sex, race/ethnicity, parental education, and college plans using a triple interaction term.

**Results:** Higher state taxes were associated with a lower probability of 30-day cigarette smoking (Average Marginal Effect [AME] = -0.006, 95% CI = -0.010, -0.003) and first cigarette initiation (AME = -0.004, 95% CI = -0.007, -0.001) among 8<sup>th</sup> graders living in counties with <100% T21 coverage compared to 8<sup>th</sup> graders living in areas with 100% coverage. There was no evidence of an interaction between T21 laws and state taxes with other smoking outcomes or in other grades. There was also no evidence to support sociodemographic differences using triple interactions.

**Conclusions:** We found evidence that higher state cigarette taxes were associated with lower probabilities of 30-day cigarette smoking and first cigarette initiation for youth living in areas with <100% T21 coverage than for those living in areas with 100% T21 coverage for 8<sup>th</sup> graders only. There was no evidence of differential associations by key sociodemographic factors. Future work should examine the interaction between T21 law coverage and other tobacco control policies and evaluate potential sociodemographic differences.

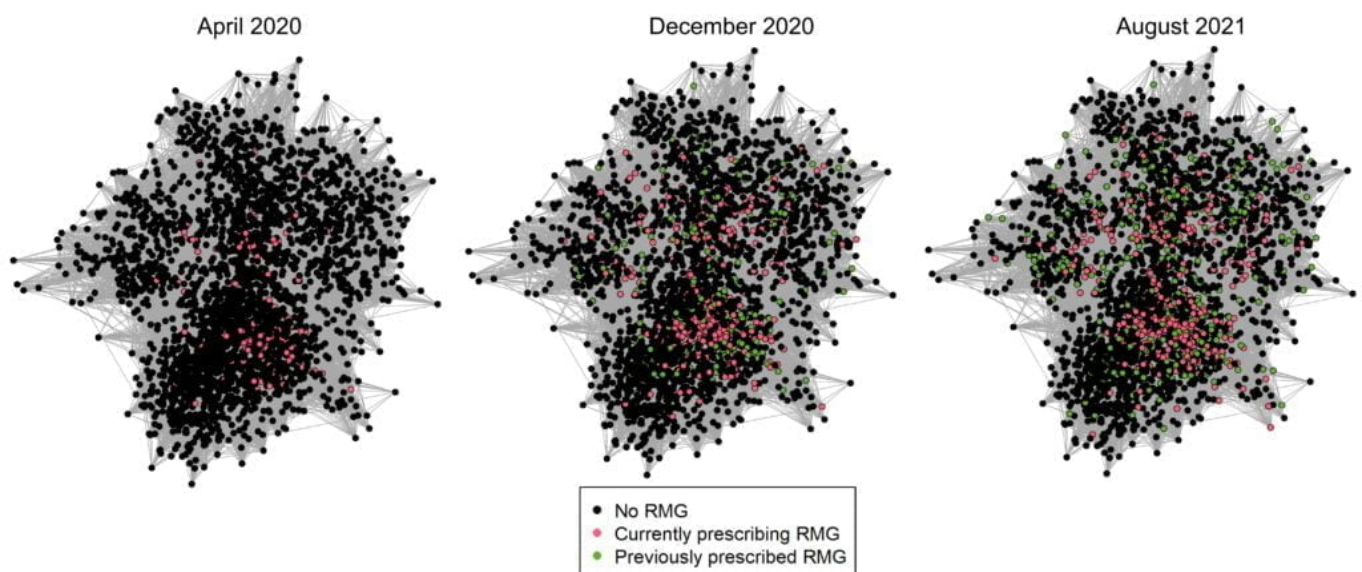
**Influence of physician networks on the implementation of pharmaceutical alternative to a toxic drug supply in British Columbia.** Megan Kurz\* Megan Kurz Bohdan Nosyk Jeong Eun Min

**Background:** We aimed to characterize the diffusion of adoption of a novel provincial policy guideline to prescribe opioids, stimulants, and benzodiazepines to individuals who were at high risk of a COVID-19 infection and drug overdose at the onset of the COVID-19 pandemic and determine the extent to which 'Risk Mitigation Guidance' (RMG) uptake operated through established networks of prescribers in British Columbia, Canada.

**Methods:** We executed a retrospective population-based study using linked health administrative data that captured all clinicians who prescribed to at least one client with a substance use disorder from 03/27/2020-08/31/2021. Social network analysis was implemented to create a network with connections between prescribers based on their shared clients. Our outcome was a clinician's uptake in a given calendar month. Our main exposure was the proportion of connected physicians that had prescribed RMG in the month prior. Generalized linear mixed modeling was used to characterize RMG uptake through the networks of clinicians.

**Results:** Among 14,137 prescribers treating clients with SUD, there were 228 early adopters of RMG (initiated before 04/30/2020) and 1,062 adopters through the end of study follow-up. Prescribers with over 25% of their peers prescribing RMG was associated with an 11-fold increase in the odds of RMG prescription (OR: 11.93 95% CI: (8.62,1 6.51)), when compared to those with no connected RMG prescribers.

**Conclusion:** RMG uptake in BC was highly dependent on the behaviour of prescribers' peer networks. These findings provide insights into the diffusion of policy uptake which can be used to improve future policy implementation strategies.



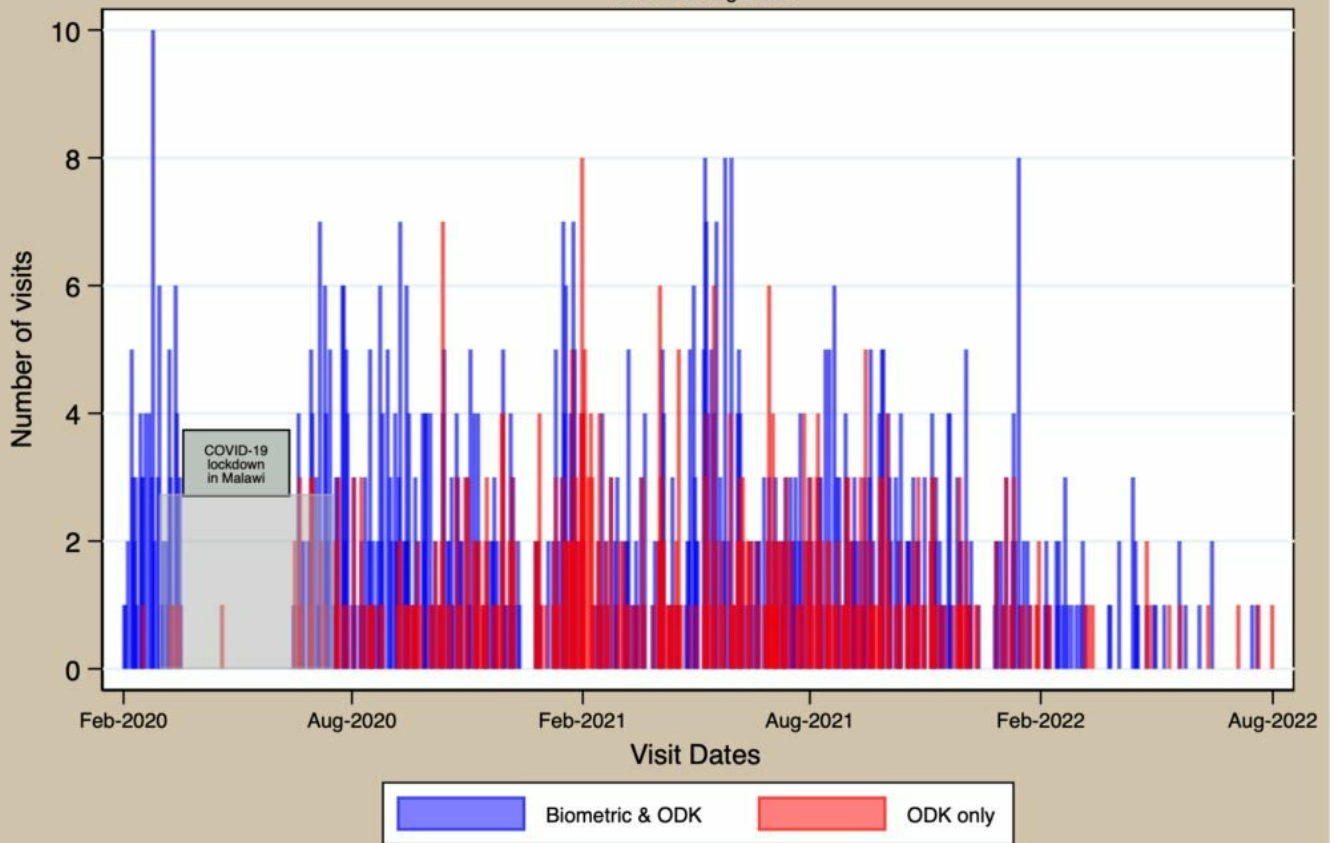
**Legend:** A connection between two prescribers is kept if the weight (number of shared clients) was in the top 20% of connections for both prescribers. This requirement was only considered for ease of display purposes. Each month displays the cumulative number of active RMG prescriber by the end of the month. Those that are currently prescribing RMG are displayed in pink. Those that prescribed RMG in previous months, but not the current month, are displayed in green. Non-RMG prescribers with SUD clients are displayed in black.

**Evaluation of biometric fingerprint scanning technology to monitor HIV care engagement among peripartum women living with HIV in Lilongwe, Malawi** Sophie Lazar\* Sophie Lazar Wiza Kumwenda Shaphil Wallie Madelyn Frey Denzel Matiya Angela Bengtson

Sustained HIV care engagement is essential for pregnant women living with HIV (PWLHIV) on lifelong antiretroviral therapy (ART). However, few strategies to improve identification and retention in HIV care in the peripartum period have been examined. In this study, we evaluate the acceptability, feasibility, and fidelity of biometric fingerprint scanning (BFS) to monitor women's engagement in HIV care across a network of clinics in Malawi using a cloud-based fingerprint biometric system and an electronic data capture system for Android, Open Data Kit (ODK). Participant data was collected on encrypted tablets by trained research assistants at enrolment into antenatal care (baseline), study visits (6-week, 6-month, and 9-month postpartum) and all usual HIV care visits. Visit data was uploaded and synced across study sites daily. During the COVID-19 lockdown in Malawi (April-May 2020), visit attendance was captured by phone. Exit interviews were conducted with a sample of participants to evaluate the feasibility and acceptability of using BFS to record HIV visits. BFS fidelity was assessed as concordance between visits captured in the BFS and ODK systems. Among 399 participants, the median age was 30 (IQR 25-35), 71% lived in an urban area, 95% were married or partnered, and 45% reported that COVID-19 impacted their ability to access health services. **Acceptability:** Of the 363 participants (91%) with exit interviews, 60% reported feeling very comfortable using BFS and 58% found BFS very easy to use. **Feasibility:** 64% reported that BFS had a positive impact on care engagement and 76% would strongly recommend BFS to be used at their clinic. **Fidelity:** 51% of the 3,561 HIV visits in the study period were captured by both the BFS system and the ODK system. PWLHIV consider BFS acceptable and feasible to register HIV visits over time and across clinics. However, fidelity to the BFS system was moderate. Further research is needed to identify optimal implementation strategies.

Figure: Concordance between biometric fingerprint scanning and electronic data capture system (ODK)

Feb 2020-Aug 2022



**The Association between Neighborhood Disadvantage and Preventable Diseases in Canines**

Christopher Pierson\* Christopher Pierson Edward Peters Kendra Ratnapradipa Joseph Fauver

Previous studies on humans have observed that neighborhood disadvantage adversely impacts human health behaviors and outcomes; however, its impact on the health of companion animals is understudied. The American Animal Hospital Association (AAHA) recommends companion dogs be vaccinated for distemper, adenovirus, parvovirus, parainfluenza, and rabies, as well as *Leptospira*, Lyme disease, *Bordetella*, and canine influenza depending on the dog's risk. Dogs and humans living in disadvantaged neighborhoods may not seek preventive care. The cost of prevention for most dogs starts at \$180/year for core vaccinations; treatment costs start at \$400. This requires veterinarians and owners to balance the cost of prevention or treatment with the owner's financial situation.

The Dog Aging Project is a longitudinal study of pet dogs across the United States; 27,538 dogs have information on their disease history and environment, including the Gini Index and a neighborhood disadvantage index. This study used cross-sectional baseline data to examine the association between disadvantage and common canine infectious diseases using log-linked Poisson generalized linear models with robust errors.

We observed that dogs in more disadvantaged neighborhoods were less likely to have a history of kennel cough (IRR: 0.903, CI: 0.83, 0.98). A dog's history of Lyme disease (adjusted for the state's Lyme endemicity) was observed to be inversely associated with neighborhood disadvantage (IRR: 0.85, CI: 0.76, 0.95). Higher-income inequality was associated with an increased history of Lyme disease (IRR: 4.11, CI: 1.30, 12.97). Neighborhood disadvantage and the Gini Index were not associated with a history of other preventable diseases.

Since we observed that dogs in more disadvantaged neighborhoods had decreased kennel cough and Lyme disease risks, veterinarians could prioritize other vaccinations over these two when balancing the cost of prevention with disease risk.



**New Long-Acting Reversible Contraceptive Insertions More Than Doubled Among a Commercially Insured, U.S.-Based Outpatient Population from 2010 to 2020** Mollie Wood\*  
Mekhala Dissanayake Clara Busse Chase Latour Sara Dejene Andrea Knittel Mollie Wood Alan Kinlaw

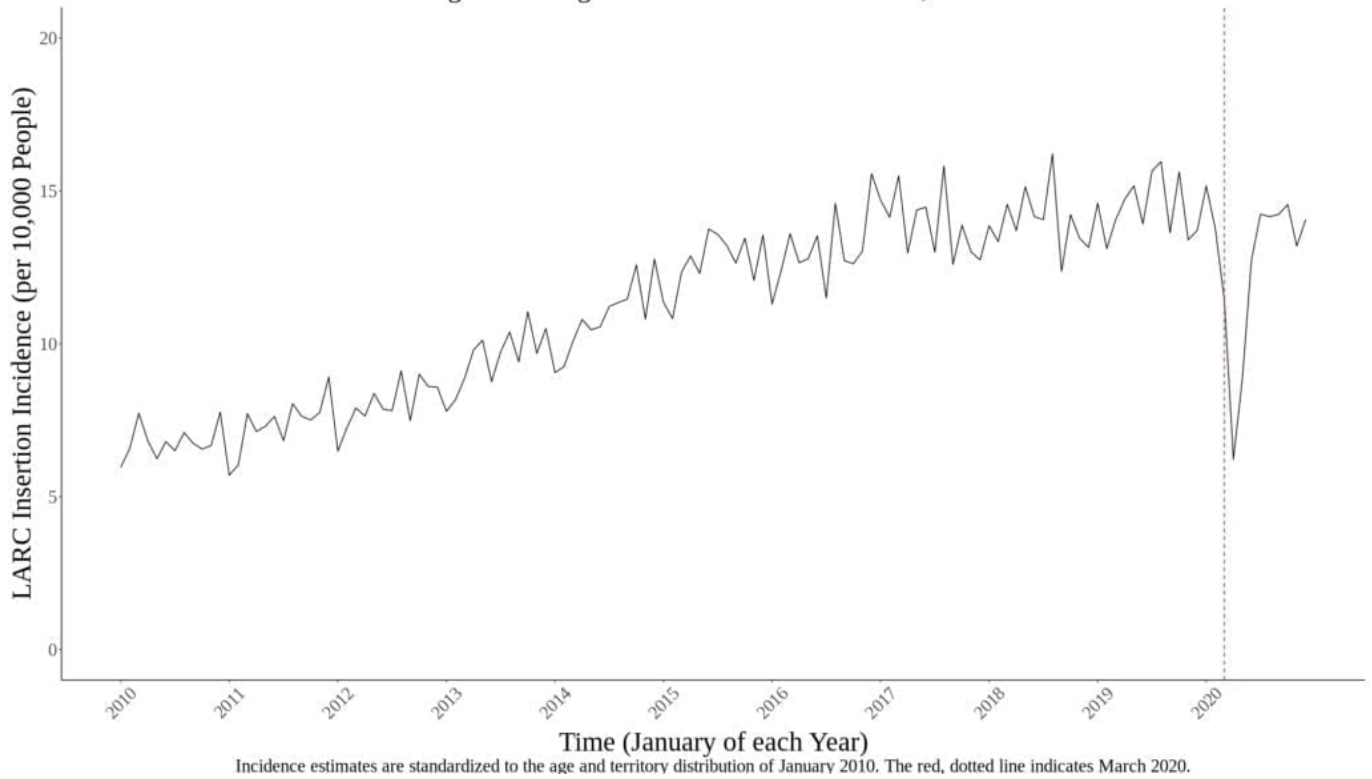
Long-acting reversible contraceptives (LARCs) are highly effective, but national trends in new use in outpatient settings are not well characterized.

We used the Merative MarketScan Commercial Claims and Encounters Database to construct a retrospective cohort of women ages 15 to 54 with  $\geq 180$  days of continuous enrollment in United States employer-sponsored private insurance from January 1, 2010 to December 31, 2020. We used Current Procedural Terminology (CPT) codes to identify LARC insertions/removals and Healthcare Common Procedure Coding System (HCPCS) codes to classify LARC type. We defined a new LARC insertion as an insertion code without a recent removal code (180 days before insertion) *and* a HCPCS code. We characterized the proportion of insertions by type: implants, non-hormonal intrauterine devices (NHIUD), hormonal IUD (HIUD). We calculated the month-level incidence of new LARC insertions per 10,000 people. Estimates are standardized to the age and state/territory distribution of January 2010.

We identified 1,372,594 new LARC insertions from 2010-2020. The monthly standardized incidence increased from 6.0 insertions per 10,000 people in January 2010 to 14.1 in December 2020. Incidence from March through May 2020 (low of 6.2) was lower than previous months (January: 15.2; February: 13.8), though incidence recovered by July (14.2). The average monthly incidence was lower in 2020 (12.7) compared to 2016-2019 (13.0-14.5). The share of LARCs that were HIUDs was stable across the study period (~68%) whereas implant use increased from 8.5% in 2010 to 21.0% in 2020, and NHIUD use decreased from 19.9% in 2010 to 10.9% in 2020.

New LARC insertion incidence doubled from 2010 to 2020. Incidence was lower early in the COVID-19 pandemic and although it returned to previous levels by July, the monthly average incidence in 2020 was still lower than prior years. Overall, our results demonstrate increasing popularity of LARCs among privately-insured users over this period.

Monthly Long-Acting Reversible Contraceptive (LARC) Insertion Incidence  
Among Women Aged 15-54 Years in MarketScan, 2010-2020



**Grip strength and risk of gestational diabetes mellitus: an observational study and Mendelian randomization analysis** Songying Shen\* Songying Shen Dongmei Wei Chang Gao Yusi Li Jianrong He Xiu Qiu

**Background:** Grip strength was found to be associated with the risk of type 2 diabetes, but its association with the risk of gestational diabetes mellitus (GDM) was less studied.

**Methods:** A total of 6888 pregnant women from the Born in Guangzhou cohort study (BIGCS) were included. Log binomial regression models were applied to investigate the prospective association between grip strength in early pregnancy and subsequent risk of GDM. Two-sample Mendelian randomization (MR) analysis was used to examine the causal association, using summary statistics from the UK Biobank and FinnGen consortium.

**Results:** The incidence of GDM in BIGCS was 17.5% (n=1204). There was a negative linear association between grip strength and GDM risk ( $p=0.0078$ ). In the multivariable-adjusted log-binomial regression models, higher grip strength was associated with a lower risk of GDM (adjusted RR [aRR] per SD increment of grip strength 0.93, 95% CI 0.88, 0.98 for left hand; aRR 0.94, 95% CI 0.89, 0.99 for right hand). In the MR analyses, an SD increment in genetically-predicted grip strength was associated with a lower GDM risk (odds ratio [OR] 0.53, 95% CI 0.36, 0.79 for left hand; OR 0.54, 95% CI 0.36, 0.81 for right hand).

**Conclusions:** Our results support a probable causal relationship between grip strength and GDM, suggesting that interventions targeting grip strength may be beneficial in preventing GDM.

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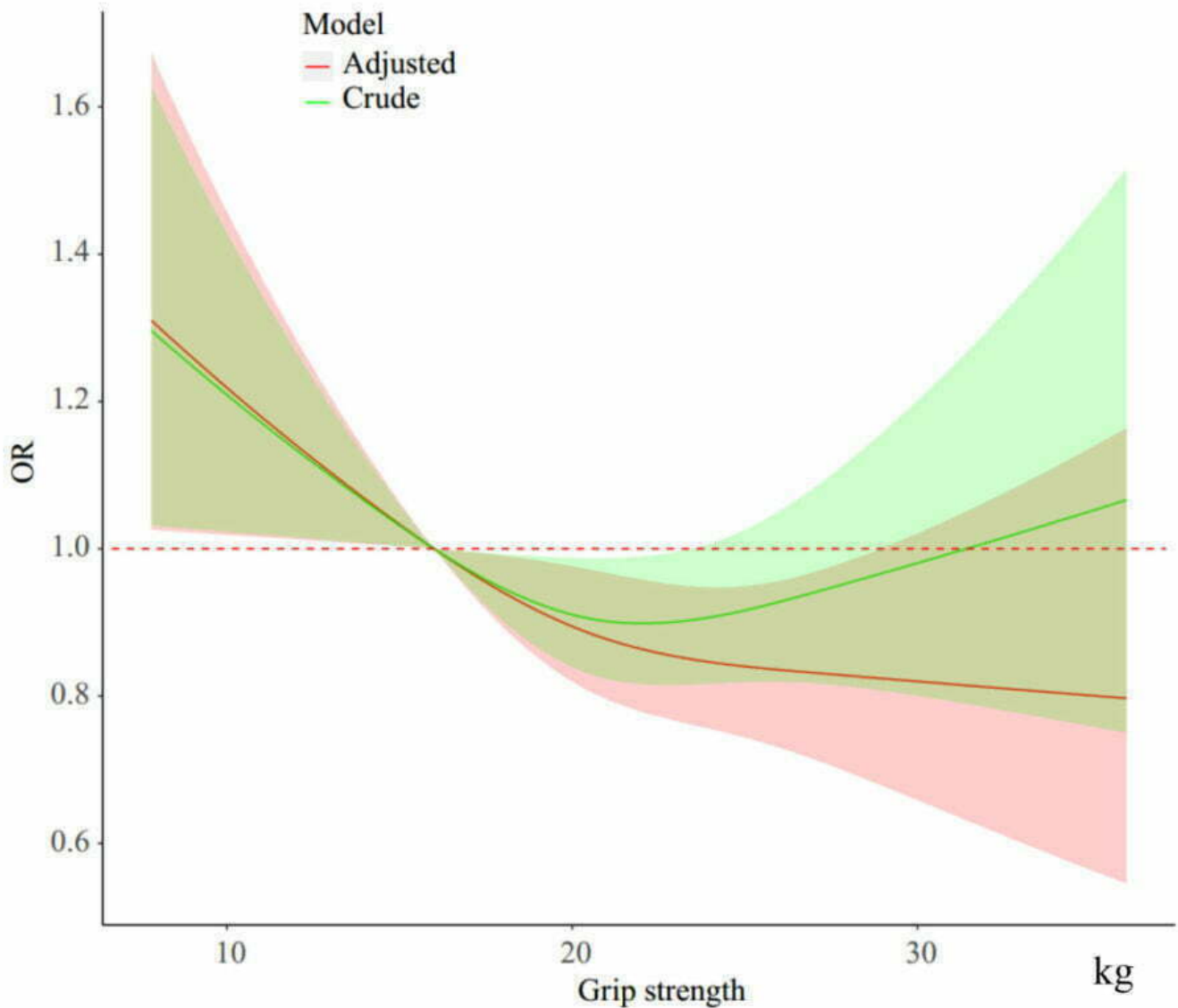


Figure 1 Association between grip strength and gestational diabetes using non-linear logistic regression analyses (smoothed cubic splines) in the Born in Guangzhou Cohort Study. Green: crude; Red: adjusted for maternal age, education level, smoking, parity, pre-pregnancy BMI, family history of diabetes, and physical activity. Grip strength of 16 kg was set as reference. Green and red shadows represent 95% confidence intervals of crude estimates and adjusted estimates, respectively.

**The association between timing of menarche, menstrual characteristics and perinatal depression: a cross-sectional study of 5953 women in Sweden** Elgeta Hysaj\* Elgeta Hysaj  
Ketty Xu Donghao Lu

**Background** Perinatal depression (PND) is a debilitating condition which occurs during or after the pregnancy when menstruations are absent or just resumed. Although menstruations and PND are intertwined because of pregnancy, the associations between menarche timing, menstrual characteristics, e.g., menstrual cycle length and dysmenorrhea, and PND are unclear.

**Methods** Leveraging the LifeGene cohort in Sweden launched in 2009, a cross-sectional analysis was conducted including 5953 women who have given birth. Self-reported Edinburgh Postnatal Depression Scale - lifetime version was used to identify probable PND. Age at menarche, the length of the menstrual cycle, and dysmenorrhea were self-reported. ORs of PND in relation to age at menarche, menstrual cycle length, and dysmenorrhea were estimated using logistic regression with adjustment for sociodemographic factors (e.g., age and civil status) and potential confounders (e.g., BMI and smoking).

**Results** At a mean age of 38.75 (SD, 7.94) years, 1415 women met the criteria of a probable PND (23.7 %). Compared to women with menarche at age 11-14, women with early menarche ( $\leq$  age 10) appeared to have higher odds of PND (OR = 1.24, 95% CI 0.88,1.72), while no association was observed for late menarche ( $\geq$ age 15). Compared to women with a menstrual cycle of 27-30 days, a positive association was observed for menstrual cycle of 23-26 days (OR = 1.27, 95% CI 1.05,1.59) and 31-34 days (OR = 1.38, 95% CI 1.02,1.85) while no significant association was observed for having cycles of  $\leq$ 22,  $\geq$ 39 days, or irregular cycle durations. Lastly, women with self-reported history of dysmenorrhea had 58% higher odds of PND than those without dysmenorrhea (95% CI 30%, 91%).

**Conclusions** Our findings suggest a positive association between dysmenorrhea and PND. Future research with a larger sample size and repeated measures on menstrual cycles is needed to determine the associations with timing of menarche and menstrual cycle length.

**Vitamin D, calcium, and timing of menopause in a large, longitudinal cohort study** Anne Marie Jukic\* Anne Marie Jukic Dale Sandler Clarice Weinberg Katie O'Brien

Vitamin D status has been inconsistently associated with ovarian reserve and menopause. We used data from the Sister Study cohort to examine the associations of vitamin D supplement use, 25-hydroxyvitamin D (25OHD) level, and calcium supplement use, with the timing of natural menopause. Vitamin D and calcium supplement use were based on a questionnaire at baseline and two follow-up time points, and characterized in multiple ways based on type, dose, and duration of use. Serum samples from a random subset of participants were analyzed for total 25OHD (25OHD<sub>3</sub>+25OHD<sub>2</sub>+epi-25OHD<sub>3</sub>) using liquid chromatography-mass spectrometry. Menopause was assessed at each follow-up as, "Have you had a menstrual period in the past 12 months?" and if not, their age at last menstrual period. We censored women at time of uterectomy or medically induced menopause, death, loss to follow-up or October, 2020. We used multivariable Cox proportional hazard models to estimate HRs and 95% CIs, adjusting for race/ethnicity, education, BMI, alcohol use, smoking status, and physical activity. Among the 13,102 eligible premenopausal participants, 8,897 experienced menopause during follow up. Combined use of a multivitamin and a single vitamin D supplement was associated with slightly earlier menopause (HR(CI): 1.10 (0.98, 1.24) (Figure 1). None of the remaining vitamin D or calcium supplement variables were meaningfully associated with timing of natural menopause. (Figure) A 25OHD level of at least 30 ng/ml was imprecisely associated with earlier menopause (HR(CI): 1.15 (0.85, 1.39), n=906). In total, vitamin D and calcium supplementation were not strongly associated with timing of menopause, though several results indicate that higher levels of vitamin D may be associated with earlier menopause.

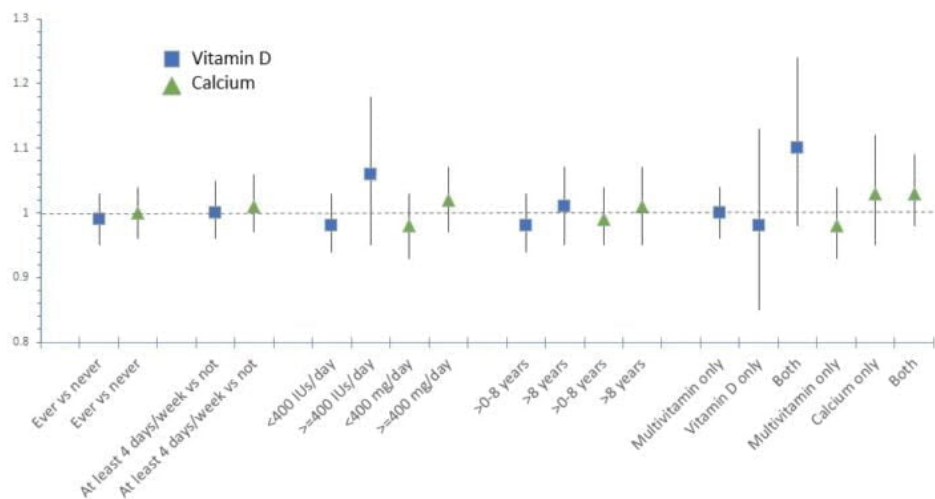


Figure 1. Estimated multivariable-adjusted hazard ratios (HRs) and 95% CIs between vitamin D and calcium supplement use and age at menopause.

**Association between peripheral blood immune cells and perinatal depression: a cross-sectional analysis of 6012 women in Sweden** Jing Zhou\* Jing Zhou Donghao Lu

**Aims:** Perinatal depression (PND) affects millions of new mothers globally. However, biomarkers are not available for early detection and clinical diagnosis. Emerging data have suggested a link between immune cytokines and PND. The association between PND and peripheral blood immune cells, which are widely tested in clinical practice at minimum cost, is yet unknown. **Methods:** We conducted a cross-sectional analysis of 6012 women in the LifeGene cohort in Sweden. PND was assessed with the Edinburgh Postnatal Depression Scale (Lifetime version) at baseline in 2009. Peripheral blood was donated at baseline to profile immune cells (i.e., lymphocytes, granulocytes, and monocytes). Logistic regression model was employed to examine the associations between log-transformed immune cell counts and PND with adjustment for demographics and potential confounders (e.g., smoking and alcohol consumption). **Results:** At a mean age of 41.92 years (SD 9.35), 1,415 (23.5%) participants met the criteria for a probable PND. A positive association was indicated between lymphocyte count and PND (OR 1.11, 95% CI 0.86, 1.45), with lower odds (OR 0.87, 95% CI 0.65, 1.15) in Q1 and higher odds in Q3 (OR 1.12, 95% CI 0.85, 1.46) compared to Q2 (P for trend =0.22). Positive associations were also suggested for monocytes (OR 1.13, 95% CI 0.88, 1.45) and eosinophils (OR 1.06, 95% CI 0.86, 1.30), while neutrophils seem to show negative association (OR 0.86, 95% CI 0.55, 1.35). However, the dose-response relationship was not observed when analyzing cell counts in tertiles. **Conclusions:** Our preliminary results based on cross-sectional data found no strong evidence on the association between blood immune cells and experience of PND. Future analysis including follow-up data on incident PND will be conducted to better understand the associations.

**Division of unpaid domestic labor, gender, and mental well-being among employed, partnered parents in Canada** Bonnie Janzen\* Bonnie Janzen Prashikchhya Parajuli

The potential hazards associated with unpaid domestic work have generally received scant epidemiological attention. The aim of this study, then, was to determine whether the division of domestic work within households was associated with the mental health of partnered mothers and fathers. Data were from Statistics Canada's 2016 cross-sectional, nationally representative General Social Survey. For this study, participants were restricted to adults in heterosexual partnerships, employed at least part time, with a child living in the household. The dependent variable, self-rated mental health (SRMH), was based on a single item assessment of participants' overall mental well-being on a five-point response scale, dichotomized into poor/fair and good/very good/excellent. Division of unpaid domestic labor was based on a series of questions asking respondents to indicate who in their household mainly took care of various domestic tasks; like items were grouped and the number of chores performed solely by the respondent summed and then dichotomized. Participants were also asked to indicate satisfaction with the division of household work (very satisfied/satisfied versus very dissatisfied/dissatisfied/neither). Covariates included socio-demographics and characteristics of paid work. Following descriptive analyses, multivariable [logistic regression](#) was conducted separately for women and men. All analyses were weighted and conducted using a robust variance estimation technique. Women were more likely than men to report sole responsibility for most household chores considered and were less likely to be satisfied with the division of labor. After adjustment for covariates which included paid work characteristics, greater sole responsibility for child rearing tasks was associated with an elevated odds of fair/poor SRMH for women (OR=2.05; 1.04-4.04) but was unrelated for men (OR=1.19; 0.52-2.72). Dissatisfaction with the current division of household work was related to poorer SRMH for both women (OR=3.67; 1.88-7.16) and men (OR=3.01; 1.39-6.52). Greater responsibility for child care tasks relative to one's partner may be a determinant of working mothers' mental health. More epidemiological research should consider unpaid domestic labor as a potentially hazardous exposure.



**Adverse childhood experiences and mental health outcomes among sexual minority women:****A population-based study** Fenfen Ge\* Fenfen Ge Thor Aspelund Unnur Anna Valdimarsdóttir1  
Edda Bjork Thordardottir

**Background:** Sexual minority women are more likely to have a history of adverse childhood experiences (ACEs) than heterosexuals. Yet to what extent the cumulative number and types of ACEs contribute to adverse mental health among sexual minorities remains to be elucidated

**Methods:** Participants were 11,454 women in the Stress-And-Gene-Analysis (SAGA) cohort, a nationally representative study in Iceland. Self-reported data were obtained on sexual orientation, exposure to 13 different ACEs (ACE-IQ), and current symptoms of depression and anxiety. We used regression models to test the associations between sexual orientation and ACEs, and mediation models to test the contribution of ACEs to mental health disparities among sexual minorities.

**Findings:** At a mean age of 44 years, 724 (6.6%) women identified as sexual minorities. Sexual minority women (22%) were more likely to report 6 or more ACEs than heterosexual women (11.3%). Compared with heterosexual women, sexual minority women were at higher odds of experiencing multiple ACEs; the odds ratio was 2.5 (95% CI 1.9-3.2) for  $\geq 6$  ACEs. Sexual minority women were more likely to report six types of ACEs than heterosexual women, specifically emotional abuse, sexual abuse, emotional neglect, mental illness of a household member, bullying and community/collective violence (OR ranging from 1.32 to 1.47). They were also more likely to report depression (OR=1.7, 95% CI 1.4-2.0) and anxiety (OR=2.1, 95% CI 1.8-2.5) of which 30% of symptoms of depression and 40% of anxiety was mediated by ACEs.

**Interpretation:** These findings suggest that ACEs is a major contributor to the mental health disparities observed among sexual minority females.

**“Breaking the Cycle: An In-Depth Look at Peru’s “Women’s Emergency Centers” Strategy for Combating Intimate Partner Violence”** Renzo Calderon Anyosa\* Renzo Calderon Anyosa

Background: Violence against women is one of the most common forms of violence worldwide, with devastating consequences. A strategy to tackle this issue in Peru includes the creation of “Women Emergency Centers” (*Centros de Emergencia Mujer* “CEM”) at the district level.

Aim: To conduct a policy analysis to evaluate the impact of the CEMs on intimate partner violence (IPV) between 2004 and 2016 in Peru and to assess the effect of misclassification on the effect estimate.

Methods:

A secondary analysis will be performed using the information available in the “domestic violence” module of the Demographic and Health Surveys from the years 2004 to 2016. The main outcome of the study is the binary probability of suffering any type of IPV (physical, psychological, or sexual) during the last 12 months. The analysis uses a difference-in-differences model and the Callaway and Sant’Anna estimator to account for the dynamic effects of the staggered implementation of CEMs in different districts.

Results:

There were 2.41 (95% CI 0.25; 5.08) more cases per 100 women of any type of intimate partner violence in exposed districts with CEMs compared to unexposed districts. Additionally, there were 4.92 (95% CI 1.36; 8.47) more cases per 100 women of psychological violence. There was no effect on physical violence (1.18 cases per 100 women, 95%CI: -2.46; 4.81) or sexual violence (0.59 cases per 100 women, 95%CI: -0.88; 2.06).

Conclusions:

Our findings suggest that while CEMs were created with the aim of reducing IPV, they may have had the opposite effect. The increase was only observed for psychological violence, which could be due to an increase in reporting rather than in incidence. However, the study also suggests that the CEMs could potentially increase the incidence of violence as a backlash for those who use the system. Overall, these findings suggest that while CEMs may have some impact on increasing IPV, further research is needed to fully understand the mechanisms by which they work and how they can be optimized to reduce IPV in different contexts. Additionally, the lack of impact on physical and sexual violence highlights the need for a multi-faceted approach to addressing IPV that includes interventions targeting different forms of violence.

**Early-Life Disadvantage and the Risk of Uterine Fibroids Among Black Women** Sefanit Admasu\* Sefanit Admasu Anissa I. Vines Alexandra Sitarik Quaker E. Harmon Chantel L. Martin Lauren A. Wise Ganesa Wegienka Donna D. Baird

**Overview:** This study examines the association between early-life disadvantage and the incidence of uterine fibroids in Black women and assesses the modifying effects of childhood supportive environment, socioeconomic status, and health behaviors.

**Methods:** Uterine fibroid incidence was determined using prospective standardized ultrasound exams to identify and measure any uterine fibroid  $\geq 0.5$  cm in diameter in 1,308 Black participants ages 23-34 years who were enrolled in the Study of Environment, Lifestyle and Fibroids and fibroid-free at baseline. Using latent class analysis, an early-life disadvantage construct was derived using childhood factors (i.e., household composition, food insecurity, household income, mother's educational attainment, neighborhood safety, and access to quiet bedroom) collected at baseline. Cox models were used to estimate the association between early-life disadvantage and uterine fibroid incidence with participant age as the time scale.

**Results:** Early-life disadvantage was not associated with an increased risk of uterine fibroids (HR=0.83; 95% CI= 0.65, 1.06), and no appreciable evidence of effect measure modification was found. However, among participants raised with low childhood support, the risk of uterine fibroids was higher for those whose mother attained less than a high school diploma compared to those whose mother attained at least a high school diploma (HR=1.95; 95% CI=1.09, 3.48).

**Conclusion:** Although there was no overall association between early-life disadvantage and uterine fibroids risk, participants born to mothers without a high school diploma and limited social support during childhood, may be at an increased risk of uterine fibroids, suggesting the importance of early childhood environment as a protective factor for uterine fibroids among Black women.

**Cervical procedures for HPV and subsequent sexual function in female pregnancy planners**

Julia Bond\* Julia Bond Katharine O White Rebecca B Perkins Lauren A Wise

**Introduction:** Cervical screening and diagnostic procedures are a critical tool in cervical cancer prevention, but studies evaluating their effect on sexual functioning have had mixed findings.

**Methods:** We used data from Pregnancy Study Online (PRESTO), a North American preconception cohort study of pregnancy planners (2013-2022). At enrollment, female participants answered questions about their history of abnormal Papanicolaou (Pap) testing and cervical diagnostic procedures. Beginning in March 2021, we invited all PRESTO participants to complete an optional survey related to sexual health which included a validated scale measuring sexual dysfunction. Participants in our analysis were residents of the United States or Canada, aged 21-45, attempting pregnancy without the use of fertility treatment, in a relationship with a male partner, and completed the sexual health questionnaire (N=3,599). We used fully conditional specification methods to impute missing data on exposures and covariates. We used log-binomial models to calculate risk ratios (RRs) and 95% confidence intervals (CIs) relating a history of abnormal Pap tests, number of abnormal Pap tests (1, 2,  $\geq 3$ ), colposcopy, and loop electrosurgical excision procedure (LEEP) to sexual dysfunction, adjusted for prespecified confounders.

**Results:** Thirty percent of the sample reported a history of abnormal Pap tests, of which 76% and 16% reported receiving a colposcopy and LEEP, respectively. The adjusted RR relating a history of abnormal Pap test to female sexual dysfunction was 1.10 (95% CI 0.97, 1.23). The RR increased with the number of abnormal Pap tests. The adjusted RR for a history of colposcopy and LEEP were 1.06 (95% CI 0.84, 1.34) and 1.06 (95% CI 0.83, 1.36), respectively.

**Conclusion:** We observed a slight increase in the risk of sexual dysfunction associated with a history of multiple abnormal Pap tests. Other cervical procedures were not appreciably associated with sexual dysfunction.

**The association of cholesterol levels with memory and memory change in a US national cohort** Silvia Miramontes\* Silvia Miramontes Erin L. Ferguson Umair Khan Marina Sirota Maria Glymour

**Introduction**

There is conflicting evidence regarding the effects of cholesterol levels on late life cognition. These inconsistencies may be due to the use of highly selected population samples or samples from clinical settings. We evaluated the association of high-density lipoprotein cholesterol (HDL), total cholesterol (TC), and estimated low-density lipoprotein cholesterol (LDL) on cognition in a national cohort.

**Methods**

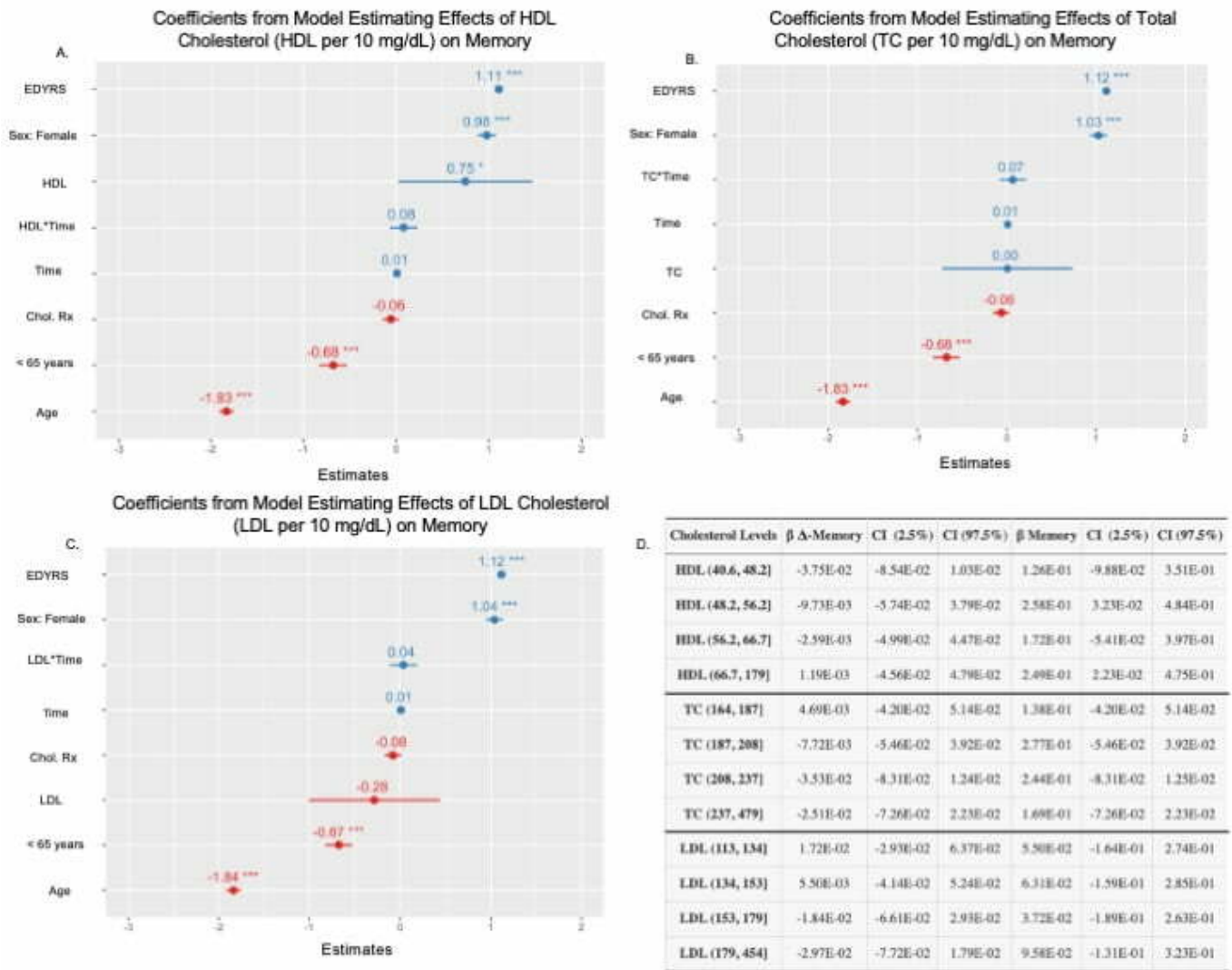
The Health and Retirement Study (HRS) is a longitudinal panel study of community-dwelling individuals ages 50+. In the years 2006 and 2008 biomarkers were collected through dried blood spots to measure HDL and TC levels (n=19,923). Total cognition was assessed every two years through 2018 using the combined results of memory assessments for immediate and delayed word recall. Linear mixed models were fit with random intercepts for participants across recorded time points, with time since baseline and its interaction with cholesterol to predict cognition; analyses were stratified by sex and age  $\geq 65$  years at the time of cholesterol measure. Covariates included age at cognitive assessments, time, years of education, sex, and use of medications for cholesterol control.

**Results**

Higher HDL at baseline was significantly associated with higher levels of memory (b=0.10 per mg/dL, 95%CI: 0.024, 0.168), but not with rate of change in memory (b=0.00, 95%CI: -0.014, 0.016). Higher TC was not associated with higher levels of memory (b=0.06 per mg/dL, 95%CI: -0.017, 0.130) or rate of change in memory (b=-0.01, 95%CI: -0.027, 0.004). Estimated LDL cholesterol was also not associated with memory (b=0.02 mg/dL, 95%CI: -0.050, 0.094), or rate of change in memory (b=-0.01, 95%CI: -0.028, 0.002), although estimates were imprecise.

**Conclusion**

While HDL is associated with higher levels of memory, the lack of association between calculated LDL, TC levels and memory suggests no large effects on cognitive aging, which is surprising given the links to cardiovascular disease.



**Fig. 1** Panels (a)-(c) depict the effect sizes of each of the outlined covariates. Here effect sizes are sorted to demonstrate the covariates with a greater effect over memory. Panel (d) describes the effects of quantile cholesterol levels (TC, HDL, and calculated LDL) among participants across each time point.

**Null association between alcohol consumption and dementia with Mendelian randomization approaches among older adults in the United States** Kyle Campbell\* Kyle Campbell Mingzhou Fu Elizabeth MacDonald Matthew Zawistowski Erin B. Ware Kelly Bakulski

Genetic causal inferences methods may help clarify previously reported mixed relationships between alcohol consumption, a modifiable risk factor, and dementia. We performed Mendelian randomization analyses using a two-sample summary statistics approach and a one-sample individual-level genetic data approach. For our two-sample analysis, we identified 59 single nucleotide polymorphisms (SNPs) that met instrument selection criteria (genome-wide significant, independent) from genome-wide association studies of weekly alcohol consumption (Liu et al., 2019, n=941,280) and late onset Alzheimer's disease (Kunkle et al., 2019, n=21,982 cases, 41,944 controls). In our one-sample analysis in the 2012 wave of the Health and Retirement Study (HRS), we tested the association between alcohol consumption ( $\log_2$  drinks per week) and impaired cognition (either Langa-Weir classified dementia or cognitive impairment without dementia versus normal cognition). We stratified models by genetic ancestry and adjusted for demographics, local genetic ancestry, and *APOE* genotype. In two-sample analyses, we observed no evidence of a causal relationship between alcohol consumption and late-onset Alzheimer's disease using the inverse variance weighted estimator (OR=1.15, 95% confidence interval (CI):[0.78, 1.72]), nor with complementary estimators. In our one-sample analysis, we again found no association between a doubling in alcohol consumption and cognitive impairment without dementia (African ancestry (n=1,673, OR=1.00, 95% CI:[0.44, 2.25]); European ancestry (n=8,072, OR=1.03, 95% CI:[0.54, 3.56])) or with dementia (African ancestry (n=1,322, OR=1.25, 95% CI:[0.58, 2.66]); European ancestry (n=8,072, OR=0.73, 95% CI:[0.36, 1.46])) using an inverse variance weighted estimator. Our one- and two-sample Mendelian randomization analyses suggest there is no inferred causal relationship between alcohol consumption and dementia.

**Factors Associated with Osteoarthritis Knee Pain During the COVID-19 Pandemic in the Multicenter Osteoarthritis Study (MOST)** Morgan Wolff\* Morgan Wolff James Torner David T. Felson Michael C. Nevitt Cora E. Lewis Tuhina Neogi Robert Wallace

Introduction: Persons with osteoarthritis had increased COVID-related hospitalizations; for those with musculoskeletal disorders, there were also delays in health care and treatments. The societal and individual pandemic-induced changes on osteoarthritis pain and progression have not been previously studied.

Methods: This cross-sectional study conducted in the Fall of 2021 investigated pandemic-induced changes in health and lifestyle behaviors among 1,150 participants in the MOST study that completed a telephone survey. A shorter survey (n=751) assessed the occurrence of COVID-19 and whether subjects had experienced a change in knee pain (increase, decrease, or neither). A longer survey (n=399) included additional questions about changes in activity, diet, medications, and residence. To determine the impact of pandemic-induced changes on osteoarthritis, pain increase (yes/no) was modeled by logistic regression with potential predictors and covariates. Modeled variables were kept if they were associated with pain increase at  $p < 0.1$ .

Results: Out of 1,150 participants, 192 reported a positive COVID-19 test (16.7%) and 1,082 reported vaccination (94.3%). Increase in pain was reported in 351 participants (30.6%). General health was rated significantly poorer in those with pain increase ( $p < 0.01$ ). Variables that were significantly related to an increase in knee pain after regression were previously measured disease status (right KL grade, right WOMAC pain, and left WOMAC pain), knee surgery, increased medications, and changes in the following behaviors during the pandemic: amount of time drinking alcohol ( $p < 0.01$ ) and watching television ( $p = 0.05$ ).

Discussion: Among this sample of persons with osteoarthritis surveyed during the COVID-19 pandemic, increased knee pain was associated with changes in lifestyle factors (possibly due to the pandemic) and decreased general health but was not related to COVID-19 infection.



**Timing of Earned Income Tax Credit (EITC) eligibility differentially predicts dementia risk: A Sequence Analysis Approach** Haobing Qian\* Haobing Qian Lucia Pacca Rita Hamad M. Maria Glymour Anusha Vable

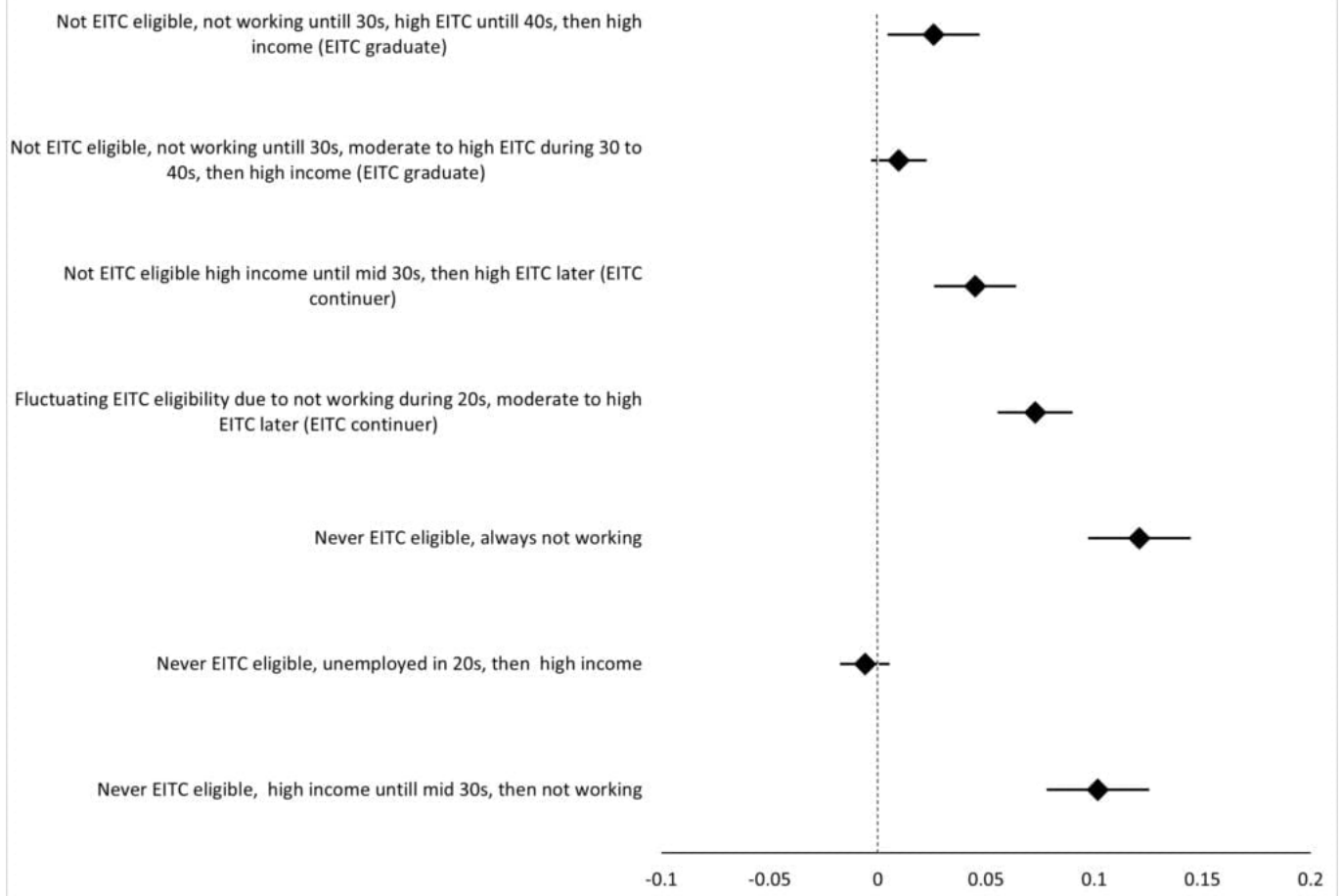
The Earned Income Tax Credit (EITC; the US's largest poverty-alleviation program), may impact later dementia risk via income support or reduced stress. To evaluate effects of EITC eligibility on long-term brain health, we must characterize lifecourse patterns in timing, duration, and amount. We fill this critical gap.

Using the National Longitudinal Survey of Youth 1979 cohort (N=7,350), we calculated annual individual EITC eligibility from ages 22-48. We classified five eligibility states based on amount (from none to >\$2500), and identified distinct EITC eligibility trajectory groups using sequence- and cluster-analysis. Our outcome was an algorithmically defined 20-year cumulative dementia probability. We used linear regression to estimate the EITC trajectory-dementia association adjusted for gender, race/ethnicity, birth year, and childhood socioeconomic status.

We identified 8 EITC trajectory clusters based on timing, EITC eligibility amount, and employment status, including 4 distinct EITC trajectories: 2 trajectories where respondents were EITC eligible, then "graduated" due to high income (EITC graduates); 2 trajectories where respondents remained EITC eligible at age 48 (EITC continuers). Compared to the reference (those who were never EITC eligible due to high income), the two EITC graduate trajectories had slightly higher dementia probability (e.g., not working in early life, eligible for high EITC in 30-40s, then EITC graduate:  $\beta=0.01$ , 95%CI:0.00,0.02), while EITC continuers had substantially higher dementia probability (e.g. fluctuating EITC eligibility due to not working in 20s, then high EITC later,  $\beta=0.07$ , 95%CI:0.06,0.09). Those who were never EITC eligible due to not working had the highest dementia probability ( $\beta=0.12$ , 95% CI:0.08,0.14).

This novel descriptive analyses summarize lifecourse EITC eligibility patterns and shows later-life EITC eligibility is associated with higher dementia risk.

Ref group= Never EITC eligible, high income



## **Association of multi-dimensional factors with Accelerating Age and constructing a Healthy Lifestyle Index** Lin Xu\* Lin Xu

### **Introduction**

Ageing process is influenced by multi-dimensional factors collectively. Previous studies examined association of one separate factor with mortality without considering different manifestations of ageing process. We investigated associations of multi-dimensional factors with Accelerating Age (AA), a proxy to quantify ageing, in older Chinese.

### **Methods**

9,831 participants from Guangzhou Biobank Cohort Study were included. Four exposure domains of 15 variables including demographic and socioeconomic factors, lifestyle factors, stress across the life course and common diseases were assessed. AA was calculated based on chronological age and eight biomarkers. Traditional multivariable linear and Bayesian Network (BN) models were used.

### **Results**

In both traditional and BN models, male sex, smoking, alcohol use, physical inactivity, greater waist circumference and body mass index (BMI) were associated with higher AA, with the adjusted  $\beta$  (95% confidence intervals (CI)) being 2.75 (2.40 to 3.09), 1.31 (0.87 to 1.76), 1.35 (0.55 to 2.15), 0.64 (0.40 to 0.88), 0.09 (0.06 to 0.11) and 0.13 (0.07 to 0.19) years, respectively. A Healthy Lifestyle Index (HLI) was constructed including the above lifestyle factors (non-smoking, non-alcohol use, physically active, non-central and non-general obesity) with a point assigned for each. A higher index indicates healthier lifestyle. Compared with participants with an HLI of 5, those with an HLI of 0-2 had 2.90 (2.48 to 3.32) years older AA.

### **Conclusions**

Male sex, smoking, alcohol use, physical inactivity, greater waist circumference and BMI were associated with higher AA by 0.09 to 2.75 years, suggesting that adopting a healthy lifestyle may alleviate process of phenotypic ageing.

## Telomere length and lifespan in men and women using a Mendelian randomization study

Mary Schooling\* C Mary Schooling Li Shun

### Abstract

**Background:** Identification of targets of intervention to promote longevity are crucial given global population aging. Telomere length is a well-established biomarker of aging. Whether telomere length is also a driver of longevity and hence a valid target of intervention remains unclear. Previous studies concerning the effects of telomere length on lifespan have not been definitive because of vulnerability to confounding and selection bias, nor have differences by sex been considered when both telomere length and lifespan differ by sex. We examined the associations of leukocyte telomere length with sex-specific lifespan (proxied by parental attained age or age at death) in a Mendelian randomization study to obviate confounding and survival bias.

**Methods:** We used summary statistics from the largest publicly available genome-wide association studies of telomere length and lifespan from the UK Biobank of 0.5 million people. Estimates were obtained using inverse variance weighted with the weighted median and MR-Egger as sensitivity analysis. Estimates were also adjusted for white blood cell count

**Results:** Telomere length was unrelated to lifespan in men (0.19 years per standard deviation of log telomere length, 95% confidence interval (CI) -0.51 to 0.90) and women (0.02, 95% CI -0.89 to 0.92). Estimates were similar in sensitivity analysis and after adjustment for white blood cell count.

**Conclusions:** Telomere length does not appear to be causally relevant to longevity; other targets of intervention to promote longevity should be sought.

### One-sample univariable MR estimates for telomere length in 472174 people (effect sizes log transformed) on lifespan (life years) in men and women from the UK Biobank (n=389,166), and multivariable MR estimates adjusted for white blood cell count

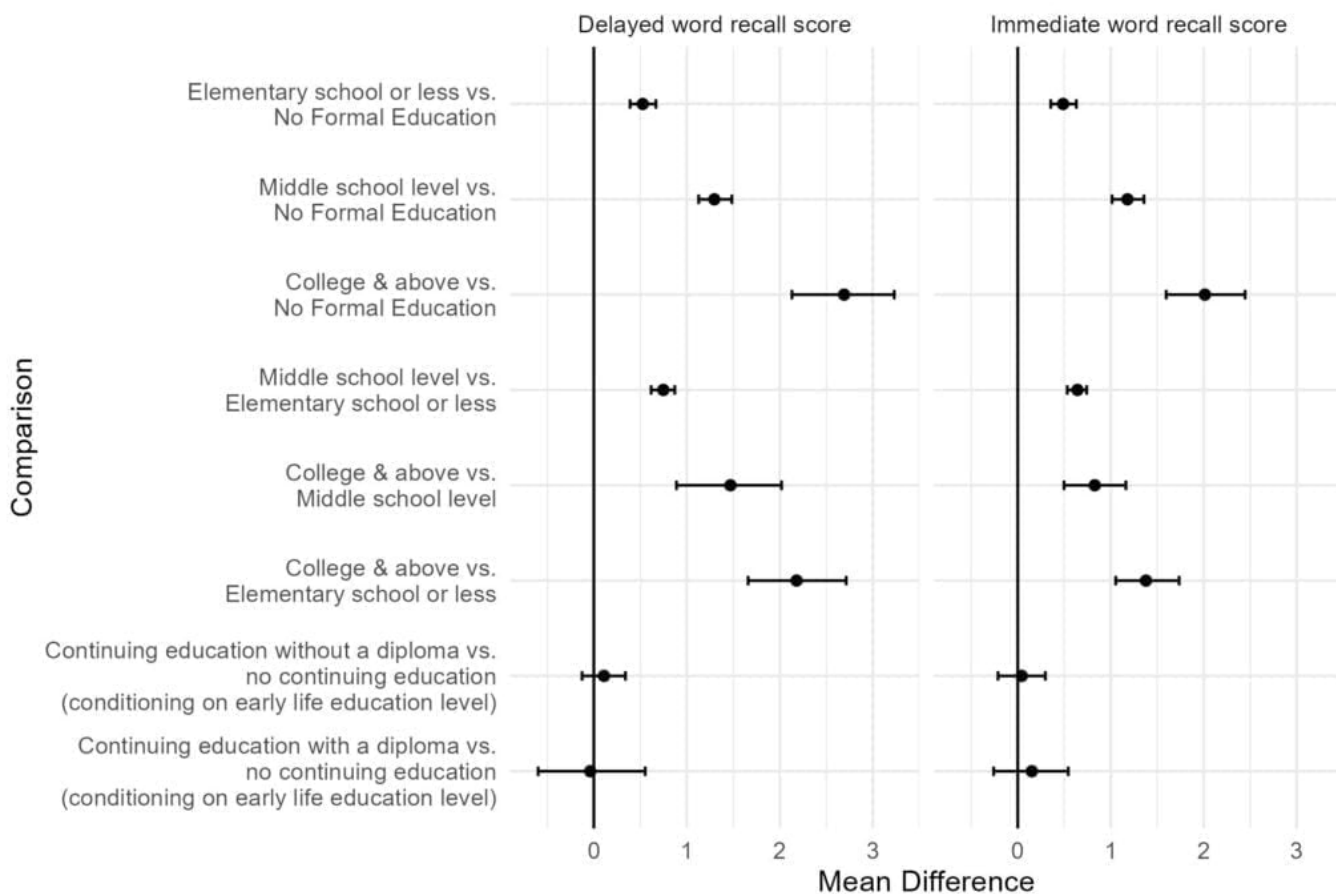
Method	#SNPs, F-stat	Men	Life years (95% CI)	p	MRE   p	Women	Life years (95% CI)	p	MRE   p
Univariable									
IVW	137, 109.2		0.20 (-0.50 to 0.90)	0.58			0.02 (-0.89 to 0.92)	0.97	
WM			0.16 (-0.54 to 0.86)	0.65			0.06 (-0.73 to 0.85)	0.88	
MRE			-0.70 (-2.00 to 0.60)	0.29	0.11		-0.92 (-2.60 to 0.76)	0.29	0.19
WBC adjusted									
MV_IVW	435, 27.2		0.08 (-0.54 to 0.70)	0.79			0.02 (-0.61 to 0.94)	0.94	
MV_Median			0.15 (-0.60 to 0.89)	0.69			0.37 (-0.47 to 1.21)	0.39	
MV_MRE			0.03 (-0.69 to 0.74)	0.47	0.75		-0.27 (-1.00 to 0.46)	0.47	0.11

IVW = Inverse variance weighted; WM = Weighted median; MRE = MR-Egger, WBC = white cell count, MV = multivariable, F-stat = F-statistic, CI = confidence interval, p = p value, MRE | p = MRE intercept p-value

**Lifecourse Education and Late-life Cognitive Function among Chinese Older Adults** Yingyan Wu\* Yingyan Wu L. Paloma Rojas-Saunero Roch Nianogo Alden L. Gross Beate R. Ritz Elizabeth Rose Mayeda

Most research on education and late-life cognitive health uses total years of education or degree attainment in US and European samples. However, the educational experiences of Chinese older adults differ substantially: more than 20% of older adults have no formal education and continuing education programs were launched for adults in 1978. We estimated effects of early-life education and continuing education in adulthood on late-life memory function among Chinese older adults. We used cross-sectional data from China Health and Retirement Longitudinal Study (CHARLS), a nationally representative study of Chinese adults aged 45+ years. The exposure was early-life education (no formal education, primary school education, middle school, and college) and continuing education (none, participated without a diploma, and participated with a diploma). Confounders included childhood socioeconomic status, occupation, marital status, and region of residence. Memory was assessed using 10-word immediate word recall and delayed word recall scores (range 0-10). Effects were estimated using g-computation and 95% CIs were obtained by 1000 bootstrap samples. 8,549 participants were included (mean age 58.2 years, mean immediate word recall score 4.0 (SD=1.6) and mean delayed word recall score 3.1 (SD=1.9). Early-life education was associated with higher memory performance. For example, the estimated mean delayed word recall was 0.53 (95%CI: 0.39-0.67) words higher for primary school versus no formal education. Associations were slightly smaller for immediate word recall. Estimated effects of continuing education were null. Higher early-life education level is associated with higher late-life memory function while the evidence does not support such a role for continuing education. Evaluation of joint effects of early-life and continuing education on late-life memory decline will provide additional insights into effects of lifecourse formal education on late-life cognitive health.

# The Estimated Effect of Education Level on Cognition



**Longitudinal association of allostatic load with depressive symptoms among urban adults: Healthy Aging in Neighborhoods of Diversity across the Life Span study** Hind A. Beydoun\*

Hind Beydoun May A. Beydoun Edward Kwon Sharmin Hossain Marie T. Fanelli-Kuczmarski Ana Maldonado Michele K. Evans Alan B. Zonderman

**Background:** Evidence suggests that lifetime exposure to stressful life events and chronic stressors may be linked to geriatric depression. Allostatic load (AL) is considered a mediator of the stress-health relationship and has been linked to psychosocial factors reflecting health disparities. The purpose of this study was to examine the longitudinal associations of AL with depressive symptoms scores among urban adults, before and after stratifying by sex and race.

**Methods:** Secondary analyses were performed using Visit 1 (2004-2009), Visit 2 (2009-2013) and Visit 3 (2013-2017) data collected on 2,298 Healthy Aging in Neighborhoods of Diversity across the Life Span study participants (baseline age: 30-64y). AL at Visit 1 ( $AL_{v1}$ ) and z-transformed probability of higher AL trajectory ( $AL_{traj}$ ) between Visits 1 and 3 were calculated using cardiovascular, metabolic and inflammatory risk indicators. The 20-item Center for Epidemiologic Studies Depression (CES-D) scale was used to calculate total and domain-specific depressive symptoms scores. Mixed-effects linear models controlled for socio-demographic, lifestyle and health characteristics.

**Results:** In fully adjusted models, a positive cross-sectional relationship was observed between  $AL_{v1}$  and "somatic complaints" depressive symptoms ( $\beta=0.21$ ,  $P=0.006$ ) score at Visit 1, whereas  $AL_{traj}$  was associated with increasing depressive symptoms score ( $\beta=0.086$ ,  $P=0.003$ ) between Visits 1 and 3. An inverse relationship was observed between  $AL_{traj}$  and "positive affect" depressive symptoms score at Visit 1 among women ( $\beta=-0.31$ ,  $P<0.0001$ ) and White adults ( $\beta=-0.32$ ,  $P=0.004$ ). Among women,  $AL_{traj}$  was also positively related to change in "somatic complaints" depressive symptoms score between Visits 1 and 3 ( $\beta=0.043$ ,  $P=0.020$ ).

**Conclusions:** Among urban adults, AL may be associated with "somatic complaints" depressive symptoms at baseline. Higher AL trajectories may predict increasing depressive symptoms (overall) and increasing "somatic complaints" depressive symptoms (among women). A higher AL trajectory may be associated with lower "positive affect" depressive symptoms at baseline among women and White adults only.

**Does type, timing and duration of lifecourse unemployment differentially predict ADRD risk? A novel application of sequence analysis** Lucia Pacca\* Lucia Pacca Haobing Qian Amal Harrati Willa D. Brenowitz Maria Glymour Anusha M. Vable

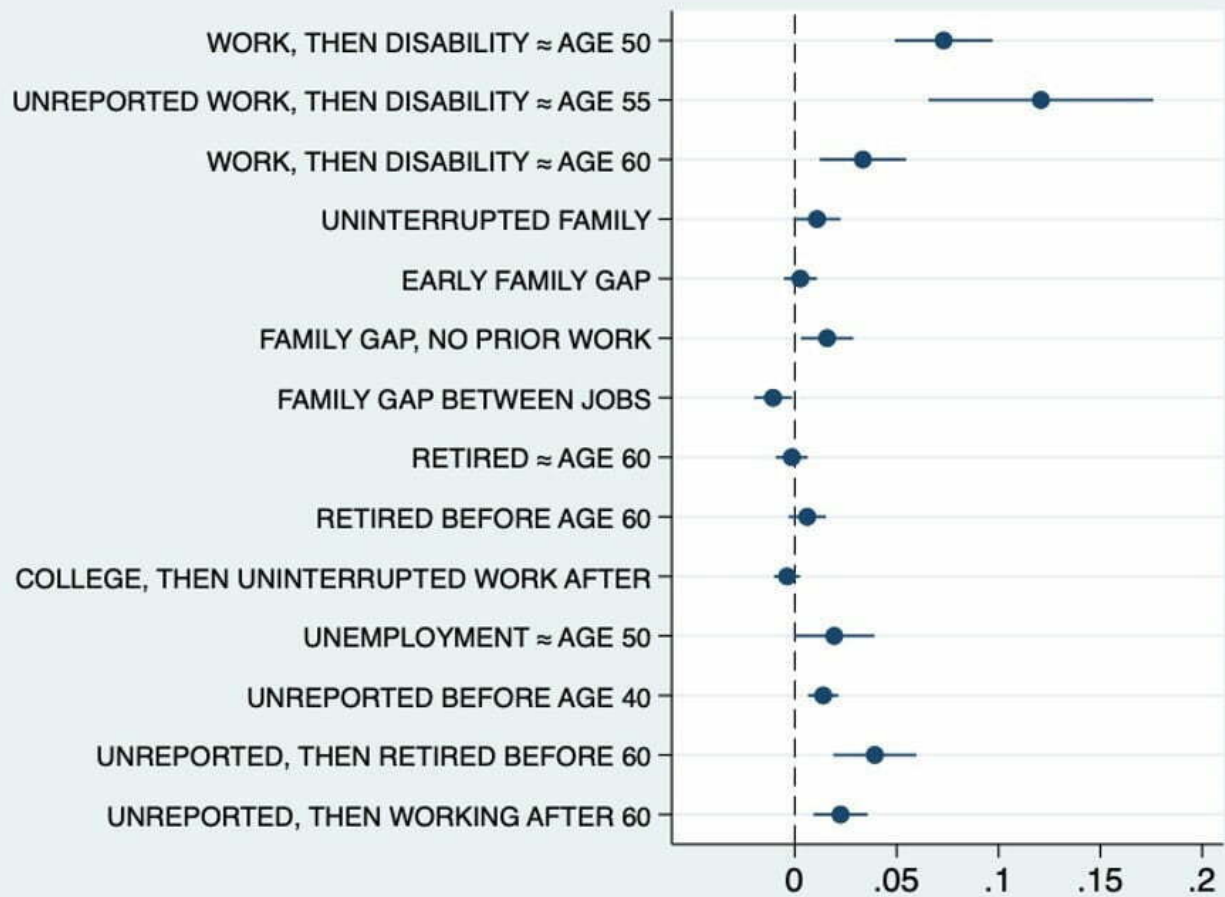
Unemployment may influence ADRD risk, but characterizing lifecourse labor market engagement is difficult and prior research is sparse. This study identifies employment trajectories age 18-65 using sequence analysis, and evaluates whether the type, timing, and duration of work gaps are associated with ADRD risk.

Data on work history came from the 2017 Life History Mail Survey supplement to the U.S. Health Retirement Study (N=5,270). Information was recorded on lifecourse participant employment, reasons for work gaps (unemployment, schooling, caregiving or disability), or unreported. We created employment trajectory clusters from age 18 to 65 using sequence analysis and cluster analysis. ADRD outcome was dementia probability score from age 70 onwards. We used generalized estimating equations to estimate the association between employment trajectories and ADRD adjusting for age, gender, birthplace, and childhood socioeconomic status.

We identified 15 employment trajectories, including three disability trajectories, and four family caregiving trajectories. Compared to uninterrupted work, disability trajectories were associated with higher dementia probability (e.g.  $b=0.07$ , 95%CI: 0.05, 0.10 for those who stopped working due to disability around age 50). Among those who cared for family members, results varied: those who did not work before a family gap had higher dementia probability ( $b=0.02$ , 95%CI: 0.002, 0.03), while those who had a family gap between jobs had lower dementia probability ( $b=-0.01$ , 95%CI: -0.02, -0.001). Those with long periods of unreported employment status had higher dementia probability.

Results suggest the type and timing of work gaps are differentially associated with ADRD risk. Work gaps due to disability or unreported employment status predicted higher ADRD risk, while work gaps due to caregiving varied by work status such that working before gaps predicted lower ADRD risk.





**Figure** - Coefficient plots for the association between work trajectories from ages 18 to 65 years and ADRD dementia probability score after age 70 compared with respondents who had uninterrupted work from age 18-65. Higher numbers for dementia probability reflect higher dementia probability (worse cognitive health).

## **Changes in a claims-based proxy for frailty in women with stage I-III breast cancer undergoing adjuvant chemotherapy compared to women without cancer**

Emilie D Duchesneau\* Emilie D Duchesneau Til Stürmer Dae Hyun Kim Jessie K Edwards Katherine Reeder-Hayes Jennifer L Lund

### **Introduction**

Frailty is a dynamic age-related syndrome characterized by a reduction in physiological homeostasis. Studies have reported clinically significant worsening in frailty in women with breast cancer (BC) during adjuvant chemotherapy (ACT), with improvements following the end of treatment. We compared changes in a claims-based proxy for frailty among women with BC receiving ACT to changes in a cohort of women without BC.

### **Methods**

We identified women (65+ years) with stage I-III BC undergoing ACT in the SEER-Medicare database. Women were required to have continuous enrollment in Medicare fee-for-service for  $\geq 180$  days prior to ACT initiation. We estimated the Faurot frailty index, a Medicare claims-based proxy measure, using demographic and billing information during the 180 days prior to key time points during BC treatment: at ACT initiation, 4 months post-ACT initiation, and 10 months post-ACT initiation. Changes in frailty were compared to age- and region-matched women without BC. Standardized mortality ratio weights were used to standardize the comorbidity distribution of the non-cancer comparator cohort to the distribution in the women with BC. Inverse probability of attrition weights were used to address informative loss-to-follow-up and death.

### **Results**

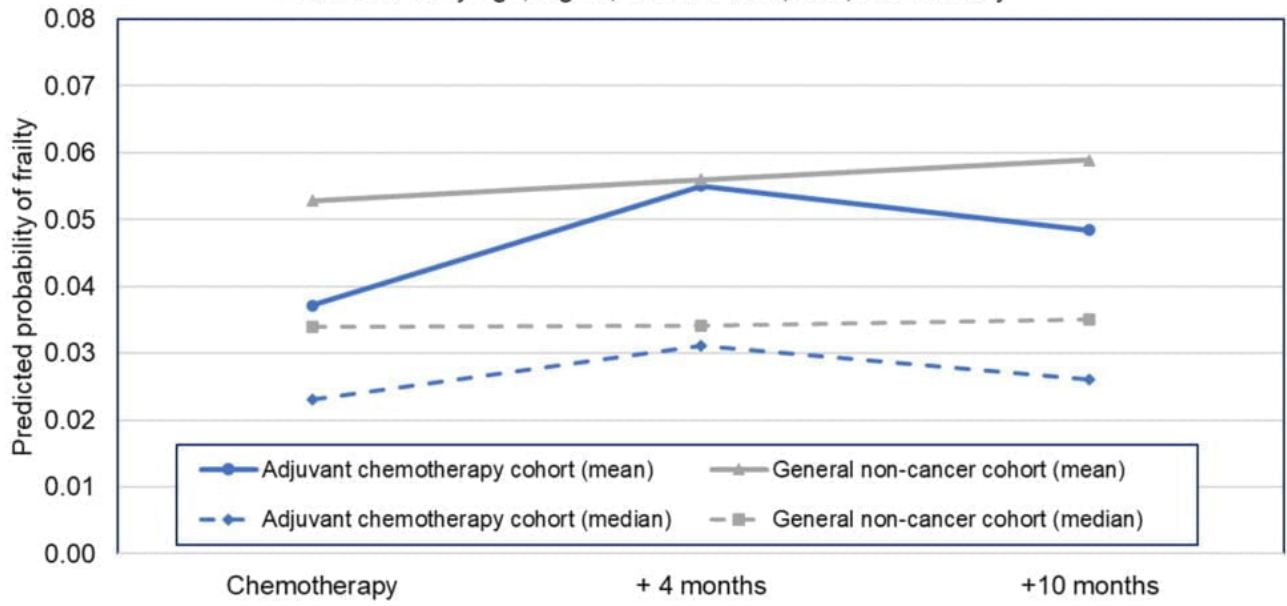
We identified 21,525 women with BC who initiated ACT. At ACT initiation, the mean predicted probability of frailty was 0.035 (median: 0.022). Mean predicted probability of frailty increased to 0.052 (median: 0.030) 4 months post-ACT initiation and subsequently fell to 0.047 (median: 0.026) 10 months post-ACT initiation (**Figure**). Women in the non-cancer comparator cohort experienced a slight increase in claims-based frailty over time.

### **Conclusion**

We observed changes in a claims-based frailty index during the BC treatment journey that were consistent with prior literature using clinical measures of frailty. These results demonstrate the feasibility of using claims data to detect changes in frailty over time.

### Change in claims-based frailty during breast cancer treatment

Standardized by age, region, comorbidities, race, and ethnicity



**Social participation and trajectories of functional disability in the last three years of life: the Japan Gerontological Evaluation Study** Takayuki Ueno\* Takayuki Ueno Junko Saito Hiroshi Murayama Masashige Saito Maho Haseda Katsunori Kondo Naoki Kondo

## Background

Functional disability has a variety of patterns from onset to death. Identifying trajectory patterns may make it possible to infer social effects, such as cost savings in health and long-term care. Although social participation is a protective factor against functional disability among older people, little is known about how social participation determines the trajectory patterns of functional disability prior to death. We aimed to assess the association between social participation, particularly horizontal and vertical organization participation, and the functional disability trajectories prior to death.

## Methods

We used 2010 survey data from the Japan Gerontological Evaluation Study for functionally independent older adults combined with public long-term care insurance system data from 2010 to 2016. (n=4,502). The outcome variable was five trajectory patterns we previously identified using a group-based trajectory modeling (i.e., persistent severe, persistent mild, accelerated, catastrophic, and minimum disability). As the explanatory variable, we used three definitions of social participation; whether to participate in any group or horizontal group (e.g., sports, hobby) or vertical group (e.g., political, religious) at least once a month. We used multinomial logistic regression analysis to calculate the odds ratios for identified trajectory patterns.

## Results

Participation in some social groups was significantly less likely to belong to “Accelerated disability” (OR=0.75), “Persistently mild disability” (OR=0.72), and “Persistently severe disability” (OR=0.59) compared to “Minimum disability.” In particular, participation in horizontal social groups was associated with less disabled trajectories.

## Conclusions

Interventions that encourage older people to participate in society, especially in horizontal social groups, may mitigate the declining levels of functional ability in the years prior to death. It is worthwhile to examine the social effects in the future.

**Cardiovascular risk factors and dementia: A genetic and phenotypic intergenerational instrumental variable analysis**

Emma L Anderson\* Emma Anderson Eirin Beate-Haug David Carslake Kaitlin Wade Sean Harrison Kate Tilling Yoav Ben-Shlomo Laura D. Howe Deborah A. Lawlor

**ABSTRACT**

**Background:** Evidence for the effect of cardiovascular risk factors (CVRFs) on incident dementia is conflicting. The pervasive issues of confounding, reverse causation and survival bias in observational studies hinder inference about the direction and magnitude of causal effects. We aimed to compare evidence from phenotypic and genetic offspring instrumental variable (IV) analyses to determine the effect of common CVRFs on dementia risk.

**Methods:** In the UK Biobank, participants reported their parents' dementia status. Participants' genetic risk scores and measures of body mass index (BMI), systolic blood pressure (SBP), glucose, total cholesterol, low- and high-density lipoprotein cholesterol (LDLc and HDLc, respectively) and triglycerides were used as IVs for CVRFs in the participants parents. The odds of parental dementia per one standard deviation greater CVRF were estimated (max N=311,816).

**Results:** Results from phenotypic and genetic offspring IV analyses largely agreed, but with a greater magnitude of effect suggested by the phenotypic analysis, potentially implying residual confounding. In the genetic analyses, there was evidence to suggest that lower BMI and SBP, and greater total and LDLc, increased odds of dementia (e.g., odds ratio for SBP on dementia risk using genetic IV: 0.64, 95% CI: 0.49-0.83, and for LDLc using genetic IV: 1.26, 95% CI: 1.14 to 1.38). There was little evidence to suggest glucose or triglycerides affected dementia risk, but odds ratios for glucose were imprecisely estimated (0.94, 95% CI: 0.67, 1.33 using genetic IV), particularly in the genetic IV analyses.

**Conclusions:** Higher total and LDL cholesterol are likely to be causal risk factors for dementia. Further research is required to understand the conflicting literature on associations between BMI, SBP and dementia.

**Chronic exposure to air pollution and multiple domains of cognitive decline in older adults**

Sindana Ilango\* Sindana Ilango Tanya Libby Claire Adam Cindy Leary Erin Semmens Annette Fitzpatrick Joel Kaufman Anjum Hajat

Evidence suggests chronic exposure to fine particulate matter (PM<sub>2.5</sub>) increases risk of dementia in older adults. We examine the effect of PM<sub>2.5</sub> on cognitive decline, an early indicator of dementia, to understand air pollution's role in domain-specific prodromal signs of dementia.

This analysis draws from the Ginkgo Evaluation of Memory Study, a clinical trial aimed at dementia prevention. Participants aged 75 years and older were enrolled between 2000 and 2002 and completed a neuropsychological battery of 10 tests repeated annually for up to eight years. Tests examined domains of memory, visuospatial abilities, language, attention, and executive function. Twenty-year exposure to PM<sub>2.5</sub> before baseline was estimated using annual averages from fine-scale spatiotemporal models and accounted for residential mobility. We used generalized estimating equations to compare trajectories of standardized scores for each domain over the study period across levels of exposure while accounting for correlations among repeated scores. We created visit-specific weights to account for differences in eligibility criteria across study visits and selective attrition. Models included demographic and socioeconomic characteristics as covariates.

This study included 2,538 individuals free of cognitive impairment at baseline. Preliminary analyses suggest exposure to PM<sub>2.5</sub> (per 5 µg/m<sup>3</sup>) was associated with marginally faster declines in standardized scores for attention and executive function ( $\beta = -0.01$ , 95%CI: -0.02, 0.01 and  $\beta = -0.01$ , 95% CI: -0.02, 0.01). Increased exposure to PM<sub>2.5</sub> was not associated with declines in other domains. Effect estimates were of negligible size and imprecise.

Preliminary findings provide some support for associations between exposure to PM<sub>2.5</sub> and worse attention and executive function. Consideration of selection processes into and out of the study is important for improving our estimation of the effect of air pollution on aging-related cognitive outcomes.

**Heterogenous trajectories of gait speed prior to incident fall** Claire Adam\* Claire Adam Erin Semmens Cindy Leary Sindana Ilango Annette Fitzpatrick

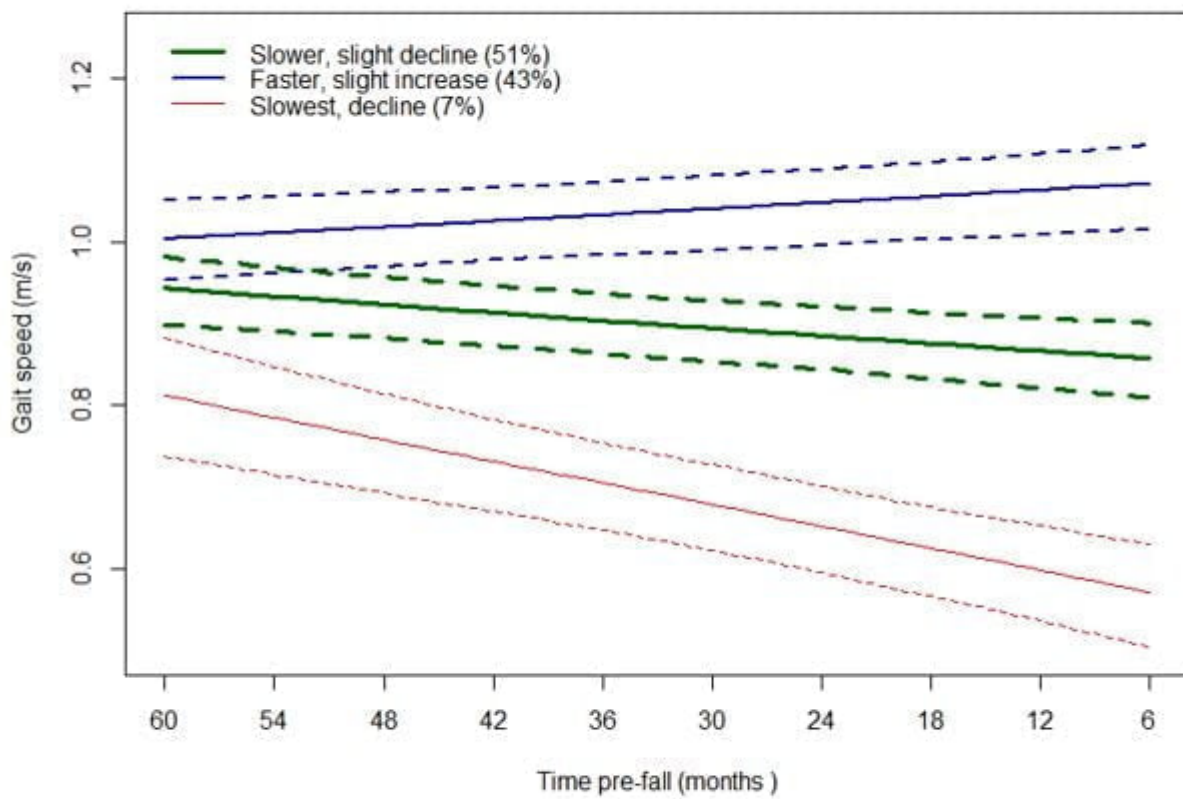
Background: Falls are frequent among adults 65 and older. Gait speed is a tool for identifying older adults with increased fall risk. While there is an association between slower gait speed and increased fall risk, not all older adults have slow gait speed (less than 1 meter/second) prior to a fall. We aim to characterize trajectories of gait speed prior to a fall and identify the features of older adults whose gait speed is greater than 1 meter/second.

Methods: Study participants were from the Ginkgo Evaluation of Memory Study (n=3069, age 75+) from four locations in the United States. Gait speed was measured annually over 15 feet with a static start. Falls were ascertained by participant report every 6 months. Latent class trajectory modeling was used to determine the trajectories of gait speed prior to incident fall. Participants who had an incident fall and at least 3 ascertainment of gait speed prior to falling were included in the latent class trajectory models.

Results: 914 participants were included in the trajectory models. A model with random effects for slope and intercept, splines, and 3 latent classes was identified as the best fit. Prior to falling, two trajectories (57% of participants), had slow, declining gait speed, while the third trajectory (43%) had fast, increasing gait speed. Older adults in the trajectory with faster gait speed were more likely to be male and younger, and were less likely to have mild cognitive impairment, a history of heart attack, or polypharmacy.

Conclusions: Older adults have heterogeneous trajectories of gait speed prior to an incident fall. Gait speed is a quick and accessible screening tool for fall risk, but it may not accurately assess fall risk in all older adults. For some populations of older adults, such as those who are male, younger, and have fewer comorbidities, clinicians may need to choose alternative screening tools to best assess fall risk.

Figure 1. Trajectories of gait speed (meters/ second) prior to a fall.



Dashed lines are confidence intervals.



**Longitudinal analysis on cardiovascular and fitness measurements over time among older adults from a park-based fitness program** Tang Li\* Tang Li Emily D'Agostino Jane Frances Pendergast Carl F. Pieper

Physical inactivity is a major risk factor for noncommunicable diseases and mortality worldwide. Older individuals are considerably more prone to physical inactivity. Park-based fitness programs can support physical activity in older adults given their proximity and affordability. This study examined the relationship between duration of program participation and changes in cardiovascular fitness across sociodemographic factors for older adults attending a low-cost, park-based exercise program in Miami, Florida.

We used three-level repeated measures linear mixed models to examine the time effects of participation in a park-based physical activity program on cardiovascular fitness outcomes across sociodemographic factors (2017-2019). Adjusted models included time of observation (continuous variable representing 4-month periods), age, gender, home-area poverty level, and race/ethnicity, as well as time×poverty, time×gender interaction terms.

The study included 352 participants (mean age 70.7 years; 85% female; 47% Hispanic, 42% non-Hispanic black). Across all participants, mean estimates for systolic and diastolic blood pressure significantly improved over time (-0.75 mmHg, 95% confidence interval [CI]: -1.18, -0.32; and -0.33 mmHg, 95% CI: -0.58, -0.08, respectively). Improvements over time also were observed for mobility, arm strength, and leg strength. Greater gains over time in arm strength were observed for females vs. males, and in pulse and mobility for individuals residing in high- vs. low-poverty areas. There was no significant change in participant's body mass index.

This study suggests that cardiovascular health of older individuals may be promoted with community park-based physical activity programs. Also, longer participation in these programs may result in greater health benefits, particularly for females and individuals residing in high-poverty areas. Future research should examine whether findings are replicated with other populations and settings.

**Sleep duration and self-rated health: Exploring sociodemographic differences** Olatokunbo Osibogun\* Olatokunbo Osibogun

**Background:** This study examined the association between sleep duration and self-rated health and whether this association is modified by age, sex, and race/ethnicity. **Methods:** Data was drawn from adults aged  $\geq 18$  years in the 2020 Behavioral Risk Factor Surveillance System (N=396,455; weighted N= 257,090,545). Sleep duration was categorized as short (<7 h), normal (7 to 9 h; reference), and long (>9 h). Self-rated health was grouped into suboptimal (fair/poor) [reference] and optimal (excellent/very good/good) health. Multinomial logistic regression tested the interaction between age, sex, and race/ethnicity with sleep duration while controlling for potential confounders. **Results:** Participants with short (adjusted odds ratio: 0.69 [95% confidence intervals 0.66-0.74]) and long (0.66 [0.59-0.74]) sleep duration had decreased odds of optimal self-rated health compared to those with normal sleep duration. There was a significant interaction with age\*sleep duration at  $p=0.01$ . Younger age (18-24 years) had the strongest association (0.58 [0.46-0.73]) for short sleep duration and self-rated health compared to the older age groups (25-34: 0.73 [0.62-0.87]; 35-44: 0.62 [0.53-0.73]; 45-54: 0.68 [0.58-0.80]; 55-64: 0.75 [0.67-0.85] and >65: 0.73 [0.67-0.80]). Those aged 35-44 (0.58 [0.40-0.84]) had the strongest association for long sleep duration compared to other age groups (18-24: 0.72 [0.50-1.05]; 25-34: 0.72 [0.47-1.11]; 45-54: 0.72 [0.52-1.00]; 55-65: 0.60 [0.46-0.78] and >65: 0.65 [0.55-0.78]). There was no evidence of a significant interaction by sex or race/ethnicity. **Conclusion:** Both short and long sleep duration are associated with lower odds of reporting optimal self-rated health among US adults. There were notable differences in this association by age. Future research should examine potential pathways linking sleep duration with self-rated health across different age groups.

**Developing A Conceptual Framework of Social Media Listening Application for Infodemiological Research** Shu-Feng Tsao\* Shu-Feng Tsao Helen Chen Samantha Meyer Zahid A. Butt

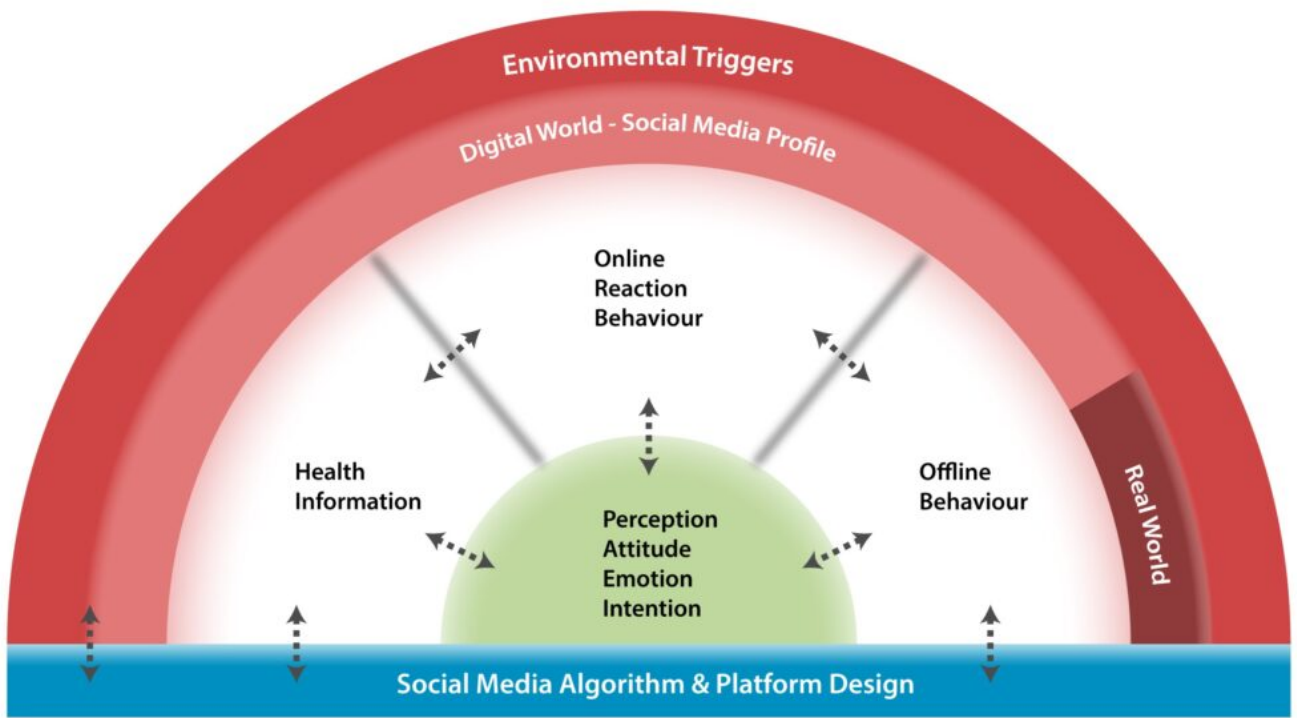
**Background:** Existing communications and behavioral theories have been adopted to address health infodemics. Although numerous studies have been published during the COVID-19 pandemic, there is no framework specially designed for social listening or infodemiological studies using social media data and machine learning techniques.

**Objective:** This study aims to propose a novel yet theory-based conceptual framework for infodemiological research.

**Methods:** We collected theories from health behaviors, communications, and infodemics to inform and design components of the proposed conceptual framework.

**Results:** We reviewed Health Belief Model, Theory of Planned Behavior/Reasoned Action, Transtheoretical Model, Social Information Processing Theory, Uses and Gratifications Theory, Social Judgment Theory, Behavioral and Social Drivers, and Social media and Public Health Epidemic and REsponse Continuum model. Accordingly, we proposed our “Social Media Listening for Public Health Behavior” Conceptual Framework by not only integrating important components of existing theories, but also adding new components, such as environmental factors and social media algorithm and platform design.

**Conclusions:** The proposed conceptual framework can be used to better understand public discourse on social media, and it can be integrated with other data analyses to gather a more comprehensive picture. The framework will continue to be revised and adopted as health infodemics evolve.



**Cue Scanning Patterns and Executive Functioning of Individuals Exposed to Repeated Stress** Gesulla Cavanaugh\* Gesulla Cavanaugh Patrick Hardigan Raymond Ownby Maria Abreu Stachyse Stanis Raina Patel

Cognitive function decline is an expected consequence of aging; nonetheless, risk factors, such as repeated exposure to stress, impact information processing regardless of age. This study examines eye-movement patterns and pupil diameter during a computerized assessment of executive function in two socioeconomic groups, proposing that individuals from disadvantaged backgrounds will demonstrate greater difficulty with executive functioning and comprehensive test performance regardless of education status. The Montreal Cognitive Assessment (MoCA) and Fostering Literacy for Good Health Today (FLIGHT)/ Vive Desarrollando Amplia Salud (VIDAS), a progressively more difficult health literacy tool, were used as the primary assessments; other assessments included grip strength, anxiety assessment, and the Trail Making test. Participants were 85 adults between 26-65 years old. Sixty-five were homeless and compared to 20 individuals with stable housing. Participants completed assessments on a laptop mounted with the Tobii Pro Nano. Visualization and numerical data were exported from Tobii ProLab and were analyzed using SPSS v.27. The results show that mean baseline pupil diameter were  $2.83\text{mm} \pm 0.5329$  (homeless) and  $2.62\text{mm} \pm 0.2366$  (control). Both groups demonstrated significant pupil dilation from baseline while progressing through the tasks divided into 8 frames  $F(8, 266156) = 1239.43, p = .000$ . A visual analysis of the data suggests that the homeless group showed the greatest change, with more guessing events, more disorganized patterns of eye-movement, and more incorrect answers ( $M = 11.34$  vs  $M = 27.57$ ). The homeless group's scattered eye-movement patterns were consistent with an increase in errors during the Trail Making Test, lower MoCA scores ( $M = 24.72$  vs  $M = 27.1$ ), weaker grip strength, and unstructured scanning for clues. The results suggest that individuals who have repeated exposure to stress may have difficulty processing information from complex cognitive tasks.

**LATEBREAKER**

Behavior

**Pain Attitudes and Pain Among People with Bleeding Disorders: Results from Community Voices in Research (CVR)** Corey\* Corey Pierce Veronica L. Irvin Marit Bovbjerg Ellen Smit Michelle Witkop James Elander

**Introduction:** In people with bleeding disorders pain is a major problem, with pain treatment often ineffective. Understanding of psychological factors involved in pain processing is limited in people with bleeding disorders. Maladaptive pain attitudes associate with worse pain outcomes and adaptive pain attitudes associate with better outcomes in high pain conditions. Relationships between pain attitudes and pain outcomes are unexplored in bleeding disorder populations.

**Aim:** Investigate relationship between pain attitudes and pain outcomes in people with bleeding disorders.

**Methods:** Pain attitudes were measured with the Survey of Pain Attitudes, containing two adaptive scales (Control and Emotion) and five maladaptive attitudes (Disability, Harm, Medication, Solicitude, Medical Cure). Adults with bleeding disorders, who had pain, and were enrolled in Community Voices in Research were eligible. Participants (n=72) completed an online pain attitudes survey. Associations between pain attitudes and pain outcomes (pain and medication use) were investigated using logistic regression.

**Results:** After adjustment, one adaptive scale (Control) was associated with most outcomes. Higher Control associated with a lower odds of medication use and lower pain. After adjustment, three maladaptive scales associated with outcomes. Increased Disability, Harm, Medication were associated with increased pain medication use and higher pain.

**Conclusions:** We presented compelling evidence of relationships between pain attitudes and pain outcomes in people with bleeding disorders, though corroboration is needed in other populations. High patient dissatisfaction with pain management in people with bleeding disorders suggests a need to explore novel pain treatment strategies. Modification of pain attitudes presents a possible avenue for intervention in improving pain outcomes.

**LATEBREAKER**

Behavior

**Development and Testing of Utility of Pain Scale (UPS) Among People with Bleeding Disorders** Corey\* Corey Pierce Veronica L. Irvin Marit Bovbjerg Ellen Smit Michelle Witkop James Elander

**Introduction:** Pain remains a daily challenge for people with bleeding disorders despite advancements in care. Complex interactions between biological and psychosocial factors are known to influence pain. Attitudes and beliefs about pain have been associated with pain outcomes, but not in people with bleeding disorders. The concept of '*pain having utility to future health*' has not been explored in pain literature. We developed and investigated novel pain attitude constructs related to 'pain utility', exploring them in relation to pain outcomes in people with bleeding disorders.

**Methods:** Utility of Pain Survey tool was developed to measure belief in pain utility. Development occurred in four phases: content development, expert validity review, patient validity review, and pilot test. Tool was administered to adults with bleeding disorders, who had pain, who participate in Community Voices in Research. Participants (n=72) completed pain attitudes survey and answered questions about pain. Regression analysis was performed to investigate relationships between attitude statements (and pain utility constructs) to outcomes (recent pain and pain medication use).

**Results:** A two-factor structure was determined for pain utility questions (factor 1: cause obscuring, factor 2: usefulness). Maladaptive statements were associated with higher average pain and greater pain medication use, while adaptive statements associated with lower average pain and lower pain medication use. Maladaptive statements (cause obscuring) were more strongly associated with outcomes than adaptive statements (usefulness).

**Conclusions:** As in other populations, these findings suggest pain attitudes associate with pain in people with bleeding disorders. Pain utility attitudes show promise in the study of pain attitudes, though further refinement of Utility of Pain Survey is needed. Further research is needed to corroborate findings, and to assess interventions to address maladaptive attitudes in people with bleeding disorders or other painful conditions.

**Leveraging behavioral sciences to augment voluntary blood donation in China: a randomized control trial and latent class analysis** Stephen Pan\* Stephen Pan Bo Li Caixia Wu Zhong Liu

**Background:** China is facing a blood shortage crisis and needs to increase its voluntary blood donation rates. Behavioral sciences can provide useful insights for developing behavioral interventions to enhance blood donation. However, there have been few empirical studies to evaluate the efficacy of such interventions. This randomized controlled trial and latent class analysis (LCA) examined the effect of online interventions on blood donation willingness, intention, and behavior in China.

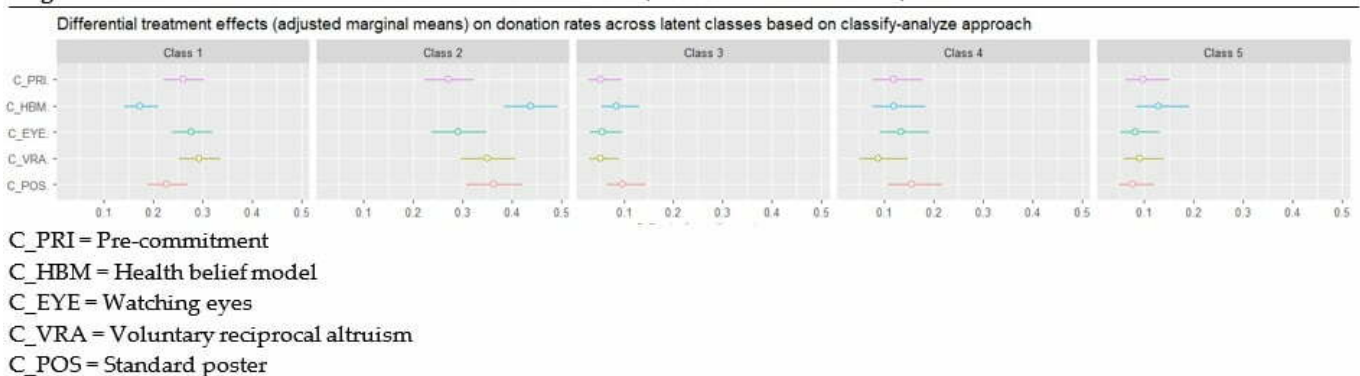
**Methods:** In 2022, 3,280 participants in mainland China population were recruited through an online survey platform and completed a baseline survey. Participants were randomized to one of five online interventions (stimulating individual standards of fairness [VRA], using eye cues to prime individuals [EYE], self-imposed penalties for goal failure [PRI], blood shortage statistics in China [HBM], a WHO blood donation poster [POS]) in the middle of the survey and provided information about where to donate blood at the end of the survey. To measure post-intervention blood donation, participants were invited to complete a follow-up survey 2-3 weeks after the baseline survey. Latent classes were determined using LCA, and differential treatment effects on actual blood donation were assessed with regression analysis based on a classify-analyze approach.

**Results:** Five latent classes were identified. HBM was significantly better than PRI or EYE in increasing actual blood donation in Class 2 (higher education, employed full-time, married with kids) but was significantly worse than them in Class 1 (lower education). No significant differences were observed among other classes.

**Conclusion:**

Presenting blood shortage statistics may be effective for stimulating blood donation among married parents with higher educational attainment and who hold full employment. However, blood shortage statistics may not be effective for augmenting blood donation among individuals with lower educational attainment.

**Figure. Differential treatment effects on outcome measures (84% confidence interval)**





**Prediction of use and affordability of oral health services using machine learning** Helena S Schuch\* Helena S Schuch Mariane Furtado Ichiro Kawachi Alexandre D P Chiavegatto Filho Hawazin W Elani

**Background:** Most dental diseases are preventable if diagnosed early, thus access to routine dental care can be a preventive and cost-effective strategy for improving the population's oral health. However, persistent disparities in oral health remain a public health challenge.

**Objectives:** To develop and validate machine learning (ML) algorithms to predict adults at risk of missing preventive dental care and inability to afford dental care.

**Methods:** We used longitudinal data from the Medical Expenditures Panel Survey (2018-2019). We developed five ML algorithms: gradient boosting, extreme gradient boosting (XGB), light gradient boosting, catboost (CB), and random forest. We used 53 variables including demographic, socioeconomic, health conditions, behavioral, and health services use. We performed feature importance analyses and examined the algorithms' fairness by conducting race and ethnicity analyses. The algorithms performances were assessed by examining several metrics including the area under the receiver operating characteristic curve (AUC).

**Results:** Our study population included 10,087 adults aged 18 and older. For the full sample, ML algorithms demonstrated high performance in predicting access to dental services. For predicting adults at risk of missing preventive dental care, the CB classifier achieved an AUC of 0.83 (95% CI 0.81; 0.84), and for the inability to afford dental care XGB had an AUC of 0.80 (95% CI 0.77; 0.82).

For the dental uninsured subpopulation (n=5,915), the XGB algorithm predicted missing preventive dental care with an AUC of 0.82 (95% CI 0.80; 0.84) and the inability to afford dental care with an AUC of 0.75 (0.72; 0.78). Race and ethnicity emerged as strong predictors for missing preventive dental care.

**Conclusions:** Our findings suggest that ML algorithms can accurately predict adults at risk of missing preventive dental care. These results can inform targeted prevention efforts to reduce disparities in oral health.

**LATEBREAKER**

Big Data/Machine Learning/AI

**Transformer-Based Topic Modeling to Examine Discussions of Delta-8 THC** Brandi Smith\*  
Brandi Smith Lara Depadilla Brooke Hoots Daniel Bowen Kristin Holland Douglas Roehler Steven A. Sumner

**Background**

Delta-8 tetrahydrocannabinol (THC) is a psychoactive cannabinoid found in small amounts naturally in the cannabis plant; it can also be synthetically produced in larger quantities from hemp-derived cannabidiol, or CBD. Most states permit the sale of hemp and hemp-derived CBD products; thus, hemp-derived delta-8 THC products have become widely available in many states, even where delta-9 THC, the most prominently occurring THC isomer in cannabis, is not currently legal. Health concerns related to delta-8 THC products and their psychoactive effects remain understudied.

**Objective**

To implement a novel topic modeling approach based on transformers, a state-of-the-art natural language processing architecture, to identify emerging topics of discussion about delta-8 THC, including potential adverse health outcomes.

**Methods**

Posts from January 2008 to December 2021 discussing delta-8 THC were isolated from cannabis-related drug forums on Reddit, a social media platform which hosts the largest online drug forums worldwide. Unsupervised topic modeling was employed to cluster posts into topics and assign labels, which were then validated by human experts.

**Results**

There were 41,191 delta-8 THC posts identified and 81 topics isolated, the most prevalent being 1) discussion of specific products, 2) comparison of delta-8 THC to other isomers, 3) and safety warnings. About 5% of the resulting topics included posts discussing health symptoms such as anxiety, sleep disturbance, and breathing problems. Until 2020, Reddit posts contained less than 50 mentions of delta-8-THC for every 100,000 posts. However, these rates increased by more than three-fold in 2020 and continued to rapidly increase into 2021.

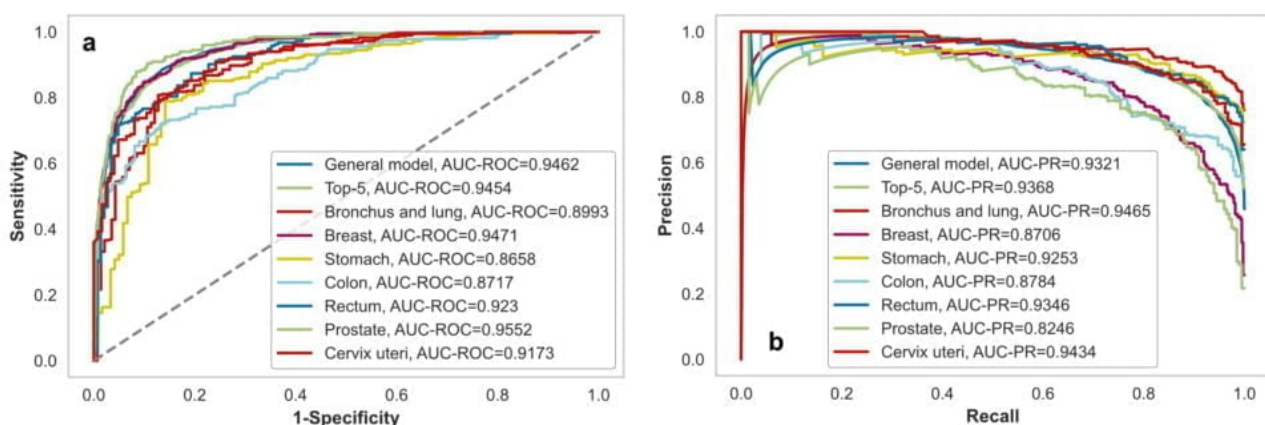
**Conclusion**

Our study provides critical and timely insights into emerging health concerns around delta-8 THC. Furthermore, we demonstrate the utility of transformer-based unsupervised learning to identify topics from unstructured discussions to enhance public health awareness.

### Machine learning for predicting longitudinal mortality risk in patients with malignant neoplasms

Gabriel Ferreira dos Santos Silva\* Gabriel Ferreira dos Santos Silva Luciane Simões Duarte Mirian Matsura Shirassu Stela Verzinhasse Peres Marco Antônio de Moraes Alexandre Chiavegatto Filho

Artificial intelligence is becoming an important tool in recent years, as machine learning algorithms have been shown to improve clinical decision-making. These algorithms will have some of their most important applications in developing regions with restricted data collection, but their performance under this condition is still widely unknown. According to the World Health Organization, about 9.6 million people died of cancer worldwide in 2018, of which around 70% were in middle- and low-income. We used public longitudinal data from São Paulo, Brazil, to develop machine learning algorithms that could predict the risk of death in patients with cancer between 12 and 24 months after the date of diagnosis. We included adult individuals (20 years or more) with diagnoses of malignant neoplasms from 2014 to 2017 and excluded cases of non-melanoma of the skin. The final sample was composed of a total of 29,194 patients. The algorithms were trained with twelve variables: sex, age, days between first physician visit and diagnosis, clinical stage of cancer, category of medical service, previous diagnosis, type of diagnosis, topography group, health regions of residence and diagnosis, morphology, and health institution habilitation. We tested different algorithms using nine separate structures: general model, top-5 cause of death model, bronchus and lung cancer, breast cancer, stomach cancer, colon cancer, rectum cancer, prostate cancer, and uterine cervix. Considering the area under the ROC curve (AUC-ROC), we obtained values of 0.946 for the general model, 0.945 for the model with the five main cancers, 0.899 for bronchial and lung cancer, 0.947 for breast cancer, 0.866 for stomach cancer, 0.872 for colon cancer, 0.923 for rectum cancer, 0.955 for prostate cancer, and 0.917 for uterine cervix cancer (**Figure, a**). Our results indicate the potential of building models for predicting mortality risk in cancer patients in developing regions using only routinely-collected data.



**Use of machine learning to predict death: an application to patients with breast cancer in a city of Paraíba, Brazil** Tiago Almeida de Oliveira\* Tiago Oliveira José Lucas Costa de Oliveira Paulo Lunardy Oliveira Diniz

It is estimated that in 2022 in Brazil, breast cancer in women was the most incident, representing more than 40% of all types of cancer. Brazil is considered the country with the most deaths from this cause, registering 20.725, that is, 24.7% of the types of cancer in 2020. Early and accurate detection, prognosis, cure, and prevention of breast cancer is a major challenge to society. Hence, a precise and reliable system is vital for the classification of cancerous sequences. Machine learning classifiers contribute much to the process of early prediction and diagnosis of cancer. In this paper, a comparative study of four machine learning classifiers such as Random Forest, Decision Tree, Lightgbm, and XGBoost is implemented for the classification of prognosis of the disease. A retrospective cohort study was conducted using 225 data from medical records of women who had breast cancer and underwent treatment between 2005 and 2015 at the "Hospital da Fundação de Assistencial da Paraíba" in Campina Grande, State of Paraíba, Brazil. Two analysis strategies were used, one which consisted of using the data as collected with a percentage of missing data using two models LightGBM and XGBoost which deal with this type of configuration. And another strategy with imputation Decision tree and Random forest models were added. When used with the missing data scenario the XGBoost model, was the best with right about 88% of the patients who would not die and about 50% of the patients who would die with an accuracy model total of 79.10%. The ROC curve was also evaluated, which had an area equal to 0.69. For the scenario with imputation, the best evaluated model was right about 95% for patients who did not die and 80% for those who died, with an accuracy of 92.59% and a ROC curve of 0.88, in the Decision Tree. Although the results of the model without missing data are quite attractive, it is noticed that when imputing the performance of the classifieds improves with a gain of 22%.

**Federated learning for health outcomes predictions in a diverse multicentric sample of hospitals** Roberta Wichmann\* Roberta Wichmann Murilo Afonso Robiati Bigoto Alexandre Chiavegatto Filho

The use of large amounts of individual patient data for the development of predictive algorithms brings new technical and ethical challenges. There is a growing use of federated learning (FL) techniques in order to preserve patient privacy, but important challenges remain. Our study aimed to develop COVID-19 mortality risk prediction algorithms using different federated learning structures in 21 Brazilian hospitals. A total of 22 predictors were used, including age, sex, heart rate, respiratory rate, pressure, temperature, and blood count data. We tested the application of two federated learning scenarios. We first evaluated the predictive performance of a Logistic Regression (RL) and a Multilayer Perceptron (MLP), in which a global model was built by aggregating the average coefficients obtained for each hospital. The second scenario used a Random Forest (RF) strategy, in which trees were built proportionally to the number of patient data from each hospital and aggregated into a single final model. The predictive performance of all three models achieved similar metrics (AUC-ROC of 0.81 for RL, 0.80 for RF and 0.80 for MLP). In both scenarios, performance gains were observed when using FL in relation to local learning, when maintaining the same hyperparameter space. Regarding local learning, RF had an average gain of 6.5%, RL 7.2% and MLP 12.8%. The lower gain presented by the RF model indicates that it had already achieved better local performance in contrast to the other options. In RF, the results from the AUC-ROC indicated a lower dispersion coefficient between the different hospitals (7.3%). In this method, a clear predictive increase was observed for hospitals with a smaller number of patients. For the RF, the highest predictive increase was 54.3%, and the worst decrease was 7.6% when FL was used instead of local learning. For RL, it was 44.0% and 14.2%, while for MLP it was 71.7% and 23.3%, respectively. MLP was the better the predictive algorithm in 9 hospitals, RL in 7, and RF in 5. Our study highlights the potential of implementing new federated learning techniques to predict health outcomes with information from multiple hospitals while protecting patient privacy.

**Physician willingness to use artificial intelligence tools in clinical practice: a multicentric prediction analysis** Roberta Wichmann\* Roberta Wichmann Tiago Almeida de Oliveira Alexandre Chiavegatto Filho

Providing an early identification of physicians with a low predisposition to use predictive machine learning algorithms can facilitate targeted interventions aimed at those more averse to the use of these technologies. An application was developed by the study to provide predictive results of the risk of COVID-19 diagnosis and prognosis, using data on gender, age, blood count, C-reactive protein, and potassium dosage of patients, obtained from 18 hospitals in all the five regions of Brazil. Physician behavior in relation to artificial intelligence algorithms, as well as data such as gender, age, and medical specialty, were collected using an online form. We developed machine learning algorithms to predict which physicians were less likely to use an AI application as assessed by the negative response to "I would use the application very often." The Likert scale variable was organized into five categories, starting with 1 (I completely disagree) and ending with 5 (I fully agree). For the purposes of the predictive analysis, these categories were recorded in a binary scale, with categories 1, 2 and 3 as the positive outcome (low willingness to use the AI application). Five different machine learning algorithms were tested (lightGBM, Extra Trees, CatBoost, Random Forest and K Neighbors). The sample division was divided in 70% for training the data and 30% for the test data, and a 10-fold cross-validation was performed in the training data set for the optimization of hyperparameters using the HyperOpt method. The Random Forest algorithms presented the highest predictive performance for identifying physicians that were less inclined to use an AI application, as measured by the AUC-ROC (0.73). The results indicate the possibility of providing targeted educational interventions for physicians on the use of artificial intelligence applications that can potentially benefit decision-making in clinical practice.

**Prevalence and Factors Associated with Marijuana Use by Cancer Survivorship among US Adults** Mariama Bah\* Mariama Bah Ling Guan Justy Antony Chiramal Holly Harris

Cancer survivors have favorable attitudes toward using marijuana to relieve cancer symptoms and manage treatment side effects. It is critical to assess the prevalence of marijuana use (MU) by cancer survivorship and to characterize MU by race/ethnicity and health care access (HCA) to inform future research and policies as marijuana becomes increasingly accessible with the rise of legalization across states.

We analyzed data for 360,888 adults who completed the Chronic Health Conditions and Marijuana Use modules in the Behavioral Risk Factor Surveillance System (BRFSS) 2018–2020. We used Mantel-Haenszel stratified analyses to determine the age-adjusted prevalence ratios (PR) of MU in the previous 30 days by non-skin cancer survivorship and effect modification by race/ethnicity and health care access, defined as a composite of health coverage and care affordability.

The overall age-adjusted prevalence of MU was higher in cancer survivors compared to non-cancer survivors, PR=1.24 (95%CI: 1.19-1.30). The PR was highest among American Indian Alaska Natives at 1.54 (95% CI: 1.37-1.74), followed by Asians, 1.42 (95% CI:1.23-1.64), Blacks, 1.38 (95% CI: (1.03-1.86), Hispanics 1.36 (95% CI:1.22-1.51) and whites 1.09 (1.01-1.17). Stratified by health coverage, the PR of MU among cancer survivors compared to non-cancer survivors was higher among those without health coverage (1.48, 95% CI:1.30-1.69) compared to those with health coverage (1.23, 95% CI:1.18-1.29). Among those with health coverage, the PR of MU was higher among those who could not afford to see a doctor (1.32, 95% CI: 1.19-1.47) compared to those who could (1.18, 95% CI: 1.13-1.24).

Cancer survivors were more likely to use marijuana than non-cancer survivors, with differences in prevalence exacerbated by race/ethnicity and HCA. Our study provides baseline data for future research investigating the reasons for MU among cancer survivors to inform health providers and policymakers as more states legalize marijuana.

**Depression and Cancer-related Mortality among Hispanic/Latino Americans in a Nationally Representative Dataset** Sri Banerjee\* Sri Banerjee Sri

There is mounting evidence that poor mental health leads to deteriorating physical health. Hispanic/Latino adults specifically experience poorer health outcomes and significantly less access to quality care than their White counterparts. Latinos are also less likely to receive treatment for depression, anxiety, and other behavioral issues than their white counterparts. In this retrospective cross-sectional analysis, we investigated the potential connection mental health and cancer outcomes in Hispanic/Latino versus Non-Hispanic Caucasian adults. Methods: We analyzed data on adults ( $\geq 20$  years) from the 2005-2010 National Health and Nutrition Examination Survey, which is a population-based survey conducted by the National Center for Health Statistics, with mortality data obtained through December 2015. All individuals from this nationally representative study were Caucasian or Hispanic and living in the United States. We assessed for major depression by using the Patient Health Questionnaire-9 measure (score  $\geq 10$ ). Due to the complex sampling design, sample weights were utilized in order to analyze the data. Comparisons were analyzed using Pearson's Chi Square, simple, and multivariable Cox regression to determine the relationship of depression and cancer-related mortality. All missing variables were excluded. Results: Data was available for 260 Latino adults in the United States population. The prevalence of depression was 1.2% (95% confidence interval [CI] 0.89%-1.5%) among Hispanic/Latinos and 4.8% (4.4%-5.6%) among Non-Hispanic Whites. The overall unadjusted hazard ratio for depression to no depression among Latinos was 2.10 (1.24-3.55,  $p < 0.01$ ). The adjusted HR was elevated, 3.32 (CI 1.81-6.10,  $p < 0.05$ ) among Caucasian adults after the results were controlled for medical (obesity, breast cancer history, C-reactive protein, cardiovascular disease status, and smoking status) risk factors and demographic (education level, gender, poverty level, and age) risk factors. Discussion: There is a significant relationship between poor mental health and cancer mortality among Latino adults. Latino adults have a much stronger relationship between poor mental health and cancer mortality than adults. Consequently, Latino adults need better access to mental health services and cancer health. Health care professionals should be made aware of mental health related racial gaps and advocate for reducing health disparities.



**The mediating role of educational attainment on the association between cancer and employment among Canadian adolescent and young adults** Giancarlo Di Giuseppe\* Giancarlo Di Giuseppe Arif Jetha Petros Pechlivanoglou Peter Smith Jason D. Pole

**Background:** Cancer in adolescents and young adults (AYAs) occurs during a critical life phase as they complete education and enter the workforce. It is unknown if cancer indirectly affects workforce participation by influencing educational completion.

**Methods:** We identified AYAs aged 18 to 39 years with a history of cancer diagnosis between the ages of 15 and 22 using multiple (n=14; years 2000 to 2017) cycles of the Canadian Community Health Survey, a nationally representative cross-sectional survey, which was linked to the Canadian Cancer Registry. Self-reported educational completion and employment, among other demographic characteristics, were captured. Marginal structural mediation models were used to decompose the total effect into the natural direct effect of cancer on employment, and the natural indirect effect through completing various levels of education. A multinomial model for employment status was measured as employed, full-time; employed, part-time; and unemployed. All analyses were sex stratified and 95% CIs were produced via bootstrapping.

**Results:** Over 200,000 individuals were eligible, of which 300 had a prior history of being diagnosed with cancer as an AYA. The average age at diagnosis was 19 years, with an average elapsed time from diagnosis to the survey of over 8-years. Compared to those who do not experience cancer, AYA cancer survivors were associated with a total effect of 1.60 (CI, 1.19 - 2.08) times the odds of unemployment vs. full-time employment. This effect was more prominent in males compared to females (OR, 1.74; CI, 1.16 - 2.50 vs. OR, 1.34; CI, 0.88 - 2.05). No indirect effect through education was observed. Results were null for the total effect of cancer when comparing part-time to full-time employment, as well as the mediating pathway.

**Conclusion:** There appears to be no evidence of a mediating effect of educational completion on the effect of cancer on employment for AYAs who experience the disease during this unique life phase.

**Lung cancer survival in Canada by individual-level socioeconomic status and geographic region: the role of stage at diagnosis.** Samia Qureshi\* Samia Qureshi Erin Strumpf

Socioeconomically and geographically disadvantaged lung cancer patients can experience worse survival which may be partly driven by higher rates of late-stage diagnosis. While the relationship between income and survival is well-documented, there is little known about the impact of other social determinants of health (education, immigration, visible minority status, and rurality) on lung cancer survival in Canada. The literature is also sparse on socioeconomic and geographic inequalities in late-stage diagnosis and on how they translate into survival inequalities. The objective of our study is to understand the association of understudied social and geographical factors with survival from lung cancer and the extent to which late-stage diagnosis drives these relationships. We use the Canadian Community Health Survey (CCHS, cycles 2001-2017), which includes self-reported information on education, immigration, and visible minority status and has been linked to the Canadian Cancer Registry (2010-2017). Our analytical cohort consists of CCHS respondents from all provinces except Quebec that subsequently developed lung cancer (n=4,031). The annual income tax return databases and the Canadian vital statistics database have also been linked for information on area of residence, family income, and death. For this study, we first estimate the association between each socioeconomic and geographic measure and 3-year survival probability from inverse probability of treatment-weighted Kaplan-Meier analyses. We then conduct mediation analyses with natural effects models to understand if late-stage diagnosis explains any observed inequalities in survival. For this method, we fit semi-parametric Aalen additive hazard models to estimate the natural indirect effect of late-stage diagnosis and the proportion of the total effect it mediates. This research will unravel potential unjust differences in lung cancer survival that may be amenable to interventions such as screening programs.

**Ambient fine particulate matter exposure and risk of endometrial cancer in the NIH-AARP Diet and Health Study** Samantha Ammons\* Samantha Ammons Rena Jones Debra Silverman Jessica Madrigal Jared Fisher Britton Trabert Alexandra White Joel Kaufman

**Background:** Fine particulate matter (PM<sub>2.5</sub>) has a heterogeneous chemical constituency with endocrine-disrupting properties. It has been consistently associated with risk of breast cancer, however, there are limited studies of other reproductive cancers and no studies of endometrial cancer. We investigated this association in a large, geographically diverse cohort.

**Methods:** Outdoor residential PM<sub>2.5</sub> concentrations were estimated using a nationwide spatiotemporal model for the NIH-AARP Diet and Health Study, located in 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan), including women with mean age 62 years at enrollment (1995-1996). We estimated average PM<sub>2.5</sub> concentrations for a 5-year historical exposure period 10 years prior to enrollment (1980-1984). We used Cox regression to estimate adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for the association per 10µg/m<sup>3</sup> increase in PM<sub>2.5</sub> and incident endometrial cancer risk. Models were adjusted for age, race/ethnicity, smoking status, educational attainment, oral contraceptive (OC) use, body mass index (BMI), and menopausal hormone therapy (MHT). We conducted stratified analyses by OC use, MHT, BMI, and catchment state.

**Results:** With follow-up through 2017, 2,820 endometrial cancer cases were diagnosed. Endometrial cancer risk increased 12% per 10µg/m<sup>3</sup> increase in PM<sub>2.5</sub> (HR=1.1 [CI:1.0-1.2]). Mean PM<sub>2.5</sub> levels were highest in Georgia and Pennsylvania, where associations were also strongest (n=81 cases; HR=4.6 [1.1-19.8]; n=505 cases; HR=1.7 [1.1-2.6]) respectively; however, the interaction was not significant (p-intx>0.05). We found no evidence of effect modification by OC use, BMI, or MHT (p-intx>0.05).

**Conclusions:** Our novel findings indicate an association between PM<sub>2.5</sub> and endometrial cancer and suggest that PM<sub>2.5</sub> chemical constituency or other region-specific factors may be drivers of risk.

**Racial Differences in Incidence and Mortality Rates of Childhood Lymphomas in the United States from 2000-2019** Emma Hymel\* Emma Hymel Josiane Kabayundo Shinobu Watanabe-Galloway

**Objectives:** Lymphoma accounts for 8% of cancers among children. Racial differences in childhood lymphoma incidence and mortality in the United States over the last two decades are unclear.

**Methods:** This population-based cohort study used Surveillance, Epidemiology, and End Results (SEER) 17 registry incidence and incidence-based mortality data to identify cancer cases and deaths of malignant lymphomas and other reticuloendothelial neoplasms from 2000-2019 among Black and White children (ages 0-19). Age-adjusted incidence and mortality trends by race (Black vs. White) were analyzed using joinpoint regression with pairwise tests for parallelism.

**Results:** 10,957 new lymphoma cases were diagnosed from 2000-2019 among Black and White children; 86.45% of cases were White. There were no significant differences in the incidence trends by race ( $p=0.71$ ). Among both races, the incidence rate increased from 2000 to 2019 (annual percent change (APC) among Blacks: 1.69, 95% CI=0.5-2.9; APC among Whites: 1.79, 95% CI=1.2-2.4). 707 lymphoma deaths occurred among Black and White children from 2000-2019; 80.91% of deaths were among Whites. From 2000-2019, the mortality rate of lymphomas was higher among Blacks compared to Whites (rate ratio=1.22, 95% CI=1.00-1.47). The mortality trends did not differ by race ( $p=0.93$ ). Among Black children, the mortality rate increased from 2000-2002 (APC=59.48, 95% CI=-28.4-255.4) and then decreased from 2002-2019 (APC=-2.23, 95% CI=-4.9-0.6). Among White children, the mortality rate increased from 2000-2002 (APC=74.53, 95% CI=25.3-143.1) and then decreased from 2002-2008 (APC=-7.26, 95% CI=-13.9-0.1) and 2008-2019 (APC=-1.02, 95% CI=-3.2-1.2).

**Conclusions:** The incidence rate of lymphoma is increasing among Black and White children. While mortality rates declined for both races, there is still a higher mortality rate among Black children. Further research is needed to understand reasons for this racial disparity in childhood lymphoma mortality.

**Distance to care among childhood leukemia cases: A report from the Children's Oncology****Group** Amanda S. Thomas\* Amanda Thomas Jenny Poynter Logan Spector David Van Riper  
Katherine Knowles Jeannette Sample Erin Marcotte

Over 15,000 children (500,000 childhood cancer survivors living in the US each year). The goal of this analysis is to understand how distance to/from designated clinic care impacts long-term effects of health (socioeconomic status, mortality) in childhood cancer survivors. We focused our analysis on acute lymphoblastic leukemia (ALL) because it is the most common type of childhood cancer.

The Children's Oncology Group Childhood Cancer Research Network (CCRN) was initiated in 2007 to provide a mechanism to facilitate non-therapeutic research and create a registry of childhood cancer patients. Data collected includes cancer diagnosis, place of residence and treatment institution. The CCRN cohort includes 15,838 ALL patients diagnosed between 2007-2017, and we have successfully geocoded addresses at time of cancer treatment for 14,755 patients. Broadly, these ALL patients are primarily of B-cell morphology (80.5%) and were diagnosed at the average age of 5 (IQR: 3-10). Large populous states (CA, TX, FL, NY) comprised the majority of cancer treatment centers at which these patients received care and greater than 85% lived in urban areas based on RUCA codes. Distance to primary cancer care while being treated showed the average straight-line distance traveled is 19.5 (IQR: 9.0-47.6) miles with rural residents traveling 4 times as far than urban. Strikingly, those that had to travel farther for care were primarily in the low/middle socioeconomic classes (Kruskall-Wallis p-value <0.001) with no considerable differences existing based on sex or age at diagnosis. Treatment at these distances can become a burden financially and potentially limit access to care. As these patients transition into survivorship care, difficulties related to distance could impact healthcare choices and ultimately long-term consequences.

**LATEBREAKER**

Cancer

**Does heavy drinking modify the association between screening for cancer and use of e-cigarettes? Results from a 2016, 2018 and 2020 national level study** Cristina Oancea\* Odele Rajpathy S. Cristina Oancea Yun Zeng

Although presented as a safer alternative to conventional cigarettes, smoking e-cigarettes (SEC) has potential oncogenicity. Heavy alcohol consumption is also oncogenic. In contrast, cancer screening is a preventative action that has contributed to substantial reductions in cancer-related deaths. In this study we aim to investigate the influence of heavy drinking on the association between receiving cancer screening and SEC.

Data from the 2016, 2018 and 2020 BRFSS study (N=124,499) was used to perform weighted and adjusted logistic regression analyses to investigate the association between screening for cancer, by sex/age recommendations, and SEC, in US adults ages 18-79, without prior cancer diagnosis. The effect modifying role of heavy drinking on this association was evaluated.

Among heavy drinking females ages 21-65 without a hysterectomy, the weighted and adjusted odds (WAO) of SEC were 52% significantly lower (95%CI: 0.30-0.76) in those who screened for cervical cancer compared to those who didn't. Among heavy drinking females ages 50-74 the WAO of SEC were 44% marginally significantly lower (95%CI: 0.30-1.05) in those who screened for breast cancer when compared to those who didn't. Among heavy drinking females ages 50-75 the WAO of SEC were 47% significantly lower (95%CI: 0.36-0.76) in those who screened for colorectal cancer when compared to those who didn't. Among non-heavy drinking females ages 50-75 the WAO of SEC were only 18% significantly lower (95%CI: 0.70-0.96) in those who screened for colorectal cancer when compared to those who didn't. No other significant associations were observed among females, or male prostate/colorectal cancer screening and SEC.

The results were indicative of a *reduction in additional cancer risk behavior due to SEC* by engaging in cancer *prevention methods, especially among heavy-drinking women*. Additional research is needed to further elucidate the findings of this study.

**Association between diabetes and cervical cancer: An analysis of NHANES 2015-2018**

Krishtee Napit\* Krishtee Napit Emma Hymel Josiane Kabayundo Dr. Shinobu Watanabe Galloway

**Background:**

Many epidemiologic studies have found an increased risk of cancer in diabetic patients. The biological evidence of diabetes and cancer risk has been established. Gynecologic cancers such as endometrial cancer have shown an unequivocal association with diabetes, but a clear relationship between cervical cancer and diabetes has not been determined.

**Objective:** 1) Examine the association between self-reported diabetes and cervical cancer among adult women ( $\geq 20$  years) in the US, and 2) identify factors associated with self-reported cervical cancer among women ( $\geq 20$  years) in the US.

**Method:**

2015–2018 National Health and Nutrition Examination Survey (NHANES) data were used. The sample included women aged 20 years or more. The sampling design was a complex, multistage, probability sampling method to select participants representative of the civilian, non-institutionalized US population. Multivariate logistic regression was used to examine the association between diabetes and cervical cancer and to identify factors associated with cervical cancer at a level of significance with a p-value of less than 0.05 and an adjusted odds ratio.

**Results**

A total of 5295 female participants were included in the analysis, where 43 (0.08%) had cervical cancer. The adjusted odds ratio was 0.78(95% CI: 0.28, 2.17) indicating there is no statistically significant association between self-reported cervical cancer and diabetes. Among all covariates: age, education, marital status, poverty, smoke, and BMI, only smoke was found significant in the adjusted model. Smokers 5.00(95% CI: 2.40, 10.43) had a higher odds of being diagnosed with cervical cancer.

**Conclusion**

Based on NHANES data, it appears women diagnosed with cervical cancer do not have association with diabetes. This may be due to very small percentage of outcome cervical cancer in NHANES data.

**Significance**

Future studies may use existing data with other risk factors for cervical cancer. Also, a survey-based research may be conducted to conduct a case-control study to examine the relationship between cervical cancer and diabetes.

**All-cause and cause-specific mortality among low-risk thyroid cancer survivors** Thi Van Trinh Tran\* Thi Van Trinh Tran Elisa Pasqual Sara J. Schonfeld Cari M. Kitahara

**Background:** Differentiated thyroid cancer (DTC) is often diagnosed in young- to mid-adulthood and is associated with high disease-specific survival. However, the optimal approach to treatment and long-term monitoring of patients with DTC is an ongoing debate, and the long-term risks of other adverse health outcomes, including second cancers and cardiovascular disease (CVD), remain unclear. To address these issues, we assessed all-cause and cause-specific mortality in patients with low-risk DTC.

**Methods:** Using the U.S. SEER-12 cancer registry database (1992-2019), we estimated standardized mortality ratios (SMRs), relative risks (RRs) and cumulative mortality for all-cause and cause-specific deaths, overall and according to patient demographics and disease characteristics among 51854 patients (81.8% women, 69.3% diagnosed before 40 years of age) diagnosed with first primary, small (<4 cm), localized DTC.

**Results:** During follow-up (median 9.5 years, range 0-28 years), 3467 deaths were recorded. The most common causes of death were second cancers (n=1035, 29.9%) and CVD (n=912, 26.3%). Thyroid cancer accounted for 4.3% of deaths (n=148) with the highest risk in the first year of diagnosis. The 15-year cumulative mortality from thyroid cancer, other cancers, and CVD was 0.5%, 3.0%, and 2.5%, respectively. DTC patients had lower mortality rates overall (SMR=0.72, 95% CI 0.70-0.75) and for most causes compared to the general population. Higher total mortality was observed in male vs. female, older vs. younger, and non-white vs. white patients. Greater tumor size and follicular carcinoma were associated with higher thyroid cancer mortality. All-cause and thyroid cancer mortality did not differ by type and extent of therapy.

**Conclusion:** Patients with low-risk DTC experienced reduced mortality rates from most causes and were more likely to die from causes other than thyroid cancer in the first three decades after diagnosis, with some variability by patient characteristics.



**Ambient fine particulate matter exposure and risk of incident liver cancer in the NIH-AARP Diet and Health Study** Xiuqi Ma\* Xiuqi Ma Jared A. Fisher Katherine A. McGlynn Linda M. Liao Vasilis Vasiliou Joel D. Kaufman Debra T. Silverman Rena R. Jones

**Background:** Fine particulate matter (PM<sub>2.5</sub>) has been associated with liver cancer incidence and mortality in limited studies, however most investigations lacked historical exposure assessment or estimates of individual-level residential exposure.

**Methods:** We used a spatiotemporal prediction model to estimate annual average historical PM<sub>2.5</sub> concentrations at the residential addresses of participants in the NIH-AARP Diet and Health Study, a cohort located in 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). Historical exposures were estimated for a 15-year period prior to enrollment (1980-1994). We used Cox regression to estimate hazard ratios (HR) and 95% CIs for risk of incident liver cancer overall and by histologic subtype per 10µg/m<sup>3</sup> increase in PM<sub>2.5</sub>. Models were adjusted for demographic characteristics, body mass index (BMI), smoking status, alcohol consumption, caloric intake, physical activity, and catchment state. We also conducted analyses stratified by smoking status, BMI, and catchment state.

**Results:** A total of 1486 liver cancers were diagnosed in follow-up through 2017. We observed a nonsignificant increased risk of liver cancer associated with PM<sub>2.5</sub> exposure (HR=1.12 [0.94-1.34] per 10µg/m<sup>3</sup>). Associations were slightly stronger for hepatocellular carcinoma (84% of cases; HR=1.15 [0.95-1.39]). No significant interactions in the PM<sub>2.5</sub>-liver cancer association were noted by smoking status, BMI, or catchment area (p-interaction all >0.05). However, associations were stronger among overweight (HR=1.24 [0.96-1.61]) and obese (HR=1.14 [0.84-1.53]) participants than among normal/underweight participants (HR=0.92 [0.66-1.27]).

**Conclusions:** Our findings from this large U.S. cohort suggest that ambient PM<sub>2.5</sub> levels at the home are associated with risk of liver cancer. BMI may influence the relationship between PM<sub>2.5</sub> and liver cancer risk.

**Sleep duration and cancer mortality in the Cancer Prevention Study-II** Sidney Donzella\*  
Sidney Donzella Emily Deubler Alpa Patel Charlie Zhong Amanda Phipps

Prior studies investigating the association of sleep duration and cancer mortality have shown mixed results. We investigated the association of sleep duration with cancer mortality, with consideration for possible sex-specific differences, among participants in the Cancer Prevention Study-II. Sleep duration was collected at baseline in 1982 among 1.2 million cancer-free US adults and categorized into 5 groups (3-5 hrs, 6 hrs, 7 hrs (referent), 8 hrs, 9-14 hrs). Cancer-specific mortality through 2018 was determined via linkage to the National Death Index. Participants were excluded from this study if they reported incomplete or implausible sleep duration, or prevalent cancer, or if they died of cancer within 2 years of baseline. We used Cox proportional hazard models to calculate HRs and 95% CIs adjusted for age, race, smoking status, body mass index, marital status, education, alcohol consumption, physical activity, fruit/vegetable intake, and comorbidity score to assess the association of sleep duration and cancer mortality, both overall and in analyses stratified by sex. Among 1,083,605 participants (56.1% female) included in these analyses, 4% slept 3-5 hrs, 16% slept 6 hrs, 34% slept 7 hrs, 39% slept 8 hrs, and 8% slept 9-14 hrs/night on average. Over 27,287,937 person-years of follow-up, there were 149,307 deaths from cancer. Shorter (6 hrs: HR 1.03, 95% CI 1.01-1.04) and longer (8 hrs: HR 1.03, 95% CI 1.01-1.04; 9-14 hrs: HR 1.07, 95% CI 1.05-1.09) sleep duration were associated with increased risk of cancer mortality. No association was seen in the shortest sleep duration group (HR 1.00 95% CI 0.98, 1.03). Sex-specific models showed slightly stronger associations among men (3-5 hrs: HR 1.06 95% CI 1.02, 1.10; 6 hrs: HR 1.04 95% CI 1.01, 1.06; 8 hrs: HR 1.03 95% CI 1.01, 1.05; 9-14 hrs: HR 1.09 95% CI 1.06, 1.12). These results indicate that sleep duration may impact risk of cancer mortality, especially among men.

**Identification of an association between Amerindian genetic ancestry and risk of hepatoblastoma** Jinhee Cha\* Jinhee Cha Nicole Branch Logan G. Spector Erin Marcotte

Although hepatoblastoma (HB) has the fastest rising incidence rate of any pediatric cancer, its literature is still in its infancy. Hepatoblastoma often occurs in the context of inherited conditions, those born at low birth weight (under 2499g) and is highest among Hispanic infants. We used genotypes derived from population-based collections of newborn dried blood spots from California (CA) and Michigan (MI) to examine the association between genomic ancestry and HB.

Hepatoblastoma cases were gathered from residual newborn dried blood spots from CA's and MI's biobanks. Controls were randomly selected from CA and MI birth records and matched to cases by sex, year of birth, birth weight and parental race/ethnicity data as listed on birth certificates. Blood spots were genotyped on the Illumina Global Screening Array and genomic proportions were generated using RFMix. We examined if proportions of European, African, Amerind (AMR), East Asian, and South Asian was associated with HB risk using logistic regression models to compute odds ratios (OR) and 95% confidence intervals (CI). We also stratified by maternal race/ethnicity and infant birth weight.

A total of 401 cases and 582 controls were included in statistical analyses. Each 10% increase in AMR ancestry was associated with increased odds of HB (OR: 1.13 [1.08, 1.19]). AMR ancestry proportion was not associated with HB risk among those born at very low or low birth weight but was associated among infants with normal (2500-3999g) and high ( $\geq 4000$ g) birth weight (OR: 1.16 [1.08, 1.25] and OR: 1.14 [1.04, 1.25] respectively). Although not statistically significant, restricting to infant of Hispanic mothers saw an increased effect estimate for each 10% increase in AMR ancestry (OR 1.10 [0.96, 1.25]).

Our results indicate that AMR ancestry is associated with an increased risk of HB and the association may be stronger among infants born at normal and high birth weights.

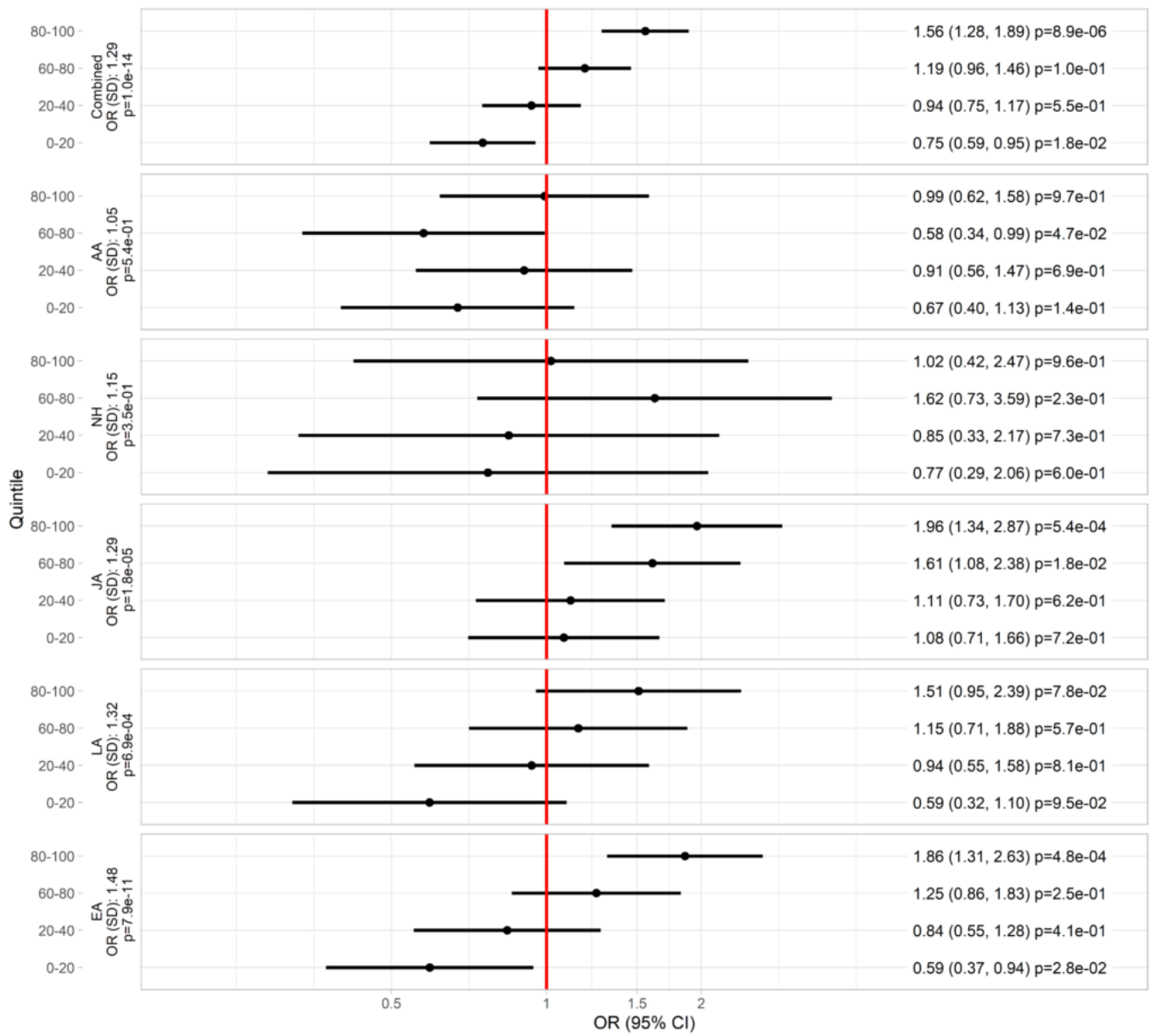
**Replication and Genetic Risk Score Analysis for Bladder Cancer in a Diverse Multiethnic****Population** David Bogumil\* David Bogumil Victoria Cortessis V. Wendy Setiawan David Conti  
Christopher Haiman Loïc Le Marchand Gertraud Maskarinec

Background: There are no replication studies of bladder cancer (BCA) associated single nucleotide polymorphisms (SNPs) outside European or Asian ancestry groups. Varying linkage disequilibrium structures across populations make cross ancestry replication important for identifying improved tagging SNPs to better understand disease mechanisms and enhance risk prediction.

Methods: We queried the National Human Genome Research Institute GWAS Catalogue and identified 25 GWAS significant SNPs associated with BCA. We estimated SNP associations in the Multiethnic Cohort Study (MEC) (n=72,323) composed of African Americans (AA), Native Hawaiians (NH), Japanese Americans (JA), Latino Americans (LA), and European Americans (EA). Cases were identified via state SEER cancer registries based on ICD site codes (C67.0-C67.9). Allelic associations were estimated using logistic regression, adjusting for age at sample collection, sex, and global ancestry. Using the variants, we calculated a polygenic risk score (PRS), weighted by the log-odds from prior GWAS.

Results: We identified 925 BCA cases (AA:153, EA:279, JA:279, LA:161, NH:53) and replicated 10/24 SNPs with MAF>5% at  $p < 0.05$  in the combined sample (EA:9, JA:5, L:3, B:2, H:0,  $p < 0.05$ ). The PRS was significantly associated with BCA in JA, EA, and LA ( $p < 0.05$ ). No association was observed in AA and NH. In the pooled sample, the PRS was associated with BCA (OR=1.30, per SD, 95% CI: 1.22, 1.39). The highest quintile was associated with a 56% increase in the odds of BCA, relative to the 40%-60% group. The association was strongest among EA (OR=1.48 per SD) and LA (OR=1.32 per SD).

Conclusion: There is limited evidence for the benefit of BCA screening among high-risk individuals. We have identified a PRS to significantly stratify BCA risk. Incorporation of a PRS in identification of high-risk individuals for urinary biomarker screening may improve screening feasibility and benefit through reducing stage at diagnosis.



**Accounting for competing risks in associations of fine particulate matter air pollution (PM<sub>2.5</sub>) with cause-specific mortality in men diagnosed with prostate cancer** Charlotte Roscoe\* Charlotte Roscoe Hari S. Iyer Timothy R. Rebbeck Francine Laden

Background: Fine particulate matter (PM<sub>2.5</sub>, particles  $\leq 2.5 \mu\text{m}$  in aerodynamic diameter) is associated with mortality in US cancer survivors. Five-year survival in men with prostate cancer (CaP) approaches 100% and CaP survivors are more likely to die from other causes, including cardiovascular disease (CVD). We assessed associations of PM<sub>2.5</sub> with cause-specific mortality (CVD, CaP) in CaP survivors, accounting for the competing event of mortality from other causes.

Methods: Using data from men diagnosed with CaP from 2000 to 2015 from California and the Seattle-Puget Sound, Washington cancer registries, we linked annual averaged PM<sub>2.5</sub> from spatiotemporal models (1km resolution) to residential addresses during year of diagnosis. For CVD and CaP mortality, we estimated cause-specific hazard ratios (HR) and 95% confidence intervals (CI) for each 5mg/m<sup>3</sup> increase in PM<sub>2.5</sub> using Cox Proportional Hazards models. To incorporate competing risks for non-CVD and non-CaP mortality, we estimated subdistribution HRs and 95% CIs using Fine-Gray models. Models were adjusted for age, diagnosis year, stage, marital status, neighborhood socioeconomic status, and population density.

Results: From 2000 through 2015, 331,877 men were diagnosed with CaP; approximately one-third died by the end of follow-up (December 31st, 2018), which included 35,015 CVD and 34,229 CaP deaths. The cause-specific HR were 1.04 (95% CI 1.03, 1.05) and 1.00 (95% CI 0.98, 1.01) and the subdistribution HR were 1.06 (95% CI 1.05, 1.08) and 1.00 (95% CI 0.98, 1.01), for CVD and CaP, respectively.

Discussion: Cause-specific analyses treat competing events as censoring and estimate HR only in men who are event free; HR have no one-to-one link to the cumulative incidence function (i.e. risk) in the presence of competing events. Subdistribution HR are estimated in men who are event free or who have experienced a competing event. We found risk of CVD, but not CaP, mortality in CaP survivors was associated with PM<sub>2.5</sub>.

**Delayed Curative Surgery Negatively Impacts Overall Survival of Male and Female Breast Cancer Patients: Findings from the National Cancer Database** Shamim Shahi\* Shamim Shahi Shamim Shahi Kendra Ratnapradipa Jane Meza Pavankumar Tandra Evi Farazi

**Background:** Prior literature on breast cancer surgery delay and overall survival has been inconclusive. The prevailing literature for female patients suggests that delaying surgery for longer intervals negatively impacts survival. However, the literature is inconclusive regarding surgery delays for <12 weeks. For male patients, to our knowledge, this association is unclear for both short and long-term delays. This study aims to evaluate whether delayed surgery impacts survival and whether gender is an effect modifier in the association between surgery delay and overall survival.

**Methods:** This retrospective cohort study utilized the National Cancer Database (NCDB) data from 2004 to 2011 with a follow-up through 2016. The NCDB is a nationwide, hospital-based, comprehensive clinical oncology database representing >70% of all newly diagnosed malignancies in the United States. We obtained crude and adjusted hazard ratios (HRs), corresponding 95% confidence intervals (CIs), and p-values from the Cox proportional hazard multivariable models adjusted for confounders. Propensity score methods, as well as landmark analysis, were used as additional analyses.

**Results:** A total of 706,154 breast cancer patients met the study eligibility criteria. Most patients received surgery within 12 weeks (94.29%). The study participants were predominantly female (99.11%), of non-Hispanic White race/ethnicity (80.19%), and between the ages of 45-74 years (72.62%). Delaying surgery for shorter periods tended to have a slightly protective effect in the combined sample of male and female patients and among female patients only. The hazard of death for those who delayed surgery for 91-180 days was 8% higher than those who received surgery in < 31 days (HR = 1.08; 95% CI: 1.04-1.12). These results mainly reflected the magnitude of associations among females, given their predominance in the study sample. Among males, the hazard of death for those who delayed surgery for 91-180 days was 64% higher than for those who received surgery in less than 31 days (HR = 1.64; 95% CI: 1.18-2.29).

**Conclusion:** We found a higher hazard of death due to surgery delay for > 12 weeks compared to 4 weeks. In stratified analysis, male patients had an elevated risk of death due to surgery delay compared to female patients.

**The effect of the sex-steroid hormone pathway on postmenopausal estrogen receptor-positive breast cancer risk: a case-cohort analysis within the Melbourne Collaborative Cohort Study**

Frances Albers\* Frances Albers Makayla Lou Brigid M. Lynch Roger L. Milne S. Ghazaleh Dashti Christopher T.V. Swain Sabina Rinaldi Vivian Viallon Lyle Gurrin Amalia Karahalios Marc J. Gunter Kristy A. Brown Dallas R. English

**Background:** Breast cancer is a hormone-driven disease. However, the endocrinological pathway is rarely disentangled from the potential confounding effects of upstream biological pathways. We estimated the effects of biomarkers from the sex-steroid hormone pathway on postmenopausal estrogen receptor (ER)-positive breast cancer risk while accounting for biomarkers of the insulin signalling and inflammatory pathways.

**Methods:** This analysis included 1,225 women (347 cases, 878 non-cases) selected for a case-cohort study of postmenopausal breast cancer within the Melbourne Collaborative Cohort Study. Plasma concentrations were measured for 20 biomarkers of the sex-steroid hormone, insulin signalling and inflammatory pathways. Weighted Poisson regression with a robust variance estimator was used to estimate RRs and 95% CIs of postmenopausal ER-positive breast cancer per doubling concentration of progesterone, estrogens, androgens, and sex hormone binding globulin (SHBG). Analyses were adjusted for lifestyle confounders and upstream biomarkers identified *a priori* via literature review and expert consensus.

**Results:** Increased risks of postmenopausal ER-positive breast cancer were observed per doubling concentration of progesterone (RR = 1.22, 95% CI: 1.03 to 1.44), androstenedione (RR = 1.20, 95% CI: 0.99 to 1.45), dehydroepiandrosterone (RR = 1.15, 95% CI: 1.00 to 1.34), total testosterone (RR = 1.11, 95% CI: 0.96 to 1.29), free testosterone (RR = 1.12, 95% CI: 0.98 to 1.28), estrone (RR = 1.21, 95% CI: 0.99 to 1.48), total estradiol (RR = 1.19, 95% CI: 1.02 to 1.39) and free estradiol (RR = 1.22, 95% CI: 1.05 to 1.41). A decreased risk was observed for SHBG (RR = 0.83, 95% CI: 0.66 to 1.05).

**Conclusion:** Progesterone, estrogens and androgens increase postmenopausal ER-positive breast cancer risk, whereas SHBG has a protective effect. These findings strengthen the causal evidence surrounding the hormone-driven nature of postmenopausal breast cancer.



**Whole genome data to explore the association between colorectal cancer and periodontitis: A case-control study in Taiwan** SHUN YI WANG\* SHUN YI WANG

**Background:** Colorectal cancer (CRC) is the leading cancer in Taiwan. Previous studies have pointed out that more than 50% of patients diagnosed with CRC have entered the advanced stage. Hence, improvement in non-invasive screening tools for CRC is needed. Periodontitis, may promote cancer by changing mucosal epithelial cells, including reducing apoptosis, DNA repair, increasing cell proliferation, and activating NF- $\kappa$ B and Wnt pathways. Therefore, the correlation of biomarkers between periodontitis and CRC in Taiwanese population is worthy to explore, so as to provide a reference for the development of non-invasive screening tools.

**Methods:** This is a case-control study. We concatenated the data from "Taiwan Biobank" and "National Health Insurance Research Database" between 2011 and 2018 to screen out the periodontitis group among CRC patients, and using 1:10 propensity score matching by sex, age, smoking, drinking and nut experience to select control group from same database. Then, genome-wide association study (GWAS) was conducted to find candidate gene locus that were highly correlated with CRC in patients with periodontitis, and further explore the interaction of the screened candidate genes with CRC.

**Results:** A total of 1,443 patients were identified in this study, including 136 cases of CRC and 1,307 among control group. Of 136 CRC patients, 103 (75.74%) got periodontitis and 33 (24.26%) didn't ( $p=0.935$ ). After conducting GWAS, we found that there are three gene locus (rs2298785, rs80246220 and rs1831016) correlated with CRC in patients with periodontitis and two of these locus are located on chromosome 18 and other is on chromosome 6. The odds ratio of these locus was 2.39, 2.35 and 2 when compared to control group, respectively.

**Conclusion:**

After correcting possible confounding factors, we found out three candidate gene locus related to CRC patients with periodontitis. Thus, it may be the reference of non-invasive screening tools for CRC. Future investigations are necessary to validate the kinds of conclusions that can be drawn from this study.

**Keywords:** Colorectal cancer (CRC), Periodontitis, Taiwan Biobank, National Health Insurance Research Database (NHIRD), Genome-wide association study (GWAS).

**Estimating 10-year risk of lung and breast cancer by occupation in Switzerland** Bernadette van der Linden\* Bernadette van der Linden Nicolas Bovio Patrick Arveux Yvan Bergeron Jean-Luc Bulliard Evelyne Fournier Simon Germann Isabelle Konzelmann Manuela Maspoli Elisabetta Rapiti Aylward Arnaud Chiolero Irina Guseva Canu

**Background:** Lung and breast cancer are important in the working-age population both in terms of incidence and costs. Associations of lifestyle-related factors with cancer risk have been explored in the literature, but accurate and easy to interpret estimates of the lung and breast cancer burden associated with occupations is lacking. The study aims to estimate the 10-year risks of lung and breast cancer by occupation and smoking status and to create age-, and sex-specific 10-year risk charts.

**Methods:** Primary malignant lung and breast cancer cases diagnosed between 2010 and 2014 from all 5 cancer registries of Western Switzerland, matched with the Swiss National Cohort were used. The 10-year risks of lung and breast cancer by occupational category were estimated. For lung cancer, estimates were additionally stratified by smoking status using smoking prevalence data from the 2007 Swiss Health Survey.

**Results:** The risks of lung and breast cancer increased with age and were highest for current smokers. Men in elementary professions had a higher 10-year risk of developing lung cancer compared to men in intermediate and managerial professions. Women in intermediate professions had a higher 10-year risk of developing lung cancer compared to elementary and managerial professions. However, women in managerial professions had the highest risk of developing breast cancer. The 10-year risk of lung cancer was higher in men than in women, and, except for current smokers, 10-year risk of breast cancer was higher than that of lung cancer in women.

**Conclusion:** The 10-year risks of lung and breast cancer differ substantially between occupational categories. Smoking led to higher 10-year risks than occupation for both sexes. The 10-year risk can help patients and health professionals to make informed choices related to cancer risk, such as screening and health behaviors. The risk charts can serve as public health indicators and to inform policies to protect workers.

**Additive effects of 10-year exposures to PM<sub>2.5</sub> and NO<sub>2</sub> on cancer incidence in American older adults** Xinye Qiu\* Yaguang Wei Mahdieh Danesh Yazdi Tszshan Ma Edgar Castro Liu Su Xinye Qiu James Healy Bryan Vu Cuicui Wang Lihua Shi Joel Schwartz

**Background:** Epidemiologic evidence on air pollution and major cancers other than lung cancer remains largely lacking.

**Objective:** To examine the simultaneous effects of 10-year exposure to fine particulate matter (PM<sub>2.5</sub>) and nitrogen dioxide (NO<sub>2</sub>) on the risks of breast, prostate, colorectal, and endometrial cancer.

**Methods:** This cohort study included national Medicare beneficiaries with continuous enrollment in the Fee-for-Service program and in Part A & B throughout the follow-up between 2000–2016. We required a follow-up period of at least 10 years during which there was no cancer diagnosis. After that, participants exited the cohort at first occurrence of cancer diagnosis, death, or end of study, whichever occurred earliest. For each cancer, we used an inverse probability weighting-based additive model to examine additive effects of moving average exposures to PM<sub>2.5</sub> and NO<sub>2</sub> over the year of diagnosis and previous two years, previous 3 to 5 years, and previous 6 to 10 years on the cancer risk.

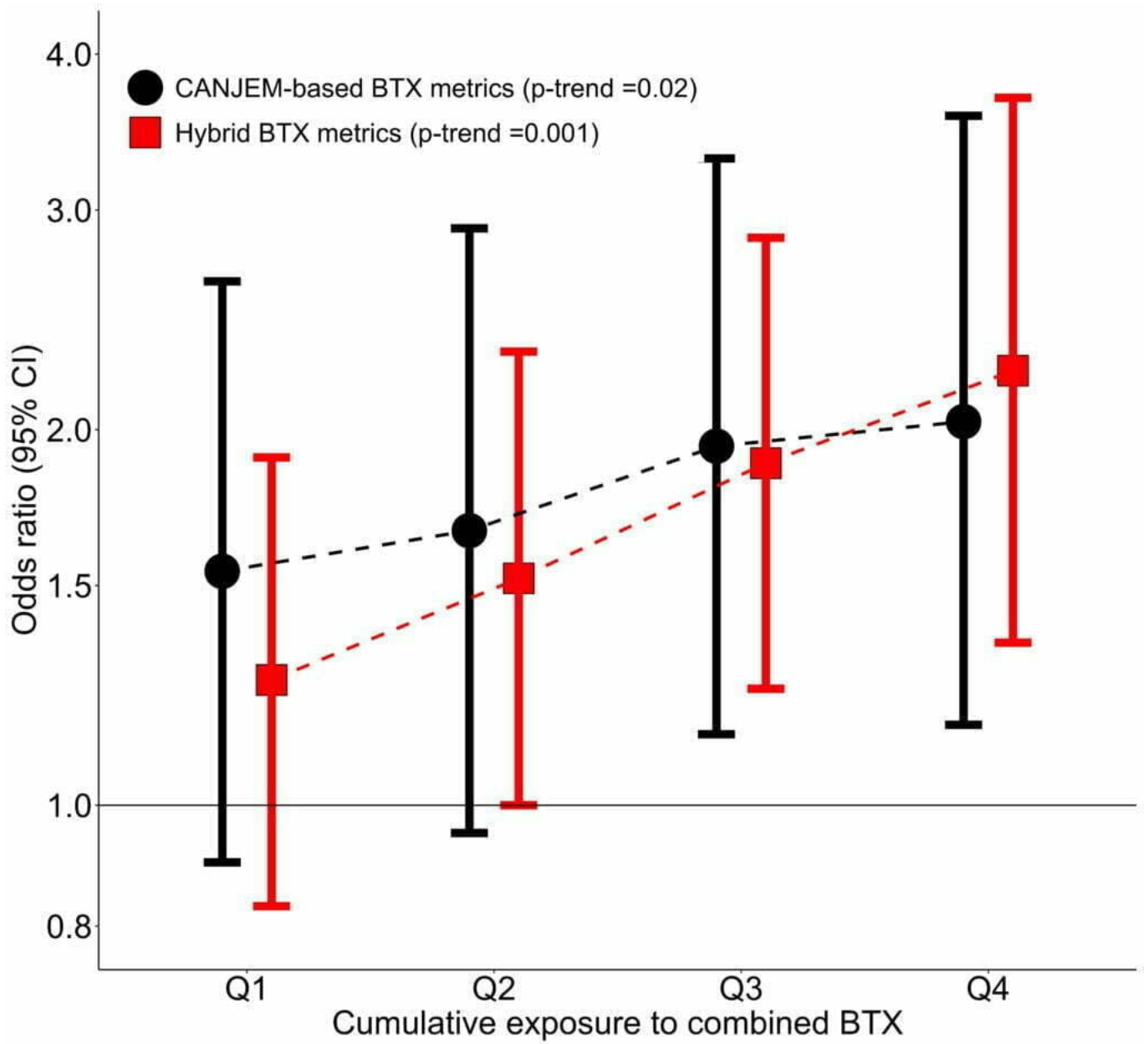
**Results:** The cohorts included 2.2–6.5 million beneficiaries for different cancers. PM<sub>2.5</sub> and NO<sub>2</sub> exposures increased absolute risks of colorectal and prostate cancer across the 10-year exposure window. Specifically, a unit reduction in PM<sub>2.5</sub> and NO<sub>2</sub> would respectively prevent 705 and 95 colorectal cancers, representing 6.2% and 0.8% of the total number of new cases per year within the cohort; a unit reduction in PM<sub>2.5</sub> and NO<sub>2</sub> would respectively prevent 460 and 223 prostate cases, representing 3.4% and 1.7% of the total number of new cases per year within the cohort. Those effects were considerably larger at exposure levels below the national standards. PM<sub>2.5</sub> and NO<sub>2</sub> exposures were not associated with endometrial cancer risk. Evidence supported adverse effects of NO<sub>2</sub> on breast cancer risk but was less clear for PM<sub>2.5</sub>.

**Discussion:** Long-term PM<sub>2.5</sub> and NO<sub>2</sub> exposures increased colorectal and prostate cancer risks. Substantial benefits of air quality management exist through cancer prevention.

**Occupational exposure to organic solvents and risk of bladder cancer** Shuai Xie\* Shuai Xie  
Melissa C. Friesen Dalsu Baris Molly Schwenn Nathaniel Rothman Alison Johnson Margaret R.  
Karagas Debra T. Silverman Stella Koutros

**Objectives:** Bladder cancer has been linked to several occupations that involve the use of solvents, including those used in the dry-cleaning industry. Here, we evaluated exposure to solvents and risk of bladder cancer in 1182 incident cases and 1408 controls from a population-based study.

**Methods:** Exposure to 21 specific solvents was quantitatively assessed using a job-exposure matrix (CANJEM). Exposure to benzene, toluene and xylene often co-occur. Therefore, we created two additional sets of metrics for combined benzene, toluene and xylene (BTX) exposure: 1) CANJEM-based BTX metrics and 2) hybrid BTX metrics, using a novel approach that integrates the CANJEM-based BTX metrics together with lifetime occupational histories and exposure-oriented modules that captured within-job, respondent-specific details about tasks and chemicals. Adjusted odds ratios (ORs) and 95% confidence intervals (95% CI) were estimated using logistic regression. **Results:** Bladder cancer risks were increased among those ever exposed to benzene (OR=1.63, 95%CI: 1.14-2.32), toluene (OR=1.60, 95%CI: 1.06-2.43), and xylene (OR=1.67, 95%CI: 1.13-2.48) individually. We further observed a statistically significant exposure-response relationship for cumulative BTX exposure, with a stronger association using the novel hybrid BTX metrics ( $OR_{Q1vsUnexposed}=1.26$ , 95% CI: 0.83-1.90;  $OR_{Q2vsUnexposed}=1.52$ , 95% CI: 1.00-2.31;  $OR_{Q3vsUnexposed}=1.88$ , 95% CI: 1.24- 2.85; and  $OR_{Q4vsUnexposed}=2.23$ , 95% CI: 1.35- 3.69) (p-trend=0.001) than using CANJEM metrics (p-trend=0.02). **Conclusions:** Our findings suggest that the integration of occupational exposure data from personal interviews improves our ability to identify an exposure-response between combined occupational BTX and bladder cancer risk, highlighting a little recognized occupational exposure that may play a role in the etiology of bladder cancer.



**Mediation of race/ethnicity disparities in physical patient reported outcomes (PROs) by socioeconomic position, comorbidities, tumor biology, and social support among elderly female breast cancer patients in the SEER-MHOS database** Kristen Champion\* Kristen

Champion Kendra Krebsbach Chloe Stallion Keith Dookeran

**Aim:** The disparity in baseline physical component summary scores (PCS) for elderly Blacks (NHB) and Hispanics compared to Whites (NHWs) with breast cancer could be due to mediation by socioeconomic position (SEP), comorbidities (CD), tumor biology (TB), and social support (SS). We examine the extent to which this race/ethnicity (R/E) disparity is transmitted through these domains.

**Methods:** Data is from the Surveillance, Epidemiology, and End Results- Medicare Health Outcomes Survey (SEER-MHOS). The analytic sample (n=17,234) included 12,943 NHW, 2,503 NHB, and 1,788 Hispanic women newly diagnosed between 2010-2017. We estimated average controlled direct associations (ACDA) using regression models with predictive margins to evaluate crude and age/body mass index (BMI)-adjusted PCS by R/E and performed a series of ACDA [with comparison of rescaled coefficients (RC)] controlling for the domains of SEP [household income ( $\leq 30K/30K-80K/>80K$ ), and education (<High School (HS)/HS/>HS)]; CD [smoking status (ever/never), diabetic (yes/no), hypertension (yes/no)]; TB [stage (local/regional/distant), grade (well/moderate/poor), subtype (luminal A/triple negative)]; SS [marital status [married/unmarried].

**Results:** NHB and Hispanic women were younger at time of diagnosis and had a higher BMI than NHW women. At baseline NHWs had PCS scores 3.5 points significantly higher than NHBs (95% CI: 2.9, 4.2) and 3.6 units higher than Hispanics (95% CI: 2.9, 4.3). Based on the RC method, of the four domains, SEP reduced the disparity the most while TB reduced it the least. While the differences were still significant, inclusion of all four domains attenuated the magnitude of the disparity between the minority groups and NHWs to a degree such that they were no longer considered minimally important differences [NHB (1.2; 95% CI: 0.14, 2.3); Hispanics (1.2, 95% CI: 0.4, 2.4)].

**Conclusion:** Our findings suggest that the observed R/E disparity in physical PROs is largely due to differences in SEP.

**Neighborhood-Wide Association Study of Incident Stroke in the REGARDS Study** Kendra D. Sims\* Kendra Sims M. Maria Glymour Tor Neilands Kirsten Bibbins-Domingo Julene Johnson

**Background:** Parsing socioeconomic and housing characteristics from interrelated area demographics may identify modifiable neighborhood determinants of Black/White stroke disparities.

**Methods:** Our sample included REasons for Geographic and Racial Differences in Stroke cohort participants (N=27829; 41% Black, aged 45-98 years, stroke-free at baseline) with data on adjudicated stroke diagnosis from 2003 to 2018. Participants were divided 50:50 into training and test datasets. Using Cox proportional hazard models, we summarized multivariable associations between each of 51 US Census American Community Survey sociodemographic, housing, and income-related census tract variables (2008-2012) and incident stroke, adjusting for individual-level factors. Neighborhood factors associated (Simes-adjusted for multiple comparisons p-value $\leq$ 0.05) with incident stroke in the training dataset were rerun in the test dataset to replicate findings. In the full cohort, we evaluated interactions between participant race and each replicated neighborhood factor on incident stroke.

**Results:** Six percent of participants had a stroke between 2003 and 2018. We observed a lower hazard of stroke among participants residing in census tracts with greater proportions of residents non-US born Non-Hispanic White, aged between 50 and 69, or in owner-occupied housing units (HR for top versus bottom tertile: 0.89; 95% CI: 0.84, 0.94). Conversely, living in census tracts with higher concentrations of sub-\$15K family income (HR: 1.21; 95% CI: 1.15, 1.28), or residents without a bachelor's degree was associated with higher stroke hazard. There was insufficiently convincing evidence of excess stroke hazard among Black versus White participants by any neighborhood factor.

**Conclusion:** Though underpowered to evaluate differential impacts of neighborhood factors by race, our findings support policies that increase home ownership and earning power to improve cardiovascular health for older Black and White adults.

**Changing clinical profile among individuals with sudden cardiac arrest: 16 years of the Oregon Sudden Unexpected Death Study** Kyndaron Reinier\* Kyndaron Reinier Harpriya Chugh Audrey Uy-Evanado Faye Norby Jonathan Jui Sumeet S. Chugh

Out-of-hospital sudden cardiac arrest (SCA), with a fatality rate of ~90%, accounts for ~20% of U.S. mortality. Improvements in prevention and treatment of cardiac disease led to a decline in SCA incidence from 1960 through 2010, which has recently leveled off. Little data is available regarding changes in the clinical profile of SCA cases over time.

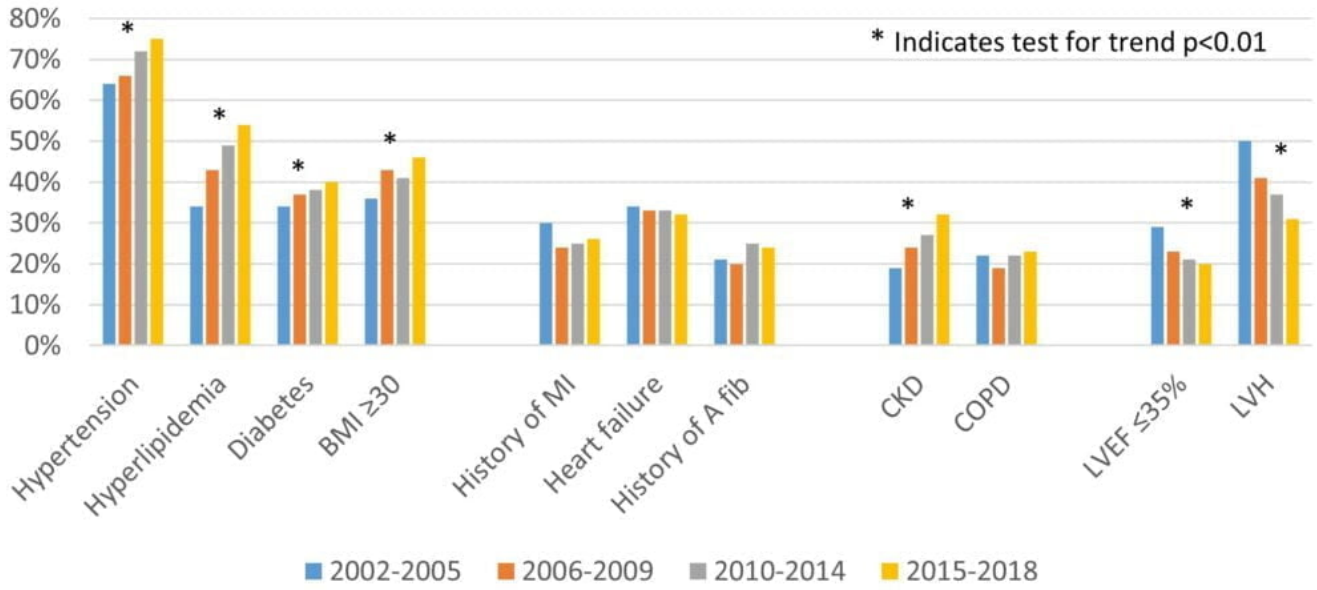
We evaluated medical history among individuals with out-of-hospital SCA (2002-2018) from the community-based Oregon Sudden Unexpected Death Study (Oregon SUDS). Medical history was obtained from medical records and was compared by 4-year periods (2002-2005, 2006-2009, 2010-2014, and 2015-2018) using 2-sided Cochran-Armitage tests and generalized linear models to test for trends over time.

Among 3,029 individuals with SCA from 2002-2018, mean age was 65 (SD 18) with no significant trend over time ( $p=0.51$ ) and 1986 (66%) were male. The prevalence of hypertension, hyperlipidemia, diabetes mellitus, obesity, and chronic kidney disease (CKD) increased significantly over time ( $p<0.01$ ) (Figure), while the proportion with history of myocardial infarction, heart failure, and atrial fibrillation did not change ( $p>0.09$ ) (Figure). In the subset of individuals with echocardiographically-assessed left ventricular ejection fraction (LVEF) and left ventricular hypertrophy (LVH) ( $n=896$ ), the proportion with  $LVEF\leq 35\%$  declined from 29% to 20% over time ( $p<0.01$ ) and with LVH from 50% to 31% ( $p<0.01$ ) (Figure).

Over 16 years of follow-up of SCA cases in a single community, the pre-SCA clinical profile changed significantly, possibly reflecting changing medical guidelines (e.g., lower cutpoints for hypertension diagnosis), increasing prevalence of some risk factors (e.g., diabetes and CKD), and decreasing prevalence of markers of cardiac damage (e.g.,  $LVEF\leq 35\%$ ) due to better treatment of existing cardiac disease. These changes highlight the need to move beyond using LVEF as the only clinical marker of high SCA risk in the general population.



### Medical history among sudden cardiac arrest cases over time



**Occupational Class in relation to Ideal Cardiovascular Health among Adults in the United States** Jamie A. Murkey\* Jamie A. Murkey Symielle A. Gaston Dana M. Alhasan W. Braxton Jackson Chandra L. Jackson

Racially minoritized groups tend to have lower 'ideal' cardiovascular health (ICVH) than non-Hispanic (NH)-White adults and are generally more likely to work in laborer or support service positions where job strain— associated with cardiovascular disease—is often high. Yet, few studies have included racially/ethnically diverse samples. Using 2004-2018 National Health Interview Survey data, we investigated standardized occupational classifications in relation to ICVH among US adults (n=230,196) by race/ethnicity. ICVH was defined as a report of 'yes' to the following: never smoked/former smoker; body mass index ( $\geq 18.5$ - $25 \text{ kg/m}^2$ ); physical activity ( $\geq 150$ - $300 \text{ min/week}$  moderate or  $\geq 75$ - $150 \text{ min/week}$  vigorous); sleep duration (7-9 hours/night); and no prior diagnosis of dyslipidemia, hypertension, or diabetes/prediabetes. Adjusting for sociodemographic, clinical factors and health behavior confounders, we used Poisson regression with robust variance to estimate PRs and 95% CIs of ICVH overall and by race/ethnicity. We performed Wald tests for interaction. Mean  $\pm$  SE age was  $41.7 \pm 0.1$  years. Latinx (53%) and NH-Black (37%) adults were more likely than NH-White adults (29%) to report laborer positions and had the lowest prevalence of ICVH (5.2% [Latinx] and 3.9% [NH-Black]). Laborer vs. professional/management occupational class positions were associated with a lower ICVH prevalence among NH-Asian (PR=0.60 [0.46-0.79]), NH-White (PR=0.80 [0.74-0.87]), NH-Black (PR=0.77 [0.58-1.01]), but with no evidence among Latinx (PR=0.94 [0.78-1.14] adults; p-interaction  $< 0.01$ ). In conclusion, working in laborer vs. professional management positions was associated with lower ICVH, except among Latinx adults. Given the higher likelihood of laborer occupations and lower prevalence of ICVH among minoritized racial/ethnic groups, social determinants related to occupational class should be considered in future studies of racial disparities in ICVH.

**Dietary Approaches to Stop Hypertension (DASH) Diet reduces blood pressure in children and adolescents in the United States**Xiang Li\* Xiang Li Tong Xia Roch Nianogo May Wang  
Onyebuchi A. Arah Liwei Chen

The Dietary Approaches to Stop Hypertension (DASH) diet has been recommended as a healthy dietary pattern to lower blood pressure among adults. Still, limited evidence is available for children and adolescents. We examined the associations between adherence to the DASH diet and blood pressure in the pediatric population and evaluated whether the level of sodium intake could modify the associations. Our analysis included 13,049 children and adolescents (8-17 years) from the National Health and Nutrition Examination Surveys (NHANES, 1999-2018). Adherence to the diet was assessed using a DASH score based on intakes of 8 DASH-targeted food groups. Systolic and diastolic blood pressure (SBP and DBP) were measured, averaging three valid values. We used multivariable linear regressions to examine the associations of DASH score with SBP and DBP, applying sampling weights to account for the complex survey design. For SBP, the mean difference (95% CI) was -0.81 mm Hg (-1.64, -0.02) in the middle tertile and -1.70 mm Hg (-2.91, -0.48) in the highest tertile compared to the lowest tertile of DASH score at the low sodium intake level (<2,300 mg/d); and was -0.88 mm Hg (-1.59, -0.18) and -1.09 mm Hg (-1.71, -0.47), respectively, at the high sodium level ( $\geq$ 2,300 mg/d). For DBP, the mean difference (95% CI) was -1.77 mm Hg (-2.94, -0.59) in the middle tertile and -2.71 mm Hg (-4.07, -1.35) in the highest tertile compared to the lowest tertile of DASH score at the low sodium intake level; and was 0.07 mm Hg (-0.66, 0.80) and -0.20 mm Hg (-1.01, 0.60), respectively, at the high sodium level. Among children and adolescents, the DASH score was associated with a reduction in SBP at both low and high sodium intake levels but only with a reduction in DBP at the low sodium intake level.

**The association between early-onset cardiovascular disease and subsequent risk of cancer**

Ce Wang\* Ce Wang Yiliang Zhang Priscilla MY Lee Chen Huang Kecheng Wei Jingjing Zhu Guoyou Qin Zhenyu Wu Yongfu Yu Jiong Li

**Abstracts****Background**

Patients with cardiovascular diseases (CVDs) have been suggested to be at a higher risk of developing cancers, but empirical findings have been inconsistent. In addition, the impact of type-specific CVDs on specific cancers remains largely unknown. We aim to examine the association of early-onset overall and type-specific CVDs with overall cancer and specific cancer types.

**Methods**

We conducted a population-matched cohort study including 132,227 patients with early-onset CVD born in Denmark during 1977-2016 and 1,322,270 individuals from the general population matched on birth year and sex. We performed stratified Cox regression to assess the association of CVD with cancer.

**Results**

During up to 42 years of follow-up, 1,575(1.19%) and 11,919(0.90%) were diagnosed with cancer among individuals with and without CVD, respectively. Individuals with CVD had a 28% increased overall risk of cancer (HR:1.28,95%CI:1.22-1.35). Sibling-matched analyses yielded a similar risk (1.37,1.24-1.51). Individuals with hypertensive disease (1.41,1.31-1.51) tended to have a higher overall risk of cancer than those with heart disease (1.15,1.00-1.32) and vascular disease (1.14,1.01-1.29). Varied increased rates of site-specific cancers were also observed, particularly for cancer of the multiple myeloma, bladder, pancreas, kidney, lung, leukemia, non-Hodgkin lymphoma, colon, central nervous system and thyroid (HRs ranging from 1.35 to 4.07). Male (1.42,1.29-1.56) or CVD diagnosed during childhood (1.42,1.26-1.59) may have a higher risk of cancer than female patients (1.23,1.16-1.31) or CVD diagnosed during early adulthood (1.25,1.18-1.33), respectively.

**Conclusions**

There was an increased risk of any cancer and several specific cancer types, among individuals with early-onset CVD, with patterns of risk varying by CVD subtypes, age at diagnosis, and sex. CVD may be an independent risk factor for cancer development and targeted strategies to prevent and manage CVD would contribute to reducing subsequent cancer risk.

**Keywords:** Cardiovascular disease, cancer, cohort study, risk factor

**Volatile Organic Compounds and Mortality from Ischemic Heart Disease: a Case-Cohort Analysis within Golestan Cohort Study** Arash Etemadi\* Arash Etemadi Mahdi Nalini Hossein Poustchi Deepak Bhandari Cindy M. Chang Benjamin C. Blount Lanqing Wang Amy L. Gross Mitchell H. Gail Christian C. Abnet Farin Kamangar Paolo Boffetta Reza Malekzadeh Neal D. Freedman

**Background:** Volatile organic compounds (VOCs) are among pollutants originating from a wide range of natural and anthropogenic sources. Although implicated in numerous health outcomes, including cardiovascular diseases, direct evidence for associations between exposure and subsequent disease is scarce.

**Methods:** In a frequency-matched (by age, sex, residence, and tobacco smoking status) case-cohort analysis nested in the Golestan cohort study (n=50,045, aged 40-75 years, enrollment: 2004-2008) in northeastern Iran, we calculated hazard ratio (HRs) and 95% CIs for the associations between urinary VOC metabolites measured in cohort baseline samples and subsequent ischemic heart disease (IHD) mortality during follow-up to 2018 using weighted Cox proportional hazard models adjusted for sociodemographic characteristics, BMI, physical activity, and other sources of VOCs.

**Results:** Data of 598 case and 575 non-case participants, mean (SD) age of 58.2 (9.3) years, 37.7% women, with a median of 8.3 years follow-up were analyzed. Among all participants, metabolites of acrylamide, acrylonitrile, acrolein, styrene, ethylbenzene, dimethylformamide/methylisocyanate, 1,3 butadiene, crotonaldehyde, isoprene, and carbon-disulfide were significantly associated with IHD mortality (HRs between 1.47 and 2.76). In subgroup analyses, statistically significant associations [HRs (95% CIs)] were observed in non-smokers for metabolites of acrylamide; [1.69 (1.02-2.79)], acrylonitrile [2.46 (1.52-3.97) and 1.99 (1.18-3.35)], acrolein; [2.30 (1.43-3.71)], styrene [1.96 (1.27-3.04)], and dimethylformamide/methylisocyanate [1.89 (1.10-3.24)]; whereas associations were not observed among tobacco smokers.

**Conclusion:** Our findings provide strong evidence for associations between exposure to several VOCs and IHD mortality many years after these exposures in the general population. These VOCs can be responsible for cardiovascular toxicity following exposure to smoke mixtures from different sources.

**Descriptive analysis of acute myocardial infarction patients with asthma: a population-based 14-year longitudinal epidemiological study** Yu-Ching Chou\* Pei-Yu Hsu Chien-An Sun

**Background:** One potential risk factor for acute myocardial infarction (AMI) is asthma, a chronic inflammatory airway disease, and the prevalence of asthma in Taiwanese adults is about 10%. However, secular trend studies of AMI with asthma are limited. This descriptive study examined the incidence of AMI with asthma in a large-scale, population-based Taiwanese cohort.

**Methods:** We conducted a descriptive study. From 2000 to 2013, 71,146 new cases with Asthma were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating the incidence rates of AMI with asthma in different sex, age groups and periods. For long term trends, we assessed the change in the incidence rates over 14 years by linear trend analysis.

**Results:** The incidence of AMI was 20.15 among asthma patients per 10,000 person-years. The incidence rate was 27.36 among men and 14.01 among women per 10,000 person-years. The incidence rate of AMI was higher in men. After stratifying age into 5 groups, we found that the incidence rate of AMI per 10,000 person-years was 0.69 in 20-29 years old, 2.16 in 30-39 years old, 9.31 in 40-49 years old, 20.70 in 50-59 years old and 41.71 in  $\geq 60$  years old. Patients have higher incidence rate of AMI when age is increasing. Also, incidence rate of AMI was 11.75, 16.42 and 23.65 by visiting 0 time, 1-3 times, and  $>3$  times in asthma clinical visits respectively.

**Conclusion:** In the past 14 years, the incidence of AMI had a profound impact on our life. By means of the big data, our finding suggested incidence rate of AMI with asthma is steadily rising. For future study, we need to test hypothesis for evaluating the correlation between asthma and AMI.

**Keywords:** Acute myocardial infarction (AMI), National Health Insurance Research Database (NHIRD), Asthma.

**LATEBREAKER**

Cardiovascular

**PTSD symptom burden since 9/11 and cardiovascular events in World Trade Center****responders: 2012-2021** Alfredo Morabia\* Leia Saltzman Leia Saltzman Sonja Swanson Maurizio Trevisan Janine Flory Alfredo Morabia

Posttraumatic stress disorder (PTSD) has been linked with cardiovascular disease in several trauma affected populations. Our previous work (2012-2016) with 9/11 World Trade Center responders demonstrated a robust association between a diagnosis of PTSD and subsequent cardiovascular events (e.g., myocardial infarction, stroke) in men and women while controlling for other recognized mental health and environmental risk factors such as depression and World Trade Center dust exposure. Our current work (2012-2021) expands on these findings to identify the relationship between PTSD symptom burden over time and distal cardiovascular events in men and women. The World Trade Center Heart Study is a prospective cohort of 6481, diverse first responders drawn from the larger World Trade Center Health Program in New York City. The cohort has 90% retention and about twice the prevalence of PTSD compared to the general population. Our analysis will link the cohort to new, just released data from the New York State hospitalization registry (SPARCS) collected up to 2021. PTSD threshold was considered positive based on a score of 44 or higher on the PCL-C and was scored across nine annual assessments from 2012-2021. WTC responders were classified into 5 groups: never met diagnostic threshold, remitting, delayed onset, recurring and chronic. Cox proportional hazard models will be used to assess the association of PTSD symptom burden and myocardial infarction, stroke, separately and pooled, in men and women. This work has implications for understanding why and how PTSD is related to cardiovascular incidents over time. It has clinical implications for the treatment and management of PTSD and the prevention of cardiovascular diseases, and coverage implications for the first responders protected by the Zadroga Act.

**LATEBREAKER**

Cardiovascular

**Is Sagittal Abdominal Diameter (SAD) the way forward for identifying visceral fat and cardiometabolic disease risk?** Shelley Ehrlich\* Suzanne Summer Jane Khoury Katherine Bowers Shelley Ehrlich

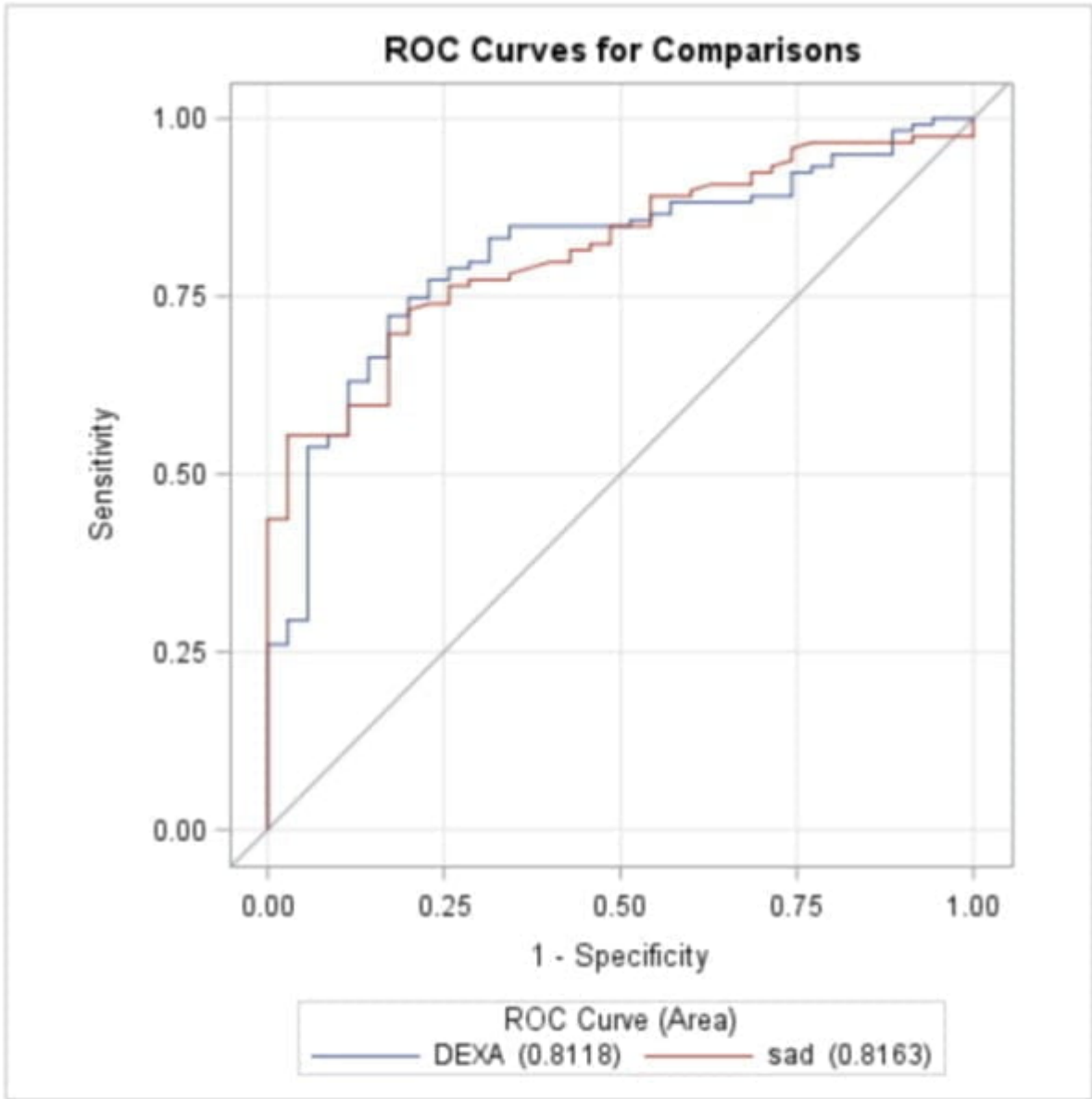
Visceral adipose tissue (VAT) is a risk factor for cardiometabolic disorders (CMD). Dual energy x-ray absorptiometry (DXA) estimates VAT but is expensive and not readily accessible. We compared DXA-VAT with sagittal abdominal diameter (SAD), a proxy for VAT, in our unique Transgenerational Effect on Adult Morbidity (TEAM) cohort - adult offspring born to moms with pregestational diabetes. TEAM participants have higher obesity prevalence compared to NHANES and are at increased risk for CMD. Our goal was to determine how well SAD agreed with DXA-VAT, and we compared their predictive probability for CMD markers.

**Methods:** TEAM participants (N=155) underwent measures of DXA-VAT, SAD, waist/hip circumference (WC, HC), and body mass index (BMI). Markers of CMD included fasting total, LDL, and HDL cholesterol, triglycerides, and hsCRP. We calculated the weighted Kappa (categorized as quartiles) for SAD and DXA-VAT to compare these measures. ROC curves were examined for each marker, comparing the area under the curve (AUC) for SAD and DXA-VAT. We also stratified by sex and waist-to-hip ratio (WHR).

**Results:** Participants (51% female; 82% white) had mean (SD) age 32.3 (4.7) years and BMI 31.5 (7.8) kg/m<sup>2</sup>. Twenty-four (15.5%) had preexisting diabetes, 17.4% had high TC and 52% LDL $\geq$ 100mg/dL, increasing risk for CMD. Mean DXA-VAT mass was 567 (304.8) g and mean SAD 23.0 (4.6) cm; the two were strongly correlated ( $r=0.81$ ,  $p<0.0001$ ) and weighted Kappa of 0.74 showed good agreement. The AUCs for the ROC curves for SAD and DXA-VAT were similar (figure), and both varied to a similar degree by sex and WHR for each of the CMD markers.

**Conclusions:** SAD is a non-invasive, inexpensive alternative to DXA-VAT that shows similar associations with markers of poor cardiometabolic health in an at-risk young adult population. Population cut-offs for SAD by sex are needed to make this tool useful to clinicians for CMD risk identification and prevention/intervention planning.





ROC Association Statistics							
ROC Model	Mann-Whitney				Somers' D	Gamma	Tau-a
	Area	Standard Error	95% Wald Confidence Limits				
DEXA	0.8118	0.0381	0.7371	0.8864	0.6235	0.6235	0.2204
sad	0.8163	0.0350	0.7478	0.8849	0.6327	0.6339	0.2237

**Epidemiologic Methods in the Firearm Policy and Mass Shootings Literature: A Scoping Review** Camerin A. Rencken, ScM\* Camerin A. Rencken Julia P. Schleimer, MPH Matthew Miller, MD, ScD, MPH Sonja A. Swanson, ScD Ali Rowhani-Rahbar, MD, PhD, MPH

Introduction: Recent reports have suggested that mass shootings are increasingly frequent in the US. However, existing literature on their prevention strategies are inconsistent and difficult to synthesize, potentially due to variations in research design and definitions of these events. To improve understanding of these discrepancies, this scoping review characterizes the methodology employed in the literature assessing the association between firearm policy and mass shootings in the US.

Methods: We included empirical articles in PubMed from 1/1/2000-9/1/2021 that examined mass shootings as an outcome and assessed any of 18 firearm policies determined *a priori* that regulate: 1) who may own, purchase, or possess firearms, 2) firearm sales and transfers, or 3) the use, storage, or carrying of firearms. Key variables extracted included how mass shootings were identified and defined, study design, analytic framework, and causal assumptions.

Results: Five articles met eligibility from 7733 screened, 2 of which studied multiple policies and 3 of which exclusively studied bans on assault weapons and high-capacity magazines sales. Outcome definitions ranged from a minimum of four to six fatalities, and two studies specified a location type (e.g., public setting). Data on mass shootings were obtained from sources such as the Mother Jones Magazine, the Supplementary Homicide Reports from the Federal Bureau of Investigation's Uniform Crime Reporting System, and the National Institute of Justice's Violence Project Dataset. Study designs included: 2 cross-sectional, 1 quasi-experimental, and 2 unspecified designs. No study was explicit about estimating a causal effect; 2 studies discussed assumptions of exchangeability and temporality.

Conclusion: The present study highlights the strikingly limited scope of evidence on the impact of firearm policies on mass shootings and identifies opportunities to improve this evidence both substantively and methodologically.

**The effect of face-to-face versus online learning on student performance in anatomy: An observational study using a causal inference approach** Joanna Diong\* Joanna Diong Hopin Lee  
Darren Reed

**Introduction:** This study aimed to estimate the causal effect of face-to-face learning on student performance in anatomy, compared to online learning, by analysing examination marks under a causal structure.

**Methods:** We specified a causal graph to indicate how the mode of learning affected student performance. We sampled purposively to obtain end-semester examination marks of undergraduate and postgraduate students who learned using face-to-face (pre-COVID, 2019) or online modes (post-COVID, 2020). The analysis was informed by the causal graph. Marks were compared using linear regression, and sensitivity analyses were conducted to assess if effects were robust to unmeasured confounding.

**Results:** On average, face-to-face learning improved student performance in the end-semester examination in undergraduate students (gain of mean 8.3%, 95% CI 3.3 to 13.4%; E-value 2.77, lower limit of 95% CI 1.80) but lowered performance in postgraduate students (loss of 8.1%, 95% CI 3.6 to 12.6%; E-value 2.89, lower limit of 95% CI 1.88), compared to online learning.

**Discussion:** Under the assumed causal graph, we found that compared to online learning, face-to-face learning improved student performance in the end-semester examination in undergraduate students, but worsened student performance in postgraduate students. These findings suggest that different modes of learning may suit different types of students. Importantly, this is the first attempt to estimate causal effects of the mode of learning on student performance under a causal structure. This approach makes our assumptions transparent, informs data analysis, and is recommended when using observational data to make causal inferences.

**Prostate-specific antigen-based screening strategies and prostate cancer mortality: emulating a target trial using electronic health records** Joy Shi\* Joy Shi Xabier García-Albéniz Nick J. Rezaee Jessica K. Wise Hanna Gerlovin J. Michael Gaziano Kelly Cho Miguel A. Hernán Barbra A. Dickerman

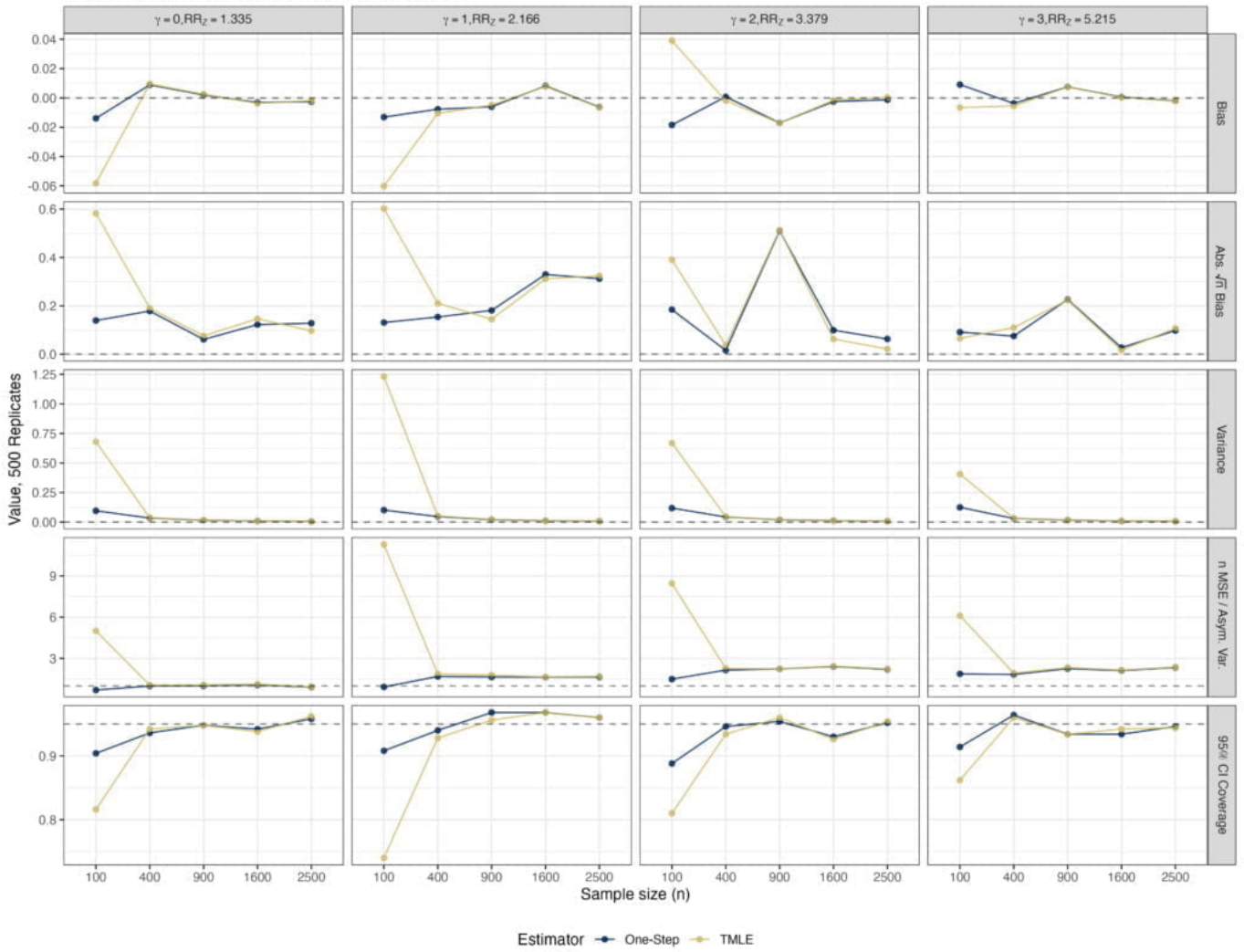
Prostate cancer screening via the prostate-specific antigen (PSA) test has declined in the U.S. over the past decade due to initial results from trials and subsequent discouragement from professional societies. In particular, the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial, which randomly assigned men to receive annual PSA screening for 6 years and digital rectal examinations (DRE) for 4 years versus usual care, is often cited as evidence for a lack of survival benefit of screening. However, the interpretation of findings from the PLCO trial is challenged by high contamination of screening in the control arm. Observational analyses provide an opportunity to benchmark and extend the results from trials, but emulating a target trial of PSA screening and prostate cancer mortality is complex. For example, one key challenge is distinguishing diagnostic from screening tests. This requires the use of a sufficiently rich database and specification of dynamic treatment strategies that excuse individuals from following the specified screening strategy upon the occurrence of certain clinical indicators that a diagnostic test may be warranted.

Here, we used nationwide observational data from the Department of Veterans Affairs, the largest integrated health care system in the U.S., to emulate a target trial of PSA-based screening strategies and prostate cancer mortality among 678,718 eligible men (mean age 62.9 years). We used inverse-probability weighted pooled logistic regression models to estimate the intention-to-treat and per-protocol effects of dynamic screening strategies on prostate cancer mortality via risk ratios and survival curves. We benchmarked the emulation against the PLCO trial at 10 years of follow-up and estimated effects in subpopulations underrepresented in the trial. In the presentation, we will further discuss challenges in benchmarking against estimates from randomized trials and potential strategies to combat them.

**Evaluating mediational vaccine efficacy under unmeasured baseline confounding using the natural direct effect** Nima Hejazi\* Nima Hejazi Philippe Boileau Ivana Malenica Mark van der Laan Sandrine Dudoit Peter Gilbert

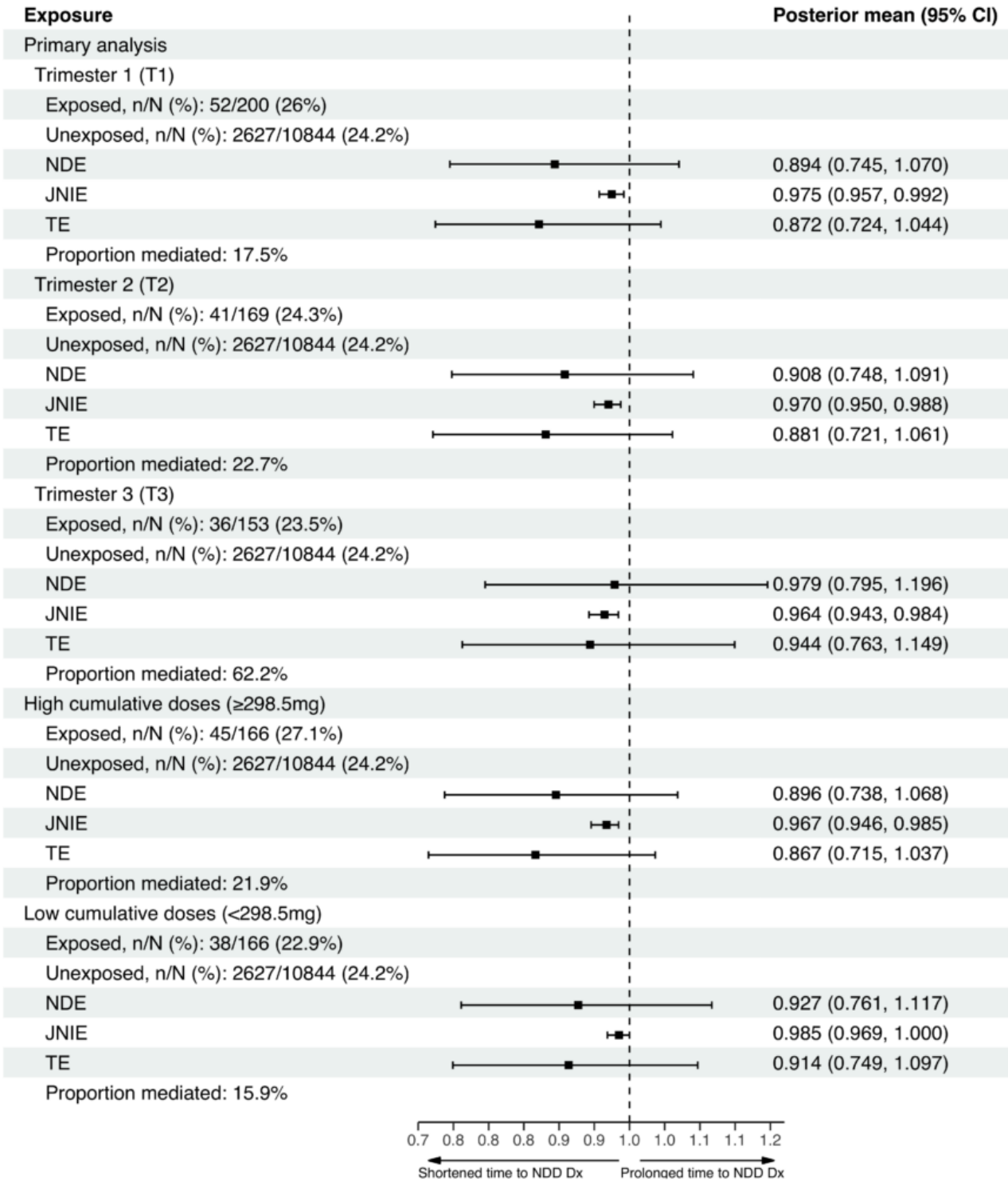
Causal mediation analysis has formulated rigorous tools for defining and estimating mechanistic effects. The natural direct and indirect effects (“(in)direct” hereafter), a canonical example, have risen to enormous popularity in epidemiologic applications, but these effects have stringent identifiability requirements, occasionally limiting their practical utility. While considerable effort has been invested in developing alternative, causal (in)direct effect decompositions with relaxed identifiability requirements, such efforts often yield effect definitions with nuanced or contrived interpretations. By contrast, relatively limited attention has been paid to relaxing identifiability assumptions of the natural (in)direct effects. Drawing on a connection between the natural direct effect (NDE) and the proportion of effect mediated, a mediational measure used in immune correlates analyses of vaccine efficacy trials, we study identifiability of the NDE under unobserved baseline confounding of the exposure-mediator pathway. We outline how multiply robust estimators of the NDE may be efficiently estimated without imposing restrictive modeling assumptions via causal machine learning. To demonstrate practical significance of our approach, we apply it to tease apart how HIV/AIDS infection status impacts susceptibility to symptomatic COVID-19 through a key immunologic marker in vaccinated adults non-naive to SARS-CoV-2 infection.

Impact of Unmeasured Confounder's Effect Size



**Prenatal Exposure to Opioids and Neurodevelopmental Disorders in Children: A Bayesian Mediation Analysis** Shuang Wang\* Shuang Wang Shuang Wang Gavino Puggioni Jing Wu Kimford J. Meador Aisling Caffrey Richard Wyss Jonathan L. Slaughter Etsuji Suzuki Kristina E. Ward Adam K. Lewkowitz Xuerong Wen

Our study sought to delineate the direct and indirect effects of prenatal opioid exposure (POE) on neurodevelopmental disorders (NDDs) in children, mediated through adverse pregnancy and birth outcomes. A retrospective cohort study was conducted using Rhode Island Medicaid claims linked to birth certificates from 2008 to 2018. A Bayesian penalized mediation analysis with elastic net shrinkage prior was developed to estimate total effect, natural direct effect (NDE), and joint natural indirect effect (JNIE) of POE by trimester that mediated through pregnancy complications, major and minor congenital malformations, and adverse neonatal outcomes. Effects were estimated as mean time to NDD diagnosis ratio using posterior mean and 95% credible intervals from Markov chain Monte Carlo algorithms. To evaluate model performance, simulations were conducted under varying scenarios. Of 11,176 eligible pregnancies, 332 pregnancies had  $\geq 2$  dispensations of prescription opioids anytime during pregnancy, including 200 (1.8%) pregnancies having  $\geq 1$  dispensation in the first (T1), 169 (1.5%) in the second (T2), and 153 (1.4%) in the third trimester (T3). A significant JNIE of opioid exposure was observed in each trimester (T1: 0.975, 95% CI: 0.957-0.992; T2: 0.970; 95% CI: 0.950-0.988; T3: 0.964, 95% CI: 0.943-0.984). Proportion of the POE-NDDs associations mediated through adverse pregnancy and birth outcomes in each trimester was 17.5%, 22.7%, and 62.2%, respectively. In conclusion, adverse pregnancy and birth outcomes jointly mediated the effect of POE on accelerated time to NDD diagnosis. The proportion mediated increased as timing of opioid exposure approached delivery, suggesting that prescription opioid exposure in different trimesters carries varying risks of neurodevelopmental outcomes via different pathways.





**Using directed acyclic graphs to identify confounders and constructing Bayesian networks to evaluate the relationship between cysticercosis knowledge and human cysticercosis (*Taenia solium*)**

Ellen Jackson\* Ellen Jackson Veronique Dermauw Guy Eyaba Tchamdja  
Mohammad Shah Jalal Amanda Janitz Athanase Millogo Rasmané Ganaba Zékiba Tarnagda Pierre  
Dorny Hélène Carabin

Bayesian networks are tools that allow epidemiologists to visualize and analyze complex systems where several, often collinear, risk factors are associated with one or several outcomes. Analyzing simultaneous risk factors is useful when choosing between control strategies. However, Bayesian networks, similar to directed acyclic graphs (DAGs), are difficult to use when cycles of transmission exist.

We have created causal DAGs of risk factors for *Taenia solium*, a zoonotic parasite with a complex life cycle including multiple correlated risk factors. Based on our full-text review of 151 articles, we created one DAG including only arcs with factors showing a strong level of causative evidence (Figure 1), and a second DAG with all arcs identified in the literature (including factors with only weak evidence).

We evaluated our DAGs using data from a cross-sectional survey of 3579 people in 60 villages in Burkina Faso conducted in 2011-12. Our DAGs have identified potential confounders (or lack of confounders, in Figure 1) of the relationship between knowledge of *T. solium* and human cysticercosis, measured by antigen seropositivity. Our hierarchical logistic regression model identified that having heard of pig cysts was a significant risk factor of human cysticercosis in both the unadjusted, strong DAG calculations (OR 3.3, 95%CI 2.0-5.4) and the results adjusted for confounding with the weak-level DAG (OR 2.0, 95%CI 1.1-3.4).

We are parameterizing a Bayesian network using a structure built from the strong-level DAG in Figure 1 and the data from the cross-sectional survey. We will compare the methods and results generated from both hierarchical logistic regression and Bayesian networks. This will be one of the first Bayesian networks made to understand the impact of multiple risk factors simultaneously on transmission of an infectious agent with a complex life cycle. With this, we aim to identify the most impactful causes to intervene upon and reduce *T. solium* transmission.

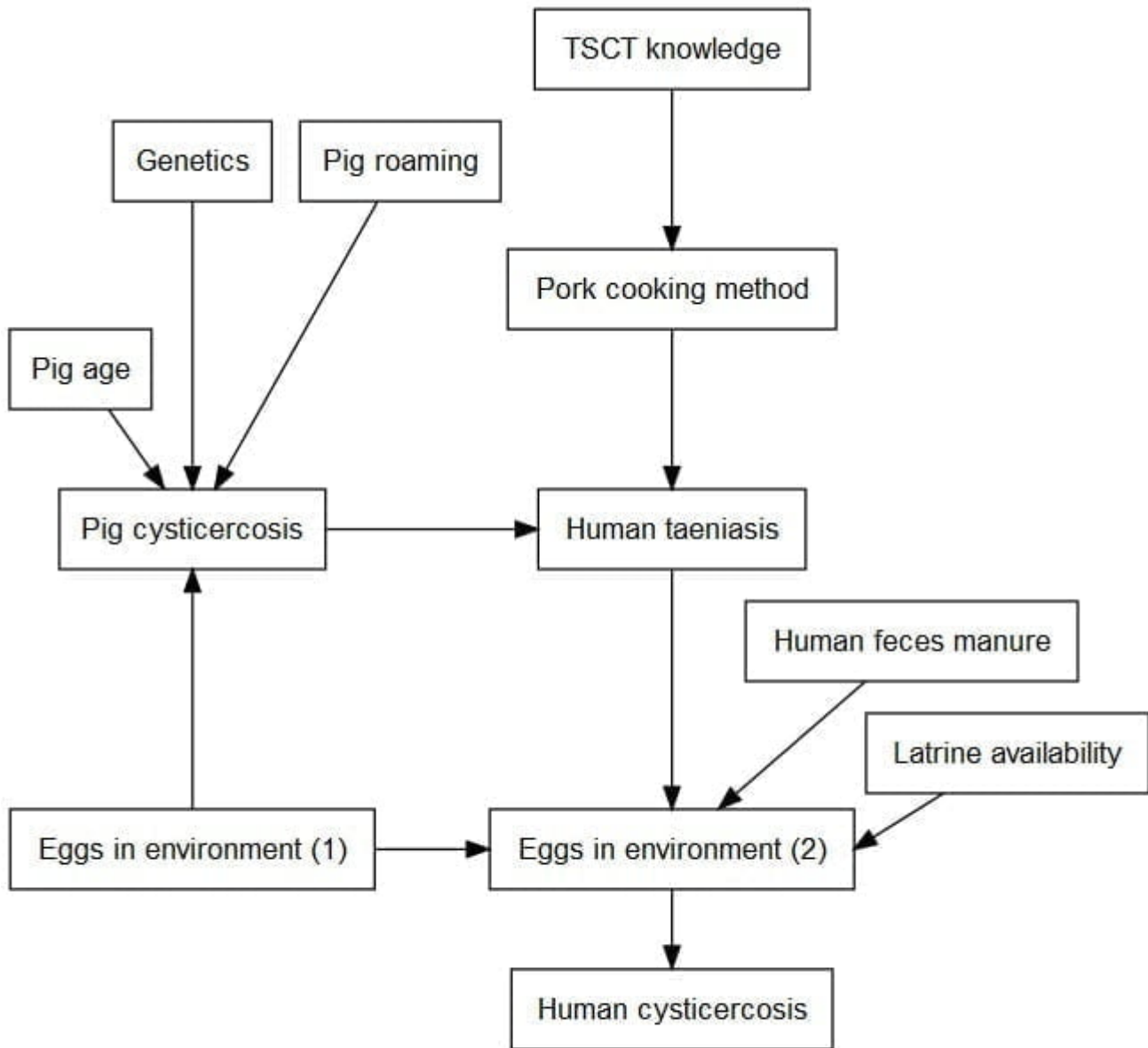


Fig. 1: Strong-level DAG and structure of the Bayesian network.

**Extending causal inference target trial emulation to veterinary observational data** Camilla Pegram\* Camilla Pegram Karla Diaz-Ordaz David Brodbelt Yu-Mei Chang David Church Dan O'Neill

Target trial emulation, which applies the design principles from randomised controlled trials to the analysis of observational data, is increasingly used within human epidemiology. Veterinary electronic clinical records potentially represent a valuable source of information to estimate real-world causal effects using causal inference approaches.

Using anonymised veterinary electronic clinical data from the VetCompass Programme, which includes data from over 20 million animals from more than 1800 UK participating veterinary practices, this study adopted the target trial framework to assess its utility for veterinary observational data. Acute diarrhoea (AD) in dogs was used as an exemplar to identify whether antibiotic prescription for AD causes increased “resolution” compared with no antibiotic prescription. Resolution was defined as no re-visit for AD within 30 days of first presentation.

Inclusion in the emulated trial required dogs, aged  $\geq 3$  months and  $< 10$  years, presenting with AD during 2019. Dogs were retrospectively assigned to antibiotic or non-antibiotic treatment. Informed from a directed acyclic graph, data on the following variables were collected: age, breed, bodyweight, insurance status, comorbidities, vomiting, reduced appetite, haematochezia, pyrexia, duration and veterinary group.

Inverse probability of treatment weighting (IPTW) was used to balance covariates between the two treatment groups. The emulated trial included random samples of 355 antibiotic cases and 539 non-antibiotic cases. The RD for resolution in antibiotic cases compared with non-antibiotic cases was 1.0% (95% CI -3.6% to 5.5%).

This study demonstrates that the target trial framework can be successfully adopted to veterinary observational data as an alternative to randomised control trials. The results show that antibiotic prescription causes no clinically meaningful difference in the need for a re-visit within 30 days for AD compared with no antibiotic prescription.

**Efficacy of the dapivirine vaginal ring accounting for imperfect adherence: An application of causal inference methods**

Marla Husnik\* Marla Husnik Renee Heffron James Hughes Barbra Richardson Ariane van der Straten Thesla Palanee-Phillips Lydia Soto-Torres Devika Singh Brenda Gati Mirembe Edward Livant Zakir Gaffoor Leila E. Mansoor Samantha S. Siva Sufia Dadabhai Flavia Matovu Kiweewa Jared Baeten

Product adherence is critical to obtaining objective estimates of efficacy of pre-exposure prophylactic interventions against HIV-1 infection. With imperfect adherence, intent-to-treat analyses assess the collective effects of complete, sub-optimal and non-adherence, providing a biased and attenuated estimate of the causal effect of an intervention. Using data from the MTN-020/ASPIRE phase III trial evaluating HIV-1 efficacy of the dapivirine vaginal ring, we conducted per-protocol, and adherence-adjusted causal inference analyses using principal stratification and marginal structural models. We constructed two adherence cut offs of  $\geq 0.9$  mg (low cutoff) and  $>4.0$  mg (high cutoff) that represent drug released from the ring over a 28-day period. The HIV-1 efficacy estimate (95% CI) was 30.8% (3.6%, 50.3%) ( $p = 0.03$ ) from the per-protocol analysis, and 53.6% (16.5%, 74.3%) ( $p = 0.01$ ) among the highest predicted adherers from principal stratification analyses using the low cutoff. Marginal structural models produced efficacy estimates ranging from 48.8% (21.8, 66.4) ( $p = 0.0019$ ) to 56.5% (32.8%, 71.9%) ( $p = 0.0002$ ). Application of adherence-adjusted causal inference methods are useful in interpreting HIV-1 efficacy in secondary analyses of PrEP clinical trials.

**Association of reversal of renin suppression with renal outcomes in medically treated primary aldosteronism** Sho Katsuragawa\* Sho Katsuragawa Atsushi Goto Satoru Shinoda Yuya Tsurutani Kosuke Inoue Kazuki Nakai Jun Saito Tetsuo Nishikawa

### Background

Renin suppression in primary aldosteronism (PA) reflects mineralocorticoid receptor activation inducing renal damage. We examined the association of reversal of renin suppression after the initiation of mineralocorticoid receptor antagonist (MRA) with renal outcomes among medically treated PA patients.

### Methods

This study analyzed 267 PA patients who started MRA (194 and 63 cases of bilateral and unilateral aldosteronism, respectively). The post-treatment renin status was defined as unsuppressed (i.e., reversal of renin suppression) when post-treatment plasma renin activity was  $\geq 1.0$  ng/mL/h; otherwise, it was defined as suppressed. The primary composite renal outcome was defined as a decline in estimated glomerular filtration rate (eGFR) to  $< 60$  ml/min/1.73m<sup>2</sup> or an increase in serum creatinine of  $\geq 0.4$  mg/dL during the follow-up. The secondary outcome was a change rate in eGFR. Cox hazard regression models and linear mixed-effects models were employed to estimate the hazard ratios (HR) of the incident primary outcome and the association of the post-treatment renin status with the change rate in eGFR, respectively.

### Results

The post-treatment renin status of 97 patients was unsuppressed and that of 170 patients was suppressed. Through the median follow-up period of 3.4 years, no significant difference in the incidence of the composite renal outcome was found between patients with the unsuppressed post-treatment renin status and those with the suppressed post-treatment renin status (HR [95%CI] = 0.80 [0.47-1.38]). However, the decline rate in eGFR was milder among patients with the unsuppressed post-treatment renin (-0.53 [95% CI, -0.74 to -0.32] ml/min/1.73m<sup>2</sup>/year) than those with suppressed renin (-1.52 [95% CI, -1.68 to -1.37] ml/min/1.73m<sup>2</sup>/year; difference, 1.00 [95% CI, 0.73 to 1.27] ml/min/1.73m<sup>2</sup>/year).

### Conclusion

Our findings indicate the importance of reversal of renin suppression for medically treated PA that could mitigate the adverse renal outcome.

**The impact of the COVID-19 pandemic on the association between physical activity for leisure and the diagnosis of coronary heart disease or myocardial infarction** S. Cristina Oancea\* S. Cristina Oancea MIchaelynn Kanichy

**Introduction:** Research on the association between leisure-time physical activity (LTPA) and heart disease by race is limited. We sought to understand how the association between LTPA and coronary heart disease or myocardial infarction (CHD-MI) compares by race, pre- and during the COVID-19 pandemic.

**Methods:** Data from the BRFSS study, years 2018 through 2021 (N=914,741), was used to perform weighted multivariable logistic regression analyses to investigate the association between LTPA and CHD-MI, by race and year, in US adults ages 18-79, without prior cancer diagnosis and who were not pregnant at the time of the survey.

**Results:** Among White people the weighted and adjusted odds (WAO) of being diagnosed with CHD-MI were significantly greater among individuals who didn't perform LTPA than among those who did, in each of the years 2018-2021. For Whites, the WAO ratio (WAOR) of CHD-MI were the greatest in 2020 (WAOR=1.29; 95%CI: 1.15-1.44) compared to the other years under investigation. Among American Indian/Alaska Natives (AI/AN) and Black/African Americans (B/AA) this association was only significant in 2020. The WAO of CHD-MI among adults who didn't perform LTPA were 1.97 times significantly greater (95%CI: 1.19-3.27), and 1.62 times significantly greater (95%CI: 1.29-2.04), than the WAO of CHD-MI in adults who did perform LTPA, among AI/AN, and B/AA, respectively. This association was not significant among Asians, for any of the years under investigation.

**Conclusion:** The odds of coronary heart disease or myocardial infarction were significantly greater, among Whites, AI/AN and B/AA people who reported no physical activity for leisure, particularly in 2020, the year of the COVID-19 pandemic shutdown. This shutdown resulted in significant life events disproportionately impacting leisure time and physical activity among the various racial groups in the US, with long term effects such as the potential development of CHD-MI as a result.

**The COVID-19 pandemic and limited preseason activities increase the anterior cruciate ligament injuries in the National Football League** Augusto César Ferreira De Moraes\* Augusto César Ferreira De Moraes Nágela Rayanne Freitas Augusto César Ferreira De Moraes

**Background.** Previous NFL preseason disruptions (2011 lockout) have been postulated to effect injury incidence. However, the effect of the 2020 preseason cancellation on injury incidence has not been empirically studied.

**Hypothesis:** We hypothesized limited activities during the COVID-19 preseason increase the odds of anterior cruciate ligament injury incidence in the NFL.

**Methods.** This is a cluster case-control study; we identify as a case group the season 2020-2021 and as a control group the seasons from 2015 to 2019. All National Football League (NFL) players who suffered anterior cruciate ligament reconstruction from 2015-16 to 2020-21 season (May 2015 to March 2021) were identified and included in this study. We applied conditional logistic regression to estimate the Odds Ratio (OR) with a 95% confidence interval (CI95%), employed when case subjects with a particular condition or attribute are matched with n control subjects without anterior cruciate ligament.

**Results.** We identified 34 injuries during the 2020/2021 season (case) and matched them with 115 between the 2015 and 2019 seasons (control). In the 2020/21 season, the number of injuries that occurred was 50% in offensive position players (17), 50% in defensive players (17), and there were no injuries in special teams players. There were statistically higher odds of suffering an anterior cruciate ligament injury in the 2020-2021 season, which did not include a complete preseason, compared to those seasons (2015-2016 to 2019-2020) with a complete preseason (OR= 1.49 [95%CI = 1.01; 2.18]).

**Conclusion.** The limited activities during the 2020 preseason increase the odds of an anterior cruciate ligament injury in NFL players compared to previous seasons (2015-19) and the highest number of injuries occurred in the first month of competitive activities. The grass surface type and team position were not founded as risk factors for anterior cruciate ligament injury.

**Development of the potential years of life lost in Czechia during the pandemic and the impact of COVID-19** Klára Hulíková Tesárková\* Klára Hulíková Tesárková

The measure of years of life lost (YLL) is often tied to the expression of the level of premature mortality and it started to be widely used during the COVID-19 pandemic for measuring the burden of the disease. In addition to the number of deaths, the YLL does not neglect the age of the deceased persons. On the other hand, many weaknesses are discussed as well. The paper consists of two parts - it presents some potential modifications of the YLL, and the proposed measures are used for illustration of the mortality development during the pandemic years in Czechia (average mortality conditions within Europe, severely hit by the pandemics). In the simplest way of calculation, the YLL is estimated as the number of deaths weighted by the expected remaining length of life, usually represented by the life expectancy. The value of YLL could be divided according to causes of death, but also according to the age of the deceased person. However, the potential length of life could be also divided into the length potentially lost during childhood, the productive age, and the senior age. Any death of a senior could lead only to YLL in senior age. On the contrary, the death of a child leads to YLL during childhood, the productive- as well as senior age. This division of YLL is illustrated using data from 2019-2021. We used the pre-pandemic (2019) potential life tables, representing the best value of life expectancy at each age group across Europe (using the Human Mortality Database). Marshall's norm for YLL estimated from the potential table was used for evaluation of the YLL in the studied population. YLL was 1.41 times higher in Czechia than the norm already in 2019. YLL per death from COVID-19 only was 12.8 in 2020 but it reached 15.1 in 2021. This represents the younger age structure of COVID victims in 2021 than in 2020. In 2021, a higher part of YLL was caused by victims in the productive age. The effect of COVID-19 was visible also in the total YLL and its age distribution.





**A mixed methods analysis of COVID-19 related stigma within a rural South African community** Nicole Kelly\* Duduzile Mashinini Nicole Kelly Palesa Mataboge Frantasia Hill Kathleen Kahn Audrey Pettifor

**Background:** Infectious disease-related stigma is a pervasive global issue that impedes disease control efforts by increasing reluctance to seek treatment or testing for fear of ostracism. Despite this, there is limited research on COVID-19 stigma in rural South Africa, which has encountered infectious disease-related stigma throughout the HIV epidemic.

**Methods:** In both 2020 and 2021, population-based surveys were conducted among 1,662 adults living in the Agincourt Health and Socio-Demographic Surveillance System (AHDSS) area in Mpumalanga. The surveys measured anticipated COVID-19 stigma from 4 (low) to 12 (high). Wilcoxon ranked sign tests compared changes in stigma between surveys. Log-binomial models estimated the association between sociodemographic factors and anticipated stigma at both intervals. In 2022, qualitative interviews were conducted among 31 adults who completed the original surveys. Thematic analysis described anticipated, perceived, and enacted stigma.

**Results:** Anticipated stigma significantly decreased from the first to the second survey (p-value: <0.0001). Stigma was significantly higher among older age groups. In 2020, those with less knowledge about COVID-19 were 2.24 times as likely to have higher levels of anticipated stigma than more knowledgeable participants (RR: 2.24, 95% CI: 1.90,2.64). Qualitative analyses revealed that fear of stigma influenced willingness to disclose infection and vaccine status. For some, fear of death and mistrust of others led to enacting stigma toward others.

**Conclusion:** COVID-19 stigma was prevalent among adults living in rural South Africa but declined over time. However, different forms of community-level stigma were associated with COVID-19 and informed participants' willingness to reveal their status. Given that South Africa has previously witnessed how infectious disease-related stigma can hinder public health efforts, government bodies should prioritize strategies to mitigate stigma in rural communities.

**LATEBREAKER**

COVID-19 Pandemic

**Job instability and job insecurity during the Covid-19 pandemic and thoughts of suicide/self-harm among Swedish employees** Linda Magnusson Hanson\* Linda Magnusson Hanson Sandra Blomqvist**Introduction**

Previous work has indicated a higher prevalence of suicidal ideation during the Covid-19 pandemic. Job loss and job insecurity are potential risk factors, but their importance during the pandemic, and the role of organizational changes for suicidal ideation, is unclear. This study examined the association between various experiences associated with job loss and insecurity during the pandemic and thoughts of suicide or self-harm in Sweden.

**Methods**

The study sample were drawn from the Swedish Longitudinal Occupational Survey of Health. Auxiliary data collections in February 2021 and 2022 assessed exposures to job loss/unemployment, furlough, workplace downsizing, or increased job insecurity versus stable employment and thoughts of suicide or self-harm (PHQ-9). The analyses were based on 1558 individuals (2 349 observations) participating in either or both waves and who had been working before the pandemic. Logistic regression models with cluster-robust standard errors were fitted, including sociodemographic factors and prior mental health problems to control for potential confounding. Measures of personality based on a brief version of the Big-five personality inventory were also added.

**Results**

The results indicated that all experiences, except furlough, increased the risk of thoughts of suicide/self-harm, when adjusting for sex, age, civil status, and socioeconomic status (job loss OR=3.70, 95% CI 1.79-7.63, downsizing OR=2.41, CI 1.24-4.70, job insecurity OR=2.77, CI 1.15-6.67) and prior mental health. The associations for job loss and insecurity were attenuated by adjustment for personality, although remained statistically significant for downsizing.

**Discussion**

The results suggested a higher risk of suicidal ideation following loss of employment and survival of a downsizing, but not a forced reduction in working times/pay during the Covid-19 pandemic. The association for subjective job insecurity was less robust and may be partly explained by personality.

**LATEBREAKER**

## COVID-19 Pandemic

**Gestational Weight Gain in Louisiana during the COVID-19 Pandemic** Nicole Cohen\* Emily Harville CL Kracht Nicole Cohen Elizabeth Sutton Maryam Kebbe Leanne Redman

**Background:** Average gestational weight gain (GWG) increased during the COVID-19 pandemic, but it is not known if this trend has plateaued.

**Methods:** In a retrospective review of birth certificate and delivery records (n=23,553 total deliveries) from March 2019 - March 2022 at the largest delivery hospital in Louisiana, GWG (total GWG and adherence to the 2009 IOM recommendations) was compared based on delivery date (cross-sectionally) and conception cohorts prior to the pandemic (March 2019-March 2020), during peak pandemic (March 2020-March 2021) and late (March 2021-March 2022), using linear and log-linear regression with control for covariates.

**Results:** In the year preceding the pandemic, 41.9% exceeded the recommended weight gain; 45.3% during peak; and 43.8% in late pandemic. Women had higher average GWG (kg: adjusted beta, SE) if they delivered peak (0.39 kg, 0.32) or late (0.82 kg, 0.30) pandemic compared to those who delivered pre-pandemic (p=0.02). When cohorts were defined by conception date, women who conceived before but delivered after the pandemic started had higher GWG compared to those whose entire pregnancy occurred before the pandemic started (0.52 kg, 0.17). This declined (p=0.01) in the pregnancies conceived after the pandemic started (0.30 kg, 0.13) and the late pandemic (0.17 kg, 0.16). Examining mean GWG month by month suggested a small dip for March 2020, followed by raised average GWG for the following year.

**Conclusions:** Women with critical timepoints of their pregnancy during the COVID-19 pandemic gained more weight compared to the previous year. The increased GWG leveled off as the pandemic progressed.

**Comparative safety and early effectiveness of mRNA vaccines for SARS-CoV-2: Assessing potential effect modification by frailty** Daniel Harris\* Daniel Harris Daniel Harris Kaleen Hayes Preeti Chachlani Andrew Zullo Vincent Mor Stefan Gravenstein

**Background:** Prior effectiveness and safety studies of the mRNA vaccines for SARS-CoV-2 have not considered effect modification by frailty, an age-related syndrome known to reduce vaccine response and increase the risk of poor health outcomes. Our objective was to compare the risk of serious adverse events and diagnosed COVID-19 between mRNA vaccines, overall and by frailty.

**Methods:** Using novel linked commercial pharmacy and Medicare data, we conducted a retrospective cohort study of US community-dwelling Medicare fee-for-service beneficiaries  $\geq 66$  years who received BNT162b2 or mRNA-1273 as their first vaccine dose between December 2020 and July 2021. We measured the risk of diagnosed COVID-19 and 13 serious adverse events (e.g., pulmonary embolism) in the 28-days following dose one. We categorized individuals as non-frail, pre-frail, and frail using a validated claims-based frailty index. Generalized linear models with product terms between frailty and vaccine were used to estimate RRs with 95% CIs adjusting for region, month, age, sex, race, and prior health services use and COVID-19.

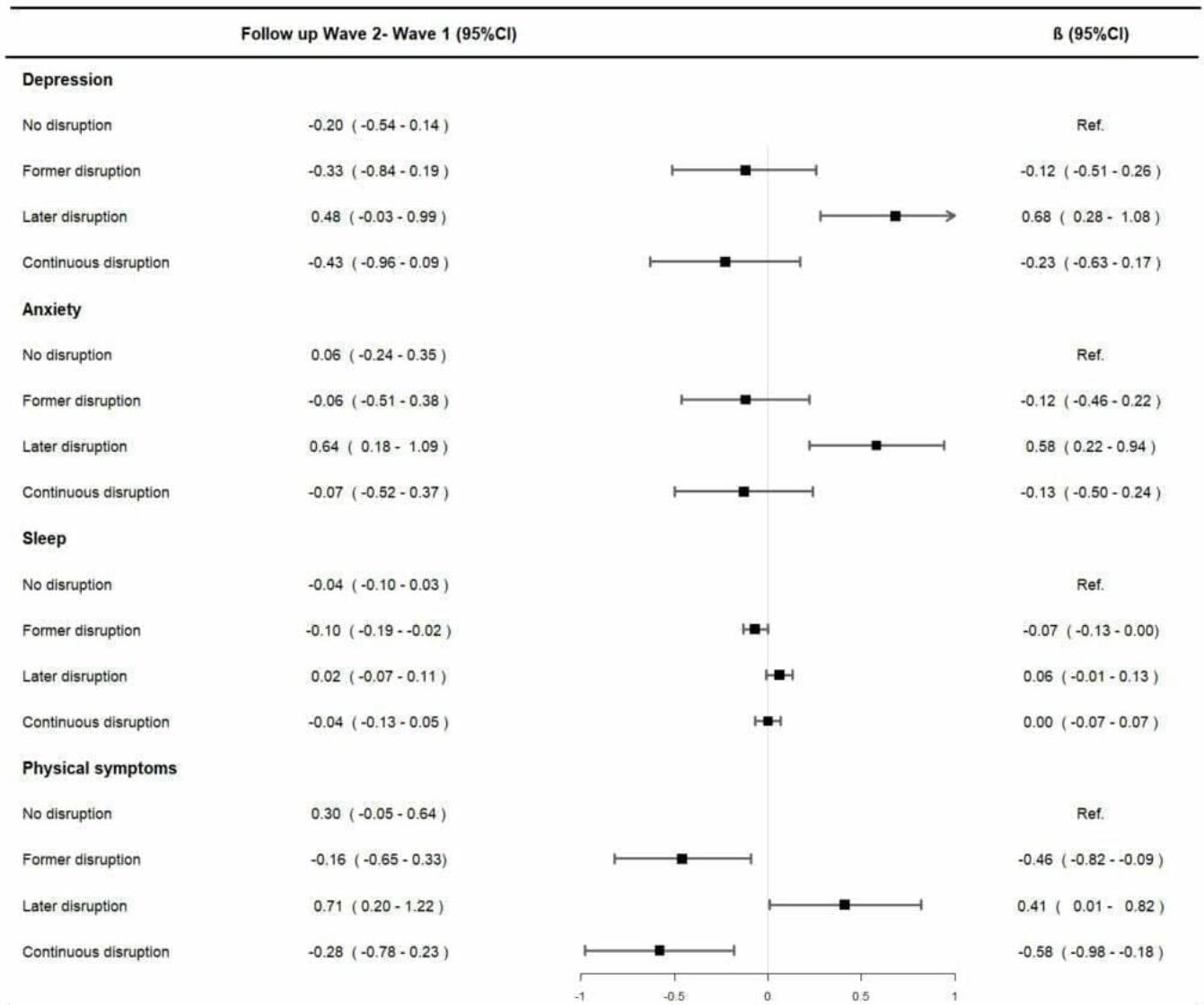
**Results:** In total, 6,388,196 persons received BNT162b2 or mRNA-1273 (median age=75 years; 59% female; 38% pre-frail; 6% frail). The risk of all outcomes was low in both vaccine groups, though elevated with greater frailty. Non-frail persons who received mRNA-1273 had a lower risk of diagnosed COVID-19 than non-frail persons who received BNT162b2 (RR=0.85; 95%CI=0.82-0.88) - an effect that was attenuated in frail persons (RR=0.94; 95%CI=0.89-0.99). The mRNA-1273 vaccine also resulted in a reduced risk of several safety outcomes, but only among non-frail persons.

**Conclusions:** The mRNA-1273 vaccine (vs BNT162b2) showed slightly better outcomes, especially in non-frail persons, possibly via improved safety or early effectiveness. Our findings suggest that the mRNA-1273 vaccine may be preferred regardless of frailty status.

**Perceived healthcare disruption during the pandemic: an observational study in Iceland**

Unnur Anna Valdimarsdóttir\* Yue Wang Thor Aspelund

**Background** COVID-19 has caused major disruptions in healthcare services worldwide. Yet little is known about the trends of healthcare disruption within the pandemic develops and its association with social-demographic factors, medical conditions and psychological well-being. The aim of our study was to investigate the prevalence of perceived healthcare disruption during the pandemic period and its impact on population mental health. **Methods** We used data from the Icelandic COVID-19 National Resilience Cohort of 15816 individuals 18 years or older who responded to questions on perceived healthcare disruption. We performed both logistic and Poisson regression to explore the association between social-demographic factors, medical conditions and perceived healthcare service disruption. We used linear regression to explore the association between duration of perceived healthcare disruption and changes in depression, anxiety, sleep quality, and somatic symptoms. **Results** The prevalence of perceived healthcare disruption was slight decreased during the pandemic period, from 12.26% in December 2020 to 10.27% in June 2021. Perceived healthcare disruption was pronounced among young adults who being sexual minorities, with lower income and had pre-existing psychiatry disorders (prevalence rates 15.75% - 16.80%). However, compared to those without COVID-19 diagnosis, no increase prevalence rate was observed among patients with COVID-19 diagnosis (11.74% vs 11.47%,  $p=0.82$ ). Furthermore, we found later perceived healthcare disruption was positively associated with changes in symptoms of mental illness ( $\beta$ s 0.41 - 0.68). **Conclusions** The disruption of healthcare services during the COVID-19 was distinctly reported by vulnerable groups, while the Icelandic healthcare system seems to have managed to maintain accessible services to individuals with COVID-19 diagnosis.



**Associations between sleep time, academic context and subjective stress in college students during the COVID-19 pandemic: 24 h movement behavior and metabolic syndrome (24 h-MESYN) study** Marcus Vinicius Nascimento-Ferreria\* Marcus Vinicius Nascimento-Ferreria

Jacyara Christina Carvalho Azevedo Lorrane Cristine Conceição da Silva Maria Isabela Alves de Almeida Silva Shirley Cunha Feuerstein Francisco Leonardo Torres-Leal Heráclito Barbosa de Carvalho Augusto Cesar Ferreira de Moraes

**Objective:** To examine the association between sleep time, academic context and perceived stress in college students during the COVID-19 pandemic.

**Methods:** This is a cross-sectional study that evaluated 195 university students (68.7% females; 44.6% aged between 21 to 25 years; 65.8% enrolled in a health sciences degree; 24.5% enrolled in the first to third semester). Data were collected during the first semester of 2021 in the city of Imperatriz, Maranhão, Brazil (Gini Index of 0.56). We collected self-reported online measures using the Perceived Stress (14-item) and Pittsburgh Sleep Quality Index (19-item). We assessed scores of positive and negative stress dimensions as outcomes (representing perceived self-efficacy and helplessness, respectively). We assessed degree program (health sciences degree or other undergraduate degree), shift (morning, evening, night or integral), time ( $\leq$  3rd semester or  $>$  3rd semester), number of classes enrolled and hours of study per day; and, the habitual sleep time (hours per night) and routine (wake up and bedtime in clock time) as exposures. The potential confounding variables were biological sex; age; ethnicity; maternal education. We examined the associations using multilevel linear regression. For a variable to be retained in the multivariate model, the significance level was set at  $p \leq 0.20$ .

**Results:** We did not observe association between academic variables and, sleep time and routine with positive domain of stress perception. Conversely, we observed that number of classes enrolled ( $\beta = 0.73$  [95% CI 0.20 to 1.26]) and bedtime ( $\beta = -0.11$  [95% CI -0.17 to -0.04]) were associated with negative dimension of perceived stress.

**Conclusion:** The number of classes enrolled was associated with perceived helplessness resulting in increased perceived stress in college students from low-income region during the COVID-19 pandemic. The delayed bedtime can be a counter response in the academic routine associated with this perception.



**Association between subjective stress and eating behavior in university students during the COVID-19 pandemic: 24h-MESYN study** Marcus Vinicius Nascimento-Ferreira\* Marcus Vinicius Nascimento-Ferreira Barbara Saldanha Lima Jacqueline Fernandes de Sá Millena Vaz de Carvalho Rhavenna Thais Silva Oliveira Shirley Cunha Feuerstein Francisco Leonardo-Torres Leal Heráclito Barbosa de Carvalho

**Objective:** To test the association between perceived stress and eating behavior in university students during the COVID-19 pandemic.

**Methods:** This study is part of the 24-hour Movement Behavior and Metabolic Syndrome (24h-MESYN) cohort study. A sample of 195 undergraduate students (68.7% females; 44.6% aged between 21 to 25 years; 65.8% enrolled in a health sciences degree; 24.5% enrolled in the 1<sup>st</sup> to 3<sup>rd</sup> semester) was recruited. Data were collected during the first semester of 2021 in the city of Imperatriz, Maranhão, Brazil (Gini Index of 0.56). We collected self-reported online measures using the Perceived Stress Scale (14-item) and the Dutch Eating Behavior Questionnaire (33-item). We assessed scores of positive and negative stress dimensions as exposures (representing perceived self-efficacy and helplessness, respectively) and scores of emotional eating, restrained eating and external eating as outcomes. The potential confounding variables were biological sex; age; ethnicity; maternal education; degree program (health sciences degree or other undergraduate degree), shift (morning, evening, night or integral), time ( $\leq$  3rd semester or  $>$  3rd semester), number of classes enrolled and, hours of study per day. We examined the associations using multilevel linear regression. For a variable to be retained in the multivariate model, the significance level was set at  $p \leq 0.20$ .

**Results:** We did not observe association between perceived stress (negative or positive dimension), and emotional and restrained eating. However, after adjusting for biological sex and age, we observed that negative domain of perceived stress ( $\beta = 0.02$  [95% CI 0.006 to 0.04]) was associated with external eating.

**Conclusion:** Perceived helplessness appeared as a unique source of stress perception related to eating behavior in university students from low-income region the COVID-19 pandemic, particularly relevant to the experience of external eating patterns.

**Spatial Variations in the Associations of COVID-19 Rates and Socioeconomic, Health, and Environmental factors in Georgia, USA** Jun Tu\* Jun Tu Jun Tu

The COVID-19 disease caused by the SARS-CoV-2 virus first identified in December 2019 has caused millions of deaths so far around the world. Controlling the spread of the disease requires a good understanding of the factors that affect virus transmission and the conditions under which it spreads. Over the past three years, numerous studies have examined the associations of COVID-19 Rates and various factors, but the results are not consistent. In this study, the county-level COVID-19 data over the two-year period of 2020 and 2021 in the state of Georgia, USA have been examined. Both Ordinary Least Squares Regression (OLS) and a spatial statistical method, Geographically Weighted Regression (GWR), were employed to model the associations of COVID-19 rates (incidence rate, death rate, and case fatality rate) with Social Vulnerability Index (SVI), chronic disease indicators, hospital discharge rates, vaccination rate, and concentrations of PM<sub>2.5</sub> and Ozone on county level. Different from the results calculated by OLS, the results obtained by GWR show that the associations of COVID-19 rates and risk factors vary over space. Positively significant, negatively significant, and non-significant relationships between COVID-19 rates and factors are all discovered in different regions of Georgia, and the varying relationships are strongly related to the varying SES (Socioeconomic Status) and urbanization level of the communities. These findings suggest that in order to more successfully control the risk of COVID-19 and other infectious diseases in general, it is necessary to consider the varying relationships between diseases and risk factors across the communities with different socioeconomic and urbanization characteristics for making and implementation of local public health policies.

**The Perceived Impact of Pandemic Scale (PIPS): Initial Development and Examination among a Sample of US Military Veterans** Julie A. Kittel\* Julie Kittel Lindsey L. Monteith Jamie Tock Alexandra L. Schneider Ryan Holliday Sean M. Barnes Lisa A. Brenner Claire A. Hoffmire

The COVID-19 pandemic has had significant impacts, including increases in mental health problems, distress, interpersonal conflict, unemployment, loss of income, housing instability, and food insecurity. Military Veterans may be particularly vulnerable to these impacts given their high prevalence of mental and physical health problems and social determinants of health. However, few measures exist to assess the impact of the pandemic, and no such measures have been validated for use with Veterans. We aimed to develop such a measure and examine its psychometric performance in a national sample of US Veterans. We created the Perceived Impact of the Pandemic Scale (PIPS) to assess perceived impact of the pandemic, with 18 items assessing impact across various domains. Survey data from 567 Veterans were collected between 12/2020 and 2/2021. To examine PIPS factor structure, we took a split sample exploratory/confirmatory factor analysis (EFA/CFA) approach to identify and test the most plausible model among the initial set of items. Based on tests of factor extraction and factor loadings, of 18 initial items, 15 clearly loaded onto three distinct factors. This structure was confirmed via acceptable model fit indices for the CFA ( $\chi^2(87)=167.39$ ,  $p<.001$ ; standardized root mean squared residual (SRMR)=0.068; root mean square error of approximation (RMSEA)=0.060 [95% CI: 0.05, 0.10], comparative fit index (CFI)=0.92). Mean factor scores were significantly correlated with measures of depression, loneliness, and social support. Results suggest the PIPS assesses three internally reliable factors comprised of perceived impact of the pandemic on interpersonal relationships, financial impact, and personal health and well-being. Construct validity with Veterans was supported. This measure may be useful for examining the potentially disparate impact of the current and future pandemics on different populations. Future research is needed to validate the PIPS in non-Veteran populations.

**Evaluating Chronic Pain as a Risk Factor for COVID-19 Complications among New York State Medicaid Beneficiaries: A Retrospective Claims Analysis** Allison Perry\* Allison Perry Katherine Wheeler-Martin Kelly Terlizzi Noa Krawczyk Victoria Jent Deborah S. Hasin Charles Neighbors Zachary L. Mannes Lisa V. Doan John R. Pamplin II Tarlise N. Townsend Stephen Crystal Silvia S. Martins Magdalena Cerdá

Chronic pain may be a risk factor for COVID-19 complications, including via inflammatory and immunosuppressant effects, impacts on immobility, and its proxy to poor general health. Opioid use disorder (OUD) may modify the effect of chronic pain on COVID-19 complications. We tested whether chronic pain was a risk factor for COVID-19 complications, and whether OUD moderated this effect. This retrospective study used New York State (NYS) Medicaid claims from March 2019-December 2020 to determine whether chronic pain increased the risk of COVID-19 emergency department (ED) visits, hospitalizations, complications, and readmissions, and whether OUD moderated this relationship. We included 18-64-year-old Medicaid beneficiaries with and without chronic pain, with 10 months of Medicaid enrollment. Individuals with chronic pain were matched to those without chronic pain on demographics, utilization, and comorbidities to control for confounders, and stratified by OUD. Complementary log-log regressions estimated hazard ratios (HR) of COVID-19 ED visits and hospitalizations, and logistic regressions estimated odds ratios (OR) of hospital complications and readmissions within three months. Among 773,880 matched adults, chronic pain was associated with greater hazards of ED visits (HR, 1.22 [95% CI, 1.16-1.29]) and hospitalizations (HR, 1.19 [95% CI 1.12-1.27]). Individuals with chronic pain and OUD experienced even greater hazards of hospitalization (HR, 1.25 [95% CI, 1.07-1.47]) and increased odds of other hepatic- and cardiac-related events (OR 1.74 [95% CI 1.10, 2.74]). Chronic pain was a risk factor for COVID-19 ED visits and hospitalizations. Comorbid chronic pain and OUD exacerbated the risk of hospitalizations and increased the odds of hepatic- and cardiac-related events. Results highlight the intersecting risks for COVID-19 complications posed by the opioid epidemic and COVID-19 pandemic and can inform targeted COVID-19 management among a vulnerable sub-population

**Previous trend of cognitive function and depression during COVID-19: a longitudinal study in rural South Africa (HAALSI)** Sun Jae Jung\* Sun Jae Jung

**Background:** In sub-Saharan Africa, people are aging rapidly, and a particular proportion exhibit a change in cognitive function. Also, mood disorders such as depression are frequent at the population level during COVID-19. However, the role of the pre-morbid cognitive function trend on depression during COVID-19 is largely untested.

**Methods:** We utilized the data from the Health and Aging in Africa: A Longitudinal Study of an INDEPTH Community in South Africa (HAALSI) study. The surveys were performed from 2014-2015(wave 1) and 2018-2019(wave 2), capturing information including demographics, education, physical functioning, depression, self-reported health history, cognitive battery, and neurological examination. In 2021, COVID-19-related factors, as well as CES-D, were measured. Among 5059 people who initially responded, we included 2375 people with valid information on both cognitive batteries at wave 1-wave 2 and CES-D at wave 3. We used k-means clustering for wave 1 and wave 2 cognitive functions for the exposure variable. CES-D during the COVID-19 period was dichotomized for outcome with a cutoff of 16. We performed logistic regression adjusting for age, sex, CES-D score, wealth index, number of children, comorbidity, and lifestyle factors, all at wave 1.

**Results:** The k-means clustering yielded four groups 1) improved (group1), 2) high function remained (group2), 3) deteriorated (group3), and 4) low function remained (group 4). Compared with the 4) low function remained group, the other three groups showed decreased likelihood for depression during COVID-19. (group1: OR=0.74, 95% CI 0.56-0.98; group2: OR=0.77, 95% CI 0.57-1.04; group3: OR=0.76, 95% CI 0.56-1.02) When stratified by sex, men and women showed different patterns.

**Conclusion:** Pre-pandemic cognitive function pattern was associated with depressive symptoms during COVID-19. People who remained lower function showed an increased likelihood of depression than those with higher function.

**Ascertaining the impact of socioeconomic status (SES) on the differential risk of SARS-CoV-2 infections with regular rapid antigen tests (RAT): a prospective longitudinal cohort study**

Nicole Ngai Yung Tsang\* Nicole Ngai Yung Tsang Hau Chi So Benjamin J Cowling Gabriel M Leung Dennis Kai Ming Ip

**Background**

COVID-19 pandemic is known to have an intensifying effect on major health inequalities. However, the lower accessibility and affordability to diagnostic facilities including RAT may have also impaired the likelihood of timely case ascertainment among socioeconomically disadvantaged subpopulations, potentially leading to an underestimation of the impact of SES on the risk of COVID-19 infection. A more standardized outcome ascertainment approach would be helpful for a less biased estimation of the differential risk between population subgroups of different socioeconomic status (SES).

**Methods**

A random and representative cohort of 10,000 individuals aged 5 or above were recruited to a large-scale prospective community surveillance in Hong Kong (HK). Free rapid antigen tests (RAT) were provided for weekly self-testing with a pooled nasal and throat swab irrespective of symptom and exposure status to monitor the risk of infection during the 5<sup>th</sup> wave in HK with omicron predominance. Sociodemographic characteristics, chronic illness and vaccination history were collected at baseline and ascertained dynamically. SES was assessed by the tertiary planning unit (TPU) level monthly household rent. A multivariate Cox proportional-hazards regression model was used to estimate the association between different sociodemographic factors and omicron infection, adjusted for vaccination status and other confounders.

**Results**

A total of 8636 participants were included in the analysis. Population with medium (3-4 persons) and large household size (5+ persons) had a significantly higher hazard ratio (HR) of 1.33 (95%CI 1.12-1.59) and 1.48 (95%CI 1.20-1.82) respectively, compared to small household size (1-2 persons). A significantly higher HR of 2.04 (95%CI 1.25-3.34) was shown in population living in public rental housing. Population with higher SES was found to have lower HR (0.68; 95%CI 0.56-0.83) of infection. Extremity of age, gender, and chronic illness were not significant predictors of higher hazard of infection ( $p > 0.05$ ).

**Conclusions**

Our findings suggest that, people with large household size, living in public estates, and lower SES were at higher risk of SARS-CoV-2 infection. Similar risk of infection was observed across different age groups and gender. Our approach with provision of free RAT may help to reduce the likelihood of differential infection ascertainment due to poor accessibility and affordability, and thus avoiding

the potential bias towards an underestimation of the impact of SES on the risk of COVID-19 infection.

**Examining the Relationship between Long-Term Exposure to Ambient NO<sub>2</sub> Pollution, Neighborhood-Level Vulnerability to Environmental Exposures, and COVID-19 Mortality in New York City Hospitalization Data** Sneha Kannoth\* Sneha Kannoth Cong Zhang Sandra S. Albrecht Alexander Azan Earle C. Chambers Perry E. Sheffield Azure Thompson Jennifer Woo Baidal Stephanie Lovinsky-Desir Jeanette A. Stingone

## Background

Spatial differences in chronic air pollution exposure and neighborhood factors may explain geographic disparities in COVID-19 mortality. We leveraged the spatial variability of New York City (NYC) residents' exposure to air pollution and neighborhood vulnerability to assess whether neighborhood vulnerability to environmental exposures modifies the relationship between chronic exposure to nitrogen dioxide (NO<sub>2</sub>) and COVID-19 mortality in NYC.

## Methods

COVID-19 hospitalization data (3/1-6/20/20) were collected from electronic health records from 5 NYC health systems. We measured NO<sub>2</sub> using the 2019 NYC Community Air Survey, and created a standardized neighborhood environmental vulnerability index (NEVI) using US Census and CDC data at the zip code level. NO<sub>2</sub> (range: 10.1-36.4 ppb) was divided into quartiles and NEVI (range: -1.8-1.3) was divided into tertiles. We stratified by NEVI and used Cox regression to estimate mortality risk associated with NO<sub>2</sub>, adjusting for age, sex, smoking, and body mass index.

## Results

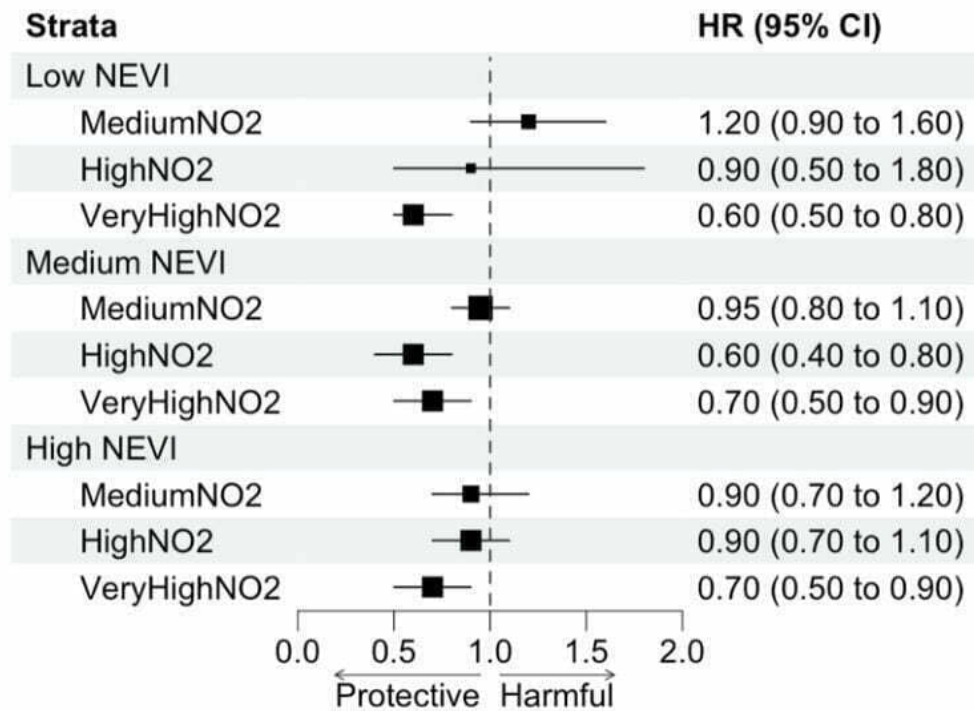
The sample included 14667 patients, of which 2836 died. We found 44% of deaths were in zip codes with high NEVI and high/very high NO<sub>2</sub>. Among those with low NEVI, relative to the 1<sup>st</sup> quartile of NO<sub>2</sub> (i.e. lowest), those in the 4<sup>th</sup> quartile had lower mortality risk (RR:0.6; 95%CI:0.5-0.8). Among medium NEVI, relative to the 1<sup>st</sup> quartile of NO<sub>2</sub>, those in the 3<sup>rd</sup> (RR:0.6; 95%CI:0.4-0.8), and 4<sup>th</sup> quartile (RR:0.7; 95%CI:0.5-0.9) had lower mortality risk. Among high NEVI, relative to the 1<sup>st</sup> quartile of NO<sub>2</sub> exposure, those in the 4<sup>th</sup> quartile had lower mortality risk (RR:0.7; 95%CI:0.5-0.9) (Figure1).

## Conclusion

We found that neighborhood environmental vulnerability does not modify the relationship between chronic NO<sub>2</sub> exposure and COVID-19 mortality and we saw an inverse relationship between chronic NO<sub>2</sub> exposure and COVID-19 mortality. This is contrary to our study hypothesis and we will assess the potential of selection bias contributing to these findings.



**Figure 1.** Cox Proportional Hazards Regression Estimates regarding the Relationship between Chronic NO<sub>2</sub> Exposure and COVID-19 Mortality Risk, within each Tertile Strata of Neighborhood Environmental Vulnerability Index (NEVI) in New York City (NYC)<sup>1-3</sup>



<sup>1</sup> Cox proportional hazards regression model adjusted for age, sex, smoking status, and body mass index

<sup>2</sup> Reference is low NO<sub>2</sub> exposure for each strata of NEVI

<sup>3</sup> Data are from a harmonized repository of electronic health records from 5 NYC health systems

**Risk of arrhythmia after mRNA (BNT162b2) and inactivated (CoronaVac) covid-19 vaccination: a self-controlled case series study** Celine Sze Ling Chui\* min FAN Francisco Tsz Tsun Lai Franco Wing Tak Cheng Ian Chi Kei Wong Celine Sze Ling Chui

**Background:** Cardiac complications were found among people following the mRNA covid-19 vaccines by many publications. However, there are limited comparative studies on the relationship between arrhythmia and covid-19 vaccinations, especially after inactivated vaccines.

**Methods:** A self-controlled case series (SCCS) design was conducted to investigate the arrhythmia risk following three doses of covid-19 vaccines. The study period was from February 23rd, 2021, to November 15th, 2022. Patients with incident cardiac arrhythmia were included. Those patients with a past history of heart failure, coronary heart disease, myocarditis, receiving heterologous vaccines, or with a positive SARS-CoV-2 polymerase chain reaction test result were excluded. Those patients with a following diagnosis of myocardial infarction, carditis, heart failure, or coronary artery disease within 28 days after arrhythmia were excluded to avoid misclassification. The day of each vaccination was defined as day 0. Risk periods of day 0, day 1-13, and day 14-28 days after each dose were defined to assess the risk of arrhythmia. Day 0 was considered a separate risk to avoid event misclassification. Any other period was considered as the baseline. An event-dependent modified SCCS was applied to avoid assumption violation since people who had arrhythmia before vaccination may avoid the vaccination. Conditional Poisson regression was used to estimate the Incidence rate ratio (IRR) and its corresponding 95% confidence interval (CI).

**Results:** During the study period, 23,317 patients were admitted to the hospital with a primary arrhythmia diagnosis. After applying the exclusion criteria, 10,020 patients with incident arrhythmia were included in the analysis: 3,035 with BNT162b2, 5,237 with CoronaVac, and 1,748 without any vaccination. Increased IRRs were found in day 14-28 (1.30 95% CI: 1.00-1.68) following the first dose after BNT162b2. No increasing risk were identified for other doses of BNT162b2 or all doses of CoronaVac.

**Conclusion:** We detected an increased risk of arrhythmia after the first doses of BNT162b2. Continuous monitoring of arrhythmia after mRNA covid-19 vaccines is needed.

**Funding:** This study was funded by the Food and Health Bureau, Hong Kong Special Administrative Region (reference COVID19F01).

**Mitigating Delayed Cancer Diagnosis during the COVID-19 Pandemic: Data-Driven Health System Planning in Alberta Canada** Emily Walker\* Emily Walker Jingyu Bu Yunting Fu Douglas Stewart Bethany Kaposhi Lorraine Shack Matthew Parliament Paula Robson

**Background.** The number of cancer cases reported to the Alberta Cancer Registry (ACR) decreased during the COVID-19 pandemic in Alberta Canada. The objective of this work was to develop a framework for analyzing this phenomenon, to support Cancer Care Alberta in planning for downstream impacts.

**Methods.** This population-based intervention study was conducted in 2020 and the effectiveness was evaluated in 2022. Cancer diagnosis data were obtained from the ACR. We used Poisson regression to estimate age-adjusted relative rates (RR) for cancer diagnosis during the pandemic vs. 2019, using the Alberta population for person-time. Interventions were developed in collaboration with clinical and administrative partners. The magnitude of the RR across COVID-19 waves was compared to evaluate the effectiveness of interventions.

**Results.** The cancer diagnosis rate was 12.4% and 4% lower than expected in 2020 and 2021, respectively. We developed a framework based on cancer-specific diagnostic pathways. The cancer-specific models were used to identify bottleneck procedures that would mediate backlog clearance. Data were presented to administrators to inform decisions around capacity. There were two interventions: public health messaging; and evidence-based health system planning. Evaluation of interventions indicates they were successful in mitigating further decreases in the cancer diagnosis rate. However, backlog clearance requires increasing diagnostic capacity beyond pre-pandemic levels, which could not be achieved during the pandemic.

**Conclusion.** While findings showed that further decreases in the cancer diagnosis rate were mitigated, we were unable to clear the diagnosis backlog. Given ongoing capacity constraints, it is unlikely that a significant surge in new diagnoses beyond normal volumes will occur.

**Post-COVID health impairments and risk factors associated with prolonged recovery: a follow-up study** Warren Szewczyk\* Warren Szewczyk Annette Fitzpatrick Alison Fohner Nicole L. Gentile Nona Sotoodehnia Surabhi Vora Jeanne Bertolli Jennifer Cope Jin-Mann S. Lin Elizabeth Unger Quan Vu

**Background:** Prolonged or non-recovery to baseline health after SARS-CoV-2 infection (COVID) is a serious public health concern; an estimated 30-50% of those infected develop sequelae persisting >3 months. Crucial to the management of post-COVID sequelae is a deeper understanding of what factors predict risk for prolonged recovery.

**Methods:** Patients in the Univ. of Washington health system with medical record confirmed COVID infection from Mar 2020 - Jan 2022 were sent surveys to collect self-report of current health. Logistic regression was used to investigate factors associated with prolonged recovery from COVID (0= <3 mo recovery, 1= >3 mo recovery or unrecovered). Demographics (age, gender, race, education), presence of a pre-COVID comorbidity, time since infection, COVID hospitalization, and acute symptom burden were examined as predictors. Unadjusted prevalence ratios were used to compare current health impairments, assessed with Patient-Reported Outcomes Measurement Information System-29 (PROMIS) v2.0 T-scores, in those who were and were not recovered.

**Results:** From May - Nov 2022, 430 patients completed surveys (mean age=53.3 years, mean time from infection=21.5 months). Acute infection severity (OR=7.25,  $p<0.001$ , highest quartile compared to lowest) and no four-year degree (OR=1.87,  $p<0.05$ , compared to advanced degree) were significant predictors of prolonged recovery. Compared to those who reported recovery to pre-COVID health, those unrecovered ( $n=178$ , 41% of total) showed increased proportions of moderate-to-severe health impairments, with the largest differences seen in fatigue, physical and social function, sleep, and pain (prevalence ratios > 3.0, all  $p<0.001$ ).

**Conclusion:** Prolonged recovery from COVID is influenced by acute infection severity. Socioeconomic position and resource access may impact recovery independent of acute infection severity. Those who remain unrecovered from COVID months after infection suffer significant health impairments.

## Impact of employment status change on depressive symptoms before and after COVID-19 in Korea Jin-Young Nam\* Jin-Young Nam SeoYeon Hwang

**Background:** The coronavirus disease has changed the daily lives of people around the world, adversely affecting their mental health and financial conditions as a result. In particular, the economically vulnerable groups were greatly impacted, resulting in a major change in their employment status. It is necessary to examine the association between employment status change and depressive symptoms to improve the mental health of workers. **Methods:** This study included 5,393 participants (aged  $\geq 19$  years) from the Korea Welfare Panel Study in 2019 and 2020. The depressive symptoms were defined by the 11-item version of the Center of Epidemiologic Studies Depression Scale. Employment status was classified into self-employed, employee, and unemployed. The Generalized Estimating Equations model was applied to identify the association between changes in employment status and depressive symptoms. **Results:** Results showed that the changes from self-employed or employee to unemployed represented a two- and 1.7-fold high risk of depressive symptoms, respectively, compared to maintaining employment status (OR = 2.03, 95% CI = 1.24-3.35; OR = 1.66, 95% CI = 1.14-2.41). Moreover, interaction effects of gender were observed, with a gender difference in the association between the change of employment and depressive symptoms. **Conclusion:** The government should provide appropriate financial and emotional supporting programs for the COVID-19 victims, to improve their mental health related to employment status.

**Table 1.** Subgroup analysis of the association between employment status change and depressive symptoms by gender

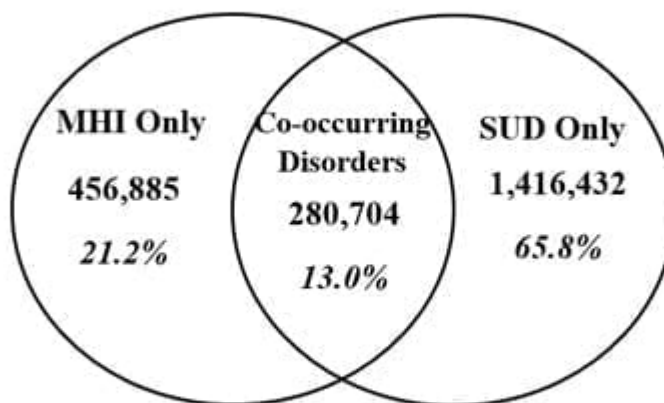
Variable	Employment status change												p-interaction				
	Employee → emplo yee	Self-employed → self-employed		Self-employed → employee		Self-employed → unemployed		Employee → self-employed		Employee → unemployed							
	OR	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI						
Gender																	
Men	1.00	2.05	1.28	3.28	1.87	0.52	6.69	6.67	3.30	13.49	3.26	1.25	8.49	1.70	0.80	3.62	0.0280
Women	1.00	0.88	0.60	1.30	0.45	0.10	1.99	0.88	0.44	1.74	0.95	0.23	3.85	1.57	1.03	2.40	

Note: Adjusted for age, region, education, marital status, house income, self-rated health, current smoking, AUDIT score.

**Adapting national hospital care survey covid-19 early release data to determine impact of mental health, substance use disorders, and co-occurring mental health and substance use in hospital encounters** Salah Shaikh\* Salah Shaikh

Concern regarding mental health issues (MHIs) and substance use disorders (SUDs) have continued throughout the COVID-19 pandemic. Hospitals are often at the forefront of treating patients with MHIs, SUDs, or co-occurring MHIs and SUDs, but available staff and access to treatment resources have become increasingly limited during the pandemic. The National Center for Health Statistics studies hospital utilization using the National Hospital Care Survey (NHCS), an annual, administrative data collection of emergency department (ED) and inpatient department encounter-level data. To meet the need for timely hospital data, procedures were developed to utilize preliminary data collected from approximately 50 NHCS hospitals to report on COVID-19 care. These data are unweighted and are not nationally representative but provide a valuable timely data source of hospital care. The preliminary data are from a select group of hospitals and contain information on 5,941,241 hospital encounters. In the data from January 1, 2020, through December 31, 2022, there were 1,890,601 MHI or SUD encounters, and among those encounters, 1,288,376 (68.1%) were SUD only, 361,285 (19.1%) were MHI only, and 240,940 (12.7%) were co-occurring MHI and SUD encounters (Figure 1). This ability of NHCS to identify to provide near real-time results on MHI and/or SUD encounters is a major feature that other data systems do not have. This poster will use the NHCS COVID-19 early release data to describe characteristics of patients with MHIs, SUDs, and co-occurring disorders. Characteristics to be examined include demographics, changes throughout the pandemic, and having a comorbid COVID-19 diagnosis.

**Figure 1: Mental health issue (MHI)-only, substance use disorder (SUD)-only, and co-occurring disorders encounters in participating hospitals**



**NOTE:** Data are not nationally representative. MHI is mental health issue. SUD is substance use disorder.

**SOURCE:** National Center for Health Statistics, Preliminary National Hospital Care Survey, 2020-2022

**Systematic review of COVID-19 vaccine decision-making, uptake, and hesitancy among adolescents aged 12 to 17 years old** Brianna Agnew\* Brianna Agnew Honorine Uwimana Marie-Claude Couture Timothy Callaghan Onyebuchi A. Arah Annette K. Regan

Vaccination remains the best strategy to prevent COVID-19-associated morbidity and mortality. COVID-19 vaccine prevalence among adolescents (61.5%) has recently stalled and remains lower than adults aged  $\geq 25$  years (82%). While prior research has focused on the parental/caregiver perspective of adolescent vaccine uptake, we need an up-to-date understanding of the adolescent perspective. We conducted a systematic review of the factors associated with COVID-19 vaccine decision-making, uptake, and hesitancy among adolescents aged 12-17 using four databases: CINAHL, EMBASE, PubMed, and SCOPUS. Inclusion criteria were: i) studies reporting on factors associated with COVID-19 vaccine uptake, hesitancy, or intention to vaccinate, ii) among adolescents aged 12 - 17 years, iii) published in English or Spanish. Two team members independently screened 4,137 research papers and agreed to full text review 299 studies for potential inclusion.

After assessing 166 full-text articles (to date), 11 studies conducted in seven countries have met eligibility criteria. A preliminary narrative analysis of four cross-sectional studies found low vaccine uptake among teens (South Korea: 50%; U.S.: 52% - 58%; Israel; 64%). The majority of adolescents reported participating with their family in vaccine decision-making (65.7%); 17.8% made their own decision, and 16.4% stated their parent/caregiver decided alone. Compared to parents/caregivers, teens reported higher levels of trust in family and friends (40%), school (20%), and social media (20%) for vaccine information and more commonly reported fear of needles (21%) and unvaccinated friends (17.1%) as reasons for vaccine hesitancy. Adolescents provide critical insights into their own COVID-19 vaccine uptake, hesitancy, and decision-making, that may diverge from their parents/caregivers. Better understanding adolescent factors associated with COVID-19 vaccination is necessary to create effective interventions to improve vaccination rates.

**The Association Between Science Knowledge and COVID-19 Vaccination** John Robert Warren\* John Warren Isabella Stade Emily Lybbert Eric Grodsky Chandra Muller

**Introduction:** There are socioeconomic, ideological, racial/ethnic, and other disparities in COVID-19 vaccination rates. To what extent are those disparities due to early life disparities in educational contexts, opportunities, and outcomes and, in turn, to late life disparities in knowledge of basic scientific information?

**Methods:** We use data from the nationally-representative High School and Beyond cohort, which has followed a probability sample of ~25,500 Americans from high school (in 1980) through age ~60 (in 2022). COVID-19 vaccination status and science knowledge are measured in 2022; educational contexts, opportunities, and outcomes and other key variables are measured in adolescence. We begin by modeling COVID-19 vaccination status as a function of educational contexts, opportunities, and outcomes; we then estimate the degree to which science knowledge in adulthood mediates the relationship between education and vaccination status. Models include covariates for childhood socioeconomic origin; religion; political ideology; and demographic attributes.

**Results:** Net of parental socioeconomic origins, religious affiliation, political ideology, and demographic attributes, we find strong associations between education—including educational attainment, but also including high school test scores and GPA—and the odds that someone got vaccinated for COVID-19. Net of all of those factors and education, we find a strong relationship between adult science knowledge and vaccination status: For every additional science item participants got correct (out of 12), their odds of getting vaccinated increased by 9 percent.

**Conclusion:** Education is strongly related to people's risk of getting vaccinated for COVID-19—but education is more than just attainment or highest degree earned. Part of that association is mediated by adult science knowledge. Better educated people know more about science in later life, and science knowledge is strongly related to vaccination decision.



**Mental health service use among childbearing parents before and during the COVID-19 pandemic in Ontario, Canada** Colleen Webber\* Colleen Webber Daniel Myran Christina Milani Simone Vigod Rahim Moineddin Anna Clarke Sarina Isenberg Jess Fiedorowicz Ye (Hailey) Jin Jasmine Gandhi Andrea Simpson Lucy Barker Claire Kendall Peter Tanuseputro

**Objectives:** Parents, and particularly those of school-aged children, have experienced unique challenges through the COVID-19 pandemic, including stressors related to school and childcare closures and subsequent impacts on workforce participation. This study evaluated changes in mental health-related physician visits by childbearing parents before and during the COVID-19 pandemic.

**Methods:** Using health administrative data, we conducted a population-based study of all childbearing parents with  $\geq 1$  child aged 1-18 in Ontario, Canada between January 1, 2016 and December 31, 2021. Using negative binomial regression, we computed the expected monthly outpatient mental health-related physician visit rate for the pandemic period (March 2020-December 2021) based on pre-pandemic visit rates. We compared the observed-to-expected rates during the pandemic period using incidence rate ratios (IRRs) and 95% confidence intervals (CIs). Differences in pandemic-related changes in outpatient mental health visits were examined according to individuals' sociodemographic and child characteristics.

**Results:** In April 2020, the observed outpatient mental health-related physician visit rate was 74.6 visits per 1,000 childbearing parents (expected=70.7 visits per 1,000 childbearing parents (IRR=1.05, 95%CI 1.02-1.09). Monthly visit rates remained between 5% and 29% higher than expected through the pandemic. This finding was consistent when visit rates were measured per 1,000 all-cause outpatient visits, suggesting the increase was not due to an overall increase in outpatient visits. The observed increases in outpatient mental health physician visits were greatest for individuals who were older, with no prior mental health diagnosis, and living in higher income or urban areas.

**Conclusion:** The COVID-19 pandemic was associated with significant increases in outpatient mental health-related physician visit rates for childbearing parents, with certain subgroups of mothers being particularly impacted.

**Online health information seeking and COVID-19 vaccination outcomes** Gabrielle

Zuckerman\* Gabrielle Zuckerman Sherine El-Toukhy

We examined associations between reactions to online health information seeking (OHIS) and COVID-19 vaccinations, if these associations were mediated by perceived risk, and if they differed by county preparedness for public health crises as determined by the Minority Health Social Vulnerability Index (SVI). Using a quasi-experimental design, we conducted an online survey (2/2022-8/2022) of 5559 US adults residing in counties that fall in the top or bottom SVI quartiles, where higher scores (i.e., top quartile) reflect greater vulnerability. Negative (i.e., effort, frustration) and positive (i.e., confidence) reactions to OHIS were exposure variables and vaccination behaviors and intentions (among the unvaccinated) for the COVID-19 primary series and boosters were outcomes. Perceived risk components - likelihood, susceptibility, severity - were mediators. Parallel mediation models were run for each exposure and outcome variable combination using PROCESS macro in R adjusting for demographics. Negative (positive) reactions to OHIS were negatively (positively) associated with COVID-19 vaccination. Negative reactions increased perceived susceptibility to ( $\beta=0.14$ ) and severity of ( $\beta=0.06$ ) COVID-19, which decreased primary series vaccination ( $\beta_{\text{sus}}=-0.07$ ,  $\beta_{\text{sev}}=-0.08$ ). Positive reactions increased perceived likelihood ( $\beta=0.15$ ) and severity ( $\beta=0.08$ ), where likelihood increased primary series vaccination ( $\beta=0.43$ ) while severity decreased it ( $\beta=-0.10$ ). Three variables decreased primary vaccination status in the overall sample and top SVI but not in the bottom SVI: (1) negative reactions to OHIS, (2) perceived susceptibility, and (3) perceived severity. Positive and negative reactions to OHIS differentially affected perceived risk, and subsequently, primary series vaccination. Resultant decreases in vaccination status were exhibited by residents of the most vulnerable counties. Accessible health information is necessary to increase uptake of vaccines among US adults.

**Excess mortality from 16 specific underlying causes of death during the COVID-19 pandemic in the US** Lauren Zalla\* Lauren Zalla Catherine Lesko

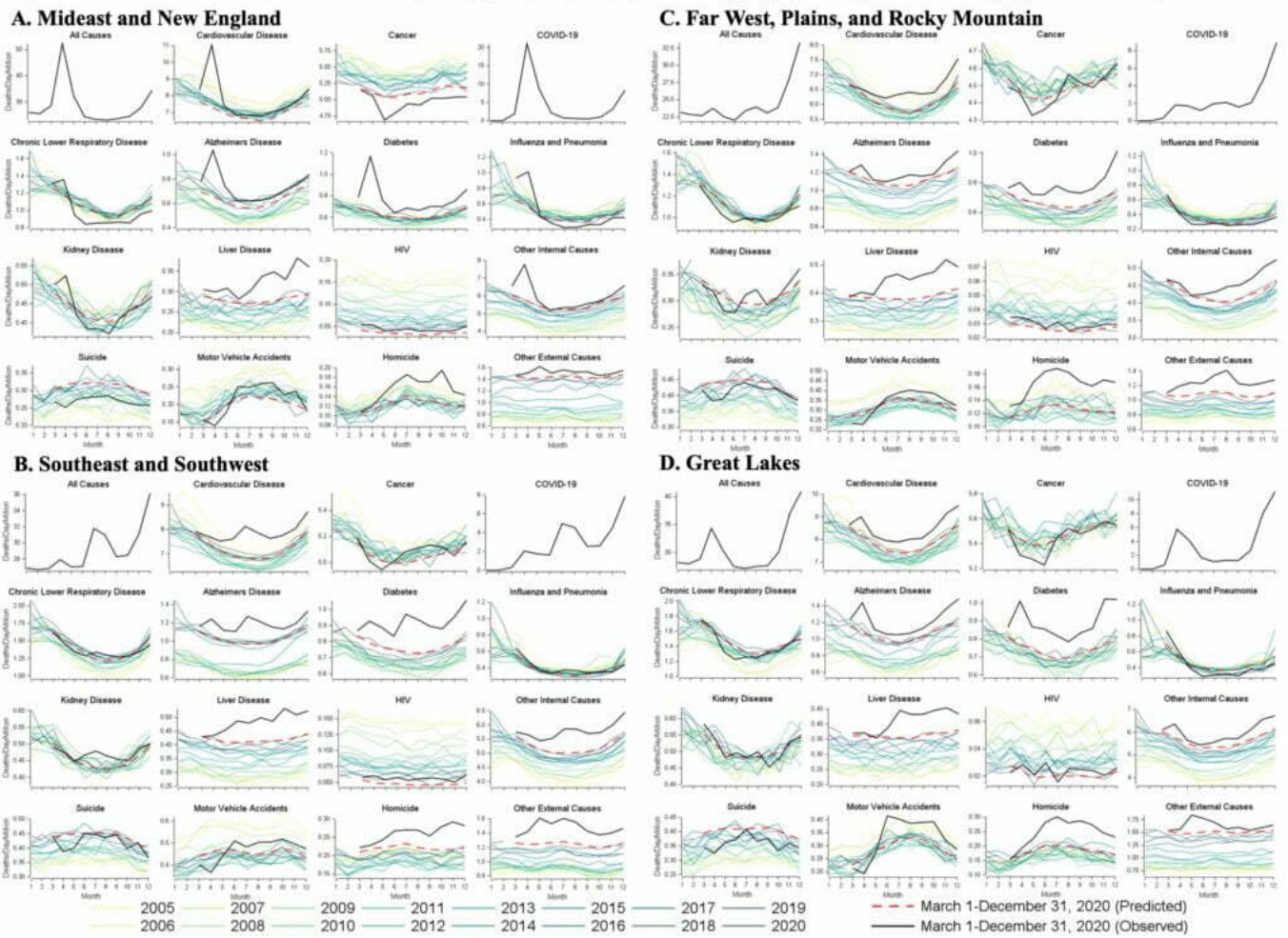
**Background:** Deaths reported to be associated with COVID-19 accounted for only 72-84% of all “excess deaths” that occurred in the US in 2020. We investigated patterns of excess deaths due to 16 specific underlying causes.

**Methods:** We used dynamic harmonic regression models to predict the number of deaths due to specific causes in 2020 using mortality data from the National Center for Health Statistics from 2005-2019. To compare temporal trends in COVID-19 vs. other causes of death, we aggregated state-level data into four regions that experienced unique pandemic surge patterns (Northeast/Mid-Atlantic; Southeast/Southwest; Far West/Plains/Rocky Mountain; Great Lakes). We estimated 95% prediction intervals (PI) by simulating each cause- and region-specific model 10,000 times.

**Results:** After deaths from COVID-19 (351,530), the greatest number of excess deaths were attributed to cardiovascular disease (63,484; 95% PI, 28,003, 98,801). The greatest relative increase was in homicide deaths (21%). There were significant increases in all other causes of death except cancer, motor vehicle accidents, chronic lower respiratory disease, influenza and pneumonia. Trends in cardiovascular disease, diabetes, and Alzheimer’s disease deaths approximated trends in COVID-19 deaths; trends in homicide, liver disease, and HIV deaths did not (Figure). Suicide deaths decreased by 6% (-2,660; -4,005, -1,323) nationally, with the largest dips occurring during surges in deaths from COVID-19.

**Conclusions:** Excess cardiovascular disease, diabetes, and Alzheimer’s disease deaths were likely either complications of COVID-19 or directly related to the pandemic (e.g., through disruptions in clinical care). Excess homicide, liver disease, and HIV deaths may be due to indirect effects of the pandemic that were less localized, or other separate causes (e.g., reaction to the death of George Floyd). Further investigation of specific causes of excess mortality may improve preparedness for future pandemics.

**Figure.** Observed and model-predicted deaths per day per 1,000,000 population by geographic region and underlying cause of death, 2005-2020



**LATEBREAKER**

Diabetes

**Maternal microchimerism and type 1 diabetes in children** Gitte Lindved Petersen\* Gitte Lindved Petersen Mads Kamper-Jørgensen Marianne Antonius Jakobsen Sofie Dolores Holm Olsen Christina Ellervik Lise Tarnow Randi Jepsen Flemming Pociot

Fetus and mother naturally exchange cells, and small numbers of maternal cells can persist in the child for decades. The phenomenon is denoted maternal microchimerism and involves a delicate balance between increased immune surveillance and triggering of autoimmunity. We aim to investigate the association between circulatory maternal microchimerism and type 1 diabetes in children.

This case-control study includes Danish children with and without type 1 diabetes (n=69 and 578, respectively). Peripheral blood from cases, controls, and mothers was used to identify an informative indel allele for each mother-child pair. Sequence-specific quantitative polymerase chain reaction assays were used to detect and quantify maternal cells in the child's blood.

A logistic regression model was used to test the crude association between maternal microchimerism presence and type 1 diabetes. Because our directed acyclic graph suggests that perinatal exposures can confound the estimate, we estimated the E-value for the crude estimate to evaluate the robustness to uncontrolled confounding.

Maternal microchimerism was detected in 54% of cases (34/63) and 17% of controls (80/459) corresponding to an OR of 5.6 (95% CI 3.2, 9.7) for having type 1 diabetes among children tested positive compared to negative for maternal microchimerism. A group of confounders should be associated with a >10-fold increased probability of testing positive for maternal microchimerism as well as of having type 1 diabetes to cause a spurious OR of this size (E-values OR 10.7, CI 5.9).

Presence of maternal microchimerism was more common in children with type 1 diabetes compared to controls, and the findings are unlikely to be explained fully by unadjusted confounding. To further assess the association, we will conduct adjusted analyses, include a quantitative exposure measure, and conduct sub- and sensitivity analyses. Laboratory results are currently being linked to register data to obtain information on covariates.

**Predicting future risk of type 2 diabetes in an ethnically and culturally diverse community in Ontario, Canada: A population-based analysis** Ghazal Fazli\* Ghazal Fazli Lorraine Lipscombe Fatema Ali Laura C Rosella

**Introduction:** Population-based risk prediction tools are important for decision-making and planning of diabetes prevention strategies. We used the Diabetes Population Risk Tool (DPoRT) to predict the 10-year risk of developing diabetes in one of Canada's most ethnically and culturally diverse communities.

**Methods:** We used population data from the Canadian Community Health Survey, a national cross-sectional survey questionnaire, to predict the 10-year risk of diabetes among adults (aged  $\geq 20$  years) living in Peel Region, Ontario, Canada. We applied DPoRT to risk factor information to predict the distribution of 10-year type 2 diabetes incidence and the number of new diabetes cases in the subsequent ten years both overall and across important subgroups.

**Results:** There were 1,462 survey respondents included in this study, of whom 167 were living with a diagnosis of diabetes and 1,295 without diabetes. Between 2017/18 to 2027/28, the DPoRT predicted a 10-year diabetes risk of 11.5% (95% confidence interval [CI] 10.6-12.3) and 102,616 new cases. The highest number of predicted 10-year risk of diabetes will occur among racialized communities (12.7% risk and 71,417 cases), low-income households (<20,000 per year (14.4% risk and 28,187 cases), those who are obese (24.0% risk and 30,382 cases), and physically inactive (13.8% risk and 42,026 cases).

**Conclusion:** In Peel Region, diabetes incidence is projected to increase rapidly, particularly among those experiencing a greater degree of socioeconomic disadvantage. In the absence of effective diabetes prevention strategies that specifically address the social determinants of health, these projected increases will pose significant challenges for individuals and the health system and disproportionately affect those from marginalized communities.

**The Influence of Preconception Hemoglobin A1c on Gestational Diabetes at First Live Birth Among New York City Adolescents, 2009-2017** Katharine McCarthy\* Katharine McCarthy Shelley Liu Luciana Vieira Victoria Mayer Teresa Janevic

Nearly one-third of adolescent girls in the U.S. have prediabetes yet less is known about how subclinical glycemic control prior to pregnancy influences the likelihood of pregnancy complications and adverse birth outcomes among adolescents. We examined the influence of preconception hemoglobin A1c level on the likelihood of gestational diabetes at first live birth among adolescents aged 10 to 24 years using a retrospective cohort of linked 2009-2017 NYC birth certificate, hospital discharge, and A1C Registry data. We included those aged 10-24 years with no history of diabetes prior to pregnancy who had at least one preconception A1c test (N=14,284). We examined mean preconception A1c values and values at last preconception test categorized as: no diabetes ( $A1c < 5.7\%$ ) or prediabetes ( $5.7 \leq A1c < 6.5\%$ ). Multivariable logistic regression was used to assess the likelihood of GDM at first birth by preconception A1c level, adjusting for pre-pregnancy characteristics. Secondary outcomes included hypertensive disorders of pregnancy, preterm birth, cesarean section and macrosomia. Most (79%) of the sample had 'no diabetes' at last preconception test, and 21% had 'pre-diabetes'. The cumulative incidence of GDM was 5.1%, with higher mean A1c values among those with incident GDM (5.7, 95% CI: 5.7-5.8) than without (5.4, 95% CI: 5.4, 5.4). Adjusting for pre-pregnancy characteristics, those with preconception prediabetes had 2.3 times the likelihood of GDM (95% CI: 1.9, 2.7) than those with no diabetes. Preconception pre-diabetes was also associated with a slight increase in the likelihood of a hypertensive disorder of pregnancy (adjusted odds ratio (aOR): 1.2, 95% CI: 1.0, 1.3), preterm delivery (aOR: 1.2, 95% CI: 1.0, 1.4%) and cesarean section (aOR: 1.1, 95% CI: 1.0, 1.2) and a nonsignificant increase in macrosomia (aOR 1.1: 95% CI: 0.9, 1.4). Results highlight adolescence as a critical window to optimize cardiometabolic health prior to pregnancy and avert excess maternal and fetal risk.

**The impact of misclassification of HbA1c tests on the relationship between HIV and type 2 diabetes in South Africa: a quantitative bias analysis**

Emma Kileel\* Emma Kileel Alana T Brennan Matthew P Fox Jacob Bor Jaya George Siyabonga Khoza Sydney Rosen Patricia Hibberd Frederick Raal Kamy Chetty Koleka Milsana Nigel J Crowther

**Background:** Many epidemiologic studies estimating diabetes prevalence in low- and middle-income countries rely on HbA1c tests. Diagnostic accuracy of HbA1c in these populations is unclear, however, particularly in people with HIV due to higher levels of hemolysis caused by some antiretroviral therapies. Using data from South Africa's National Health Laboratory Service National HIV Cohort, we conducted a quantitative bias analysis adjusting for diabetes misclassification to estimate the risk of diabetes diagnosis among people age  $\geq 45$  years with (PWH) and without (PWOH) HIV.

**Method:** Data from patients with both HbA1c and fasting glucose tests were used as internal validation data, using fasting glucose as the gold standard, to estimate bias parameters by HIV status. Validation data were used to adjust the RR among those with only HbA1c available for diagnosis. Beta distributions were specified as: PWH sensitivity:  $\sim\text{beta}(2055, 2364)$ , specificity  $\sim\text{beta}(1275, 1914)$ ; people without HIV (PWOH): sensitivity  $\sim\text{beta}(21735, 24149)$ , specificity  $\sim\text{beta}(10344, 17290)$ . We ran 100,000 Monte-Carlo simulations, randomly sampling values of sensitivity and specificity from the distributions and using standard formulas to obtain an adjusted RR of diabetes diagnosis. Simulations accounting for random and systematic error were summarized using the median as the point estimate and the 2.5<sup>th</sup>-97.5<sup>th</sup> percentiles as the 95% simulation interval (SI).

**Results:** Crude estimates showed a 16% decrease in risk of lab-diagnosed diabetes among PWH vs PWOH (RR: 0.84; 95% CI: 0.84-0.85). After accounting for random and systematic error, the median adjusted RR of lab-diagnosed diabetes was 0.79, corresponding to a 21% decrease in risk of lab-diagnosed diabetes among PWH vs PWOH (95% SI: 0.74-0.84).

**Conclusion:** HbA1c tests resulted in an overdiagnosis of diabetes among PWH. Accounting for outcome misclassification, results indicate PWH have a lower risk of lab-diagnosed diabetes compared to PWOH.



**Association of alcohol use with type 2 diabetes risk: Evidence from a prospective cohort study and Mendelian randomization in the UK Biobank** Shiu Lun Au Yeung\* Shiu Lun Au Yeung Shan Luo Tommy Hon Ting Wong Shiu Lun Au Yeung

Background: Observational studies suggested inverse association of moderate alcohol use with type 2 diabetes (T2D) risk although the association could be due to confounding. Previous Mendelian randomization (MR) studies may not account for potential non-linearity appropriately. We assessed the association of alcohol use with T2D risk using a prospective cohort study and non-linear MR design.

Method: This study was based on UK Biobank (n=315,750), a large prospective cohort study in United Kingdom. Alcohol use was ascertained based on self-reports whilst T2D incidence ascertainment was based on record linkage. Association of alcohol use (in categories and in units/week) with T2D risk was assessed using Cox proportional hazard model, adjusted for potential confounders. Non-linear MR with doubly-ranked stratification method was used to assess the same association using a weighted genetic risk score based on 71 genetic predictors of alcohol use, with replication in DIAMENTE (n=933,970), a large genome wide association study of T2D. Systolic blood pressure (SBP) was used as a positive control outcome.

Results: After a median follow up of 12.4 years, 8,888 incident T2D was observed. Observationally, all drinker categories had lower risk of T2D compared to lifelong abstainer (Sensible: HR (0.64, 95%CI 0.59 to 0.70); Moderate: (0.52, 95%CI 0.48 to 0.58); Hazardous: (0.49 (0.45 to 0.55); and Harmful: (0.54, 95%CI 0.49 to 0.59)), with similar findings using continuous alcohol trait. However, non-linear MR suggested a positive association, with potential non-linearity (p value = 0.003). Both analyses showed alcohol use positively associated with SBP.

Conclusion: Alcohol use unlikely protects against T2D but instead could increase T2D risk. The discrepancies between observational and MR findings are possibly an indication of confounding.

**Fine particulate matter and preterm birth: a causal survival approach** Michael Leung\*

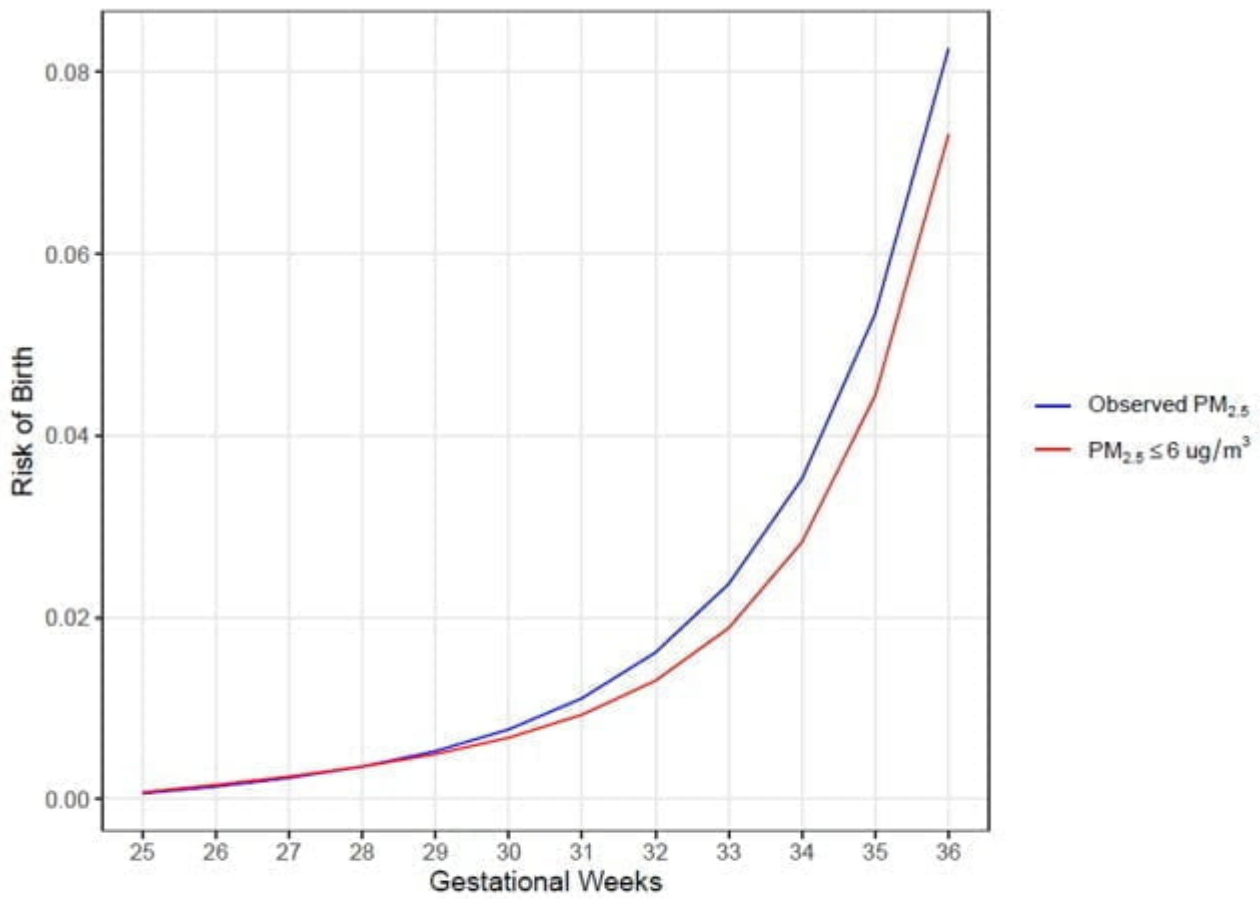
Michael Leung Anna M Modest Michele R Hacker Hari Iyer Jaime E Hart Yaguang Wei Joel Schwartz Brent A Coull Francine Laden Marc G Weisskopf Stefania Papatheodorou

**Background:** There is substantial interest in understanding the impact of environmental exposures on preterm birth (<37 weeks). The standard approach treats prematurity as a binary outcome and cannot examine time-varying exposures during pregnancy. Here, we reframe preterm delivery as a time-to-event outcome and use a causal survival approach (amenable to dealing with time-varying covariates) to assess its association with particulate matter  $\leq 2.5 \mu\text{m}$  ( $\text{PM}_{2.5}$ ).

**Methods:** We used data on 9,446 births from 2011-2016 in a Massachusetts-based cohort. We considered two  $\text{PM}_{2.5}$  exposure windows which depend on gestational week —the cumulative exposure from conception to week and 1-week prior to week — and estimated the effect of a hypothetical intervention reducing  $\text{PM}_{2.5}$  exposure to  $6 \mu\text{g}/\text{m}^3$  in each window.  $\text{PM}_{2.5}$  was taken from a 1-km grid model and assigned to address. Risk ratios (RR) and differences (RD) of preterm birth were estimated by fitting discrete-time hazards models adjusted for sociodemographic characteristics, time trends, temperature, and nitrogen dioxide; and then standardizing the estimated risks to the distribution of baseline covariates.

**Results:** There were 805 (8.5%) preterm births in this cohort. Average  $\text{PM}_{2.5}$  was  $7.4 \mu\text{g}/\text{m}^3$  for the cumulative exposure (87% had  $>6 \mu\text{g}/\text{m}^3$ ) and  $7.3 \mu\text{g}/\text{m}^3$  for the 1-week window (98% had  $>6 \mu\text{g}/\text{m}^3$ ). We found that setting the cumulative  $\text{PM}_{2.5}$  exposure ceiling to  $6 \mu\text{g}/\text{m}^3$  was associated with a lower risk of preterm birth; for example, the RR was 0.89 (95% CI: 0.78, 1.01) and the RD was -0.01 (95% CI: -0.02, 0.0004), which translates to about 89 (95% CI: -4, 167) fewer preterm births in this cohort.  $\text{PM}_{2.5}$  in the 1-week window was not associated with preterm birth.

**Conclusions:** We show that higher cumulative  $\text{PM}_{2.5}$  exposure was associated with increased risk of preterm birth. A causal survival framework can accommodate time-varying covariates and quantify the change in the number of preterm births for a given exposure contrast.



**Figure 1.** The absolute risk of birth <37 gestational weeks for the observed PM<sub>2.5</sub> distribution (blue) and had the PM<sub>2.5</sub> exposure ceiling been set to 6  $\mu\text{g}/\text{m}^3$  (red).

**Bidirectional associations between posttraumatic stress symptoms and sleep quality among older survivors of the 2011 Great East Japan Earthquake and Tsunami** Aki Yazawa\* Aki Yazawa Koichiro Shiba

Sleep problems are frequently observed following traumatic experiences, especially for those suffering from posttraumatic stress disorder (PTSD). Although sleep problems are considered a central symptom of PTSD, the temporal relationship between sleep and PTSD is not firmly established; it has been suggested that pre-existing sleep disturbances may facilitate PTSD onset in response to trauma exposures, as well as they may impede recovery from PTSD. In this study, we sought to examine the bidirectional associations between disaster-related posttraumatic stress symptoms (PTSS) and sleep quality in a sample of older disaster survivors. We used 4 waves (2010, 2013, 2016 & 2020) of the Iwanuma Study, a 9-year follow-up study of older survivors of the 2011 Great East Japan Earthquake and Tsunami. A unique strength of the cohort is the availability of pre-disaster assessment of sleep. Poisson regression analysis was used to examine the bidirectional associations between sleep problems and PTSS. Individuals reporting sleep problems before the disaster were more likely to develop PTSS after exposure to disaster trauma, while there was no effect modification, i.e., prevalence ratios of onset PTSS did not vary according to the severity of disaster-related trauma. Individuals reporting sleep problems after the disaster were less likely to recover from PTSS, and more likely to experience delayed onset of PTSS five years after the disaster. Individuals who recovered from PTSS nine years after the disaster still remained at higher risk of having sleep problems compared to those who never had PTSS. The association between PTSS and sleep problems was bidirectional. Intervention to address lingering sleep problems may benefit the recovery of disaster survivors from post-traumatic symptoms.

**Sensitive time windows of exposure to indoor air pollutants and psychosocial factors and their association with psychopathology at school-age in a South African birth cohort**

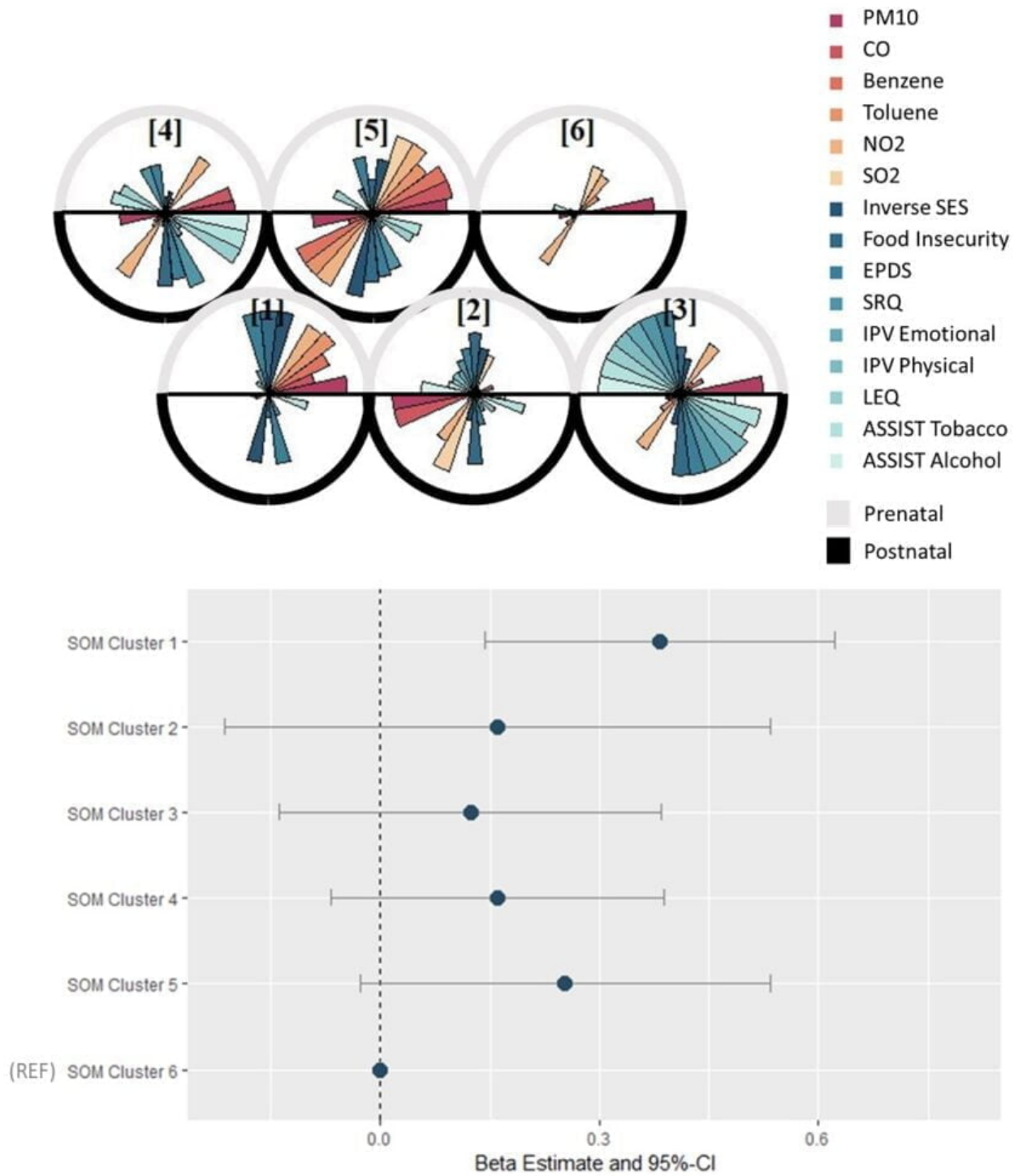
Grace Christensen\* Grace Christensen Michele Marcus Aneesa Vanker Susan Malcolm-Smith Shakira Suglia Howard Chang Heather Zar Dan Stein Anke Huels

Gestation and early life are critical periods of brain development. Exposure to indoor air pollutants (IAP) and psychosocial factors (PF) during gestation and early life have been shown to impact psychopathology in childhood. In previous studies pre- and postnatal exposures have been investigated separately not taking the other exposure period into account. This study aims to evaluate the joint effects of exposure to IAP and PF in gestation and early life on psychopathology at 6.5 years old.

We used data from the Drakenstein Child Health Study (N=599), a South African birth cohort. Exposure to IAP and PF was measured during the second trimester of pregnancy and 4 months postnatal. The Childhood Behavior Checklist (CBCL) was administered at 6.5 years old to assess child psychopathology (total problems score). Joint effects of IAP and PF in both time periods were summarized using self-organizing maps (SOM) to create profiles of joint exposures across exposures and timepoints. Linear regression models were adjusted for maternal age, ancestry, and maternal HIV status.

SOM cluster 6 was used as the reference cluster in linear regression modeling, as it is characterized by low PF exposure and low-moderate IAP exposure at both timepoints (Figure 1). In adjusted linear regression modeling, all SOM clusters showed harmful associations with CBCL total problem score compared to cluster 6. Specifically, cluster 5 characterized by high pre- and postnatal IAP (beta: 0.25; 95% CI: -0.03, 0.53), and cluster 1 characterized by high prenatal IAP and high pre- and postnatal PFs (0.38; 0.14, 0.62) showed the strongest association with CBCL.

Exposure to high levels of IAP, particularly during pregnancy, was associated with higher CBCL total problems score, indicating pregnancy as a sensitive period for exposure. Determining sensitive periods of exposure is necessary to ensure exposure reduction interventions have the highest impact on health outcomes.



**Exposure to high ambient temperatures across spermatogenesis and semen quality** Carrie J Nobles\* Carrie Nobles Timothy P Canty Lindsey M Russo Neil J Perkins Pauline Mendola Enrique Schisterman Sunni Mumford J Richard Pilsner

**Introduction:** Spermatogenesis is uniquely susceptible to heat stress, including decrements in sperm count, morphologic differentiation, and acquisition of motility. Despite the anticipated global increase in high-temperature exposures, few clinical studies have evaluated the relationship of ambient temperatures with semen quality.

**Methods:** The Folic Acid and Zinc Supplementation Trial (FAZST) enrolled 2,015 men from couples seeking infertility treatment near Salt Lake City, Utah (2013-2017). Semen samples were collected at enrollment and at 2-, 4-, and 6-months and evaluated for sperm concentration, morphology, and motility. Ambient temperature was abstracted from weather stations and averaged across spermatogenesis and four susceptible windows of spermatogenesis: spermiation (0-10 days prior to ejaculation), spermiogenesis (11-32 days), meiosis I+II (33-58 days), and mitosis (59-74 days). Linear mixed models estimated differences in semen quality parameters during the warm (Apr. 1-Sept. 30) vs. cold (Oct. 1-Mar. 31) seasons. Sperm concentration and morphology were log-transformed and models adjusted for fine particulate matter and participant characteristics.

**Results:** Median (IQR) daily ambient temperature was 22.7 (16.0, 26.8)°C in the warm season and 4.6 (-0.2, 10.0)°C in the cold season. A 2°C increase in ambient temperature during spermatogenesis was associated with lower sperm concentration during the warm season (% difference -0.87, 95% CI -1.74, 0.02) and lower percent morphologically normal sperm in both the warm (% difference -0.99, 95% CI -2.40, -0.36) and cold (% difference -1.10, 95% CI -2.36, 0.17) seasons. Associations with sperm concentration were greatest in the warm season during spermiogenesis (% difference -1.04, 95% CI -1.96, -0.12) and meiosis (% difference -0.85, 95% CI -1.64, -0.04).

**Discussion:** Associations of high temperatures with decrements in semen quality may have important implications for men's fertility in a changing climate.

**Nickel exposure is associated with an ADHD diagnosis in children aged 6-14 years old living near coal-fired power plants.** Kelsey M Maclin, MS\* Kelsey Maclin Lonnie Sears, PhD John Myers, MS Kristina Zierold, PhD

**Background and Aim:** Attention-deficit/hyperactivity disorder (ADHD) is a neurodevelopmental disorder characterized by disorganization, weakened attention levels, and/or hyperactivity. ADHD can affect a child's ability to learn in school and act in social situations. Heavy metals are known to affect neurodevelopment. Limited research has investigated the relationship between the neurotoxic metal, nickel, and ADHD diagnosis. The objective of this study was to investigate the association between nickel and ADHD in children aged 6 to 14 years old.

**Methods:** This was a community-based study with children living near coal-fired power plants. Toenails and fingernails were collected to determine heavy metal body burden. Nickel was determined using Inductively coupled plasma mass spectrometry (ICP-MS). To assess the association between nickel exposure and clinically diagnosed ADHD, two statistical methods were used. The Wilcoxon test for continuous exposures and logistic regression for dichotomized exposures.

**Results:** There were 283 children enrolled in this study and 17% of children were diagnosed with ADHD. There were slightly more males than females and 26% of children self-identified as nonwhite. Based on Wilcoxon analysis, nickel was found to be significantly higher in children with a diagnosis of ADHD ( $p=0.006$ ). The nickel values were log transformed and results from logistic regression supported the Wilcoxon results.

**Conclusions:** Limited research has investigated nickel, a known neurotoxin, in relationship to children diagnosed with ADHD. Our study found that children exposed to nickel were significantly more likely to be diagnosed with ADHD compared with children not exposed to nickel. Nickel is a neurotoxin and further research needs to be conducted to confirm this finding and to understand how childhood exposure to nickel may be associated with ADHD.



**Long-term exposure to ozone pollution and kidney function: A cohort study of Thai adult workers** Kanawat Paoin\* Kanawat Paoin Chanathip Pharino Prin Vathesatogkit Arthit Phosri Suhaimee Buya Krittika Saranburut Kayo Ueda Xerxes Tesoro Seposo Thammasin Ingviya Chagriya Kitiyakara Nisakron Thongmung Piyamitr Sritara

Some previous studies reported that long-term ozone (O<sub>3</sub>) exposure was positively associated with the risk of chronic kidney disease (CKD). However, there is still insufficient and inconsistent evidence to support the association between O<sub>3</sub> and kidney function indicators. We investigated the association between long-term exposure to O<sub>3</sub> and estimated glomerular filtration rate (eGFR) in adult Electricity Generating Authority of Thailand (EGAT) workers in the Bangkok metropolitan region (BMR), Thailand. This longitudinal study involved 2,022 adult workers from the EGAT3 cohort study (2009–2019; aged 25–55 years at baseline). The calculation of eGFR was based on the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation. Outcome variables, including eGFR, were measured in 2009, 2014, and 2019. Exposure to air pollution (i.e., particulate matter with an aerodynamic diameter ≤10 μm (PM<sub>10</sub>), O<sub>3</sub>, nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), and carbon monoxide (CO)) was estimated using the kriging method in BMR during 2009 to 2019. The average exposure for each participant was one year prior to the follow-up date. We used linear mixed-effects models to estimate the association of O<sub>3</sub> with eGFR. A random intercept was given to each participant. The result of eGFR was shown as a percentage change per interquartile range (IQR) increase in O<sub>3</sub>. There were also two-pollutant models performed. We included 2,022 study participants with 5,623 eGFR measurements. The annual participants' average exposure to O<sub>3</sub> was 33.6 ppb during the follow-up period. An IQR increase in O<sub>3</sub> concentration (4.8 ppb) was associated with lower eGFR [-1.31% (95%CI: -1.68, -0.93)] after controlling for potential confounders. The association of O<sub>3</sub> with eGFR in two-pollutant models showed no marked change when PM<sub>10</sub>, NO<sub>2</sub>, SO<sub>2</sub>, and CO were added to the model. In conclusion, long-term exposure to O<sub>3</sub> was associated with the progression of kidney dysfunction in Thai adult workers.

**Cadmium exposure and risk of breast cancer: A meta-analysis from epidemiological studies**

Victor Florez\* Victor Florez Edwin Guevara Maren Hawkins Leonelo Bautista Tara Jenson Justin Yu  
Amy Kalkbrenner

**Background:** Cadmium is a heavy metal with carcinogenic properties, highly prevalent in industrialized areas worldwide. Prior reviews evaluating whether cadmium influences breast cancer have been inconclusive and not reflected several recent studies. **Objective:** To evaluate the association between cadmium exposure and female breast cancer incidence, with an emphasis on separately estimating dietary vs. airborne vs. biomarker measures of cadmium and studies published until October 2022. **Methods:** We evaluated risk of bias using set criteria and excluded one study judged to have high risk based on self-report of breast cancer and insufficient adjustment. We conducted a random effects meta-analysis of epidemiological studies, including subgroups by exposure route and by menopausal status. **Results:** A total of 17 studies were eligible for our meta-analysis. Only 2 studies addressed airborne cadmium directly. Breast cancer risk was elevated in women exposed to higher levels of cadmium across all studies – pooled odds ratio: 1.13 (95% confidence interval: 1.00, 1.28), with notable heterogeneity between studies ( $I^2=77%$ ). When examining separately by exposure route, dietary cadmium was not linked with an elevated risk – (OR: 1.05; 95%CI: 0.91, 1.21;  $I^2=69%$ ), consistent with prior reviews, but biomarker-based studies showed an elevated but non-significant pooled measure (OR: 1.37; 95%CI: 0.96, 1.94;  $I^2=84%$ ). We did not observe any clear patterns of different risk by menopausal status. **Conclusion:** Findings from our meta-analysis suggest that exposure to higher cadmium increases the risk of breast cancer in women, but with remaining questions about whether non-dietary exposure may be more risky or whether residual confounding by constituents of tobacco smoke may be at play.

**Environmental factors and their interaction with glutathione S-transferase genes in relation to blood mercury concentrations of Jamaican children** Sheikh Farzana Zaman\* Sheikh Farzana Zaman Maureen Samms-Vaughan Sepideh Saroukhani Jan Bressler Manouchehr Hessabi Megan L. Grove Sydonnie Shakspeare-Pellington Katherine A. Loveland Mohammad H. Rahbar

Mercury (Hg) is a highly toxic heavy metal, xenobiotic and known neurotoxicant that affects children's neurodevelopment. There is no safe limit for Hg exposure. Food of both animal (fish) and plant (grains and vegetable) origin are considered the key sources of environmental Hg exposure in children. We used data from 375 typically developing (TD) 2-8-year-old Jamaican children who were enrolled as controls in an age- and sex-matched case-control study in Jamaica. We explored additive and interactive associations of environmental factors and glutathione S-transferase (GST) genes in relation to blood Hg concentration (BHgC). Findings from our interactive multivariable general linear models (GLMs) showed that the child's age, consumption of saltwater fish, and string beans were significantly associated with 21%, 35%, and 17% higher mean BHgCs, respectively (all  $P \leq 0.04$ ). However, the consumption of starches (pasta, macaroni, noodles) showed an inverse association with mean BHgC (28% lower) ( $P < 0.01$ ). Additionally, we identified the *GSTP1* gene as an effect modifier for the consumption of canned fish (sardine, mackerel) in relation to BHgC using either a co-dominant or recessive genetic model (overall interaction  $P = 0.01$  and  $P < 0.01$ , respectively). In the co-dominant genetic model for the *GSTP1* Ile105Val polymorphism, we found that consumption of canned fish (sardine, mackerel) was associated with a significantly higher mean BHgC only among children with Ile/Ile (59% [Ratio of mean Hg (95% CI) = 1.59 (1.09, 2.32),  $P = 0.02$ ]) and Ile/Val (46% [Ratio of mean Hg (95% CI) = 1.46 (1.12, 1.91),  $P = 0.01$ ]) genotypes, and in the recessive genetic model for *GSTP1*, only children with Ile\* (Ile/Ile or Ile/Val) genotypes had a 50% [Ratio of mean Hg (95% CI) = 1.50 (1.20, 1.87),  $P < 0.01$ ] higher mean BHgC than children who did not consume these canned fish. Since this is the first study from Jamaica that reports these findings, replication is warranted in other countries or populations.

**Effects of Prenatal Chemical Exposures on Early Menarche: A Scoping Review of Prospective Studies** Melanie R Sandquist\* Melanie Sandquist Somdat Mahabir

Age at menarche is an important risk factor for health and disease, including breast cancer. While emerging evidence indicates that prenatal exposures to certain chemicals in the environment result in increased risk of early menarche, much remains unknown. Many of the environmental chemicals that children are exposed to prenatally are known endocrine disruptors. Since prenatal environmental exposures are an important public health concern, potentially modifiable, and offer opportunities for disease prevention, we conducted a scoping review to assess the state of the published literature. This scoping review assesses the state of epidemiologic research on prenatal chemical exposure and age at menarche. Searches conducted in PubMed, SCOPUS and Embase returned 149 papers. Based on established exclusion/inclusion criteria, we included twenty-two prospective studies in our analysis. The literature search assessed several chemical categories, such as agricultural chemicals, metals, phthalates, phenols, biphenyls, per-/polyfluoroalkyl (PFAS) substances, medications, and tobacco smoke in relation to age at menarche. Relevant information was then extracted from each study, tabulated, and synthesized. Several chemical exposures impacted age at menarche. Contraceptives, smoking, atrazine, several phenols, phenyls and PFAS were associated with early menarche. This scoping review shows that prenatal chemical exposures may have potentially harmful health effects later in life by pathways that affect age at menarche. There are large gaps in knowledge that must be filled to improve understanding of prenatal environmental chemicals as well as the mechanisms by which they affect menarche. Many of the published prospective analyses of prenatal chemical exposures and menarche are based on ancillary studies to parent cohorts. There is a need for diverse prospective pregnancy cohorts with a priori aims that address prenatal chemical exposures and their effects on the age of menarche.

**Long-term exposure to air pollution and infant mortality: a systematic review and meta-analysis** Adrien Wilkie\* Adrien Wilkie Kristen Rappazzo Alison Krajewski Fanny Njie Kevin Park Sarah Zelasky Thomas Luben

Background/Aim: Infant mortality - a common global indicator of population health - is a pressing public health concern. In this systematic review and meta-analysis, we reviewed the available literature for epidemiologic evidence of the association between long-term criteria air pollution exposure and all-cause infant mortality.

Methods: Relevant publications were identified through PubMed and Web of Science databases using comprehensive search terms then screened using predefined inclusion/exclusion criteria. We extracted data from included studies and applied a systematic rubric for evaluating study quality across domains including participant selection, outcome, exposure, confounding, analysis, selective reporting, sensitivity, and overall quality. When more than 2 eligible studies provided effect estimates, we performed meta-analyses, using both fixed and random effects methods, and estimated pooled odds ratios (ORs) and 95% confidence intervals (95%CI) for criteria pollutants (nitrogen dioxide (NO<sub>2</sub>), sulfur dioxide (SO<sub>2</sub>), coarse particulate matter (PM<sub>10</sub>), fine particulate matter (PM<sub>2.5</sub>), ozone (O<sub>3</sub>), carbon monoxide (CO)) and all-cause infant mortality.

Results: Our search returned 549 studies. We excluded 490 studies in the abstract screening phase and an additional 37 studies in the full text screening phase, leaving 22 studies for inclusion. Among these 22 studies, 7 included extractable effect estimates for PM<sub>2.5</sub>, 5 for PM<sub>10</sub>, and 3 for CO. We could not conduct meta-analyses for O<sub>3</sub>, NO<sub>2</sub>, or SO<sub>2</sub> because each had 2 eligible studies with extractable effect estimates. The pooled OR (95%CI) for a 5-µg/m<sup>3</sup> increase in PM<sub>2.5</sub> concentration was 1.52 (95%CI: 0.54, 4.22), for a 1-ppm increase in CO concentration was 1.07 (95%CI: 1.00, 1.14), and for a 5-µg/m<sup>3</sup> increase in PM<sub>10</sub> concentration was 1.04 (95%CI: 1.03, 1.06).

Conclusions: We identified long-term exposures to two criteria pollutants - CO and PM<sub>10</sub> - are associated with all-cause infant mortality across studies.

**The Association Between Urban Heat and Crime in the United States: A Systematic Review**

Alexander Azan\* Alexander Azan Jin Choi Byoungjun Kim

**Background:** The root causes of urban crime are structural. Neighborhood disinvestments, such as poor housing stock and lack of green space, are associated with stress-responsive behaviors, such as crime. These same environmental conditions absorb and re-emit solar energy at high levels, disproportionately exposing disinvested communities to extreme urban heat. Global studies have demonstrated various relationships between heat exposure and urban crime, with few studies based in the United States (U.S.). This systematic review aims to summarize current evidence from cities in the U.S.

**Methods:** We used PRISMA guidelines to review empirical studies examining the association between urban heat exposure and crime in the U.S. between January 2000 and December 2022. We examined the comparability of study designs, geographic and temporal units of analysis, definitions and operationalization of urban heat exposure and crime variables, covariate selection, statistical analyses, study results, and interpretive framing.

**Results:** Fifteen studies met our inclusion criteria. All but one study found positive associations between exposure to high temperature and various types of crime at the city-level. The majority of studies reported a linear relationship between temperature and crime, except for two studies, which found curvilinear, inverted U-shaped relationships. Only two studies framed the interpretation of results within an environmental justice framework.

**Conclusions:** A small number of studies have demonstrated a positive association between heat exposure and urban crime in the U.S. This literature is composed of varied statistical approaches, has limited spatial granularity, and lacks the integration of justice-oriented frameworks. Further study of this relationship is essential to informing climate resiliency planning efforts. Integrating environmental justice frameworks in future research will help ensure related policies are community-centered and equitable.

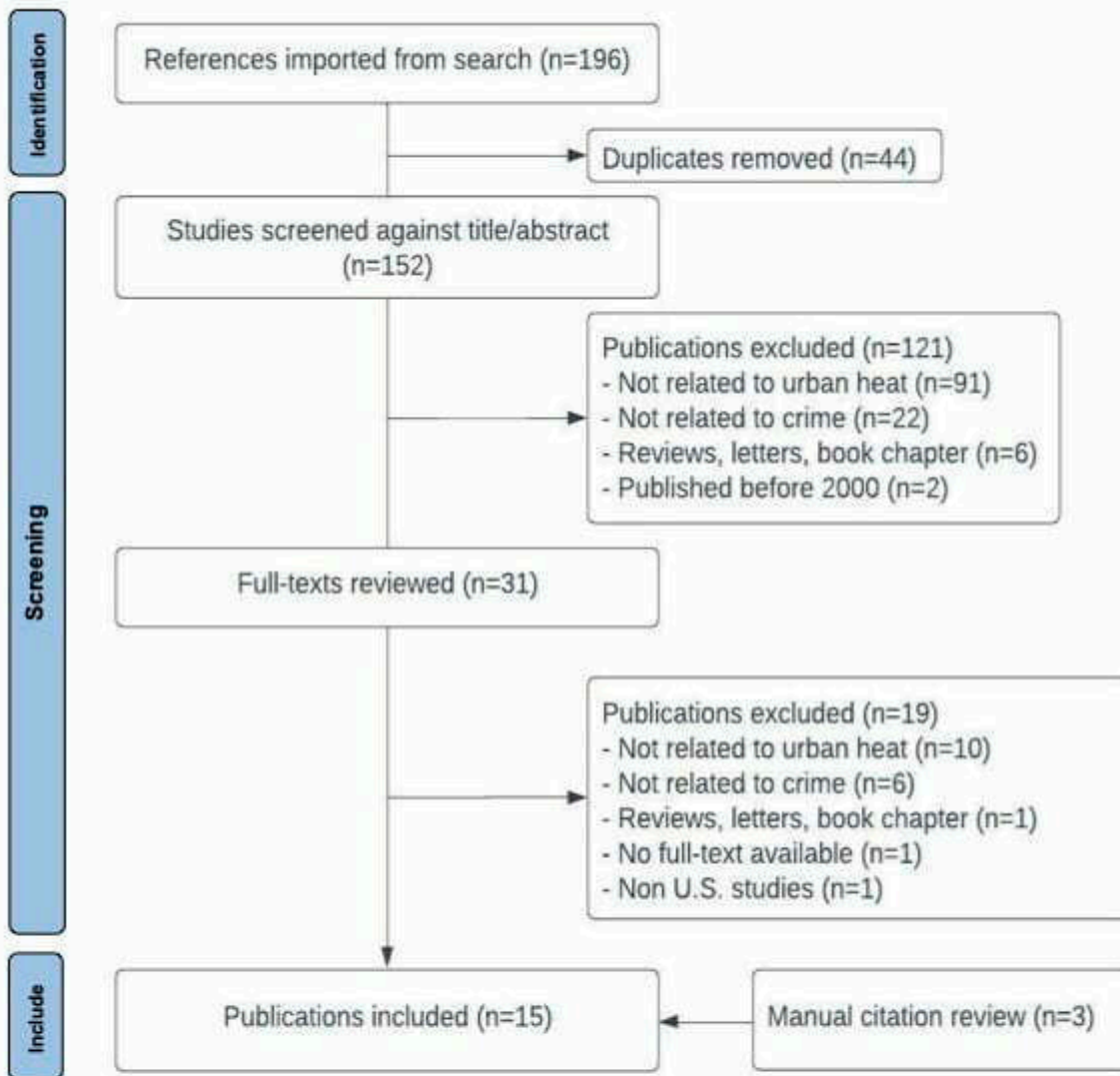


Figure 1. PRISMA flow diagram.

**Racialized experience, biomarkers of lead exposure, and later-life cognition: a mediation analysis** Tara Jenson\* Tara Jenson Amy E. Kalkbrenner Kelly Bakulski Linda Wesp Ira Driscoll Keith Dookeran

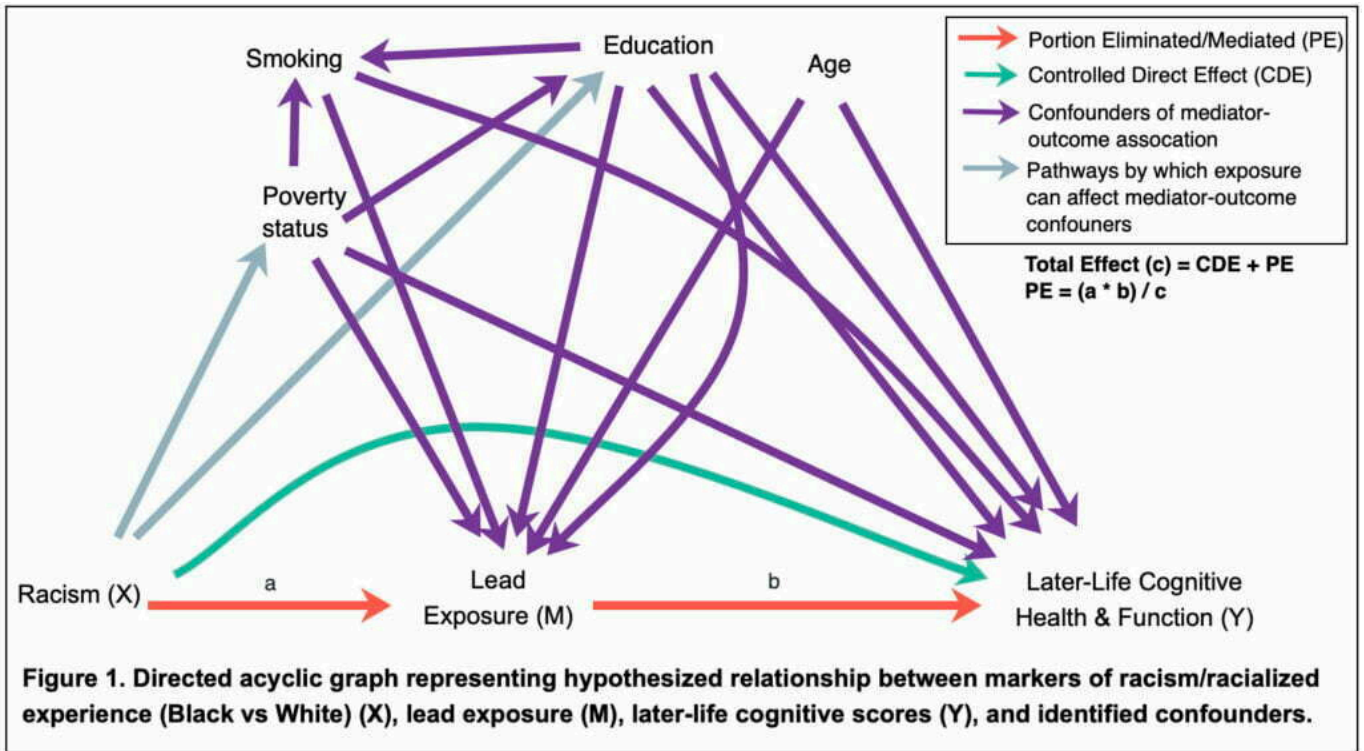
**Background:** Racial disparities in environmental lead (Pb) exposure and later-life cognition are well documented. We evaluated the portion of later-life cognitive deficit for persons of Black race, a marker of racialized experience, that may be mediated by higher exposures to neurotoxicant Pb.

**Methods:** We included NHANES participants (1999-2002, 2011-2014) 60+ years of age, randomly sampled for blood collection, identifying as non-Hispanic Black (N=1,085) or White (N=2,839). To reflect long-term Pb exposure, we estimated patella bone Pb levels via previously established predictive models using blood Pb (mean 2.5 ug/dL, st. dev 2.3) and demographics. Concurrent cognition (processing speed, sustained attention, working memory) was measured by Digit Symbol Substitution Test (DSST) and standardized. We used multiple imputation to recapture persons with missing data (N=833). We used Baron and Kenny's mediation model to conduct separate linear regressions adjusted for NHANES cycle and sampling weights to evaluate total and partitioned associations (Fig. 1). To obtain portion mediated, we divided the product of regression coefficients for race on Pb (+1.7  $\mu\text{g}$  Pb per g bone higher for Black race, 95% CI: 0.91, 2.57) and Pb on DSST adjusted for race, and additionally adjusted for confounders age, education, poverty income ratio, and smoking status (-0.12 DSST z-score per 10 ug/g increase in Pb, 95% CI: -0.22, -0.02) by total association of Black race on DSST: -0.87 z-score.

**Results:** Of the association of Black race on DSST (about a 16-point decrement), we observed that 2.4% was mediated directly through patella Pb levels.

**Discussion:** We demonstrate a mediation analysis where confounder adjustment is limited to the mediator-outcome path. We report that avoidable lead exposure driven by environmental injustice is one avenue by which later-life cognitive health disparities may be impacted, noting that a large proportion of the pathway of systemic racism harming cognition remains.





**Prenatal exposure to particulate matter and birthweight in the Upstate KIDS cohort** Ian Trees\* Ian Trees

**Background:** Air pollution has been associated with adverse perinatal outcomes. This study explores how prenatal exposure to particulate matter (PM) at different time windows during pregnancy impacts birthweight.

**Methods:** We included 4,959 mother-infant pairs from the Upstate KIDS cohort born in New York State. Air pollution data were gathered from the EPA's Community Multiscale Air Quality model and matched to home addresses at the census tract level. Birthweight and gestational age were gathered from vital records. We ran multiple linear regressions adjusting for maternal socio-demographics, traffic-related pollutants (O<sub>3</sub>, NO, and SO<sub>2</sub>), infant sex, plurality, and seasonality.

**Results:** Participants were exposed to relatively low levels of PM during pregnancy (median PM<sub>2.5</sub>: 5.89 µg/m<sup>3</sup>, median PM<sub>10</sub>: 8.14 µg/m<sup>3</sup>). Nevertheless, higher PM exposure across virtually all windows of pregnancy was associated with lower birthweight in unadjusted models (**Table**). After controlling for traffic co-pollutants (Model 2), PM<sub>2.5</sub> and PM<sub>10</sub> exposure around conception and during the 3rd trimester remained associated with lower birthweight, as did PM<sub>10</sub> around delivery. However, further accounting for maternal and infant characteristics attenuated associations for the peri-conception window, while PM<sub>10</sub> exposure during the 3rd trimester (-45.0g; 95% CI: -79.4, -10.7) and around delivery (-25.5g; 95% CI: -45.8, -5.3) remained associated with lower birthweight. PM exposure was not associated with gestational age in fully adjusted models, suggesting that at least some birthweight results were not due to changes in gestational age.

**Conclusion:** Prenatal exposure to PM may impact birthweight depending on other pollutants and specific windows of exposure. Prenatal exposure to PM during specific pregnancy windows, particularly later in pregnancy, requires further research. In addition, studies using more precise exposure assessment methods and looking at a wider range of pollutants are necessary.

**Table** Linear regression results for the impact of prenatal exposure to PM<sub>2.5</sub> and PM<sub>10</sub> on infant birthweight in grams

Exposure Window	Pollutant	IQR $\mu\text{g}/\text{cm}^3$	IQR Effect	95% CI	p-value	IQR Effect	95% CI	p-value	IQR Effect	95% CI	p-value
14 days post-conception	PM <sub>2.5</sub>	3.80	-33.8	-58.4, -9.3	0.007	-40.8	-78.1, -3.5	0.032	-3.9	-35.2, 27.3	0.805
	PM <sub>10</sub>	4.98	-31.8	-56.1, -7.4	0.011	-32.9	-66.4, 0.6	0.054	-7.4	-35.5, 20.7	0.606
Trimester 1	PM <sub>2.5</sub>	2.67	-26.6	-52.4, -0.8	0.041	-19.8	-64.3, 24.7	0.384	-9.9	-46.9, 27.2	0.601
	PM <sub>10</sub>	4.98	-40.7	-75.5, -6.0	0.022	-37.1	-89.7, 15.5	0.167	-30.8	-76.4, 14.8	0.185
Trimester 2	PM <sub>2.5</sub>	2.61	-31.5	-57.0, -5.9	0.016	-24.5	-69.5, 20.4	0.285	-8.8	-46.3, 28.6	0.643
	PM <sub>10</sub>	3.68	-34.8	-60.3, -9.2	0.008	-26.0	-65.7, 13.7	0.200	-11.4	-45.6, 22.8	0.514
Trimester 3	PM <sub>2.5</sub>	2.58	-32.6	-58.1, -7.2	0.012	-52.5	-96.9, -8.0	0.021	-31.9	-68.8, 5.1	0.091
	PM <sub>10</sub>	3.59	-51.3	-77.0, -25.7	<0.001	-76.0	-115.7, -36.3	<0.001	-45.0	-79.4, -10.7	0.010
14 days pre-birth	PM <sub>2.5</sub>	3.48	-17.0	-41.2, 7.1	0.167	-25.5	-59.8, 8.9	0.146	-21.0	-49.3, 7.3	0.146
	PM <sub>10</sub>	3.55	-27.6	-46.4, -8.7	0.004	-38.6	-62.6, -14.5	0.002	-25.5	-45.8, -5.3	0.014
Whole Pregnancy	PM <sub>2.5</sub>	2.43	-35.3	-62.0, -8.7	0.009	-19.5	-75.0, 36.0	0.492	-2.8	-49.2, 43.6	0.906
	PM <sub>10</sub>	4.78	-58.9	-95.1, -22.7	0.001	-49.9	-118.7, 18.8	0.155	-24.9	-83.5, 33.8	0.407

\*Model 1 did not control for any variables

\*\*Model 2 adjusted for O<sub>3</sub> + NO + SO<sub>2</sub> in each respective exposure window

\*\*\*Model 3 further adjusted for maternal age, race, education, and smoking status; private insurance status; infant plurality and sex; and seasonality

Each model was run separately for each of the six exposure windows

**LATEBREAKER**

Environment/Climate Change

**Migraines and air pollution: Validating the use of migraine smartphone app records compared to emergency room discharge data for environmental exposures and transient health outcomes** Andrea Portt\* Andrea Portt Dr. Hong Chen Dr. Erjia Ge Dr. Christine Lay Dr. Peter Smith

**Background:** Migraine is a chronic, debilitating neurologic condition affecting more than 1 billion people worldwide. Migraine attacks cause headache, nausea, and sensitivity to light and/or sound. Migraine is the second leading cause of years lived with disability. Although migraine-specific drugs exist, they are expensive, under-prescribed, and can have challenging side effects. Therefore, many migraine patients are left to avoid situations, foods, drinks, and odours that trigger attacks in order to manage their condition.

Environmental exposures including air pollution are a timely concern for many health conditions. Despite this and the prevalence and impact of migraine, little is known about pollution triggers for migraine. Existing literature suggests that particulate matter 2.5 or less microns in diameter (PM<sub>2.5</sub>), ozone (O<sub>3</sub>) and nitrogen dioxide (NO<sub>2</sub>) may all precipitate attacks. However, outcome measures have generally been limited to single pollution exposures and administrative data such as emergency room (ER) visit data. As an additional challenge, the interplay between multiple air pollutants is difficult to model with administrative data and existing analytic methods.

**Methods:** Fortunately, modern data sources and analytic methods are available. Migraine Buddy is a well-established smartphone app with approximately 3 million users worldwide. Users who consent to share their data donate a wealth of individual-level, longitudinal, repeated-event data. The case time series is a newly developed modeling technique that harnesses longitudinal individual-level data in relation to environmental exposures. This method allows for simultaneous modelling of multiple exposures more readily than previous methods.

**Objectives:** To compare the association between mean ambient NO<sub>2</sub>, PM<sub>2.5</sub> and 8-hour maximum O<sub>3</sub>, and ER visits vs smartphone app records for migraine. We expect the richness of the Migraine Buddy data and the analytic strength of the case time series method to yield new insights into the effects of multiple air pollutants on migraine. Our overarching goal is to validate the use of self-reported smartphone app data compared to administrative data in the context of environmental exposures and health outcomes.

**Results:** Analyses will be conducted in early 2023 and results will be discussed.

**Association of traffic-related air pollutant exposures with cognitive decline and incident Alzheimer's dementia in the Chicago Health and Aging Project**

Ryan M. Andrews\* Ryan Andrews Sara D. Adar Adam A. Szpiro Joel D. Kaufman Cami C. Christopher Todd Beck Kumar B. Rajan Klodian Dhana Denis Evans Jennifer Weuve

**Background:** Epidemiologic evidence suggests that long-term exposure to traffic-related air pollution may increase the risk of adverse cognitive outcomes. This study examined associations between tailpipe-related (oxides of nitrogen and nitrogen dioxide) and non-tailpipe-related (coarse particulate matter copper and zinc) air pollutants and cognitive decline and dementia.

**Methods:** Study data came from the Chicago Health and Aging Project (CHAP; N=7,638), a population-based cohort of older adults that collected data triennially over six study waves from 1993-2012, including cognitive test scores, clinically diagnosed dementia, and residential locations for baseline exposure to air pollution. Using generalized estimating equations, we estimated adjusted associations of air pollutants with cognitive decline and incident dementia. All models incorporated weights to address post-enrollment attrition bias. We also conducted analyses with CHAP-inspired simulation data to explore the potential influence of pre-enrollment survivorship bias on our results.

**Results:** Overall, we found limited evidence of associations between air pollutant exposures and cognitive decline or incident dementia. The strongest observed association was between oxides of nitrogen and incident dementia (OR per 1 SD = 1.24, 95% CI: 1.00, 1.66). Our simulations suggest that survivorship bias may have influenced our results, under the plausible assumptions that (1) air pollution exposure negatively affects cognition, (2) air pollution exposure decreases one's probability of surviving long enough to enroll in CHAP, and (3) individuals who are more susceptible to air pollution's effects on mortality are also more susceptible to its effects on cognition.

**Discussion:** In this prospective cohort study, we found few adverse associations between traffic-related air pollutant exposure and cognitive decline or incident dementia. However, survivorship bias may have impeded our ability to detect these associations.

**Ambient fine particulate matter exposure and risk of non-Hodgkin lymphoma in the NIH-AARP Diet and Health Study** Jared Fisher\* Jared Fisher Xiuqi Ma Linda M. Liao Joel D. Kaufman Debra Silverman Rena Jones

**Background:** Particulate and dust exposure has been associated with non-Hodgkin lymphoma (NHL) in occupational settings, but studies of ambient PM<sub>2.5</sub> are scarce. We aimed to investigate this association for the first time by histologic subtype.

**Methods:** We estimated outdoor PM<sub>2.5</sub> concentrations at the residential enrollment (1995-1996) address for 451,202 participants of the NIH-AARP Diet and Health Study, a cohort located in 6 states (California, Florida, Louisiana, New Jersey, North Carolina, and Pennsylvania) and 2 metropolitan areas (Atlanta, Georgia, and Detroit, Michigan). We used annual estimates from a national spatiotemporal model to assess PM<sub>2.5</sub> concentrations for a 5-year pre-enrollment period (1990-1994). We used Cox regression to estimate associations (hazard ratio, HR; 95% confidence interval, 95%CI) with NHL and major histologic subtypes per interquartile range (IQR; 4.4µg/m<sup>3</sup>) increase in PM<sub>2.5</sub>, adjusting for demographic characteristics, body mass index (BMI), smoking status and intensity, and census-tract median household income. We also examined models stratified by BMI and state.

**Results:** There were 6,466 incident cases of NHL diagnosed through 2011. We found a positive and statistically significant association with follicular lymphoma (HR<sub>IQR</sub>=1.16; 95%CI=1.02-1.31; 788 cases); associations for other subtypes were not apparent. An overall NHL association was not apparent (HR<sub>IQR</sub>=0.99; 95%CI=0.95-1.04), and no differences were observed by BMI (*p*-int >0.05). NHL risk was significantly elevated with PM<sub>2.5</sub> levels in Pennsylvania (HR<sub>IQR</sub>=1.28; 95%CI=1.06-1.54), but a test for interaction by state was not significant (*p*-int>0.05).

**Conclusions:** Our findings from this large U.S. cohort indicate that PM<sub>2.5</sub> may be associated with risk of follicular lymphoma. Future investigations of NHL and PM<sub>2.5</sub> should consider histologic subtypes and examine whether differences in regional PM constituency influence risk.

**The role of C-reactive protein in the associations between urinary benzene and ethylbenzene concentrations and mortality among US adults** Nasser Laouali\* Nasser Laouali  
Tarik Benmarhnia Youssef Oulhote

**Background:** Chronic exposure to volatile organic compounds (VOCs) has been consistently associated with an excess risk of premature mortality. Oxidative stress and inflammation have been hypothesized to partially explain such relationships. However, empirical evidence quantifying the mediating role of such biomarkers is not available at the population level. The present study examines the associations between exposure to benzene and ethylbenzene, and mortality, and the extent to which inflammation-biomarkers may mediate these associations.

**Methods:** We used data on 532 adults aged  $\geq 20$  years enrolled in the NHANES-III between 1988 and 1994 and followed up through Dec 31, 2015. Urinary concentrations of benzene and ethylbenzene were measured using ultra-performance liquid chromatography, and mortality was determined from the National Death Index records. Serum concentrations of C-reactive protein (CRP) were measured in blood samples. We used a causal mediation analysis with Aalen additive hazards models to decompose the total effect of VOCs on all-cause, cardiovascular, and cancer mortality into natural direct and indirect (through CRP levels) effects while controlling for a priori-defined confounders. 10,000 iterations were performed for bootstrapping the hazard rate difference and 95% confidence intervals. We also estimated the proportion mediated.

**Results:** Median follow-up was 22.5 years, and 105 participants died (13 from cardiovascular diseases, and 24 from cancer). Each unit increase in benzene concentrations was associated with excess deaths from all-cause (250.1 per 10000 person-year [95% CI 102.5 to 426.2]), and cancer (179.8 per 10000 person-year [95% CI 37.4 to 357.2]). The corresponding excesses that can be attributed to subsequent increases in CRP were 1.6 per 10000 person-year [95% CI -6.7 to 17.4] and 0.9 per 10000 person-year [95% CI -2.1 to 8.1], and the proportions mediated were (95% CI -1.3% to 13.7%) for all-cause and cancer mortality, respectively. We did not identify an association for cardiovascular mortality (5.0 per 10000 person-year [95% CI -56.9 to 99.2]). For the exposure to ethylbenzene, we observed similar patterns but the estimates were less statistically precise.

**Conclusion:** Our findings confirm the harmful effects of VOCs on premature mortality, however, they do not support the hypothesis that inflammation as measured by circulating CRP levels mediates this relationship.

**Improving the integration of epidemiological data into human health risk assessment: What risk assessors told us they need** Ali Hamade\* Sandrine Deglin Raghavendhran Avanasig Igor Burstyn Denali Boon Matthew Gribble Ali Hamade Mark Johnson David Miller Jennifer Reed

Environmental epidemiology has proven critical to study potential associations between environmental exposures and adverse human health effects. However, there is a perception that it does not always sufficiently inform risk assessment or is not always reliable. To help address this concern, the Health and Environmental Sciences Institute initiated a project in 2017 that engaged the epidemiology, toxicology, exposure science, and risk assessment communities. This included representation from government agencies, industry, and academia in a dialogue on the use of environmental epidemiology for quantitative risk assessment.

As part of this project, in 2022, the committee initiated a survey of toxicologists and risk assessors regarding their use of epidemiology, and how it might be better integrated into the derivation of hazard thresholds (e.g., reference doses). To better understand the practical needs risk assessors/toxicologists may have regarding epidemiology, we explored the perceived relative value of epidemiology studies for the derivation of these benchmarks and what might help make epidemiology data more useful. The survey is ongoing and more responses are anticipated.

Preliminary analyses of the 38 responses collected by January 5, 2023 are summarized. Most respondents have used or considered using epidemiology in risk assessment. Responses came from 12 countries (but mostly the US) and most respondents were employees of government agencies (47%). Furthermore, survey data revealed that were lacking in many epidemiological studies and improvements in this area were most valued (45%). This was followed by wishes for a (18%) and increased transparency of study protocols and data reporting (10%). Almost all respondents indicated that epidemiology has the potential to play a more prominent role in hazard benchmark derivation. We will also provide an analysis of the responses according to activity sectors and training histories. A detailed thematic analysis of "rare" requests will be undertaken to ensure that a full breadth of views is captured. Based on the insights into wishes of risk assessors/toxicologists, we will propose actionable steps aimed at better realizing the full potential of human data in risk assessment.



**A causal association between HbA1c levels and NAFLD development? A Mendelian randomization analysis approach** Hye Ah Lee\* Hye Ah Lee Hyesook Park Bomi Park

The causal direction of the association between impaired glucose status and nonalcoholic fatty liver disease (NAFLD) risk remains questionable, as given studies reported a bidirectional association. Therefore, using Korean Genome and Epidemiology Study (KoGES) cohort data (16-year follow-up), we assessed the causal effect of HbA1c predicted by genetic instruments on the incident NAFLD risk using Mendelian randomization (MR) analysis. From previous studies, including a meta-analysis of genome-wide association studies, 25 genetic variants associated with hemoglobin A1c (HbA1c) were selected and a weighted genetic risk score (GRS) was calculated. Incident NAFLD was assessed based on a hepatic steatosis index (HSI)  $\geq 36$ . This study included 5322 subjects (50.0% male). The causal effect of the MR analysis was expressed as a Wald ratio. As a sensitivity analysis, individual single nucleotide polymorphisms (SNPs) were evaluated using an inverse-variance weighted (IVW) method, MR-Egger method, and the Mendelian randomization pleiotropy residual sum and outlier (MR-PRESSO) test. During the 16-year follow-up, the cumulative incidence of NAFLD was 28.3%. A weighted GRS for 25 HbA1c-related SNPs showed a null association with incident NAFLD (Wald ratio = 0.186, 95% CI: -0.494, 0.865). An unweighted GRS gave similar results (Wald ratio = 0.190, 95% CI: -0.545, 0.925). Of the 25 SNPs, only rs174570 of *FADS2* was significantly associated with incident NAFLD (Wald ratio = 2.641, 95% CI: 0.729, 4.552). In addition, causal estimates of individual SNPs synthesized using the IVW and MR-egger methods showed no causal association. Horizontal pleiotropy was not detected in the MR-PRESSO test. The average HSI during the follow-up period did not differ significantly across the quartiles of weighted GRS ( $P = 0.516$ ). The MR results did not support a causal relationship between the genetically determined HbA1c level and incident NAFLD risk.

**Funding:** This work was supported by the National Research Foundation of Korea (NRF) grant funded by the Korea government (MSIT) (No. 2021R1A2C1003176).

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**LATEBREAKER**

Genetics

**Feasibility of a Traceback Approach to Facilitate Genetic Testing in the Genetic Risk Analysis in Ovarian Cancer (GRACE) Study** Sheila Weinmann\* Sheila Weinmann Jessica Ezzell Hunter Yolanda K Prado Tia Kauffman Ana A. Reyes Jamilyn M. Zepp Mahesh Maiyani Jennifer Sawyer Larissa Lee White Sarah Vertrees Alan F. Rope Sheila Weinmann Nora B. Hendrikson Sandra Soo-Jin Lee Heather Spencer Feigelson

**Introduction:** Individuals with a prior ovarian cancer diagnosis who have not received genetic testing represent missed opportunities to identify families with inherited high risk cancer variants. Using a novel “traceback testing” approach, the Genetic Risk Assessment in Ovarian Cancer (GRACE) study aims to address this significant healthcare gap by identifying these individuals and offering genetic risk information to them and their family members.

**Methods:** Tumor registry and electronic medical record (EMR) data at two integrated health care systems (Kaiser Permanente Northwest and Kaiser Permanente Colorado) were used to identify survivors of ovarian cancer diagnosed from 1998 to 2020 who either did not receive genetic testing or had genetic testing limited to *BRCA1* and *BRCA2* and could benefit from testing using a comprehensive panel of cancer risk genes. Individuals were contacted and offered testing; subsequent genetic testing of the familial variant was offered to first- and second-degree relatives if a pathogenic or likely pathogenic variant was detected.

**Results:** Of the 317 living individuals eligible for recruitment, 10 (3%) had invalid contact information, 136 (43%) were considered “passive decliners” after multiple contact attempts, 16 (5%) were on hospice or had evidence of cognitive decline (personal representatives of these individuals will be contacted for recruitment later), 76 (24%) were contacted and declined participation, and 79 (25%) were contacted and consented for testing. Sixteen of the 79 individuals who enrolled (21%) were found to carry a pathogenic or likely pathogenic variant in a cancer risk gene. Of the 79 at-risk relatives eligible for cascade testing, 20 underwent genetic testing (25% cascade testing uptake) of which nine were found to carry the familial variant. Interestingly, though we expected enrollment to be higher among survivors with more recent cancer diagnoses, years since diagnosis and rate of consent were not significantly associated.

**Conclusions:** Overall, these findings indicate the promise of traceback testing to provide potentially life-saving information to individuals and their family members at increased genetic risk for cancer who may otherwise be missed. Subsequent analyses will include findings from outreach to relatives of deceased individuals.

**LATEBREAKER**

Global Health

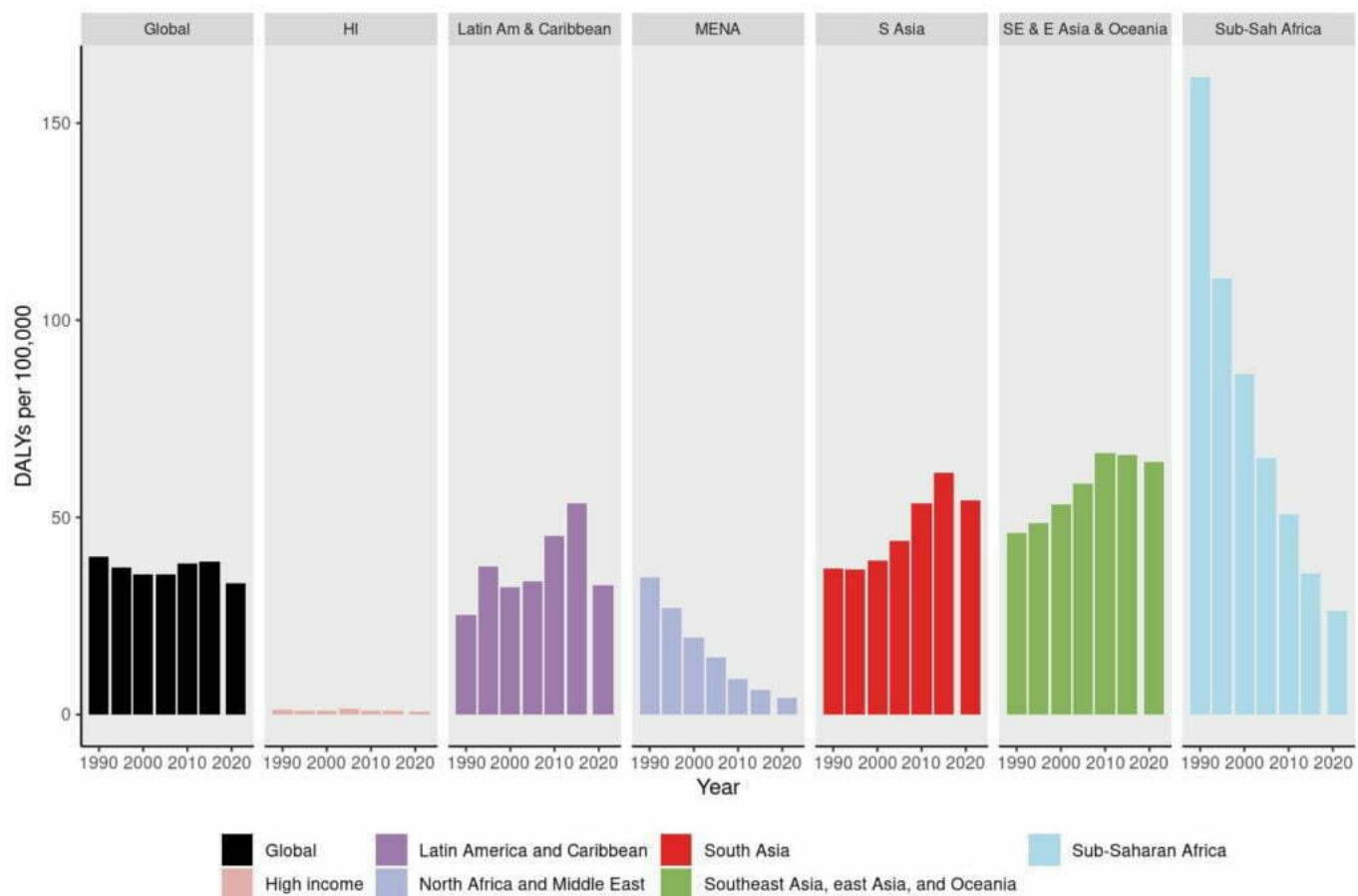
**The global burden of arboviral diseases (Dengue, Yellow Fever, and Zika virus): analysis for the Global Burden of Disease Study 2021** Ewerton Cousin\* Ewerton Cousin Cathleen Keller Taren Gorman Olivia Nesbit Lydia Plante Joanna Whisnant Stephanie R. M. Zimsen Quince Hara Jonathan Mosser

Arboviral diseases are caused by arthropod vectors, predominantly mosquitos. Dengue, yellow fever (YF), and Zika virus are among the most prevalent of these diseases and can lead to epidemics. Many arboviral diseases are endemic in low-and-middle-income countries (LMICs). We aim to describe the global burden of three arboviral diseases included in the Global Burden of Disease (GBD) study (dengue, YF, and Zika virus) and their trends from 1990 to 2021.

We estimated separately the burden of each disease. To model the fatal burden, we either used vital registration and verbal autopsy as input data and ran cause-of-death ensemble models or used case-fatality ratio models. For the non-fatal burden, we used case reports, surveillance data, and surveys and ran spatiotemporal Gaussian process regression and mixed-effects negative binomial models. Disability Adjusted Life Years (DALYs) were calculated as the sum of Years of Life Lost and Years Lived with Disability.

We present here preliminary results of the GBD 2021. There were 33.0 ([95%UI] 17.6 to 48.0) age-standardized DALYs per 100,000 due to dengue, YF, and Zika virus in 2021, a 16.8% (-54.6% to 32.3%) decrease compared to 1990. Age-standardized DALYs rate had the largest decrease in Sub-Saharan Africa and North Africa and Middle East, and the largest increase in South Asia. Of the total fraction of the burden, 39% was in South Asia, 37.4% in Southeast Asia, East Asia, and Oceania, and 14.3% in Sub-Saharan Africa. The YF age-standardized DALYs rate decreased by 73.4% (66.8% to 79.5%) since 1990. However, dengue increased by 27.8% (-39.5% to 80.0%) in the same period.

Arboviral diseases are still an important cause of burden in LMICs. Even with the decrease in the YF burden, the expansion of dengue and Zika virus make these causes a public health threat. Actions for vector control, vaccines, prevention programs, and adequate and prompt health care would be extremely important to reduce this burden.



**Spatial diarrheal disease risks and antibiogram diversity of diarrheogenic *Escherichia coli* in selected access dams of a notable freshwater resource in the Eastern Cape Province, South Africa: Implications for public health** Chidozie Declan Iwu\* Chidozie Declan Iwu

Nolonwabo Nontongana Chinwe Juliana Iwu-Jaja Brilliance Onyinyechi Anyanwu Anthony Ifeanyin Okoh

**Introduction:** Freshwater sources, often used for domestic and agricultural purposes in low- and middle-income countries are repositories of clinically and epidemiologically significant bacterial pathogens. These pathogens are usually diversified in their antibiogram profiles posing global health threats. This cross-sectional study evaluated the spatial diarrhoeal disease risk and antibiogram diversity of diarrheogenic *Escherichia coli* (DEC) recovered from four access dams of the Buffalo River, Eastern Cape Province, South Africa.

**Methods:** The DEC (n=180) and their antibiogram profiles were characterized using standard microbiological and molecular methods. The diarrhoeal disease risk attributed to the DEC was estimated using the Quantitative Microbial Risk Assessment and Monte Carlo simulation with 10,000 iterations. The antibiogram diversity of the DEC was assessed using the Whittaker's single alpha-diversity modelling.

**Results:** A high diarrhoeal disease risk of  $25.0 \times 10^{-2}$  exceeding the World Health Organization's standard was recorded across the study sites. The average Single and Multiple Antimicrobial Resistance Indices of the DEC were highest in the Eluxolzwi dam [SARI:0.52 (SD: 0.25, 95% CI: 0.37 to 0.67)] and King William's Town dam [MARI: 0.42 (SD: 0.25, 95% CI: 0.27 to 0.57)] respectively. The prevalent antibiotic resistance genes detected were *tetA*, *bla*<sub>FOX</sub> and *bla*<sub>MOX</sub> plasmid-mediated *AmpC*, *bla*<sub>TEM</sub> and *bla*<sub>SHV</sub> extended-spectrum  $\beta$ -lactamases, which co-occurred across the study sites on network analysis. At least, three phylogenetic clades of the DEC with initial steep descent alpha-diversity curves for most of the test antimicrobials were observed across the study sites, indicating high diversity.

**Conclusion:** The occurrence of diversified multi drug resistant DEC with diarrhoeal disease risks in the Buffalo River substantiates the role freshwater sources play in the dissemination of drug-resistant bacterial pathogens with public health implications.

**Poly-substance use, treatment completion, and contact with the justice system: a multistate analysis of treatments for substance use disorders between 2010-2019, Chile**

Andrés González-Santa Cruz\* Andrés González-Santa Cruz Mariel Mateo Pinones Álvaro Castillo-Carniglia

**Background:** Substance use can affect health and multiple social dimensions, including criminal behaviors and the likelihood of contacting the criminal justice system. We aim to estimate the effects of polysubstance use at baseline (vs single substance use) on the probabilities of completing baseline drug treatment(i) and contacting the criminal justice system after treatment(ii), using multistate survival models at 1, 3 and 5-years follow-ups.

**Methods:** We used a population-based record-linkage retrospective cohort, merging records of adults in publicly funded Chilean SUTs programs with the Prosecutor's Office (PO) data of offenses at the national level between 2010-2019. Patients were weighted by the inverse probability of polysubstance use based on several predictors; Weights were truncated at the 1st and 99th percentiles. We then calculated Aalen-Johansen estimator for transition probabilities(Figure 1, Panel A). Codes and markdowns are available at [bit.ly/3w9wygJ](https://bit.ly/3w9wygJ).

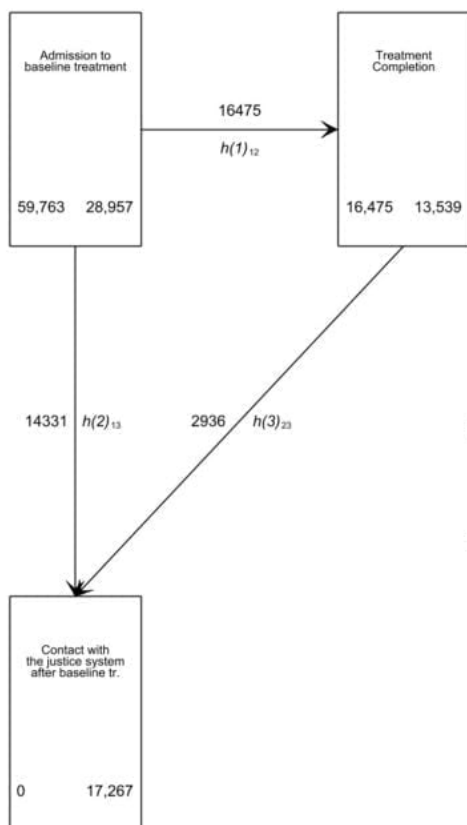
**Results:** Of the 85,048 SUT patients with one or more treatments between 2010-2019, 70,863(83%) were eligible to be matched with PO data. Of the sample, 19,276(27%) completed baseline treatment, and 22,287 (31%) had contact with the justice system.

The weighted sample had 59,763 patients with 16,475(28%) complete treatments and 17,267(29%) with at least one contact with the justice system(Figure 1, Panel B).

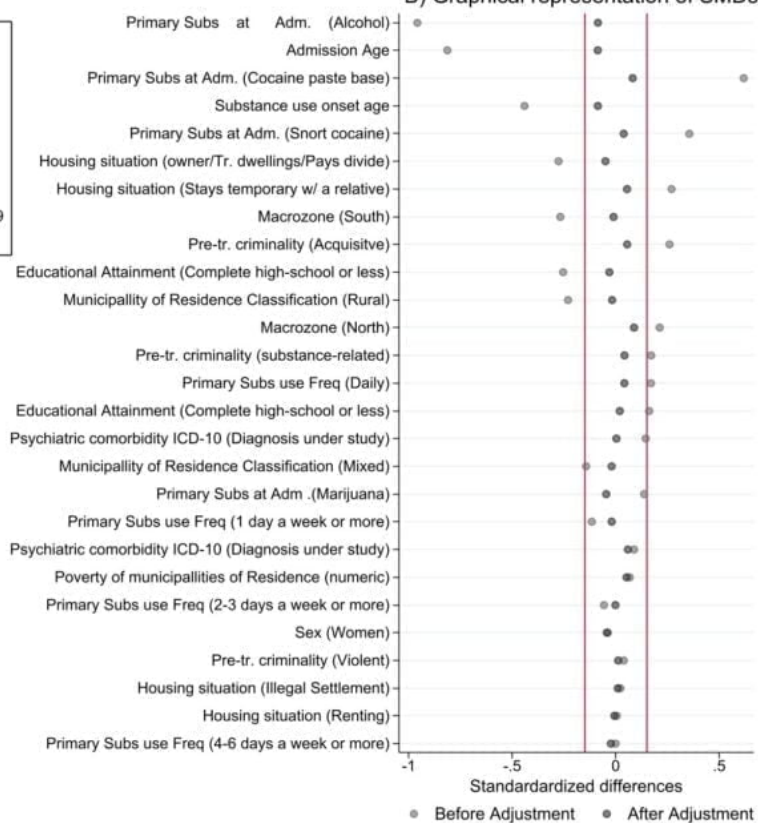
The lowest differences were at one year. People with polysubstance use had lower likelihoods of treatment completion(14.4% 95% CI 14.1%, 14.6%) than people with single substance use(17.2% 95% CI 16.9%, 17.6%). Polysubstance users had greater likelihoods of contact with the justice system(incomplete: 7.5% 95% CI 7.3%, 7.8%; complete: 8.5% 95% CI 7.4%, 9.6%) than single-substance users(incomplete: 6.4% 95% CI 6.2%, 6.6%; complete; 4.5% 95% CI 3.9%, 5.2%).

**Conclusions:** People with polysubstance use had lower probabilities of completing baseline treatment and were more likely to contact the justice system.

A) Multistate scheme



B) Graphical representation of SMDs



Note: Red lines depict standardized differences of -0.15 and +0.15

## **Development and Validation of Rapid Culture-based Detection Methods of Enteric Bacterial Pathogens from Soil** Alexis Kapanka\* Alexis Kapanka Megan

Globally, 1.6 million people die from diarrheal disease each year, with one in ten deaths of the under-five group caused by enteric pathogens. Soil is an important fomite for this age, as it provides a linkage between fecal deposits containing various pathogen species in the open environment and contamination of household water supplies, hands, objects, and food that can be directly consumed by young children. No standardized protocol exists for soil detection and quantification of enteric pathogens. We aimed to develop and validate a protocol for rapid, simultaneous detection of the most common diarrheal bacteria, *Salmonella enterica*, *Shigella spp.*, *Listeria monocytogenes*, *Campylobacter jejuni*, and *Escherichia coli* from soil. We evaluated the detection of these pathogens by manipulating soil quantity and sterility, pathogen concentration ( $10^1$  to  $10^4$  cfu/gram), length of primary enrichment time, and secondary enrichment conditions. Our protocol yielded simultaneous multiple pathogen recovery with a 15hr universal primary enrichment and 5hr secondary enrichment using pathogen specific secondary selective enrichment broths followed by selective plating. *E. coli*, *L. monocytogenes*, and *C. jejuni* were recovered in all samples at  $10^1$  cfu/gram in .25, 2.5, and 25-grams in both environmental and sterile soil. *S. enterica* was recovered at  $10^3$  cfu/gram in all soil volumes and sterilities. Microbial validation of species recovery confirmed these results in *E. coli* and *S. enterica*, and is still undergoing for *L. monocytogenes*, and *C. jejuni*. Only *Shigella spp.* had unreliable recovery in all concentrations and soil samples using this protocol for simultaneous detection. Overall, we developed a novel protocol for the rapid, simultaneous, and quantitative detection of *S. enterica*, *L. monocytogenes*, *C. jejuni*, and *E. coli* from soil, which is currently being used to study routes of community transmission in children under five within Kenya.



**Racial Disparities Among Mpox Cases and Vaccinations in Tennessee** Caleb Wiedeman\*  
Jennifer Wang Caleb Wiedeman

**Background:** The Centers for Disease Control and Prevention has reported ~30,000 confirmed cases of mpox and 19 deaths as of December 2, 2022. Robust evidence of racial disparities among cases and vaccine uptake is limited and needed to appropriately identify vulnerable groups, target communication, and prioritize equitable distribution of resources.

**Methods:** Individuals with laboratory-confirmed mpox and individuals who received at least one dose of the JYNNEOS vaccine in Tennessee (TN) were identified through the National Electronic Disease Surveillance System Base System and the TN Immunization Information System between July 11, 2022 and December 2, 2022. Population data were obtained from the TN Department of Health's Annual Estimates of the Resident Population. Individuals with complete race data were analyzed to calculate 1) proportions of cases and vaccinations by race and 2) case and vaccination rates by race.

**Results:** Of 381 mpox cases in TN, 233 (61.2%) were Black while comprising 17.0% of the TN population, 97 (25.5%) were white while comprising 78.3% of the TN population, 34 (8.9%) were other race or multi-racial, and 17 (4.5%) were unknown race. Among 8,037 individuals who received the JYNNEOS vaccine, 1,359 (16.9%) were Black, 5,928 (73.8%) were white, 669 (8.3%) were other race or multi-racial, and 81 (1.0%) were unknown race. As of December 2, 2022, the race-specific case rate for Black individuals was 19.7 per 100,000 individuals compared to 1.8 per 100,000 individuals for whites. In assessing vaccination uptake, race-specific vaccination rates between Black individuals (117.5 per 100,000) and whites (110.0 per 100,000) were comparable.

**Conclusions:** In Tennessee, Black individuals are overrepresented in mpox cases and underrepresented in vaccinations relative to their risk of illness. Prevention measures, provider education, and communication strategies for mpox should be prioritized and tailored for this group to mitigate growing racial disparities.

**LATEBREAKER**

Health Disparities

**Multistage Carcinogenesis and differences in Lung Cancer Incidence between Non-Hispanic Black and Non-Hispanic White adults in the Multiethnic Cohort Study** Sarah Skolnick\* Sarah Skolnick Pianpian Cao Jiyoung Jeon S. Lani Park Loïc Le Marchand Rafael Meza

**Purpose:** Despite smoking less, Non-Hispanic Black (NHB) individuals have higher lung cancer rates than Non-Hispanic White (NHW) individuals. We use a multistage carcinogenesis model, the Two-Stage Clonal Expansion model (TSCE), to explore the impact of smoking on lung cancer development and incidence in NHB and NHW individuals in the Multiethnic Cohort (MEC) Study.

**Methods:** The MEC Study is a longitudinal cohort for investigating the development of cancer and other chronic illnesses in a multiethnic population. The TSCE can explicitly examine the effects of smoking on the rates of tumor initiation, promotion, and malignant conversion. The TSCE has been used to study lung cancer incidence in other prospective cohorts, replicating well temporal smoking and lung cancer risk patterns. Maximum likelihood methods were used to estimate model parameters and assess differences by race, gender, and smoking history.

**Results:** The final model reproduced well the age-specific lung cancer risk patterns by smoking status, race, and gender in MEC. Smoking increased promotion and malignant conversion, but did not affect tumor initiation. Nonsmoking-related initiation, promotion, and malignant conversion and smoking-related promotion and malignant conversion differed by race and gender.

**Conclusions:** Our analysis provides insights into the biological and epidemiological mechanisms underlying lung cancer incidence differences between NHB and NHW individuals. The findings are novel in suggesting that while smoking plays an important role in lung cancer risk, background risk not dependent on smoking also plays a considerable role in explaining race differences. Ultimately, the resulting TSCE will be used to inform race-specific Lung Cancer natural history models to assess the impact of prevention interventions on US lung cancer outcomes and disparities by race.

**Does the association of play and early childhood development in acutely ill children in low-resource settings differ depending on sex assigned at birth** Riffat Ara Shawon\* Riffat Ara

Shawon Harriet Babikako Margaret Nampijja Emmie Mbale Christopher Lwanga Lynnth Turyagyenda Christina L. Lancioni Melissa Gladstone Judd L. Walson James Berkley Ezekiel Mupere Meta van den Heuvel on behalf of the CHAIN Neurodevelopment Group

Acute and chronic illnesses in young children have been linked with delayed child development. Exploring factors associated with improved neurodevelopment in children recovering from illness and identifying specific groups at high risk may help optimize interventions.

Childhood Acute Illness & Nutrition Network (CHAIN) enrolled acutely ill hospitalized children aged 2-23 months in a cohort study between 2017 and 2019. In a sub-study, sites in Uganda, Malawi, and Pakistan collected data from home visits after discharge on the number of play items and caregiver-child interactions using the Family Care Indicator (FCI) tool. Neurodevelopment was assessed with the Malawi Developmental Assessment Tool (MDAT) at discharge and after 6 months. We determined the association between 6 month-neurodevelopmental outcomes and FCI measures using linear regression analysis with robust standard errors adjusting for site, assets, HIV, and prematurity in all children and in sex-based subgroups.

We included 521 eligible children (55% male, mean age 12.4 months) and found that with each unit increase in the number of play items and interaction score, the combined MDAT z-score was raised by 0.34 (95% CI:0.24, 0.43; p-value:<0.001) and 0.29 (95% CI:0.13, 0.46; p-value:<0.01) units. There were appreciable differences between coefficients for male and female children for both exposures: play items (male:0.61 vs. female:0.32) and interaction (male:0.43 vs. female:0.19), albeit not statistically significant at a 5% alpha level. We noted a similar pattern in domain-specific developmental outcome scores, which alludes that play items and caregiver-child interaction had a comparatively lower impact on the developmental outcomes of female children than male children recovering from acute illness in low-resource settings. These findings point to the need for further evaluation of the difference in the nature and quality of interaction and play items between male and female children in these settings.

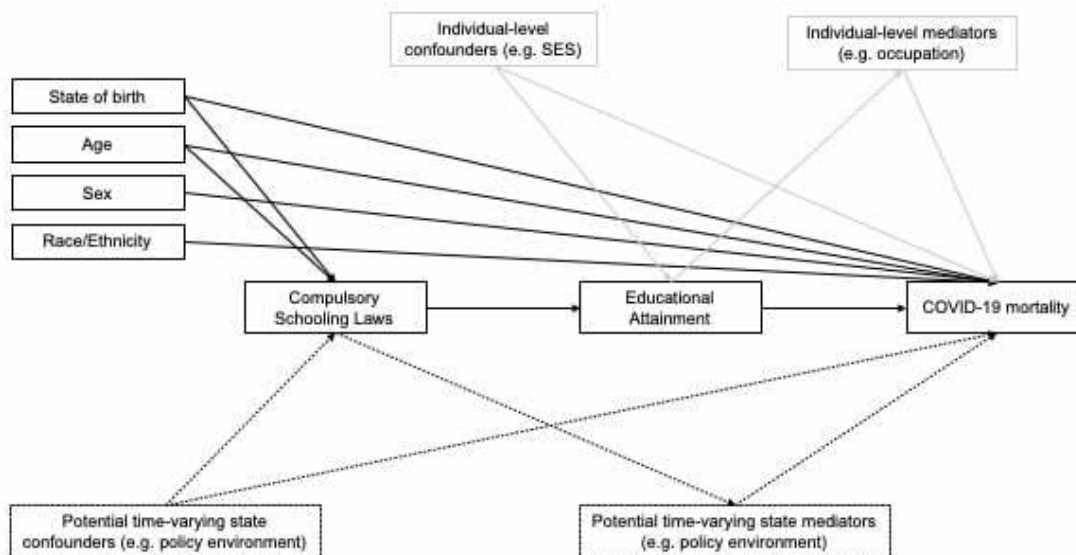
**Effects of educational attainment on COVID-19 mortality: A natural experiment using changes in state-level compulsory schooling laws** Whitney Wells\* Whitney Wells Yea-Hung Chen Ruijia Chen Andrew Stokes Alicia Riley Mathew V Kiang Jacqueline Torres Erika Meza Shelley DeVost Scott Zimmerman Marie-Laure Charpignon M. Maria Glymour

Disparities in COVID-19 mortality are well documented, including higher mortality among those with lower educational attainment. It is unclear if the association is due to a causal effect of education on COVID-19 mortality or confounding by other factors (e.g. early life socio-economic conditions). We used instrumental variable (IV) analysis based on changes in historic state compulsory schooling laws (CSLs) to evaluate the effect of education on COVID-19 mortality.

We included people born in the US pre-1964 given CSL availability. From US death certificate data we included deaths Mar-Dec 2020 with COVID-19 as an underlying cause (n=246,661). We used 2016-2020 five-year ACS PUMS (n=4,831,187) with population weights for the denominators. We used federal reports on state-level CSLs to create two instruments (mandatory enrollment age with drop-out age; or with work permit age) to predict education (8-level ordinal variable:  $\leq 8^{\text{th}}$  grade; some high school (HS); HS degree/GED; some college; associate; bachelor; master; PhD/prof. degree). We used two-stage least squares estimation controlling for birth state fixed effects, age and age-squared in 2020, sex, and race/ethnicity. For comparison, we conducted linear regressions of COVID-19 mortality on observed education.

The first-stage estimates of IVs were strong (partial  $F=29.9$ ). Each increment in level of education attributable to CSLs was associated with lower COVID-19 mortality ( $b=-0.015$ , 95% CI:-0.020- -0.011). The association between observed education and COVID-19 mortality was closer to the null ( $b=-0.00048$ , -0.00049- -0.00047).

These preliminary findings should be interpreted cautiously but suggest the association between more education and lower COVID-19 mortality is causal. Investments in education decades ago may have reduced COVID-19 mortality for select birth cohorts. Next steps will assess robustness of the model to alternative specifications and falsification tests and heterogeneity by sociodemographic factors.



**Figure 1.** Directed acyclic graph for the hypothesized effects of compulsory schooling laws (CSLs) on COVID-19 mortality. Individual-level confounding and mediating pathways are shown in light gray, given CSLs are not influenced by individual-level characteristics. Potential time-varying state confounding and mediating pathways are shown with dotted lines given these represent potential limitations in isolating the pathway between CSLs and COVID-19 mortality via instrumental variable analysis.

**Do the harms outweigh the benefits? Examining within-city and between-city child mortality inequalities for the urban poor in Ghana.** Honor Bixby\* Honor Bixby Jill Baumgartner Brian E Robinson James Bennett Ayaga A Bawah Raphael E Arku Alexandra M Schmidt Samuel Agyei-Mensah George Owusu Alicia Cavanaugh Jacqueline D Anum Samuel K Annim Samilia E Mintah Charles Agyei-Asabere Majid Ezzati

Countries in sub-Saharan Africa suffer the highest rates of child mortality worldwide. Despite improvements over recent decades, wide geographic and socio-economic inequalities persist. Urban areas tend to have more favourable rates than rural areas, however, within-city inequalities are of growing concern in this rapidly urbanising region. Little evidence is available to target support to the urban poor. We aimed to empirically quantify child mortality among the poorest urban households in Ghana and examine the variation across cities and neighbourhoods.

We accessed the 2010 census microdata on over 135,000 women living in the poorest 20% of urban households in four cities of Ghana: Accra, Kumasi, Tamale and Sekondi-Takoradi. We summarised counts of child births and deaths by five-year age group of women and neighbourhood (n=427). We applied indirect methods to convert summarised counts to population probabilities of death under-five years of age and assign each to a reference year. We fitted a Bayesian spatio-temporal model to the neighbourhood child mortality probabilities to obtain estimates for the year 2010.

In 2010, child mortality among the poor ranged from 9 (95% credible interval (CrI): 1-26) to 269 (95% CrI: 122-456) deaths per 1000 live births across city neighbourhoods in Ghana (Fig. 1). Rates were on average highest in the northern city of Tamale and lowest in Accra, Ghana's capital, however, within-city inequalities were largest in Accra. We found no evidence of a relationship between area deprivation and child mortality among the poorest residents.

Reducing inequalities in child mortality requires accelerated improvement among the poor. Combining fine-scale socio-economic and spatial data reveals large child mortality inequalities among the poor within cities. Here we show that the child mortality advantages of living in Ghana's wealthiest cities extend to only some of the poorest residents. For others, the harms seem to outweigh the benefits.

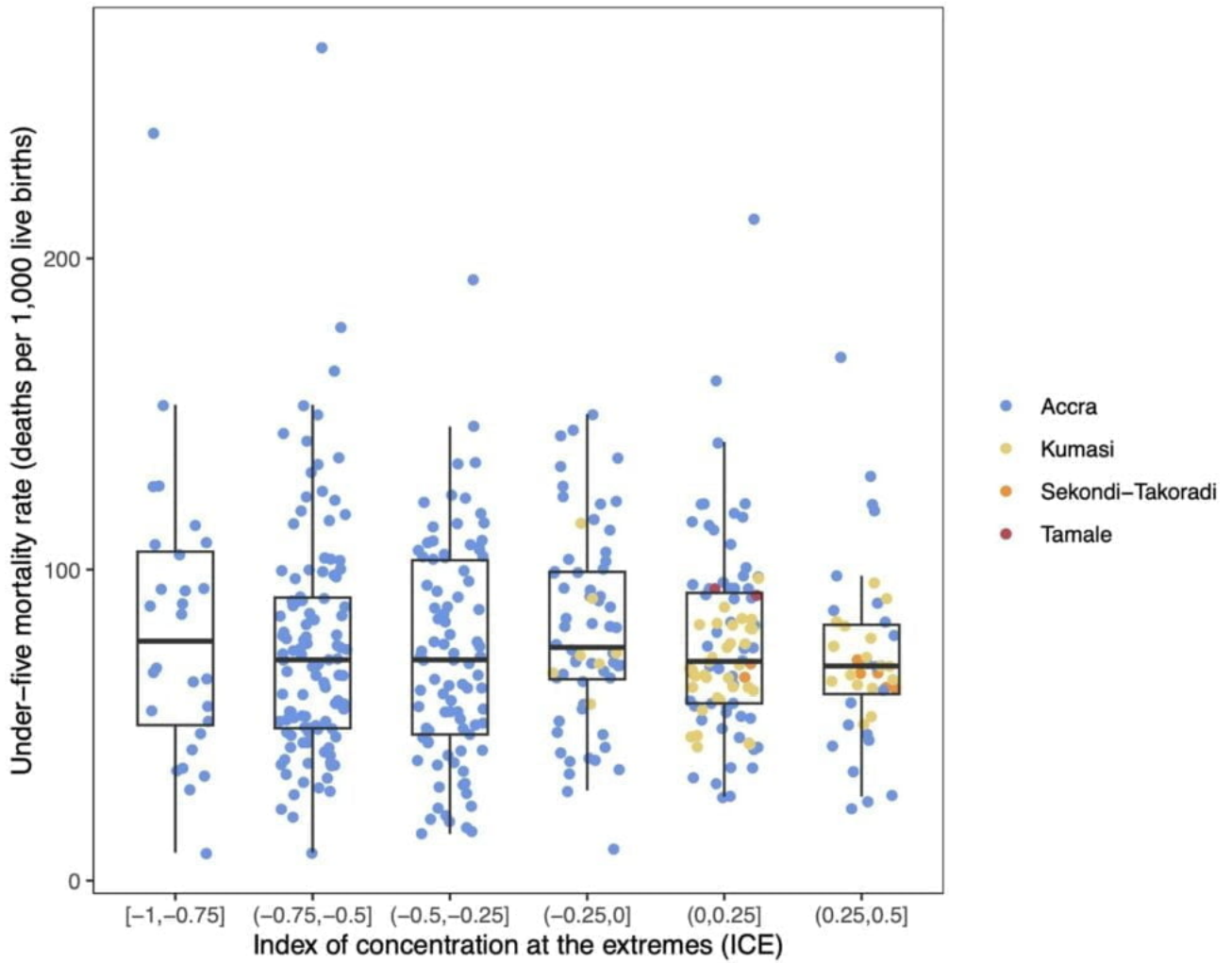


Fig. 1: Under-five mortality rates for the poorest 20% of households in city neighbourhoods by neighbourhood deprivation. Index of concentration at the extreme values below 0 and tending to -1 indicate increasing neighbourhood deprivation; values above 0 and tending 1 indicate increasing neighbourhood affluence.

**Characterizing possible disparities in the incidence of salmonellosis in the United States by urbanicity and community-level social determinants of health** Reese Tierney\* Reese Tierney  
Daniel Weller Beau Bruce Erica Rose

**Background:** Understanding differences in salmonellosis burden among different populations in the United States is useful for developing effective, equitable prevention programs.

**Methods:** Using nationwide data from the Laboratory-based Enteric Disease Surveillance System from 1996 to 2018, we calculated age-adjusted county-level salmonellosis incidence (per 100,000 people) and linked county-level data from federal and non-profit sources on social determinants of health (SDOH; e.g., urbanicity, food environment [FEI]). Continuous variables were categorized into quintiles (Q), with Q1 representing counties experiencing the least and Q5 the most disadvantage. Differences in geometric mean (dGM) incidence between Q4 and Q2 were calculated. Incidence was stratified by SDOH alone and by SDOH and urbanicity. A positive difference indicated a possible disparity.

**Results:** Incidence was higher in large urban (GM=8.0; 95% confidence interval [CI]=7.6-8.5) and suburban counties (GM=7.3; CI=7.1-7.5) than rural counties (GM=3.3; CI=3.2-3.4). Counties with an index representing a high percentage of the population that identified as a racial or ethnic minority group or spoke English less than well had a higher incidence than those with a low percentage (dGM=2.1; CI=2.11-2.14). Differences were also observed among counties when stratified by FEI (dGM=0.6; CI=0.58-0.55), food insecurity (dGM=0.4; CI=0.43-0.45), and the percentage of the population without access to a car (dGM=1.5; CI=1.47-1.50). For some SDOH, disparities were only observed when incidence was also stratified by urbanicity.

**Discussion:** Our analysis suggests that salmonellosis differentially affects persons in counties with populations that differ in SDOH profiles. These findings provide insights that can guide follow-on, quantitative studies, and develop population-specific prevention efforts.



**Prevalence, symptoms and awareness of knee osteoarthritis in Vietnamese (Viet)-Americans: The VietAmerican Health Pilot Study** Uyen-Sa Nguyen\* Uyen-Sa Nguyen Wenjun Li Yuqing Zhang Emily Spence Russell Wagner Ngoc Nguyen Christine Vu Alena Pham Thanh Tran Patricia Franklin

Osteoarthritis (OA) causes pain and disability. Prevalence and symptoms of OA differ by race/ethnicity, yet few studies included Asian Americans. We conducted a pilot study to investigate the occurrence, symptoms, knowledge and management of OA in Viet-Americans, a marginalized and hard-to-reach population. From 07/01/2022 - 08/31/2022, we recruited participants through community leaders from faith-based and community organizations serving Viet-Americans living in Dallas-Fort Worth, TX. Eligibility criteria included being  $\geq 45$  years old, ambulatory, cognitively able, and provide informed consent. Participants were asked to complete a survey on demographics, height, weight, doctor-diagnosed medical conditions, Knee Injury and Osteoarthritis Outcome Survey (KOOS), and awareness and management of knee OA. These instruments were adapted and translated from English to Vietnamese using the Translation, Review, Adjudication, Pretesting, and Documentation Model (TRAPD). Of those invited to participate, 272 (82%) completed the questionnaire. Our study included 53% women and 54%  $\geq 65$  years old. Also, 21% and 6% reported being overweight and obese, respectively. Average stay in US was 30 years ( $\pm 12.8$ ). Knee OA occurred in 20% men, 25% women. Of note, 13% of men and 22% of women said they have rheumatoid arthritis (RA). About 1/3 of men and women reported knee pain (KOOS pain score  $< 70$ ). Only 34% of women and 48% of men knew that an optimal weight can prevent knee OA. Most people (84%) used alternative pain management, including massages, herbal medicines, and acupressure. Compared with a year ago, 50% of men and women rated their physical health as slightly/much worse. Participants reported high prevalence of OA and RA, despite low prevalence of overweight/obesity. Most people were unaware that weight management can prevent OA, and there may be a lack of understanding of differences in OA and RA. We need to understand risks, awareness, and prevention of OA in Viet-Americans.

**Racial/Ethnic Disparities in Palliative Care Use among Breast Cancer Patients by Metastatic Status: A National Cancer Database Analysis** Jincong Freeman\* Jincong Freeman  
Yong Gun Lee Xinyi Li Victoria Umutoni Ted Akhiwu Jared Hara

**Background:** Palliative care (PC) remains underutilized among breast cancer patients (pts), and racial/ethnic disparities in PC use by metastatic status (MS) are unknown.

**Methods:** Data came from the 2004-2019 National Cancer Database (NCDB), a joint project of the Commission on Cancer of the American College of Surgeons and the American Cancer Society. Per NCDB, PC, including surgery, radiotherapy, systemic therapy, and/or other pain management, was performed to relieve symptoms. PC use was dichotomized as yes/no. MS was categorized as non-metastatic (NM, i.e., stage I-III) and metastatic (M, i.e., stage IV) per the American Joint Committee on Cancer staging. Race/ethnicity included Asian, Black, Hispanic, and White. Multivariable logistic regression was used to assess racial/ethnic disparities in PC use by MS, adjusting for sociodemographic and clinical characteristics.

**Results:** Of 2,596,176 pts (mean age 62 [SD 13] years), 79.8% were White, followed by 11.3% Black, 5.6% Hispanic, and 3.3% Asian; 94.8% and 5.2% had NM and M disease, respectively. We observed significant differences in sociodemographic and clinical characteristics by race/ethnicity. Overall, 1.3% of the pts used PC; 1.8% of Black, 1.2% of White, 1.0% of Hispanic, and 0.9% of Asian pts used PC. By MS, 0.3% of Black, 0.2% of White, 0.2% of Hispanic, and 0.1% of Asian NM pts used PC; 21.0% of White, 19.4% of Black, 17.1% of Asian, and 15.2% of Hispanic M pts used PC. In the adjusted models, Black NM pts had higher odds of PC use than White pts (adjusted OR [aOR] 1.3, 95% CI: 1.2-1.5); PC use was similar between White and Asian or Hispanic NM pts. Black (aOR 0.9, 95% CI: 0.8-0.9), Asian (aOR 0.8, 95% CI: 0.7-0.9), and Hispanic (aOR 0.7, 95% CI: 0.6-0.7) M pts had lower odds of PC use than White pts.

**Conclusion:** PC use was low among breast cancer pts, overall and by MS. Our findings highlight racial/ethnic disparities in PC use and suggest that breast programs addressing equitable PC access may be needed.

**Association Between Socioeconomic Status and Prevalence of Hypersensitivity Diseases and Autism: A Nationwide Study of Children** Tsung Yu\* Tsung Yu Tzu-Jung Wong

**Objective:** Prior research suggests that children with a low socioeconomic status (SES) background are at an increased risk for special healthcare needs. Conversely, however, for hypersensitivity-related diseases, many studies have reported a lower risk among children with lower SES. We aimed to evaluate the association between SES and several hypersensitivity diseases and autism in a representative American sample.

**Methods:** We used data from the 2016, 2017 and 2018 US National Survey of Children's Health. A total of 102,341 children aged 0-17 years were included. The dependent variables were doctor-diagnosed allergies, arthritis, asthma, diabetes, and autism. The main SES indicators were family poverty levels, highest education of the reported adults and difficulty in family income (i.e., hard to get by). Our analysis used logistic regression that accounted for the survey sampling design.

**Results:** The sample had a mean age of  $9.4 \pm 5.3$  years. The weighted prevalence for allergies was 24.4%, 0.3% for arthritis, 11.9% for asthma, 0.5% for diabetes and 2.6% for autism. Children with adults reporting higher educational levels had greater odds of allergies (adjusted odds ratio and 95% CI: 1.48, 1.23-1.78) than those with lower educational levels. But for all other diseases, most findings suggested that a higher odds of disease was associated with lower SES instead of higher SES. **Conclusions:** A low SES background remains an important risk factor for hypersensitivity diseases in children. Most of our results suggested that children with low SES were associated with a higher risk of hypersensitivity diseases and autism.

**General health, oral health, and cancer transversality: Results from the Chilean National Health Survey** Matias Muñoz-Medel\* Matias Muñoz-Medel Doris Durán Rhodia Colomé Ignacio N. Retamal

## Background

The prevalence of systemic and oral health diseases changes within social gradients, decreasing when socioeconomic risk is also reduced. Analyzing public data from the Chilean National Health Survey which includes general health, oral health, and cancer questionnaires, we aim to describe how self-perceived health, along with the prevalence of systemic diseases and cancer, relate to social gradients in Chile.

## Methods

We selected demographical, socioeconomic, and health variables from 6233 participants of the Chilean National Health Survey 2016-2017. The prevalence of these conditions was determined for each level of scholary ( <12 years, =12 years, and >12 years). Additionally, a logistic regression model incorporating independent variables was performed, with an analysis of variance of significant variables to understand their association with household income. Furthermore, we obtained odds ratios of these conditions for each level of scholary.

## Results

From 6233 subjects, scholary data was available in 6174. As expected, we observed that the prevalence of all conditions per 100 subjects at risk had a negative association with a higher scholary level (Kruskall-Wallis p-value 12-years: 4.26 [95%CI:3.24-5.48], p-value = 0.121).

## Conclusion

This is the first report on the prevalence of general health, oral health, and cancer conditions in the same universe of subjects in Chile. Based on the results of the epidemiological data, cancer is a transversal disease, whose prevalence is not altered by socioeconomic level. Further studies on cancer financing and survival by social gradients are necessary to fully address the impact of cancer in Chilean society.

**Sexual orientation-based differences in endometriosis diagnosis in the Nurses' Health II Study—a cohort of U.S. women** Ariella R Tabaac\* Ariella Tabaac Amy L Shafir Leslie V Farland Frances Grimstad Stacey A Missmer S Bryn Austin Brittany M Charlton

**INTRODUCTION:** Endometriosis is estimated to affect 10% of women in the United States, but we do not know how endometriosis can vary as a function of sexual orientation.

**AIMS:** We proposed to examine lifetime prevalence of endometriosis across several dimensions of sexual orientation in a prospective cohort of cisgender women from the Nurses' Health Study II (NHSII).

**METHODS:** In a sample of 101,657 women, using log-binomial models producing risk ratios (RR) and 95% confidence intervals (CI), we examined age- and age at menarche-adjusted differences in any endometriosis diagnosis, surgically-confirmed endometriosis diagnosis, and clinician-confirmed endometriosis diagnosis across four dimensions of sexual orientation: lifetime sexual minority status (no, yes), sexual orientation identity (completely heterosexual, mostly heterosexual, bisexual, gay/lesbian, another identity), sexual/romantic attraction (men only, women only, both men and women), and sex of sexual partners (only men, only women, both men and women, no partners).

**RESULTS:** Endometriosis was diagnosed in 15.1% of heterosexual women and 16.5% of sexual minority women in the NHSII cohort. Women who ever identified as a sexual minority were more likely to report any endometriosis diagnosis (RR=1.09, 95% CI: 1.03-1.15) or a surgically-confirmed diagnosis (RR=1.10, 95% CI: 1.03, 1.17). Bisexual women were more likely than completely heterosexual women to report any endometriosis diagnosis, surgically-confirmed diagnoses, and clinician-confirmed diagnoses (RRs=1.30-1.68).

**CONCLUSION:** Findings indicate that endometriosis diagnosis appears higher among bisexual women, further work should examine further differences in time-to-diagnosis, treatment, and sociodemographic factors by sexual orientation identity.

**Development of novel urban residential mobility indicators for Canada** Sarah Mah\* Sarah Mah Emmalin Buajitti Lief Pagalan Lori Diemert Laura Rosella

**Background:** Lack of longitudinal data and standard approaches for summarizing residential histories have led to an absence of research on the long-term health impacts of residential instability. Our objective was to develop a generalizable and transferable methodology for deriving and validating individual-level indicators of residential mobility using comprehensive encounter-based residential history data from Ontario's single-payer health care system.

**Methods:** We accessed a record-linked cohort of Ontario respondents of the Canadian Community Health Survey (CCHS 2000-2014) for whom longitudinal residential postal codes are captured and routinely updated when an individual moves or has a health system interaction. We first developed a measure of residential instability based on the number of moves captured before survey interview date. We used descriptive statistics to compare and optimize indicator definitions (varying lookback windows, distributed lag, etc.) to maximize variation across urban populations. We will quantify associations with premature mortality data for Ontario (2000-2021) to assess explanatory power for population health.

**Results:** Among the 169,211 CCHS respondents, approximately 87% lived in large population centres, which rendered a sample size  $N = 147,647$ . Descriptive analyses showed that 12.1% of urban CCHS respondents moved within a year before their survey date, 29.7% moved within 3 years, and 42.3% moved within 5 years. Over a 5-year lookback period, 28.9% moved once whereas 13.4% moved two or more times. Frequency of moves was greater among respondents aged  $<35$  (53.2% within 5 years), those living in low-SES neighbourhoods (48.3%), and those not owning their residential dwelling (59%).

**Conclusions:** Developing novel approaches for measuring residential mobility will give population health value for studying an understudied social determinant of health and will enrich research and planning for healthy cities.

### Time to kidney transplant referral among patients with lupus nephritis-associated end-stage kidney disease

Laura McPherson\* Laura McPherson Rachel E. Patzer

Lupus is a multisystem autoimmune disease that can result in a kidney manifestation known as lupus nephritis-associated end-stage kidney disease (LN-ESKD). There are two treatments for LN-ESKD patients, and research suggests that kidney transplant provides a survival benefit over dialysis. A majority of LN-ESKD patients are initiated on dialysis and it is unknown how their early access to kidney transplant compares to patients with ESKD unrelated to LN (other-ESKD). Adults who began ESKD treatment at any Southeast (GA, NC, SC), Northeast (CT, MA, ME, NH, NY, RI VT), and Ohio River Valley (IN, KY, OH) dialysis facility from 1/1/14 to 12/31/18, followed through 12/31/20, were identified from the US Renal Data System. Referral data were collected from 29 transplant centers across these regions. The exposure was primary cause of ESKD and categorized as a dichotomous (LN-ESKD vs other-ESKD) and categorical (diabetes, hypertension, glomerulonephritis, LN, other, and unknown) variable. The outcome was referral for evaluation, which is the first step in the kidney transplant process. We used crude and multivariable cause-specific hazard models to quantify the association between primary cause of ESKD and referral. Patients were censored for event (referral), death, or study end (12/31/20). Among 112,669 patients (ages 18-75 years) on incident dialysis, 0.4% had LN-ESKD. Majority of LN-ESKD patients were female (81%), Black (56%), and a median age of 40 years (IQR: 51, 68) (vs 61 years for other-ESKD). Half of LN-ESKD patients were referred before study end, with a median of 27 months on dialysis (IQR: 3, 70). Over 16% of LN-ESKD patients died prior to referral compared to 28% of patients with other-ESKD. In multivariable analyses, LN-ESKD patients were less likely to be referred compared to other-ESKD patients (specifically causes of diabetes, hypertension, and glomerulonephritis), which is likely driven by the younger age of the LN-ESKD patient population (Table 1).

**Table 1.** Cause-specific modeling results for the association of provider attributed primary cause of ESKD with time to referral for kidney transplant in 29 transplant centers among incident ESKD patients across the Northeast, Southeast, and Ohio River Valley regions of the United States: 2014-2018, followed through 2020

Provider attributed primary cause of ESKD	N (%)	Referred N (%)	Hazard Ratio (95% CI)	
			Crude	Adjusted <sup>1</sup>
LN-ESKD (ref)	415 (0.4)	209 (50.4)	-	-
Other-ESKD <sup>2</sup>	112,254 (99.6)	40,240 (35.8)	0.73 (0.63, 0.84)	1.10 (0.97, 1.26)
Diabetes	53,867 (47.8)	18,429 (34.2)	0.69 (0.60, 0.79)	1.11 (0.97, 1.27)
Hypertension	30,813 (27.4)	11,982 (38.9)	0.79 (0.69, 0.91)	1.15 (1.00, 1.31)
Glomerulonephritis	9,735 (8.6)	4,361 (44.8)	0.95 (0.82, 1.09)	1.17 (1.02, 1.34)
Other cause	16,238 (14.4)	5,024 (30.9)	0.63 (0.54, 0.73)	0.96 (0.83, 1.10)
Unknown cause	1,601 (1.4)	444 (27.7)	0.52 (0.43, 0.63)	0.86 (0.72, 1.03)

CI, confidence interval; ESKD, end-stage kidney disease; LN, lupus nephritis

<sup>1</sup>Model adjusted for categorical age, sex assigned at birth, race/ethnicity, body mass index  $\leq 35$  kg/m<sup>2</sup>, cardiovascular disease, dialysis duration, treatment modality, primary source of health insurance, and access to nephrology care prior to ESKD

<sup>2</sup>Includes all other ICD-9/ICD-10 codes listed as the provider-attributed primary cause of end-stage kidney disease: diabetes, hypertension, glomerulonephritis, other cause, and unknown cause

**Black people and White people respond differently to social capital: what racial differential item functioning reveals for racial health equity** Ester Villalonga-Olives\* Ester Villalonga-Olives Majercak KR Wang W Dean L Ransome Y

**Introduction:** Social capital has been conceptualized as features of social organization such as networks and norms that facilitate coordination and cooperation for mutual benefit. Because of long-standing anti-Black structural racism in the US, social capital may be associated with health differently for Blacks than for other racial groups. The reason for this difference, however, may not be due to race per se, but point to underlying structural issues with the measures. We examined the psychometric properties of social capital indicators to identify whether there is Differential Item Functioning (DIF) in social capital by Black and White race.

**Methods:** An item displays DIF if the probabilities of responding in different response options within a variable vary across study groups, given equivalent levels of the underlying concept. We used data from n=2,048 respondents who participated in the Southeastern Pennsylvania Household Health Survey in 2004, residing in Philadelphia PA, a large racially and socioeconomically diverse city. Social capital items were perceived 'trust in neighbors', 'belongingness to the neighborhood' and 'people helping their neighbors'. We used Item Response Theory methods with a Graded Response Model accounting for educational level.

**Results:** The item 'belonging to the neighborhood' displayed DIF. Whites were consistently more likely to report higher belongingness scores than Blacks ( $\chi^2=18.84$ ,  $df=3$ ,  $p<0.01$ ). The item "'trust in neighbors' displayed DIF. Blacks were more likely to report lower trust than Whites ( $\chi^2=24.12$ ,  $df=4$ ,  $p<0.01$ ).

**Conclusion:** We found significant DIF by race in social capital measures used in health research. These results underscore the need to interrogate how structural biases and assumptions impact how we interpret existing items and associations with health outcomes. We must use an equity-based lens to correct measurement error and to develop new items to ensure racial and cultural congruence and equivalence.



**LATEBREAKER**

Health Services/Policy

**Emergency department use and hospital admissions among community-dwelling older adults and those in residential care facilities in Ontario, Canada, 2013 to 2019** Derek Manis\*  
Derek Manis Paul Katz Natasha Lane Susan Bronskill Paula Rochon Samir Sinha Kali Thomas Ross  
Andel George Heckman David Kirkwood Andrew Costa

**Objective:** We examine annual rates of emergency department (ED) visits and hospital admissions among older adults who resided in the community and residential care facilities.

**Methods:** We conducted a repeated cross-sectional study using linked, individual-level health system administrative data on community-dwelling persons, home care recipients, residents of assisted living facilities, and residents of nursing homes aged 65 years and older in Ontario, Canada from January 1, 2013 to December 31, 2019. We calculated rates of hospital-based care per 1,000 individuals per population per year. We used a generalized linear model with generalized estimating equations, gaussian distribution, log link, and heteroskedasticity-consistent standard errors to model rate ratios.

**Results:** There were 1,893,230 older adults in the community and 136,655 older adults in residential care facilities in 2013, and 2,410,718 older adults in the community and 152,900 older adults in residential care facilities in 2019. Residents of assisted living facilities had the highest rates of ED visits (1,260.69<sub>2019</sub> v. 1,174.91<sub>2013</sub>) and hospital admissions (482.63<sub>2019</sub> v. 480.19<sub>2013</sub>). Residents of assisted living facilities also had significantly higher rates of ED visits (RR 3.30, 95% CI 3.23, 3.38) and hospital admissions (RR 6.23, 95% CI 6.02, 6.45) relative to community-dwelling older adults.

**Interpretation:** The disproportionate use of hospital-based care among residents of assisted living facilities may be attributed to fragmented regulation of the sector and variable models of care. The implementation of interdisciplinary, team-based approaches to home and primary care in assisted living facilities is warranted to reduce potentially avoidable use of hospital-based care among this population.

**Care trajectories and health outcomes of people with diabetes in Quebec** Divine-Favour Ofili\*  
Divine-Favour Ofili Amélie Quesnel-Vallée

Diabetes presents large inequities both in its prevalence and management in the Canadian population, especially in consideration of immigrant groups. This is concerning as people with diabetes already have higher rates of resource utilization and avoidable healthcare visits in Canada; these are in turn associated with adverse health outcomes. Yet, there exists a knowledge gap in the long-term healthcare utilization patterns, the drivers and health risks of these avoidable visits and how to equitably prevent them in people with diabetes. In view of this, this study leverages the novel *Care Trajectories-Enriched Dataset* (TorSaDE) which links Quebec's health administrative data (1996-2016) to the Canadian Community Health Survey data (2007-2014) and adopts an equity lens to highlight factors that may influence healthcare use and outcomes of people with diabetes over time. Using state sequence analysis methods, we will map individuals' healthcare use after diabetes diagnosis into care trajectories, and then determine trajectory membership by individual-level factors like age, immigrant status, language, race/ethnicity, etc. Next, we will assess the risk of *emergency department visits* (ED) and *avoidable hospitalizations* (AH) (coded independently as binary variables) based on the trajectories, and other individual-level factors using binary logistic regression models. Furthermore, as immigrants have higher rates of diabetes than the host population and are also disproportionately experiencing avoidable healthcare visits, we will use the Blinder-Oaxaca decomposition method to assess how much of the differences in ED/AH across the trajectories are explained by immigrant status. Results from this study will inform policy on the development of equitable diabetes care protocols for people with diabetes, which is a critical priority in a diverse country like Canada. This will thus reduce the economic and health burden of diabetes on both the patients and healthcare systems.

**Adverse employment histories and barriers to healthcare access** Hanno Hoven\* Hanno Hoven  
Insa Backhaus Ichiro Kawachi

**Background:** Research suggests that people in disadvantaged social positions have an elevated risk of perceiving healthcare access barriers, especially to specialists and preventive services. In this study, we analyze if adversity during past employment histories is linked to healthcare access barriers later on, independently of later wealth and income. Additionally, we investigate if the associations vary according to healthcare access and quality indicators. **Methods:** We use data from the Survey of Health, Ageing, and Retirement in Europe with a study sample of 55,416 men and women aged 50-80 years from 26 countries. Data include retrospective information on employment histories that allows us to derive characteristics of past careers, including the number of unemployment periods, main occupational position, and pension contributions. Healthcare access is measured by self-perceived forgone care due to costs and waiting time at up to four follow-up periods (2011 to 2020). Healthcare indicators include for instance the total healthcare expenditure. We apply multilevel Poisson regression for binary outcomes and test for cross-level interactions between career characteristics and healthcare system. **Results:** Career characteristics are linked to later healthcare access barriers for men and women, consistently in case of cost barriers and less consistently for waiting time barriers. For instance, the risk for forgone care due to costs or waiting time is 1.20 (95% CI: 1.06-1.35) higher for men who experienced one unemployment period and 1.22 (95% CI: 1.01-1.48) higher for men with two or more periods as compared to men without an unemployment period. Associations are similar for men and women and, although diminishing, persist when considering current wealth. Estimates do not vary according to macro-level indicators. **Conclusions:** Our study adds to existing research by highlighting the need to link inequalities in access barriers with adversity during previous working lives.

**Effect of non-benzodiazepine hypnotics on motor vehicle crashes among older adults**

Marzan A. Khan\* Marzan Khan Nina R. Joyce Melissa R. Pfeiffer Seth A. Margolis Brian R. Ott  
Allison E. Curry Katie Konieczny Andrew R. Zullo

**Background:** Non-benzodiazepine hypnotics (i.e., “Z-drugs”) are often prescribed to treat insomnia and may increase the risk of motor vehicle crash (MVC) through prolonged drowsiness and delayed reaction times, though the effect is unknown.

**Objective:** To estimate the causal effect of Z-drug initiation on the risk of MVC among older adults in a sequential target trial emulation.

**Methods:** We linked New Jersey (NJ) driver licensing and police-reported MVC data to Medicare claims. We emulated a new target trial each week from July 1, 2007 through October 7, 2017 in which Medicare fee-for-service beneficiaries aged  $\geq 66$  years and licensed in NJ were classified as Z-drug initiators or non-initiators at baseline and followed for MVCs over 12 weeks. We used inverse probability of treatment and censoring weights (IPTW and IPTC) to estimate risk ratios (RR) and risk differences (RD) with 95% robust confidence limits (CLs) adjusting for potential confounding and selection bias by 30 investigator-specified and empirically derived covariates.

**Results:** Across 695,564 unique beneficiaries there were a total of 7,812,504 person-trials. Comorbidities and healthcare utilization were more prevalent among the 103,371 Z-drug initiators compared to the 7,709,133 non-initiators who experienced 976 and 63,489 MVCs respectively. The intention-to-treat (ITT) RR was 1.02 (95% CLs 0.92, 1.12) and the RD was 2 MVCs per 10,000 person-trials (95% CLs -7, 10). When accounting for treatment discontinuation and switching in the per-protocol (PP) estimand, there were 800 MVCs among initiators and 63,250 MVCs among non-initiators (RR 0.83 [95% CLs 0.75, 0.93]; RD -9 MVCs per 10,000 person-trials [95% CLs -21, -6]).

**Conclusion:** Sustained use of Z-drugs after initiation resulted in a lower MVC risk, but initiation alone resulted in a slightly higher risk. More work is necessary to understand the divergence of the ITT and PP effect estimates.

**Prevalence and characteristics of healthcare utilization with different providers among Canadians with chronic back problems from 2001 to 2016: A population-based study** Jessica Wong\* Jessica Wong Dan Wang Sheilah Hogg-Johnson Silvano Mior Pierre Côté

**Background:** Understanding healthcare utilization by Canadians with back problems informs healthcare planning nationally. The study aimed to determine the prevalence of utilization of healthcare providers (medical doctors, chiropractors, physiotherapists, nurses), and associated characteristics among Canadians with chronic back problems (2001-2016).

**Methods:** Canadian Community Health Survey data (2001-2016) were analyzed, restricting to respondents with chronic back problems (aged  $\geq 12$  years). Outcomes were self-reported consultation with healthcare providers (medical doctor, chiropractor, physiotherapist, nurse; 2001-2010) and regular healthcare provider (2015-2016). 12-month period prevalence of utilization with providers was calculated. Modified Poisson regression was used to assess sociodemographic, health, and behavioural factors associated with utilization of providers.

**Results:** From 2001-2010 and 2015/2016, respectively, prevalence of utilization of medical doctors was 87.9% (95%CI 87.6-88.2) and 86.7% (95%CI 85.9-87.5); chiropractors 24.0% (95%CI 23.6-24.4) and 14.5% (95%CI 13.8-15.3); physiotherapists 17.2% (95%CI 16.9-17.6) and 10.7% (95%CI 10.0-11.4); nurses 14.0% (95%CI 13.7-14.2) and 6.6% (95%CI 6.1-7.0). Females were more likely to see any provider than males. Persons of lower socioeconomic status were less likely to consult chiropractors or physiotherapists (2001-2016), or nurses (2001-2010). Immigrants were less likely to consult chiropractors or nurses. Persons aged  $\geq 65$  years were less likely to consult chiropractors or physiotherapists, and those with fair/poor general health were less likely to consult chiropractors, but more likely to consult other providers.

**Conclusion:** Medical doctors were most consulted by Canadians with back problems, then chiropractors and physiotherapists. Characteristics of healthcare utilization varied by provider. Findings inform the need to strengthen healthcare delivery for Canadians with back problems to mitigate burden.

**The role of child maltreatment in the association between earned income tax policies and adolescent suicide mortality: a mediation analysis** Yana B Feygin\* Yana Feygin Natalie DuPre Liza Creel Anne Wallis Richard Baumgartner Nicholas Peiper

### **Objective**

Suicide mortality is difficult to predict at the individual level; however, by decreasing risk factors associated with suicide, such as child maltreatment, the rate can be reduced at the population level. This study aims to describe the associations between the presence of a refundable state Earned Income Tax Credit (EITC), child maltreatment rates, and adolescent suicide mortality rates over time. Our central hypothesis is that a refundable state EITC may reduce the adolescent suicide rate by decreasing child maltreatment rates.

### **Methods**

Maltreatment rates from NCANDS and publicly available data on suicide rates among adolescents aged 10-19 years, the presence of a refundable state EITC, household firearm ownership, unemployment, bachelor's degrees, poverty, mental health professionals, and public pre-kindergarten access were obtained for US states, 2005-2019. Mixed effect regression models were used to assess factors associated with maltreatment (linear) and suicide rates (hurdle), clustered by state and year. Mediation analysis assessed whether the refundable state EITC had an indirect effect on suicide rates through maltreatment rates.

### **Results**

The presence of a refundable EITC was associated with a 10.95% decrease in maltreatment rates, with the effect moderated to an 8.63% decrease when unemployment rate increases by 1% point from the mean. EITC was also associated with a decrease in the adolescent suicide rate, though non-significantly, and moderated by household firearm ownership rates. No significant mediation effects were found.

### **Conclusions**

Although mediation was not found in the study, results imply a significant role for a refundable state EITC in reducing the rate of child maltreatment and potentially adolescent suicide. While residual confounding may explain some of these findings, focusing on population level primary prevention through state policy may be an important strategy for preventing child maltreatment and suicide among adolescents.

**Who has used telehealth? A cross-sectional survey of Nebraska adults** Kendra Ratnapradipa\*  
Kendra Ratnapradipa Snehal Jadhav Josiane Kabayundo Lisa Smith Hongmei Wang

**Background:** COVID-19 spurred uptake of telehealth to facilitate patients' access to medical care. Despite the increased availability of telehealth, there are still disparities in accessibility and use of telehealth services. Hence identifying facilitators and barriers to telehealth should be prioritized.

**Objective:** To identify characteristics associated with ever use of telehealth. **Methods:** A stratified random sample of Nebraska households (n=5300) with oversampling of census tracts with at least 30% African American, Hispanic, or Native American populations received a mailed survey (English, Spanish) about social determinants of health and healthcare access in late 2020. Survey weights were used for all calculations. Prevalence ratios (PR) with 95% CI for ever used telehealth were calculated in SAS using robust Poisson regression. **Results:** Response rate was 20.8% (n=1101). An estimated 25.5% of Nebraska adults had ever used telehealth, and 97% had internet access. Internet and rurality were correlated so rurality was not modeled. In univariate models, internet access, age, sex, ethnicity, education, and no chronic health condition were significant. When adjusted, education was not significant but internet access (PR 5.36; 1.60-17.88), age <45 (PR 4.60; 1.90-11.16) and age 45-64 (PR 7.78; 2.01-30.10), female (PR 1.55; 1.04-2.31), non-Hispanic (PR 6.96; 2.31-20.95), and no chronic condition (PR 1.97; 1.25-3.10) were. Chronic condition by age interaction was not significant. **Conclusions:** The digital divide is a known barrier to telehealth, and internet access was a strong predictor of telehealth ever use. Older adults, people with a chronic health condition, and Hispanics were significantly less likely to use telehealth, which may indicate need for targeted support. Our sampling weights adjusted to make the sex and age distribution representative of the Nebraska population, but we were unable to adjust for race and rural responses were diluted with weighting.

**Restrictive abortion Laws and Antenatal and Postpartum Mental Health** Sarah McKetta\*

Sarah McKetta Brittany Charlton

Background: Half of all pregnancies in the U.S are unintended and state-level laws largely determine abortion access. This variable legal climate contributes to major depression and PTSD, particularly among women of reproductive age. However, little is known about how abortion laws impact prenatal and postpartum depression including among women who become pregnant unintentionally.

Methods: We quantified the risk of depression during and after pregnancy using longitudinal data from Nurses' Health Study 3 in 2010-2015 (N=3,075 participants with 5,572 pregnancies). Restrictive abortion laws were measured using a standardized index of 18 restrictive laws. After controlling for sociodemographics and state economic measures (poverty rate and Gini index), multilevel logistic models with repeated measures were used to elucidate the interaction pregnancy intention (i.e., unintended versus intended).

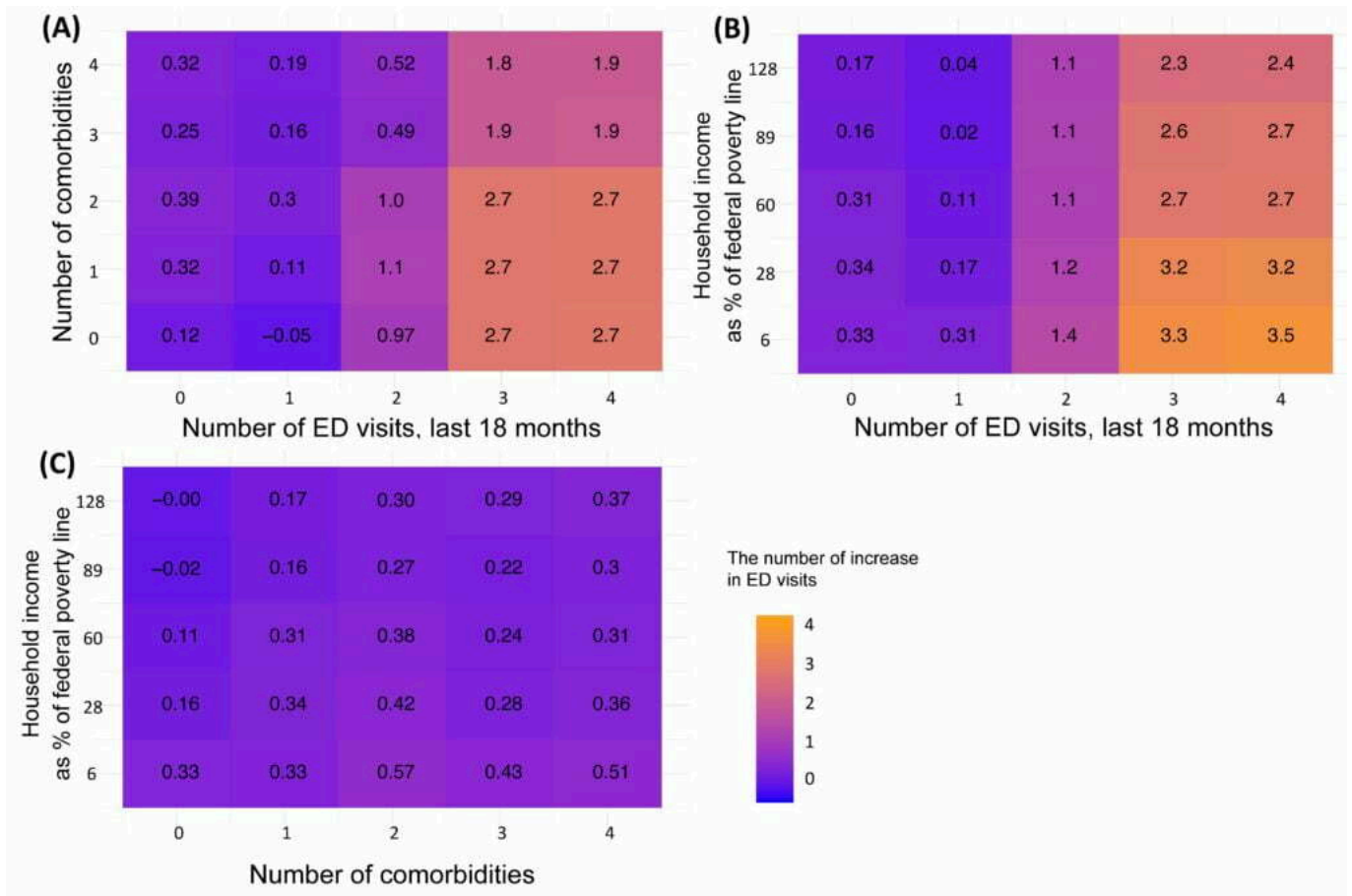
Results: When we grouped intended and unintended pregnancies together, depression during pregnancy was similar in states with restrictive abortion laws compared to those with less restrictive laws (OR=1.06, 95% CI 0.86, 1.31). However, among those with unintended pregnancies, restrictive abortion laws strongly predicted increases in depression during pregnancy (OR=2.57, 95% CI: 1.19, 5.53). Restrictive abortion laws were not associated with mental health after pregnancy among participants with intended or unintended pregnancies.

Conclusions: Women with unintended pregnancies are at risk for adverse mental health during pregnancy, particularly those living in states with restrictive abortion laws.



**Heterogeneous Effects of Medicaid on Emergency Department Visits: A Machine Learning-Based Analysis of Oregon Health Insurance Experiment** Yusuke Tsugawa\* Itsuki Osawa Kosuke Inoue Ryunosuke Goto

The Oregon Health Insurance Experiment (OHIE)—a randomized controlled trial to estimate the effects of the 2008 Medicaid expansion in Oregon—showed that Medicaid coverage increased emergency department (ED) visits. Given that non-emergent visits for conditions that might be treatable in primary care settings accounted for most of the increase in ED visits, the identification of individuals likely to disproportionately increase ED use with Medicaid expansion is critical. In this context, to find previously unidentified subgroups who visited the ED more frequently with Medicaid coverage, we applied the machine learning-based causal forest algorithm to data from the OHIE. Among 5,564 low-income individuals aged 19 to 64 years in the OHIE, we found heterogeneity in effects of the Medicaid expansion on ED visits based on *ex ante* observable individual characteristics. Top 10% of the increases in the number of ED visits due to Medicaid in 18 months after randomization was about 7 times higher than among those in the remaining 90% (increase in ED visits [95% CI]: +2.2 [+1.5 to +2.8] times in 18 months vs. +0.31 [+0.10 to +0.53] times in 18 months;  $P < 0.001$ ). By comparing the characteristics of individuals with higher versus lower estimated effects of Medicaid on ED visits, individuals with higher estimated effects of Medicaid on ED visits tended to have more preexisting conditions (e.g., asthma, depression), poorer self-reported health, lower socioeconomic status, and greater numbers of ED visits prior to randomization. We found that the interactions between the number of ED visits prior to Medicare coverage and other determinants could have a large impact on changes in the number of ED visits (**Figure**). Our findings could aid policymakers in designing expansions of the Medicaid program without increasing the inefficient and expensive use of EDs.



**Tracking sexually transmitted infections in cisgender women seeking care at a safety-net hospital to identify HIV pre-exposure prophylaxis candidates** Brandi Moore\* Brandi Moore Antoinette Oot Farzana Kapadia Colleen Denny Melinda Katz Richard Greene Robert Pitts

**Background:** Per CDC's HIV prevention guidelines, recent infection with a bacterial sexually transmitted infection (STI) is an indicator of eligibility for pre-exposure prophylaxis (PrEP), an effective HIV prevention tool. Despite this, cisgender women who are at heightened risk for HIV are often missed for PrEP. To understand the gap in bacterial STI diagnosis and PrEP prescription, we examined correlates of bacterial STIs among women seeking care at a Women's Health Clinic in NYC to identify potential candidates for PrEP.

**Methods:** A retrospective review of electronic health record data of gonorrhea and chlamydia tests was conducted for cisgender women not living with HIV who obtained care between 09/2021-09/2022. Analyses described overall trends in incident infections and log binomial regression models were fitted to examine factors associated with incident bacterial STIs.

**Results:** Among n=7,601 women (mean age=37.5 yrs (SD: 11.2); 16.4% Black, 7.0% White, 5.3% Asian, 3% Native Hawaiian/Alaskan/Pacific Islander, 62.7% Other Race; 49.6% Spanish as a primary language; 44.5% utilized Medicaid, 36.6% were self-pay, 16.6% had private insurance, 2.2% had Medicare/other public insurance) who received care, n=202 (2.7%) incident chlamydia and n=19 (0.3%) gonorrhea infections were identified. No women with either type of infection during the study period received a PrEP prescription post-STI diagnosis. Chlamydia or gonorrhea infection risk decreased with age (RR=0.90, 95%CI 0.88, 0.93), but was higher in women divorced/widowed/separated (RR=3.81, 95%CI 1.62, 8.94), with Spanish as a primary language (RR=1.66, 95%CI 0.98, 2.82), and who utilized Medicare/other public insurance (RR=6.81, 95%CI 2.13, 21.73) or were self-pay (RR=2.11, 95%CI 0.94, 4.73).

**Conclusions:** Cisgender women in the US continue to be underserved by HIV prevention programs, particularly in accessing PrEP. More effective strategies are needed to identify at-risk individuals and expand use of PrEP.

**Long-Term Relationship Between Opioid Use and Change in HIV Disease Severity: A Prospective Cohort Study** Fiona Bhondoekhan\* Fiona Bhondoekhan Coraline Danieli Michal Abrahamowicz Brandon D.L. Marshall M-J Milloy

**Aim:** We sought to model the cumulative, long-term effect of self-reported opioid use using weighted cumulative exposure (WCE) models on change in Veterans Aging Cohort (VACS) Index score, a measure of HIV disease severity, among people with HIV (PWH).

**Methods:** ART-exposed PWH who enrolled from December 2005 to November 2017 in the AIDS Care Cohort to Evaluate Exposure to Survival Services prospective cohort study in Vancouver, Canada were studied. Baseline surveys collected sociodemographic and substance use information, and follow-up occurred every six months. Opioid use was defined as self-reported illicit use of prescription opioids and/or heroin in the past six months. The outcome was VACS Index score. WCE models estimated the relative impact of past opioid use on the current change in VACS Index score. Conventional linear mixed models were used as a comparative reference to the WCE models.

**Results:** The study comprised 483 ART-exposed PWH, 21.2% (n=102) of whom used opioids at baseline. Median age was 44.1 years, 42.4% identified as Indigenous, and 34.2% were female. Median VACS Index score at baseline was 21 (IQR= 12 - 29), and median follow-up time was 6.7 years (IQR= 3.5 - 8.6 years). The results from the WCE model indicated that opioid use from approximately the past 1.5 - 3 years were associated with statistically significant decreases in the current VACS index score. The conventional linear mixed model estimated that ever using opioids in the past 6 months resulted in an average 0.04 point (95%CI: -0.83 - 0.76) decrease in VACS Index score.

**Conclusion:** WCE models capture dynamic patterns of self-reported opioid use that may inform more realistic modeling of substance use behavior on health outcomes.

**Occupational stigma and sexual health outcomes: Findings from a community-based cohort of women sex workers in Metro Vancouver, Canada (2014-2022)** Kirstin Kielhold\* Kirstin Kielhold Kate Shannon Jennie Pearson Emma Ettinger Charlie Zhou Andrea Krusi Shira Goldenberg

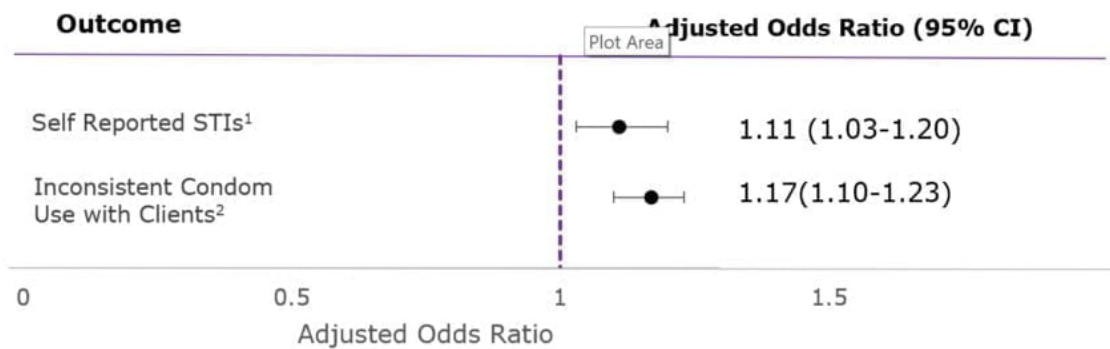
**Background:** Women sex workers (SWs) face high rates of health disparities due to structural barriers including criminalization and high rates of occupational stigma. Stigma is generally associated with HIV and STI related health inequities among marginalized populations, however we know less about the nature and impacts of sex work-specific stigma on sexual health risks among women SWs. Given these research gaps and the disproportionate burden of stigma faced by SWs, we evaluated the association between experiences of sex work occupational stigma and sexual health outcomes of (1) self-reported sexually transmitted infection (STI) diagnoses and (2) inconsistent condom use with clients, both measured in the last 6 months.

**Methods:** Baseline and semi-annual **questionnaire** data from a prospective, community-based cohort of SWs in Vancouver, Canada from 2014-2022. We used bivariate and multivariate logistic regression with generalized estimating equations (GEE) to analyze the relationship between occupational stigma (measured using a validated sex work scale,  $\alpha = 0.96$ ) and outcomes of (1) self-reported STI diagnoses, and (2) inconsistent condom use with clients.

**Results:** Among participants ( $n=574$ ), the median age was 39 (IQR:31-46) and 42.3% ( $n=243$ ) identified as Indigenous. 17.9% ( $n=103$ ) had at least one self-reported STI diagnosis, and 32.1% ( $n=184$ ) reported inconsistent condom use with clients during the study period. In separate multivariate confounder models, occupational stigma was independently associated with recent STI diagnosis (aOR1.11, 95% CI: 1.03-1.20) and inconsistent condom use (aOR1.17, 95% CI: 1.10-1.23) after adjustment for confounders.

**Conclusion:** SWs who face more stigma face higher odds of self-reported STIs and inconsistent condom use. Interventions addressing the role of occupational stigma as a determinant of health are needed, including peer-delivered sexual health services and structural changes to decriminalize and destigmatize sex work.

Figure 1: Adjusted odds ratios (AORs) and 95% Confidence Intervals (CIs) for the association between sex work stigma and Self Reported STI's and Inconsistent Condom Use with Clients in the last 6 months among women sex workers in Metro Vancouver, Canada (N=574, 2014-2022)



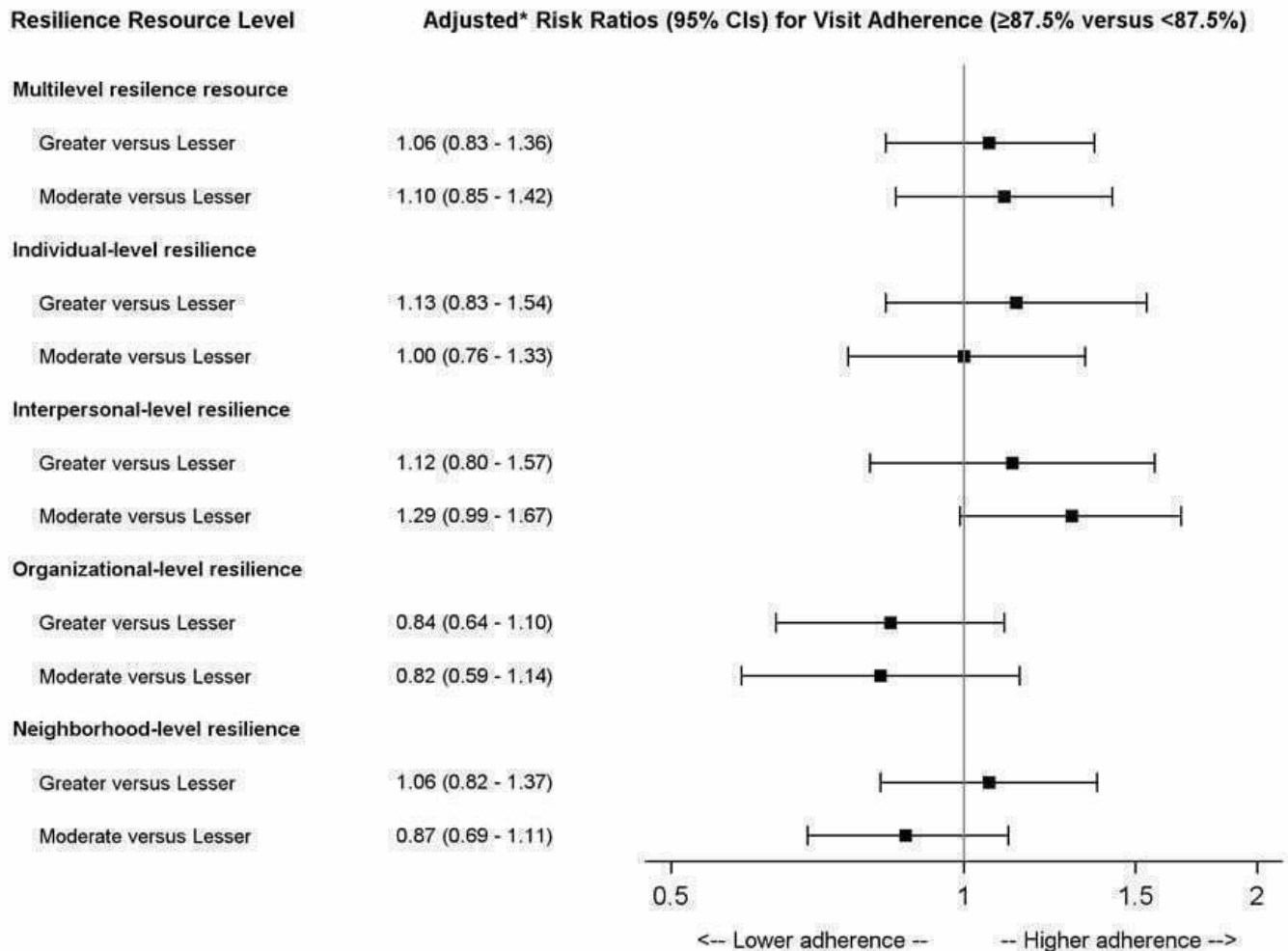
1. Model one adjusted for Indigenous ancestry, violence from perpetrators posing as clients, sexual minority, gender minority, age, injection drug use, street/public solicitation, unstable housing, police harassment, and difficulty accessing condoms

2. Model two adjusted for age, injection drug use, indigenous ancestry, sexual minority, gender minority, street solicitation, violence from perpetrators posing as clients, and unstable housing

All variables time updated to last six months

**Multilevel resilience and visit adherence among African American/Black adults living with HIV in the southeastern United States** Marta G. Wilson-Barthes\* Jee Won Park Marta G. Wilson-Barthes Joseph W. Hogan Michael J. Mugavero Sonia Napravnik Michael P. Carey Joseph L. Fava Sannisha K. Dale Valerie A. Earnshaw Bernadette Johnson Sarah Dougherty-Sheff Deana Agil Chanelle J. Howe Akilah J. Dulin

Attending clinic appointments is critical for achieving viral suppression among adults with HIV, yet racial disparities in clinic attendance are documented. Multilevel resilience resources (e.g., self-compassion) may help to reduce such disparities. Data from 293 African American/Black participants in two HIV clinical cohorts in southeastern U.S. were used to prospectively examine the relationship between resilience resources and clinic visit adherence. Resilience was assessed via the Multilevel Resilience Resource Measure (MRM), where endorsement of a MRM statement indicated agreement that a resource helps continue HIV care despite challenges or is present in a respondent's neighborhood. Visit adherence was an indicator of attending  $\geq 87.5\%$  of scheduled clinic appointments during 12-months of follow-up. Modified Poisson models estimated adjusted risk ratios (aRRs) for visit adherence as a function of MRM tertiles, controlling for potential sources of confounding and selection bias. We assessed for effect modification by neighborhood disadvantage, crime risk and assault risk. Participants had a median age of 51 years at enrollment, were 36% female, and had 55% visit adherence. The overall aRR (95% CI) for higher visit adherence comparing participants with greater (versus lesser) resilience resource endorsement was 1.06 (0.83-1.36). Adjusted corresponding overall findings were similar for resilience resources at the individual-, interpersonal-, and neighborhood-level. However, the corresponding overall aRR for organization-level resilience was 0.84 (0.64-1.10). There was evidence of modification by levels of neighborhood disadvantage and assault risk, but minimal evidence by neighborhood crime risk. Promoting resilience resources at specific levels (e.g., interpersonal) among certain subgroups (e.g., residents of more disadvantaged neighborhoods) may improve visit adherence and reduce racial disparities in clinic attendance. Further study in a larger sample is needed.



**Figure.** Associations between multilevel resilience resources and adherence to scheduled HIV clinic appointments (≥87.5% versus <87.5%) among 293 African American/Black participants in two HIV clinical cohorts in the southeastern United States.

\* Adjusted for age at enrollment, gender at enrollment, sexual orientation at enrollment, neighborhood disadvantage at enrollment, neighborhood murder index at enrollment, neighborhood assault index at enrollment, health insurance status at enrollment, at-risk alcohol use at or in the year prior to enrollment, drug use at or in the 3 months prior to enrollment, depression at or in the 2 weeks prior to enrollment, panic syndrome at or in the 4 weeks prior to enrollment, other mental health diagnoses at or in the 4 weeks prior to enrollment, AIDS-defining illnesses at or in the 2 years prior to enrollment, time since ART initiation, last CD4 cell count in the 2 years prior to enrollment, and last virologic suppression status (i.e., HIV-1 RNA levels below 50 copies/milliliter) in the 2 years prior to enrollment.



**Early Influenza Activity, Surveillance Trends, and Severity Indicators – Tennessee and Georgia, October-December 2022** Elizabeth White\* Elizabeth White Sarah Winders Audrey Kunkes Christine Thomas Noah Kojima Mary-Margaret Fill Caitlin Newhouse Keipp Talbot Carlos Grijalva Caleb Wiedeman Dylan Proctor Rene Borroto Cherie Drenzek Kyle Openo Jessica Pavlick Matthew Biggerstaff Danielle Iuliano Alissa O’Halloran Brendan Flannery John Dunn Melissa Rolfes

**Background:** In October 2022, Tennessee and Georgia reported early influenza activity. We used surveillance data to characterize the intensity and severity of this early influenza circulation.

**Methods:** We analyzed historic and current data on the percent of emergency department visits for influenza-like illness (ILI-ED visits, 2016-17-current) and rates of influenza-associated hospitalization from the Emerging Infections Program (2012-13-current; adjusted for influenza testing practices) for the Atlanta, Georgia and Nashville, Tennessee metropolitan areas. We restricted 2022-23 season data to October 2-December 3, 2022, as of December 14, 2022. We stratified analyses by age (<18, 18-64, ≥65 years). We calculated weekly changes in ILI-ED visits and hospitalizations for each season. To assess severity, we compared weekly hospitalizations from the 2022-23 season to a probability distribution built from the three highest weekly rates from each prior season.

**Results:** During October 2-December 3, 2022, weekly percent ILI-ED visits and influenza-associated hospitalization rates in Atlanta and Nashville were greater than during the same period in previous seasons. In both areas, weekly changes in age group-specific ILI-ED visits and influenza-associated hospitalizations were within the 75<sup>th</sup> percentile of changes seen in prior seasons. The greatest weekly changes during the 2022-23 season occurred among those aged <18 years. Among children, percent ILI-ED visits reached 23% in Atlanta (prior season peak range: 18-31%) and 29% in Nashville (range: 14-34%). Weekly influenza-associated hospitalization rates among children approached (in Atlanta) or exceeded (in Nashville) the 90<sup>th</sup> percentile of standardized peak rates.

**Conclusions:** In Atlanta and Nashville, the 2022-23 influenza season began early and with high rates of hospitalization, particularly among children. Prevention measures including influenza vaccination are important to reduce the potential severity of this season.

**Mathematical modeling of spatial-demographic heterogeneity in urban malaria epidemics to assess the impact of insecticide-treated bed nets in Accra, Ghana** M. Koissi Savi\* Merveille Koissi Savi Lauren M. Childs Christian Borgemeister

Over 650,000 people die each year because of malaria in sub-Saharan Africa. Existing frameworks for decision-making do not always include community behaviors, and often include misrepresentations of policymakers. Our objectives are to 1) assess community knowledge and behavior regarding urban malaria prevention, 2) develop some reality-based scenarios explaining urban malaria dynamics based on the findings of the community survey, 3) develop a metapopulation framework that enables checking the developed scenarios, 4) determine the mathematical validity of the mechanistic model, 5) understand the magnitude of community behavior on disease infectivity. In our study, we developed a mechanistic model with Lagrangian movement between communities that was patch- and age-structured. Three scenarios were simulated compared to spatially isolated communities with a fraction of 60% using insecticide-treated bed nets (ITN). The rate of use of ITN is constant and varies with the spatial area, ii) the rate of use of ITNs depends on their coverage, and ii) the rate of use of ITNs varies with their chemical and physical integrity. According to our survey, malaria poses a threat to the surveyed communities. Having an ITN does not imply that the community will use it. Simulations show that malaria reproduction rates double when ITNs are compromised. To effectively control the disease, it is imperative to consider the behavior of the community. Consequently, there is a need to educate communities and encourage their use of ITN.

**Comparing Influenza Vaccine Adherence Among Diabetes Patients and Non-Diabetes US Population in the Pre- and During the COVID-19 Eras** Amanda Phipps\* Herve Fossou Orvalho Augusto

**Background:** Diabetes patients are at elevated risk for complications from influenza infection. The SARS-CoV-2 infection (COVID-19) led to unanticipated disruption in the healthcare system. We compared influenza vaccine adherence among people living with diabetes vs. the non-diabetes population before and during the COVID-19 era.

**Method:** Using the Behavioral Risk Factor Surveillance System (BRFSS), we compared influenza vaccine adherence among people with diabetes in the states where the optional module for diabetes was collected in 2018-2019 (pre-COVID-19) and in 2020-2021 (during COVID-19). We used age-standardized proportions and 95% CIs to describe influenza vaccine adherence between these periods among people with diabetes. We also used a difference-in-differences analysis to compare the change in influenza vaccine adherence between periods in people with and without diabetes.

**Results:** The average proportions of influenza vaccine adherence among BRFSS participants with diabetes ranged from 0.538 (0.573, 0.593) to 0.673 (0.664, 0.683), respectively, in the pre- and during-COVID-19. Among participants without diabetes, the average adherence respectively ranged from 0.457 (0.453, 0.460) to 0.556 (0.552, 0.560), between these time periods. Thus, influenza vaccine adherence proportions and changes in those proportions over time were similar among those participants with versus without diabetes.

**Conclusion:** Influenza vaccine adherence increased before and during COVID-19, and the increases were similar in magnitude regardless of diabetes status. However, adherence remains much lower than the 80% to 90% of influenza vaccine adherence recommended by the CDC, respectively, for non-diabetes and diabetes, to achieve herd immunity and prevent complications from influenza. Therefore, developing efficient strategies for improving adherence should be a priority.

**Evaluating methods of measurement for antibiotic exposure in hospitalized patients** Neal Goldstein\* Jessica Webster Neal D. Goldstein

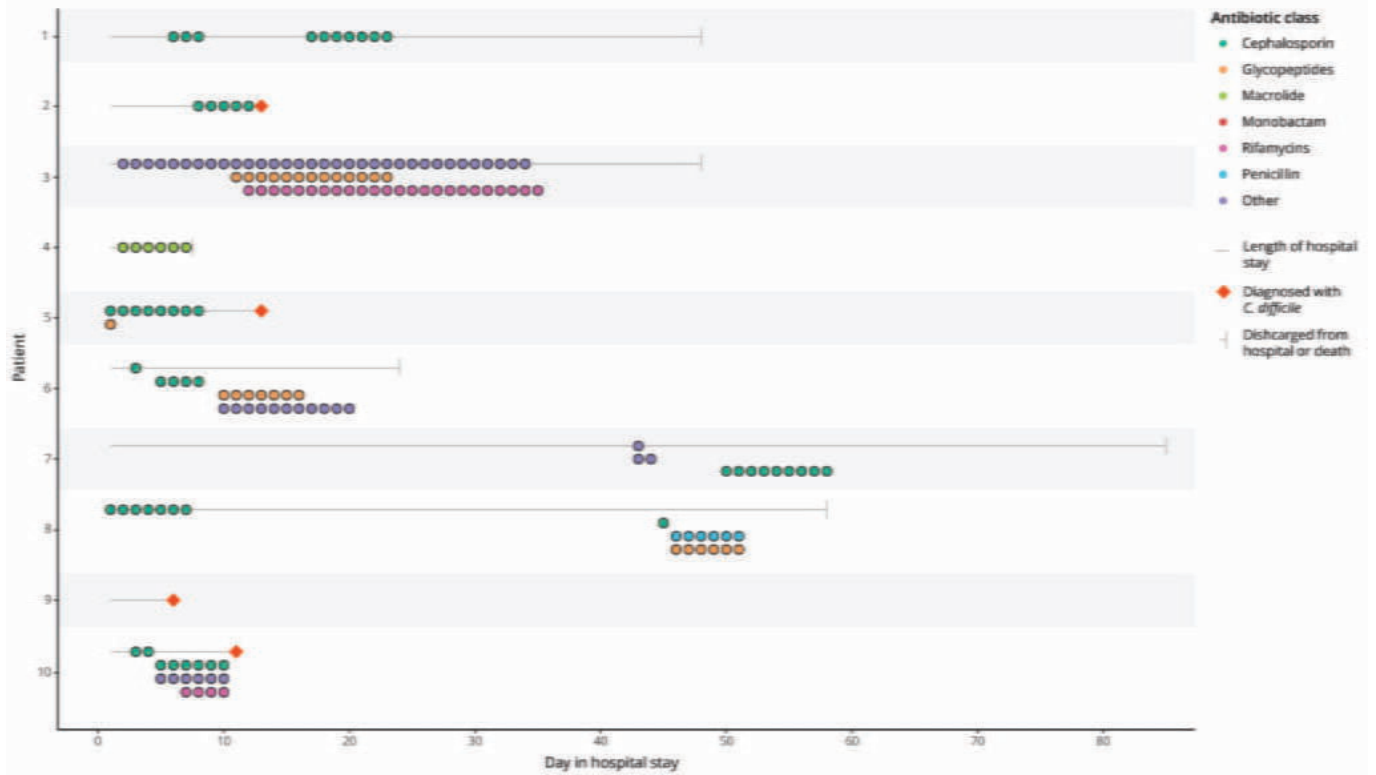
Antibiotic administration is often evaluated as a dichotomous treatment in clinical research of hospitalized patients, despite it being a complex exposure with a range of characteristics constantly changing over the course of a patient's hospital stay. These characteristics may include type and class of medication, treatment dose, length of treatment, route of administration, and timing of treatment within the stay, all of which could vary between patients as well as within patients prescribed multiple courses. We sought to compare and contrast methods of measuring and operationalizing antibiotic treatment and illustrate how each would be calculated using sample data.

We identified six aspects of antibiotic treatment that may be used for measuring exposure: receipt of any antibiotic, cumulative number of antibiotic courses, length of antibiotic course, type and class of medication, dosage, and route of administration. These measures can be calculated in various ways, depending on the investigator's research question and study design (cross-sectional versus longitudinal).

To illustrate the calculations and interpretations of the various treatment decisions, we applied these measures to an inpatient cohort followed until healthcare-associated *Clostridioides difficile* infection, discharge, or death. The **Figure** displays the complex exposure patterns in patients' hospital stays for a subset of the cohort. Exposure measurements differed with respect to the calculation of interest: for example, among 667 patients in the cohort, 449 (66%) received any antibiotic. Among patients that received an antibiotic, 347 (77%) had >1 course, 337 (75%) had >1 class, and the median duration of therapy was 7 days (IQR: 11 days).

Investigators studying antibiotic exposure should consider multiple aspects of treatment informed by their research question. Failure to consider the complexities of antibiotic exposure measurement may lead to misclassification and biased results.

### Variations in antibiotic exposure and *Clostridioides difficile* diagnosis in hospitalized patients



### **3D Printers in Hospitals: Bacterial Contamination of Common and Antimicrobial 3D-printed Material** Katelin Jackson\* Katelin Jackson Douglas Call Eric Lofgren

**Background:** COVID-19 has presented hospitals with unique challenges. A survey of hospitals showed that 40% reported “limited” or worse levels of personal protective equipment (PPE), and 13% were self-producing PPE to address those deficits, including 3D printed items. We previously found that 3D-printed materials can be disinfected, but the level of disinfection was variable and bacterial populations recovered hours after disinfection. Two filaments, PLACTIVE and PUREMENT, claim to be antimicrobial; they use copper nanocomposites and silver ions to reduce bacterial populations. We assess how PLACTIVE and PUREMENT may be contaminated and how well they reduce contamination versus Polylactic Acid (PLA), a standard 3D-printed material.

**Methods:** We grew pathogens commonly found in hospital environments, methicillin-resistant and susceptible *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae* on 3D-printed disks. We conducted bacterial survival assays to determine if bacteria grow on PLA, PLACTIVE, and PUREMENT. We performed a time series (with 3- and 24-hour dry times) followed by serial dilutions to attain colony-forming unit (CFU) averages for each strain per disk. PLACTIVE and PUREMENT CFU averages were compared to PLA CFU averages to see how well the antimicrobial material decreased bacterial load.

**Results:** PLA is readily contaminated with bacteria common in hospitals and can sustain that contamination. PLACTIVE and PUREMONT had lower levels of bacterial contamination when compared to PLA. However, PLACTIVE had lower overall CFU averages.

**Conclusion:** Using appropriate materials for 3D printing is essential for controlling contamination. 3D printers and their products can be invaluable for hospitals, especially when supplies are low and healthcare worker safety is paramount. Environmental services should be made aware of the presence of 3D-printed materials, and patients should be discouraged from printing their own items for use in hospital environments.

**Assessing the Impact of Inpatient Antibiotic Use on Bloodstream Infection Resistance: A Time-Series Analysis** Juan Gago\* Juan Gago Bo Shopsis Victor Torres Lorna Thorpe

Bloodstream infections (BSI) are associated with high morbidity and mortality. While increased antimicrobial use is correlated with an increased incidence of difficult to treat antimicrobial resistant infections at the population-level, the role of in-patient antimicrobial use on hospital-associated BSI and resistance patterns are not well explored. Here, we assessed correlations between inpatient antimicrobial use and trends of resistance in nosocomial BSI in one large tertiary care hospital system using time-series analysis. We aggregated monthly rates of daily doses of antibiotics per 10,000 admissions and incidence of BSI (cases per 10,000 admissions) among adult inpatients from 2017 to 2021. We stratified BSI by type of pathogen and resistance, and performed a cross-correlation analysis of time series data on antibiotic use and lagged incidence of nosocomial BSIs. We observed an overall increase in antibiotic use for the period 2017-2021 (88.7% increase in daily dose rate). The overall incidence of BSI during this period also increased (14.33 vs. 23.74 cases per 10,000 admissions). Upon stratifying the results by nosocomial or community-acquired BSI, we found that nosocomial resistant infections remained stable, while there was a surge in community-acquired antimicrobial susceptible BSI. These ecologic trends suggest that higher use of in-patient antibiotics does not seem to be driving a higher incidence of resistance in nosocomial BSI within our patient population. We further explore whether the increase in community-acquired susceptible BSI are associated with hospital readmission (misclassified as community-acquired). Our data point to potential implications for short-stay hospitalizations and exogenous forces such as the opioid epidemic.

**Predicting COVID-19 hospitalizations from wastewater surveillance data in New York State, USA** David A. Larsen\* Dustin Hill Mohammed Alazawi Joe Moran Lydia Bennett Ian Bradley Mary B. Collins Christopher J. Gobler Hyatt Green Tabassum Insaf Brittany L. Kmush Dana Neigel Shailla Raymond Mian Wang Yinyin Ye David A. Larsen

*Background:* The public health response to COVID-19 has largely shifted to reducing deaths and hospitalizations, and ensuring that health systems are not overwhelmed. The amount of SARS-CoV-2 RNA fragments in wastewater are known to correlate with clinical data including cases and hospital admissions for COVID-19. We develop and test a predictive model for incident COVID-19 hospital admissions in New York state using wastewater data and other covariates.

*Methods:* Using county-level COVID-19 hospital admissions and wastewater surveillance covering 13 million people across 30 counties in New York, we fit a generalized linear mixed model with a Poisson distribution predicting new hospital admissions from wastewater concentrations of SARS-CoV-2 RNA from 2020-2022. We included covariates for comorbidities such as COVID-19 vaccine coverage in the county, rate of individuals with cancer in the county, demographics such as median age, social vulnerability, and seasonality.

*Findings:* Wastewater concentrations of SARS-CoV-2 correlate with new hospital admissions per 100,000 population up to ten days prior to the day of admission. Models that include wastewater and covariates have higher predictive power than models that include clinical cases and covariates without wastewater. Predicted hospital admissions had a correlation of 0.87 with observed admissions.

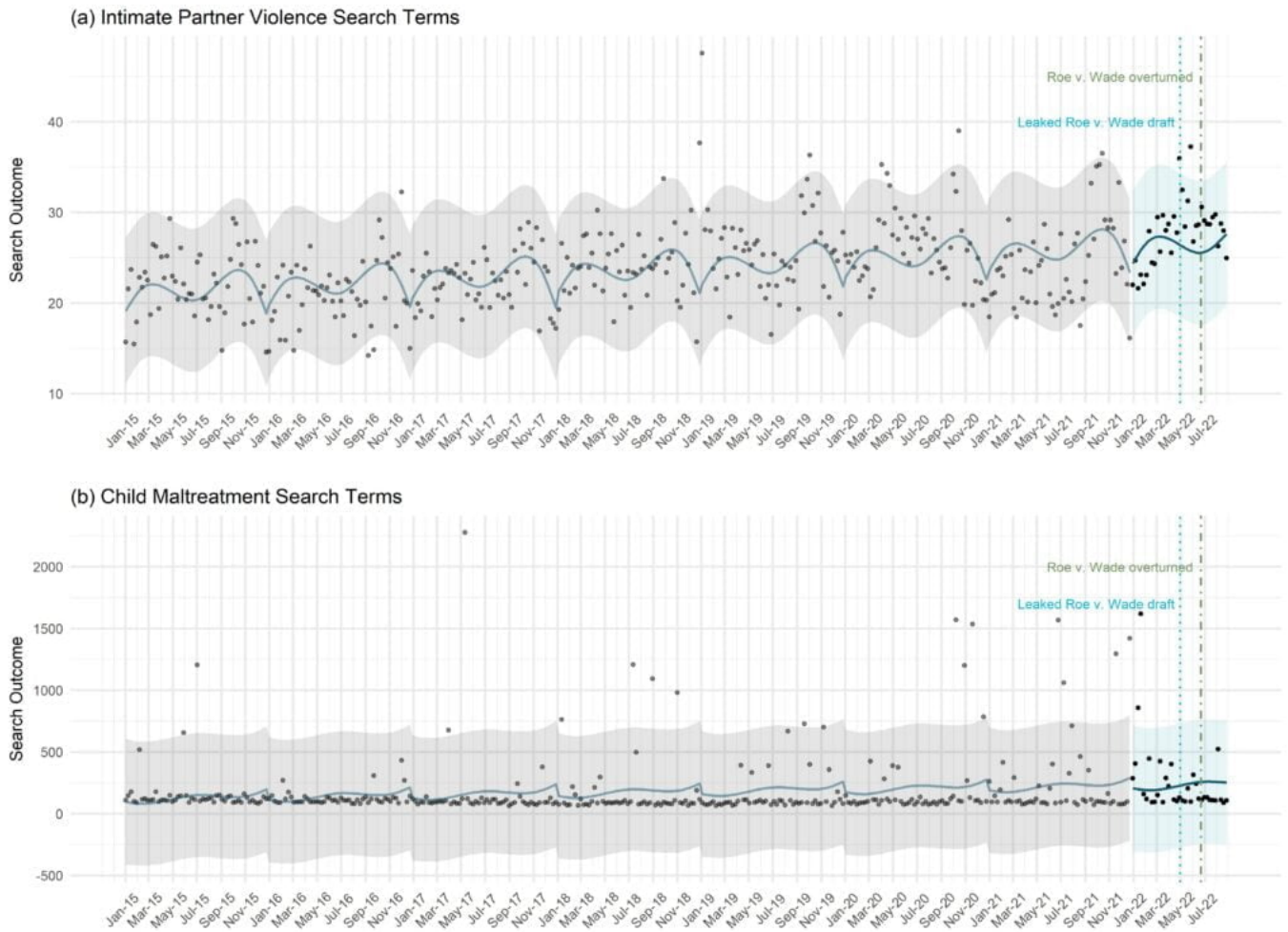
*Interpretation:* Using wastewater to predict future hospital admissions due to COVID-19 is accurate and effective. The observed lead time of ten days could improve resource allocation and preparation for seasonal surges.



**Impact of overturning Roe v. Wade on family violence in the United States** Krista Neumann\*  
Krista Neumann Kriszta Farkas N. Jeanie Santaularia Susan M. Mason

The overturning of Roe v. Wade on June 24, 2022 by the United States Supreme Court rescinded the constitutional right to an abortion. Research shows that lack of abortion access increases risk of violence, but the full range of consequences of rescinding Roe v. Wade are unknown given the new extent of restrictions, differential policies by state, and limited real-time data. Previous work has used Google search data to analyze the real-time impact of policies on family violence. The goal of this study is to better understand the impacts of the overturning of Roe v. Wade on family violence, including intimate partner violence and child maltreatment, which we hypothesize may increase via stress pathways (e.g., due to additional financial burdens, unwanted pregnancies, legal threats). We obtained national- and state-level weekly Google search volume data from January 2015 to September 2022 (most recent), via the Google Health Trends application programming interface, for terms indicative of intimate partner violence and child maltreatment victimization. We evaluated whether there were excess Google searches post-Roe v. Wade by comparing observed searches to expected searches, had the court decision not happened. We used a linear regression prediction model with restricted cubic splines to capture seasonal variation and looked for observed data points outside calculated 95% prediction intervals. Preliminary national-level results do not suggest a clear increase in relative search volume indicative of intimate partner violence or child maltreatment post-Roe v. Wade for the US as a whole (Figure 1). The results of this study are the first of its kind documenting the potential impacts of overturning Roe v. Wade on family violence. While these initial national-level results do not suggest associations in the first weeks after the court decision, in ongoing research we will examine longer post-policy periods and state-specific impacts that could be masked by aggregation.

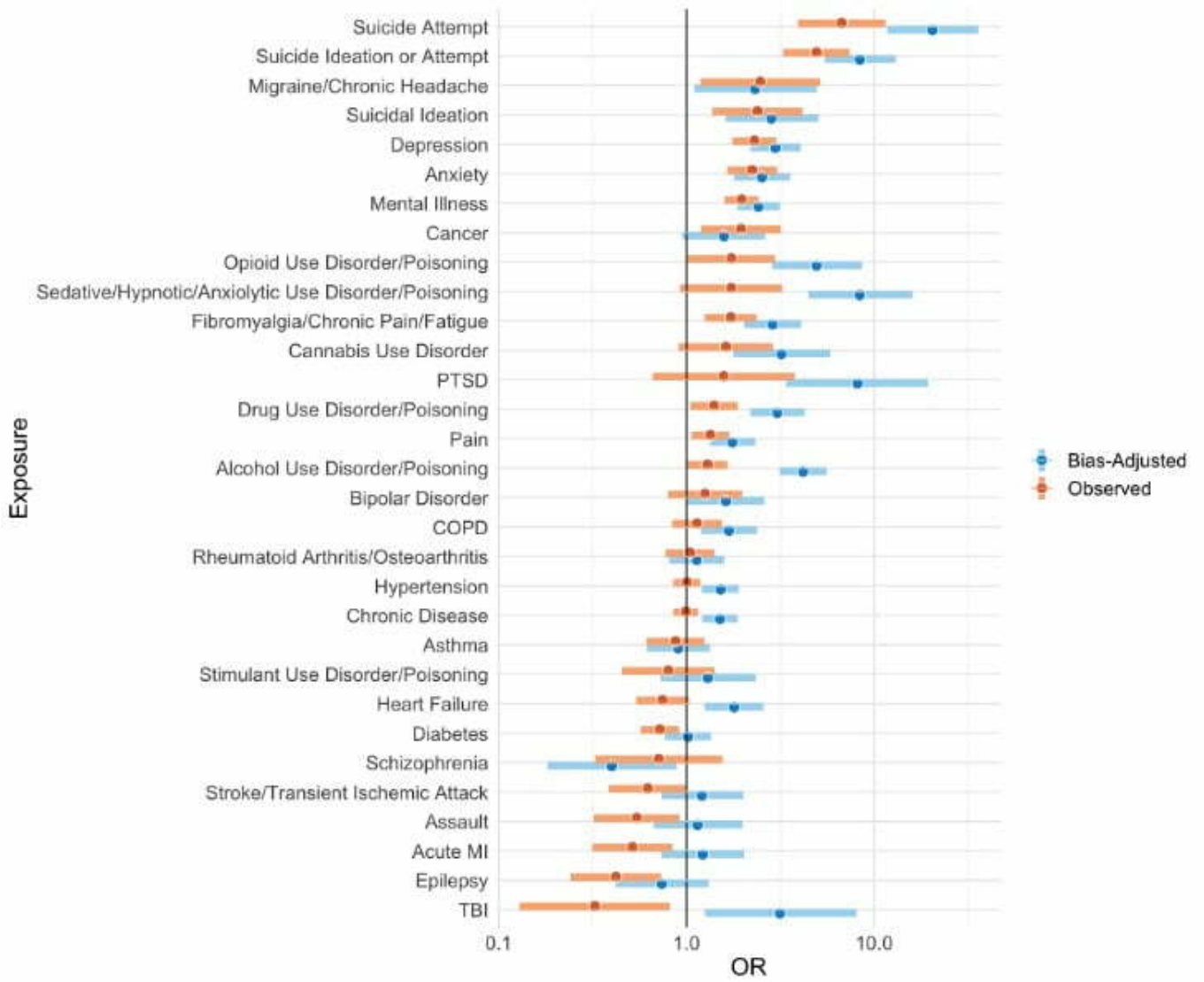
Figure 1: Excess Google Searches at the National Level



Note: Average weekly Google search volume (points) alongside predicted Google search volume (curve) and 95% prediction intervals (grey bands representing years 2015-2021 and blue bands representing the year 2022)

**Association of medical conditions and firearm suicide among legal handgun purchasers in California** Julia Schleimer\* Julia Schleimer Rose Kagawa Hannah Laqueur

Certain health conditions are markers of suicide risk, but more research is needed on clinical risk factors for suicide among firearm owners. Our goal was to examine associations of emergency department (ED) and inpatient hospital visits for behavioral and physical health conditions with firearm suicide among handgun purchasers. This was a case-control study of 5,415 legal handgun purchasers in California who died between 1/1/2008-12/31/2013. Cases were firearm suicide decedents; controls were motor vehicle crash (MVC) decedents. Exposures were ED and hospital visits for six categories of health diagnoses in the three years prior to death. Probabilistic quantitative bias analysis (QBA) quantified selection bias due to deceased controls. There were 3,862 firearm suicide decedents and 1,553 MVC decedents. In multivariable models, suicidal ideation/attempt (OR=4.92; 95% CI=3.27-7.40), mental illness (OR=1.97; 95% CI=1.60-2.43), drug use disorder (OR=1.40; 95% CI=1.05-1.88), pain (OR=1.34; 95% CI=1.07-1.69), and alcohol use disorder (OR=1.29; 95% CI=1.01-1.65) were associated with higher odds of firearm suicide. When adjusting for all conditions simultaneously, only the associations for suicidal ideation/attempt and mental illness remained. QBA indicated that observed associations were generally biased downward. Encounters with the healthcare system provide opportunities to identify firearm owners at high risk of suicide and implement tailored interventions.



**Population-level patterns of health care utilization in the 12-months following an emergency department encounter for sexual assault in a universal health care system**

Katherine Muldoon\* Katherine Muldoon Hailey Mitchell Robert Talarico Kari Sampsel Douglas Manuel

**Background:** Little is known about health care utilization among survivors of sexual assault. The objective of this study was to document health care utilization patterns 12-mo following an emergency department (ED) encounter for sexual assault.

**Methods:** This retrospective cohort study uses health administrative data from 2013-2018 to identify survivors of sex assault who presented for care at 197 EDs in Ontario, Canada. Cases were identified through the National Ambulatory Care Reporting System, Discharge Abstract Database, and Registered Persons Database. Follow-up encounters were identified through the Ontario Health Insurance Plan, a single-payer universal health insurance plan, and specialists were identified through specialty designation codes. Data are presented in proportions and median (med) and interquartile ranges (IQR) for continuous.

**Results:** Between 2013-2018, there were 17 552 ED encounters for sex assault, 15 365 (87.5%) among female individuals. The median age for females was 21 years (IQR:17-31) and 10 (4-26) for male. In the 12-mo post-sex assault, Primary Care Providers provided care to 12 930 (84.5%) female survivors within med 42 (IQR:12-115) days and 1638 (75.2%) male survivors within med 47 (IQR:13-133) days of the assault. Psychiatrists provided care to 4725 (30.9%) female survivors within 45 (IQR:10-143) days and 519 (23.8%) male survivors within 37 (IQR:8-135) days. Emergency specialists provided care for 3394 (22.2%) female survivors within 96 (IQR:22-205) days and 356 (16.3%) males within 84 (IQR:15-211) days. OBGYNs provided care to 2330 (15.2%) females survivors within 137 (IQR:50-242) days. Only 767 (5.0%) females and 154 (7.1%) male survivors did not have any encounter with the health care system.

**Conclusion:** This study found a surprisingly high level of timely engagement with the healthcare system for survivors of sexual assault with care most commonly provided by family medicine, psychiatrists, emergency physicians and OBGYNs.

**Intersectionality and the Role of Firearm and Alcohol Involvement in Violent Deaths: A Decomposition Analysis** Hoisum Nguyen\* Hoisum Nguyen James Macinko

Violence is a public health priority. It is also a matter of social justice that requires nuanced understanding of the interplay among different individual-level and structural factors that serve as root causes of societal disadvantage. Through applying intersectional theories, we analyze different combinations of alcohol and firearms involvement (exposure) on different types of violent death (outcome) and its relationship to race, where we consider both “non-additive intersectionality” and “switch-intersectionality” as: 1) one’s intersectional identity would influence one’s life more than if each identity were considered separately, and 2) some causal relationships are activated/deactivated specifically for individuals that occupy an intersection of certain identity positions and are otherwise not present for those “outside” of that intersection.

Utilizing data from the NVDRS (National Violent Death Reporting System, 2018-19), we demonstrate an intersectional approach to understanding health inequities by quantifying differential exposures and effects via 3- and 4- way decomposition, with an exploration of pure (natural) direct and indirect effects, and reference and mediated interaction effects among individuals involved in firearm-related, alcohol-related and both firearm- and alcohol-related suicides and homicides.

Preliminary results suggest that different combinations of firearm and alcohol involvement vary across intersections of social identity and status. For example, despite White individuals composing most of the study sample, Black, Asian, and Hispanic/Latino individuals comprise a disproportionately large portion of those with combinations of firearm and alcohol involvement. Pursuing an intersectional approach to this decomposition analysis will bridge quantitative causal methods to qualitative social constructs that can target policy intervention for specific groups of people and identities.

**Table 2. Distribution of Involvement Between Firearms and Alcohol in the Types of Violent Death and Relevant Sociodemographic Characteristics (N=107,747)**

	N (%)	Combinations of Involvement Between Firearms and Alcohol <sup>2</sup>			
		Firearms Only	Alcohol Only	Firearms and Alcohol	Neither Firearms nor Alcohol
<b>Types of Violent Death</b>					
<b>Suicide</b>					
No	38,513 (35.74)	14,992 (38.93)	6,711 (17.43)	5,157 (13.39)	11,653 (30.26)
Yes	63,482 (58.92)	23,690 (37.32)	7,590 (11.96)	8,924 (14.06)	23,278 (36.67)
<b>Homicide</b>					
No	76,282 (70.80)	24,984 (32.75)	8,167 (10.71)	12,269 (16.08)	30,862 (40.46)
Yes	25,713 (23.86)	13,698 (53.27)	6,134 (23.86)	1,812 (7.05)	4,069 (15.82)
<b>Sociodemographic Characteristics</b>					
<b>Biological Sex of Victim</b>					
Male	83,987 (77.95)	33,158 (39.48)	12,536 (14.93)	9,974 (11.88)	23,820 (28.36)
Female	23,751 (22.04)	5,524 (23.26)	1,765 (7.43)	4,107 (17.29)	11,105 (46.76)
<b>Race/Ethnicity</b>					
White	69,437 (64.44)	24,183 (34.83)	7,741 (11.15)	9,519 (13.71)	24,430 (35.18)
Black or African American	21,642 (20.09)	9,568 (44.21)	3,961 (18.30)	1,938 (8.95)	4,593 (21.22)
Asian	1,468 (1.36)	302 (20.57)	239 (16.28)	359 (24.46)	550 (37.47)
Hispanic/Latino	11,148 (10.35)	3,644 (32.69)	1,990 (17.85)	1,670 (14.98)	3,473 (31.15)
Native Hawaiian/Pacif. Islander	2,565 (2.38)	545 (21.25)	170 (6.63)	362 (14.11)	1,346 (52.48)
American Indian/Alaska Native	313 (0.29)	83 (25.52)	23 (7.35)	43 (13.74)	120 (38.34)
<b>Education Level</b>					
12 <sup>th</sup> Grade or Less	22,463 (20.85)	8,263 (36.78)	2,816 (12.54)	2,474 (11.01)	7,562 (33.66)
High School Graduate/GED	45,372 (42.11)	16,878 (37.20)	6,648 (14.65)	5,870 (12.94)	13,680 (30.15)
Some College Credit/AA Degree	22,735 (21.20)	8,115 (35.69)	3,152 (13.86)	3,232 (14.22)	7,183 (31.59)
Bachelor's Degree	10,068 (9.34)	3,289 (32.67)	1,088 (10.81)	1,474 (14.64)	3,645 (36.20)
Graduate-Level Degree <sup>3</sup>	7,109 (6.60)	2,137 (30.06)	597 (8.40)	1,031 (14.50)	2,861 (40.24)
<b>Mental Health Problem at Time of Death</b>					
No	73,776 (68.47)	29,814 (40.41)	10,919 (14.80)	8,324 (11.28)	20,773 (28.16)
Yes	33,971 (31.53)	8,868 (26.10)	3,382 (9.96)	5,757 (16.95)	14,158 (41.68)

<sup>1</sup> Missingness from "combinations of firearm and alcohol involvement" (n=5,752; 5.34%); sex (n=9, 0.01%); race/ethnicity (n=1174, 1.09%)

<sup>2</sup> Row percent was used across combinations of involvement between firearms and alcohol

<sup>3</sup> Graduate-level degree = master's, doctorate, or professional degree

**Survey on Sexual Harassment among SER Members** Ruiqi Cen\* Ruiqi Cen Wendy N Nembhard  
Martha M Werler

Background: “#Me Too” went global in 2018 as a social movement against workplace gender-based harassment and abuse. A 2018 report in *Nature* stated the prevalence of sexual harassment in academia was higher than that in industry and government in the US. Although considered a public health issue, sexual harassment has rarely been studied in the workplace of public health professionals.

Methods: We emailed Society for Epidemiologic Research members in 2021, inviting them to complete an online survey, without incentive provided. Survey questions were designed based on literature and existing surveys, and asked whether the respondent had ever experienced sexual harassment as a graduate student, in the workplace, and at a professional conference, and, if so, its impact and consequence. Data on gender and years since graduation with highest degree were also collected.

Results: Among 630 respondents, 78% identified as women; 14% were students, while 26%, 20%, 21%, and 18% had graduated 20 years previously. Among women, the prevalence of having experienced sexual harassment was 45%, compared to 15% among those identifying as men. Sexual harassment in the workplace was reported by 29%, as a graduate student by 17%, and at professional conference by 9% of respondents. Among those reporting sexual harassment, 6% of men and 22% of women stated a definite negative impact; no men and 23% of women reported it to a higher authority. Women who graduated <5 years before had the highest percent reporting to a higher authority (31%), while women who graduated >20 years before had the lowest reporting rate (13%). Fear of negative consequences and feeling it was useless were the top reasons for not reporting to higher authority. Verbal warning issues and reporting to the police were the most and least consequences for harassers.

Conclusion: Sexual harassment in epidemiology training, work, and conference spaces is high; prevention training is needed.



**Predicting Violent Crime Among Handgun Purchasers in California Using Handgun Purchase Trends and Criminal Histories** Aaron Shev\* Aaron Shev Mona Wright Garen Wintemute Hannah Laqueur

**Background:** Firearm purchasing records are a potentially critical and unexplored resource for the development of risk prediction tools to identify individuals at high risk for violence. In this study, we use machine learning methods to develop models to predict firearm violence among legal purchasers of handguns.

**Methods:** Our data consists of all individuals with records of transaction in California's Dealer Record of Sale (DROS) database, from 1996 through 2020. We extract features to describe purchase history including age at first purchase, temporal purchase patterns, firearm caliber and price, and others. Purchaser information is linked to criminal records to identify firearm-related major violent crime, our primary outcome, as well as criminal history predictors. Using gradient boosted models with Cox Proportional Hazards loss functions, we fit a validated predictive model of individual risk of violence. Handgun purchasing and criminal history features are included in the model as time-varying covariates summarizing the previous year and lifetime of the purchaser. We also include time-invariant community characteristics of the purchasers as additional predictors. The gradient boosted model is ideal for this application as it can efficiently identify the most important features, and interactions of features, for prediction.

**Results:** Results are forthcoming. Our data comprises 3,521,963 legal handgun purchasers in California. Among those purchasers, 837,307 (23.8%) had at least one arrest on record, and 190,837 (5.4%) purchasers had at least one arrest for a major violent crime

**Conclusions:** We demonstrate the utility of gun sale records in identifying higher risk handgun purchasers and relevant risk factors. Effective utilization of these data may help aid efforts to reduce firearm related death and injury.

**Rate of self-inflicted firearm injuries in Veterans and associated healthcare costs** Sarah Shull\* Elizabeth Hooker Elizabeth R Hooker Tess A Gilbert Sarah Shull Lauren Maxim Kathleen F Carlson

**Background:** Compared to civilians, Veterans have 1.5 times the rate of suicide mortality and a higher proportion of suicide mortality from a firearm injury. Healthcare settings like the Department of Veterans Affairs (VA) are evaluating approaches to reduce firearm suicide and other firearm injury (FAI) risks. To inform these efforts, this study examines the rate of VA-treated FAIs among VA healthcare-using Veterans and compares their health care costs to those without a FAI.

**Methods:** Using VA administrative data and International Classification of Diseases diagnosis codes, we identified 9,818,194 Veterans who had at least one healthcare visit to a VA facility between 2010-2019. For the cost analysis, we matched each Veteran with a FAI visit to two Veterans without, based on index visit date, demographic data, and previous healthcare usage. We calculated FAI rates per 100,000 Veteran-years and conducted t-tests to assess the cost difference between Veterans with and without a FAI.

**Results:** We found 15,157 Veteran-years (12,384 unique Veterans) had at least one FAI-related visit from 2010-2019, for an overall rate of 26.8 per 100,000 Veteran-years. Of these Veteran-years, 2,308 (15.2%) were self-inflicted FAIs (4.1 per 100,000 Veteran-years). The average cost of health care for Veterans with a FAI was 1.9 times higher in the following year than matched Veterans without a FAI (\$29,266 (95% CI: \$26,719, \$31,813) vs \$15,282 (95% CI: \$14,341, \$16,222);  $p < 0.001$ ). However, those with a self-inflicted FAI had almost 4 times higher average cost than their matched controls (\$54,504 (95% CI: \$34,818, \$74,191) vs \$14,262 (95% CI: 12,654, 15,870);  $p < 0.001$ ).

**Conclusions:** Veterans with a FAI had nearly twice the annual health care costs compared to matched controls without a FAI; this ratio is even higher among Veterans with a self-inflicted FAI. These data support the need for healthcare-delivered FAI prevention measures such as suicide screening and lethal means counseling.

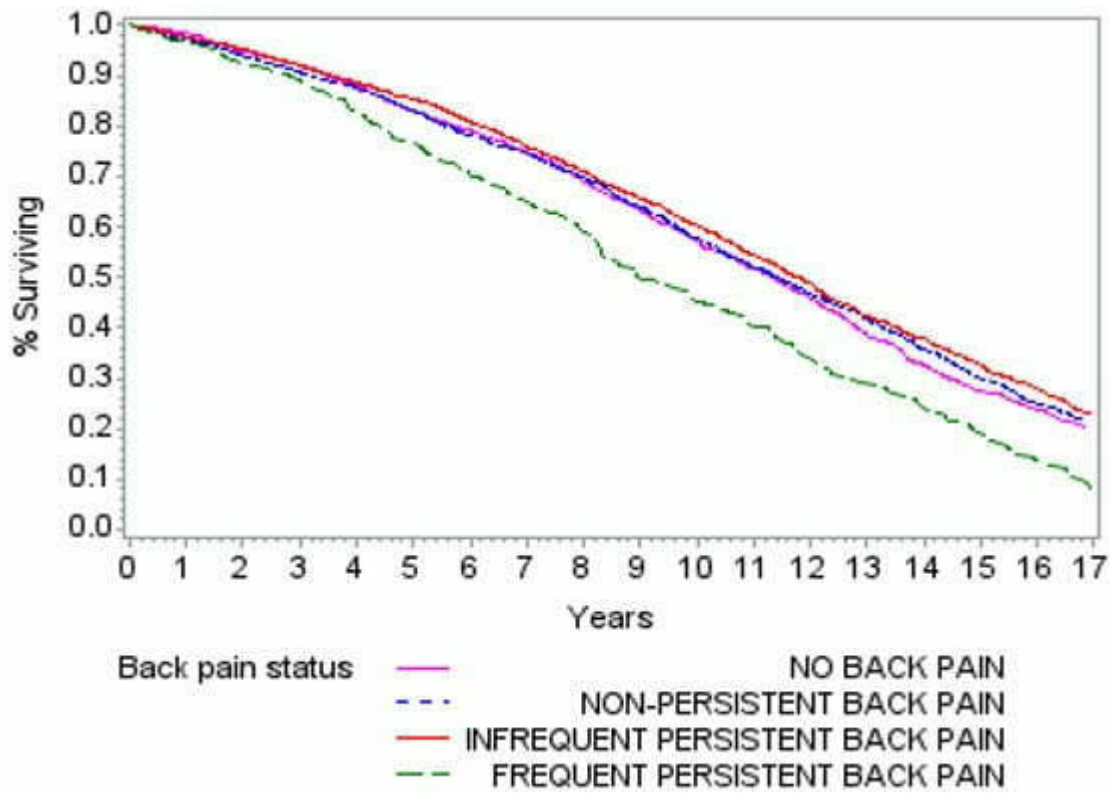
**Association of back pain with mortality in older men: a cohort study** Howard A. Fink\* Eric Roseen David McNaughton Stephanie Harrison Aron Downie Cecilie Krage Øverås Casper G. Nim Hazel Jenkins James J. Young Jessica Wong Jan Hartvigsen Katie L. Stone Kristine Ensrud Lynn Marshall Soomi Lee Peggy Cawthon

**Background:** A recent meta-analysis found severe back pain (BP) is associated with increased mortality among women but not men. However, few studies of men had a detailed BP exposure that considered frequency or persistence of symptoms.

**Methods:** We examined the association of BP with mortality in the Osteoporotic Fractures in Men (MrOS) study, a prospective cohort of 5994 older men with detailed BP measurement over time. We hypothesized that compared to men with no BP, those with frequent and persistent BP would have a higher mortality risk. We included data from 5215 men (mean age 73, SD=5.6) who reported whether they experienced BP in the past year at both visit 1 (2000-02) and visit 2 (2005-06). We defined presence of any BP in the year prior to both visits as "persistent" and, for each visit, BP present all or most the time during the past year as "frequent." We created a 4-category exposure: no BP; non-persistent BP; infrequent persistent BP; or frequent persistent BP. Vital status was confirmed with death certificates. All-cause mortality was estimated by hazard ratios (HR) adjusted for sociodemographic and health variables.

**Results:** After visit 2, 3463 men died over a mean follow up of 10.3 (SD=5.2) years. A higher proportion of men with frequent persistent BP died (76%=283/370) versus those with no BP (67%=797/1192) (sociodemographic adjusted HR=1.27, 95%CI:1.11-1.46). This association was attenuated after also adjusting for differences in health variables (HR=0.99, 95%CI:0.85-1.14). No association was observed for other BP groups.

**Conclusions:** Compared to no BP, frequent persistent BP was associated with increased mortality in older men accounting for sociodemographic factors. However, the association was explained by differences in 'excellent' health, smoking, obesity, prevalent vertebral fracture, fall history, COPD, hypertension, diabetes, hip pain and arthritis. Future analyses should clarify whether these factors are confounders, mediators, or both.



**Leveraging Spanish/Latinx media use to further our understanding of mental health mass communication and stigma: a natural effects mediation study** Melissa DuPont-Reyes\* Melissa DuPont-Reyes Alice Villatoro Lu Tang

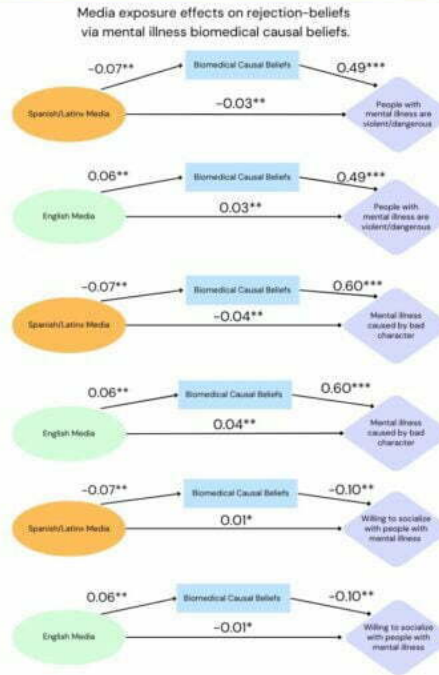
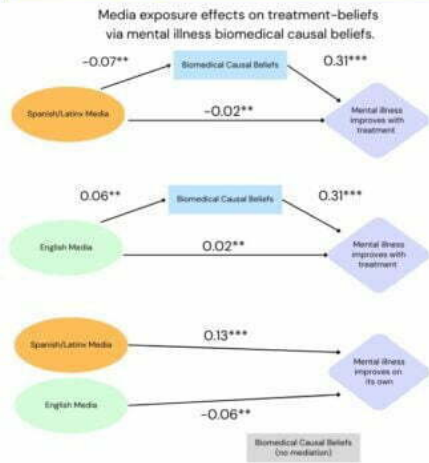
**Background:** Mass media—Internet, TV, Radio, Print, social media—is powerful for conveying mental health information like knowledge about mental illness as well as their treatment and portrayals. Yet extant literature is limited to English-language media overlooking heterogeneity in language/cultural preferences. This study examines how mental illness socio-biomedical causal beliefs mediate mass media impacts on treatment and social rejection beliefs.

**Method:** In 2021, a purposive US-based Latinx sample ages 13-86 (N=2058) completed a survey assessing Spanish/Latinx and English language/cultural media use and scanning/seeking of mental health information ( $\alpha=.86-.94$ ). Also assessed were beliefs about mental illness, 1) socio-biomedical causes—stress, genetics, environment, brain chemistry; 2) treatment—improves with treatment or on its own; and 3) rejection—violent/dangerous, bad character, unwilling to socialize. Structural equation models estimated direct and indirect effects of Spanish/Latinx and English media exposures on treatment and rejection beliefs via causal beliefs adjusting for individual/family factors.

**Results:** Spanish/Latinx media was negatively associated with causal beliefs while English media was positively associated ( $p<.01$ ). Causal beliefs in turn were positively associated with treatment and rejection beliefs ( $p<.01$ ), simultaneously. Indirect pathways of media exposures were also significant ( $p<.05$ ). Proportion mediated on treatment beliefs was one-third for Spanish/Latinx and two-thirds for English media. Proportion mediated on rejection beliefs for all media exposures averaged  $\geq 1$ .

**Conclusion:** Spanish/Latinx media consumers report lower mental illness causal knowledge which impedes treatment beliefs. In contrast English media consumers with knowledge of mental illness causes and treatment consequently hold rejection beliefs. Mental health content in media must be studied and practiced judiciously to help promote help-seeking without social rejection.

Leveraging Spanish/Latinx Media to Further Understanding of Mental Health Mass Communication and Stigma



Method: Structural equation models (N=2058; 2021) control for sex, race, ethnic origin, nativity, household income, education, ethnic attachment, acculturation, PHQ4, and family/household mental illness/substance abuse. \*\*\*p<0.001, \*\*p<0.01, \*p<0.05

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**Metabolic profile and the risk of developing depression, anxiety, and stress-related disorders: Experience from the Swedish AMORIS cohort.** Charilaos Chourpiliadis\* Charilaos Chourpiliadis Anikó Lovik Niklas Hammar Maria Feychting Fang Fang

Introduction: Biomarkers of lipid, apolipoprotein, and carbohydrate metabolism have been previously suggested to be associated with the risk for depression, anxiety, and stress-related disorders with inconsistent results. Methods: The Swedish AMORIS cohort included 212442 participants undergoing laboratory investigations for occupational health screening between 1985-1996 in the Stockholm region. Blood measurements included biomarkers of lipid, apolipoprotein, and carbohydrate metabolism. We examined the association between biomarker levels and the risk of developing depression, anxiety, and stress-related disorders up to 35 years after recruitment using Cox proportional regression models with adjusted hazard ratios and 95% CI. In addition, we conducted nested case-control analyses, including all incident cases of depression, anxiety, and stress-related disorders and up to ten controls matched using incidence density sampling and individually matched for year of birth, sex, and year of enrollment. Population trajectories were used to illustrate time trends in biomarker levels for cases and controls. Results: Glucose and triglyceride levels were positively associated (HR=1.08 (95% CI: 1.04-1.12), HR=1.10 (95% CI: 1.06-1.14), respectively), while High-Density Lipoprotein, and Apolipoprotein A-I were negatively associated (HR=0.90 (95% CI: 0.86-0.95), HR=0.91 (95% CI: 0.86-0.96), respectively) with the risk for depression, anxiety, or stress-related disorders when comparing high vs low biomarker levels. These results were similar for males and females. During the 20 years preceding diagnosis, the levels of glucose, triglycerides, total cholesterol, and Apolipoprotein B, and up to 10 years, the levels of Apolipoprotein A-I, were higher among cases compared to controls. Conclusion: Biomarkers of carbohydrate, lipid, and apolipoprotein metabolism might be linked to the risk of future depression, anxiety, and stress-related disorders.

**Age differences in the association between social contact pattern, social capital, and happiness in Taiwan** Wu, Yun-Hsuan\* Yun-Hsuan Wu Lai, Yueh-Ting Tsai, Meng-Han**Introduction:**

Age-based differences in social contacts and social capital may translate into age-related differences in mental health, and mental health plays a part in achieving happiness. Given limited studies evaluating age differences, our study aimed to examine the association between social contacts, social capital, and happiness across different age groups in Taiwan.

**Methods:**

Data from the 2017 Taiwan Social Change Survey (n= 1724) were used in this study. Happiness was our outcome of interest and used to evaluate mental health. Social capital (cognitive, structural and network social capital) and social contacts were our primary exposures of interest. We classified social contacts into four contact patterns based on low and high face-to-face contact (FFC) and non-face-to-face contact (NFFC). Multivariate ordinal logistic regression was applied to examine the abovementioned association within the 18-34, 35-49, 50-64, and  $\geq 65$  age groups among Taiwanese.

**Results:**

The primary contact pattern was high FFC and high NFFC in the < 65 age groups and was low FFC and low NFFC in the  $\geq 65$  age group. In addition, people aged < 65 year had higher level of social capital when comparing with the  $\geq 65$  age group. In the 18-34 age group, having high FFC and low NFFC (OR= 2.59, 95% CI: 1.15-5.82) as well as higher cognitive social capital (OR= 1.50, 95% CI: 1.04-2.14) were more likely to be happier. Conversely, having structural social capital was negatively associated with happiness (OR= 0.51, 95% CI: 0.30-0.87). In addition, the positive association between network social capital and happiness were only found in the 50-64 age group (OR= 1.32, 95% CI: 1.00-1.75).

**Conclusion:**

Our finding suggests that the influence of social contacts and social capital on happiness vary across different age groups. Future interventions that focus on building individuals' social contacts and social capital considering age-related differences may benefit their mental health.



**Perinatal Depression as a Risk Factor for Cardiovascular Disease** Emma Bränn\* Emma Bränn  
Krisztina Laszlo Donghao Lu

Perinatal depression (PND) has been associated with inflammation, oxidative stress, stress-related neuroendocrine or cardiometabolic changes, behavioral/lifestyle changes, and recurrent psychiatric episodes – all playing important roles in the development of cardiovascular disease (CVD). The association between PND and CVD is largely unexplored.

Leveraging all pregnancies in Sweden during 2001-2014 (1,347,032 pregnancies in 878,595 women), we conducted a population-based matched cohort study of 55,543 women with PND and 545,614 matched unaffected women. PND and CVDs were assessed by International Classification of Diseases-codes registered in the Swedish national health registers. Using multivariable cox regressions, we estimated hazard ratios (HR) of any CVD among women with PND. We conducted stratified analyses for history of psychiatric disorder and analyses for type-specific CVDs.

PND was diagnosed at an age of 30.8 (SD 5.6) years on average. During a mean follow-up of 10.5 (SD 3.5) years, 1,484 (2.7%) women with PND and 8,393 (1.5%) unaffected women developed CVD. Compared to matched unaffected women, women with PND had a 38% higher risk of subsequent CVD (adjusted HR = 1.38, 95% CI: 1.30-1.47). The risk elevation was stronger for women with postnatal depression (HR = 1.51, 95% CI: 1.39-1.63) than that for antenatal depression (HR = 1.23, 95% CI: 1.12-1.35). Largely comparable results were found for women with and without history of psychiatric disorder ( $p$  for interaction = 0.164). Highest risks were observed for heart failure (HR = 1.66, 95% CI: 1.09-2.53), hypertensive disease (HR = 1.48, 95% CI: 1.32-1.65), and ischemic heart disease (HR = 1.44, 95% CI: 1.01-2.05).

Our findings suggest that women with PND have a higher risk of CVD in middle adulthood. Further work could help establish whether there is a causal association between PND and CVD and identify relevant pathways. These findings may be relevant to clinicians working with perinatal patients.

**Estimation of the Relationship between Core Depressive Symptoms** Katherine M. Keyes\*  
Debbie Huang Ezra Susser Kara E. Rudolph

The psychiatric symptom network paradigm emerged in response to controversies about the measurement and diagnosis of depression that pose challenges for etiology and disease management. The validity of the network paradigm for depression is premised on the causal relationship between depressive symptoms; however, this premise has not been tested. Previous studies have had limited inference regarding causality because of two methodological challenges - study design and ability to meet inference assumptions. The current study sought to investigate symptom dynamics and address existing challenges. We utilized data from Project Transitions (n=779 young adults). We estimated the relationship between two depressive symptoms - sadness and anhedonia - using an inverse probability treatment-weighted regression estimation approach. After adjusting for potential confounders, results showed an average one-month effect of sadness on anhedonia 2.77 (95% CI: 1.92, 4.01) and vice versa 2.76 (95% CI: 1.95, 3.90), over the course of 24 months. The current study is a first attempt to test assumptions underlying the network paradigm for depression. Future research to further evaluate the assumptions for the network paradigm is critical to a valid understanding of depression phenomenology.

**Political and socio-cultural determinants of gender differences in major depression and alcohol use disorder among Asian and Pacific Islander Americans** Emily Goldmann\* Daniel Hagen Emily Goldmann

Background:

Major depressive disorder (MDD) and alcohol use disorder (AUD), leading causes of disease burden, exhibit marked gender differences whose magnitude may be associated with area-level social policies and norms. Given the differences in adherence to traditional gender norms, mental health stigma, expression of psychological distress, attitudes to alcohol consumption, and experience of discrimination between racial/ethnic groups, an examination of macro-level determinants of gender differences in MDD and AUD specifically among Asian/Pacific Islander Americans is warranted.

Methods:

Gender differences in prevalence and manifestation of current MDD and AUD were examined among Asian/Pacific Islander respondents to the 2006 and 2008 Behavioral Risk Factor Surveillance System (BRFSS) (n=6,368) and compared to the overall sample (n=234,020). Predicted probabilities of MDD/AUD prevalence and predicted means of 8 MDD symptoms and 3 AUD dimensions (drinking frequency, quantity, and frequency of heavy episodic drinking) were computed using modified Poisson and negative binomial regression models with interaction terms between gender (male vs. female) and state-level social policy generosity, public support for gender equality, and reproductive rights, respectively.

Results:

In the Asian/Pacific Islander subsample, public support for gender equality was associated with greater gender differences in AUD prevalence, with the predicted excess prevalence among men ranging from -0.2% in states with lowest to 21.4% in states with highest support ( $p=0.003$ ). Similar results were found for frequency of alcohol consumption and of heavy episodic drinking. None of these associations were detected in the overall sample at  $p<0.05$ .

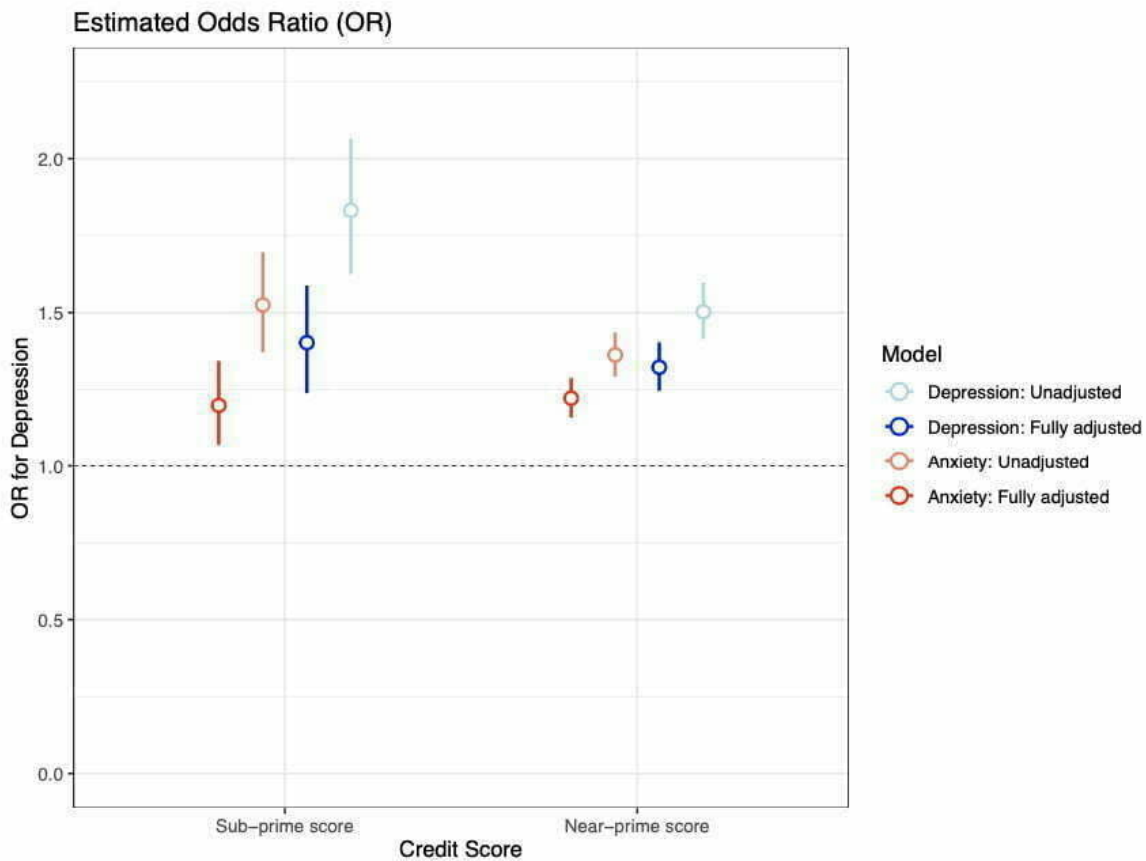
Conclusion:

Political and socio-cultural factors appear to modify the association of gender with prevalence and different dimensions of AUD among Asian/Pacific Islander Americans but not in the overall population, which underscores the need for subgroup analyses.

**Credit scores, depression, and anxiety in Pennsylvania adults during the COVID-19****pandemic** Catherine Ettman\* Catherine Ettman Elena Badillo Goicoechea Elizabeth A. Stuart  
Lorraine T. Dean

During the COVID-19 pandemic, more than one quarter of U.S. adults reported symptoms of depression or anxiety, possibly driven both by individual- and neighborhood-level risk factors. Consumer credit scores are novel measures of economic status; area-level credit scores represent a neighborhood's access to resources, which may have downstream consequences for mental health. Using a weighted sample of adults in Pennsylvania who completed the COVID-19 Trends and Impact Survey from November 2021 - June 2022 (N= 111,971) we assessed the relationship between pre-COVID area-level credit scores in 850 PA ZIP codes and individual-level anxiety and depression during the COVID-19 pandemic. We defined depression and anxiety as feeling depressed or anxious "most" or "all" of the time. We used area level average VantageScore credit score tiers in December 2017, defined as subprime ( $\leq 700$ ), near prime (701-800), or prime ( $> 800$ ). We used multilevel models to separately estimate the prevalences of depression and anxiety, controlling for individual-level characteristics: age, gender, race and ethnicity, employment, educational attainment, and percentage of people in the ZIP code with the same race as the respondent. We also conducted analyses stratified by race/ethnicity. In the fully adjusted model, lower average area-level credit score tier was associated with greater odds of depression (near prime: OR:1.32, 95%CI 1.25,1.40; sub-prime: OR:1.40, 95% CI 1.23,1.59) and anxiety (near prime: OR:1.22, 95%CI 1.16, 1.29; sub-prime: OR:1.20, 95% CI 1.07,1.34) relative to the higher credit score tier. However, analyses stratified by race showed non-significant associations for area-level credit score tier and mental health for Non-Hispanic Black and Hispanic adults. Findings suggest that area-level credit scores may provide insights about how economic resources play a role in shaping population mental health but may be more salient for White adults than racial/ethnic minoritized adults.

Figure 1. Odds of reporting frequent feelings of depression and anxiety by average area-level credit score tier



Note: Fully adjusted model controlled for age, gender, race/ethnicity, employment, educational attainment, percent of people of the same race in the ZIP code, clustered at the ZIP code level. Prime average area-level credit score tier was the reference group.

**Poorer subjective mental health among girls: artefact or real? Examining whether interpretations of what mental health means vary by sex** Afshin Vafaei\* Afshin Vafaei Fiona Costello Naomi Gazendam Susan P. Phillips

**Background:** Girls consistently report poorer self-rated mental health (SRMH) than boys but demonstrate greater resilience, academic achievement and less risk-taking. We examined whether this apparent paradox might be an artefact arising from girls' and boys' different interpretations of the meaning of SRMH.

**Methods:** Data collected via an online survey of youth aged 13-18 included self-rated mental health and individual and social circumstances shaping that rating. Principal component analysis (PCA) identified potential latent factors within the items that participants considered important in rating their mental health. The robustness of the analysis was assessed by estimating the Kaiser-Meyer-Olkin (KMO) measure of sampling adequacy and Bartlett's test of sphericity.

**Results:** Poor SRMH was reported by 47% of 506 girls and 27.8% of 216 boys. In general, circumstances considered important to this rating were similar, although boys focused more on sense of identity, self-confidence, physical well-being, exercise, foods eaten and screen time, while girls paid more attention to having a boyfriend or girlfriend, comparisons with peers, and school performance. Common to boys and girls were five emerged domains of resilience, behavior/community, family, relationships with peers and future vision. Given that the KMO measures were greater than 0.60 the size of the sample was deemed adequate. Furthermore, the statistical significance of Bartlett's test suggested that the five-common factor solution was sufficient to explain the correlations.

**Conclusions:** Girls' poorer SRMH did not arise from a more expansive interpretation of mental health. Instead it may reflect perceived or real disadvantages in individual or social circumstances. Alternatively, girls' known greater resilience could underly lower SRMH which might then be used motivate future achievement and avoid the complacency of thinking that 'all is well'.

**Temporal patterns in the annual incidence of common mental dis** Jen Dykxhoorn\* Jennifer Dykxhoorn David Osborn Kate Walters Shamini Gnani Antonio Lazzarino

**Background:** Common mental disorders (CMD) including depression, anxiety, and stress are very common, but it is unclear whether the last two decades of social, economic, and political change have impacted incidence of CMD. This study explored longer-term temporal trends in the incidence of CMD in the UK.

**Methods:** We used data from general practices in the UK (Clinical Practice Research Datalink) to estimate the incidence of news episodes of CMD, including of symptom, diagnosis, or pharmaceutical treatment. Trends were explored by age group, sex, ethnicity, deprivation, and physical comorbidity.

**Results:** We included 29,480,164 individuals followed for 12.5 years on average (SD=6.4 years). The incidence of CMD episodes was 55.9 per 1,000 person-years in 2000 (95% CI 55.8–56.1), increasing to 79.6 per 1,000 person-years in 2019 (95% CI 79.5–79.8). Females had higher incidence rates, as did those living in more deprived areas. There were differing patterns of incidence by ethnic group, with a steeper increase in Asian, Black, and Mixed groups in recent years. We observed striking patterns by age over time, with rates in ages 16–24 increasing from 40.2 per 1,000 in 2000 (95% CI 39.8–40.5), to 107.8 per 1,000 in 2019 (95% CI 107.0–108.6). In contrast, the rates in those aged 55 or older decreased since 2014.

**Conclusions:** Overall, the incidence of recorded CMD in UK general practice increased between 2000 and 2019 with a small decrease in 2020. We found large differences across demographic characteristics, which may have implications for primary, secondary, and tertiary prevention.

**Perceived stress and memory decline in older Chinese: the Guangzhou Biobank Cohort****Study** Lin Xu\* Lin Xu**Background** Previous studies on associations of perceived stress with poor memory performance in older adults showed inconsistent results.**Objective** We examined the prospective associations of perceived stress with memory decline.**Design** Longitudinal cohort study.**Setting** Guangzhou Biobank Cohort Study in China.**Subjects** 9,656 participants (72% women) with mean age 61.6 (standard deviation=6.4) years**Methods** Perceived stress was measured by the Perceived Stress Scale (PSS) at baseline (2003-2006) (score 0-41), greater scores indicating greater stress. Memory function was measured by delayed 10-word recall test (DWRT; 0-10) and immediate 10-word recall test (IWRT; 0-30), with greater scores indicating better performance, at baseline and follow-up (2008-2012) examinations, analyzed as mean annual change in scores.**Results** During an average follow-up of 4.4 years, after adjusting for baseline IWRT/DWRT scores and 14 confounders, each one-point greater PSS score was significantly associated with mean annual decline in DWRT scores ( $\beta$  (95% CI) = -0.005 (-0.008 to -0.002)). Regarding the subscales of PSS, greater perceived helplessness scores, but not perceived self-efficacy scores, was associated with greater mean annual decline in DWRT and IWRT scores ( $\beta$  (95% CI) = -0.005 (-0.009 to -0.001) and -0.012 (-0.018 to -0.005), respectively). Interaction analysis showed that the association of greater PSS with greater decline in DWRT scores was observed only in those with low family income ( $\beta$  (95% CI) = -0.08 (-0.13 to -0.04), P for interaction=0.03).**Conclusions** Greater perceived stress was associated with a greater decline in delayed recall memory and the association was observed only in those with low family income.



**LATEBREAKER**

Mental Health

**Maternal factors associated with global developmental delay in children at one year: Findings from the MAASTHI cohort study in Bengaluru, India** Giridhara Rathnaiah babu\*  
Giridhara Rathnaiah Babu Onno CP van Schayck

**Introduction:** Global developmental delay (GDD) is a significant public health concern that affects a child's physical, social, cognitive, and emotional development. Identifying the risk factors associated with GDD is essential to improve early intervention and management strategies. This study aimed to investigate maternal and infant factors associated with GDD in children at one year of age in the MAASTHI cohort study in Bengaluru, India.

**Methods:** A nested case-control study design was conducted with 151 GDD cases among children who completed one year of follow-up assessments on time. Controls were selected in a 1:5 ratio and were matched based on gestational age. Maternal and infant characteristics, feeding practices, and GDD outcomes were assessed through direct observation and caregiver responses. Logistic regression models were used to estimate the odds of GDD associated with maternal and infant factors.

**Results:** Maternal factors such as gestational diabetes mellitus (GDM), anemia, elective C-section, and postpartum depressive symptom score were significantly associated with GDD at one year. Infant factors such as birth weight, feeding practices, and GDD outcomes at 14 weeks were also associated with GDD at one year. Maternal depressive symptoms during pregnancy significantly increase the odds of a child having developmental delay at one year by 5 times per unit increase in symptom score, and by 15% for depressive symptoms at birth after adjusting for confounding factors, including social support, increases the odds. Confounders adjusted for include maternal age, socio-economic status, spousal smoking, anemia, formula fed status, gestational age at delivery, delivery type, gender of the child, and weight at birth.

**Conclusion:** This study highlights the importance of identifying and addressing maternal risk factors, including GDM, anemia, and depressive symptoms during pregnancy, to reduce the risk of GDD in children. Early identification of GDD is crucial to provide timely interventions and improve developmental outcomes for children.

**LATEBREAKER**

Mental Health

**COVID-19 infection during the early pandemic is associated with multiple mental health impairments: results from a national online mental health survey in confirmed patients**

Dongkyu\* Dongkyu Lee Hyejin Kim Sun Jae Jung

**Objective:** While psychiatric sequelae after COVID-19 infection has been reported, it is unclear whether patients infected during certain time frames are at greater risk. We assessed whether the period of COVID-19 infection is associated with heterogeneous psychiatric outcomes.

**Method:** Data from 99,055 adults aged 18-99 were obtained from COVID-19 confirmed patients who responded to an online mental health questionnaire provided by the Korea National Center for Disaster and Trauma. Data was collected from patients who were infected between January 1<sup>st</sup>, 2020 and July 31<sup>st</sup>, 2022. Period of infection was categorized by quarter (Q), ranging from 2020Q1 to 2022Q3. Reference period was set as 2022Q1. Outcomes were measured using validated questionnaires, with Patient Health Questionnaire-9 (PHQ-9) for depression, Generalized Anxiety Disorder-7 (GAD-7) for anxiety, Primary Care Post-Traumatic Stress Disorder-5 (PC-PTSD-5), Patient Health Questionnaire-15 (PHQ-15) for somatization, and P4 suicidality screener for suicidal ideation. Outcomes were binomial, with a screening criteria of  $\geq 10$  points for PHQ-9 and GAD-7,  $\geq 3$  points for PC-PTSD-5,  $\geq 15$  points for PHQ-15, and being a high-risk group in P4. Log-binomial regression was used to estimate prevalence ratios with age, sex, area of residence, and experience of family member infection or mortality from COVID-19 as covariates.

**Result:** Periods of maximum risk for depression (2020Q3, PR: 2.02, 95% CI: 1.64-2.49), anxiety (2020Q2, PR: 2.66, 95% CI: 2.06-3.45), PTSD (2020Q2, PR: 2.31, 95% CI 1.94-2.75), somatization (2020Q2, PR: 1.69, 95% CI: 1.15-2.48), and suicidal ideation (2020Q1, PR: 2.92, 95% CI: 1.90-4.48) were focused during early periods of the COVID-19 pandemic.

**Conclusion:** Patients who were infected at the early stages of the pandemic experienced a higher risk for psychiatric illnesses. Healthcare providers should be aware of possible worsened prognosis in mental health after COVID-19 infection in the early pandemic.

**LATEBREAKER**

Methods/Statistics

**Conflict of interest and funding in health communication on social media: a systematic survey** Vanessa Helou\* Vanessa Helou Fatima Mouzahem Adham Makarem Hussein A. Noureldine Rayane Al Khoury Dana Al Oweini Razan Halak Layal Hneiny Joanne Khabsa Elie A. Akl

**ABSTRACT**

**Objectives:** To synthesize the available evidence on the reporting of conflicts of interest (COI) by individuals posting health messages on social media, and on the reporting of funding sources of studies cited in health messages on social media.

**Data Sources:** Medline(OVID) (2005-March 2022), Embase (2005-March 2022) and Google Scholar (2005-August 2022), supplemented with a review of reference lists and forward citation tracking.

**Design:** Reviewers selected eligible studies and abstracted data in duplicate and independently. We appraised the quality of the included studies using the relevant section of Mixed Methods Appraisal Tool. We summarized the results in both narrative and tabular formats. We followed the PRISMA 2020 checklist for reporting our study.

**Results:** Of a total of 16,645 retrieved citations, we included 17 eligible studies. The frequency of reporting of conflicts of interest varied between 0-60%, but it was mostly low. In addition, a significant proportion, ranging between 15-80%, of healthcare professionals using social media have financial relationships with industry. However, three studies assessed the proportion of conflicts of interest of physicians identified through Open Payment Database (OPD) but not reported by the authors and found that 99-100% of these relationships with industry are not reported when communicating health-related information. Also, two studies showed that there is evidence of a potential association between COI and the content of posting. No studies were found on the reporting of funding sources of studies cited in health messages on social media.

**Conclusions:** While a significant proportion of healthcare professionals using social media have financial relationships with industry, lack of reporting on COI and undisclosed COI are common. We did not find studies on the reporting of funding sources of studies cited in health messages on social media.

**Funding:** None

**LATEBREAKER**

Methods/Statistics

**Model specification for outcome predictors in inverse probability weighting** Leah Sadinski\*

Leah Sadinski Rachael Ross Alexander Breskin

Inverse probability weighting (IPW) is a common standardization method used to estimate marginal effects. A correctly specified model for the exposure (i.e., propensity score model, PS) is needed for valid estimates when using IPW. Covariate selection for the PS model is informed by the relationship of covariates with exposure and outcome. Investigators may include predictors of the outcome in the PS model to reduce variability between comparison groups and improve precision. However, there is minimal guidance on how to consider specification of outcome predictors in the PS model. We use simple simulations to investigate the impact of outcome predictor inclusion and specification on bias, precision, and mean squared error (MSE) of the RD using IPW.

We simulated two binary confounders to predict a binary exposure. To generate a binary outcome, we used the two confounders and an independent outcome predictor. We considered two scenarios. In Scenario 1, the outcome predictor was binary, and the outcome model included the main term for the predictor and an interaction between the predictor and one confounder. In Scenario 2, the outcome predictor was continuous, and the outcome model included a quadratic term for the predictor.

In both scenarios, inclusion of the main term of the outcome predictor in the PS model improved precision compared to omission of the predictor; inclusion of the interaction term in scenario 1 and the quadratic term in scenario 2 resulted in greater precision gains. In both scenarios, there was negligible bias regardless of specification of the outcome predictor. Thus, the MSE decreased monotonically with inclusion of the outcome predictor's main term and inclusion of the appropriate interaction/quadratic term.

This work has implications for investigators planning to use outcome predictors in IPW in observational and randomized trial research, as the inclusion and correct specification of outcome predictors can lead to meaningful precision gains.

**Simulated application employed for evaluating models predicting prior risk using randomized controlled trial data** Guiyou Yang\* Guiyou Yang Henk Groen Sanne Gordijn Wessel Ganzevoort Gerton Lunter

**Background/aim:** For any prediction model, preliminary evaluation of clinical impact is wise before prospective impact studies. Specifically for evaluating models predicting treatment benefit, a method was proposed applying the results of randomized trials to individual patients (simulated application); for models predicting prior risk, decision curve analysis (DCA) may be useful. However, DCA has downsides, e.g., likely overestimated net benefit and non-intuitive results. We propose to use simulated application to evaluate models predicting prior risk, and illustrate this procedure with an example.

**Method:** A published model predicting maternal clinical deterioration in women with hypertensive disorders of pregnancy was used as an example. DCA showed using the prediction model led to a net benefit over “treating all/none” policies for cut-off values around 0.4. At this hypothetical cut-off value (0.4), reflecting how the harm of a false negative prediction was weighed against that of a false positive prediction, simulated application was applied to examine the impact of the model on the rate of maternal deterioration when DCA suggested benefits of using the model. Cesarean section rate was used as an alternative outcome. Fisher’s exact test was used to compare the rates of outcomes between the “treating all” group and the group where treatment arm suggested by the model coincided with random allocation.

**Results:** Fisher’s exact tests showed statistically significant differences ( $p$  value < 0.001) for both outcomes between the two groups. The rate difference (95% CI) of cesarean section was 5.0% (-0.4%, 10.5%), and that of maternal clinical deterioration was 15.6% (8.3%, 22.7%).

**Conclusion:** Simulated application is a feasible method to preliminarily assess the impact of models predicting prior risk. It provides easily interpretable results to clinicians. The results can be used as guidance for selective prospective impact studies.

**Proposing the observational-implementation hybrid approach (designing observational research for rapid translation) and applying it to collect data regarding the implementation of evidence-based practices to support drinking reductions among Black sexual minority men**

Justin Knox\* Justin Knox Sheree Schwartz Brett Dolotina Dustin Duncan Sandro Galea Elvin Geng

### Objective

We recently proposed the observational-implementation hybrid approach, or the incorporation of implementation science elements into observational studies. This allows for the collection of information to anticipate, estimate, and/or infer the effects of interventions and implementation strategies. We describe this approach, including how we are applying it in an ongoing observational cohort study of Black sexual minority men (BSMM) to collect implementation data on the use of evidence-based practices to address alcohol misuse.

### Methods

We will employ various methods to collect information on how to deliver alcohol interventions that we identified as relevant [electronic screening and brief intervention, motivational interviewing, HealthCall, naltrexone) to BSMM.

### Results

Among n=240 BSMM in the cohort who report heavy drinking, we are using survey measures to collect factors related to transportability (e.g., access to a primary care physician, treatment-seeking) of the identified alcohol interventions, and a discrete choice experiment to collect preference data on the delivery of these alcohol interventions. Among a further sub-sample (n=30), we are using a human-centered design approach to collect journey maps of BSMM experiences accessing HIV prevention and care service. We are also conducting in-depth interviews with n=10 HIV service providers to assess implementation factors related to co-locating alcohol interventions into HIV prevention and care services.

### Conclusions

Applying the observational-implementation hybrid approach provides an opportunity to conduct observational research in ways that will allow it to achieve more rapid translational gains in terms of understanding how to deliver evidence-based practices. In future waves of data collection, we will use this approach to collect implementation data relevant to interventions for cannabis use, stimulant use, HIV prevention and HIV care, and we will apply the approach in other studies.

Figure 1a

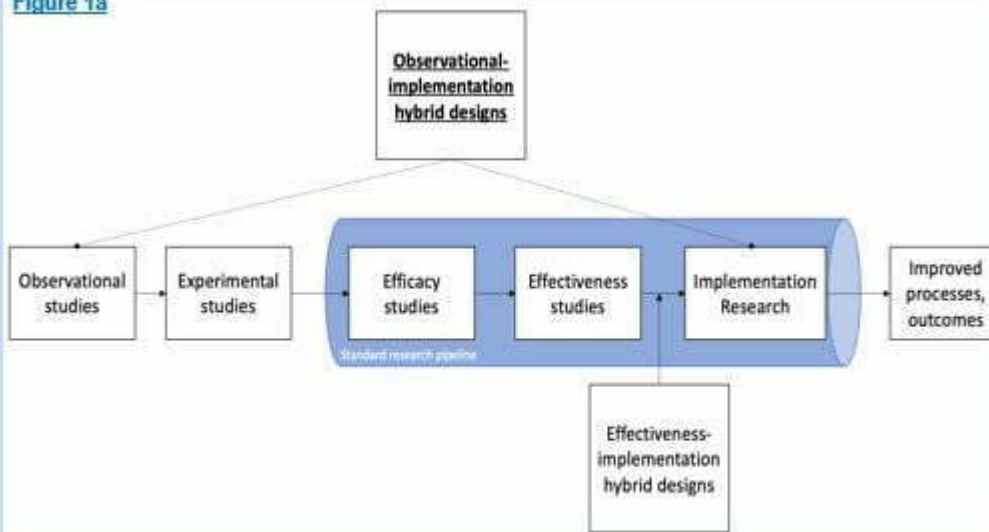
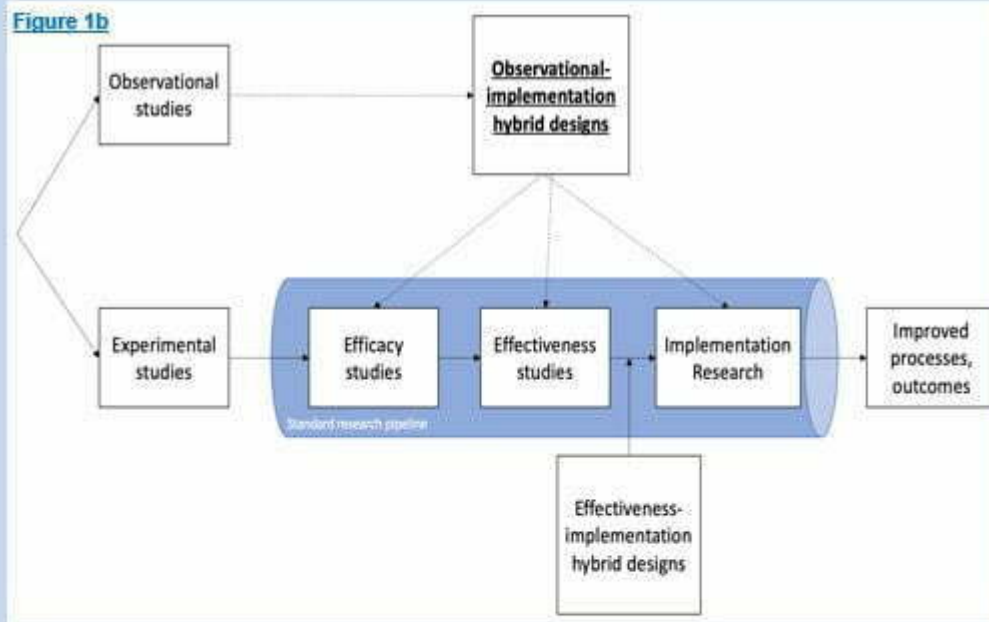


Figure 1b



**The observational-implementation hybrid approach could increase efficiency and effectiveness of the research pipeline** whether observational research is conceptualized as a **precursor** to experimental research (**Figure 1a**) or as on a distinct pathway as experimental research (**Figure 1b**).

**Impossible Values in Probabilistic Bias Analysis: A Simulation Study Comparing Three**

**Methods** Allison Domingues\* Allison Domingues Allison Domingues Erin Marcotte Timothy Lash  
Matthew Fox Thomas Ahern Tyler Richter Logan Spector Richard MacLehose

**Background:** Misclassification is a common concern in epidemiologic studies; however, if estimates of bias parameters are available, one may adjust for this bias. In simple methods, point estimates of bias parameters are used to estimate a misclassification-adjusted point estimate. When there is uncertainty in estimates of bias parameters, distributions may be assigned to the parameters, and probabilistic bias analysis (PBA) can be used to adjust for misclassification while incorporating that uncertainty in the interval around the adjusted estimate. Not all bias parameter values are compatible with a given data set, and PBA may result in impossible values, such as negative cell counts in the bias-adjusted  $2 \times 2$  table. **Objectives:** This study compared three methods used in practice to overcome this issue—1) discard all PBA iterations that result in impossible values, 2) change the distribution of the bias parameters to decrease the likelihood of impossible values, or 3) use Bayesian methods, which automatically prohibit impossible values. **Methods:** To compare these three methods, we conducted a simulation study for a variety of sample sizes, exposure prevalences, sensitivities, and specificities. We implemented all three methods on each data set and compared the median bias-adjusted estimate to the true OR to calculate bias, coverage probability, and mean squared error. Each method was also applied to data from an existing study of maternal smoking and childhood cancer. **Results:** When bias parameter distributions resulted in no impossible values, all three methods performed similarly. As the proportion of impossible values across PBA simulations increased, the Bayesian method produced the least biased adjusted estimates, while altering bias parameter distributions produced the most bias. **Discussion:** Authors should consider adopting procedures such as Bayesian methods when there is evidence of nontrivial incompatibility between bias parameters and observed data.



**Parameterization of beta distributions for bias parameters of binary exposure****misclassification in probabilistic bias analysis** Qi Zhang\* Qi Zhang Timothy L Lash Lindsay Collin Richard Maclehorse Thomas P Ahern

**Background:** To account for bias due to misclassification of dichotomous variables, beta distributions are often assigned to bias parameters, e.g., positive predictive value (PPV) and negative predictive value (NPV), in probabilistic bias analysis (PBA). The distribution for the predictive values is usually specified using only data in the validation study. However, zero cell frequencies can occur in the cross tabulation of the measured and gold-standard values due to sparse data, which can be a result of smaller sample size in validation sub-studies. In such cases, assigning prior distributions to the predictive values might be helpful.

**Methods:** We simulated cohort studies of varying sizes, comprising a binary exposure and outcome, as well as an internal validation sub-study for exposure classification. PBA was conducted under five scenarios of prior distribution specification for NPV and PPV: (1) conventional method without a prior or a continuity correction; (2) a uniform prior beta ( $\alpha = 1, \beta = 1$ ); (3) a Jeffreys prior beta ( $\alpha = 0.5, \beta = 0.5$ ); (4) a continuity correction factor of 0.5 to the  $\alpha$  and  $\beta$  values of beta distributions only when zero-cell problem existed in validation data; and (5) same as scenario 4 except the continuity correction factor of 1 was used. Different scenarios were compared by evaluating coverage probability, bias and mean squared error (MSE).

**Results:** For sparse validation data, methods (2)-(5) all produced substantially better coverage and lower MSE than the conventional method, among which using a +1 prior yielded the greatest coverage, lowest bias and MSE. However, little difference between methods was observed when the validation sub-study did not contain any cells with zero observations.

**Conclusion:** If sparse data, especially zero cells, are expected in the validation data, using a +1 prior for the beta distribution of bias parameters will improve the validity of bias adjusted measures.

**Quality Assessment of the Natural Course Simulation of the Parametric G-formula: an Illustration Using the Diesel Exhaust in Miners Study (DEMS)** Wenxin Lu\* Wenxin Lu Sally Picciotto Sadie Costello Alex Keil Stella Koutros Debra Silverman Ellen Eisen

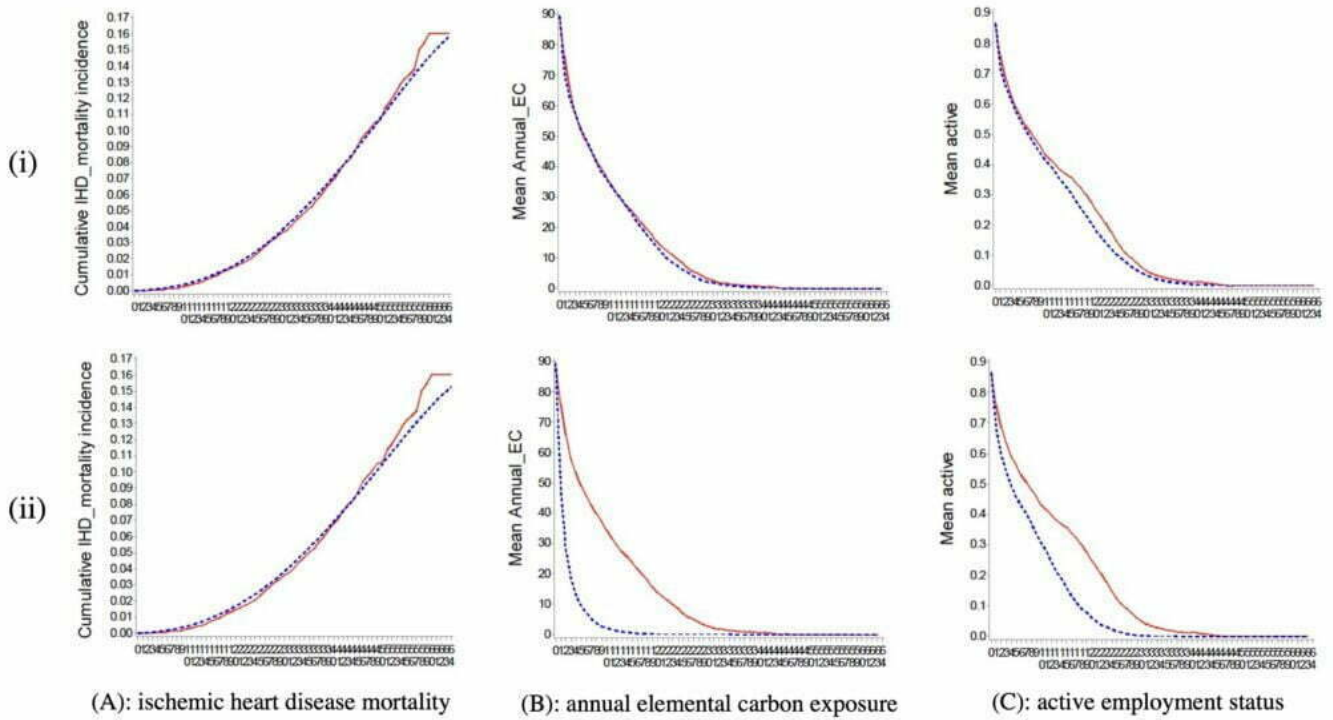
**Background:** Healthy worker survivor bias is common in occupational epidemiology but can be mitigated using the parametric g-formula to simulate counterfactual scenarios under potential interventions. Like all parametric methods, it assumes correct specification of models, usually assessed by comparing the observed outcome data with the simulated natural course of the outcome with no intervention. However, there is no consensus on how to determine whether the simulated natural course is close enough to the observed data, and the literature does not discuss whether other covariates should also be considered.

**Methods:** We applied parametric g-formula to examine effects of occupational exposures on ischemic heart disease mortality in the Diesel Exhaust in Miners Study (DEMS). 10780 male workers in 8 US mines were followed to 2015. We generated 23 simulations of the natural course based on different sets of parametric models. We ranked them qualitatively based on visual assessment of how closely the natural courses resembled the observed scenario for all time-varying variables during follow-up. We also calculated the sum of Akaike information criterion (AIC) across all variables as a potential quantitative indication of total model misspecification.

**Results:** The Figure shows that close approximation of the natural course to the observed outcome risk does not guarantee good simulation of other covariates: poor predictions of exposures and time-varying covariates may still exist and cause biased effect estimation of potential interventions. Sum of AICs across models was not consistent with qualitative visual assessment.

**Conclusion:** We recommend reporting graphic predictions over time of the outcome variables, intervened variables, and other time-varying covariates when applying parametric g-formula. Objective criteria for model misspecification need to be developed.

Observed (red solid line) and natural course (blue dotted line) estimates of outcome (A), exposure (B), and employment status (C) by follow-up years, from the best (i) and worst (ii) performing models in parametric g-formula



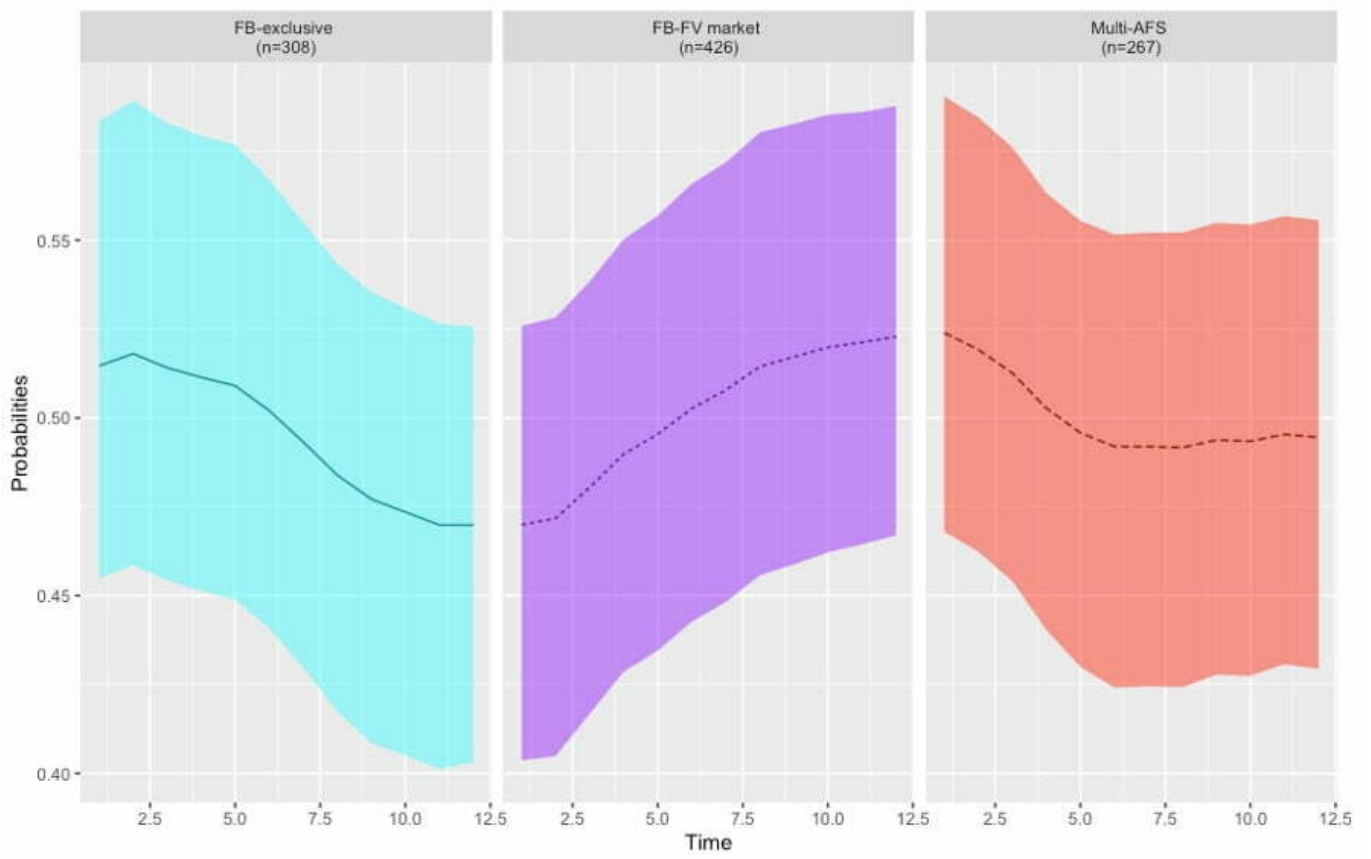
**Examining the relationship between alternative food source utilization and trends of food donations use among newly food bank users** Mabel Carabali\* Elsurry Pérez Mabel Carabali Geneviève Mercille Marie-Pierre Sylvestre Federico Roncarolo Louise Potvin

**Background:** Food donations (FD) are important source of relieve for people experiencing or at risk of experiencing severe food insecurity, defined as reduction in the amount of food consumed due to lack of money. FD use is part of complex food acquisition strategies that include several alternative food sources (e.g., Fruit and vegetable (F&V) markets, community gardens, food banks (FB)). We examine the association of alternative food source utilization (AFSU) and trends of FD use.

**Methods:** We use data from the *Parcours study*, a prospective study of 1,001 newly enrolled FB users from 2018-2021 and analyzed their first 12 months of food bank use. First, we used latent class analysis to identify baseline AFSU profiles based on food source type, frequency, and travel time. Further, we fitted Bayesian hierarchical mixed-effects models using Integrated Nested Laplace Approximation for the association between AFSU profiles and monthly use of FD. We used inverse probability of censoring weighting to address the attrition. All models were adjusted for individual/household and area-level covariates, accounting for spatial clustering and temporal correlation. To examine trends of FD use by AFSU profile, we assessed interaction between the ASFU profiles and time.

**Results:** Three profiles of AFSU were identified: a) exclusive FB-users; b) FB-F&V-market users; and c) Diverse-AFS users, which were linked to sociodemographic characteristics and settings. Bayesian hierarchical mixed-effects models showed that each profile had a different trend of FD use over their first 12-months, but there were not statistically significant differences of FD use for the fruit & vegetable or diverse AFSU users compared to exclusive FB users.

**Conclusion:** FD use depends on sociodemographic and setting conditions, varying over time. Further research must explore determinants of AFSU profiles to target interventions aimed at an improved use of and FD's effect among those in need.

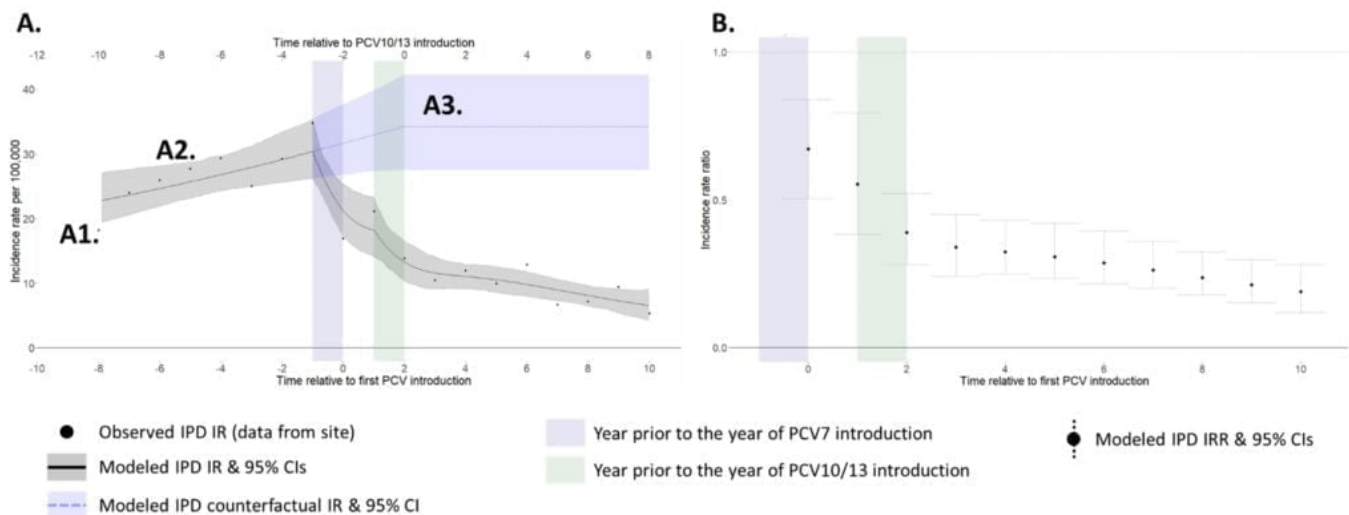


## Application of Bayesian multi-level Poisson regression for estimating global pneumococcal conjugate vaccine impact

Julia C. Bennett\* Julia C. Bennett Maria Deloria Knoll Scott L. Zeger

Population-level pneumococcal conjugate vaccine (PCV) impact studies are critical for informing policy. Such studies are typically conducted using invasive pneumococcal disease (IPD) surveillance data. However, small sample sizes can limit the precision of single surveillance site analyses. Attributing single-site changes in IPD incidence rates (IRs) over time to PCVs may also be biased by external events unrelated to PCVs that impact IPD IRs. Thus, methods that aggregate surveillance data across many sites may provide more robust estimates. Historically, multi-site PCV impact studies have used random effects meta-analysis (REMA), where annual incidence rate ratios (IRRs) comparing pre- and post-vaccine periods are estimated for each site and then pooled across sites for each post-vaccine year. This approach has several limitations that can be overcome using a Bayesian multi-level model. First, REMA of site-specific IRRs can only include sites with both pre- and post-vaccine data, while the Bayesian multi-level model can use data from all sites. Second, a Bayesian approach allows estimation of counterfactual PCV effects that adjust for site-specific pre-vaccine trends, a critical component of modeling vaccine impact as all inferences are relative to a baseline rate of disease. Third, the Bayesian multi-level model appropriately accounts for uncertainty both within and between sites. Finally, a Bayesian approach provides confidence intervals for the entire site-specific relative incidence curve, not just the pre-post comparison. Improving upon REMA multi-level PCV impact studies using a Bayesian approach strengthens the evidence base on which PCV policy decisions are made, with important implications for vaccine program funding, advocacy efforts, and recommendations for PCV use.

**Figure.** Bayesian, multi-level method for estimating annual IPD IRRs comparing the pre-PCV period to each post-PCV year: example using all serotype IPD data for children <5 years from one country.



### A. Annual IPD IRs.

A1. Plot A points show observed annual IPD IR. A2. Plot A black curve shows the modeled IR and surrounding 95% CIs estimated for years of available data using Bayesian multi-level, mixed-effects Poisson regression. Model includes all available data from other countries for children <5 years with a population denominator offset and random effects for the intercept and slope. A non-linear break is included one year prior to each PCV introduction to capture the change from the year prior to introduction to the year of PCV introduction and cubic spline knots are included at years +1 and +3 post-each PCV introduction to allow for flexibility in the IR. A3. Plot A blue curve shows the counterfactual IPD IR and surrounding 95% CIs in the absence of PCV introduction estimated by extending the pre-PCV IR slope for three years post-PCV before flattening to a slope of zero at the estimated rate onward.

B. Annual modeled IPD IRRs in each post-PCV year. The site-specific modeled IPD IR and counterfactual IR are used to estimate site-specific annual IRRs in each post-PCV year with the mean of the posterior distribution of rate ratios (the modeled IR in each post-PCV year: the counterfactual IR).

**Time trends in classification parameters: detection and approach** Katherine Lawson-Michod\*  
Katherine Lawson-Michod Julie Barberio Richard F. MacLehose Thomas P. Ahern Timothy L. Lash  
Lindsay J. Collin

**Background:** Validation substudies are an important component of epidemiologic research that enable quantification of bias due to misclassification of a variable of interest, often the exposure or outcome, and subsequent bias analysis. Our work in validation substudy design has identified time trends in classification parameters. Time trends in classification parameters may have important implications for approaches to validation substudy design and quantitative bias analysis. In this study, we use simulations to demonstrate methods to detect time trends in classification parameters and approaches to account for time trends in classification parameters using quantitative bias analysis.

**Methods:** We simulated multiple cohorts of 10,000 individuals with a 10-year enrollment and an average follow-up of 10-years to examine exposure and outcome misclassification. We assumed a true exposure prevalence of 15% in each simulated cohort and a hazard ratio of 2. We induced nondifferential misclassification of the exposure or outcome under various scenarios, including in the absence of a time trend and the presence of linear or logarithmic time trends. To detect a time trend, we iteratively sampled blocks of 10 individuals based on the observed exposure/outcome status and computed the positive and negative predictive values within these blocks. Once a time trend in the classification parameter was detected, we then sampled individuals for the validation substudy at two later time points—at the middle and end of cohort enrollment/follow-up. These validation data were then used to impute the predicted classification parameters over the course of cohort enrollment/follow-up.

**Results and Future Directions:** In our preliminary results, the ability to detect a time trend in the classification parameters was dependent on the degree of change in outcome and exposure misclassification over cohort enrollment and follow-up. Subsequent adaptation of the validation substudy approach based on time trend detection allowed for imputation of classification parameters over the course of the study period. Continued work on this project will outline approaches for validation substudy design in the presence of a time trend in classification parameters and methods to account for time trends in bias analysis.

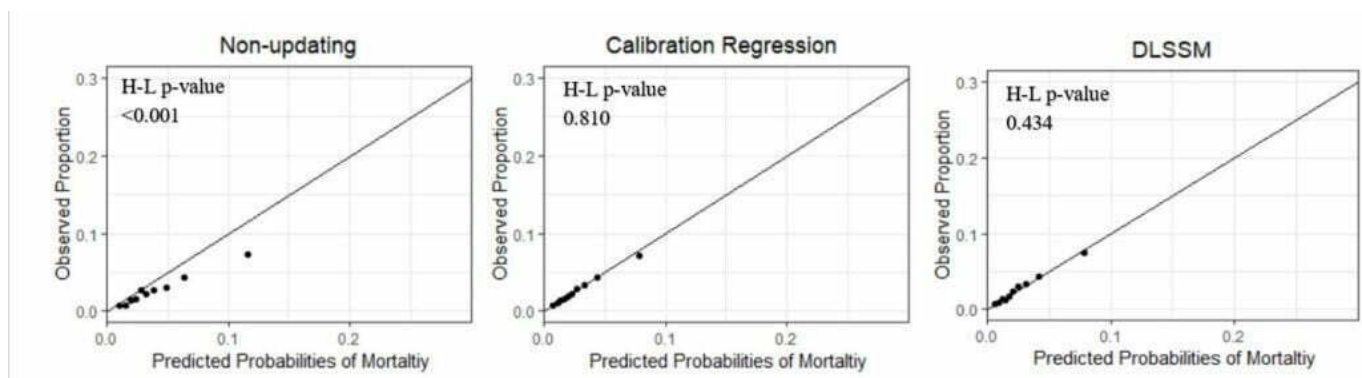
**Dynamic Prediction Modeling of Postoperative Mortality among Surgical Aortic Valve Replacement (SAVR) Patients in a State-Wide Cohort over a 12-year period** Jackie Pollack\*  
Jackie Pollack Wei Yang Stephen Kimmel

**Background:** Clinical prediction models are important tools for decision-making regarding patient care, but they are infrequently updated and often perform poorly over time. Despite recent work to develop methods for model updating, rigorous testing and comparisons of these methods with regular, frequent, model updating are lacking. This study aimed to compare a non-updating model's predictive ability to two dynamic model updating methods: calibration regression and the novel dynamic logistic state space modeling (DLSSM).

**Methods:** A population of 44,546 adults who received an isolated surgical aortic valve replacement from January 1, 1999 - December 31, 2018, in Pennsylvania were chronologically split into a 40% training and 60% validation set. In the non-updating strategy, a baseline model predicting 30-day postoperative mortality was fit by least absolute shrinkage and selection operator (Lasso) regression in the training set. Calibration regression started with the baseline model and annually updated its intercept and slope in the validation set while the DLSSM modeled varying coefficients using smoothing splines and annually updated its coefficients. Calibration, discrimination, and overall measures of accuracy were considered to measure prediction performance.

**Results:** The risk of mortality decreased significantly during the validation period ( $p < 0.01$ ). Both updating methods performed better than non-updating. In the order of non-updating, calibration regression, and DLSSM methods: calibration (Hosmer-Lemeshow (H-L) chi-square statistic 156.5, 4.9, 8.0, respectively; see figure) discrimination (C-statistic 0.685, 0.687, 0.696), and overall accuracy (Brier score 0.256, 0.253, 0.252).

**Conclusion:** Dynamic prediction updating can improve model accuracy, discrimination, and calibration. The decision as to which method to use may depend on which measure is most important in each context.





**Modeling SARS-CoV-2 transmission dynamics between a university population and the surrounding community during multiple outbreaks** Matthew Mietchen\* Matthew Mietchen  
Erin Clancey Eric Lofgren

Prior studies suggest that heterogeneity in SARS-CoV-2 transmission occurs in geographically defined populations (e.g., county), leading to outbreaks among specific communities. During the fall of 2020, many US universities and the surrounding communities experienced a high incidence of reported COVID-19, with a high disease burden among students. We explore the transmission dynamics of an outbreak of COVID-19 among university students, how it impacts the non-student population, and how it could influence pandemic planning and response.

Using surveillance data of reported SARS-CoV-2 cases, we developed a two-population SEIR model to estimate transmission parameters and evaluate how these sub-populations interacted during the 2020 Fall semester. We estimated the transmission rate among the university students ( $\beta_U$ ) and community residents ( $\beta_C$ ), as well as the rate of cross-transmission between the two subpopulations ( $\beta_M$ ) using simulation-based methods. Tau-leaping was used to simulate the mechanistic model and particle Markov chain Monte Carlo (pMCMC) to maximize the likelihood function.

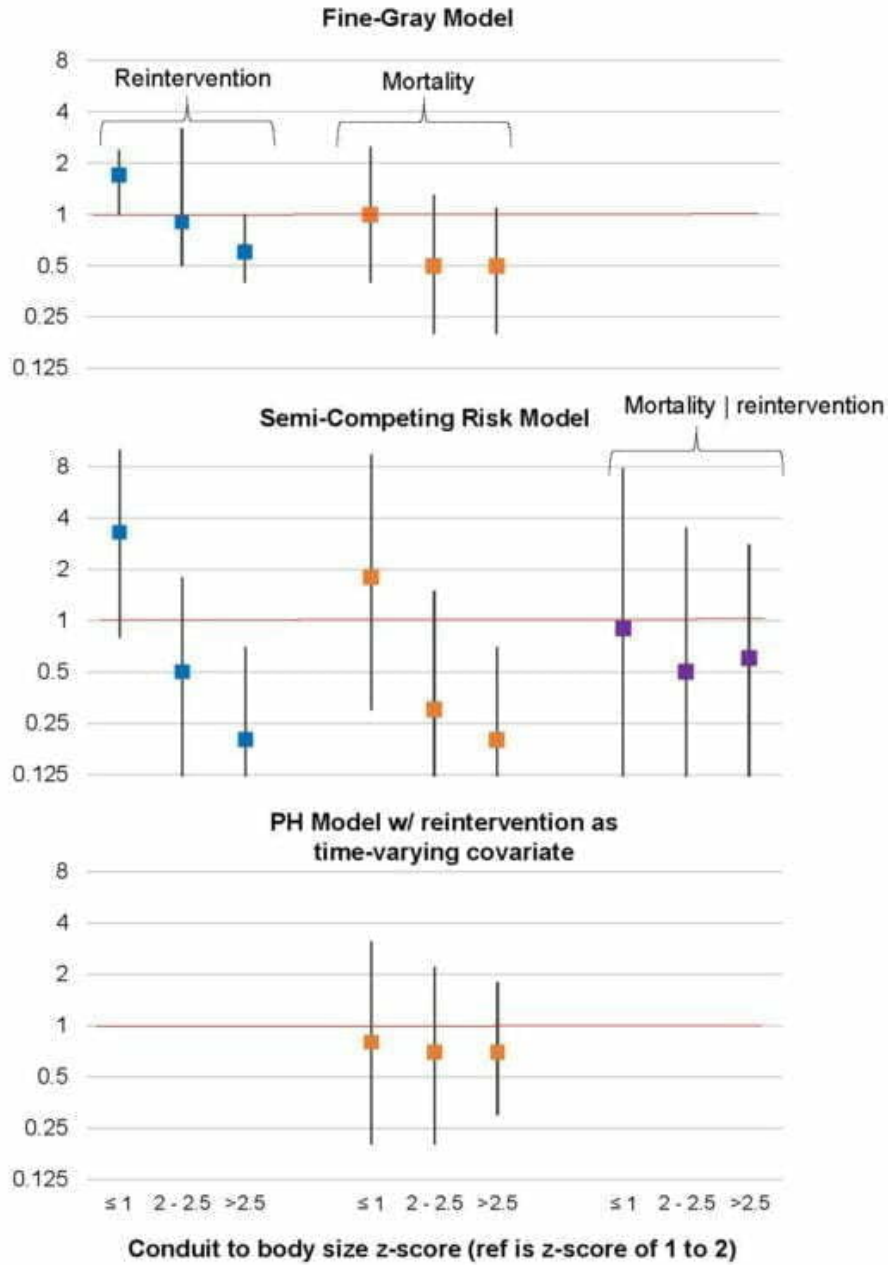
We found that both populations were more likely to interact with others in their group. The cross-transmission estimate ( $\beta_M$ ) was considerably smaller [ $0.02 \times 10^{-5}$  (95% CI:  $0.01 \times 10^{-5}$ ,  $0.11 \times 10^{-5}$ )] compared to the community estimate ( $\beta_C$ ) at  $1.44 \times 10^{-5}$  (95% CI:  $0.72 \times 10^{-5}$ ,  $1.73 \times 10^{-5}$ ) and university estimate ( $\beta_U$ ) at  $24.5 \times 10^{-5}$  (95% CI:  $20.2 \times 10^{-5}$ ,  $36.8 \times 10^{-5}$ ). The individual transmission rates were considerably higher (0.01225 times and 0.00072 times, respectively) than the cross-transmission rate, suggesting that these two populations did not transmit between each other heavily, despite their geographic overlap.

Assumptions that well-mixed populations at a county level during a respiratory viral pandemic should be reconsidered. Models structured to multiple populations could assist with better-targeted interventions for local public health and healthcare facilities.

**Surviving model choice with terminal and non-terminal events: comparison of Fine-Gray, semi-competing risk, and time-varying adjustment approaches to evaluate the impact surgical factors on reintervention and survival after pediatric congenital heart surgery** Tzu-Chun Chu\* Jessica Knight Tzu-Chun Chu Krisy Kuo Lazaros Kochilas

Reintervention and survival are main outcomes of interest after corrective repair of congenital heart defects for which certain surgical considerations can result in a trade-off between these outcomes. For example, in patients with truncus arteriosus (TA), a conduit is needed to improve pulmonary flow. Use of a larger conduit can delay need for replacement as the child grows but may cause untoward complications leading to earlier mortality. Though several methodological approaches are available to address these questions, it is not clear how results from these methods compare and which is optimal for reporting. Therefore, we compared results for the association of conduit size on reintervention and survival in patients surgically treated for TA obtained from Fine-Gray competing risk, semi-competing risk, and reintervention as a time-varying covariate in hazard models. The Pediatric Cardiac Care Consortium database was used to identify children surgically treated for TA in participating US hospitals between 1982 and 2003. Reintervention within five years of the index surgery and z-score for conduit size relative to body size were abstracted from clinical records and linked to the National Death Index for survival information through 2020. Of 209 eligible children who survived to hospital discharge, 104 underwent reintervention (median time=1.3 yrs after discharge) and 40 died (median=2 yrs), 19 after reintervention. As shown in the Figure, each method similarly found small conduits led to faster reintervention, but the magnitude and precision varied. Fine-Gray and semi-competing risk models found large conduits protective against reintervention and mortality. This effect on mortality was attenuated when reintervention was adjusted for as a time-varying covariate. Further work will assess the effects of assumptions, estimation methods, and compare results for different types of heart defects with varying incidence of and association between reintervention and survival.

**Figure.** Adjusted hazard ratios (aHR) for reintervention and mortality comparing conduit size relative to body size z-score (reference category is z-score of 1-2 standard deviations larger than current size of the infant) across three different types of models.



**Methods and software for estimating adjusted risk ratios and risk differences** Konrad H.\*

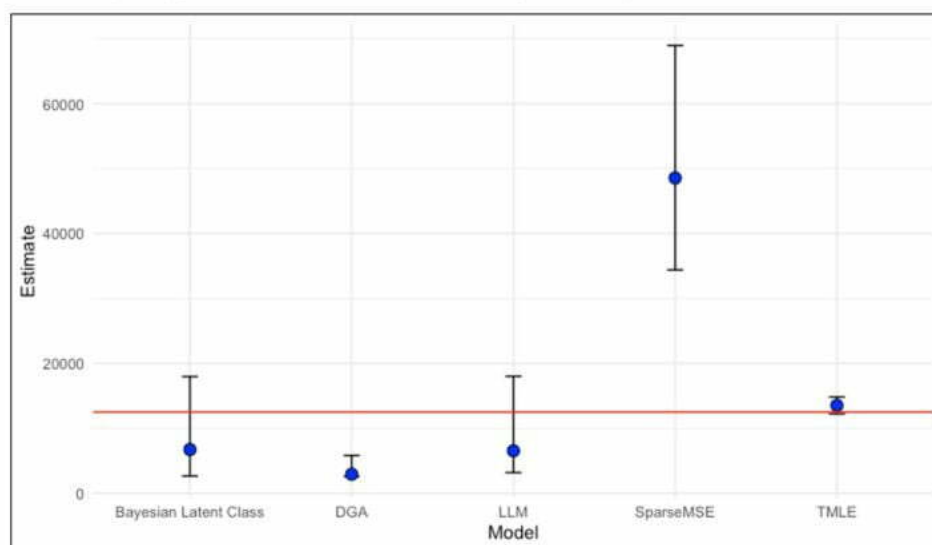
Konrad H. Stopsack

Comparing risks (or prevalences) as risk ratios (RRs) or risk differences (RDs) is a core task of inference in epidemiology. There is no shortage on tutorials explaining how to estimate adjusted RRs and RDs from simplified example data with binary outcomes. However, more advanced programming skills than for fitting a logistic regression model are typically required, and consequently many applied studies simply report odds ratios, despite their limited interpretability. Which approach to estimating RRs and RDs is preferable in real datasets is also unclear. This study implemented several regression model-based approaches to estimating RRs and RDs from binary outcomes and compared feasibility (convergence), differences in point estimates (bias), and width of confidence intervals (variance). Starting from a simple cohort study that has historically been used for illustration purposes, a wide range of datasets that epidemiologists might encounter was simulated. These data showed empirically that binomial regression models were, as expected, neither a feasible nor a valid approach in many datasets, even with improved maximum likelihood estimation techniques. Widely used Poisson regression models for RRs with robust variance also frequently did not converge. In contrast, a marginal standardization (g-computation) approach based on the logistic model had excellent convergence, bias, and variance properties for both adjusted RRs and RDs, with confidence intervals estimation implemented via bootstrapping and the delta method. For RRs, a case-duplication approach proposed by Miettinen that had not been available in standard statistical software also performed well. All approaches are accessibly implemented in the new R package *risks*, leaving no more excuse for estimating odds ratios when RRs or RDs are the actual estimands of interest for causal inference.

**Evaluating a Targeted Minimum Loss-based Estimator for Capture-Recapture Analysis: An Application to HIV Surveillance in San Francisco, CA** Paul Wesson\* Paul Wesson Manjari Das Mia Chen Ling Hsu Willi McFarland Edward Kennedy Nicholas Jewell

Capture-recapture is a common tool in epidemiology and public health surveillance to estimate the size of “hidden” populations based on incomplete and overlapping lists of the target population. The population size estimate is then used to correct the under-ascertainment of cases, establish the true denominator for the population at risk to determine rates of disease burden, and to set public health priorities. Log-linear regression models are often used to estimate the population size yet rely on untestable assumptions and may produce implausible and unreliable estimates due to model misspecification and small cell sizes. A novel Targeted Minimum Loss-based Estimation (TMLE) model recently developed for capture-recapture makes several notable improvements to conventional modeling: “targeting” the parameter of interest to reduce bias and improve statistical efficiency, flexibly fitting the data to alternative functional forms, and limiting bias from small cell sizes. Using simulations and empirical data from the San Francisco Department of Public Health’s HIV surveillance registry, we evaluated the performance of the TMLE model and compared results to other common models (Log-Linear Models [LLM], Bayesian Latent Class models, Decomposable Graph Approach [DGA, a Bayesian Model Averaging approach], and SparseMSE). Based on 2,584 people observed on at least one of three selected lists reporting to the surveillance registry, the TMLE model estimated the number of San Francisco residents living with HIV as of December 31, 2019, to be 13,523 (95% CI: 12,222 – 14,824). This estimate, compared to a “ground truth” of 12,507, was the most accurate and precise of all models examined. The TMLE model represents a significant advancement in capture-recapture research, leveraging modern statistical methods (e.g., SuperLearner, cross-validation) to improve the accuracy and reliability of prevalence estimates of hidden populations.

Population size estimates for the number of San Francisco residents living with HIV as of December 31, 2019, comparing TMLE model to conventional capture-recapture estimation models.



Note: Horizontal line indicates “ground truth” from HIV surveillance registry (n=12,507)

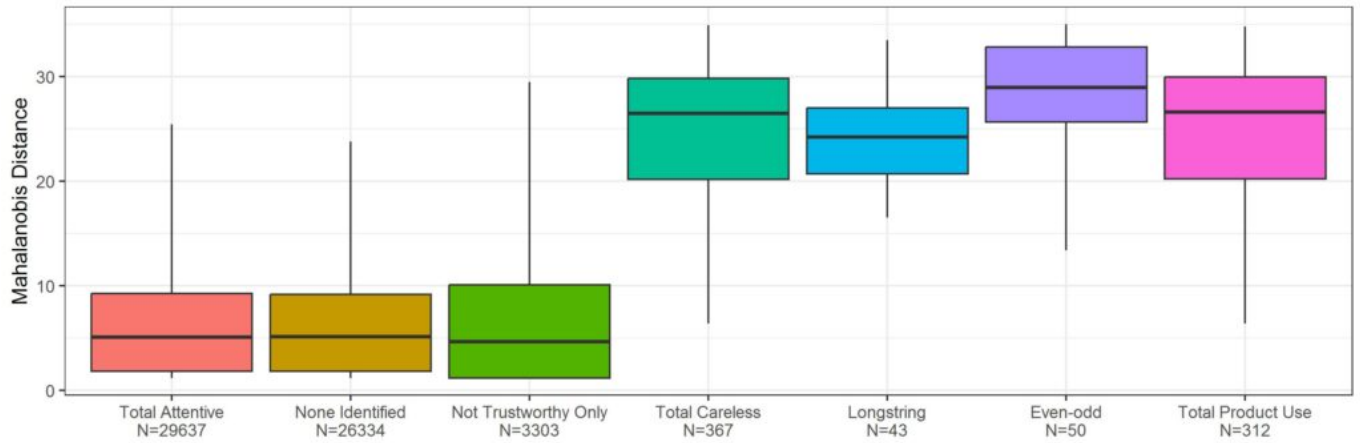
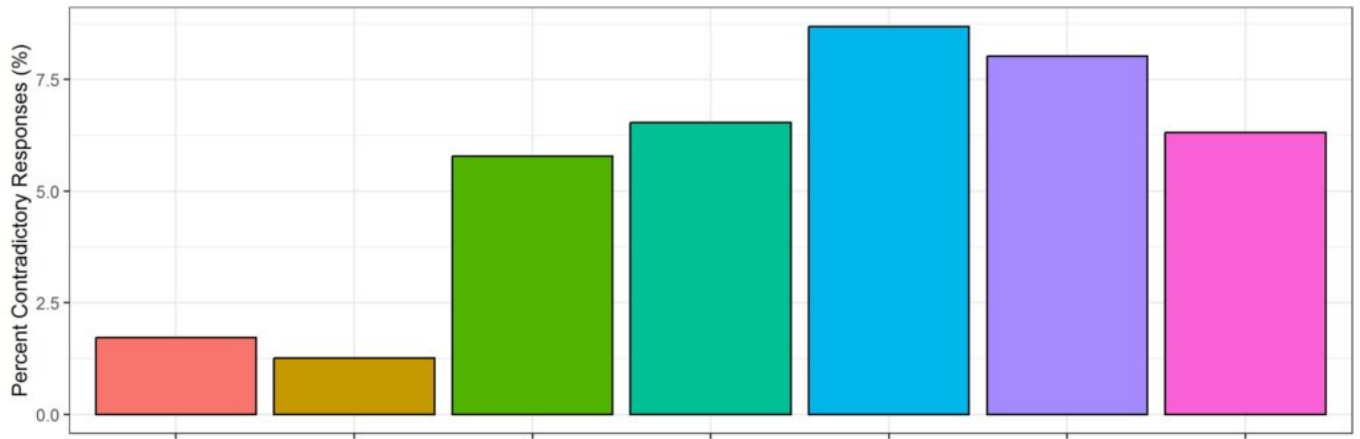
**Removal of bias due to careless response criteria in online health surveys** Karilynn M Rockhill\* Karilynn Rockhill Annika Czizik Hannah Burkett Elizabeth Bernis Joshua C. Black

Background: As online surveys become more common, survey panels provide advantages (lower costs, engaging interfaces, anonymity). Companies assure data quality (bot detection, targeted samples, etc.), but additional vetting is needed regarding careless behaviors. Our objective was to assess careless response influence in the 2022 RADARS® System Survey of Non-Medical Use of Prescription Drugs (NMURx) Program.

Methods: Criteria to identify careless respondents were literature-based or answer pattern-based: time to complete question set (<2 seconds/question), longstring analysis (consecutive endorsement  $\geq 16$  drugs), even-odd analysis ('yes'/'no' alternating drug endorsement, 4 sets), outlier analysis (total endorsement  $\geq 25$  drug products), and a trustworthiness question. Validation metrics used to confirm removal, median Mahalanobis distance of 80 drug use behaviors, and percent of contradictory responses are shown. To demonstrate impact of removing careless responders, we compared weighted prevalence for last year use of cannabis (common) and heroin (rare).

Results: 367/30,0004 (1.2%) surveys were identified as careless respondents. Figure 1 shows breakdown across criteria (N=0 for question timing); 89% qualified by a single criterion. Trustworthiness was excluded given deviation was not confirmed by external metrics. Careless compared to attentive respondents demonstrated more deviant answers (M-distance 24.8 vs. 5.1) and more contradictory answers (6.5% vs. 1.7%). Removal of these respondents reduced relative prevalence by 0.4% for cannabis use (21.6% to 21.5%) and 14.0% for heroin use (0.7% to 0.6%).

Conclusions: Multiple criteria are needed to evaluate response quality, as most respondents only exhibit one behavior. While careless respondents represent a small portion of the sample, they can bias estimates especially on rare survey outcomes. Careless response tools should be included in survey design to detect and remove careless responders post data collection.



**Age and sex differences in the association of insomnia symptoms with all-cause mortality among community-dwelling stroke survivors: a prospective cohort study**

Wendemi Sawadogo\* Wendemi Sawadogo Tilahun Adera

**Background and Objectives:** Insomnia is more frequently reported in stroke survivors but the independent role of insomnia in mortality in this vulnerable group is unknown. The purpose of this study was to investigate the association of insomnia symptoms with all-cause mortality among stroke survivors.

**Methods:** The Health and Retirement Study from 2002 to 2018 was used as the data source. The exposure variable of interest was insomnia symptoms and was derived from sleep-related factors including difficulty initiating sleep, difficulty maintaining sleep, waking up too early, and nonrestorative sleep. Cox proportional hazards regression models were employed to investigate the association between insomnia symptoms and all-cause mortality.

**Results:** A total of 3,501 participants were included in this analysis. Over a mean follow-up of 6 years, 1,782 deaths occurred. Overall, every one unit increase in insomnia symptoms score was associated with a 2% increased risk of death after adjusting for demographic, socioeconomic, and behavioral risk factors (hazard ratio (HR) = 1.02, 95% confidence interval (CI): 1.00, 1.04). However, differences by age and sex were observed. The association was stronger in males aged less than 65 years (HR=1.12, 95%: 1.02, 1.23), followed by females aged less than 65 years (HR=1.06, 95%: 0.97, 1.16), males aged 65 years and over (HR=1.04, 95%: 1.00, 1.08), and females 65 years and over (HR=0.97, 95%: 0.93, 1.00).

**Conclusion:** Our study indicates that insomnia symptoms increased the risk of death, especially in males and those who are younger than 65 years of age. Increased awareness and management of insomnia symptoms may contribute to the prevention of death among stroke survivors.



**Adaptive and innate immunity are key drivers of age at onset of multiple sclerosis** Elina Misicka\* Elina Misicka Yunfeng Huang Stephanie Loomis Nilanjana Sadhu Elizabeth Fisher Arie Gafson Heiko Runz Ellen Tsai Xiaoming Jia Ann Herman Paola Bronson Tushar Bhangale Farren Briggs

**Background.** Age at onset (AAO) is an objective predictor of long-term multiple sclerosis (MS) outcomes independent of disease duration. A higher burden of MS risk variants, including *HLA-DRB1\*15:01*, confer an earlier AAO. However, there has been sparse research characterizing the influence of other genetic variants.

**Objective.** To investigate the mechanisms driving MS onset using a genome-wide association study (GWAS).

**Methods.** The study population consisted of 3,905 unrelated, non-Latinx persons with MS from 3 Biogen clinical trials: ADVANCE (N=665), ASCEND (N=582), and DECIDE (N=1,076); and 3 Genentech clinical trials: OPERA1 (N=528), OPERA2 (N=539), and ORATORIO (N=500). GWAS were conducted in each trial for AAO (rank-normalized) using linear additive models adjusting for sex and genetic ancestry. Results were meta-analyzed. Gene-based tests of association and pathway enrichment analyses were performed. Mendelian randomization (MR) analyses examined whether known risk factors for MS also influenced AAO.

**Results.** The mean AAO was 31 years (SD=9). After filtering for heterogeneity ( $I^2 < 0.75$ ) there were  $8.3 \times 10^6$  variants. Two loci met genome-wide significance. rs28672722T ( $p = 1 \times 10^{-9}$ ,  $\beta = 0.17$ ; *HLA-DQB1* regulatory variant in modest linkage disequilibrium with *HLA-DRB1\*15:01* [ $R^2 = 0.03$ ,  $D' = 0.78$ ]) and rs37411T ( $p = 3.6 \times 10^{-8}$ ,  $\beta = -0.25$ ; a *LOC105375167* [lncRNA] variant). At the gene-level, *HLA-DRB1* was associated with AAO ( $p = 5 \times 10^{-3}$ ) and the most significant associations ( $p = 5 \times 10^{-5}$ ) were for *HLA-C*, *PSORS1C2*, *KLHL7* and *METTL5*. Pathways involved in both adaptive and innate immunity were enriched amongst AAO-associated genes, including MHC I/II antigen presentation ( $p < 5 \times 10^{-6}$ ) and complement activation ( $p < 0.005$ ). MR suggested a role for earlier puberty with earlier MS onset ( $p = 0.03$ ), but not for body-mass index or vitamin D levels.

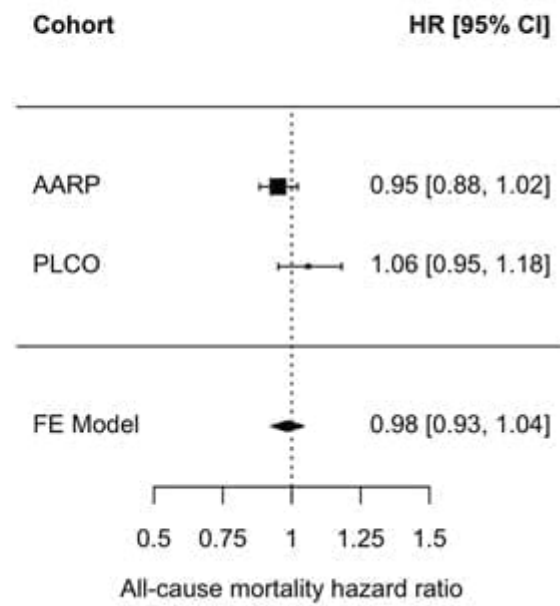
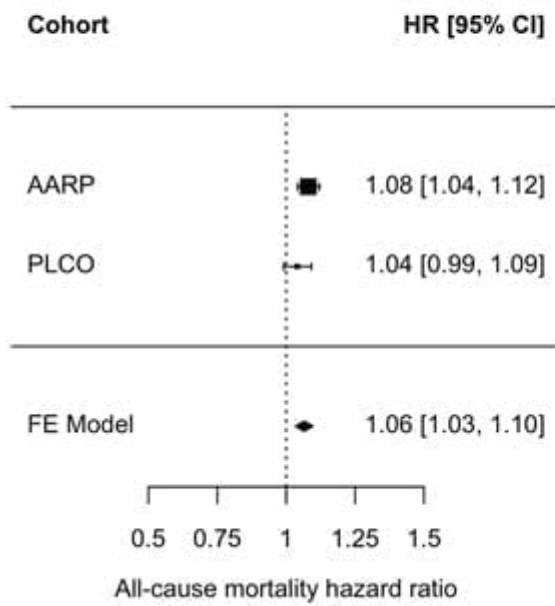
**Conclusions.** Here we present findings from a GWAS of MS AAO, and results implicate genetic mechanisms involved in both adaptive and innate immunity as key drivers.

**Time-varying analysis of multivitamin use and mortality risk in two large, prospective US cohorts** Erikka Loftfield\* Erikka Loftfield Caitlin O'Connell Christian Abnet Barry I. Graubard Linda Liao Neal D. Freedman Rashmi Sinha

In the US, 1 out of every 3 adults use multivitamins (MV), and usage is higher among women and older Americans. The primary motivation for MV use is to enhance health and prevent disease; thus, mortality studies can inform public health guidance. In 2022, the US Preventative Services Task Force reviewed data on MV supplementation and all-cause mortality from randomized controlled trials and found insufficient evidence for determining benefits or harms owing, in part, to limited follow-up time and external validity. Observational evidence is also mixed potentially owing to competing issues of confounding by healthy lifestyle (i.e., healthy user effect) and reverse causation whereby those diagnosed with chronic disease may start MV use (i.e., sick user effect). To address limitations of prior studies, we used Cox proportional hazards regression models with time-varying covariates to estimate multivariable-adjusted hazard ratios (HR) and 95% confidence intervals (CI) in two large, prospective, and geographically diverse, US cohorts, the NIH-AARP Diet and Health Study (N=244,138; n=130,149 deaths) and the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial Study (N=50,251; n=20,807 deaths). Both had repeat assessments of MV use, detailed information on lifestyle, and >20 years of follow-up. We modeled risk estimates in the first and second half of follow-up due to a violation of the proportional hazards assumption. Daily MV users, as compared to nonusers, had fewer mortality risk factors. They were more likely to be never smokers, female, college educated, and normal BMI but were also more likely to report a history of cancer. After adjustment for potential confounders, MV use was not associated with lower mortality risk in either cohort; summary HR estimates for daily MV users versus nonusers were 1.06 (95% CI=1.03-1.10) and 0.98 (0.93-1.04) during the first and second half of follow-up, respectively (**Figure 1**). Results were similar in age and sex-stratified analyses. A weak association between daily MV use and higher mortality risk was observed earlier in follow-up after excluding those with poor self-rated health or a history of chronic disease, arguing against the sick user effect. Overall, we found that MV use was not associated with a mortality benefit but may be associated with modest harm.

Follow-up Period 1

Follow-up Period 2



**Weight cycling, body satisfaction, and eating attitudes among college students** Megan W. Harvey\* Megan Harvey Chelsea Allison Jennifer Fields Lydia Smith

Background: Weight cycling is associated with a variety of adverse health effects, including increased total body fat, increased central adiposity, increased risk of future weight gain, higher fasting glucose levels, impaired glucose tolerance, stress on the cardiovascular system including fluctuations in blood pressures, heart rate, sympathetic activity, and lipid profile, some type of cancer including renal cell carcinoma, endometrial cancer, and non-Hodgkin's lymphoma, and a higher risk of all-cause mortality. The practice has also been found to be associated with an increased risk of disordered eating behavior. We conducted a survey among college students in a small traditional college in the Northeast to evaluate the prevalence of weight cycling, body satisfaction, eating attitudes, and risk of disordered eating and to explore potential risk factors for future morbidity and mortality.

Methods: The Health-Related Knowledge and Attitudes Study is a cross-sectional study of undergraduate and graduate college students between the ages of 18-30. Data was collected between November and December 2022. Students who signed informed consent answered questions about their knowledge, attitudes, and behaviors around nutrition, their current eating behaviors, level of physical activity, and food security status, and demographic information.

Results: The sample was 59.5% male and 97% White. Most students (59.6%) reported never having weight cycled, defined as losing and gaining 20 or more pounds. More than a third (35.5%), however, reported having experienced one weight cycle. More than one weight cycle was uncommon. About 2% (1.8%) reported two weight cycles, about 1% (0.9%) reported 3 weight cycles, and about 2% (2.2%) reported 4 or more weight cycles. Nearly a quarter (24.8%) of the sample answered questions indicating that they are at risk for disordered eating. More than a quarter (27.0%) of the sample reported often, usually, or always being occupied with a desire to be thinner.

Conclusion: Weight cycling, body dissatisfaction, disordered eating behaviors, and a desire to be thinner are common among college students. Future analysis will use current eating behaviors and attitudes to understand frequency of weight cycling.

**Early life socioeconomic position contributes to adult obesity independent of adult socioeconomic factors: Findings from the Sister Study cohort** Jennifer M.P. Woo\* Jennifer Woo Deborah B. Bookwalter Geannette Greene Dale P. Sandler

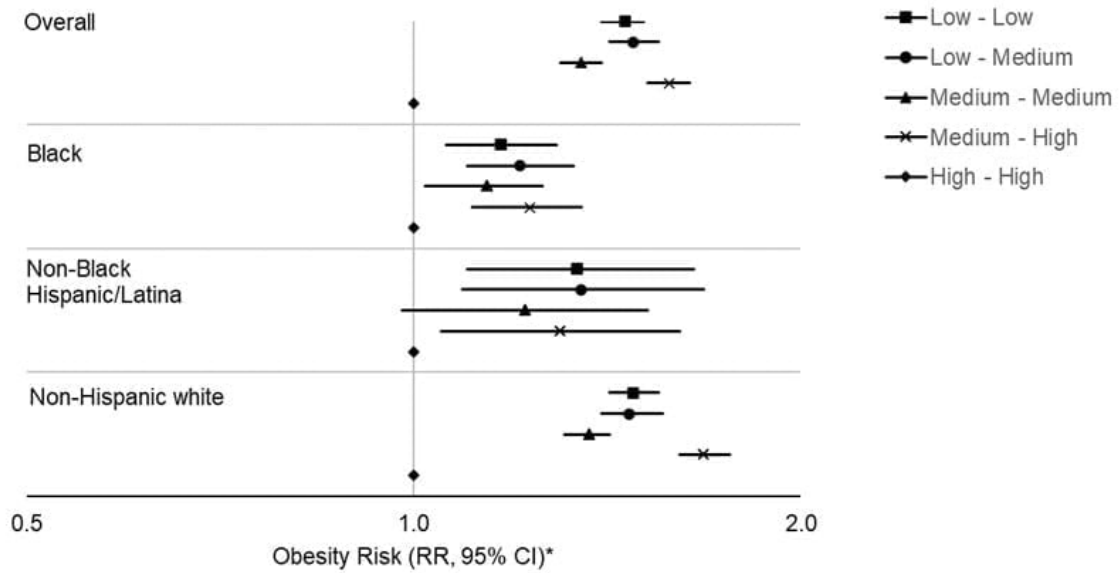
Although low socioeconomic position (SEP) has been associated with obesity within the same life stage, less is known about the association between childhood SEP in the context of life course SEP and adult obesity risk. Changes in SEP over the life course may directly or indirectly alter downstream obesity risk. Research is needed to understand the impact of childhood SEP independent of the effects of adult SEP and how SEP trajectories may influence adult obesity risk.

**Methods:** We use data from the Sister Study, a prospective U.S. cohort of women aged 35–74 years (N=50,884; enrollment: 2003-2009). Childhood SEP was assessed as a continuous latent variable (confirmatory factor analysis-7 indicators) and 5 SEP trajectories were identified using latent class analysis. We use log-binomial regression to estimate RR for adult obesity (body mass index  $\geq 30$  kg/m<sup>2</sup>) at enrollment associated with childhood SEP and SEP trajectory in overall and race and ethnicity-stratified models. We further estimated the direct effect of childhood SEP on adult obesity and mediation by adult SEP.

**Results:** Approximately 30% of participants were obese at enrollment. Lower childhood SEP was associated with greater obesity risk (RR=1.16, 95% CI: 1.15-1.17). In race and ethnicity-stratified models, RRs were elevated in all groups though lower for Black and Hispanic/Latina participants. The direct effect of childhood SEP on adult obesity persisted in mediation models independent of adult SEP (RR=1.10, 95% CI: 1.08-1.12), with adult SEP mediating approximately 40% of the total effect. Furthermore, adult obesity risk was elevated for all SEP trajectories compared to persistent high advantage (high-high). Upward SEP trajectory did not reduce adult obesity risk among participants who experienced less than high advantage in childhood.

**Conclusion:** Lower childhood SEP, independent of adult SEP, may be an important risk factor for adult obesity and a potential point for intervention in obesity prevention.

**Figure 1.** Association between life course socioeconomic position (SEP) trajectory and risk of obesity in adulthood (compared with healthy weight), overall and by race and ethnicity.



\*Adjusted for race and ethnicity (for Overall model only), age, and birth cohort

**Measuring Sociodemographic Factors and Hunger among Food Pantry Users in Eastern****Massachusetts** Alyson Codner\* Alyson Codner Rachel Zack Xinyang Liu Candice Bangham Eva Nelson Jacqueline Milton Hicks Jacey Greece

**Background:** Food assistance programs that aim to relieve hunger are beneficial but often inadequate and there is a need for shorter, validated tools to measure hunger in these settings. Determinants of hunger pre-COVID-19 have been exacerbated by the pandemic. We assessed determinants of hunger among food pantry clients to inform future emergency responses.

**Methods:** 611 food pantry users across 10 food pantries in Eastern Massachusetts completed a cross-sectional survey at the pantry that utilized a modified, validated Household Hunger Scale to efficiently quantify hunger into ordinal categories. Mixed effect logistic regression models assessed the relationship between hunger and household sociodemographic and economic characteristics and adjusted for food pantry site as a random effect with all other covariates controlled for as fixed effects.

**Results:** 19.14% of food pantry users experienced severe hunger, while 20.13% reported moderate hunger. Experiencing economic hardship resulted in larger odds of severe hunger (aOR: 4.78, 95%CI:2.49-9.19) than odds of moderate hunger (aOR 1.95, 95% CI:1.10-3.48). Participation in food assistance programs such as SNAP (aOR 0.53; 95%CI: 0.32-0.88) and WIC (aOR 0.20; 95% CI: 0.05-0.78) were protective against severe hunger. Pantry users already experiencing risk factors for hunger (i.e., single or separated; less than high school education; unemployed or working part-time; lower income; and, experiencing economic hardships such as death, debt, and eviction) were most likely to experience severe or moderate hunger.

**Conclusion:** This study provides insight into the determinants of hunger among food pantry users and offers a practical way to measure hunger in a fast-paced setting. This is important as the economic context has changed due to the pandemic and as more people access resources. It will continue to shift in the aftermath including job loss, unexpected medical or other expenses, and loss of stable housing.

**Type of infant feeding at 4 months of age and effect on growth in early and middle****childhood** Priscilla K. Clayton\* Priscilla Clayton Diane L. Putnick Ian R. Trees Akhgar Ghassabian  
Jordan N. Tyriss Edwina H. Yeung

The prevalence of childhood obesity continues to rise, affecting more than 47 million children in the United States. Early infant growth trajectories have been linked to obesity risk. One suggested modifiable factor associated is breastfeeding.

We explored type of feeding at 4 months of age and child anthropometric measures in children from the Upstate KIDS cohort. All singletons and one randomly selected multiple from each family were included. Parents reported weight and height acquired from pediatrician visits at 24-36 months (n=2007) and at 7-9 years (n=1296). Age- and sex-standardized weight-, height-, and body mass index (BMI)-for-age z-scores were calculated using the World Health Organization reference. Parents reported whether they were breastfeeding, partially breastfeeding, or formula feeding. Association between type of feeding at 4 months and repeatedly assessed anthropometric measures were estimated using linear mixed models.

About 24% infants were exclusively breastfed, 26% partially breastfed, and 50% formula fed at 4 months. Exclusive breastfeeding was associated with higher education and lower twinning (p<.0001). Compared to those formula fed, BMI-for-age z-scores (-0.28; 95% CI: -0.46, -0.11) and weight-for-age z-scores (-0.16;-0.29, -0.03) were lower than for those exclusively breastfed. Partial breastfeeding was associated with lower BMI (-0.24; -0.40, -0.07) but not weight (-0.09; -0.22, 0.02). Results remained similar after adjusting for maternal age, maternal education, pre-pregnancy BMI, race/ethnicity, gestational age, multiple status, and use of fertility treatment. Fully adjusted models using BMI-for-age z-scores at 7-9 years of age show associations persisted for exclusive (-0.25; -0.66, -0.24) and partial (-0.22; -0.42, -0.02) breastfeeding.

Infants exclusively breastfed had lower BMI-for-age z-scores. We confirm evidence of an inverse association with exclusive and even partial breastfeeding on early BMI compared to formula feeding.



**LATEBREAKER**

Nutrition/Obesity

**The association between measures of acculturation and healthy lifestyle behaviors in pregnancy among Latinas** Sofija Zagarins\* Sofija Zagarins Katherine Tucker Bess Marcus Milagros Rosal JoAnn Manson Lisa Chasan-Taber

Studies of the impact of acculturation on pregnancy behaviors have focused on women of Mexican descent although women of Puerto Rican heritage experience higher rates of unhealthy nutrition and low physical activity (PA). We evaluated these associations using data from 103 predominantly Puerto Rican participants in Proyecto Mamá, a randomized controlled trial conducted in Massachusetts (2014-18). We assessed acculturation via the Psychological Acculturation Scale (PAS), language preference, and birthplace. We calculated Alternate Healthy Eating Index-Pregnancy (AHEI-P) scores using data from 3 24-hour recalls collected at a mean of  $14.2 \pm 4.3$  weeks gestation. We measured PA via the Pregnancy PA Questionnaire (PPAQ); meeting American College of Obstetricians and Gynecologists (ACOG) guidelines for PA in pregnancy was defined as at least 30 min/day of moderate intensity sports/exercise. Mean PAS score was  $2.16 \pm 0.77$ , and 34.0% of women reported Spanish language preference; 46.5% of women were born outside the continental US. Mean AHEI-P was  $57.6 \pm 13.6$ , and 34.0% of women met ACOG guidelines. In unadjusted models, women born outside the continental US had 5.5-unit higher AHEI-P scores as compared to women born in the continental US ( $SE=2.6$ ;  $P=0.03$ ), although this association was attenuated with adjustment for age, pregnancy BMI, and energy intake. In multivariable models, a one-unit increase in PAS was associated with a 42.0-MET-hrs/wk increase in total PA including sedentary behavior ( $SE=19.6$ ;  $P=0.03$ ); being born in the continental US was associated with a 63.2-MET-hrs/wk increase in total PA relative to being born outside the US ( $SE=28.7$ ;  $P=0.03$ ). In summary, higher degrees of acculturation were associated with poorer diet quality and higher PA in Puerto Rican women, suggesting that dietary choices may be a larger part of self-identity than PA. Public health interventions aimed at improving pregnancy outcomes in this population should be tailored to acculturation level.

**Dietary Quality and Timing across Days and throughout a Workday Stratified by Shiftwork Status among Nurses** Michael D. Wirth\* Michael Wirth Emily Farrell Robin M. Dawson James W. Harden Gabrielle M. Turner-McGrievy

**Background:** Night and day workers have similar energy intake, but diet quality and timing differ. However, detailed assessment of dietary quality and timing in nurses is lacking. This study examined differences in diet between work and off days, and between times throughout the day stratified by shiftwork status among nurses.

**Methods:** In this cross-sectional study, nurses (n=121) provided detailed assessment of diet quality and timing up to seven consecutive days using the ASA24®. Work schedules, health behaviors, anthropometrics, and psychosocial metrics were self-reported. The Healthy Eating Index (HEI), Energy-density Dietary Inflammatory Index (E-DII), and fasting duration were calculated. Adjusted linear mixed models assessed associations between workday status (work vs. off day) and the HEI, E-DII, and fasting duration. Relationships between food timing (before, during, or after a work shift) and the DII were assessed. Shiftwork status (day vs. night) was assessed as an effect modifier.

**Results:** Nurses were primarily white (84%), females (95%). Fasting duration was 1 hour shorter (11.5 vs. 12.5,  $p<0.01$ ) on workdays compared to off days. Among day workers no association was observed, but a difference in fasting length was found in night workers (workday = 10.5 vs. off day = 12.8 hours,  $p<0.01$ ). No significant results were observed for the EDII or HEI by work vs. off day. The E-DII was lower during a shift compared to before or after a shift (0.50 vs. 1.06 vs. 1.60, all  $p<0.05$ ). Both night shift (1.79 vs. 0.18,  $p<0.01$ ) and day (1.49 vs. 0.64,  $p=0.01$ ) workers had higher E-DII scores after a work shift compared to during work ( $p$  for shiftwork interaction  $<0.01$ ).

**Conclusions:** The E-DII during a shift was the healthiest, and fasting was the shortest on workdays. Future interventions could target the workdays for increasing fasting duration and diet quality before and/or after a shift as a starting point for dietary interventions among nurses.

**Associations between job control and time to pregnancy in a preconception cohort** Erika L. Sabbath\* Erika Sabbath Mary Willis Amelia Wesselink Elizabeth E. Hatch Tanran Wang Craig J. McKinnon Lauren A. Wise

**Background:** Low job control is associated with acute and chronic health conditions, but few studies have examined its association with reproductive health outcomes. We evaluated associations between low job control (operationalized as low job independence and low freedom to make decisions) and time to pregnancy.

**Methods:** We used self-reported data from Pregnancy Study Online (PRESTO), a preconception cohort study of U.S. and Canadian pregnancy planners aged 21-45 years who self-identified as female (2018-2022). We restricted analyses to 3,110 employed participants with  $\leq 6$  cycles of attempt time at baseline. We used the NIOSH Industry and Occupation Computerized Coding System to match participants' occupation and industry with standardized occupation codes, which we then matched to O\*NET job exposure matrix scores for job independence and freedom to make decisions. Participants reported pregnancy status on bimonthly follow-up surveys. We estimated fecundability ratios (FRs) and 95% CIs via proportional probabilities regression models, adjusting for age, education, intercourse frequency, race, ethnicity, education, geographic region, and income.

**Results:** The lowest quartiles of job independence were associated with reduced fecundability (FR for first quartile 0.91, 95% CI 0.82-1.04; FR for second quartile 0.84, 95% CI 0.74-0.95). The lowest quartile of freedom to make decisions was associated with slightly reduced fecundability (FR 0.92, 95% CI 0.80-1.05). Spline analyses were consistent with these patterns. Sensitivity analyses affirmed findings.

**Conclusions:** Low job control may be a risk factor for longer time to pregnancy. As job control is a condition of work (i.e., not modifiable by individuals), these results—if causal—strengthen the case for improving working conditions as a means of improving worker health and wellbeing (including fertility), particularly among working women.

**Heavy lifting at work is associated with metabolic syndrome in U.S. workers** Jian Li\* Jian Li  
Onyebuchi A. Arah Liwei Chen

**Objective:** Although current physical activity (PA) guidelines state that all domains of PA are beneficial to cardiometabolic health, recent epidemiological studies suggest a paradoxical association of occupational PA, such as lifting in the workplace, with manifested cardiometabolic disorders. This study aimed to examine associations of lifting at work with metabolic syndrome (MetS), a cluster of risk factors for cardiovascular diseases.

**Methods:** In total, 587 workers were identified from the Midlife in the United States (MIDUS) Wave II Study with detailed medical examinations. Frequency of lifting at work [never/little (reference group), some, and most/all of the time] was measured by 3 questions regarding levels of lifting load (i.e.,  $\geq 50$  pounds, 10-50 pounds, and  $\leq 10$  pounds). MetS was defined according to the National Cholesterol Education Program–Adult Treatment Panel III guideline. Multivariable logistic regression was performed to quantify the associations, adjusting for age, sex, race, marital status, education, income, smoking, alcohol consumption, leisure-time PA, and job strain.

**Results:** The overall prevalence of MetS was 34.07%. Across the 3 lifting frequency categories, adjusted odds ratios (95% confidence intervals) were 1.11 (0.65-1.89), and 2.54 (1.01-6.40) for the lifting of  $\geq 50$  pounds at work; 1.15 (0.74, 1.80), and 1.22 (0.73, 2.05) for the lifting of 10-50 pounds; and 1.00 (0.63-1.57), and 0.88 (0.55, 1.40) for lifting of  $\leq 10$  pounds.

**Conclusion:** We found that frequent exposure to a high level of lifting at work ( $\geq 50$  pounds) was associated with elevated odds of MetS, whereas frequent exposure to low levels of lifting at work ( $\leq 10$  pounds) was not associated with MetS, demonstrating the importance of both lifting frequency and load in the workplace. Given the cross-sectional design of the present study, future research is warranted to explore the contribution of lifting at work to cardiometabolic health.

**Cause-Specific Mortality Among the Millennium Cohort Project Service Members and Veterans** Yunnuo Zhu\* Yunnuo Zhu Clinton Hall Neika Sharifian Satbir Boparai Felicia R. Carey Rudolph P. Rull

**Purpose:** To compare cause-specific mortality among U.S. service members and veterans, a group with unique occupational exposures and life stressors, with the general adult population.

**Methods:** This study used data from the Millennium Cohort Study, a prospective study of current and former U.S. military service members. Vital status and underlying cause of death were confirmed through 2018 using four military and federal data sources. Standard mortality ratios (SMR) with 95% CIs, adjusted for age, sex, race, ethnicity, and calendar year, were calculated to compare cause-specific mortality among study participants with the general U.S. population, overall and by sex.

**Results:** Among 201,618 participants, 3,017 (1.5%) had a recorded death by December 31, 2018. Among all deaths, 57.0% were due to natural causes, 20.1% to accidents, and 17.1% to suicides; the relative proportion of deaths due to natural causes was higher for non-Hispanic Black participants (70.8%) and the proportion due to accidents and suicides was higher among single, never married participants (31.1% and 26.7%, respectively). Compared with the U.S. population, deaths due to natural causes (SMR 0.36; 95% CI 0.34-0.38), accidents (SMR 0.47; 95% CI 0.44-0.51), and assaults (SMR 0.22; 95% CI 0.17-0.29) were lower among service members and veterans. When stratified by sex, deaths from suicide overall were higher for military women (SMR 1.65, 95% CI 1.31-2.05) but not men (SMR 0.96, 95% CI 0.87-1.05), while deaths from suicide by firearm were elevated for both military women (SMR 2.83, 95% CI 2.04-3.82) and men (SMR 1.33, 95% CI 1.18-1.49).

**Conclusions:** Service members and veterans displayed higher mortality from suicide by firearms compared with the general U.S. population; women specifically showed higher mortality from suicide overall. Policies and programs focused on understanding and reducing the unique stressors and excess risk of mortality due to suicide among service members are needed.

**The Effects of Playing Professional American Football on Longevity** John Robert Warren\* John Warren Gina Rumore

**Introduction:** Does playing professional American football impact longevity? Do any longevity effects of playing football vary across playing positions? Previous research—which has typically featured inappropriate comparison groups that ignore selection into treatment—has found playing football to be positively associated with longevity. This is surprising given the frequency of traumatic brain injuries and other negative health repercussions among players.

**Methods:** We use data on every man drafted to play professional football in the 1950s; if alive, these men would now be at least 83. Some men subsequently played professional football; others never did, despite being selective on similar dimensions as men who did play. We improve on prior research by comparing men who played professional football to otherwise comparable men who, for whatever reason, did not play professionally. Both groups were drafted to play (thus making them similar with respect to skill, size, etc.); they also share the regional, educational, socioeconomic, racial/ethnic, physiological, cultural, and other attributes that make football players systematically different from American men in general.

**Results:** In contrast to almost all prior research, we find no difference in longevity between men who played American professional football and otherwise comparable men who did not: Both groups lived for an average of 77.7 years. In preliminary analyses, we also find no differences by position played.

**Conclusion:** Because of their reliance on inappropriate comparison groups, prior research has incorrectly concluded that the longevity benefits (e.g., fitness, athleticism, income) associated with playing professional American football outweigh possible longevity detriments (e.g., head trauma, CVD). Using a stronger research design, we find no evidence that American professional football players live any longer (or shorter) than comparable men.

**LATEBREAKER**

Occupational

**The Working Life Expectancy of American Adults Experiencing Depression** Kathleen Dobson\*  
Kathleen Dobson Monique Gignac Cameron Mustard

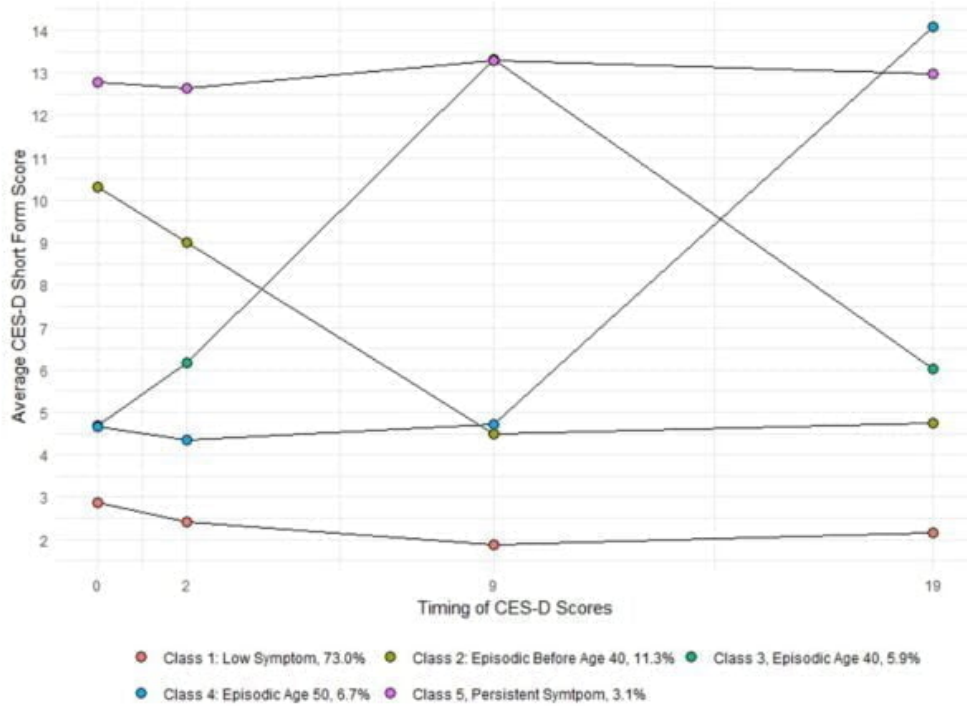
**Objectives:** To estimate the working life expectancies (WLE) of American men and women with depression, examining depression by symptom trajectories from the late 20s to early 50s, and estimate WLE by race/ethnicity and educational attainment.

**Methods:** Data from 8,223 participants collected from 1979 to 2018 in the US National Longitudinal Survey of Youth 1979 cohort were used. Depression was measured using the *Center for Epidemiologic Studies Depression Scale Short Form* at four time points (ages 28-35, ages 30-37, age 40, and age 50). Labor force status was measured monthly starting at age 30 until ages 58-62. Depressive symptom trajectories were estimated using growth mixture modeling and multistate modeling estimated WLE from age 30-60 for each gender and depressive symptom trajectory.

**Results:** Five latent symptom trajectories were established: a low symptom trajectory (n=6,005), an episodic trajectory with high symptoms occurring before age 40 (n=928), an episodic trajectory with high symptoms occurring around age 40 (n=483), a trajectory with high symptoms occurring around age 50 (n=550), and a persistent high symptom trajectory (n=257). The WLE for men at age 30 was 30.8 years for the low symptom trajectory, 23.5 years for the episodic before 40 trajectory, 19.6 years for the episodic around age 40 trajectory, 18.6 years for the episodic around age 50 trajectory, and 13.0 years for the persistent symptom trajectory. Results were similar for women. Disparities between WLE trajectories grew when stratified by race/ethnicity and education level.

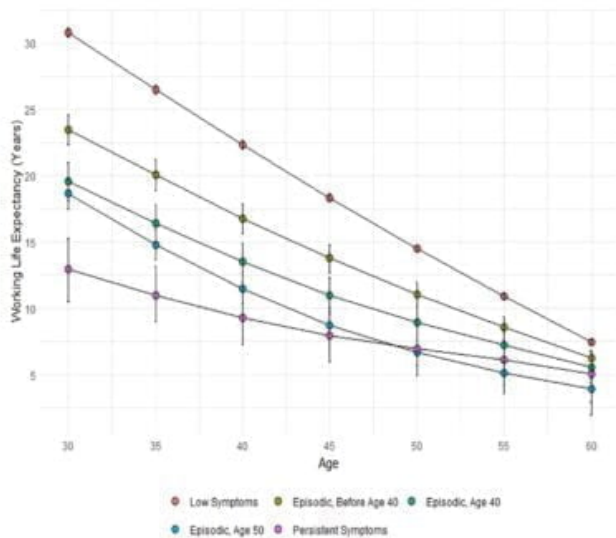
**Conclusions:** Most individuals experience episodic depressive symptoms. However, despite periods of low depressive symptoms, individuals were expected to be employed ~7.3 to 17.8 years less at age 30 compared to those with low/no symptoms. Accessible employment and mental health disability support programs across the working life course may be effective in maintaining work attachment and improving WLE among those with depression.

**Figure 1. Average CES-D-SF Scores, Stratified by Latent Trajectory Membership, NLSY79 Sample (n=8,223)**

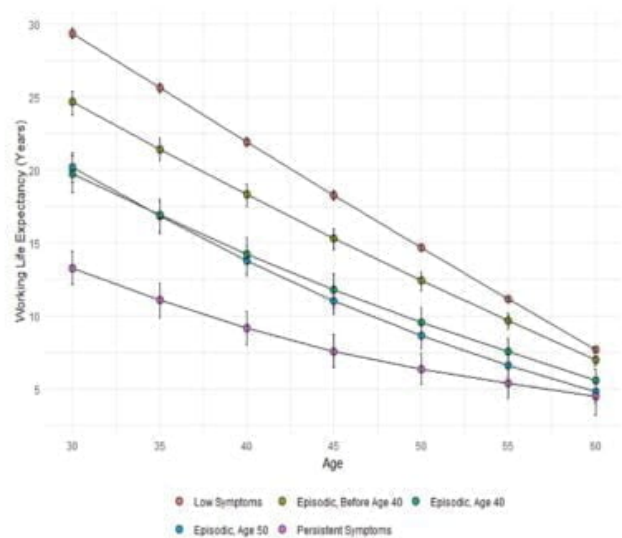


**Figure 2. Estimated Working Life Expectancy by Gender and Depressive Symptom Trajectory**

**Panel A. Men**



**Panel B. Women**





**LATEBREAKER**

Perinatal &amp; Pediatric

**The association between maternal adherence to vegetarian diets and perinatal health: findings from two British birth cohort studies** Peiyuan Huang\* Peiyuan Huang Gemma Sharp  
Kate Northstone Carolina Borges

**Objectives:**

To examine the associations between adherence to vegetarian (V) diets during pregnancy and perinatal health in the Avon Longitudinal Study of Parents And Children (ALSPAC) and Born in Bradford (BiB) study.

**Methods:**

Dietary data were available in 11852 and 3871 singleton pregnancies in ALSPAC and BiB, respectively. Due to small sample sizes, semi-V, pesco-V, lacto-ovo-V, and vegans were combined as broadly defined V (N=614 [5.2%] in ALSPAC; N=139 [3.6%] in BiB). A total of 20 maternal, pregnancy, and offspring outcomes were examined. Results from each study were meta-analysed and corrected for multiple testing using 5% false discovery rate (FDR). Residual confounding by socioeconomic position (SEP) was explored by comparing results between BiB mothers of European (N=1955) and non-European (N=1912) ancestry given differing confounding structures in two groups.

**Results:**

Higher adherence to V-diets was associated with increased odds of maternal anaemia during pregnancy (OR: 1.61 [95% CI: 1.24, 2.10],  $P_{\text{FDR}}=0.006$ ,  $I^2=0\%$ ) and longer breastfeeding (BF) (BF  $\geq 6$  months OR: 1.66 [1.33, 2.06],  $P_{\text{FDR}}<0.001$ ,  $I^2=0\%$ ). The increased risk of maternal anaemia was lower in women with iron supplementation compared to those without (OR: 1.29 [0.91, 1.82],  $I^2=0\%$  vs. 2.36 [1.55, 3.59],  $I^2=0\%$ ). In BiB, the association with BF was fully attenuated in women of non-European (OR: 1.09 [0.65, 1.82]) compared with European (2.62 [1.67, 4.11]) ancestry. No associations were observed with other perinatal outcomes, e.g., hypertensive disorders of pregnancy, C-section, preterm birth, birth weight, Apgar scores, etc.

**Conclusions:**

Evidence from two cohorts consistently showed a higher risk of maternal anaemia associated with V-diets adherence in pregnancy, which was attenuated among iron supplement users; the observed association with BF seemed to reflect residual confounding by SEP. We are replicating these findings in larger samples and exploring potential differences between V-subgroups.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Trends in spontaneous and medically indicated preterm births in Massachusetts** Ruby Barnard-Mayers\* Ruby Barnard-Mayers Collette Ncube

**Background:** More than a third of infant deaths are due to causes related to preterm birth (PTB). PTB rates in Massachusetts (MA) increased prior to the mid-2000s, and since then have oscillated between 8.4% and 9.0%. PTB subtypes are infrequently examined, and the degree to which either subtype is a primary driver of temporal changes in racial disparities in MA is unclear.

**Objective:** To describe how racial and ethnic disparities in PTB, and its subtypes (spontaneous vs. medically indicated), have changed 2011-2018.

**Methods:** Using MA birth record data obtained from the U.S. National Center for Health Statistics, we examined temporal trends in PTB (livebirths <37 weeks gestation), by racial and ethnic group (Asian/Pacific Islander, Black, Hispanic, White). Using joinpoint regression, we calculated the average annual percent change (APC) in PTB rate for each racial and ethnic group, as well as by PTB subtype. Differences in trends by plurality were explored. To identify spontaneous and medically indicated deliveries, we used a validated birth-certificate based algorithm.

**Results:** PTB rates generally increased 2011-2018. Among Black individuals, PTB rates decreased until 2014 (APC=-2.77%) and increased thereafter (APC=3.44%). Among White individuals, PTB rates decreased until 2015 (APC=-3.25%) and increased thereafter (APC=2.28%). PTB rates among Asian/Pacific Islander and Hispanic individuals fluctuated with no discernable pattern. Medically indicated PTB rates generally increased 2011-2018. Among Hispanic (APC=4.5%) and Black (APC=4.9%) individuals indicated PTB rates increased during this period. Spontaneous PTB rates fluctuated throughout 2011-2018. Among Hispanic and White individuals spontaneous PTB rates were mostly unchanged, decreasing only slightly. PTB rates among singletons mirrored overall PTB trends.

**Conclusion:** Increases in overall PTB appear to be driven primarily by changes in medically indicated delivery.

**LATEBREAKER**

Perinatal &amp; Pediatric

**Proportion of orofacial clefts attributable to known risk factors differs for Hispanic and non-Hispanic White individuals** Erin Sley\* Erin Sley Tania Desrosiers A.J. Agopian Suzan Carmichael Joanna Maselko Daniela Stores-Alvarez Mollie Wood Elizabeth Ailes Mark Canfield Mimi Le Andrew Olshan

**Background**

In the United States, orofacial cleft (OFC) prevalence varies by race and ethnicity. Compared to non-Hispanic White (NHW) individuals, Hispanic individuals have a lower prevalence of cleft palate (CP) and cleft lip (CL) but higher prevalence of cleft lip with cleft palate (CLP). However, risk factors for OFCs have been examined in primarily NHW cohorts. To examine whether risk factor profiles for OFCs vary between Hispanic and NHW individuals, we estimated population attributable fractions (PAFs) for 13 risk factors using data from the National Birth Defects Prevention Study (NBDPS).

**Methods**

NBDPS is a multi-state case-control study of births from 1997-2011. Our sample included 956 cases (n=198 CL, 259 CP, and 499 CLP) and 2,820 infants without a birth defect (controls) born to Hispanic individuals, and 2,405 cases (n=646 CL, 810 CP, and 949 CLP) and 6,392 controls born to NHW individuals. We calculated average-adjusted PAFs (aaPAFs) and 95% CIs to estimate the fraction of cases attributable to infant sex, maternal age, education, body mass index, smoking, secondhand smoke, alcohol, pregestational diabetes, parity, folic acid supplementation, dietary folate intake, fever, and acculturation.

**Results**

The proportion of cases explained by all risk factors was similar for CLP (50.2% Hispanic, 50.8% NHW) but higher among Hispanic CL (44.8% Hispanic, 35.8% NHW) and CP (54.9% Hispanic, 19.3% NHW). Among Hispanic individuals, the lowest quartile of dietary folate intake (5.7% CLP, CI:2.8-9.5) and secondhand smoke (8.9% CP, CI:3.7-16.1; 6.4% CL, CI:0.3-8.8) had the highest modifiable aaPAFs. Maternal smoking had the highest aaPAFs among NHW individuals (7.4% CLP, CI:4.3-10.8; 4.6% CP, CI:2.4-7.7; 1.4% CL, CI:0.0-5.1), but one of the lowest among Hispanic CP (0.8%, CI:0.0-3.4).

**Conclusions**

Differences in attributable risk profiles for Hispanic versus NHW individuals may aid in understanding differences in OFC prevalence and inform population-focused prevention strategies.

**Investigation of a Transient Increase in Omphalocele Prevalence in a U.S. Military Birth****Cohort** Jackie Lanning\* Jackie Lanning Clinton Hall Sandra M. Magallon Anna T. Bukowski Gia R. Gumbs Ava Marie S. Conlin

**Background:** The Department of Defense Birth and Infant Health Research (BIHR) program conducts ongoing surveillance of birth defects among infants born to military families. Omphalocele is a major abdominal wall defect with a yearly prevalence of ~2 per 10,000 births in BIHR data, but an unexpected increase was observed from 2017 to 2019, peaking at 6.4 per 10,000 births in 2018; rates returned to baseline in 2020. To investigate this transient increase in prevalence, this study aimed to validate all omphalocele cases in BIHR data from 2016 to 2021.

**Methods:** Using the BIHR birth cohort and associated medical encounter data, omphalocele cases were identified by the presence of International Classification of Diseases, Tenth Revision (ICD-10) code Q79.2 on one inpatient or two outpatient infant encounter records in the first year of life. Cases were validated using available maternal and infant electronic health records. Characteristics of true and false positive cases were assessed using bivariate analyses and compared over time.

**Results:** Of 638,905 live births 2016-2021, 230 met the ICD-10 case definition for omphalocele; 138 (60.0%) of these cases had available electronic health records, of which 68 (49.3%) were true positives. Among the 70 false positives, 36 (51.4%) were cases of misdiagnosed umbilical hernia. The mean time from birth to first ICD-10 omphalocele diagnosis was 0.4 (standard deviation [SD]): 2.4) days for true positives and 57.5 (SD: 83.2) days for false positives ( $p < 0.0001$ ). Rates of misdiagnosed umbilical hernia and delayed omphalocele diagnosis (i.e., >7 days after birth) were elevated during the 2017-2019 period. No temporal trends in maternal, hospital, or geographic characteristics were noted.

**Conclusions:** Higher misuse of ICD-10 code Q79.2 during 2017-2019 likely explained the associated increase in omphalocele prevalence. Timing of first diagnosis should be considered for omphalocele case definitions based on medical encounter data.

**Prevalence and factors associated with excessive weight during pregnancy in South**

**Carolina: 2015-2021** Sarah Simpson\* Sarah Simpson Angela M. Malek Chun-Che Wen Brian Neelon Dulaney A. Wilson Julio Mateus John Pearce Kalyan Chundru Jeffrey E. Korte Hermes Florez Kelly J. Hunt

**Background:** The objective of the study was to assess the prevalence and associated factors of excessive weight gain during pregnancy among a population-based cohort in South Carolina.

**Methods:** This study included 301,553 live full term singleton births from 173,722 Non-Hispanic White (NHW), 91,036 Non-Hispanic Black (NHB), 22,387 Hispanic and 14,408 women of other race/ethnic groups from 2015 to 2021. Pre-pregnancy BMI based on CDC classification was collected via birth certificate. Gestational weight gain (GWG) adequacy was defined as inadequate, adequate and excessive based on IOM 2009 recommendations for weight gain during pregnancy based on pre-pregnancy BMI. GWG adequacy was dichotomized as excessive vs. inadequate and adequate.

**Results:** 24.9% gained inadequate weight, 25.5% gained adequate weight and 49.7% gained excessive weight during pregnancy. The prevalence of excessive weight gain among underweight, normal, overweight, and obese women was 29.5%, 39.5%, 60.1% and 55.6 %, respectively. Trends in excessive weight gain remained stable over time across race-ethnic groups. Being overweight (RR=1.57, 95% CI: 1.55-1.58) or obese (RR=1.47, 95% CI: 1.46-1.49) prior to pregnancy was associated with excessive weight gain compared to normal weight, while less likely among underweight (RR=0.75, 95% CI: 0.72-0.77). High school education, some college and college education or higher was associated with excessive weight gain. Smoking and parity were also associated with excessive weight gain. NHBs, Hispanics, and other racial/ethnic minorities were less likely to gain excessive weight than NHWs. Age, Medicaid, WIC and residence were not associated with excessive weight gain.

**Conclusions:** The prevalence of excessive weight gain during pregnancy remains high. Pre-pregnancy overweight and obesity was associated with excessive weight gain. Additionally, race/ethnicity, education, parity, and smoking are significant predictors of excessive weight gain during pregnancy.

<b>Factors associated with excessive weight gain during pregnancy in South Carolina.</b>	
<b>Characteristic</b>	<b>Odd Ratios (95% CIs)</b>
Time	0.99 (0.99-1.00)
Age (10-year unit increase)	0.99 (0.98-0.99)
<b>Race/Ethnicity</b>	
Non-Hispanic White	1.00
Non-Hispanic Black	0.85 (0.84-0.86)
Hispanic	0.79 (0.78-0.81)
Other	0.81 (0.79-0.83)
<b>BMI Classification</b>	
Normal	1.00
Underweight	0.75 (0.72-0.77)
Overweight	1.57 (1.55-1.58)
Obese	1.47 (1.46-1.49)
<b>Education</b>	
Less than high school	1.00
High school graduate	1.09 (1.07-1.10)
Some College	1.15 (1.13-1.16)
>= College Graduate	1.15 (1.14-1.17)
<b>Medicaid Status (yes vs. no)</b>	0.98 (0.97-0.99)
<b>Women, Infants and Children (WIC) (yes vs. no)</b>	1.02 (1.01-1.03)
<b>Residence (rural vs. urban)</b>	0.99 (0.98-1.00)
<b>Previous Live Birth/Still Born (no vs. yes)</b>	1.15 (1.14-1.16)
<b>Smoking (yes vs. no)</b>	1.10 (1.08-1.11)

**Variation in risk for neonatal intensive care among TRICARE insured newborns at military and civilian hospitals** Celeste Romano\* Celeste Romano Clinton Hall Anna Bukowski Thornton S. Mu Gia Gumbs Ava Marie S. Conlin Rasheda J. Vereen JoAnna K. Leyenaar David C. Goodman

**Objective:** To characterize differences in the TRICARE-insured neonatal population and risk for neonatal intensive care unit (NICU) admission between US military and civilian hospitals.

**Methods:** Singleton births identified in DoD Birth and Infant Health Research program data October 2015–December 2020 were stratified by birth location (military treatment facility [MTF] or civilian hospital); births occurring at civilian hospitals within 40 miles (the catchment area) of an MTF were also ascertained. NICU admission rates (per 100 births) and the frequency of newborn risk factors were calculated by birth location. Modified Poisson regression models estimated associations with risk factors, and marginal  $R^2$  values were calculated to assess model fit.

**Results:** Of 470,605 births, 36.8% occurred at an MTF, 20.4% at a civilian hospital within an MTF catchment area, and 42.9% at a civilian hospital outside an MTF catchment area. The NICU admission rate was 8.9 and 10.4 among births at MTFs and civilian hospitals, respectively; for births at civilian hospitals within MTF catchment areas, the rate was 12.5. Births at civilian hospitals within MTF catchment areas vs at MTFs were similarly more likely to be preterm (9.1% vs 5.3%) and have low birthweight (5.9% vs 3.9%) and birth defects (5.0% vs 3.1%). Positive associations were observed between risk factors and NICU admission regardless of birth location, but there was greater unexplained variation among births at MTFs ( $R^2$ : 0.14) and civilian hospitals outside MTF catchment areas ( $R^2$ : 0.19) vs civilian hospitals within MTF catchment areas ( $R^2$ : 0.25).

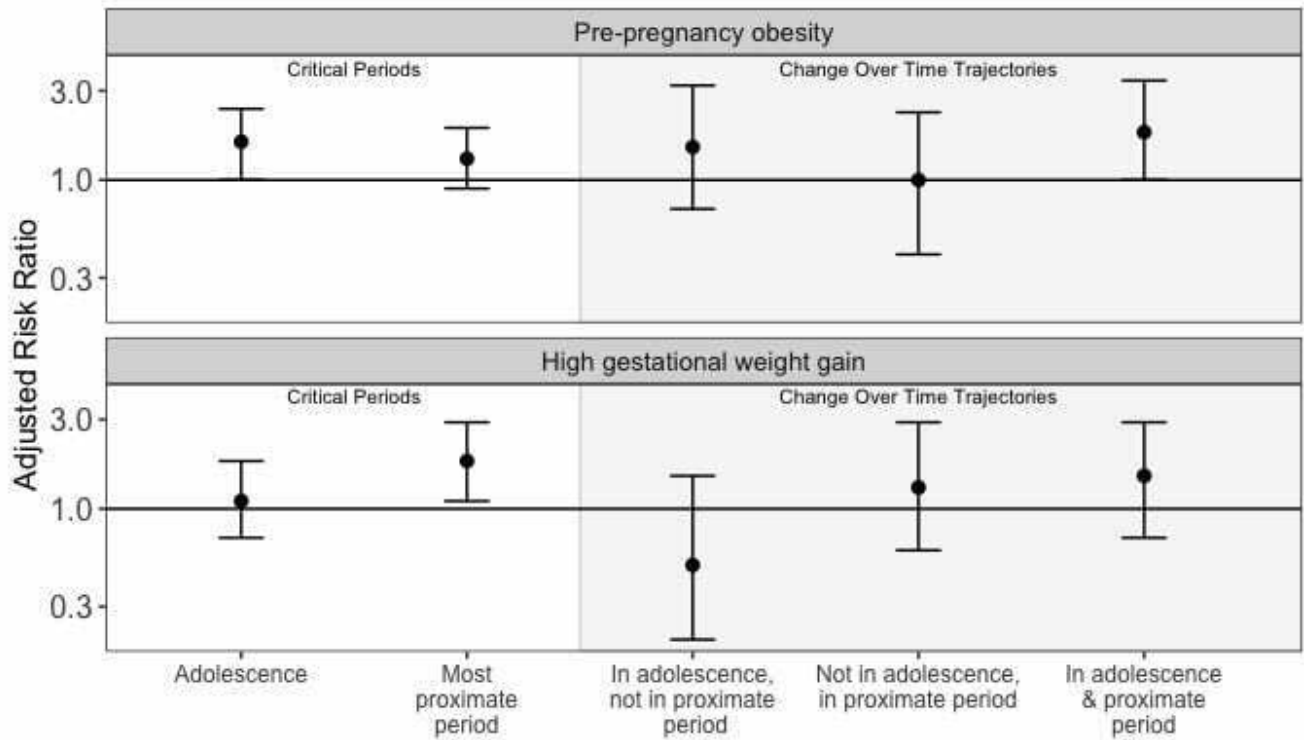
**Conclusions:** Births at MTFs were at lower risk for NICU admission relative to those at civilian hospitals, particularly civilian hospitals within MTF catchment areas. Furthermore, NICU admission for births at MTFs was not well explained by predictors of newborn need. Baseline population differences should be considered when comparing care received at MTFs vs civilian hospitals.

**Associations of pre-pregnancy depression trajectories with pregnancy-related weight****outcomes** Kriszta Farkas\* Kriszta Farkas Rebecca L. Emery Tavernier Sydney T. Johnson Lisa M. Bodnar Richard F. MacLehose Susan M. Mason

Research has shown preconceptional depression to be associated with pregnancy weight outcomes, including gestational weight gain (GWG). However, less is understood about the influence of depression earlier in the life-course. In the Life-course Experiences and Pregnancy study (n=656), we estimated associations of depression trajectories from adolescence to young adulthood with pre-pregnancy obesity and high GWG in each participant's first pregnancy. We examined two critical periods (adolescence and most proximal survey wave prior to pregnancy) and trajectories of change over time from adolescence to most proximate period. Using modified Poisson regression, we estimated risk ratios (RR) and 95% CIs adjusted for confounders, including race, childhood socioeconomic status, and education. In bias-adjusted analyses for outcome misclassification, we used multiple imputation techniques to adjust self-reported pregnancy weight from surveys using medical record data on a participant subset. Preliminary analyses with only non-imputed self-report survey data show depression in each critical period to be associated with pre-pregnancy obesity (adolescence: RR=1.6 [1.0, 2.4]; most proximate period: RR=1.3 [0.9, 1.9]; Figure 1). Depression during both adolescence and the most proximate period was also associated with higher pre-pregnancy obesity risk (RR=1.8 [1.0, 3.4]). Depression only in the most proximate period was related to greater risk of high GWG (RR=1.8 [1.1, 2.9]). Change over time trajectories also showed positive, although imprecise, relations with high GWG. Overall, these early findings suggest that adolescent depression may be more salient for pre-pregnancy obesity risk, whereas depression in the most proximate period prior to pregnancy may be more relevant for high GWG risk. They also support the potential importance of examining depression across the life-course for understanding pregnancy-related weight.



Figure 1. Associations of pre-pregnancy depression trajectories with pregnancy weight outcomes



Note: No depression served as the reference category for each of the life-course depression exposures examined.

**Breastfeeding and late adolescent ApoB: a Hong Kong birth cohort study** C Mary Schooling\*

C Mary Schooling Shiu Lun Au Yeung Man Ki Kwok Gabriel M Leung

**Background:** Breastfeeding is widely promoted although experimental evidence concerning long-term benefit is limited. Observational studies are open to bias from confounding by socio-economic position. We assessed the association of breastfeeding with late adolescent lipid sub-fractions, particularly apolipoprotein B (ApoB), overall and by sex, in a setting with minimal association of breastfeeding with higher socio-economic position using the population-representative “Children of 1997” birth cohort comprising 88% of births in Hong Kong in April and May 1997 in which many of the results from randomized controlled trials of breastfeeding promotion have been replicated.

**Methods:** Associations of breastfeeding in the first three months of life (never, mixed, exclusive) with lipid sub-fractions were obtained using linear regression adjusted for potential confounders, including parental socio-economic position, maternal place of birth, type of delivery, gestational age and birth weight. Differences by sex were assessed. Multiple imputation and inverse probability weighting were used to recover the original sample.

**Results:** Of the 3408 participants included, average age 17.6 years, 48.8% were girls and mean ApoB was 0.74g/L (standard deviation 0.15). Exclusive breastfeeding was associated with lower ApoB (-0.027g/L, 95% confidence interval -0.046 to -0.007, p for trend 0.016) with similar estimates by sex. No such association was seen for triglycerides or high-density lipoprotein cholesterol.

**Conclusions:** Breastfeeding may provide lifelong protection against cardiovascular disease. This study supports established policies aimed at promoting breastfeeding as a modifiable exposure that forms part of a healthy start in life as an investment for lifelong cardiovascular disease prevention.

**Predictors of early childhood residential mobility in urban and rural Pennsylvania****populations** Cassandra Clark\* Cassandra Clark Nicole Deziel Joshua Warren James Saiers Xiaomei Ma Michelle Bell

**Background.** Exposure assessments in perinatal and pediatric epidemiology commonly use residential address at birth to assign exposure. However, expectant parents have a high rate of residential mobility, which can introduce exposure misclassification. Additionally, factors predicting mobility may vary by urbanicity.

**Methods.** We examined predictors of early-life residential mobility and compared these between urban and rural children within a registry-based population of 400 Pennsylvania children diagnosed with leukemia for whom birth and diagnosis addresses were available. Residential mobility between birth and diagnosis was assessed by three metrics: whether a child moved, distance moved, and whether the child changed census tracts. These metrics were compared in urban and rural populations using chi-square, t-tests, and logistic regression.

**Results.** A greater proportion of rural subjects moved (66.7%) and moved further (median: 3.5 km) compared to suburban (60.7%, 0.3 km) or urban (57.1%, 0.5 km) subjects.

Comparable proportions of urban and suburban/rural children changed census tracts upon moving (173 [48.5%] and 20 [46.5%], respectively). Within urban populations, moving was associated with race ( $p=0.009$ ), educational attainment ( $p=0.003$ ), using food stamps ( $p<0.001$ ), census tract-level income ( $p<0.001$ ), and a higher (i.e., more vulnerable) Social Vulnerability Index ( $p<0.001$ ). Specifically, urban Black mothers were 5.03 times more likely to move than white mothers (95% CI: 1.70-14.92), and mothers using food stamps were 2.64 times more likely to move than mothers who did not move (95% CI: 1.67-4.17). Conversely, moving in suburban/rural populations combined was not statistically significantly associated with any demographic/SES factor.

**Conclusions.** We identified several SES/demographic factors associated with early-life residential mobility in urban children, though patterns in the suburban/rural population are less clear. Our results suggest that residential mobility occurs differentially both within and across urban and suburban/rural populations, which has implications for spatial exposure assessment methods using birth address in regional studies.

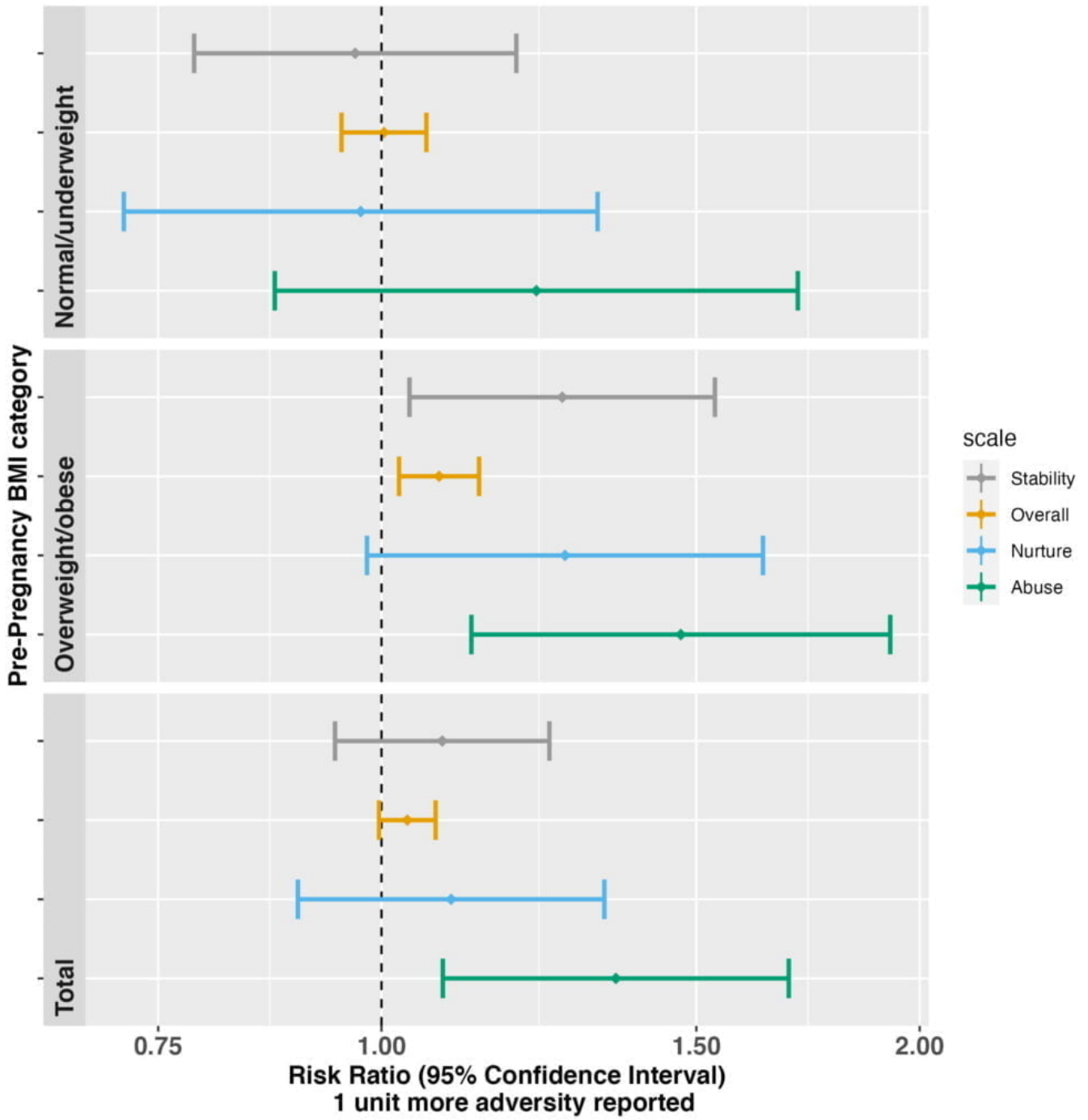
**Understanding the role of childhood nurture, abuse, and stability on incident gestational diabetes in the Coronary Artery Risk Development in Young Adults study (CARDIA)** Kaitlyn Stanhope\* Kaitlyn Stanhope Erica Gunderson Shakira Suglia Sheree Boulet Denise Jamieson Catarina Kiefe Kiarri Kershaw

**Objective:** To estimate the association between positive (nurture, stability) and negative (abuse) aspects of maternal childhood family environment with gestational diabetes (GDM) and effect modification by pre-pregnancy body mass index (BMI) or maternal race.

**Methods:** We used CARDIA data over 30 years (1985-2016) on individuals with >20 week pregnancies after baseline (1985-86), no pre-pregnancy diabetes and complete data on the Childhood Family Environment Questionnaire (retrospectively assessed once at year 15, 2000-01). We used the overall score and three subscales: abuse, nurture, and stability as continuous, separate exposures. We fit log binomial models with generalized estimating equations to account for multiple pregnancies per individual and calculated crude and adjusted risk ratios and 95% confidence intervals. Age at delivery, parity, race (black or white), and parental education (as a proxy for childhood SES) were potential confounders and pre-pregnancy BMI and race potential effect modifiers.

**Results:** We included 748 individuals (39% Black, age at baseline 18-32 years) with 1891 pregnancies, 142 of which (7.5%) were complicated by GDM; For all four exposures, a worse childhood family environment was associated with increased risk of GDM. The estimated association was strongest for abuse, with a 1 point increase on the abuse subscale (e.g., from “rarely or never” to “some or little of the time”) associated with a 40% increased risk of GDM (aRR: 1.4, 95% CI: 1.1, 1.7). There was multiplicative interaction by BMI with a stronger association among individuals who were overweight/obese at the preceding CARDIA exam than among those who were normal/underweight. There was no evidence of interaction by race.

**Conclusions:** Higher levels of childhood trauma were associated with increased risk of GDM, with possible effect modification by BMI.



**Maternal leukocyte telomere length, hypertensive disorders of pregnancy, and risk of fetal growth abnormalities** Jessica L Gleason\* Jessica Gleason Fasil Tekola-Ayele Zhen Chen Kathryn Wagner Cuilin Zhang

**Background:** Leukocyte telomere length (LTL) is a marker of cellular aging with links to fetal programming. Non-pregnant individuals with hypertensive disorders have shorter LTL than normotensives, but few studies have evaluated maternal LTL in relation to risk of hypertensive disorders of pregnancy (HDP) or extremes of birthweight, small and large-for-gestational age (SGA and LGA).

**Methods:** LTL was measured in maternal blood samples at 10-13 weeks' gestation in a case-control study nested in the NICHD Fetal Growth Studies (n=310), which excluded women with chronic hypertension. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for risk of any HDP (n=19) as well as risk of SGA (birthweight <10<sup>th</sup> percentile, n=13) and LGA (birthweight>90<sup>th</sup> percentile, n=31). All analyses were weighted by inverse probability of selection into the case-control study and adjusted for maternal sociodemographics.

**Results:** Compared to the 3<sup>rd</sup> (longest) tertile of LTL, risk of HDP was higher for those in the 2<sup>nd</sup> (OR=1.85; CI 0.93, 3.69) and 1<sup>st</sup> (shortest) tertiles (OR=30.4; CI 16.2, 57.1). Associations between LTL and SGA appeared to be non-linear as those in the 2<sup>nd</sup> tertile had lower odds of SGA (Figure), with inconsistent results in the 1<sup>st</sup> tertile. Risk for LGA was lower in both the 2<sup>nd</sup> and 1<sup>st</sup> tertiles (Figure), but associations again appeared non-linear. Results were robust to sensitivity analyses, including stratification by age group (above/below 30 years) and restriction to no other pregnancy complications (n=201), which included no HDP for SGA and LGA.

**Conclusion:** Shorter maternal LTL in the first trimester was associated with an elevated risk of developing hypertensive disorders of pregnancy, which may indicate sub-clinical vascular disturbances. Shorter LTL was also a signal for lower risk of LGA, even among those without hypertensive disorders. Findings indicate maternal LTL may be an important determinant for pregnancy complications and inter-related fetal growth.

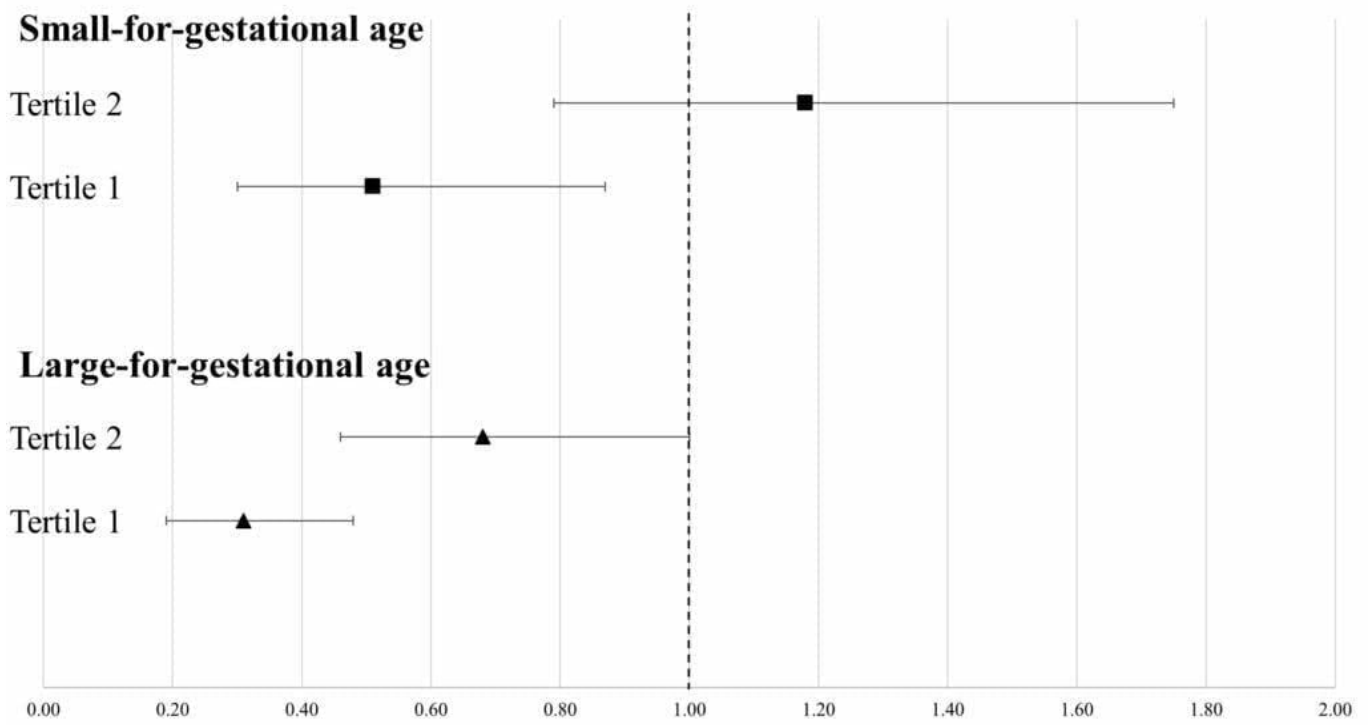


Figure. Odds of small-for-gestational age (SGA) or large-for-gestational age (LGA) by leukocyte telomere length compared to tertile 3 (longest telomeres) adjusted for maternal age, race/ethnicity, pre-gravid BMI, parity, marital status, education, and infant sex

**Differences in Assisted Reproductive Technology Use among Cisgender Women with Same-Sex versus Different-Sex Partners: Findings from a Prospective Cohort across the U.S.**

Kodiak R. S. Soled\* Kodiak Soled Tabor Hoatson Brent Monseur Bethany Everett Payal Chakraborty Colleen A. Reynolds Aimee K. Huang Sebastien Haneuse Brittany M. Charlton

**Background:** Women with same-sex partners form biological families in myriad ways, including through sexual intercourse, and, for those without access to sperm, social networks and medically assisted reproductive technology (ART). Emerging evidence suggests this population increasingly wants to form biological families, yet little is known about their ART use.

**Methods:** The Growing Up Today Study is a longitudinal cohort based in the U.S. (n=27,805). Participants were 9–16 years of age at baseline (1996 initial enrollment) and biennial follow-up is ongoing. We identified cisgender women with same-sex and different-sex partners and assessed ART use using logistic models, accounting for participant clustering using generalized estimating equations. We also assessed pregnancy status, conception attempts, and ART methods.

**Results:** A sizable portion of participants were pregnant or trying to conceive in 2019 (15% of those with same-sex partners vs 26% of those with different-sex partners). Nearly 80% of pregnant participants with same-sex partners (n = 29) used ART from 2005 - 2019 compared to 17% of those with different-sex partners (n = 588;  $p < 0.0001$ ). Among participants who used ART, those with same-sex partners used different ART methods compared to those with different-sex partners ( $p < 0.0001$ ); differences were largest for intrauterine insemination (55% among those with same-sex partners vs 21% among those with different-sex partners), gamete/zygote intrafallopian transfer (7% vs 0%), intracytoplasmic sperm injection (7% vs 11%), and ovulation medication alone (0% vs 30%).

**Conclusions:** A burgeoning number of cisgender women with same-sex partners are forming biological families and using ART more often than their peers with different-sex partners to achieve this. Differences in ART methods reflect different clinical needs (e.g., ovulation medications alone indicate infertility). Providers need to be prepared to competently care for this growing population.



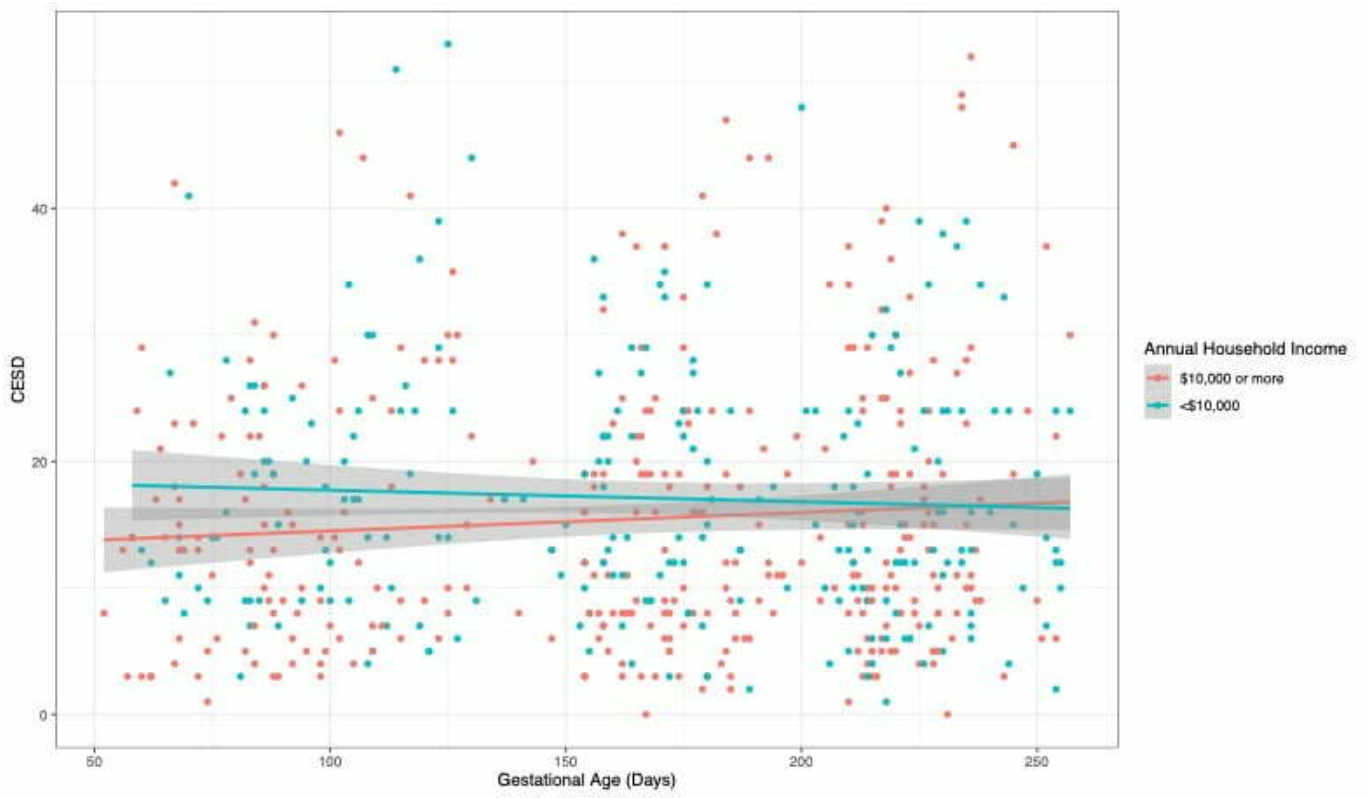
**Depressive symptoms across pregnancy in Black women** Sarah Vaughan\* Sarah Vaughan Dalia Khalil Suzanne Hyer Naida Saadat Dawn Misra Carmen Giurgescu

**Background:** Understanding how depressive symptoms change across pregnancy is necessary for screening and intervention efforts. Most research to date has relied on measuring symptoms at a single time point in pregnancy among mostly White women. We describe here a longitudinal analysis of depressive symptoms across pregnancy in a sample of Black women.

**Methods:** We conducted a secondary data analysis of 187 Black pregnant women from the prospective cohort study, Biosocial Impact on Black Births, recruited from the Midwestern U.S. Participants completed questionnaires, including the Center for Epidemiological Studies Depression scale (CES-D), at three timepoints during pregnancy. Hierarchical linear modeling was used to assess CES-D over time. Maternal age, annual household income, marital status, work status, cigarette use, and alcohol use were assessed as individual-level predictors.

**Results:** Women with an annual household income <\$10,000 had significantly higher CES-D scores at baseline than women with an annual household income  $\geq$ \$10,000 ( $p=0.01$ ). There was a significant interaction between annual household income and time ( $p=0.04$ ). CES-D scores for women with an annual household income <\$10,000 decreased across pregnancy whereas CES-D scores for women with an annual household income  $\geq$ \$10,000 increased across pregnancy (Figure 1). Cigarette smoking was significantly associated with increased CES-D at baseline ( $p=0.05$ ), but there was no interaction between smoking and time.

**Conclusions:** Black women with an annual household income of  $\geq$ \$10,000 are at higher risk for increasing depressive symptoms as pregnancy progresses compared to women with an annual household income of <\$10,000. Screening and interventions for depressive symptoms in Black women may be most effective in early pregnancy; however, providers should screen throughout pregnancy as symptoms may increase over time for certain groups of women.



**Sex and obesity status modify the association between vitamin D and eczema among adolescents** Abdullah Al-Taiar\* Abdullah Al-Taiar Ali Ziyab Reem Al-Sabah Lemia Shaban Zainab Almousa Anwar AlBaloul

**Background:** Epidemiological studies have reported inconsistent associations between vitamin D and eczema. This study sought to assess whether sex and obesity status could modify the association between vitamin D and eczema.

**Methods:** A cross-sectional study enrolled 763 adolescents in Kuwait. 25-hydroxyvitamin D (25(OH)D) was measured in venous blood using liquid chromatography tandem mass spectrometry (LC-MS/MS). Current eczema was defined according to clinical history and characteristic morphology and distribution.

**Results:** In sex-stratified analysis, decreased 25(OH)D levels were associated with increased current eczema prevalence among males (adjusted odds ratio (aOR)<sub>tertile 1 vs. tertile 3</sub>: 2.14, 95% confidence intervals (CI): 1.07-4.56), but not among females (aOR<sub>tertile 1 vs. tertile 3</sub>: 1.08, 95% CI: 0.71-1.66). Further stratification by obesity status showed that lower 25(OH)D levels were associated with increased current eczema prevalence among overweight/obese males (per 10-unit decrease in 25(OH)D levels: aOR: 1.70, 95% CI: 1.17-2.46). Such an association was weaker and not statistically significant among overweight/obese females (per 10-unit decrease in 25(OH)D levels: aOR: 1.26, 95% CI: 0.93-1.70).

**Conclusions:** Sex and obesity status modified the association between vitamin D and eczema, with an inverse association observed among overweight/obese males, but not among overweight/obese females. These results suggest that preventive and clinical management strategies should vary by sex and obesity status.

**Water fluoridation and birth outcomes in California** Dana Goin\* Dana Goin Amy Padula Tracey Woodruff Allison Sherris Kiley Charbonneau Rachel Morello-Frosch

**Background:** Evidence suggests fluoride consumption may affect neurodevelopment among children, but there is a lack of research on the reproductive effects of fluoride.

**Methods:** We linked California birth records from 2000-2018 to annual average fluoride levels by community water system. Fluoride levels were collected from consumer confidence reports using Freedom of Information Act requests. Births were geocoded to the address at delivery and the fluoride level in the year of pregnancy was determined, using a weighted average if the pregnancy spanned multiple years. We estimated the effects of a hypothetical intervention reducing water fluoride levels to 0.7 ppm and 0.5 ppm on birthweight and gestational age using G-computation with a linear regression model and a natural cubic spline to allow for non-linearity. Individual covariates included maternal age, race/ethnicity, insurance type, educational attainment, and the month and year of conception. Area-level covariates included water system size, county-level unemployment, income inequality, temperature and urbanicity. Inference was calculated using a clustered bootstrap with Wald-type confidence intervals.

**Results:** There was no estimated effect of the hypothetical intervention to reduce fluoride levels to 0.7 ppm on birthweight (-2.1 g, 95% CI -4.4, 0.1). We did observe a negative association of the hypothetical intervention to reduce fluoride level to 0.5 ppm (-5.3 g, 95% CI -9.5, -1.1). We also observed small associations for the 0.7 or 0.5 ppm intervention on gestational age (-0.009 weeks, 95% CI -0.017, -0.001 and -0.012 weeks, 95% CI -0.03, 0.006, respectively).

**Conclusions:** Contrary to our hypotheses, we found small negative associations of hypothetical interventions of reducing fluoride levels to 0.5 ppm on birthweight, and small associations for reductions to 0.7 ppm and 0.5 ppm on gestational age.

**Prevalence and temporal trends of epilepsy in Canadian children between 2002 and 2020: A retrospective birth cohort study.** Bénédicte Driollet\* Bénédicte Driollet Emmalin Buajitti Asma Ahmed Jennifer Hutcheon Laura C. Rosella Seungmi Yang

**Objective.** Epilepsy is one of the most common chronic neurologic disorders in children. Few studies have examined the burden of this disease notably in high-income countries but there is a lack of data concerning temporal trends according to child and maternal characteristics. The objective of this study is to examine the occurrence and temporal trends of epilepsy according to specific characteristics.

**Methods.** We identified all in-hospital births between 2002 and 2019 in the province of Ontario, Canada, and linked their health records to various administrative data (N=2 342 739). We estimated the prevalence of epilepsy in children under 18 years old, overall and by specific characteristics. We also estimated temporal trends in epilepsy rates in young children (ages 0-10) by their year of birth, between 2002 and 2010 to allow for an equal follow-up time of 10 years for all children.

**Results.** Overall prevalence of epilepsy in our cohort was 31.6 per 1000 live births (95% Confidence interval 31.3-31.8). Epilepsy rates in ages 0 to 10 years rates seemed to be stable over time with the lowest rate in the 2003 birth cohort at 30.2 (95%CI 29.2-31.09) per 1000 live births followed by a slight increase over time (e.g., 33.6 (95%CI 32.6-34.5) in the 2020 cohort). As expected, preterm births have higher rates over time (37.7 (95%CI 33.44-42.01) in the 2002 cohort vs. 46.8 (95%CI 42.4-51.1) in the 2010 cohort). Rates were higher among girls and children with lower socioeconomic characteristics, while it was lower among children born to immigrant mothers over time (e.g. 31.2 (95%CI 29.4-33.0) vs. 34.5 (95%CI 33.3-35.7) of Canadian-born mothers in the 2010 cohort).

**Conclusion.** In a large representative sample of births in Canada, we observed a modest increase in epilepsy rates in more recent births. Disparities by gender, socioeconomic position, and maternal immigration status persisted over time. Further research is needed to better understand these disparities.

**Supplement Use Among Couples Seeking Fertility Treatment and Associations with Live Birth** Naria Sealy\* Naria Sealy Sunni L. Mumford Ellen C. Caniglia Julia DiTosto Chanele D. Lomax Erica Boiman Jim Hotaling Bradley Van Voorhis Enrique F. Schisterman Stefanie N. Hinkle Ginny Ryan Pauline Mendola

**Background:** Dietary supplements are increasingly being marketed towards couples attempting to become pregnant. Studies indicate that micronutrients found in these supplements may be important for pregnancy and fertility, there are limited data on use of dietary supplements within couples seeking infertility treatment and on its association with live birth.

**Methods:** This was a secondary analysis of data from couples seeking fertility treatment within the Folic Acid and Zinc Supplementation Trial (FAZST) and Impact of Diet, Exercise, and Lifestyle on Fertility Study (IDEAL). Information on supplement use was collected at baseline. Descriptive statistics of supplement use were collected. Poisson models with robust variance were used to estimate risk ratios (RR) and 95% CI for associations between supplement use and live birth, adjusting for confounders.

**Results:** Among 2370 couples 67% of females used any supplement (66% used a multivitamin) and 45% of males used any supplement (38% used a multivitamin) at baseline. The most used individual supplements among females were folic acid (8%) and fish oil (6%). Fish oil was the most used individual supplement among males (11%), followed by vitamin C (11%). Overall, 35% of couples achieved a live birth. Female use of any supplement use was associated with an increased chance of live birth (adjusted RR: 1.22, 95% CI: 1.04, 1.43). Male use of supplements was not associated with live birth (adjusted RR: 0.98, 95%: 0.87, 1.09). Supplement use within couples was associated with live birth when only the female partner used a supplement (adjusted RR: 1.25, 95% CI: 1.04, 1.50).

**Conclusion:** Among couples seeking infertility treatment, supplement use was common among both male and female partners, with the majority taking a multivitamin. There is evidence that supplement use in female, but not male, partners is associated with increased likelihood of live birth.

**Systematic differences in birth weight percentiles between twins and singletons across socially and economically marginalized subgroups** Anna Booman\* Anna Booman Dang Dinh Jean O'Malley Teresa Schmidt Jonathan M. Snowden Sarah-Truclinh Tran Kimberly K. Vesco Janne Boone-Heinonen

**Background:** Fetal growth is different according to plurality and social conditions, yet little is known about twin birth weight (BW) distributions in socially/economically marginalized populations. Further, no United States (US)-based twin BW reference is available. To highlight the need for a representative twin BW reference, we compared twin and singleton BW percentiles among socially/economically marginalized subgroups.

**Methods:** We used Oregon BW data linked to the PROMISE study cohort, an electronic health record-based study derived from a network of community health centers. Infants with a recorded BW born between 22 and 44 gestational weeks were included, resulting in 352 twin and 24,102 singleton infants. Reference data from 2009-2010 US live birth files of singleton births were used to calculate weight-for-gestational-age percentiles. Percentile data for infants born from singleton and twin gestations are presented and compared; BW percentile was calculated for each twin rather than averaging them.

**Results:** Overall, mean BW percentile was 50.6 in singletons and 29.2 in twins. Infants of Black mothers had the lowest BW percentile among singletons (43.9) but the highest among twins (33.5). Thus, the smallest difference between singletons and twins of any racial/ethnic group was among infants of Black mothers (10.4); the difference was over two-fold higher among the other racial/ethnic subgroups. Infants with private insurance had the smallest BW percentile difference between singletons and twins (13.8) while larger differences were seen for those with government insurance (22.9, 24.1) or self-pay (24.3).

**Discussion:** Findings indicate that there are systematic differences in BW percentiles between singleton and twin infants across all social factors examined. The vastly different sample sizes of singletons and twins may have produced unstable estimates among twins. Still, these findings support the need for a representative US-based twin-specific BW reference.

**Beyond MAVRIC: The effect of transabdominal versus transvaginal cerclage for prevention of early preterm birth in a lower-risk obstetric population** Chelsea Messinger\* Chelsea Messinger Sonia Hernández-Díaz Albert Hofman Jessica Young Thomas McElrath

The 2020 MAVRIC trial found a strong protective effect of transabdominal cerclage (TAC) relative to transvaginal cerclage (TVC) for the prevention of spontaneous delivery (birth or late miscarriage) prior to 32 weeks. Trial participants had a prior failed TVC and an average 2.8 prior spontaneous deliveries <28 weeks. Since MAVRIC, some question whether TAC should be offered to patients with fewer risk factors for recurrent spontaneous preterm delivery. We emulated a target trial to estimate the effect of TAC relative to TVC on preterm delivery <34 weeks within a lower risk population of patients.

We identified a retrospective cohort of adult singleton pregnancies in the United States who received history-indicated cerclage and had 1 prior spontaneous deliveries <34 weeks with or without history of a failed TVC. All eligible patients who received TAC and a random sample of eligible patients who received TVC were included. To estimate risk differences (RD), risk ratios (RR) and 95% confidence intervals (CI), we used inverse probability weighted estimation of cumulative incidence to adjust for confounding and censoring.

195 patients were eligible for inclusion: 91 received TAC and 104 received TVC. Overall, 42% of patients had a history of a failed TVC and an average 1.5 0.7 prior spontaneous deliveries <34 weeks. Preterm delivery <34 weeks occurred in 13.2% of pregnancies. The weighted risk of preterm delivery prior to 34 weeks was 6.0% for TAC (95% CI 2.5%, 10.1%) and 19.1% for TVC (95% CI 7.5%, 30.7%), RD=-13.5% (95% CI -24.8%, -0.1%), RR=0.31 (95% CI 0.12, 0.99). This estimate was robust to several sensitivity analyses.

In a lower risk obstetric patient population than that of the MAVRIC trial, TAC was strongly protective for preterm delivery prior to 34 weeks compared to TVC. These results must be considered against the risks of TAC, which include mandatory Cesarean delivery at ~37 weeks, for determining whether TAC should be offered to lower-risk women.



**In Utero Opioid Analgesics Exposure and Birth Outcomes: Do Duration and Timing Matter?**

Yi Wang\* Yi Wang Lawrence Berger Christine Durrance Russell S. Kirby Daphne Kuo Jessica Pac  
Deborah B. Ehrental

**Background:** In utero opioid exposure is associated with higher risk of adverse birth outcomes. Few studies investigate these associations by duration and timing of exposure.

**Aim:** To estimate the associations between prenatal opioid exposure and neonatal intensive care unit (NICU) admission, neonatal opioid withdrawal syndrome (NOWS), and being small for gestational age (SGA) by duration and timing of exposure.

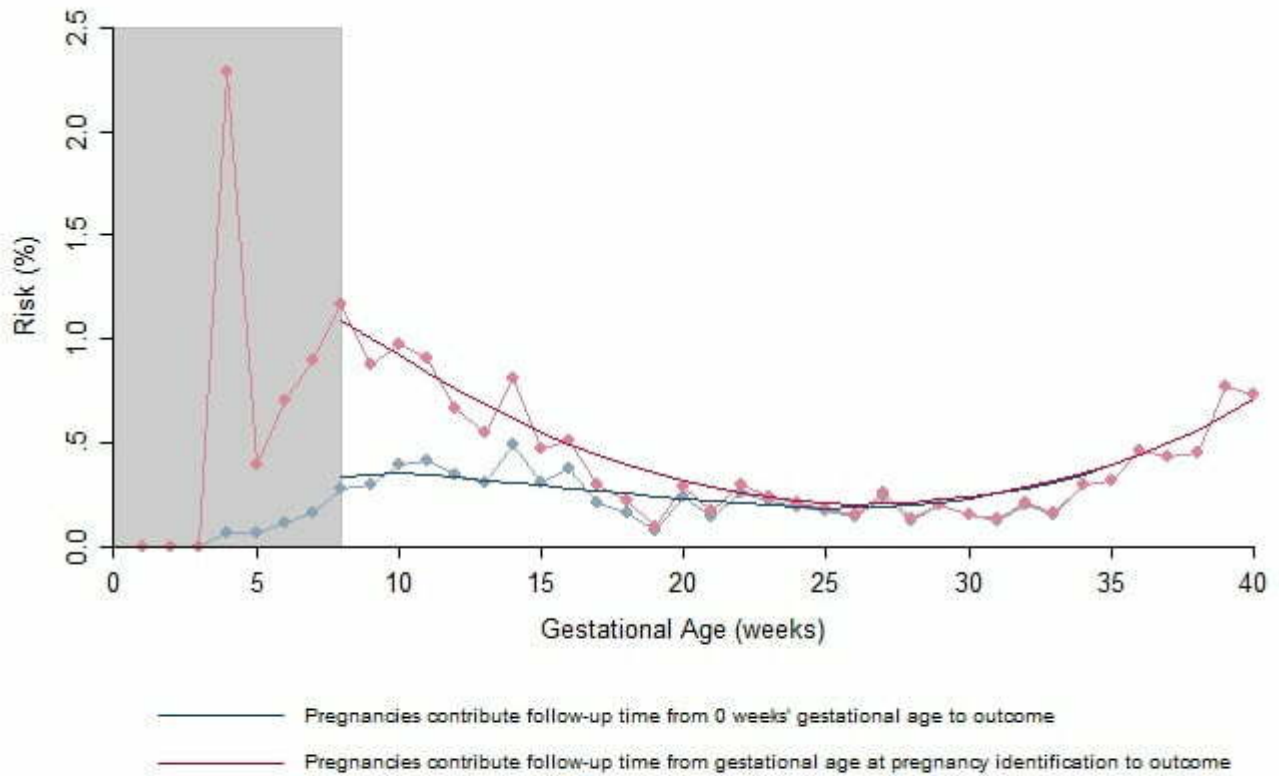
**Method:** Exposure was identified using claims for prescription opioid analgesic fills during the prenatal period for Wisconsin Medicaid-covered live births 2011-2019. Duration of exposure was measured as 0-6, 7-29, 30-89, and 90+ days; timing was measured as early (first 2 trimesters) and late (3rd trimester, regardless of earlier use). We used logistic regressions to assess the odds of adverse birth outcomes for infants with exposure. Propensity score matching was used to reduce selection bias.

**Results:** Infants with any prenatal opioid exposure had higher odds of NICU ( $OR=1.09$ , 95% CI: 1.04, 1.14), NOWS ( $OR=2.31$ , CI: 2.05, 2.60), and SGA ( $OR=1.07$ , CI: 1.03, 1.12). Exposure for <7 days had no increased risk of any outcome. Increasing duration of exposure was associated with greater odds of (a) NOWS: 7-29 days ( $OR=1.58$ , CI: 1.24, 2.02); 30-89 days ( $OR=3.28$ , CI: 2.49, 4.31) and 90+ days ( $OR=6.24$ , CI=4.68, 8.32); (b) SGA: 30-89 days ( $OR=1.27$ , CI: 1.11, 1.45) and 90+ days ( $OR=1.23$ , CI=1.05, 1.44); (c) NICU: 90+ days ( $OR=1.87$ , CI: 1.60, 2.20). Infants with late exposure had higher odds of NOWS ( $OR=1.70$ , CI: 1.40, 2.07). The interaction terms between duration and timing show late exposure increased the risk of NOWS for 7+ days exposure and added additional risk of NICU for 90+ days exposure.

**Conclusion:** More than a week of prenatal opioid exposure was associated with greater risk of adverse birth outcomes, and this risk increased with more exposure. Late exposure was associated with higher risk of NOWS and more likely to harm infants with more exposure.

**Investigating the Patterns and Determinants of Pregnancy Loss: The Unique Opportunity of a Preconception Cohort in Pakistan** Michelle Dimitris\* Michelle Dimitris Sajid Soofi Arjumand Rizvi Yaqub Wasan Imran Ahmed Zulfiqar Bhutta

**Introduction:** Pregnancy loss is the outcome of approximately 30% of conceptions. Early pregnancy losses are often systematically missing from datasets, which may bias studies of prenatal exposures and postnatal outcomes. We examined the patterns and determinants of pregnancy loss in a population-based cohort in rural Pakistan. **Methods:** The Matiari Empowerment and Preconception Supplementation Study (MaPPS), of which our study is an extension, was a cluster randomized-controlled trial that investigated the effect of preconception multiple micronutrient supplementation on nutrition and birth outcomes. The MaPPS trial quarterly monitored women aged 15-24, regardless of pregnancy intent, for ongoing pregnancy. We examined risk of pregnancy loss by gestational age, and stratified risk curves by pre-pregnancy characteristics. **Results:** Among 17048 consenting households in which 25447 eligible women lived, we analyzed 4401 pregnancies of which 377 ended in pregnancy loss (243 miscarriages/abortions and 134 stillbirths). Mean (standard deviation) gestational age at pregnancy detection was 8.9 (3.7) weeks among those that ended in miscarriage/abortion, 14.7 (7.0) weeks among stillbirths, and 14.5 (6.9) weeks among livebirths. Accordingly, we calculated risk of loss by allowing pregnancies to contribute follow-up time from: a) 0 weeks gestational age and b) the gestational age at pregnancy detection. Risk of pregnancy loss tended to decline from 8 to 20 weeks gestational age (Figure), though absolute risks differed by method of calculation; risks ranged from 0.3-1.2% at 8 weeks and 0.2-0.3% at 20 weeks. Preliminary results indicated that this pattern differed by pre-pregnancy self-reported health status. **Conclusion:** In this population-based cohort, the risk of pregnancy loss was highest at the lowest gestational ages, and steadily decreased to mid-pregnancy. Our completed study may provide insight on the correlates of pregnancy loss, and whether it is amenable to intervention.



**Figure.** Scatter plot and lowess curve of the risk of pregnancy loss by gestational age. Absolute risk of pregnancy loss by gestational age is displayed when pregnancies contribute follow-up time from 0 weeks gestational age (blue) and from gestational age at pregnancy detection (red).

**Evaluation of the Mediating Role of Neighborhood Deprivation on the Relationship Between Racial Residential Segregation and Hypertensive Disorders of Pregnancy**

DaShaunda Taylor\* DaShaunda Taylor Derek Chapman Karen D. Hendricks-Muñoz Robert A. Perera Emily Zimmerman

**Background.** Hypertensive disorders of pregnancy (HDP) occur in 5-8% of pregnancies in the United States, and recent trends indicate a rise in this condition. HDP can have lifelong as well as transgenerational consequences, such as poor later-life cardiovascular health for mothers. Research on upstream social determinants of health, including racial residential segregation (RRS) and neighborhood deprivation, suggests that these factors have a substantial influence on perinatal health outcomes. **Objective.** Therefore, this study evaluated the mediating role of neighborhood deprivation on the relationship between RRS and HDP. **Methods.** Birth certificate data from singleton births in Richmond, Virginia from 2011-2019, neighborhood-level indicators from the U.S. Census Bureau's 2006-2010 American Community Survey, and the 1990 decennial census were utilized to examine these associations. Principal component analysis was conducted to determine variables for inclusion in the neighborhood deprivation index. Mediation was assessed using multilevel structural equation modeling, specifically path analysis. **Results.** In analyses stratified by race/ethnicity, the Index of Dissimilarity and the Interaction Index - measures of RRS - were associated with HDP among non-Hispanic White women (OR: 0.63, 95% CI: 0.46-0.88 and OR: 1.73, 95% CI: 1.37-2.17, respectively), and the Index of Dissimilarity was significantly related to HDP for non-Hispanic Black women (OR: 1.60, 95% CI: 1.17-2.19). Among non-Hispanic Black women, higher RRS was associated with increased likelihood of HDP; approximately 70% of this relationship was mediated by neighborhood deprivation. Non-Hispanic White women experienced reduced odds of HDP when RRS was higher. **Conclusions.** Findings indicate that RRS is detrimental to non-Hispanic Black women but beneficial for non-Hispanic White women regarding HDP likelihood. Future studies should continue to explore the impact of RRS on HDP among differing racial/ethnic groups.

**A Scandinavian collaboration enabling the evaluation of cancer risk in patients with inflammatory bowel disease** Jessica C. Young\* Jessica Young Lise Mørkved Helsingen Erle Refsum Vera Perrin Rasmus Hvidbjerg Gantzel Rune Erichsen Amanda Hogden Weimin Ye Anita Berglund Hans-Olov Adami Tine Jess Johannes Blom Miguel Hernán Mette Kalager

### **Background**

Treatments for inflammatory bowel disease (IBD) reduce inflammation and may thus affect cancer risk. However, there exist substantial barriers to evaluating IBD therapies and the risk of cancer. Randomized trials require long follow-up and large samples, and adequately sized observational data typically lack detailed clinical information.

### **Objective**

To fill a persistent gap in knowledge on cancer risk in persons with IBD, we established an IBD cohort combining registry and clinical data in Norway, Sweden, and Denmark.

### **Methods**

Individuals with IBD were identified from nationwide registries. Using a case-cohort design, we efficiently sampled IBD cases with cancer (small intestinal, colorectal, hepatobiliary, or non-Hodgkin's lymphoma) and randomly selected controls, regardless of case status. Detailed medical chart abstraction included date of symptom onset, symptoms prior to diagnosis, disease extent and severity at diagnosis, longitudinal evaluation of endoscopy and pathology reports, and the timing of and reasons for initiation and discontinuation for medical therapies.

### **Results**

Chart abstraction was completed for 3,068 individuals with a median age at diagnosis of 41 years (IQR:26, 60). Date of symptom onset was recorded for 89% and extent at diagnosis for 88%. Among the 97% of people with at least one endoscopy, the median number of endoscopies was 6 (IQR:3, 10). Systemic aminosalicylates were the most documented medication (76% of individuals). The most used biologics were infliximab and adalimumab with 11% and 6% having recorded use, respectively.

### **Impact**

This cohort leverages national register data combined with medical chart review from three countries. We will use the target trial framework with these case-cohort data to evaluate the effectiveness of IBD therapies on cancer risk, demonstrating how causal inference methods and efficient data collection can be used to answer clinical questions when evidence from trials is unattainable.

**Unravelling potential sex-specific effects of cardiovascular medications for longevity using Mendelian randomization** C Mary Schooling\* Man Ki Kwok C Mary Schooling

**Background:** Establishing the efficacy of widely used cardiovascular medications in reducing mortality in women and men is pivotal to evidence-based clinical practice, but few trials have assessed differences by sex. This study evaluated sex-specific effects of commonly prescribed and potential cardiovascular medications on longevity using two-sample Mendelian randomization (MR).

**Methods:** Genetic variants in the relevant protein-encoding gene targets were used to mimic drug effects, and applied to genetic associations with lifespan (from parental attained age) in the UK Biobank by sex and overall. Estimates were obtained using inverse variance weighting with sensitivity analysis.

**Results:** For lipid-lowering drugs, genetically mimicked proprotein convertase subtilisin/kexin type 9 (PCSK9) inhibitors were associated with longer lifespan in men (2.39 years per standard deviation LDL-cholesterol reduction, 95% confidence interval [CI] 0.42 to 4.36). Genetically mimicked potential lipid-lowering treatments targeting *APOC3* or *LPL* (and possibly *LDLR*) were also associated with longer lifespan. For antihypertensives, genetically mimicked beta blockers and calcium channel blockers were associated with longer lifespan particularly in men (beta blockers 7.89 years, 95% CI 3.77 to 12.02; calcium channel blockers 4.36 years, 95% CI: 0.70 to 8.02). For anti-diabetic drugs, genetically mimicked metformin was associated with longer lifespan in both sexes (2.27 years, 95% CI 1.00 to 3.54). No such associations were found for genetically mimicked statins, ezetimibe or ACE inhibitors. Sensitivity analysis gave a similar interpretation.

**Conclusions:** PCSK9 inhibitors, beta blockers and calcium channel blockers may prolong lifespan more in men than women. Targeting *APOC3* or *LPL* (and possibly *LDLR*), and metformin may be relevant to both sexes. Whether the lack of association found for statins, ezetimibe and ACE inhibitors is due to medication use or lack of efficacy requires investigation.

**Vaccine patterns among patients diagnosed with Guillain-Barré Syndrome: a matched cohort study in older adults with Medicare Supplemental insurance, 2000-2020** Samantha Eiffert\* Samantha Eiffert Til Stürmer Betsy L Sleath Carolyn T Thorpe Rebecca Traub Sudha R Raman Alan C Kinlaw

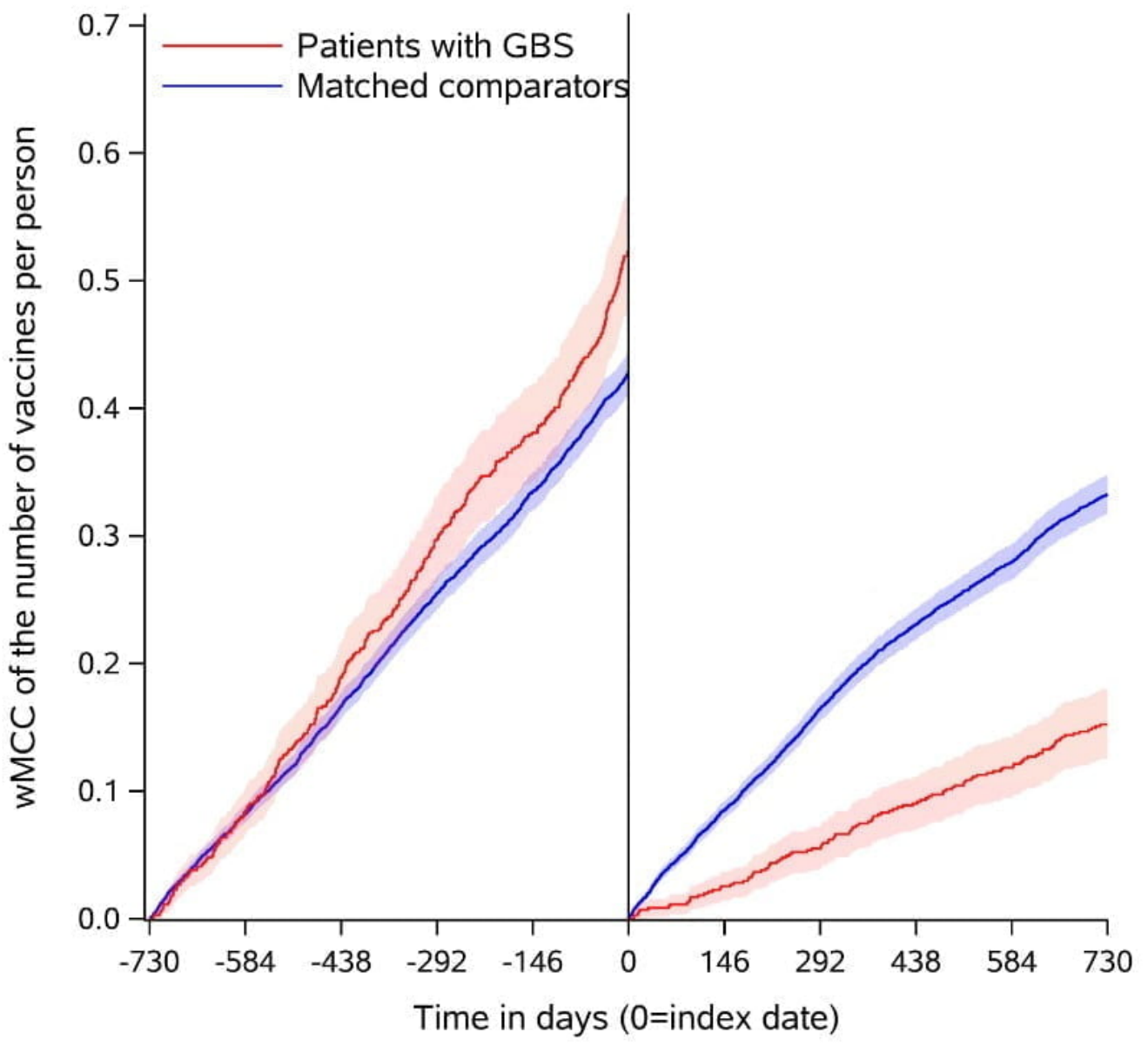
Some vaccines have a small risk of triggering Guillain-Barre Syndrome (GBS), an autoimmune disorder where nerve damage leads to paralysis. Adults and their doctors may consider a prior GBS diagnosis when making decisions about vaccines. There is no guidance beyond a CDC warning for patients whose GBS was vaccine-triggered. Our objective was to describe vaccine patterns before and after a GBS diagnosis.

We conducted a matched cohort study using the Merative MarketScan® Medicare Supplemental and Coordination of Benefits Database, 2000-2020. We included patients  $\geq$  age 65 at GBS diagnosis (index date) with two years of prior continuous enrollment. We matched each GBS patient to 10 comparators on sex and age. Vaccines included the 10 CDC recommended vaccines for ages  $\geq$ 65 and measles-mumps-rubella and human papillomavirus vaccines. We used standardized mortality ratio weights to balance healthcare use, frailty and comorbidity measures. We estimated weighted mean cumulative counts (wMCC), which account for competing events and differential follow-up, of vaccines received during two years before and up to two years after GBS diagnosis.

Patients with GBS (n=709) had a higher wMCC (0.52 vaccines/person) prior to diagnosis than matched comparators (0.43); wMCC difference: 0.10 (95% CI 0.05, 0.15). At the end of follow-up, patients with GBS had a lower wMCC (0.15) than comparators (0.33); wMCC difference: -0.18 (95% CI -0.21, -0.15). The 2-year vaccine wMCC difference in differences was -0.28.

Patients diagnosed with GBS received 0.28 fewer vaccines over the 2 years after diagnosis than matched comparators. The wMCC prior to diagnosis is higher among GBS patients even before the 42-day risk window for vaccine-triggered GBS. This is likely due to unmeasured confounding. These results cannot elucidate the vaccine related decision-making process. Future work should assess real-world doctor recommendations and patient motivations for vaccine use among adults with a history of GBS.

### Weighted mean cumulative count of the number of vaccines received per person before and after the index date

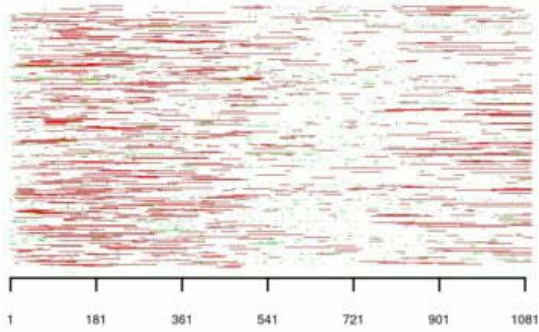




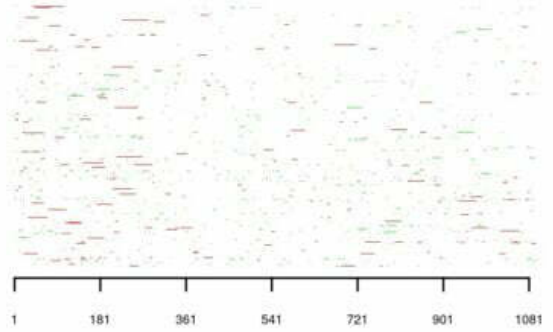
**Jail-based medication for opioid use disorder and patterns of community re-entry after release: A sequence analysis** Sungwoo Lim\* Sungwoo Lim Teena Cherian Monica Katyal Keith S. Goldfeld Ryan McDonald Ellen Wiewel Maria Khan Noa Krawczyk Sarah Braunstein Sean M. Murphy Ali Jalali Philip J. Jeng Zachary Rosner Ross MacDonald Joshua D. Lee

Treatment with methadone and buprenorphine medications for opioid use disorder (MOUD) during incarceration may help transition to the community from jail, but evidence on this relationship has been mixed. It may be because existing measures such as recidivism rate are poor proxies for unsuccessful community re-entry. This study aimed to 1) identify re-entry patterns using sequence analysis of 3-year post-release recidivism, emergency department visits, and hospitalizations data, and 2) test the association between in-jail MOUD and a pattern defined by rare occurrence of reincarceration and preventable healthcare utilization (= stability pattern). Data came from a retrospective, observational cohort study of 6066 adults with opioid use disorder who were incarcerated in New York City jails and released to the community during 2011-14. The outcome was community re-entry patterns via sequence analysis. The exposure was receipt of in-jail MOUD versus out of treatment (42% vs. 58%) for the last 3 days before discharge. We performed propensity score matching to address confounding, considering baseline demographic, clinical, behavioral, housing, and criminal legal characteristics, and marginal multinomial logistic regression. Five re-entry patterns were identified: stability (64%), hospitalization (23%), delayed reincarceration (7%), immediate reincarceration (4%), and continuous incarceration (2%). After addressing confounding, 64% and 54% followed the stability pattern among MOUD and out-of-treatment groups who were released from jail in 2011, respectively. In 2012-14, the prevalence of following the stability pattern increased year-by-year while a consistently higher prevalence was observed among those with in-jail MOUD. Sequence analysis helped define post-release stability based on health and criminal legal system involvement. We also found that receipt of in-jail MOUD was associated with successful community re-entry.

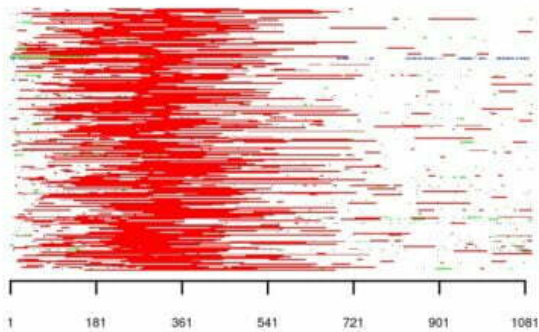
Hospitalization (N=1424)



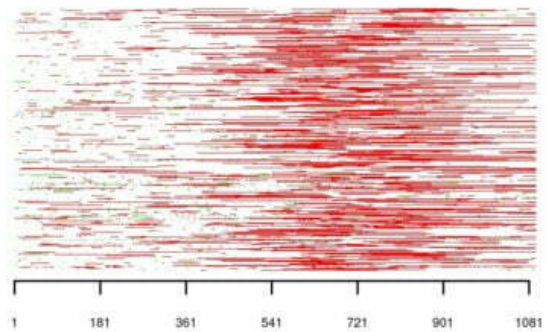
Stability (N=3862)



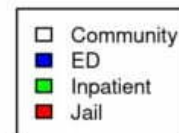
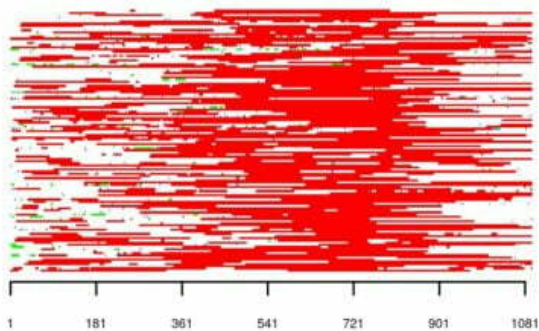
Immediate return to jail (N=223)



Late return to jail (N=435)



Continuous incarceration (N=122)



**LATEBREAKER**

Policing/Incarceration

**Longitudinal associations between maternal gestational weight and physical growth at birth, mid-childhood and early adolescence: a birth cohort**

Yingze Zhu\* Yingze Zhu Liang Wang Qi Qi Yue Cheng Zhonghai Zhu Lingxia Zeng

**Background**

Maternal adiposity during pregnancy has been identified as predictors of offspring physical growth, nevertheless it remains unclear whether this relationship has changed over time.

**Methods**

We used a birth cohort data from a randomized controlled trial of antenatal micronutrient supplementation in rural western China (ISRCTN08850194). Maternal weight and height were collected during the first, second and third trimester, and weekly weight gains during second and third trimester were calculated and classified following the IOM-2009 guidelines. Offspring length/height and weight were standardly assessed at birth, mid-childhood (age 7-10 years) and early adolescence (age 10-14 years), which were then converted into z scores (BAZ and HAZ) using the INTERGROWTH-21st and WHO growth standards, respectively. We conducted generalized linear models to examine the associations of maternal weight status during pregnancy with BAZ and HAZ at birth, mid-childhood and early adolescence, respectively, with adjustments for common covariables.

**Findings**

A total of 586 mother-offspring pairs were analyzed and most are boys (60%). Per kg/m<sup>2</sup> increase of maternal BMI during first trimester was associated with offspring higher BAZ. The adjusted mean differences (aMD) were 0.06 (95% Confidence Interval [CI] -0.004, 0.12) at birth, 0.07 (95% CI 0.03, 0.11) at mid-childhood, and 0.11 (95% CI 0.06, 0.17) at early adolescence. In addition, maternal excessive weight gain during second and third trimester was associated with higher HAZ at birth, mid-childhood and early adolescence. The corresponding aMD was 0.15 (95% CI -0.24, 0.54), 0.27 (95% CI 0.002, 0.55) and 0.48 (95% CI 0.21, 0.75), respectively.

**Interpretation**

Maternal adiposity during pregnancy had long-lasting impacts on offspring BAZ and linear growth, and the association strength tended to become stronger as they grow older.

**Suicide mortality in people formerly incarcerated in North Carolina prisons compared to the North Carolina general population, 2000 - 2020** Kate Vinita Fitch\* Kate Vinita Fitch Brian W. Pence Monica E. Swilley-Martinez Andrew L. Kavee Vanessa E. Miller Bradley N. Gaynes Timothy S. Carey Shabbar I. Ranapurwala

**Objective.** Compare the rates and characteristics of suicide mortality in FIPs to the general population in North Carolina (NC).

**Methods.** We conducted a retrospective cohort study of 272,579 FIPs released from NC prisons 476,724 times between January 1, 2000 and March 15, 2020. We calculated standardized mortality rates and ratios (SMRs) using indirect standardization by sex, age, and calendar year of release to compare FIPs to the NC general population. We evaluated effect modification by race/ethnicity, sex, age, and firearm involvement.

**Results.** FIPs had twice the rate of overall suicide mortality compared to the general population for three years after release. SMRs varied by means of suicide completion in that FIPs had 1.4 (1.2, 1.6) times the firearm-involved suicide mortality rate of the general population but 2.9 (2.5, 3.2) times the non-firearm-involved suicide mortality rate of the general population. Effect modification analyses indicated that female, white, and young adult FIPs had greater elevation of suicide mortality compared to their general population peers than did other FIP groups.

**Conclusions.** Formerly incarcerated persons have significantly higher rates of suicide mortality even several years following release.

**Life course economic hardship and fecundability** Molly N. Hoffman\* Molly Hoffman Collette N. Ncube Sharonda M. Lovett Ruth J. Geller Chad M. Coleman Amelia K. Wesselink Lauren A. Wise

**Background:** The influence of life course economic hardship on fertility is not well studied.

**Methods:** We examined the association between life course economic hardship and fecundability (per-cycle probability of conception) among 6,014 participants enrolled in Pregnancy Study Online, a North American preconception cohort study. We estimated fecundability from follow-up questionnaires completed every 8 weeks. Beginning in 2019, we invited past and current participants to complete a supplemental questionnaire about adversity across the life course. Economic hardship was defined by self-report of “not having enough money to pay for food, rent, or mortgage,” “having to borrow money to pay for medical expenses,” or “receiving public assistance or welfare” in the following life stages: childhood (age  $\leq 11$ ), adolescence (ages 12-17), and adulthood (age  $\geq 18$ ). Current wealth was defined by self-reported length of time participants could maintain their standard of living and stay in their home had they suddenly lost all sources of household income. We used proportional probabilities regression models adjusted for age and socio-demographic factors to estimate fecundability ratios (FRs) and 95% CIs.

**Results:** Economic hardship (ever vs. never) was associated with reduced fecundability (FR=0.90; 95% CI 0.84-0.95). Fecundability was further reduced among those who experienced economic hardship in all life stages (FR=0.83; 95% CI 0.75-0.92) and adulthood only (FR=0.87; 95% CI 0.80-0.95). Compared with those who could maintain their standard of living for >1 year had they lost all sources of income, those able to maintain their standard of living for <2 months had slightly lower fecundability (FR=0.92; 95% CI 0.84-1.01).

**Conclusions:** Life course cumulative exposure to economic hardship, economic hardship in adulthood, and less current wealth were associated with delayed conception.

### Fecundability Ratio (95% CI)

#### Economic hardship ever reported\*

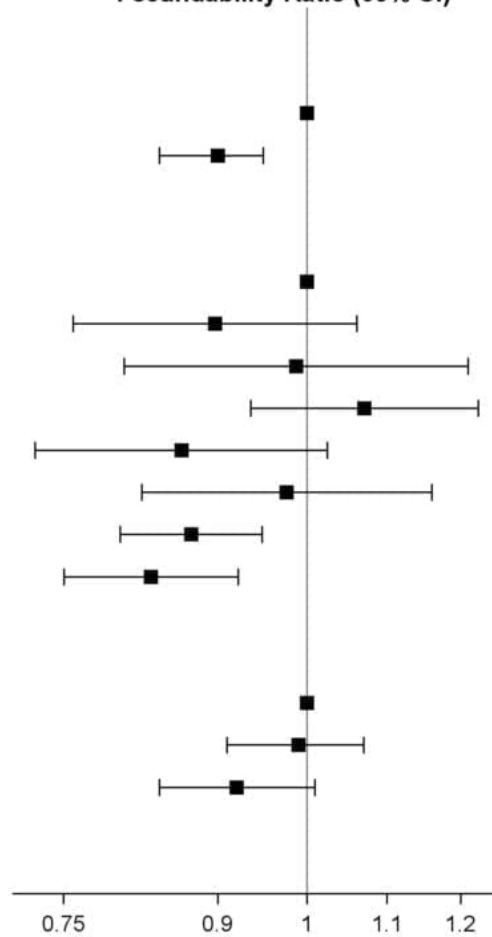
Never	1.00 (Reference)
Ever	0.90 (0.84, 0.95)

#### Life course economic hardship\*

No economic hardship	1.00 (Reference)
During childhood only	0.90 (0.76, 1.06)
During adolescence only	0.99 (0.81, 1.21)
During childhood and adolescence only	1.07 (0.94, 1.23)
During childhood and adulthood only	0.86 (0.73, 1.02)
During adolescence and adulthood only	0.98 (0.82, 1.16)
During adulthood only	0.87 (0.80, 0.95)
During all life stages	0.83 (0.75, 0.92)

#### Current wealth\*\*

More than one year	1.00 (Reference)
2 months to 1 year	0.99 (0.91, 1.07)
Less than two months	0.92 (0.84, 1.01)



\*Model adjusted for age and parental education

\*\*Model adjusted for age, income, education and trying to improve chances of pregnancy

**A prospective study of subjective preconception sleep health and hypertensive disorders of pregnancy** Chad M. Coleman\* Chad M. Coleman Amelia K. Wesselink Traci N. Bethea Tanran R. Wang Andrea S. Kuriyama Elizabeth E. Hatch Lauren A. Wise

**Background:** Hypertensive disorders of pregnancy (HDP)—defined as gestational hypertension, preeclampsia, and eclampsia—are leading causes of pregnancy-related morbidity and mortality in the United States. While studies report associations between sleep-disordered breathing and HDP, few studies have evaluated subjective (self-assessed) sleep health and HDP.

**Methods:** We examined prospectively the association between subjective sleep health and HDP risk among 5,730 participants enrolled in Pregnancy Study Online, a North American preconception cohort study. On the baseline questionnaire, participants reported their sleep duration (hours/night) in the past month and their frequency of trouble sleeping at night in the past two weeks (all the time, most of the time, slightly more than half the time, slightly less than half the time, some of the time, and at no time). We identified HDP diagnoses via questionnaires and birth registries. We used log-binomial regression models to estimate risk ratios (RRs) and 95% CIs for the association between both sleep measures and HDP risk, adjusting for socio-demographic, behavioral, and reproductive factors.

**Results:** About 14% of participants with a pregnancy that progressed beyond 20 weeks of gestation and no pre-pregnancy hypertension had a HDP diagnosis. 21% of participants slept <7 hours/night in the past month and 18% experienced trouble sleeping  $\geq$ half the time. Compared with 7-<9 hours/night (recommended sleep), RRs for sleep durations of <6, 6-<7, and  $\geq$ 9 hours/night were 1.18 (95% CI 0.88-1.58), 1.05 (95% CI 0.87-1.26), and 0.99 (95% CI 0.75-1.31), respectively. Compared with participants who had no trouble sleeping, RRs for participants who had trouble sleeping <half the time and  $\geq$ half the time were 0.98 (95% CI 0.84-1.15) and 1.06 (95% CI 0.87-1.29), respectively.

**Conclusions:** Short preconception sleep duration may be associated with increased HDP risk. We will evaluate sleep during pregnancy in future analyses.

**Fine particulate matter during susceptible windows of spermatogenesis and impact on semen quality** Lindsey M. Russo\* Lindsey M. Russo J. Richard Pilsner Timothy P. Canty Neil J. Perkins Pauline Mendola Enrique F. Schisterman Sunni L. Mumford Carrie J. Nobles

**Background:** Studies have suggested a detrimental association between fine particulate matter (PM<sub>2.5</sub>) and semen quality in countries with high levels of air pollution. However, a data gap exists in exploring the relation between PM<sub>2.5</sub> and semen quality parameters in countries with low to moderate PM<sub>2.5</sub> levels, such as the U.S.

**Methods:** We examined the relation between PM<sub>2.5</sub> and semen quality in the Folic Acid and Zinc Supplementation Trial (FAZST) (2013-2017) in male partners (ages 18+) of couples seeking infertility treatment in the Salt Lake City, Utah region (n=2,015). We evaluated four windows of susceptibility to ambient PM<sub>2.5</sub> during spermatogenesis (Mitosis, Meiosis I-II, Spermiogenesis, Spermiation). Semen quality parameters were assessed at enrollment, and at 2-, 4-, and 6-month intervals. PM<sub>2.5</sub> was abstracted from EPA Downscaler models for the Salt Lake City region and averaged across each susceptible window. Generalized estimating equations considered four repeated semen sample measurements for each participant, and adjusted for season, ambient temperature, and participant characteristics. Season was assessed as a potential effect modifier.

**Results:** Overall, a 1 µg/m<sup>3</sup> increase in PM<sub>2.5</sub> across the 74-day spermatogenesis window [PM<sub>2.5</sub> median (IQR): 7.2 (6.0, 9.0) µg/m<sup>3</sup>] was associated with lower sperm concentration in the warm season (% change: -2.00 (-3.95, -0.01)). PM<sub>2.5</sub> was associated with lower percent motility and percent progressive motility in the warm season, particularly during spermiation [% progressive motility, aMD: -0.35 (-0.60, -0.10)] and spermiogenesis [aMD: -0.60 (-0.89, -0.32)], the periods where sperm acquire motility due to epididymal transit. No clear associations were observed between PM<sub>2.5</sub> and morphology, or with motility in the cold season.

**Conclusion:** Findings from this study help fill in the research gap showing that low to moderate concentrations of PM<sub>2.5</sub> exposure in the U.S. may impact the spermatogenesis developmental process.



**Sexual orientation-related disparities in fetal and neonatal outcomes** Payal\* Payal

Chakraborty Colleen A. Reynolds Sarah McKetta Kodiak Soled Aimee K. Huang Brent Monseur Jae Downing Juno Obedin-Maliver A. Heather Eliassen Jorge E. Chavarro S. Bryn Austin Bethany Everett Sebastien Haneuse Brittany M. Charlton

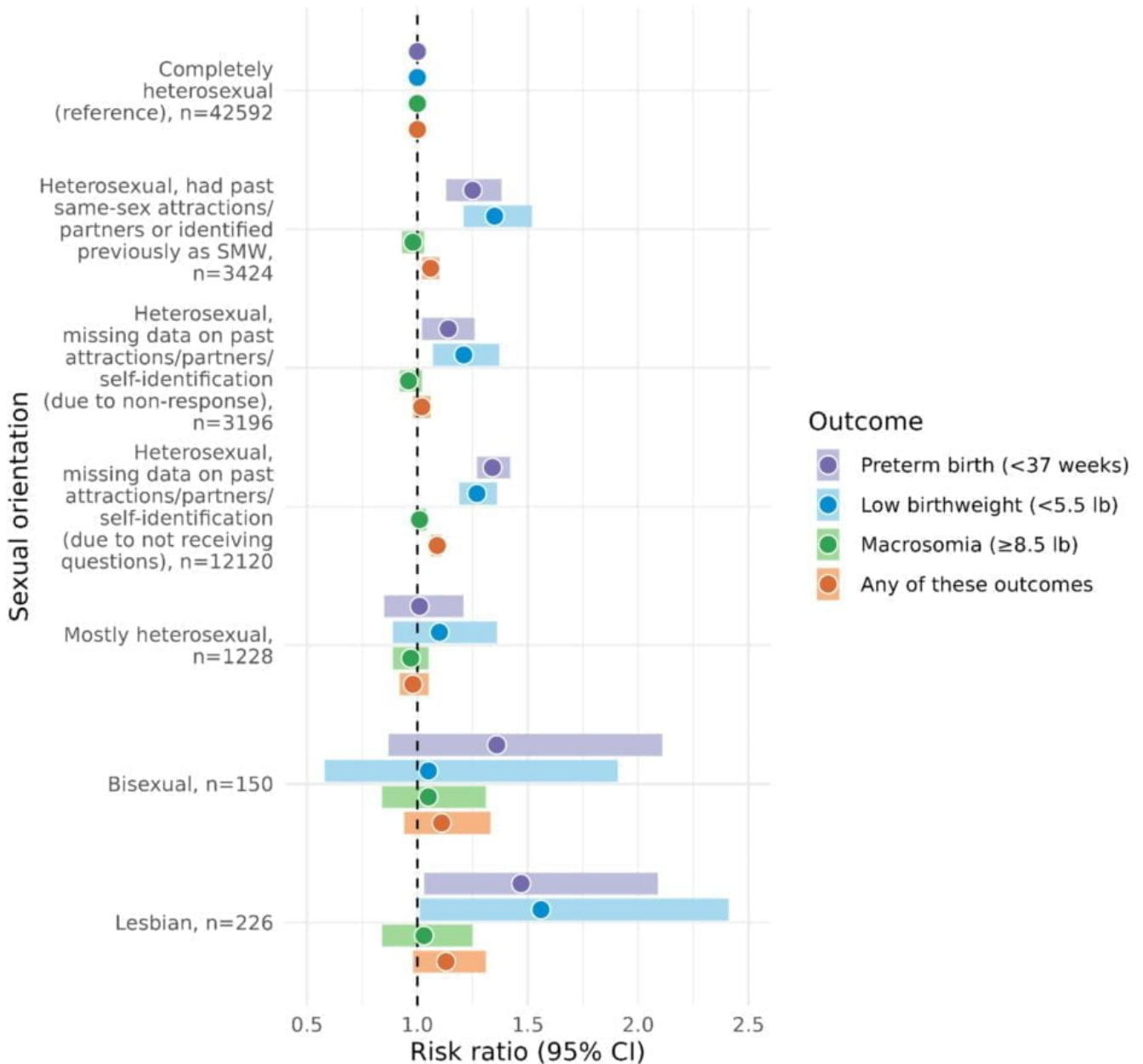
**Background:** Sexual minority women (SMW; i.e., those with same-sex attractions/partners or identify as lesbian/gay/bisexual) experience structural inequities that result in adverse perinatal health. Compared to heterosexual women, SMW have less healthcare access, lower social support during pregnancy, and higher maternal stress. Thus, SMW may be at risk for adverse obstetrical outcomes.

**Methods:** We used data from the Nurses' Health Study II—a cohort of nurses across the US—restricted to those who had live births (N=63,001). Participants were asked about sexual orientation identity (current/past) and past same-sex attractions/partners. We examined disparities in self-reported preterm birth (PTB), low birthweight (LBW), and macrosomia among seven groups: (1) completely heterosexual (reference), (2) heterosexual, had past same-sex attractions/partners or identified previously as SMW, (3) heterosexual, missing data on past attractions/partners/self-identification (due to non-response), (4) heterosexual, missing data on past attractions/partners/self-identification (due to not receiving questions), (5) mostly heterosexual, (6) bisexual, and (7) lesbian. We used log-binomial models to estimate risk ratios (RRs) for each outcome and used weighted generalized estimating equations to account for multiple pregnancies per person over time and informative cluster sizes.

**Results:** Compared to completely heterosexual women, offspring born to parents in all SMW groups (groups 2, 5-7) had higher risks of PTB and LBW, but not macrosomia. RRs were statistically significant for lesbian women (RR[95%CI] for PTB: 1.47[1.03-2.09] and LBW: 1.56[1.01-2.41]), heterosexual women with past same-sex attractions/partners or SMW identification (PTB: 1.25[1.13-1.38], LBW: 1.35[1.21-1.52]), and both heterosexual missing data groups.

**Conclusions:** These findings highlight the need to examine health risks among SMW due to heterogeneity in identity and behavior, which meaningfully influences PTB/LBW risk.

Figure. Risk ratios (and 95% confidence intervals) of adverse fetal/neonatal outcomes by sexual orientation using log-binomial models with weighted generalized estimating equations.

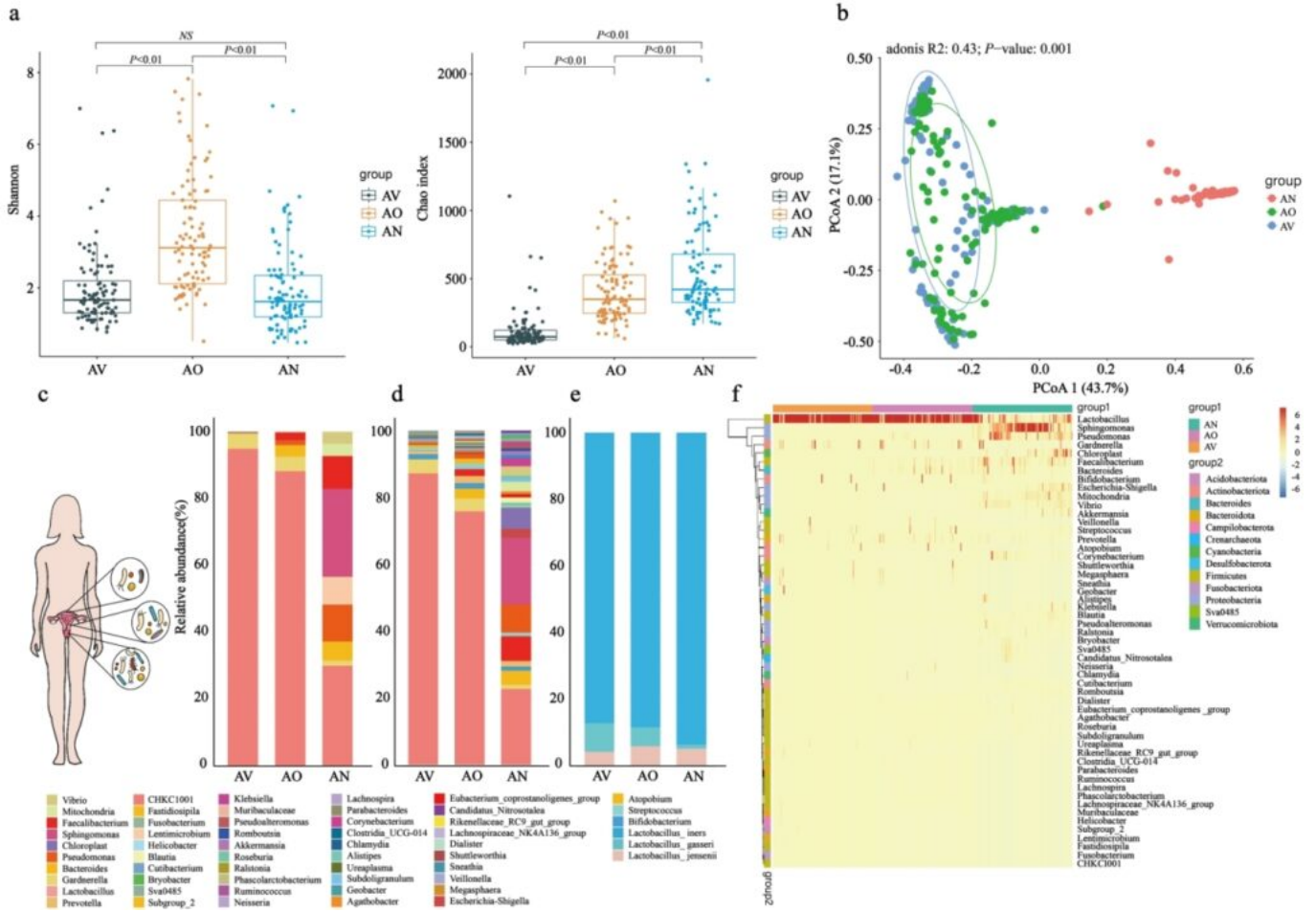


Note: The reference group of completely heterosexual participants are those who reported heterosexual identity, never having past same-sex attractions/partners, and never identifying previously as SMW.

**Vaginal, cervical, and endometrial microbiota at 4-9 weeks of gestation in healthy women**

Shi Wu Wen\* Hong Gao Na Zhu Yahui Chen Qiao Liu Lingling Tan Huanhuan Li Genlin Li Xiaolan  
Wang Daniel Corsi

Reproductive tract microbiota play important role in establishment and maintenance of human pregnancy. However, microbial composition, their interactions, and impacts of host factors in human pregnancy remain unknown. We have therefore conducted a study at two affiliated hospitals University of South China in Hengyang, China between September 2021 and March 2022. We obtained approval from the ethical review board of the University before the commence of the study. Healthy women who were 18 to 45 years of age with a live pregnancy without sexual life within 48 hours and requested for an induced abortion at 4 to 9 weeks of gestation were invited to participate. Written consent was obtained from all enrolled women. Demographic data was collected and microbiological samples before (for vaginal and cervical samples) or during (for endometrial samples) induced abortion were collected by on-duty gynecologists according to strict protocol. 16S rRNA gene amplicon sequencing was use to profile microbiota. Subsequent analysis, meta-analysis, Shannon index, and Chao index were used to describe the distribution of microbiota and to test differences in alpha diversity and beta diversity among the three sites. Spearman correlation coefficient was used to test the interactions among microbial species in the three sites. Statistical Analysis of Metagenomic Profiles was used to compare the composition of microbiota under different host factors. A total of 100 eligible women were enrolled. The primary microbiota was *Lactobacillus* in all three sites but major variations existed among all dominant microbiota. The abundance of *Lactobacillus* was negatively correlated with the most vaginal microbe and cervical microbe but positively correlated with endometrial microbiota. Maternal age, pre-pregnancy body mass index, and history of pelvic surgery impacted on the composition of the reproductive tract microbiota. Our study confirms that the microbial have unique compositions in the vagina, cervix, and endometrium and they interact each other and these interactions vary according to specific reproductive tract site. Reproductive tract microbiota also changes dynamically according to host factors.



**Target trial emulation of preconception serum vitamin D levels on live birth and pregnancy**

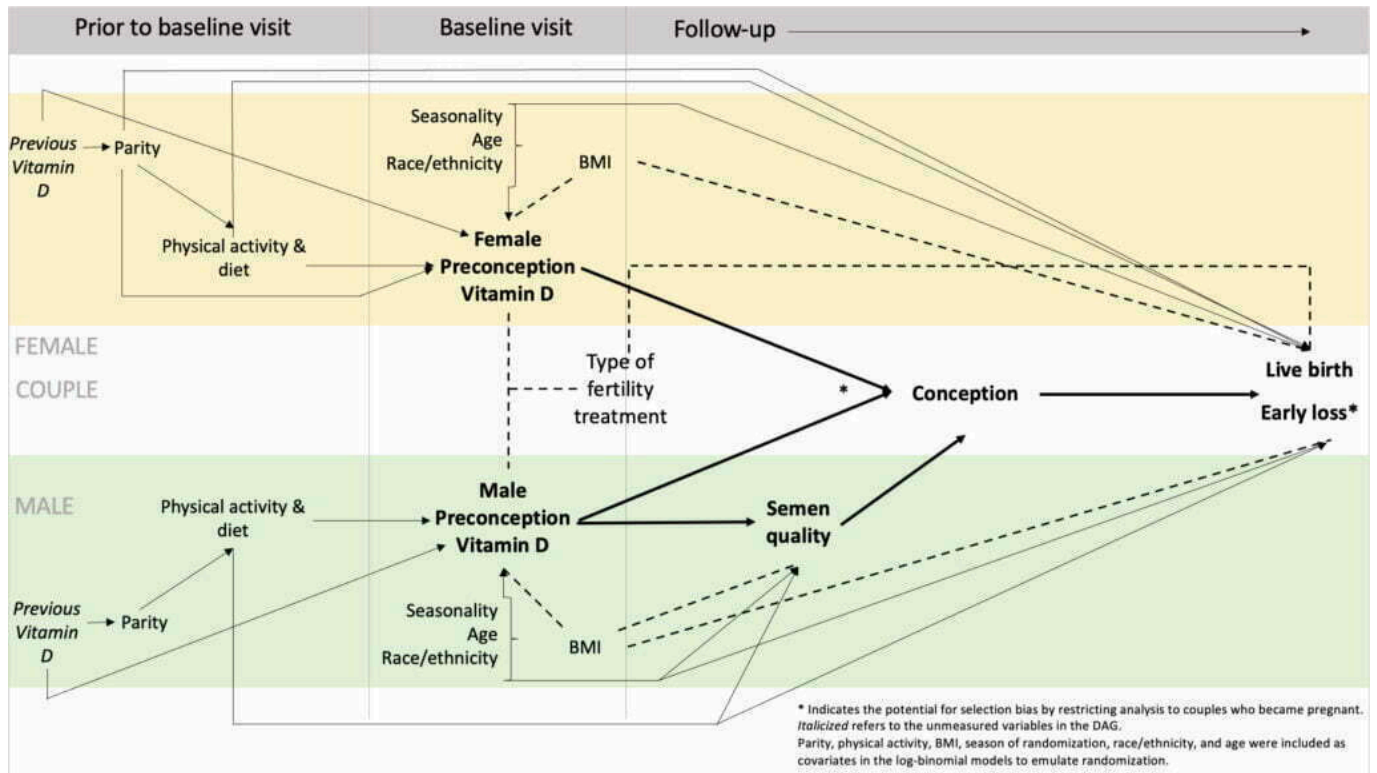
**loss: a couples-based approach** Julia D DiTosto\* Julia DiTosto Ellen C Caniglia Stefanie N Hinkle Naria Sealy Chanele D Lomax Enrique F Schisterman Erica Johnstone Pauline Mendola Jim Hotaling Ginny Ryan Sunni L Mumford

**Background:** Previous studies suggest that higher preconception vitamin D is associated with improved fertility; however, they largely focused on female partners or couples undergoing in-vitro fertilization. We evaluated associations between preconception vitamin D levels in both male and female partners on live birth and pregnancy loss in couples seeking infertility treatment that was primarily ovulation induction/intrauterine insemination.

**Methods:** Baseline serum 25(OH)D was measured in both partners (N=2370 couples). A target trial framework was used to emulate randomization based on preconception vitamin D status [deficient (<20 ng/mL, ref), insufficient (20-29.9 ng/mL), sufficient ( $\geq$ 30 ng/mL)]. Individual and couple-based models were considered. Log-binomial regression models with multiple imputation for missing data estimated likelihood of live birth adjusting for confounders (Fig). Inverse probability weights account for conception in pregnancy loss models.

**Results:** At baseline, a majority of female and male partners were vitamin D deficient or insufficient (females 19% and 40%, males 29% and 50%, respectively) while 11% of couples were both deficient. Female vitamin D levels were associated with live birth (sufficient vs. deficient RR 1.3, 95% CI: 1.1, 1.6; insufficient vs. deficient: RR 1.2, 95% CI: 1.0, 1.5). Male vitamin D levels were inconsistently associated with live birth (sufficient vs. deficient RR 1.1, 95% CI: 0.9, 1.3; insufficient vs. deficient: RR 1.2, 95% CI: 1.0, 1.4). Couples who were both sufficient or insufficient vs. both deficient had an increased likelihood of live birth (RR 1.4, 95% CI: 1.1, 1.7). No associations with pregnancy loss were observed.

**Discussion:** Using a target trial framework, higher preconception vitamin D levels among couples, particularly female partners, were positively associated with live birth and not with pregnancy loss. These results further support an association between preconception vitamin D levels and fertility.



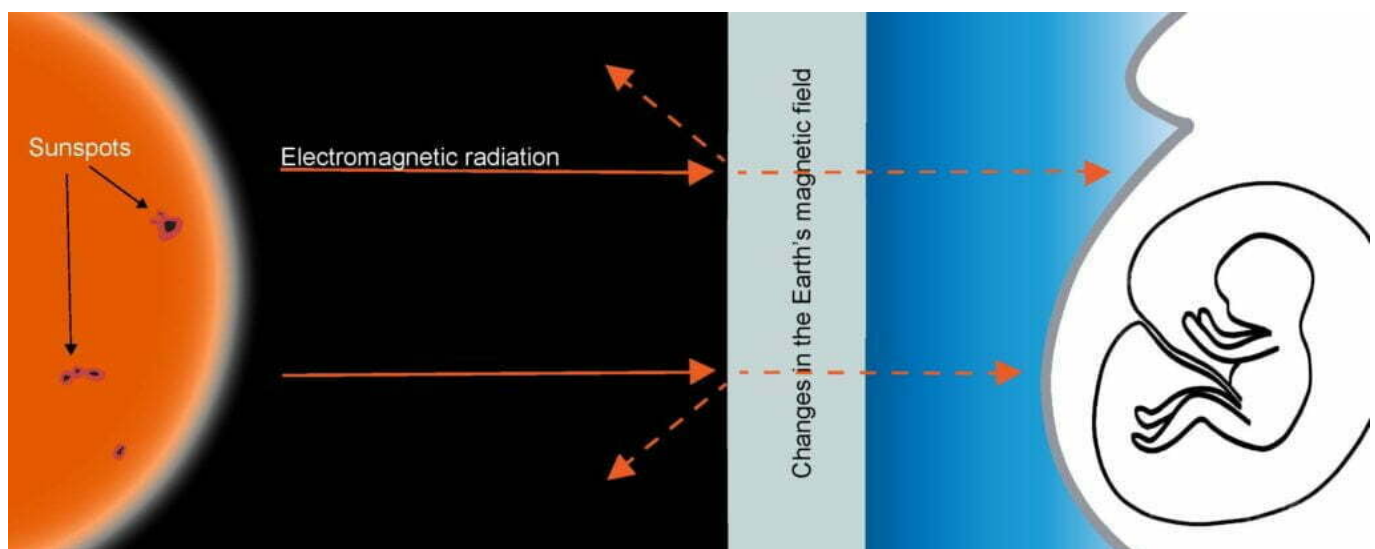
**Association of Solar and Geomagnetic Activity with Fetal Growth** Veronica A. Wang\* Veronica A. Wang Michael Leung Anna M. Modest Michele R. Hacker Carolina L. Zilli Vieira Joel Schwartz Brent A. Coull Petros Koutrakis Stefania Papatheodorou

**Background:** Solar and geomagnetic activity have been shown to suppress melatonin, an important hormone for fetal development, motivating the investigation of their association with fetal growth.

**Methods:** We included 9,573 singleton births with routine ultrasounds at an academic medical center in Eastern Massachusetts from 2011 through 2016. Three exposure windows of sunspot number and Kp index from NASA Goddard Space Flight Center were considered, including the first 16 weeks of pregnancy, one month prior to fetal growth measurement, and conception until fetal growth measurement (cumulative). Ultrasound scans from which we extracted biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC) measurements were categorized as anatomic (<24 weeks' gestation) or growth scans ( $\geq 24$  weeks' gestation). Ultrasound parameters and birth weight were standardized, and linear mixed models adjusted for long-term trends were fitted. Maternal race and fetal sex were considered as modifiers separately.

**Results:** Prenatal solar and geomagnetic activity were positively associated with anatomic scan head parameters, negatively associated with growth scan ultrasound parameters, and not associated with birth weight. Associations were strongest for cumulative exposure in growth scans, where an interquartile range increase in sunspot number was associated with a -0.17 (95% CI: -0.26, -0.08), -0.25 (95% CI: -0.36, -0.15), and -0.13 (95% CI: -0.23, -0.03) difference in mean BPD, HC, and FL z-score, respectively. An interquartile range increase in cumulative Kp index was associated with a -0.11 (95% CI: -0.22, -0.01) and -0.11 (95% CI: -0.20, -0.02) difference in mean growth scan HC and AC z-score, respectively. White participants and male fetuses may be particularly vulnerable in early pregnancy.

**Conclusions:** Solar and geomagnetic activity were associated with fetal growth. Future studies are needed to better understand its impact on clinical endpoints.



**Prenatal Solar Exposures and Pregnancy Loss in Eastern Massachusetts** Veronica A. Wang\*  
Veronica A. Wang Michael Leung Man Liu Anna M. Modest Michele R. Hacker Carolina L. Zilli Vieira  
Marc Weisskopf Joel Schwartz Brent A. Coull Stefania Papatheodorou Petros Koutrakis

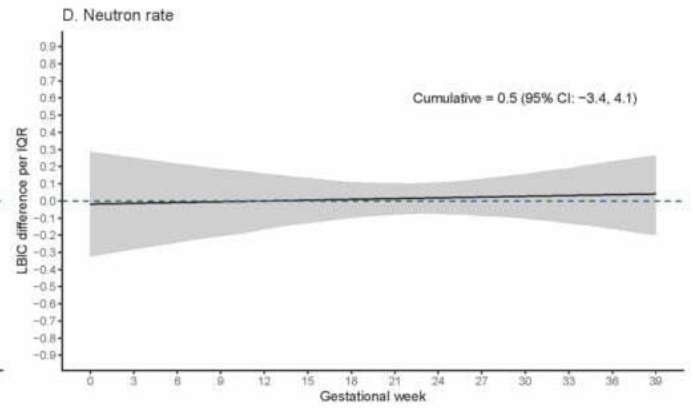
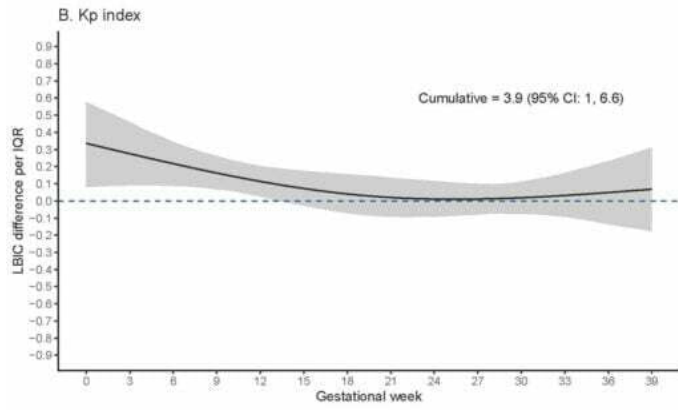
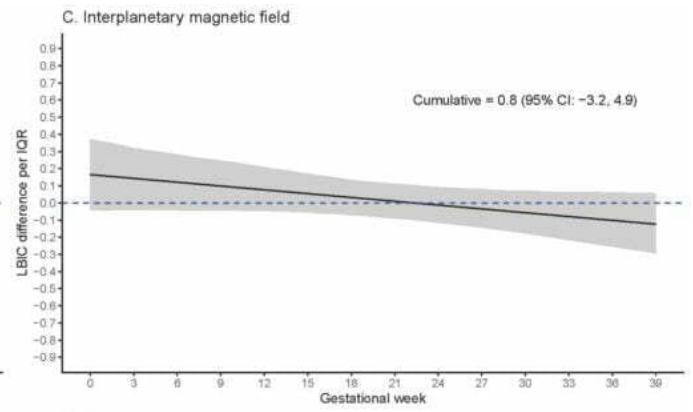
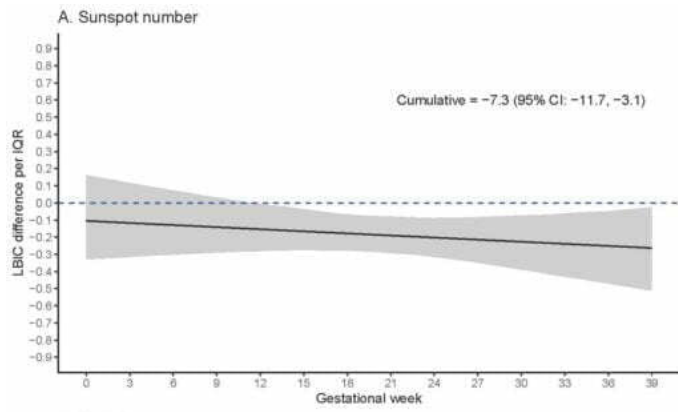
**Background:** Previous studies have linked solar activity to folate and melatonin levels, which may be important to sustaining a pregnancy. Thus, we aimed to examine the association with pregnancy loss.

**Methods:** Our study included singleton term births at an academic medical center in 2002-2015 in Eastern Massachusetts. We considered several solar exposures, including sunspot number and interplanetary field intensity, and solar-driven exposures, including Kp index, a measure of geomagnetic activity, and neutron rate, a measure of galactic cosmic rays, collected by the NASA Goddard Space Flight Center and the Bartol Research Institute. We used a novel time series method to identify pregnancy loss based on the number of live birth-identified conceptions (LBICs)—the difference between the total number of conceptions and those that result in loss for each week—and fitted distributed lag models adjusted for time trends.

**Results:** There were, on average, about 30 conceptions per week during our study period. An interquartile range increase in sunspot number throughout pregnancy was associated with 7.3 (95% CI: 11.7, 3.1) fewer LBICs (i.e., more pregnancy loss), with weeks 13 to 39 identified as a critical window of exposure. Interestingly, an interquartile range increase in exposure to Kp index across pregnancy was associated with 3.9 (95% CI: 1.0, 6.6) more LBICs (i.e., fewer pregnancy loss), with exposure from conception to week 13 identified as a critical period. Prenatal exposure to interplanetary field intensity and neutron rate were not associated with pregnancy loss.

**Conclusions:** Whether solar activity was beneficial and/or deleterious to sustaining a pregnancy varied by exposure metric. Solar activity is a complex phenomenon, and more studies are needed to better understand the ranges of electromagnetic spectrum captured by each metric and its relation to human health.





**The association between vitamin D and infertility: an analysis of NHANES data, 2013-2018**

Alice Lee\* Alice Lee Meng-Han Tsai Heather Franson

**Background:** It is well-known that vitamin D is essential for musculoskeletal health. However, there is emerging evidence of vitamin D's role in female reproduction. Since most of the existing evidence is primarily based on animal and in vitro studies, we explored the association between vitamin D and infertility in women in the United States (U.S.).

**Methods:** We conducted a cross-sectional analysis utilizing data from the 2013-2018 National Health and Nutrition Examination Survey (NHANES). Females, ages 20-44 years who were currently not pregnant and had laboratory serum 25-hydroxyvitamin D (a metabolite of vitamin D) data were included. Our exposure of interest was vitamin D, our outcome of interest was infertility, and the covariates considered included demographics as well as reproductive and lifestyle factors. Multivariable logistic regression models were used to quantify the association between vitamin D levels and infertility. We also conducted subpopulation analyses within body mass index (BMI) categories. All analyses were weighted to represent the general U.S. female population.

**Results:** The mean serum vitamin D level in women who did not report infertility issues was 65.16 nmol/L versus 63.08 nmol/L in women who reported infertility issues. Women who did not have optimal levels of vitamin D (defined as <75 nmol/L) were significantly more likely to experience infertility compared to women whose vitamin D levels were considered optimal (OR=1.85, 95% CI, 1.12-3.08). Among women with a BMI of 30+ (i.e. obese), those with less than optimal vitamin D levels were close to three times as likely to report issues with infertility (OR=2.77, 95% CI, 1.22-6.27).

**Conclusions:** Our results add to the growing evidence of vitamin D's importance in female reproductive health. Given that vitamin D deficiency remains a public health problem, strategies that improve vitamin D levels may be relevant, particularly among women of childbearing age.

**Is Treatment Efficacy in Clinical Trials Modified by Access to Healthcare?** Lizbeth Gomez\*

Lizbeth Gomez Jane E. Clougherty Ellen J. Kinnee Fernando Holguin

*Background:* Randomized clinical trials rarely include social or environmental co-exposures known to alter underlying disease and treatment efficacy in their analysis. For asthma clinical research, this is concerning as asthma disproportionately affects lower-income urban communities, where air pollution and social stressors are pervasive and can impact response to therapy.

*Methods:* We reexamined AsthmaNet's Step-Up Yellow Zone Inhaled Corticosteroids to Prevent Exacerbations (STICS) RCT. In it, 254 children aged 5 to 11 were randomized to either a low-dose inhaled glucocorticoids (fluticasone at 44 µg/inhalation) or a quintupled high-dose (fluticasone at 220 µg/inhalation) two inhalations twice daily at the onset of an exacerbation. We geocoded participant residences and estimated mean exposures to PM<sub>2.5</sub>, NO<sub>2</sub>, and O<sub>3</sub> during each participant enrollment period, using a validated national spatiotemporal model for fine particles. We derived census block group indicators for health provider shortage areas (HPSA). We tested whether these co-exposures altered the treatment efficacy on time prednisone use, time to treatment failure, and number of exacerbations.

*Results:* High ICS treatment was associated with shorter time to prednisone use, compared to low ICS treatment only among those living in non-HPSA areas (p= .01). Likewise, randomization to the high ICS treatment was associated with more prednisone courses only among older children (p=.04) and those living in non-HPSA (p=.002). Exposures to air pollutants did not predict number of exacerbations in these analyses.

*Conclusions:* Living in non-HPSA designated census blocks modified observed treatment efficacy in STICS. In less-deprived areas or those with more healthcare access, higher ICS doses conferred *shorter* times to prednisone use. RCTs should consider the role of social and environmental co-exposures to understand intervention impacts and identify subgroups for whom interventions may be differentially effective.

**Variability in ppFEV1 Predicts Mortality or Lung Transplant** Jonathan V. Todd\* Jonathan Todd Joshua Ostrenga Elizabeth Cromwell Wayne J. Morgan Raksha Jain Rhonda Szczesniak Oisin J. O'Connell Albert Faro

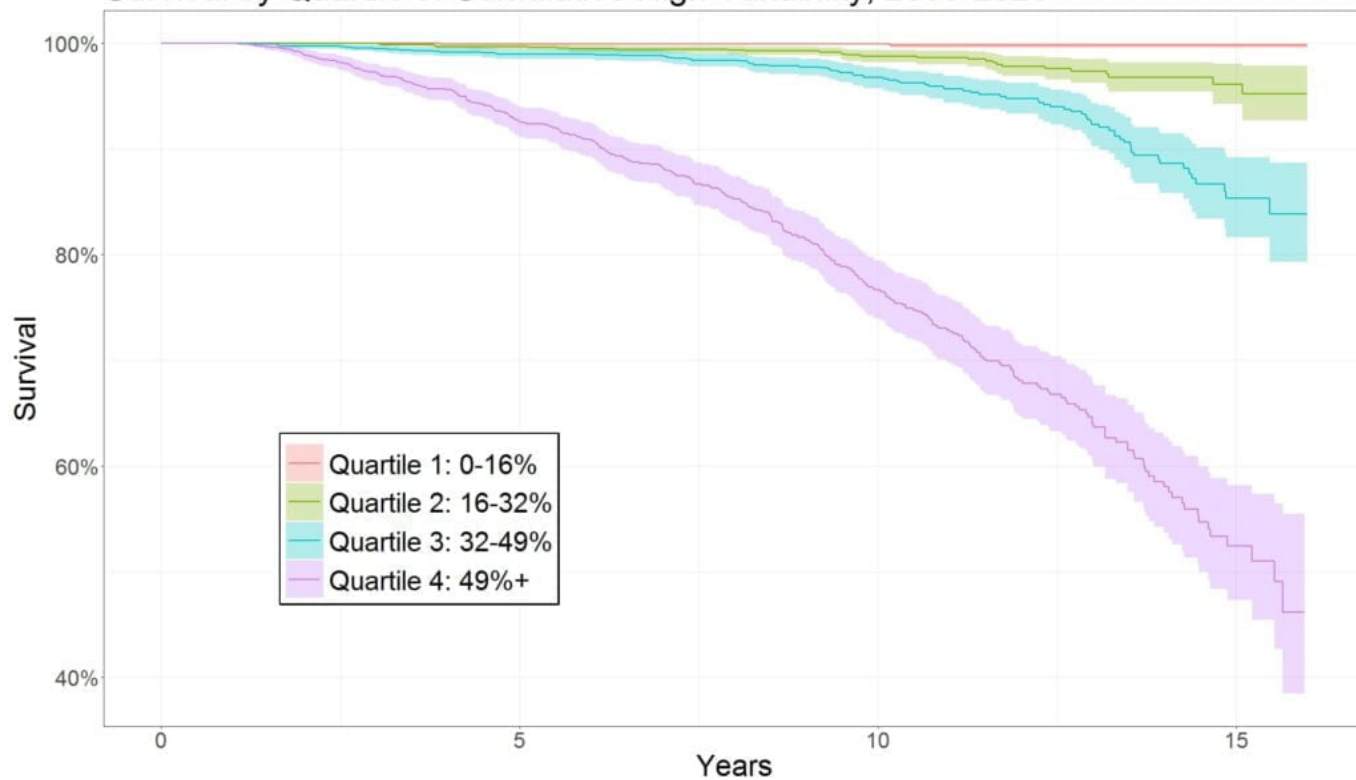
**Background:** Declines in percent predicted Forced Expiratory Volume in 1 Second (ppFEV<sub>1</sub>) are an important marker of clinical progression of Cystic Fibrosis (CF). The relevance of ppFEV<sub>1</sub> variability, or patterns of changes in ppFEV<sub>1</sub> involving large drops or rises in ppFEV<sub>1</sub>, in predicting mortality or lung transplantation is less well understood.

**Methods:** We used the US CF Foundation Patient Registry to estimate the association between ppFEV<sub>1</sub> variability and a combined outcome of lung transplant or death. We included children ages 8 or above with CF and two prior years of ppFEV<sub>1</sub> data before baseline between 2005 and 2020. We defined ppFEV<sub>1</sub> variability as a relative increase or decrease of at least 10% in ppFEV<sub>1</sub> from a two-year averaged baseline, updated from measurements in the previous two years from each time point ppFEV<sub>1</sub> was measured. A marginal structural Cox proportional hazards model was used to estimate the association between ppFEV<sub>1</sub> variability and time to either lung transplant or death. Results were weighted for age, sex, race, baseline ppFEV<sub>1</sub>, time-updated ppFEV<sub>1</sub>, Forced Vital Capacity (FVC), any steroid use, bronchodilator use, and leukotriene use. Patients were censored at the first instance of lung transplant, death, one full year without ppFEV<sub>1</sub> measurements, or December 31, 2020. We also examined a cumulative measure of ppFEV<sub>1</sub> variability, defined as the cumulative proportion of visits with ppFEV<sub>1</sub> variability at each visit. Kaplan-Meier estimates were used to generate survival curves based upon quartiles of the cumulative distribution of ppFEV<sub>1</sub> variability.

**Results:** We included 9,155 CF patients in our cohort. The median age at baseline was 8.3 years (interquartile range 8.2 - 8.4), 50% female, 94% Caucasian, and baseline ppFEV<sub>1</sub> percent predicted was 94.4. The unadjusted HR for increased ppFEV<sub>1</sub> variability on lung transplant/mortality was 4.29 (95% CI 3.59 - 5.14) and the weighted HR was 1.77 (95% CI 1.36 - 2.30). Survival curves stratified by quartile of cumulative variability demonstrated an increased hazard of lung transplant/mortality as the proportion of cumulative ppFEV<sub>1</sub> variability increased.

**Conclusions:** Using a marginal structural Cox proportional hazards model, we found an association between ppFEV<sub>1</sub> variability and lung transplant or mortality in a cohort of people with CF in the US.

Survival by Quartile of Cumulative High Variability, 2005-2020



**Association of post-World Trade Center (WTC) mortality with pre-WTC-exposure lung function: a twenty-year longitudinal study** Madeline Cannon\* Rachel Zeig-Owens Madeline Cannon Rachel Zeig-Owens Charles B Hall Jaeun Choi Michael Weiden

**Background:** Forced expiratory volume in 1s (FEV<sub>1</sub>) decline is associated with all-cause and cause-specific mortality in occupational and other cohorts. The association between baseline FEV<sub>1</sub> in the normal range and mortality is poorly described. We aimed to assess the association of baseline lung function (FEV<sub>1</sub> and forced vital capacity (FVC)) with subsequent mortality.

**Methods:** The cohort was World Trade Center (WTC)-exposed rescue/recovery workers with baseline (pre-WTC exposure) FEV<sub>1</sub> and FVC from 1/1/98 to 9/10/01; associations of baseline FEV<sub>1</sub> and FVC with mortality (all-cause and cause-specific) were assessed with multivariable Cox proportional-hazards models adjusted for age, sex, race/ethnicity, job description and smoking status. Cause of death was obtained from the National Death Index. Follow-up began on 9/12/01 and ended at death or 12/31/21.

**Results:** Baseline lung function was measured in 11270 participants; 6963 (61.8%) had FEV<sub>1</sub> ≥100% predicted and 3964 (35.2%) had FEV<sub>1</sub> between 80 and 100%. Over 225091 person years of follow-up, 540 (4.8%) died. Baseline lung function predicted mortality. Relative to those with a baseline FEV<sub>1</sub> ≥100% predicted, the HRs for all-cause mortality, cancer-caused mortality, respiratory disease-caused mortality and heart disease-caused mortality among those with FEV<sub>1</sub> from 80% to 100% predicted were 1.47 (95%CI 1.23-1.76), 1.42 (95% CI 1.03-1.95), 1.82 (95%CI 0.72-4.60) and 1.68 (95% CI 1.15-2.47), respectively; for those <80% predicted the HRs were 2.31 (95%CI 1.66-3.23), 3.15 (95% CI 1.85-5.35), 5.73 (95%CI 1.48-22.20) and 2.45 (95% CI 1.22-4.93). FVC results were similar.

**Conclusion:** Baseline lung function is associated with elevated all-cause, cancer-caused, respiratory disease-caused and heart disease-caused mortality in the 20 years following WTC exposure. Further investigation is needed to define the pathways connecting normal variation in baseline lung function and post-exposure all-cause and cause-specific mortality.

**LATEBREAKER**

Respiratory

**Respiratory emergency department visits during a hydrogen sulfide emergency in Southern Los Angeles County, CA** Arbor Quist\* Arbor Quist Jill Johnston

In October 2021, thousands of residents in Carson, California began complaining of noxious odor and respiratory issues. Hydrogen sulfide (H<sub>2</sub>S), a toxic odorous gas, was measured at concentrations up to 7000 parts per billion (ppb) and remained above California's acute air quality standard of 30 ppb for 4 weeks. While the adverse respiratory effects of high concentrations of H<sub>2</sub>S exposure are well known, research on the association of low- and medium-level H<sub>2</sub>S exposure and respiratory outcomes has yielded conflicting results. Few studies have examined how H<sub>2</sub>S emergencies affect diverse communities like Carson. We calculated daily rates of emergency department (ED) visits for all chronic lower respiratory diseases (CLRD), asthma, and chronic obstructive pulmonary disease (COPD) in Carson area ZIP codes (<5 km from Carson) and in Los Angeles County ZIP codes >15 km from Carson (control). Using controlled interrupted time series, we compared ED visit rates during the 4 weeks of the H<sub>2</sub>S incident in Carson to the predicted rates had this event not occurred, based on 2018-2021 ED trends, and controlling for ED visit rate changes in control areas of Los Angeles County. We examined effect measure modification by age. We observed a 21% increase (rate ratio (RR): 1.21, 95% CI: 1.19, 1.43) in ED visit rate for CLRD, a 38% increase (RR=1.38, 95% CI: 1.24, 1.52) for asthma, and 24% increase (RR=1.24, 95% CI: 0.98, 1.50) for COPD in Carson during the 4 weeks of the event. These effects were strongest among adults ages 40-59 years (CLRD RR=1.81, 95% CI: 1.56, 2.06). We observed dose response relationships when we examined larger exposure areas from the event (CLRD, 5 km exposure buffer: RR=1.31, 95% CI: 1.19, 1.43; 10 km exposure: RR=1.17, 95% CI: 1.10, 1.24; 20 km exposure: RR=1.09, 95% CI: 1.04, 1.14). Exposure to H<sub>2</sub>S and other malodors are often under-prioritized in environmental justice communities. H<sub>2</sub>S releases harm respiratory health, even at low and medium exposure levels.

**LATEBREAKER**

## Screening

**Testing acceptability of an organ inventory designed to reduce misclassification of transgender, nonbinary, and intersex people in cancer screening and research**

Heidi Moseson\* Heidi Moseson Sachiko Ragosta Anu Manchikanti Gómez Juno Obedin-Maliver

Epidemiological data highlight that transgender, nonbinary, and intersex people bear a disproportionate cancer burden, while being less likely to receive appropriate cancer screening. Gender-based cancer screening protocols may misclassify people based on assumptions about body parts. To address this misclassification problem, we collaborated with a community advisory board and used feedback from six focus groups to develop an inclusive, evidence-based organ inventory to capture relevant information on eligibility for cancer screening, care, and research than captured by gender or sex. We used an online survey to evaluate the organ inventory. We recruited survey participants via social media and physical flyers. Eligible participants were any gender, at least 15 years old, spoke English or Spanish, and resided in the United States. Over 8 months in 2022, 333 individuals completed the survey: 34% identified as transgender or nonbinary, 44% as cisgender, and 14% as intersex. Cancer screening inequities existed: for example, 78% of cisgender people with a cervix reported having a pap smear in the past 5 years, compared to 56% of transgender and nonbinary people and only 33% of intersex people ( $p < 0.05$ ). Participants rated the organ inventory as acceptable for use in both health care and research settings: 73% found it very easy to understand, and 65% found it very comfortable to fill out. We found substantial misclassification when gender identity alone was used to recommend screening. For instance, 64 (19%) participants were eligible for mammogram screening based on organ inventory responses indicating having breast tissue but would have been missed by restricting to only those who indicated “woman” as their gender identity, and 43 (12.9%) would have been missed relying on “female” as their sex assigned at birth. Using an organ inventory instead of gender or sex-based screening questions could reduce disparities in screening and reduce misclassification in research.



**Validating Screening Measures in the Absence of a True Gold Standard: Lessons Learned from LEAD Panels** Brad Cannell\* Brad Cannell Sharon Jason Burnett David Burnes Doug Livingston Katelyn Jetelina Rabiya Mian

Elder mistreatment (EM) is commonly defined as an intentional act, or failure to act, by a caregiver or another person in a relationship involving an expectation of trust, that causes harm or creates a risk of harm to an older adult. EM includes financial abuse/exploitation, neglect, emotional/psychological abuse, physical abuse, and sexual abuse. Exposure to EM is often chronic and commonly involves multiple types. The annual prevalence of EM among cognitively intact adults is approximately 10% and higher among those with dementia. Further, EM is linked with increased risk of physical injury, hospitalizations, emergency room visits, psychological distress, morbidity, and early mortality. Despite the scope and seriousness of this problem, EM is difficult to detect and often goes unrecognized. One of the biggest challenges to understanding and preventing EM is poor detection and reporting. While efforts to create screening tools intended for research, pre-hospital, and emergency department (ED) settings have been in existence since at least the 1970s, there remains a lack of rigorous evaluation establishing the validity and reliability of these screeners across settings. A key challenge with evaluating screening instrument(s) is the inevitable need to validate them against a gold standard. But what is the gold standard measure of EM? Currently, the two most commonly used gold standards are Adult Protective Services investigations, which have a number of limitations in a research context, and Longitudinal, Experts, All Data (LEAD) panels. This session will introduce the audience to LEAD panels, discuss critical issues with using LEAD panels as a gold standard measure of EM in practice, discuss potential alternatives to LEAD panels (e.g., the Delphi method), and facilitate an interactive discussion about the future of the LEAD panels as a tool to validate EM screening instruments in the absence of an objective gold standard measure.

**Impact of Mass Screening Using Chest X-Ray on Mortality Reduction Among Pulmonary Tuberculosis Patients** Sayada Zartasha Kazmi\* Ji Yoon Baek Sayada Zartasha Kazmi Myung-Hee Shin Jayoun Lee Hongjo Choi Aesun Shin

**Background:** Although chest x-ray (CXR) screening was introduced in Korea in the 1950s, the incidence of pulmonary tuberculosis (PTB) remains still high. This study evaluated the effect of CXR screening on mortality reduction by comparing cases who are detected through screening and cases who are diagnosed routinely at health care facilities.

**Methods:** A retrospective analysis on a cohort of PTB patients was performed using the claims data from the National Health Insurance Service. From 2004 to 2020, PTB cases were defined as having a diagnosis of PTB by ICD-10 codes (A15, A16, A19). The patients were divided into two groups according to a history of CXR screening within 6 months prior to their initial diagnosis of PTB. Cox proportional hazards model was used to estimate the association between screening and all-cause mortality or TB-specific mortality. For adjustment, severity of PTB, age and sex were used as covariates. A subgroup analysis including the PTB cases with prescription of TB treatment drugs was conducted.

**Results:** Among a total of 86,830 PTB patients, 15,916 (18.8%) were screening-detected and 68,914 (81.2%) were unscreened. The screened group had a lower risk in all-cause mortality (adjusted HR: 0.66 [95% CI: 0.63-0.68]) and TB-specific mortality (0.38 [0.32-0.46]) compared to the unscreened group. In the subgroup analysis with 52,491 PTB patients who were diagnosed and had TB drug treatment, a similar pattern in all-cause mortality (0.71 [0.68-0.75]) and TB-specific mortality (0.41 [0.34-0.49]) was observed.

**Conclusion:** The screened group showed a lower risk of death by all-cause as well as TB-specific compared to the unscreened group. This may indicate CXR screening leads to reducing the burden of mortality of PTB patients.

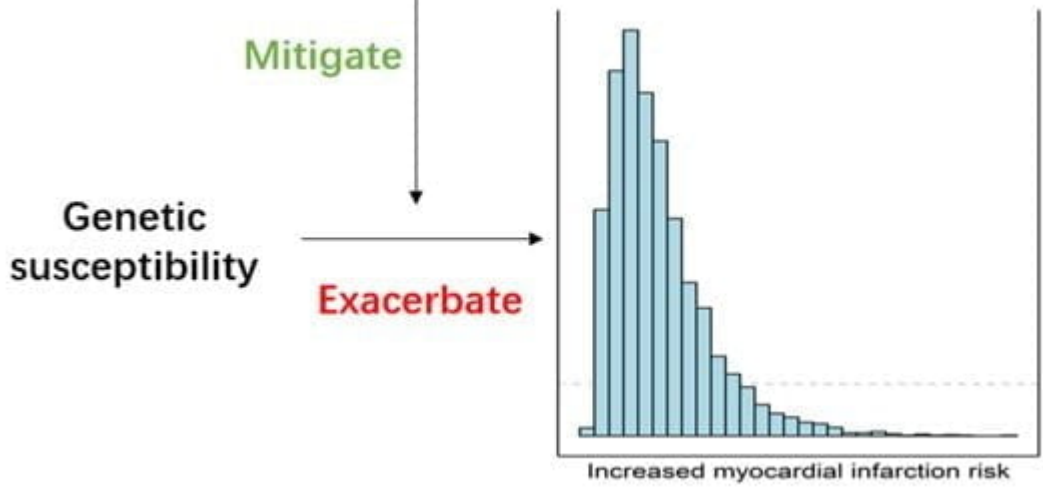
## **The Association of Joint Genetic and Social Environmental Risk with Incident Myocardial Infarction: Results from the Health and Retirement Study** Chenkai Wu\* Chenkai Wu

**Background:** Myocardial infarction (MI) is a significant clinical and public health problem worldwide. However, little research has assessed the interplay between genetic susceptibility and social environment in the development of MI.

**Methods:** Data were from the Health and Retirement Study. The polygenic risk score and polysocial score for MI were classified as low, intermediate, and high, respectively. Using Cox regression models, we assessed the race-specific association of polygenic score and polysocial score with MI, respectively; we examined the association between polysocial score and MI within each polygenic risk score category. We also examined the joint effect of genetic (low, intermediate, and high) and social environmental risk (low/intermediate, high) on MI.

**Results:** 612 Black and 4,795 White adults aged  $\geq 65$  years initially free of MI were included. We found a risk gradient of MI across the polygenic risk score and polysocial score among White participants, respectively; no significant risk gradient across the polygenic risk score was found among Black participants. A disadvantaged social environment was associated with a higher risk of incident MI among older White adults with intermediate and high genetic risk but not those with low genetic risk. We revealed the joint effect of genetics and social environment in the development of MI among White participants.

**Conclusions:** Living in a favorable social environment is particularly important for persons with an intermediate and high genetic risk for MI. It is critical to develop tailored interventions to improve the social environment for disease prevention, especially among adults with a relatively high genetic risk.

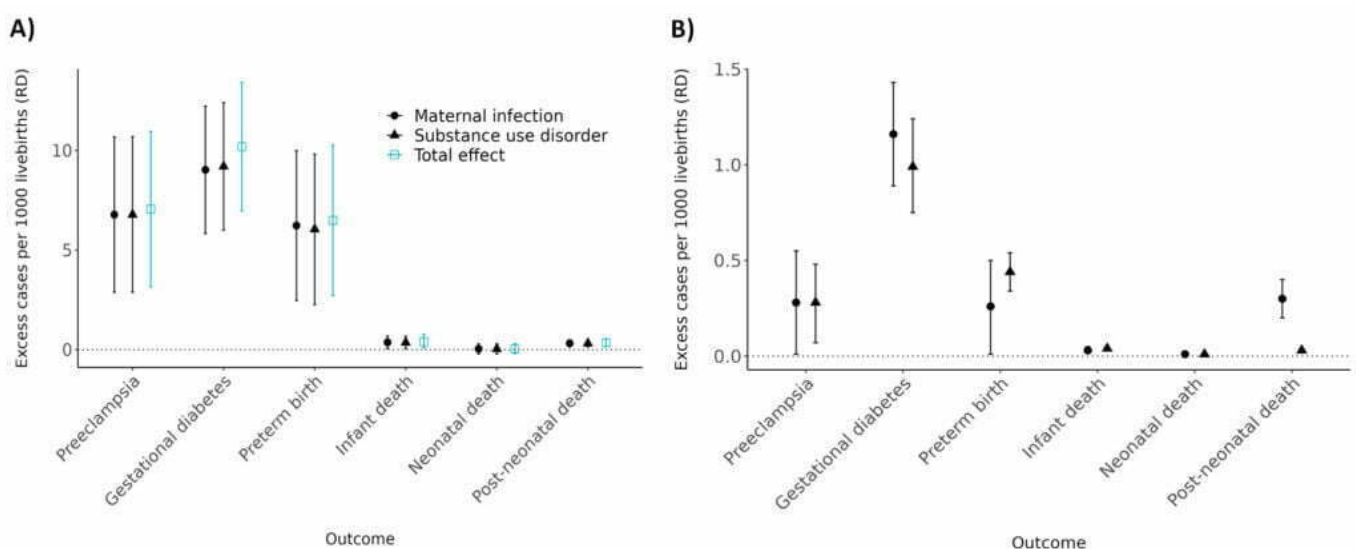


**Mediators of Community Violence and Perinatal Outcomes in California** Emily Liu\* Emily Liu Shelley Jung Caitlin Chan Dana Goin Kara Rudolph Kristen Marchi William Dow Paula Braveman Mahasin Mujahid Mark van der Laan Jennifer Ahern

Persistent disparities in maternal and infant health likely reflect underlying structural and social inequities. The burden of community violence is a determinant that may contribute to adverse perinatal outcomes via behavioral and biologic mechanisms, however, the pathways have not been elucidated in prior studies.

We examined mediators that could explain the relationship between community violence and multiple perinatal outcomes using a cohort of singleton live births in California (2007-2011). Data were obtained from hospital birth records linked to 12-month average levels of community violence (rates of death and injuries due to assault) at the ZIP code tabulation area (ZCTA) level. We used propensity scores to identify ZCTAs with comparable characteristics but different levels of community violence and analyses were limited to the area of common support. We estimated natural direct and indirect effects using targeted maximum likelihood estimation to assess mediation by prenatal infection and substance use disorder on risk of preeclampsia, gestational diabetes mellitus (GDM), preterm birth, infant death, neonatal death, and post-neonatal death.

Analysis included 72% of live births retained on support ( $n = 1597122$ ). Living in a high-violence community (75th percentile and above) was associated with an increased risk of all outcomes, excluding neonatal death (Fig 1A, Total effect). For the mediators, the natural indirect effects had varied magnitudes across outcomes (Fig 1B). Respectively, the indirect effect of substance use and maternal infection during pregnancy explained a proportion of the total effect of high community violence on preeclampsia (3.9% and 4.0%), GDM (9.7% and 11.4%), preterm birth (6.8% and 4.0%), infant death (10.1% and 8.1%), neonatal death (21.8% and 15.8%), and post-neonatal death (9.1% and 7.5%). Results suggest that substance use and maternal infection during pregnancy mediate a non-trivial proportion of multiple perinatal outcomes.



**Figure 1.** Total, natural direct (A) and natural indirect (B) effect estimates and 95% confidence intervals examining the mediators of maternal infection and substance use disorder during pregnancy by perinatal outcomes. Note that the effects are graphed on different scales.

## **The association between social fragmentation and deaths of despair among Canadian adults** Stephen Hunter\* Stephen Hunter Gregory Farmer Roman Pabayo

### Background

Social fragmentation (low community integration) has been theorized and empirically associated with suicide in prior research. However, there remains a dearth of information about whether social fragmentation is associated with deaths attributed to alcohol or drug use. The purpose of this research was to examine the association between social fragmentation and deaths attributable to alcohol use, drug use, and suicide (deaths of despair) among a population-based, representative sample of Canadian adults.

### Methods

Participants were 15,324,645 Canadians within 288 census divisions between 2006 and 2019. Mortality data from the Canadian Vital Statistics Database was linked with census division socioeconomic data from the 2006 Canadian census using the Canadian Census Health and Environment Cohorts. A census division social fragmentation index was created consisting of the proportion of lone parent households, the proportion of households tenured as renters, and the proportion of households who moved within the last 5 years. Cox-proportional hazard regression with survey weights and the sandwich co-estimator were used to account for clustering of individuals (level-1) nested within census divisions (level-2) was used.

### Results

After adjusting for individual-level and census division-level confounders, social fragmentation was associated with an increased hazards of all-cause mortality (HR = 1.04; 95% CI: 1.02, 1.07), suicide (HR = 1.09; 95%CI: 1.01, 1.18), drug overdose related mortality (HR = 1.13; 95%CI: 1.03, 1.24), and deaths of despair (HR = 1.10; 95% CI: 1.04, 1.16), but not significantly associated with alcohol related liver disease (HR = 1.06; 95% CI: 0.91,1.23).

### Conclusion

Social fragmentation is associated with an increased hazard of deaths of despair among Canadian adults. Efforts to improve social cohesion in areas characterized by high social fragmentation need to be evaluated.

**LATEBREAKER**

Social

**The rocky road to freedom: number of countries passed through defection and risk of metabolic syndrome among North Korean Refugees in South Korea** Doo Woong Lee\* Doo Woong Lee Hoon Sang Lee Sin Gon Kim Kyeong Jin Kim Sun Jae Jung

**The rocky road to freedom: number of countries passed through defection and risk of metabolic syndrome among North Korean Refugees in South Korea**

## 1. INTRODUCTION

The Korean War, which broke out on June 25, 1950, has had far-reaching implications for North Koreans, with many escaping to South Korea for a variety of reasons. Initially, the majority of these refugees were motivated by political aspirations. However, the South Korean economy experienced rapid growth from the late 1970s, widening the economic disparity between the two countries. Thus, the primary motivation for North Korean refugees (NKR) gradually shifted from political to economic concerns, with more people choosing to move to South Korea in search of a better life. As of December 2021, the cumulative number of NKR living in South Korea is 33,815. This figure does not include those who have escaped but are stranded in China or other Asian countries in an attempt to reach South Korea.

Defection from North Korea is a highly risky process, with the possibility of being thrown into a political prison camp or executed if caught. The refugees are also subjected to extreme levels of stress while fleeing the country, with the constant fear of being tracked by Chinese authorities or North Korean secret police in China until they obtain help from the South Korean government or find a way to enter the country. This can have a detrimental impact on the physical and mental health of the refugees, who are also forced to find basic necessities such as food, water, and shelter in the transit countries. As a result, they are highly likely to experience traumatization, which can later manifest in the form of physical and psychological illnesses.

Previous research has indicated that psychological distress and mental disorders can lead to a higher mortality rate than the general population. Post-traumatic stress disorder (PTSD) is known to be connected to various types of chronic diseases, such as cardiovascular and metabolic diseases, which are associated with the pathogenic process of PTSD.

This study hypothesized that the risk of metabolic syndrome (MetS) among NKRs would vary depending on the severity of the trauma experienced while defecting. It was expected that drastic changes in lifestyle and diet in South Korea would lead to health problems, particularly metabolic problems, which are known to be highly associated with these factors. Accordingly, the number of countries and the period from defection until arrival in South Korea were used as quasi-measurements to determine the degree of the traumatic event. The study also investigated whether the risk of the MetS by the number of countries the NKR transited varied depending on their residence period in South Korea, sex, and age.

## 2. METHODS

### 2.1. Data source and study population

The North Korean Refugee health in South Korea (NORNS) Study was established with the goal of evaluating the medical status and health determinants of North Korean defectors living in South Korea. It aimed to analyze six domains: demographic and migration information, disease history, mental health, health-related lifestyle, female reproductive health, and socio-cultural adaptation. This research utilized the data from the NORNS study and excluded 212 participants due to missing information. To account for lifestyle variables (alcohol drinking frequency and days of exercise) which are known to be major factors affecting the MetS, multiple imputation based on the multivariate normal distribution was implemented to reduce the missing values to 20%. This left 847 participants in the final study population. To ensure accuracy and transparency, this study followed the STROBE reporting guideline.

### 2.2. Measures

The participants of the survey all visited the Korea University Anam Hospital, located in Seoul. It was mandatory for them to fast from the day prior. The survey took 30 minutes, comprising of questions about demographics, medical history, mental health, lifestyle habits and women-specific conditions. Additionally, medical exams were conducted measuring anthropometric measurements, blood pressure, atherosclerosis and biochemical measurements. To ensure the accuracy and validity of the data, a NKR doctor was present to assist with the questionnaires. A more detailed description of the measurements is reported in the study by Lee et al.

#### 2.2.1. Outcome: metabolic syndrome

MetS was defined in this study with the modified National Cholesterol Education Program Adult Treatment Panel III criteria, using the Asian cut-off values for waist circumference. Waist circumference varies amongst ethnicities, and is associated with the prevalence of MetS among different ethnic groups. In order to be considered as having the MetS, participants had to meet three of the five criteria outlined: waist circumference (men  $\geq 90$  cm, women  $\geq 85$  cm), high triglyceride  $\geq 150$  mg/dl, low high density lipoprotein cholesterol (HDL-C) (men  $< 40$  mg/dl, women  $< 50$  mg/dl), hypertension  $\geq 130/85$  mmHg, and high fasting glucose  $\geq 100$  mg/dl.

#### 2.2.2. Exposure: traumatic experiences of the NKRs during defection

The exposure of the NKRs to traumatic experiences during defection was also taken into account, as the NKRs often face poverty, political imprisonment, and life-threatening situations if arrested by the police during defection. In addition, due to their chronically illegal status in a third country, they may experience prolonged insecurity. Thus, the number of transit countries and the period from defection till arrival in South Korea were utilized as quasi-measurements to determine the extent of exposure of the NKR to traumatic experiences.

#### 2.2.3. Covariates



As a moderating factor, the period of residence in South Korea was also taken into consideration, as the prevalence of mental disorders in the NKR may differ based on their period of residence in South Korea, due to better adaptation to a new environment over a period of time. Covariates such as sex, age, average monthly household income, pack-year of smoking, current alcohol drinking frequency, days of vigorous-intensity exercise per week, depressive symptoms (CES-D-20) and comorbidities, such as hyperlipidaemia, stroke, myocardial infarction, angina pectoris and diabetes, were also taken into account. Furthermore, body mass index and Total cholesterol were also included as continuous variables.

### **2.3. Statistical analysis**

The general characteristics of the study population were evaluated using  $\chi^2$ -tests and t-tests, which yielded frequencies and relative percentages for categorical variables, and mean and standard deviations for continuous variables. To identify the optimal model, the Akaike Information Criterion, Bayesian Information Criterion, and -2 log likelihood were considered, with lower scores indicating a better fit relative to other candidate models. Subsequently, a multivariable logistic regression analysis was conducted to estimate ORs and 95% CIs. Crude models were utilized to evaluate the bivariate association between the number of transit countries and the MetS, and further adjusted models (Models 1-3) were developed to include period of defection and residence in South Korea, sex, age, monthly household income, lifestyle factors, and health status. Model 3 was identified to have the best goodness-of-fit. Subgroup analyses were conducted for the period from defection till arrival in South Korea, the residence period in South Korea, sex, and age group. All statistical tests were two-tailed, with a p-value of  $< 0.05$  considered to be statistically significant. Analyses were carried out using SAS version 9.4 software (Cary, NC, USA).

### **2.4. Ethics approval**

This study was conducted in accordance with the ethical standards of the Institutional Review Board of Korea University Medical Center (approval number: Ed08023).

## **3. Results**

Of 847 NKR participants dwelling in South Korea, 682 (80.5%) were women and the mean age of the participants was 42.3 ( $\pm 11.9$ ) years. The least number of NKR were those who had defected to South Korea by transiting three countries (117; 13.8%). Mean period from defection till arrival in South Korea was 49.99 ( $\pm 51.7$ ) months, and the mean period of residence in South Korea was 40.9 ( $\pm 40.9$ ) months. Of all, 111 NKR (13.1%) had MetS. There was a different distribution for those with and without the MetS according to their age, sex, income, health related characteristics, number of transit countries, period from defection till arrival in South Korea, and period of residence in South Korea.

NKR who had transited three countries during defection had significantly higher odds for MetS than those who had arrived directly in South Korea (adj.OR 2.66, 95% CI: 1.16-6.10). Additionally, a marginally significant trend was identified between the number of countries transited during defection and higher odds for MetS (p-for trend 32.4 months, median month), albeit a marginal statistical significance (transited three countries: adj.OR: 4.86, 95% CI: 0.89-26.60, two countries:

adj.OR: 4.47, 95% CI: 0.91-22.02). Furthermore, for the NKR who had a longer period of defection and the more number of transited countries, the more likely they were to have MetS (p-for trend = 0.031). For the NKR who had settled in South Korea for a shorter period (<25.6 months, median month), the association was stronger (adj.OR: 3.42, 95% CI: 1.15-10.21). Those aged >41 (median) also had a higher association (adj.OR: 3.14, 95% CI: 1.16-8.56).

#### 4. Discussion

This study has provided evidence that the traumatic experiences of NKR in the process of defection are associated with an elevated risk of developing MetS. By using novel data from the NORNS, the researchers found that a greater number of transit countries had a significant association with an increased risk of the MetS. Moreover, the association strengthened if the NKR had a longer duration of defection, a shorter duration of residence in South Korea, and the NKR was older.

From the perspective of behavioral psychology, stress induced by traumatic experiences can lead to poor health habits and lifestyle choices (poor diet and sedentary behaviors), and consequently increase disease risk, especially the MetS and cardiovascular diseases. Biochemically, chronic stress of traumatic experiences can cause overeating, co-elevation of cortisol, insulin and fat angiogenesis, and suppression of certain anabolic hormones, which can result in metabolic dysfunction.

As observed in this study, the NKR who have been settled in South Korea only for a shorter period showcased a greater correlation between traumatic experience and the MetS. This can be interpreted as an adaptation difficulty to South Korean society and lifestyle, likely due to unhealthy lifestyle habits and poor dietary choices. These findings suggest a positive association between the extent of traumatic experience and MetS, emphasizing the need to understand not only the health implications, but also the potential adaptation difficulties faced by NKR.

Considering the ample amount of evidence that indicates a higher risk of the MetS in vulnerable populations, such as military veterans or refugees from other countries, and the socio-economic vulnerability of the NKR, it can be concluded that there exists a significant association between trauma and the development of the MetS. In light of this, priority policy intervention for vulnerable population groups is necessary.

This study provides meaningful evidence regarding the NKRs' trauma and its persistence even after arrival in South Korea, as well as its negative effect on their metabolism. However, it has several limitations that should be taken into consideration. The NORNS data is non-representative of all the NKR dwellings in South Korea since it was initially recruited from NKR aged  $\geq 30$  living in Seoul, the capital city of South Korea, with no statistical sampling methods employed. This may have introduced a selection bias in the results. Further, most of the questionnaires were self-reported, raising the possibility of a recall bias. Additionally, there were no questionnaires that encapsulated specific types of traumas and their severity among the NKR. Because the study was a cross-sectional design, causal relationships cannot be inferred. Future studies should employ longitudinal data with a sufficient study population to confirm a causal mechanism of traumatic experience leading to any health problem.

#### 5. Conclusion

Appropriate social support from the government and society are needed to provide them with continuous opportunities for adaptation to the unfamiliar environment in South Korea. Furthermore,

psychological and health care support may be necessary if needs arise. Future studies should consider employing longitudinal data with a sufficient study population to confirm the causal mechanisms of traumatic experience leading to any health problem.

**Income inequality and mental health in adolescents during COVID-19, results from COMPASS, 2018-2021** Claire Benny\* Claire Benny Brendan Smith Karen Patte Scott Leatherdale Roman Pabayo

**Introduction.** The ongoing impact of the COVID-19 pandemic has negatively affected the mental health of Canadians youth. Pre-pandemic research has linked income inequality in schools to adolescent depression, however, it is unclear if the onset of the pandemic exacerbated the effects of income inequality on adolescent mental health. The current study aimed to quantify the association between income inequality and adolescent mental health following the pandemic.

**Methods.** Longitudinal data come from three waves (2018/19 to 2020/21) of the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking, and Sedentary behaviour (COMPASS) school-based study. The sample included 29,722 secondary school students across 43 Census Divisions in British Columbia, Alberta, Ontario, and Quebec, Canada. Growth Curve modelling was used to assess the association between income inequality and mental health before and after the onset of the pandemic. Income inequality was assessed using Gini coefficient and adolescent depressive and anxiety scores were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D) and General Anxiety Disorder-7 (GAD-7), respectively.

**Results.** Adjusted analyses indicated that the relationship between income inequality on anxiety scores was strengthened following the COVID-19 onset ( $B=0.02$ , 95% CI= $0.0004$ ,  $0.03$ ), indicating that income inequality was associated with a greater increase in anxiety scores, but was not associated with changes in depressive scores during the pandemic, as compared to before COVID-19.

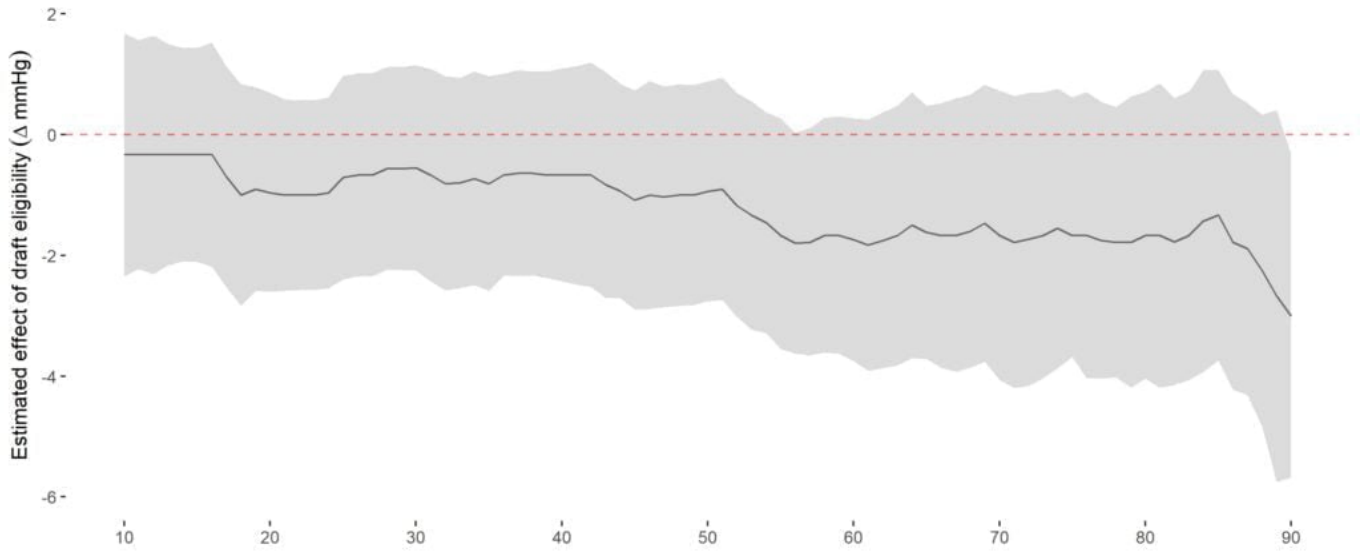
**Discussion.** The study results indicate that the association between income inequality and adolescent anxiety was heightened at the onset of the COVID-19 pandemic. These results add to evidence of inequitable impacts of the pandemic and highlight the importance of upstream approaches to improving adolescent mental health. This study can inform policy and programs toward an equitable pandemic recovery for young Canadians.

**Impact of Vietnam-era GI Bill eligibility on the distribution of later-life blood pressure: evidence from a natural experiment** Aayush Khadka\* Aayush Khadka Lucia Pacca M. Maria Glymour Kirsten Bibbins-Domingo Justin S. White Sanjay Basu Fei Jiang Anusha M. Vable

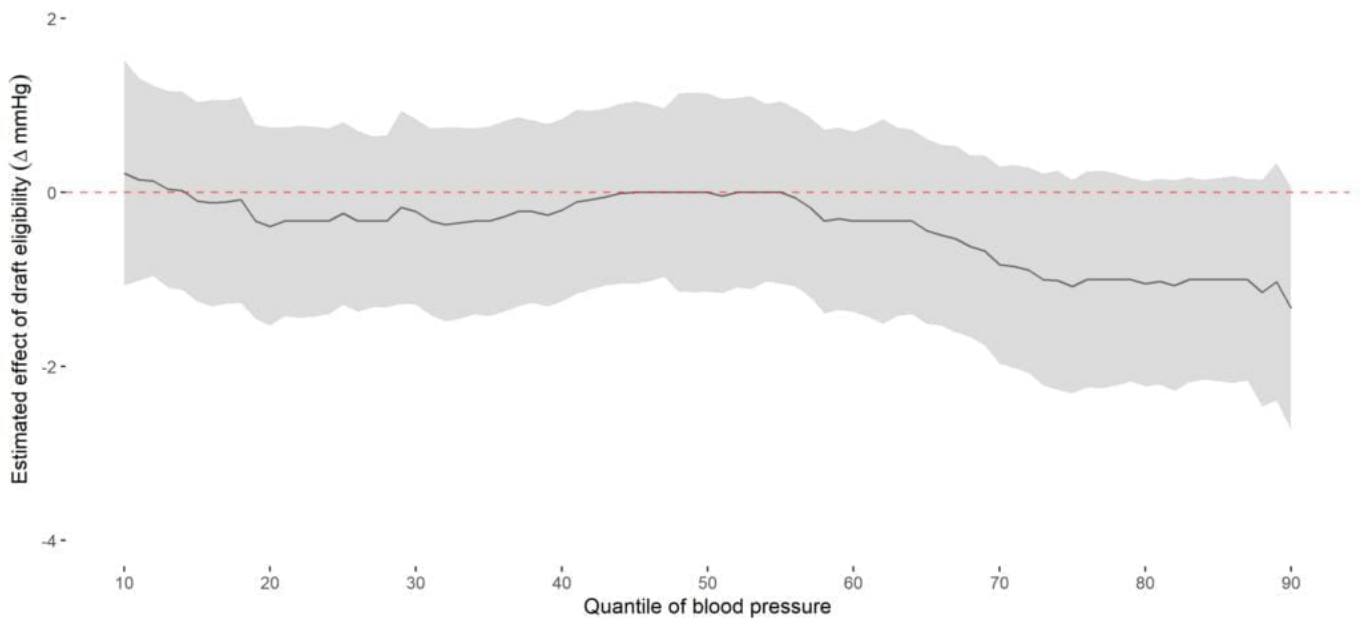
Interventions with larger protective effects at higher blood pressure levels relative to lower ones can have greater population health impact due to blood pressure's nonlinear relationship with cardiovascular disease (CVD) risk. Education may have such heterogeneous effects on blood pressure, but this question is rarely studied as most research focuses on effects on average blood pressure. We investigated the effects of Vietnam-era GI Bill eligibility, a policy that subsidized college education for veterans, on the distribution of later-life blood pressure by exploiting the Vietnam draft lottery natural experiment. Using US Health and Retirement Study data (2006-2018) for men born 1947-1953 (n=1,970), we proxied GI Bill eligibility using draft eligibility, a binary variable defined using draft lottery numbers. Outcomes were repeated, biennial measures of systolic and diastolic blood pressure (SBP, DBP). We estimated intention-to-treat effects at the mean and at the 10th-90th percentiles of blood pressure using linear and quantile regressions. We investigated effect modification by childhood socioeconomic status (cSES), defined using a previously validated index. We adjusted for year of outcome measurement and month-and-year-of-birth fixed effects and used a cluster-robust variance estimator in all regressions. Draft eligibility reduced mean SBP and DBP (e.g., estimate for SBP: -1.3mmHg [95% CI -2.9,0.2]). Draft eligibility had larger effects at the highest blood pressure decile than at the lowest decile (e.g., estimates for SBP at the 10th and 90th percentiles:  $\beta_{10}$ : -0.3mmHg [95% CI -2.4,1.7];  $\beta_{90}$ : -3.0mmHg [95% CI -5.7,-0.3]). Draft eligibility had protective effects in men with low and medium cSES but not high cSES. GI Bill eligibility shifted and reshaped the blood pressure distribution to one of lower CVD risk and reduced cSES disparities in blood pressure. Focusing only on average effects may underestimate the health benefits of social interventions.

# Intention-to-treat effect at quantiles of the blood pressure distributions

i) Systolic blood pressure



ii) Diastolic blood pressure



## Quantifying associations between child health and neighborhood social vulnerability: Does the choice of index matter? Nrupen Bhasvar\* Anna Zolotor Ro Huang Nrupen Bhavsar

**Background:** Disadvantage indices combine population-level social, economic, and health data to quantify the overall social vulnerability of a geographic area. While they are often used interchangeably, index choice may influence results due to the population or outcome under consideration. We compared the cross-sectional associations between three common indices (Social Vulnerability Index (SVI), Area Deprivation Index (ADI), and Child Opportunity Index (COI)) and infant well-child check (WCC) attendance and adolescent obesity.

**Methods:** Electronic health record (EHR) data from Duke University Health System (DUHS) from 2014-2018 was linked to the 2014 SVI, 2015 ADI, and 2015 COI 2.0 (coded so higher scores indicate greater disadvantage) based on patient address at the census tract level. Included patients lived in Durham and were 0-15 months old for WCC and 11-17 years for obesity. Outcomes were: 1) WCC attendance: attending less than six WCC in the first 15 months of life, and 2) Adolescent obesity: BMI  $\geq$  the 95<sup>th</sup> percentile at both the most recent encounter and a prior encounter 9-36 months earlier. Multivariate logistic regression models quantified the associations.

**Results:** Of the 14961 patients in the obesity cohort, 20% ( $n=2933$ ) were obese. Of the 10175 patients in the WCC cohort, 20% ( $n=2073$ ) had less than six WCC. The median (IQR) decile SVI, ADI, and COI for Durham County tracts were 5 (2-9), 4 (2-6.75), and 5 (2-9), respectively. All three indices were associated with both obesity and WCC. Each index decile increase was associated with 10-12% greater odds of meeting the WCC measure and 5-8% greater odds of adolescent obesity (Table 1).

**Conclusions:** Higher social risk as defined by all three indices was similarly associated with both adolescent obesity and infant WCC. While these results suggest that the indices may be used interchangeably, results may differ in other geographic areas with greater heterogeneity in index scores.

**Table 1. Adjusted odds ratios and confidence intervals for increasing deciles of each index<sup>◇</sup>**

	Obese	Well Child Check Measure*
	Adjusted ** odds ratio (95% CI)	Adjusted *** odds ratio (95% CI)
<b>SVI</b>	1.05 (1.04-1.08)	1.10 (1.08-1.12)
<b>ADI</b>	1.08 (1.06-1.10)	1.10 (1.08-1.12)
<b>COI</b>	1.07 (1.05-1.08)	1.12 (1.10-1.14)

◇ ADI rolled up to census tract level to align with COI and SVI geographies; all indices coded so that higher scores indicate greater disadvantage

\* < 6 well child checks in first 15 months of life

\*\* adjusted for age, sex, race, ethnicity

\*\*\* adjusted for sex, race, ethnicity

**Deepening measures of structural racism to include laws that shape racialized inequities**

Taylor Riley\* Taylor Riley Mienah Z. Sharif Anjum Hajat

**Introduction:** The study of structural racism and its health consequences is rapidly expanding in epidemiology. Recent studies measuring structural racism take distinct analytic approaches (e.g. index, latent class) that include indicators reflective of social determinants of health (e.g. education inequities between the Black and White population). While the most frequently used measures, these area-based inequities capture a spatialized *outcome* of structural racism rather than how structural racism operates through and is embedded in laws and policies. Thus far, no studies have compared how structurally racist policies align with and shape the frequently used manifestations of structural racism at the same geographic level.

**Methods:** We utilized the Dr. Madina Agenor et al.'s 2021 database of structural racism-related state laws and compared those to state-level indicators of racialized inequities derived from the American Community Survey, Vera Institute of Justice, and the National Conference of State Legislatures. We conducted a latent profile analysis, which assumes collinearity among the observed state-level indicators of inequities that jointly capture structural racism as a latent construct. State-level latent profiles were compared to frequency and type of state laws.

**Results:** Preliminary analyses using indicators of structural racism identified five latent profiles of structural racism across the 50 states. Most states across all latent profiles had enacted laws that disproportionately discriminate against and criminalize racially minoritized people. Policy analyses are in progress.

**Discussion:** While there is unlikely to be a single best operationalization of structural racism, understanding the relationships between active processes of structural racism via laws versus area-based inequities that are manifestations of structural racism will advance the alignment of theory and measurement of structural racism and its translation to policy.



**Historic redlining and accelerated biological aging in the Health and Retirement Study**

Helen C.S. Meier\* Helen Meier Jessica Faul Colter Mitchell Bruce Mitchell Jeffrey Wing Margaret Hicken

**Introduction:** Historic redlining resulted in social divisions of property and power that have perpetuated inequalities in social and economic resource distribution resulting in intense racial residential segregation and disparities in place-based resources.

**Objective:** To examine if historic redlining, a marker of institutional racism, is associated with DNA methylation-based age acceleration (DNAmAA), an indicator of accelerated biological aging.

**Methods:** The Health and Retirement Study (HRS) is a nationally representative sample of US adults over the age of 50. Analyses were conducted on a subsample of participants living in urban areas in 2016 with historic redlining data, DNAmAA measurement, and non-missing information on covariates (N=2,146). We calculated a historic redlining score from the weighted sums of the proportion of Home Owners' Loan Corporation (HOLC) graded areas within each census tract. A 5-level categorical variable was created using an indicator for urban area ungraded tracts and historic redlining scores segmented into four equal intervals. Weighted linear regressions were used to examine the association between redlining interval (referent= low redlining) and DNAmAA from thirteen epigenetic clocks adjusting for age, gender, race/ethnicity, and cell composition. A combined race and redlining variable evaluated the association of redlining for Black participants vs. non-Hispanic Whites.

**Results:** Greater historic redlining was significantly associated with DNAmAA for three of the 13 epigenetic clocks, including GrimAge, DunedinPoEm and Zhang. Black participants living in historically redlined census tracts, low redlining tracts, and urban ungraded tracts had greater DNAmAA than non-Hispanic Whites living in low redlining tracts for GrimAge and DunedinPoEM.

**Conclusions:** Redlining, a historic racist policy and determinant of present-day place-based resources, was associated with accelerated biological aging, a possible indicator of weathering.

**Examining the Interaction of Anticipatory Racism Threat and Racial Discrimination on Mental Health among African American Women** Amanda D. Perez\* Amanda Perez Tyan Parker Dominguez Thu T. Nguyen David H. Chae Amani M. Allen

**Pre- and post-move exposure to air pollution and neighborhood socioeconomic status**

Chelsea Liu\* Chelsea Liu Erin E. Bennett Katie M. Lynch Xiaohui Xu Eun Sug Park Qi Ying Richard L. Smith James D. Stewart Eric A. Whitsel Joel D. Kaufman Emma Stapp Melinda C. Power

**Introduction:** Nearly 10% of the U.S. population moves in a given year. We aim to examine the change in neighborhood socioeconomic status (nSES) and air pollution exposures before and after a move.

**Methods:** We included 11,523 participants from the Atherosclerosis Risk in Communities Study with geocoded address data at Visit 2 (V2; 1990-1992) and Visit 3 (V3; 1993-1995). Census tract-level variables reflecting nSES in 1991 and 1994 were obtained from the 1990 census; these values did not change between visits for non-movers. Concentrations of  $PM_{2.5}$ ,  $O_3$  and  $NO_2$  in 1991 and 1994 were estimated at geocoded participant addresses using national or regional universal kriging with land use regression and partial least squares regression; these values changed for non-movers due to time trends in air pollution exposures. We defined long and short distance moves according to whether they moved more or less than the median move distance (4.3 miles).

**Results:** Short-distance movers (N=817) moved to better neighborhoods (+2% census tract % of adults age 25+ with a high school degree, +\$2325 census tract mean family income), while long-distance movers (N=390) moved to worse neighborhoods (-7% census tract % of adults age 25+ with a high school degree, -\$6637 census tract mean family income). On average, non-movers and short-distance movers experienced similar change in air pollution exposures from 1991 to 1994 ( $-1.1\mu g/m^3$   $PM_{2.5}$ ;  $-0.19$  ppb  $O_3$ ;  $+0.7$ ppb  $NO_2$  for both groups). Change in air pollution exposures differed for long-distance movers ( $-1.8\mu g/m^3$   $PM_{2.5}$ ;  $-0.9$ ppb  $NO_2$ ;  $+1.2$ ppb  $O_3$ ).

**Conclusions:** On average, short distance movers relocate to areas with better nSES and similar time trends in air pollution exposure, while long-distance movers relocate to areas with worse nSES and different trends in air pollution exposure. Thus, failure to account for residential mobility could lead to substantial misclassification of these contextual variables.

**Interdisciplinary methods to study a complex environmental health issue: wood pellet production facilities** Anne M Weaver\* Anne Weaver Mallory Turner Taylor Minich Elizabeth D Hilborn Anna Jalowska Ann Chelminski

Emerging complex issues present opportunities for epidemiologists to work collaboratively with scientists from other disciplines. Here, we discuss interdisciplinary methods to study environmental and health impacts of the wood pellet industry. Since 2016, the wood pellet industry has grown by about 60%, with most wood pellet production facilities (WPPFs) located in the Southeastern US. They may be a significant source of water and air pollution that impacts the health of local communities. Residents of communities where WPPFs are located have also expressed concerns about environmental injustice. However, the environmental and health impacts of WPPFs have not been systematically characterized in the scientific literature.

Geospatial experts will map locations of WPPFs and source forests in the Southeastern US. These data will be linked to Census-based data on demographics and socioeconomic status of local populations, existing air pollution data, water quality data, and watershed data to assess environmental and environmental justice impacts of WPPFs. Epidemiologists will then use Medicare data to conduct an ecologic study of potentially related health outcomes (asthma, COPD, cardiovascular disease, mortality) in communities with WPPFs before and after WPPFs became operational. Social scientists will interview community members to better understand environmental, social, economic, and health concerns of impacted populations. Finally, exposure scientists, epidemiologists, and medical experts will measure individual-level air pollutant exposures and health metrics, assessing potential associations.

Interdisciplinary teams are required to fully understand the scope of emerging environmental and health concerns. As epidemiologists, we have immense opportunities to collaborate with scientific colleagues.

This abstract does not necessarily reflect EPA policy.

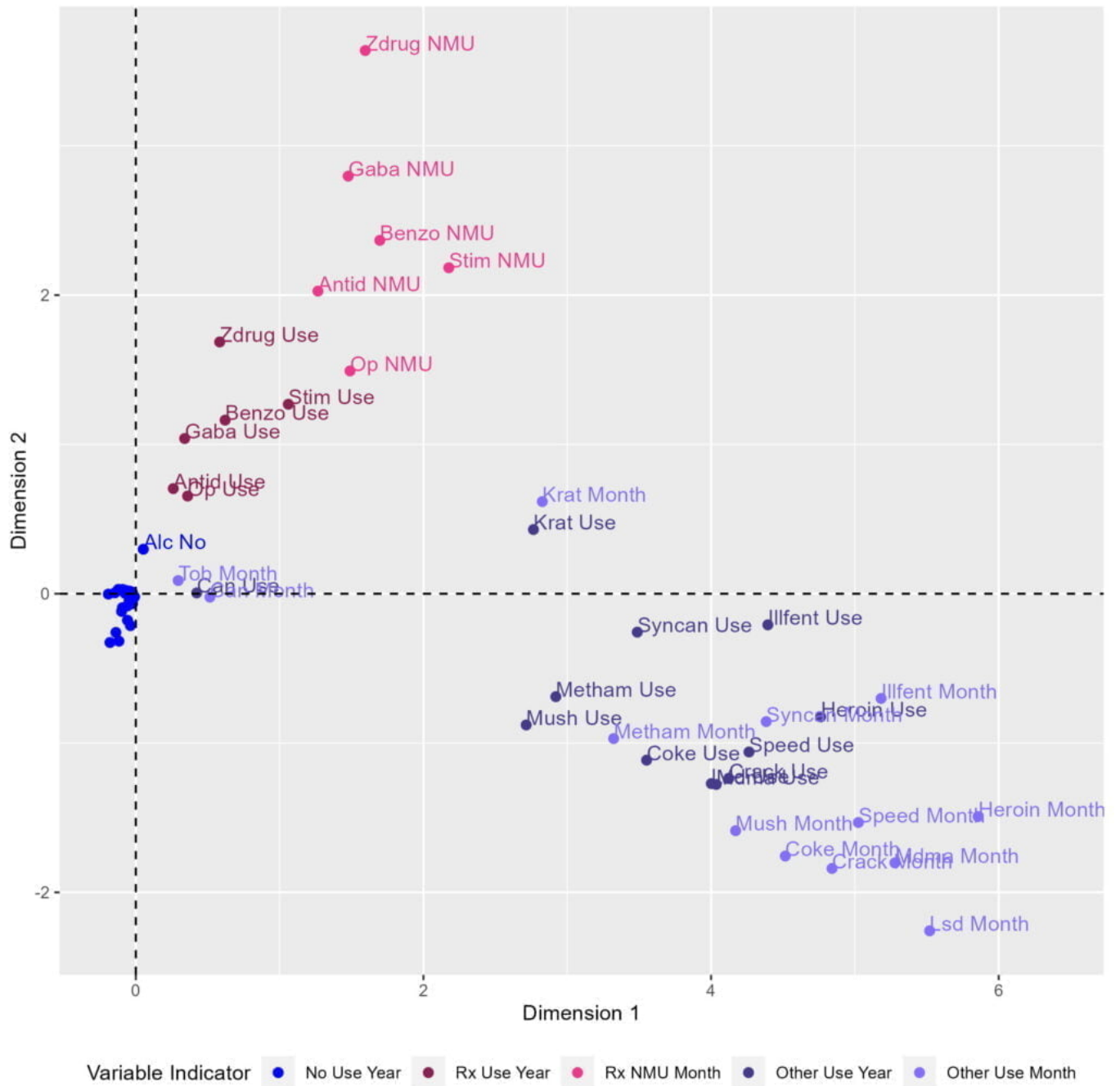
**How should we define polysubstance use? Using dimensionality reduction methods to remove the guess work** Karilynn M Rockhill\* Karilynn Rockhill Janetta Iwanicki Alison Abraham Joshua C. Black

**Background:** The drug epidemic is evolving, and polysubstance use is growing and is associated with unmet healthcare needs, substance use disorders, and mortality. However, no uniform definition of polysubstance use exists, often studies including either type of drug or frequency of use. Our objective was to discover patterns of drug use in the general population to inform future definitions of observed present-day polysubstance use.

**Methods:** We used a national drug use survey among adults (18+), the RADARS® System Survey of Non-Medical Use of Prescription Drugs Program. Those who reported  $\geq 1$  last year drug use were included (N=47,321). A multiple correspondence analysis, a principal components method, was conducted to allow data-driven combinations across the 20 most prevalent drugs and frequency measures of last year (6 prescription, cannabis, 11 illicit, alcohol), and month use (additionally tobacco) to emerge.

**Results:** Last year alcohol use was most common (46.3%), then cannabis (21.4%), and prescription opioids (21.4%), while illicit drugs were  $< 1.8\%$ . Overall, 65.5% reported  $\geq 2$  drugs used. The first two dimensions explained 15.2% and 6.3% of the variance. Dimension 1 seemed to characterize perception of risk; values increased across prescription drug use to non-medical use to illicit drug use (Figure). Dimension 2 separated all prescription drug use from a progression of illicit pain relievers to stimulants and psychedelics, possibly separating by neurologic effect. Recency of use did not define dimensions. Alcohol use did not appear with other drugs, indicating it did not explain drug combinations.

**Discussion:** Polysubstance use is a highly prevalent and widely varied behavior. We observed that drug choice mattered in defining use combinations, but frequency did not. An apparent neurologic separation appeared which deserves more exploration. Polysubstance drug use definitions should identify individuals by use of either prescription or illicit drugs but not alcohol.



**Examining the alcohol harm paradox: socioeconomic position, heavy drinking and 100% alcohol-attributable emergency department visits in Canada from 2000-2017** Erin Hobin\*  
Erin Hobin Christine Warren Alessandra Andreacchi Brendan Smith

**Background:** Lower socioeconomic groups have higher rates of alcohol-attributable harm despite reporting lower alcohol use. Heavy drinking is one proposed explanation for this “alcohol harm paradox”, however this has not been quantified in Canada. Our objective was to estimate the joint effect of socioeconomic position (SEP) and heavy drinking on 100% alcohol-attributable emergency department (ED) visits.

**Methods:** We conducted a cohort study among current and former alcohol consumers aged 15-64 living in Ontario and Alberta from Canadian Community Health Surveys (CCHS, 2000-08) linked to ED records through 2017. SEP was measured using equivalized household income quintiles. We used Fine and Gray subdistribution hazard models to estimate the association between income and incident 100% alcohol-attributable ED visits, with all-cause mortality as a competing risk. We estimated the interaction between dichotomized income (quintiles 1-3 (low) vs. 4-5 (high)) and heavy drinking ( $\geq 5$  standard drinks in an occasion  $\geq$  once a month in the past year) on ED visits. Canadian population weighted and bootstrapped models were adjusted for age, sex, marital status, immigration, rurality, province and cycle.

**Results:** An inverse gradient was observed between income and 100% alcohol-attributable ED visits, ranging from 2.4 (95%CI:1.4,2.4) to 1.2 (95%CI:1.0,1.5) times greater in quintile 1 (lowest) and quintile 4 compared to quintile 5 (highest), respectively. Relative to high income non-heavy drinkers, the risk of 100% alcohol-attributable ED visit was highest among low income heavy drinkers (HR=5.0, 95%CI:4.0,6.2) followed by high income heavy drinkers (HR=3.0, 95%CI:2.5,3.6), with elevated risk also observed in low income non-heavy drinkers (HR=1.6, 95%CI:1.3,1.9)

**Conclusions:** The association between low SEP and 100% alcohol-attributable ED visits cannot be explained by heavy drinking in Canada. Research on other potential mechanisms is required to understand the alcohol harm paradox.

**Initiation of medications for opioid use disorder in commercially insured individuals with opioid use disorder** Marissa Seamans\* Marissa Seamans

Medications for opioid use disorder (MOUD) are safe and effective but underutilized in the US. We examined disparities in MOUD use among commercially insured patients. We conducted a retrospective cohort study of patients 16 years or older who were diagnosed with OUD between 2016-2019 using the OptumLabs Data Warehouse. Patients were required to have continuous enrollment with prescription drug coverage and no previous OUD diagnosis or use of MOUD (buprenorphine/naloxone, methadone, and extended-release naltrexone) in the 180 days prior to OUD diagnosis. We examined characteristics associated with MOUD initiation using modified Poisson regression. Of the 42,782 patients with an initial OUD diagnosis between 2016-2019, the median age was 56 years, 50% were female, 58% were White, 10% were Black, and 6% were Hispanic. The most common comorbidities were anxiety (34%), depression (31%), and Hepatitis C (29%). Overall, 8% initiated MOUD within 30 days of OUD diagnosis. Patients with mental health comorbidities were more likely to initiate MOUD than those without comorbidities. Compared to White patients, Hispanic patients were less likely to initiate any MOUD (aRR: 0.83, 95% CI: 0.72-0.96), and median days supply of buprenorphine was lower (10 days versus 14 days). Treatment length was also shorter among Hispanic patients than White patients (median length: 118 days versus 139 days). Our results suggest that MOUD continues to be underutilized among commercially insured patients, particularly Hispanic patients. Understanding factors underlying disparities in MOUD use is needed to inform interventions to close these treatment gaps.



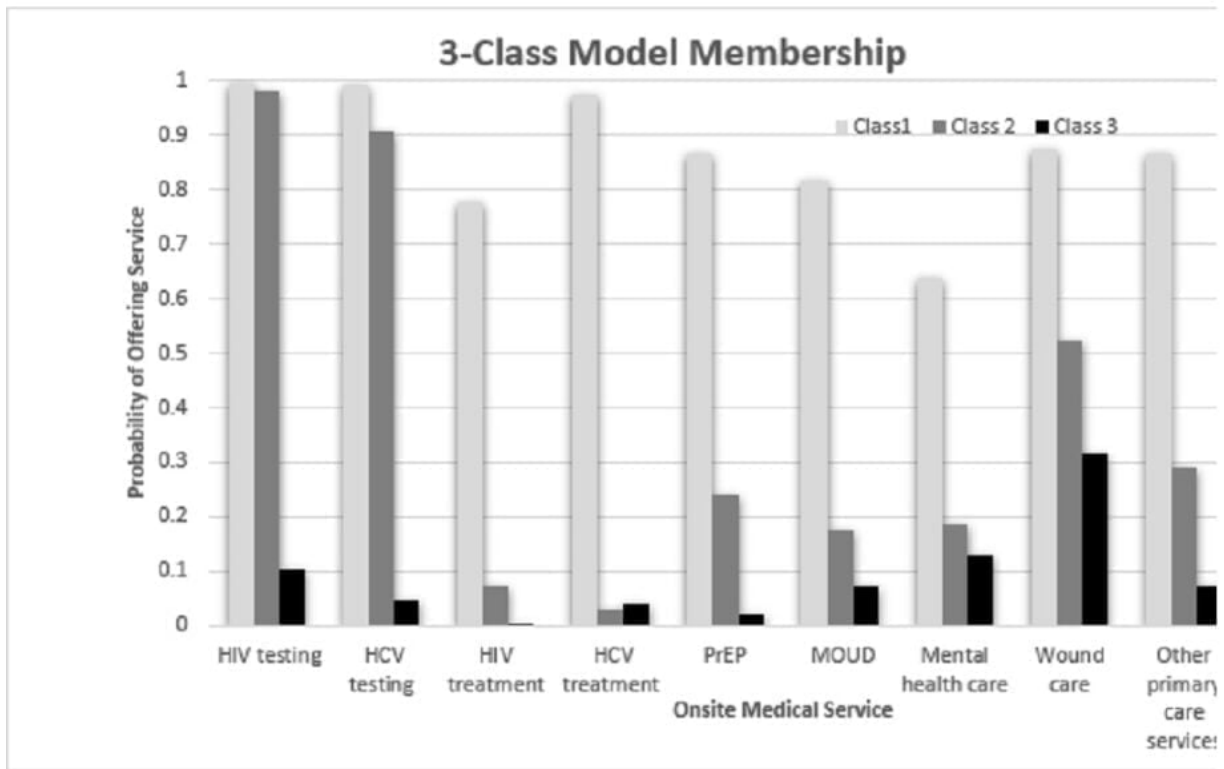
**A latent class analysis of health service delivery models at syringe services programs in the United States** Czarina Behrends\* Czarina Behrends Don C. Des Jarlais Xinlin Lu Grace Corry Sara N. Glick Shashi N. Kapadia David C. Perlman Bruce R. Schackman

People who use drugs have a high need for health care services but insufficient access to these services. Syringe services programs (SSPs) are places where health services may be provided, but little is known on what health service delivery models are most common at SSPs.

We used the national Dave Purchase Memorial survey (N=153) to identify health services offered at SSPs in 2019. Health model classes were defined by combinations of health services offered on site, including HIV and hepatitis C testing and treatment, HIV pre-exposure prophylaxis, wound care, other primary care, medications for opioid use disorder, and mental health care. We conducted a latent class analysis, using measures of BIC, AIC, and entropy to determine the best fit class model. We assessed the association between SSP characteristics (i.e., organization type, geography, public funding, program size, and budget) and class membership using multinomial logistic regression.

A 3-class model was the best fit model. The three classes included 1) a broad health service model with a high probability of offering all health services (11%), 2) a moderate health service model with a high probability of providing HIV/HCV testing and wound care, and a lower probability of offering other services (57%), and 3) a minimal health service model with a low probability of offering any health services (32%). SSPs with over 50% of funding from public funds had higher odds of a broad health service model (OR=9.1, 95% CI:1.1, 78.2) and a moderate health service model (OR=5.9; 95% CI:1.1, 33.6) than a minimal health model. Rural SSPs had lower odds of having a broad health service model than a minimal service model (OR=0.08; 95% CI:0.01, 0.93).

Rural SSPs and SSPs with less public funding may need resources to implement more robust health models. Recent expansion of public funding provides an opportunity to expand medical services to SSP clients. Future research will describe these health models in more detail.



## **Clinical Characteristics and Outcomes of Veterans Hospitalized with Alcohol Withdrawal**

Kirsha S. Gordon\* Kirsha Gordon Matthew Ronan Michael Krug Patrick Godwin Daniel Heppe Matthew Hoegh Joel C. Boggan Jeydith Gutierrez Perez Micah Pescetto Peter J. Kaboli Michelle Guidry Peter Caldwell Christine A. Mitchell Erik Ehlers Nazima Allaudeen Jessica E. Cyr Andrea Smeraglio Peter Yarbrough Richard Rose Anand Jagannath Jaclyn Vargas Paul B. Cornia Meghna Shah Matthew Tuck Cherinne Arundel James D. Laudate Joel Elzweig Benjamin A. Rodwin Joyce Akwe Meredith Trubitt Mary Charles Craig G. Gunderson

### **Background**

Alcohol withdrawal (AW) is a common reason for hospitalizations in the Veterans Health Administration (VHA). Little is known about optimal management for AW due to scarcity of evidence and variation in treatment protocols. Also lacking is the risk of poor outcomes such as ICU transfer, complicated withdrawals, and treatment duration. We sought to describe patient characteristic and determine factors associated with treatment duration and complicated withdrawal.

### **Methods**

We used data collected from the Alcohol withdrawal study (AWS), a cohort of hospitalized patients with chart review confirmed AW from 19 VHA sites across the US. Treatment duration was the total number of days of treatment, defined as last date minus first date of receiving AW medication. Complicated withdrawal (CW) was defined as having delirium and/or seizure at admission (yes/no). Using a Poisson model, factors associated with treatment duration were examined, and a logistic regression model was used to examine factors associated with CW. Both models included demographic, clinical characteristics, treatment type, and medications.

### **Results**

There were 594 patients with confirmed AW of whom 96 % were male, 74% white, and 60% unemployed. More than half had an AW admission in the prior year. Prior delirium, ICU admission, and AW medications (Ativan, Phenobarbital, and Gabapentin) were associated with longer treatment duration. In contrast, symptom triggered treatment was associated with lower treatment duration. Odds of CW were higher in patients with prior delirium (AOR [95% CI]=2.30 [1.21, 4.39]), prior seizures (2.10 [1.13, 3.92]), Thrombocytopenia, (2.17 [1.24, 3.81]), and Black patients compared to white (3.11 [1.52, 6.38]).

### **Conclusions**

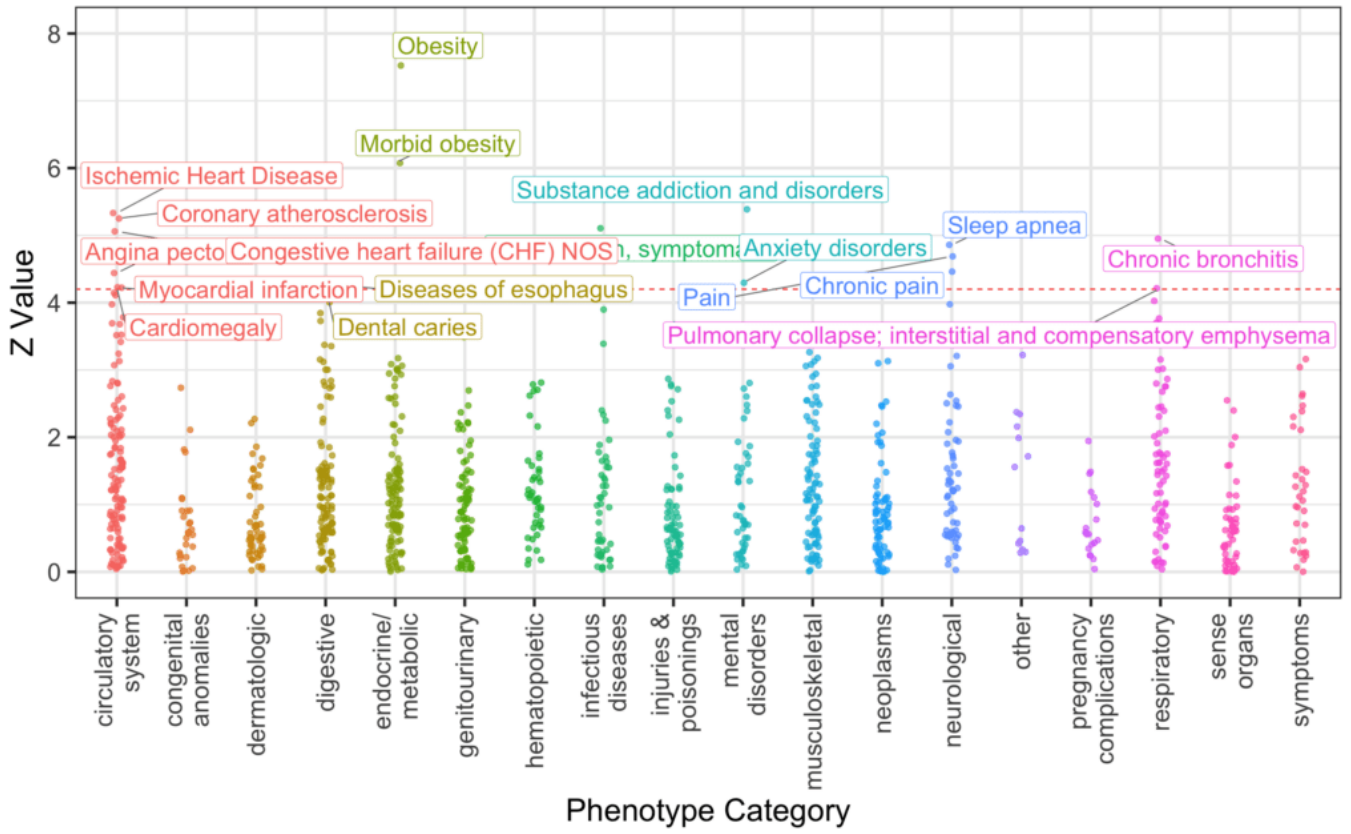
In a national sample of patients hospitalized with AW, history of delirium was associated with both longer treatment duration and CW. For treatment duration, attention to medication will be important. Future work is needed to better prevent CW in Black patients.

**Polygenic scores for tobacco use provide insights into systemic health risks in a diverse EHR-linked biobank in Los Angeles** Vidhya Venkateswaran\* Vidhya Venkateswaran Kristin Boulter Yi Ding Ruth Johnson Arjun Bhattacharya Bogdan Pasaniuc

Tobacco use is heavily influenced by environmental factors with significant underlying genetic contributions. Here, we use a polygenic score (PGS) for tobacco use disorder (TUD) trained in European ancestry individuals from UK Biobank to study the effects of tobacco-use-predisposing genetic variants in UCLA ATLAS - a multi-ancestry, hospital-based biobank (Johnson et al Gen Med 2022). We evaluate the predictiveness and potential shared effects of the PGS across 1847 phecodes (aggregated ICD-codes) extracted from the electronic health records of ATLAS participants (n=26,517)

We find that TUD-PGS is associated with TUD phecode in European American (EA) (OR: 1.22, CI: [1.18, 1.27]), Hispanic/Latin American (HL) (OR:1.21, CI: [1.13, 1.31]), and East Asian American (EAA) (OR: 1.23, CI: [1.08, 1.40]) genetically inferred ancestry groups (GIAs) but not in African American (AA) GIA. (OR: 1.05, CI: [0.90, 1.22]). TUD-PGS offered strong risk stratification across PGS quantiles in the EA and HL GIAs but inconsistently in EAA and AA GIAs. In a cross-ancestry phenome-wide association meta-analysis (PheWAS), TUD-PGS correlated primarily with cardiac, respiratory, psychiatric, and metabolic phecodes (21 phecodes at  $P < 2.57e-5$ ). In a PGS-PheWAS of **never-smokers**, TUD-PGS was associated with obesity and alcohol-related disorders ( $P = 3.54E-07$ ,  $1.61E-06$ ). Mendelian Randomization (MR) analysis provides evidence of a causal association between tobacco use and adiposity measures.

The inconsistent performance of this TUD-PGS in non-European ancestries suggests that equitable clinical translation of TUD-PGS mandates the inclusion of diverse ancestries at all levels of TUD genetic research. Associations between TUD-PGS and obesity and alcohol use disorder **in the absence of smoking behavior** suggest shared biological pathways between these traits. Consequently, TUD-predisposed individuals may require comprehensive tobacco use management approaches to address underlying addictive tendencies.



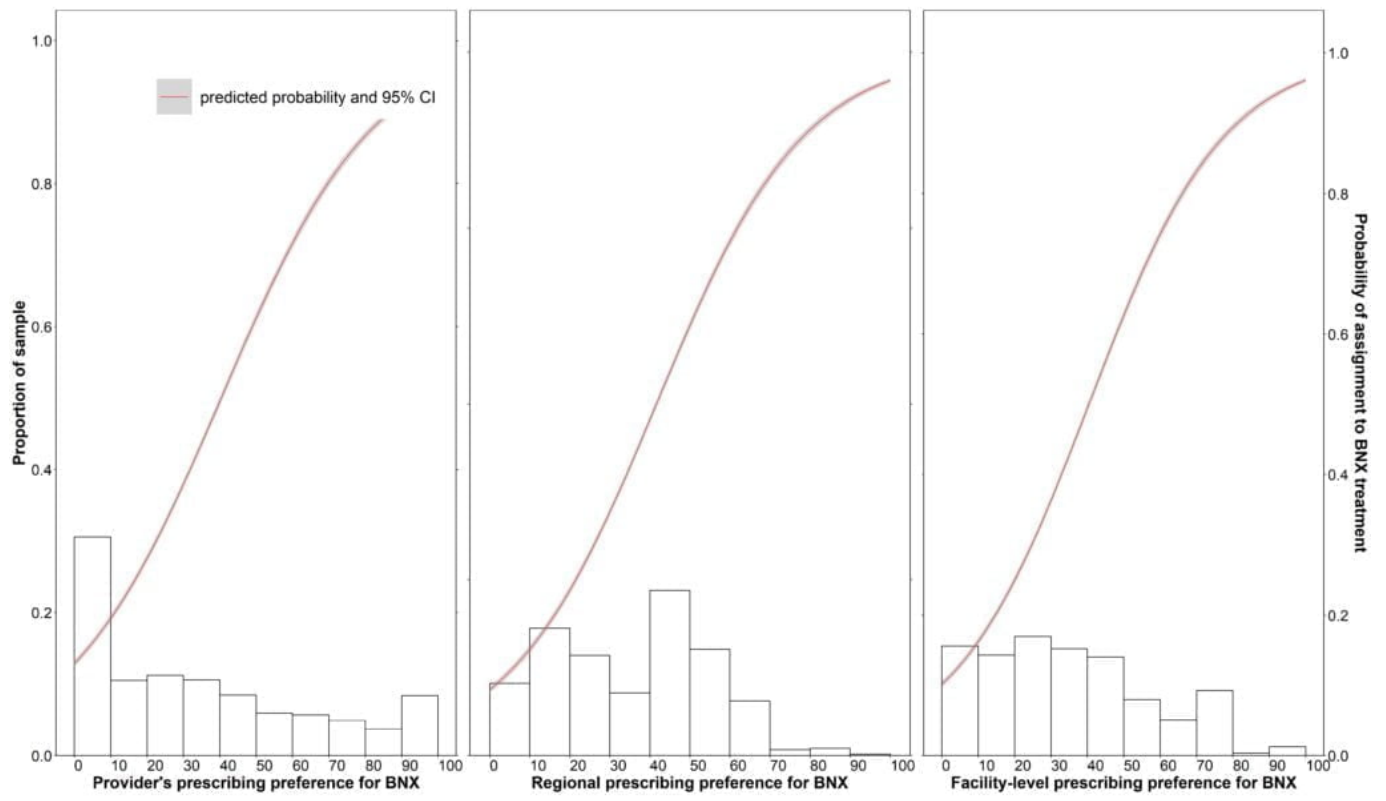
**Comparative analysis of instrumental variables on the assignment of buprenorphine/naloxone or methadone for the treatment of opioid use disorder** Fahmida Homayra\* Fahmida Homayra Benjamin Enns Jeong Eun Min Megan Kurz Paxton Bach Julie Bruneau Sander Greenland Paul Gustafson Malcolm MacLure Lawrence McCandless Kevin Schnepel Hitoshi Shigeoka Uwe Siebert Eugenia Socias Evan Wood Bohdan Nosyk

**Background:** Instrumental variable (IV) analysis provides a means of addressing uncontrolled confounding by indication. Our objective was to evaluate the suitability of prescriber preference and calendar time as potential IVs to evaluate the comparative effectiveness of buprenorphine/naloxone versus methadone for the treatment of opioid use disorder (OUD).

**Methods:** Using linked population-level health administrative data we constructed five IVs: prescribing preference at the individual, facility, and region level (continuous and categorical variables), calendar time, and a hybrid IV for an intent-to-treat analysis using both incident-user and prevalent-new-user designs. The primary outcome was treatment discontinuation. Using published guidelines, we assessed and compared each IV according to the four necessary assumptions for IVs using both empirical assessment and content expertise. We confirmed the robustness of our results through a series of sensitivity analyses.

**Results:** The study sample included 35,904 incident-users (43.3% on buprenorphine/naloxone) initiated on opioid agonist treatment by 1,585 prescribers during the study period. We found that while all candidate IVs were strong (A1) according to conventional criteria, assumptions of exclusion (A2), independence (A3), monotonicity (A4a) and homogeneity (A4b) were upheld for prescribing-preference-based IV but did not hold for calendar-time-based IV, by empirical criteria and expert opinion, respectively. We determined that provider-level-prescribing preference, measured on a continuous scale, was the most suitable IV for the comparative effectiveness of buprenorphine/naloxone and methadone for the treatment of OUD.

**Conclusions:** This study demonstrates the suitability of measures of prescriber preference as IVs in comparative effectiveness studies of treatment for OUD.



**Estimation of prevalences of opioid misuse in New York State counties** Julian Santaella-tenorio\* Julian Santaella-Tenorio David M. Kline Staci Hepler Ariadne Rivera Magdalena Cerda

**Introduction:** An important challenge to addressing the opioid overdose problem is the lack of information on the size of the population misusing opioids (people using illegal opioids or prescription opioids without a prescription) in local areas. In this study we aimed to estimate the prevalence of people misusing opioids in New York State (NYS) counties applying newly published methodology.

**Methods:** We used 2010-2018 NYS-level data on the prevalence of opioid misuse, and county-level data on opioid-related outcomes (patients receiving buprenorphine and methadone, fatal and nonfatal opioid overdoses) and covariates that could predict these opioid-related outcomes and also opioid misuse. To estimate the prevalence of people misusing opioids we used a Bayesian spatio-temporal integrated abundance model. This model assumes that each opioid-related outcome reflects a partial count of the number of people misusing opioids. Similar to capture-recapture, we leverage multiple sources of partial information to infer the size of the hidden population of interest - people misusing opioids. Using this model, we integrate data from multiple aggregate data sources while accounting for spatio-temporal dependence, covariates, and spatial scale. Estimation of the count of people who misuse opioids provides us with the denominator needed to estimate rates of each outcome among the affected population of interest.

**Results:** Most counties experienced a reduction in the prevalence of opioid misuse from 2010-2018 (Figure 1). Overall, the highest prevalences were observed in the Hudson Valley area, in Niagara and Genesee counties. The rate of opioid overdoses among the people misusing opioids greatly increased in southern NYS, and in Erie and Rochester counties.

**Conclusions:** Using multiple sources of aggregate data we estimated the population misusing opioids in NYS counties. This information can be used to better understand the needs across counties and improve the allocation of resources.

**Figure 1. Estimated rate of opioid misuse in New York counties**





**Demographic/Health Characteristics and Medical Marijuana Product Use Patterns among Individuals with and without Chronic Pain: Findings from a Statewide Survey** Kendall

Robinson\* Kendall Robinson Yan Wang Robert Cook Hannah Fechtel Ruba Sajdeya Gabriel Spandau

**Background:** Chronic pain is among the most common reasons for using medical marijuana (MMJ). However, there are limited data on patient characteristics, comorbidities, and MMJ product use patterns associated with using MMJ for chronic pain. This analysis aimed to compare these variables between people using MMJ for chronic pain versus others.

**Method:** A total of 632 physician-certified MMJ users were recruited across the state of Florida and completed the cross-sectional survey of the Medical Marijuana & Me (M<sup>3</sup>) Study. 278 participants indicated chronic pain as a main reason for using MMJ. T-tests and chi-square tests were used to compare demographic characteristics and product use patterns between groups.

**Results:** Individuals using MMJ for chronic pain were significantly older than those using it for other reasons (mean (SD): 50.1 (12.8) vs. 43.2(14.8),  $p < 0.0001$ ). Other demographic characteristics did not differ between the two groups. Individuals with chronic pain also reported higher numbers of diagnosed health conditions (mean (SD): 5.5(2.3) vs. 3.6 (2.1),  $p < 0.0001$ ) and were more likely to report problems related to sleep or insomnia (56.5% vs. 39.0%,  $p < 0.0001$ ). Individuals with chronic pain were more likely to report using MMJ for “mostly or completely medical” motives (80.2% vs. 61.0%,  $p < 0.0001$ ) rather than recreational motives. The three most frequently used products for individuals with chronic pain were flower (86.9%), vape (77.9%), and edibles (64.8%), which did not differ from those using MM for other conditions. Both groups used MMJ with primarily or only THC rather than a balanced ratio of CBD vs. THC or CBD-dominant products.

**Conclusions:** In our study, individuals who use MMJ for chronic pain were older, had more diagnosed comorbidities, and were more likely to use THC-dominant products. Additional research evaluating the safety and efficacy of high-THC products in older adults with chronic pain and other comorbidities is warranted.

**Impact of tobacco 21 and flavor restrictions on youth tobacco use** Summer Hawkins\* Summer Hawkins Naoka Carey Rebekah Levine Coley Christopher F. Baum

Declining trends in use of conventional tobacco products among youth have been increasingly countered by electronic nicotine delivery systems (ENDS). Innovative tobacco control policies have been proposed to curb rising levels.

Using 2011-2021 data on 256,409 18-24-year-olds from 50 states and DC in the Behavioral Risk Factor Surveillance System, we conducted fixed effects probit regression models to examine the impact of tobacco 21 (state and Federal T21) laws and flavor restrictions on cigarette, smokeless tobacco, and ENDS use controlling for demographics, other tobacco control policies, time trends and state fixed effects. We included interactions to test differential effects of T21 laws by age (18-20 vs 21-24). We report average marginal effects from adjusted regression models.

The Federal T21 law decreased use of cigarettes (-0.016 [-0.027, -0.004]) and smokeless tobacco (-0.012 [-0.019, -0.005]) overall. A significant interaction ( $p=0.004$ ) revealed larger effects on smokeless tobacco use among 18-20 (-0.018 [-0.025, -0.011]) than 21-24-year-olds (-0.007 [-0.015, 0.001]). Since 2016, ENDS data were available on a subset of 77,617 youth. The Federal T21 law decreased ENDS use (-0.068 [-0.106, -0.030]) overall and a significant interaction ( $p=0.04$ ) indicated larger effects among 18-20 (-0.077 [-0.120, -0.035]) than 21-24-year-olds (-0.053 [-0.093, -0.013]). There was no evidence for effects of state T21 laws or flavor restrictions overall or by age. In sensitivity analyses using data through 2019, prior to the Federal T21 law and COVID-19 pandemic, there were no effects of state T21 laws or flavor restrictions on any outcomes overall or by age.

We found evidence that implementation of the Federal T21 law reduced tobacco use, with larger effects among youth under age 21 who were directly impacted by the law. We will further test components of state T21 laws and flavor restrictions to better understand and inform future iterations of these policies.

**The Impact of Selection Bias on The Relationship Between Quitline Services and Tobacco Cessation** Ami E. Sedani\* Ami Sedani Summer G. Frank-Pearce Sixia Chen Jennifer D. Peck Ann F. Chou Janis E. Campbell Laura A. Beebe

**Introduction:** State quitline effectiveness is evaluated by measuring tobacco abstinence at 7-months post-registration. Follow-up response rates have been decreasing despite utilization of a variety of prevention methods. Restricting the analysis to the uncensored data opens the door for potential selection bias. This study assessed the impact of selection bias on the association between quitline services and tobacco cessation among individuals enrolled in the Oklahoma Tobacco Helpline (OTH).

**Methods:** The study used data for OTH participants who were randomly selected for the 7-month follow-up from April 2020-December 2021. We fit marginal structural models to estimate the effect of intervention intensity on 30-day abstinence, using Inverse Probability of Censoring Weighting (IPCW) to adjust for selection bias. We truncated the total weights to mitigate the influence of extreme weights and to avoid near positivity violations. To facilitate comparison to conventional analyses, the stabilized weighted Risk Ratio (RR) was compared to complete case analysis.

**Results:** The analytic sample included 4,332 individuals and 64% received high intensity cessation services. A total of 2,065 individuals had responded to the follow-up survey with approximately 35% reporting 30-day tobacco abstinence at follow-up. Age, race/ethnicity, health insurance, and time to first tobacco use are measured determinants of censoring and the exposure of interest; therefore, were used for IPCWs. The weighted RR (1.14; CI: 1.02, 1.27) was slightly higher than the complete case RR (1.10; 95% CI: 0.98, 1.23).

**Discussion:** Despite similar point estimates, the IPC weighted confidence interval excluded the null value suggesting that failing to account for selection bias may underestimate the true impact of quitline programs. Findings will have implications for delivering and evaluating quitline services since even a small error in the estimation of effect sizes can greatly impact program decisions.

**Factors associated with carrying naloxone among people who inject drugs in New York City**

Sarah Kimball\* Sarah Kimball Don des Jarlais Courtney McKnight Allen Weng

**Background**

The United States experienced over 100,000 overdose deaths in 2022, with the majority of deaths attributed to opioids. naloxone is an effective medication to reverse opioid overdoses, particularly if used quickly. Carrying naloxone allows for quick access to this vital medication. As the overdose crisis continues, it is important to understand factors that affect carrying naloxone.

**Methods**

Utilizing respondent-driven sampling, people who currently inject drugs in New York City completed a survey on substance use and risk factors for overdose and HIV (n=248). naloxone carrying behavior was measured dichotomously with never/occasionally and often/always. Variables related to demographics, current substance use, overdose history, treatment history, syringe sources, and prior naloxone use and training were analyzed. Bivariate analyses were conducted using logistic regression and a multivariate model was built using purposeful selection.

**Results**

In the sample, 123 (49.6%) reported carrying naloxone often/always. In the bivariate analysis, the odds of carrying naloxone were significantly higher among those who were female, younger, had a history of overdose, used syringe service programs (SSP), had prior naloxone training, ever used naloxone on someone, or used a higher number of different drugs in the past 30 days. In the multivariate model, the odds of carrying naloxone were significantly higher among those who were female (aOR: 2.15; 95% CI: 1.22, 3.86), ever used naloxone on someone (aOR: 2.88; 95% CI: 1.67, 5.03), whose main drug was an opioid (aOR: 2.42; 95% CI: 1.07, 5.72), and used a higher number of different drugs in the past 30 days (aOR: 1.17; 95% CI: 1.05, 1.30).

**Conclusions**

Slightly less than half the sample consistently carried naloxone. Modifiable factors such as SSP access and naloxone training should be further explored as they may increase the odds of carrying naloxone.

**The relationship between marijuana use and permanent tooth loss: A Behavioral Risk Factor Surveillance System 2020 cross-sectional study** Omolara Akingba\* Omolara Akingba  
Eric Bakwa Herve Fossou Noel Weiss

**Background:** According to the CDC, about 5% of adults aged 20-64 years are lacking teeth and 52% have at least one missing tooth. Periodontitis, the leading cause of adult tooth loss, is linked with age, race, gender, and tobacco use. However, little is known about the association between marijuana use and permanent tooth loss. Notably, previous research has not specifically examined the effect of marijuana use method and frequency on permanent tooth loss. This study investigates this association among adults aged 18-64 years using the Behavioral Risk Factor Surveillance System (BRFSS) 2020 dataset.

**Methods:** The exposures, “# of days of marijuana use in the past 30 days” and “how did you use marijuana in the past 30 days”, were in a state-optional module given by 21 states. The outcome, “permanent tooth loss”, was collected by all states in even years. We conducted Mantel-Haenszel stratified analyses adjusting for age, annual household income, and smoking status. We report adjusted prevalence ratios (PR) with 95% CI at a 5%  $\alpha$ -level.

**Results:** Of 92,733 participants with complete data, 38% had lost at least one permanent tooth. 12% reported marijuana use in the past 30 days; 5% (1-10 days), 2% (11-20 days), and 5% (21-30 days). Compared to no marijuana use, the PR of permanent tooth loss was 1.03 (1.00-1.05) for any reported marijuana use, 1.04 (1.01-1.07) for inhalation method, and 1.09 (1.06-1.12) for 21-30 days of past use.

**Conclusions:** We report a near-null association between marijuana use, method and frequency, and permanent tooth loss. Thus, marijuana use is not likely a big driver of permanent tooth loss. Intervention efforts could focus on more prominent potential causes. Due to this cross-sectional design and the short, reported exposure period (30 days), additional research, e.g. longitudinal studies, is required to substantiate these findings.

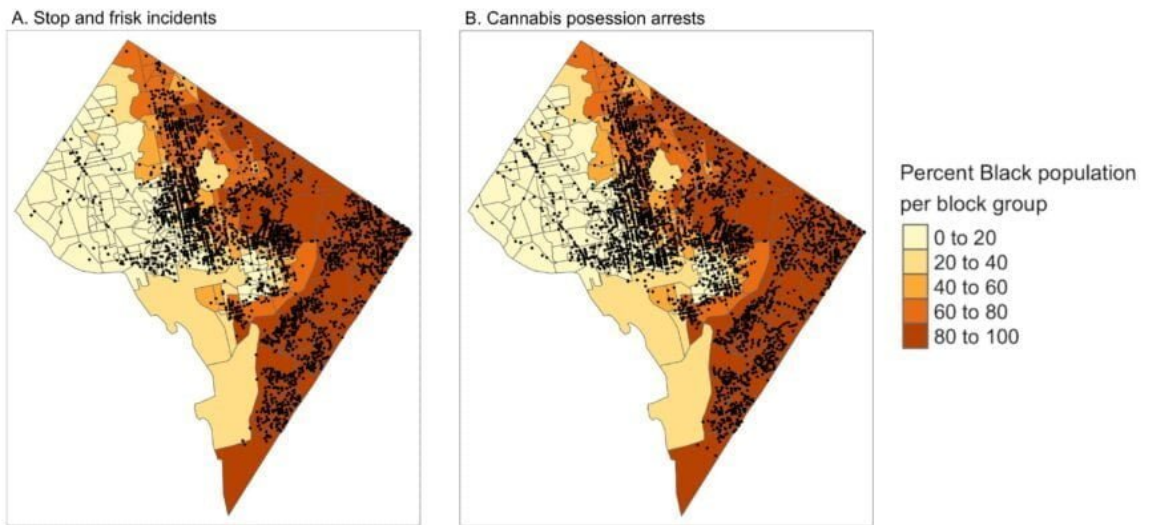
**Spatial relationships between racial disparities in cannabis possession arrests and hot spot policing in Washington, DC 2012-2017** Ariana N Gobaud\* Ariana N Gobaud Christina A Mehranbod Sarah Gutkind Brady Bushover Christopher N Morrison

**Background:** Black and White people use cannabis at roughly the same rate, yet Black people are more likely to be arrested for cannabis possession. Hot spot policing (i.e., concentrating police in areas of higher crime) has been heavily criticized for inequitably targeting minority neighborhoods, resulting in racial disparities in arrests. Decriminalizing cannabis is one intervention that has reduced racial disparities in arrests for cannabis possession among adults. The aim of this study was to determine whether the rate of hot spot policing practices (e.g., stop and frisk) and cannabis arrests changed after cannabis possession was decriminalized in Washington, DC on February 26, 2015.

**Methods:** This cross-sectional ecological study used data from the Metropolitan Police Department on cannabis arrests and stop and frisk incidents for 2012-2017 aggregated within block group years (n = 2,700). We conducted a longitudinal spatial panel analysis using Bayesian conditional autoregressive Poisson models to estimate associations between cannabis possession arrests among adults before and after decriminalization, accounting for spatial dependencies.

**Results:** A total of 8,916 cannabis possession arrests and 10,086 stop and frisk incidents occurred from 2012-2017. Block groups with more stop and frisk incidents had a higher rate of cannabis possession arrests (IRR: 1.015, 95% CI: 1.002, 1.028). There was a significant reduction in cannabis possession arrests after decriminalization went into effect, with a greater decrease for block groups with a higher proportion of Black residents.

**Conclusion:** Cannabis decriminalization has a greater impact on possession arrests in block groups with a greater proportion of Black residents in Washington, DC. A systematic effort to understand the intended and unintended consequences of hot spot policing practices is needed to inform whether it should be continuously used as a proactive policing strategy.



**Figure 1.** Maps of (A) Stop and frisk incidents and (B) Cannabis possession arrests by block group in Washington, DC 2012-2017

**Exploring Application of an Ecologic Study Design for Childhood Lead Exposure****Surveillance in Washington County, Oregon** Lauralee Fernandez\* Lauralee Fernandez Blanca Perez Ryan Ames Kathleen Rees Kimberly Repp

**Background:** Standard childhood lead screening is well structured to identify risks at the household level. However, many risk factors for lead exposure are influenced by sociobehavioral characteristics, including shared culinary practices, and travel habits in communities. In settings where lead exposure associated with community behavior is prevalent, surveillance methods at the aggregate level should be considered for targeted outreach.

**Objective:** To demonstrate and discuss the application of ecologic study design for childhood lead exposure surveillance in a setting where use of imported and traditional goods has previously been a primary exposure source.

**Methods:** We conducted an ecologic study in Washington County, Oregon of elevated blood lead level (BLL) rates in children under 6 years by census tract. We imported 2018-2022 data from Oregon Public Health Epidemiologist User System for children with BLL >5ug/dL . We used population counts from the 2019 American Community Survey to calculate childhood rates of elevated BLL by census tract. Using ArcGIS Pro, we calculated global and local Moran's I with weighting based on inverse distance, polygon continuity, and nearest neighbor (4, 5, and 6) to test if the spatial distribution of rates in census tract were random.

**Results:** We included 102 children with elevated BLL across 104 census tracts. Moran's I was significant with inverse distance of 22350, 22500, and 23500 (P=0.01) meters, with nearest neighbor(4 &5, P=0.01; 6, P=0.02) and with polygon continuity (P=0.02). We identified 4 census tract clusters.

**Conclusion:** Census tract aggregated geospatial clustering analysis of elevated BLL rates among children under 6 years is feasible with existing data and facilitates identification of geographic areas that could benefit from increased lead exposure outreach. Exploration of vulnerability indices, including community characteristics associated with the use of lead containing goods, in these areas is warranted.



**Associations between maternal cervical cancer screening and adolescent HPV vaccination**

Adino Tesfahun Tsegaye\* Adino Tesfahun Tsegaye John Lin Allison M. Cole Adam A. Szpiro Darcy W. Rao Judd L. Walson Rachel L. Winer

**Background:** Less than 2/3 of US adolescents are up to date with HPV vaccination. In general, mothers engaged in preventive care are more likely to seek preventive care for their children. However, the association between maternal cervical cancer screening (CCS) and adolescent HPV vaccination is underexplored.

**Method:** To assess the association between maternal CCS and adolescent HPV vaccination, we used electronic medical record data from a large health system in Seattle, USA (UW Medicine). Adolescents (11-17 years) and their mothers were included if each had  $\geq 1$  primary care visit between 2018-2020. Outcomes were initiation and completion of the adolescent HPV vaccine series. The primary exposure was maternal CCS adherence, defined as up-to-date with guideline-recommended intervals. Secondary exposures were maternal breast cancer screening adherence (restricted to mothers  $\geq 52$  years) and maternal receipt of  $\geq 1$  wellness visit within two years. Poisson regression with robust standard errors adjusted for adolescent age and sex and maternal age was used to estimate prevalence ratios and 95% CIs, and explore effect modification by adolescent sex.

**Results:** Of 4,192 adolescents, 3,453 (82%) initiated HPV vaccination, 2,051 (49%) completed the series, and 3,002 (72%) had a CCS adherent mother. CCS adherence was associated with higher HPV vaccine initiation (aPR:1.11, 95%CI:1.02-1.20) and completion (1.20, 1.08-1.33). Recent maternal wellness visit was not significantly associated with vaccination (initiation:1.03, 0.96-1.10, completion:1.09: 1.00-1.19). There was a non-significant trend towards association of maternal breast cancer screening (n=511 eligible) with vaccine completion (1.23, 0.91-1.66). There was no evidence of effect modification by adolescent sex.

**Conclusion:** The observed association between maternal CCS and adolescent HPV vaccination suggest that integrating HPV vaccination with CCS and other maternal encounters could improve HPV vaccination coverage.

**How is the newborn's weight and length at birth affected by maternal diabetes?** Thomas Skogvold\* Thomas Skogvold Nils-Halvdan Morken Linn Marie Sørbye Rolv Skjærven Kari Klungsøyr

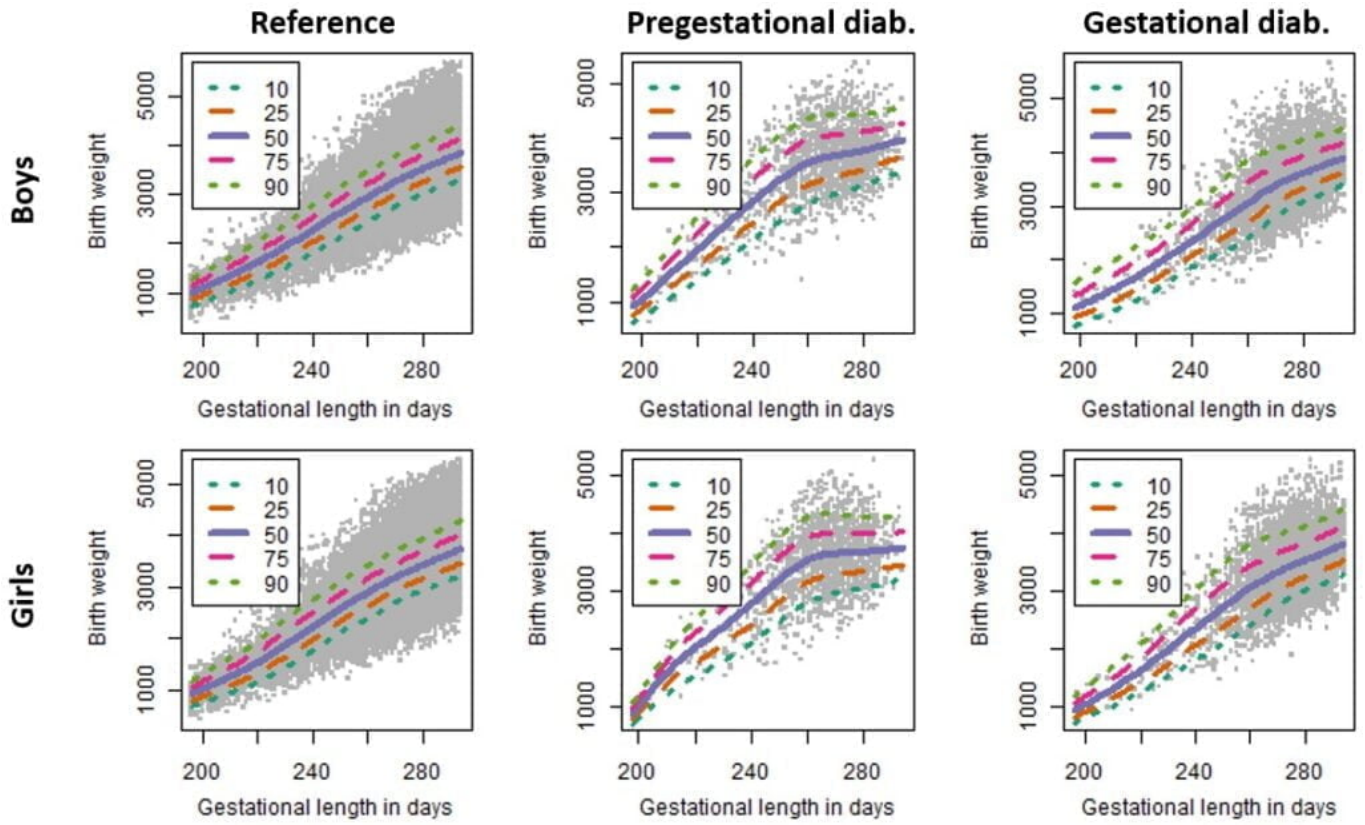
**Introduction:** While gestational diabetes is a complication of the pregnancy, type 1 and type 2 diabetes are chronic conditions. Diabetes during pregnancy is known to increase average birthweight of the fetus. Less is known about whether the different subtypes affect fetal size differentially.

**Aim:** To explore how maternal diabetes subtypes differentially affect fetal weight and length at birth.

**Method:** We identified 483 346 nulliparous women who gave birth to a viable singleton child between 1999-2020 using the Medical Birth Registry of Norway. We studied newborn size in diabetic mothers stratified by infant sex and diabetes subtype (pregestational -type 1 and type 2, or gestational diabetes), with non-diabetic mothers as the reference group. Generalized additive models (GAMLSS) in R were used to describe size by length of gestation. Mean values and 95% confidence intervals (CI) were evaluated by analysis of variance.

**Results:** Among nulliparous women giving birth in Norway 3% were registered with diabetes during their first pregnancy. Of these women 0,7% had pregestational and 2,1% gestational diabetes. Newborn length and weight differed by diabetes subtype (pregestational or gestational). Mean birthweight at week 38 for offspring of non-diabetic mothers (3217g, 95%CI 3213-3220g) was lower than for pre-gestational and gestational diabetes (3641g, 95%CI 3612-3671g and 3381, 95%CI 3363-3400g, respectively). The effects were more pronounced for weight than length at birth. The largest relative difference in size was found among those born between gestational week 28 and 38 (day 196 and 266).

**Conclusion:** In the Norwegian population, maternal pregestational diabetes was associated with higher average birthweight and average body length. Gestational diabetes does not affect weight and length at birth to the same degree.



**LATEBREAKER**

Women's Health

**Racial inequalities in symptoms and additional treatment in a cohort of pre-menopausal women treated with a hormonal intrauterine device** Michael J Green\* Michael Green Mollie E Wood Kemi M Doll Erin T Carey Joacy G Mathias Whitney R Robinson

**Objective:** Hormonal intrauterine devices (IUDs) can be an early treatment for benign gynecological conditions. We investigated racial inequalities in symptoms at time of IUD insertion and more invasive concurrent and follow-up treatments.

**Methods:** With electronic health records from a large healthcare system in the US South (2014-2019) we created a prospective cohort of 907 pre-menopausal women (non-Hispanic White n=525; non-Hispanic

Black n=244; Hispanic n=138; mean ages=32.5, 33.7 and 36.2 years respectively) who had an IUD inserted for a benign gynecological condition. Medical record abstraction provided data on symptoms in

the 4 months before IUD insertion and additional treatments (median follow-up: 1.86 years). Racial inequalities were assessed using chi-square tests and cox proportional hazard models.

**Results:** Compared to White patients, Black and Hispanic patients had more severe bleeding but less severe pain symptoms recorded (Figure), and were more likely to receive the IUD in conjunction with a myomectomy (White: 2.3%; Black: 8.2%; Hispanic: 7.2%;  $p<0.01$ ). We did not find racial differences in hysterectomy rates post-IUD insertion (White: 9.3%; Black: 9.8%; Hispanic: 8.7%;  $p=0.934$ ) or time to

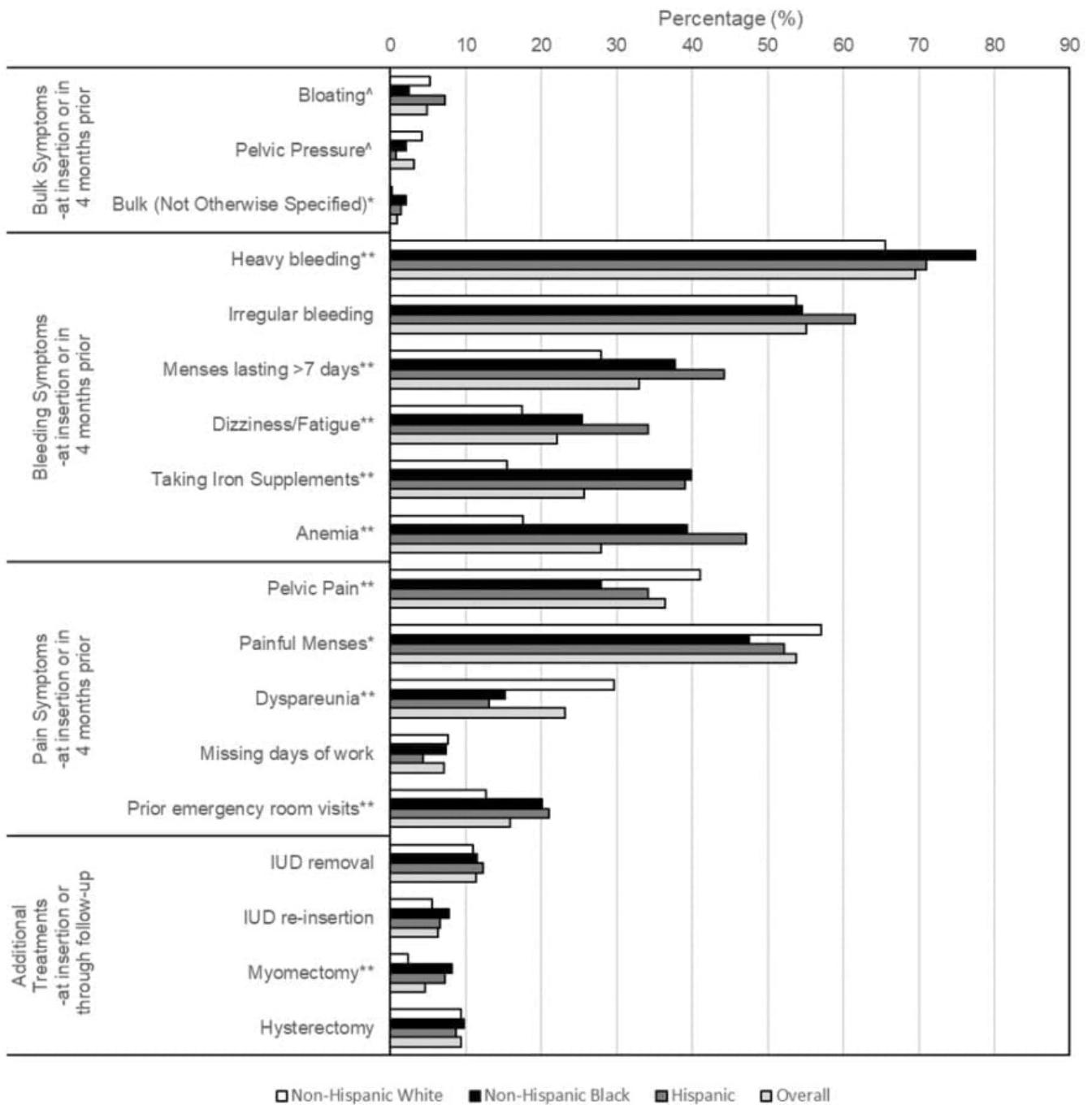
hysterectomy (mean time: 1.2 years; age, symptom and myomectomy adjusted HRs[95% CIs] in reference to White: Black: 0.76[0.45-1.27]; Hispanic: 0.63[0.32-1.23]). Findings on inequalities in symptoms and hysterectomy rates were similar among patients who did not get a myomectomy (n=865).

**Conclusions:** At time of IUD insertion, Black and Hispanic patients had more severe symptoms than White patients, and were more likely to receive the IUD as part of a more invasive procedure.

Nevertheless, hysterectomy rates in years following IUD insertion were similar. Higher prevalence of IUD insertion concurrent with myomectomy indicates that IUDs may be underutilized for Black and Hispanic patients earlier in the clinical course, prior to invasive surgical procedures.

# Racial inequalities in symptoms and additional treatments among IUD patients

P-values for racial inequalities: ^p<0.1; \*p<0.05; \*\*p<0.01



**Access to contraceptives among sex workers in Vancouver, British Columbia** Emma Stirling-Cameron\* Emma Stirling-Cameron Andrea Krusi Jennie Pearson Charlie Zhou Esteban Valencia Shira Goldenberg

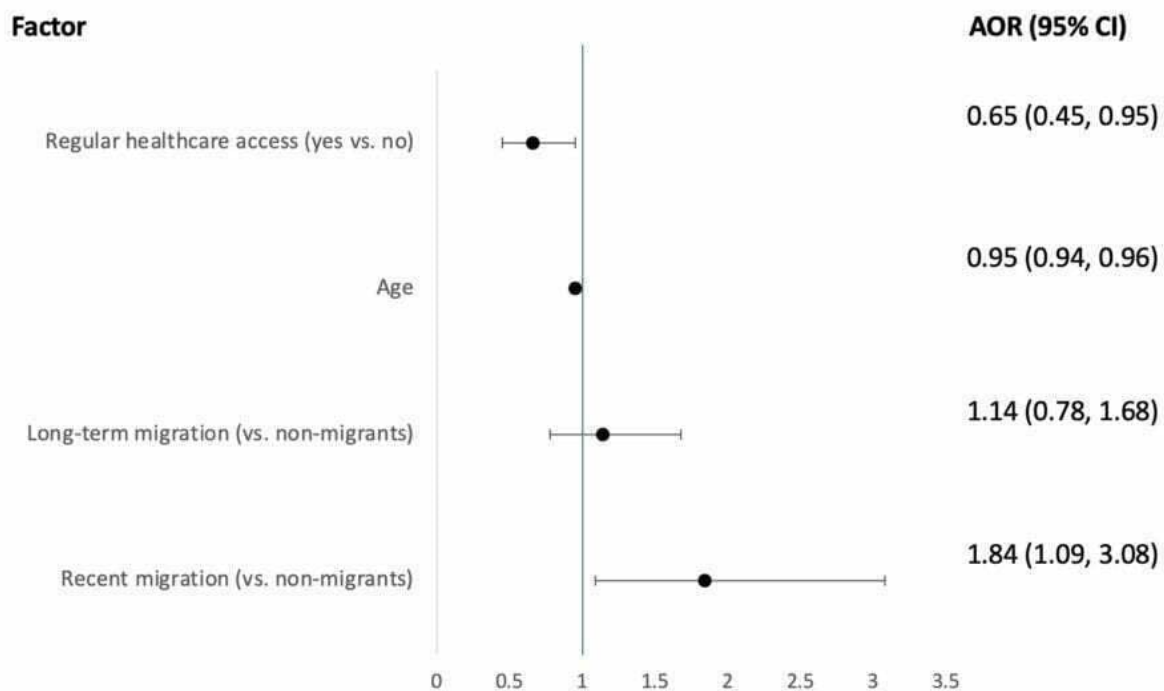
**Background:** Women sex workers (SWs) face substantial health inequities, including reduced access to contraceptives and reproductive healthcare. Migrant women are overrepresented in precarious employment, including sex work, and face additional barriers to healthcare due to intersecting socio-structural factors including immigration status, stigma, and criminalization. Given limited epidemiological evidence regarding socio-structural barriers to non-barrier contraceptive access—including the role of migration—we examined socio-structural factors associated with contraceptive access among a prospective cohort of women SWs in Metro Vancouver, Canada, from 2010-2021.

**Methods:** Baseline and semi-annual questionnaire data were drawn from an open, community-based cohort of women SWs (January 2010 - September 2021). Complete case bivariate and multivariable logistic regression using generalized estimating equations (GEE) modeled socio-structural correlates of experiencing difficulties accessing contraceptives in the past 6 months, including the role of migration timing. Non-barrier contraceptive use included pills, IUDs, injectables, and emergency contraception.

**Results:** Analyses included 7340 observations among 958 SWs. Over the course of follow-up, 22.4% of participants (n = 214) reported difficulties in accessing non-barrier contraceptives. Multivariable GEE analysis indicated that both recent migrants (<5 years; AOR: 1.84, 95% CI: 1.09, 3.08) and long-term migrants to Canada (>5 years; AOR: 1.14, 95% CI: 0.78, 1.68) faced higher odds of experiencing difficulties accessing non-barrier contraceptives. Self-reported regular healthcare access (AOR: 0.66, 95% CI: 0.45, 0.95) and age (AOR: 0.95, 95% CI: 0.94, 0.96) were associated with lower odds of experiencing barriers to contraceptives.

**Conclusion:** To address enhanced barriers to contraceptive access among migrant women in sex work, there is a critical need to expand universal health coverage and scale-up of newcomer-specific, culturally-safe, and confidential sexual and reproductive health services, alongside structural interventions to decriminalize and destigmatize sex work.

**Figure 1: Associations between socio-structural factors and difficulties in accessing non-barrier contraceptives in the last 6 months among women sex workers in Vancouver, BC, 2010 - 2021: Adjusted odds ratios (AORs) and 95% confidence intervals (CIs) from multivariable logistic regression using generalized estimating equations, (n=441).**



**Mortality risk among women with premenstrual disorders: a nationwide population-based matched cohort study in Sweden** Marion Opatowski\* Marion Opatowski Donghao Lu

**Background:** Premenstrual disorders (PMD) are characterized by psychological and physical symptoms occurring few days before menstruation. Despite the negative impact of PMD on women's physical and mental quality of life, the mortality risk has never been explored. Therefore, this study aimed to examine the association between PMD and overall and cause-specific mortality.

**Methods:** Leveraging national Swedish registers, we conducted a cohort study of women diagnosed with PMD during 2001-2018 randomly matched with 5 PMD-free women on year of birth. PMD were identified from in-/outpatient diagnoses and drug dispensing. Individuals were followed through 2018 for deaths, ascertained from the Causes of Death Register. Conditional cox regressions were conducted for overall and cause-specific deaths, adjusted for age, socioeconomic status, Charlson index, and psychiatric comorbidities.

**Results:** In total, 67,748 women with PMD were matched to 338,740 women at a mean age of 36 years. During a mean follow-up of 6.2 years, 367 and 1,958 deaths occurred among women with and without PMD, with a mortality rate of 9/10,000 person-years. Compared to unaffected women, women with PMD were not at increased risk of overall mortality (adjusted HR=0.9, 95% CI [0.8-1.0]). However, the risk was higher for women diagnosed before age 25 (HRa=2.5 [1.4-4.4]); the association was not significant for other age-groups. The most common causes of death were suicide, cardiovascular diseases, cancers, accidents, and nervous system diseases. Cause-specific analyses showed a higher risk of suicide (HRa=1.9 [1.4-2.6]), regardless of age at diagnosis. No association was found for other causes.

**Conclusion:** Our findings suggest that women with PMD are not at risk for premature death overall. However, the risk was elevated among young women and for suicide. This supports the importance of careful follow-up for young women with PMD and highlight the need to develop suicide prevention strategies for these women.



**Menstrual cycle characteristics throughout the reproductive lifespan and cognitive****function in middle-aged women** Diana C. Soria\* Diana Soria Jiaxuan Liu Rebecca B. Lawn Jan L. Shifren Alexandra Purdue-Smithe Francine Grodstein Karestan C. Koenen Jorge E. Chavarro Emily Oken

Menstrual cycle irregularities reflect alterations in the hypothalamic-pituitary-ovarian axis and signal an unbalanced hormonal milieu that may contribute to a later risk of cognitive impairment. We evaluated the associations between menstrual cycle characteristics during the reproductive years and cognitive function around midlife in the Nurses' Health Study II.

We studied 13,751 nurses with data on cognitive function and menstrual cycle characteristics. We evaluated cognitive function in 2014-2019 with the Cogstate Brief Battery (composite z-scores capturing global cognition, psychomotor speed and attention, and learning and working memory). Cycle regularity (very regular [ref.], regular, irregular/no period) and length ( $\leq 25$ , 26-31 [ref.],  $\geq 32$  days/too irregular to estimate) were self-reported at baseline in 1989 for ages 14-17 and 18-22 and again in 1993 when the nurses were 28-48 y. We used linear regression models adjusted for age at the assessment of cycle characteristics, age at cognitive assessment, race and ethnicity, childhood and adulthood socioeconomic status, education, age at menarche, body fat and lifestyle factors at ages 14-17, 18-22 or 28-48, depending on the exposure.

Mean (SD) age at cognitive assessment was 60.8 (4.6) y. Women with irregular cycles at 28-48 y, vs. those with very regular cycles, had a lower z-score in the learning and working memory composite ( $\beta$  -0.04 [95% CI -0.08, 0.00]). We did not observe differences in cognitive function by cycle regularity at 14-17 or 18-22 y or by cycle length at 28-48 y. However, women with cycles  $\leq 25$  days at 18-22 y had a lower score in the learning and working memory composite ( $\beta$  -0.09 [-0.16, -0.03]).

Women with irregular cycles at 28-48 y and with cycles  $\leq 25$  days at 18-22 y had a lower performance in learning and working memory cognitive tasks. The associations were inconsistent across the lifespan but may support a role for reproductive hormones on cognition seen in other studies.

**Maternal history of fibroids and uterine fibroid development in offspring in a prospective ultrasound study of Black/African American women** Christine Langton\* Christine Langton  
Quaker Harmon Donna Baird

Uterine fibroids are highly prevalent benign tumors of the uterine muscle. Fibroids are the leading indication for hysterectomy, and Black/African American women are disproportionately burdened. Family history of fibroids may be a risk factor for fibroid development, but results from prior studies have been mixed, and none utilized ultrasounds to prospectively assess fibroid incidence and growth.

We evaluated the association between maternal history of fibroids and fibroid development among self-identified Black/African American women aged 23-35 years in the Study of Environment, Lifestyle & Fibroids (SELF). For most participants, maternal fibroid history was gathered directly from their mothers (89%). A standardized ultrasound examination was conducted during 4 clinic visits over 5 years to detect fibroids  $\geq 0.5$  cm in diameter. We used Cox regression models to estimate hazard ratios (HRs) and 95% CIs for the association between maternal history of fibroids (any history as well as early onset - diagnosed before age 35) and incident fibroids. Fibroid growth was calculated as change in log-volume per 18 months for fibroids matched at successive visits. Both incidence and growth models were adjusted for maternal and participant factors.

Of 1,187 fibroid-free participants at enrollment, 424 participants (36%) had mothers with fibroids, 38% of whom had early onset. Over the study, 285 participants (24%) developed incident fibroids. Participants with maternal history of fibroids had higher risk of incident fibroids compared with those without (aHR=1.21; 95% CI: 0.96, 1.52), but the elevated risk was limited to those whose mothers had early onset (aHR=1.46; 95% CI: 1.07, 1.99 vs. aHR=1.03; 95% CI: 0.78, 1.36). Average fibroid growth differed little by maternal history of fibroids.

Results from this first ultrasound-based, prospective fibroid study support maternal history of fibroids as a risk factor for incident fibroids, particularly when the mother is diagnosed at an early age.

**Body mass index and uterine fibroid development: a prospective study** Quaker Harmon\*

Quaker Harmon Stacy Patchel Sheri Denslow Ganesa Wegienka Donna Baird

Fibroids are hormonally dependent benign tumors of the uterus with significant morbidity. Increased adiposity, as measured by body mass index (BMI), alters hormone concentrations, and has inconsistent associations with fibroid prevalence. We assessed the association between repeated measures of BMI and fibroid incidence and growth in the Study of Environment, Lifestyle & Fibroids (SELF). SELF followed 1,610 women self-identified as "African American" or "Black", ages 23-35 from the Detroit, Michigan area with ultrasound every 20 months for 4 visits (5 years). Weight and height were measured at enrollment and weight was measured at every follow-up visit. Baseline BMIs  $\geq 30$  kg/m<sup>2</sup> were common (59%). Participants with incident fibroids (n=294) were identified among those who were fibroid free at the enrollment ultrasound (n=1230). Fibroid incidence was modeled using Cox models. Fibroid growth, scaled to 18-months, was estimated for individual fibroids as the difference in log-volume between visits and was modeled using linear mixed models accounting for within-woman and within-fibroid correlations. All models used time-varying BMI, and adjusted for time-varying demographic, reproductive, and contraceptive factors. Compared to BMI < 25 kg/m<sup>2</sup> those with BMI 30- < 35 kg/m<sup>2</sup> had increased fibroid incidence (adjusted hazard ratio (aHR) 1.37, (95% CI 0.96, 1.94)) while those with BMI  $\geq 40$  kg/m<sup>2</sup> had reduced incidence (aHR 0.61, (95% CI 0.41, 0.90)). A non-linear association was corroborated using continuous BMI with a restricted cubic spline (p-value=0.0007, indicating nonlinearity) (Figure 1). Fibroid growth had inconsistent and mostly small magnitude associations with BMI. BMI is only a crude measure for studying the health effects of adiposity. More detailed measures of hormonal, metabolic, and DNA-damaging sequelae of adiposity are needed to better understand the non-linear association we observe.

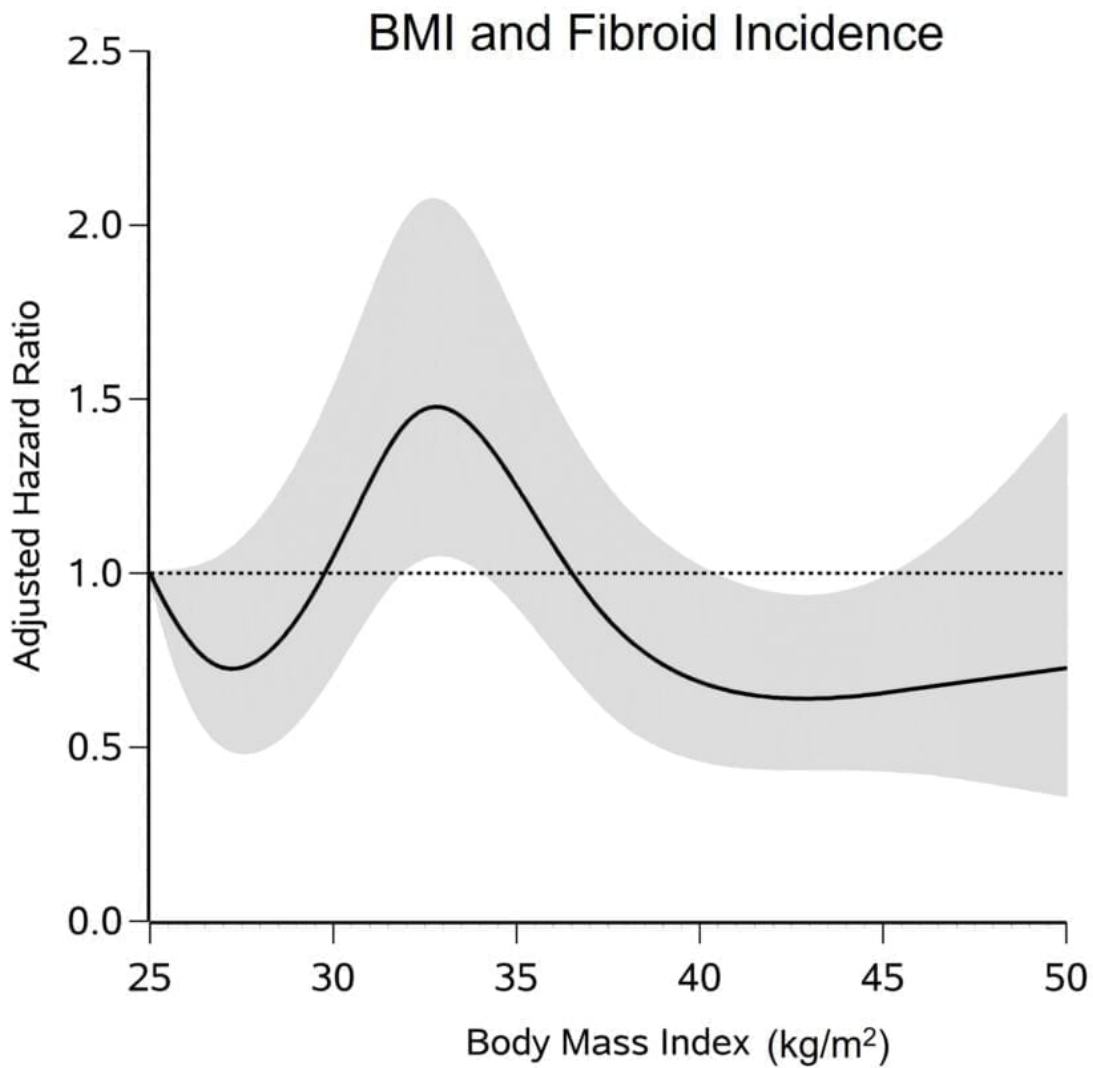


Figure 1. Continuous BMI (kg/m<sup>2</sup>) modelled using Cox regression with a restricted cubic spline with 5 knots and a reference value of 25 kg/m<sup>2</sup>. BMI values <25 kg/m<sup>2</sup> assigned value of 25. BMI trimmed to values <50 kg/m<sup>2</sup> to avoid sparse data. Solid line captures the adjusted hazard ratio, shaded areas represent the 95% confidence interval.

**The intergenerational transmission of preeclampsia: examining the unaffected daughters**

Aditi Singh\* Aditi Singh Sage Wyatt Liv Grimstvedt Kvalvik Kari Klungsøyr Rolv Skjærven

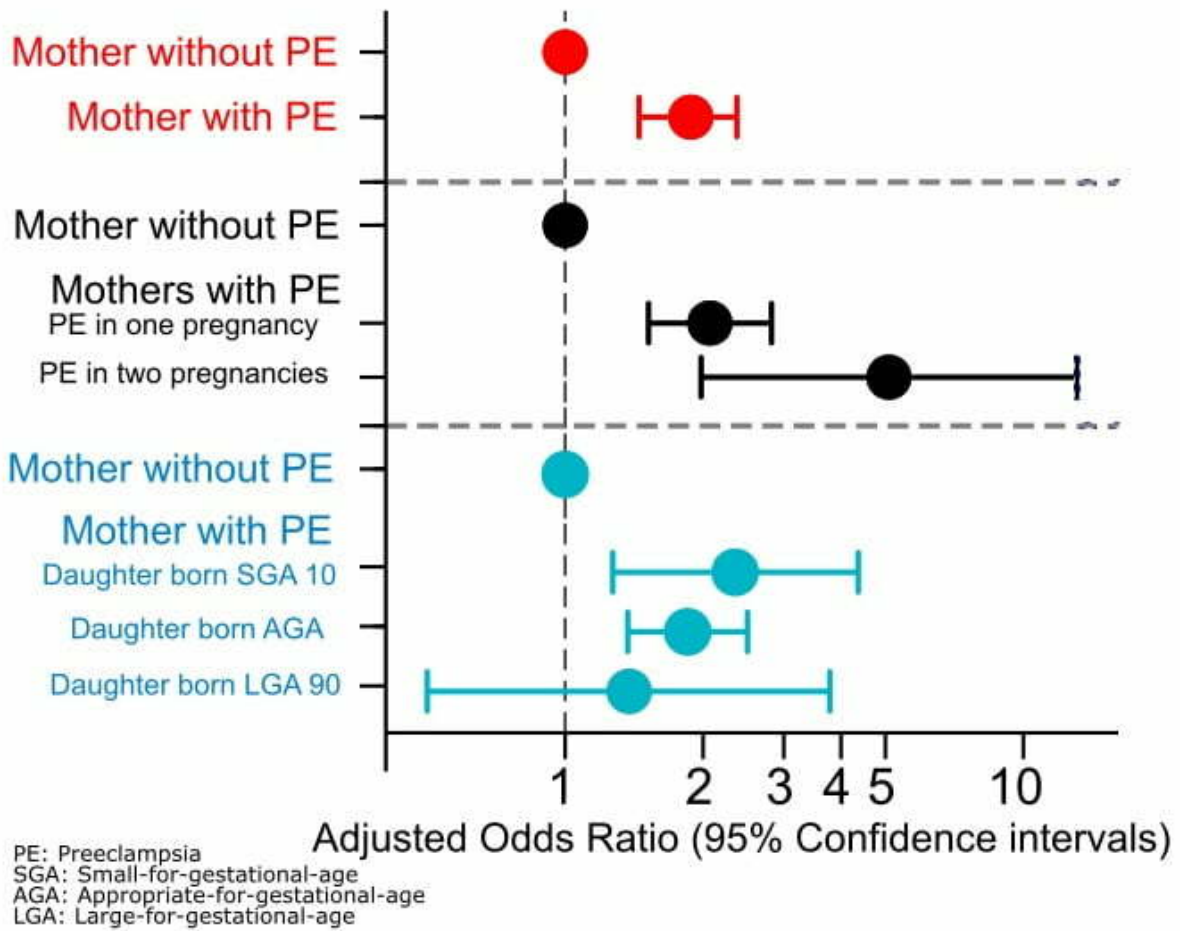
**Introduction:** Previous research has shown that daughters born to mothers with preeclampsia (PE) have an increased risk of developing PE, regardless of their prenatal exposure to PE. To gain further insight into the intergenerational transmission of PE, we examined the risk of PE in the first pregnancies among daughters not prenatally exposed to PE and born to mothers with PE in other pregnancies.

**Methods:** Using the Medical Birth Registry of Norway (1967-2020), we identified 403 917 mother-daughter units where the daughter was prenatally unexposed to PE. We calculated odds ratio (OR) and 95% confidence intervals (CI) using logistic regression to evaluate the association PE in daughters' first pregnancies and mothers' reproductive history. Daughters born to mothers without PE were the reference group. Models were adjusted for the mothers' and daughters' age at first pregnancy and highest educational status, and daughters' year of birth.

**Results:** Among daughters unexposed to PE (N=403 917), 0.2% (n=924) were born to mothers with PE pregnancies. Of these daughters, 6.6% (n=61) had PE in their first pregnancy. Daughters born to mothers with PE had an increased risk of developing PE in their first pregnancy (OR 1.88, 95%CI 1.45-2.25). Moreover, daughters had a higher risk of a first PE pregnancy if born to mothers with two pregnancies complicated by PE (OR 5.09, 95%CI 1.98-13.09) than if born to mothers with PE in only one pregnancy (OR 2.07, 95%CI 1.52-2.82). Daughters born to mothers with PE who themselves were born small-for-gestational-age had a higher risk of having a first PE pregnancy (OR 2.4, 95%CI 1.3-4.4) than daughters born appropriate-for-gestational-age (OR 1.85, 95%CI 1.37-2.50); while this was less evident for daughters born large-for-gestational-age (OR 1.38, 95%CI 0.50-3.78).

**Conclusion:** These findings highlight the heterogeneity in the intergenerational transmission of PE by perinatal factors that need further investigation.

## Risk of preeclampsia in the first pregnancy of daughters not prenatally exposed to preeclampsia



**Violence victimization-related morbidity among pregnant and postpartum women using a population-based, longitudinal dataset** Shaina Sta. Cruz\* Shaina Sta. Cruz Claire Margerison  
Alison Gemmill Sidra Goldman-Mellor

Violence against women, including during pregnancy and the postpartum period, is a major public health problem worldwide. Homicides during the perinatal period have recently increased (Wallace 2022), yet, concerningly, these deaths reflect only the most extreme manifestation of violence-related victimization. Far less is known about trends and disparities in pregnancy-associated violence morbidity. Examining emergency department (ED) utilization for violence-related injuries in this patient population can shed light on overall incidence and patterns of risk, despite ED visits comprising a subset of all violent victimization. In this study, we examined trends and disparities in pregnancy-associated violent injury morbidity from 2010-2019 using individually-linked longitudinal, all-payer, population-based statewide data from California. The sample comprised all women with a live-birth hospital delivery in each year from 2010-2018 (~3 million). Annual cohorts of women were followed for 12 months after their delivery hospitalizations to identify subsequent nonfatal ED visits for violent injury (defined using ICD-9/10-CM codes). Analyses included trends in annual incidence rates, including disparities by race/ethnicity and payer. In the 2010 cohort, 12-month incidence of ED visits for pregnancy-associated violent injury was 0.46%; this remained stable for several years and then declined to 0.41% in the 2018 cohort (an overall decrease of 10.9%). In every year, Black women had the highest incidence of ED visits for violent injury compared to White, Hispanic, and Asian/Pacific Islander women. Next steps are to analyze the timing of violence victimization in the perinatal period and investigate sociodemographic trend heterogeneity. While relatively rare, pregnancy-associated violence victimization still affects large numbers of women each year. Better surveillance and prevention efforts are needed.

### Validation of obstetric comorbidities index on severe maternal morbidity in South Korea: 16-year cohort study Jin-Young Nam\* Jin-Young Nam

**Objective:** An obstetric comorbidity index has been developed and validated to predict severe maternal morbidity (SMM) or maternal death for a last decade; however, few studies have been performed a validation of the index on SMM. Therefore, this study aimed to validate the obstetric comorbidity index and to estimate the comorbidity prevalence and discriminative performance of the index on various severe maternal outcomes using the nationwide population-based delivery cohort in Korea. **Methods:** This study was used the National Health Insurance Service Delivery Cohort in South Korea from 2003 to 2019, which included whole cases of delivery in South Korea. The obstetric comorbidities were identified using the Bateman's obstetric comorbidities index. Outcomes were SMM which was developed by US-CDC, severe acute maternal morbidity (SAMM) from the EURONET, and maternal death within 30 days postpartum. The predictive and discriminative ability of the index was calculated by Brier score and the area under the receiver operating characteristic curve (AUC). Multivariate logistic regression was used to estimate odds ratio (OR) with 95% confidence interval (CI). **Results:** Of the 6,527,810 delivery cases, 2.2% (n=143,392), 1.3% (n=84,994), and 0.0% (n=555) experienced US-CDC's SMM, EURONET's SAMM, and maternal death, respectively. 68.8% women did not have any condition of the index and approximately 0.1% had a score >10. The prediction ability and discriminative performance of the OB-CMI was constant for SMM, SAMM, and maternal death within 30 days postpartum (SMM: Brier score=0.02, AUC=0.72; SAMM: Brier score=0.01, AUC=0.67; maternal death: Brier score=0.00, AUC=0.78). **Conclusion:** The Obstetric Comorbidity Index showed similar performance characteristic in the previous research and it had a good ability to predict and discriminate SMM, SAMM and maternal death in a nationwide delivery cohort in South Korea. This finding suggests that the Obstetric Comorbidity Index may be a useful tool to predict an adverse maternal health outcome globally.

Table 2. Validation of the obstetric comorbidity index by various outcomes

Bateman's score	Severe maternal morbidity in US-CDC				Severe Acute Maternal Morbidity in EURONET			Maternal death within 30 days postpartum		
	Stratification Capacity n (%)	Association OR (95% CI)	Discrimination ability AUC (95% CI)	Calibration accuracy Brier score	Association OR (95% CI)	Discrimination ability AUC (95% CI)	Calibration accuracy Brier score	Association OR (95% CI)	Discrimination ability AUC (95% CI)	Calibration accuracy Brier score
0	4,493,632 (68.8)	Ref	0.72	0.02		0.67	0.01	Ref	0.78	0.00
1-2	1,823,015 (27.9)	1.39 (1.37-1.41)			1.56 (1.53-1.59)			2.40 (1.91-3.02)		
3-4	116,525 (1.8)	2.26 (2.20-2.33)			2.65 (2.26-2.76)			7.95 (5.55-11.40)		
5-6	16,610 (0.3)	15.18 (14.62-15.76)			39.20 (37.79-40.65)			29.55 (19.53-44.71)		
7-8	55,130 (0.8)	4.07 (3.96-4.19)			4.87 (4.69-5.06)			9.94 (6.93-14.26)		
9-10	18,642 (0.3)	4.38 (4.20-4.57)			4.96 (4.66-5.27)			13.18 (7.87-22.07)		
>11	4,256 (0.1)	7.46 (6.95-8.02)			7.17 (6.47-7.96)			38.19 (20.90-69.80)		