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Marginal sufficient component cause model: an emerging causal model with authenticity?

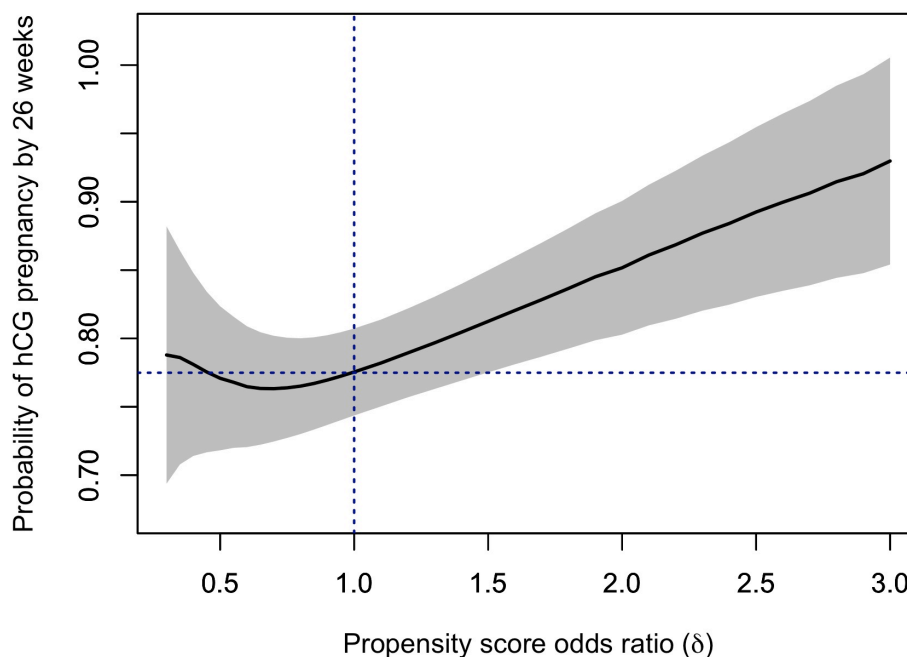
Etsuji Suzuki* Etsuji Suzuki Eiji Yamamoto

For decades, the sufficient cause model and the counterfactual model have shaped our understanding of causation in biomedical science, and the link between these two models has enabled us to obtain a deeper understanding of causality. Recently, a new causal model—the marginal sufficient component cause (mSCC) model—was proposed and applied in the context of interaction or mediation. In the mSCC model, “all possible combinations of background conditions for each sufficient cause [in the conventional sufficient cause model] are recategorized and transformed into mutually exclusive and exhaustive conditions” (Lin et al., *Stat Med* 2019;38:2467-2476). In other words, mSCC is simply a form of representation of the response types defined in the counterfactual model. The proponents of the mSCC model have emphasized its utility in visualizing the presence of “agonism” in the counterfactual framework, claiming that the concept of agonism has not been clearly defined in causal inference and that agonistic interaction cannot be visualized by the conventional sufficient cause model. In this presentation, we illustrate that a careful scrutiny based on the conventional sufficient cause model yields further insights into the concept of agonism in a more biological sense. We primarily focus on the following three points: a) “agonism” defined in the counterfactual model can be visualized as *sets* of sufficient causes in the conventional sufficient cause model; b) although the so-called independent competing assumption or no redundancy assumption may seem irrelevant in the mSCC model, researchers do need to assume that potential completion times of relevant mSCCs differ; c) possibly differing potential completion times of mSCCs cannot be discerned until the hidden mechanistic paths of the mSCCs are considered in the conventional sufficient cause model. In this rapidly progressing field of research, decades after its introduction, the sufficient cause model retains its authenticity.

Time-varying incremental propensity score estimation of the effect of aspirin on pregnancy in the Effects of Aspirin in Gestation and Reproduction trial Jacqueline Rudolph* Jacqueline Rudolph Kwangho Kim Edward Kennedy Ashley Naimi

In many settings, the average causal effect, which compares counterfactual outcomes had we intervened to expose all versus none of a sample, is an unrealistic contrast. Effects of more realistic interventions may have greater public health relevance. One novel approach - incremental propensity score estimation - allows us to estimate the effect of shifting each individual's probability of being exposed. This method has two further advantages: it does not require the positivity assumption and can be implemented using flexible machine learning tools while still being optimally efficient. Prior work has shown how to apply this method in time-fixed settings. We here demonstrate how to use the approach in the time-varying setting, using data from the Effects of Aspirin in Gestation and Reproduction trial, which assessed the effect of preconception, low dose aspirin on pregnancy outcomes. Compliance to aspirin or placebo was summarized weekly and may have been affected by time-varying confounders such as bleeding or nausea. Our outcome was the probability of human chorionic gonadotropin confirmed pregnancy by 26 weeks. We used incremental propensity score estimation to quantify what the probability of pregnancy would be if we multiplied each woman's probability of taking aspirin in each week by ORs between [0.30, 3.00]. Under no intervention (OR=1), the probability of pregnancy was 0.78 (95% CI: 0.74, 0.81), which matched the observed risk. As we shifted a woman's probability of taking aspirin, we saw a non-linear relationship. Decreasing her probability had little effect on pregnancy, e.g. the probability for OR=0.5 was 0.77 (95% CI: 0.72, 0.82). However, when we increased the probability of taking aspirin, the probability of pregnancy increased, from 0.85 (95% CI: 0.80, 0.90) for OR=2 to 0.93 (95% CI: 0.85, 1.00) for OR=3. In our time-varying example, incremental propensity score estimation allowed us to obtain results which were both highly interpretable and robust.

Incremental propensity score estimation of the effect of aspirin on hCG pregnancy in the EAGeR trial

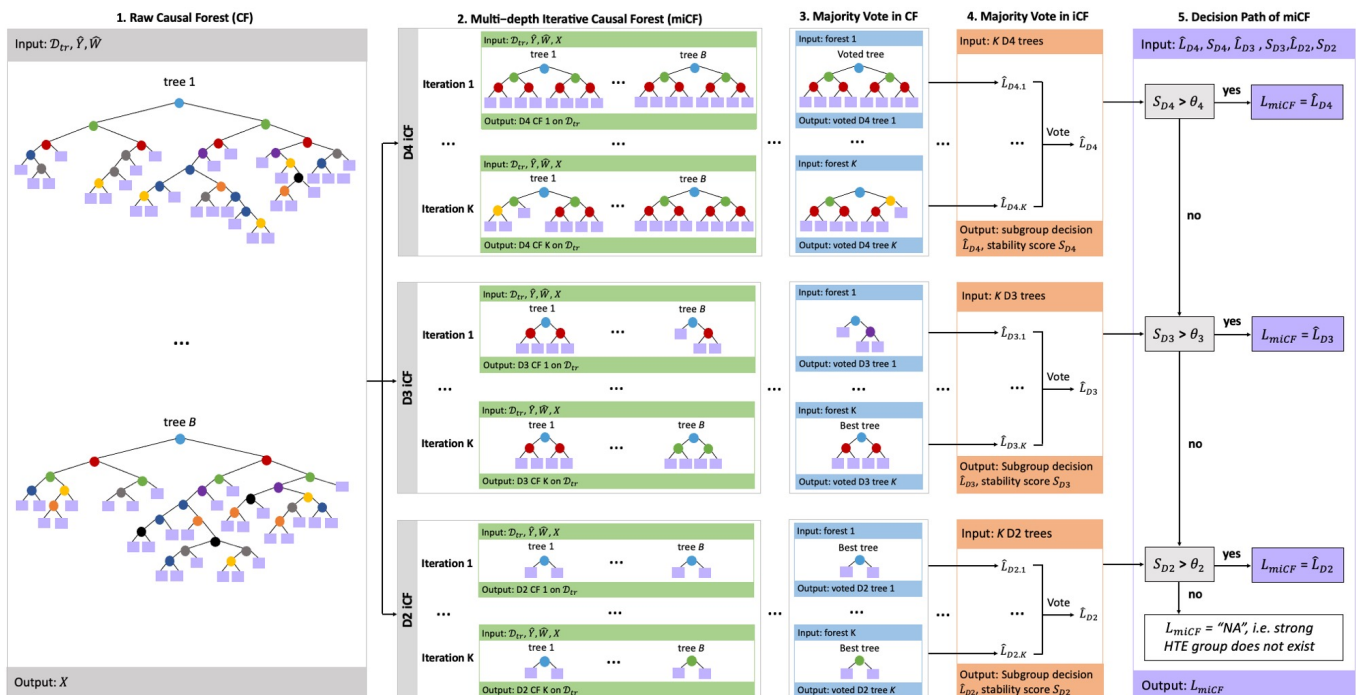


A comparison of regression discontinuity and propensity score matching to estimate the causal effects of statins using electronic health records Michelle Odden* Michelle Odden Sebastian Calonico Adina Zhang Neal Jawadekar Annabel Tan Soohyun Kim Adina Zeki Al Hazzouri

Quasi-experimental designs, such as regression discontinuity (RD), are gaining popularity in epidemiologic studies aimed at deriving causal estimates from observational data. In this methodologic investigation, we compared the estimates of effect of statins on myocardial infarction (MI) using RD and propensity score matching; the protective effect of statins on MI is well-established. For comparison, we used motor vehicle accidents as a negative control outcome. In the RD analysis, we leveraged a 2008 UK guideline that recommends statins if a patient's 10-year cardiovascular disease (CVD) risk score >20%. We used electronic health record data (2008-2018) from the Health Improvement Network (THIN) on 21,413 adults aged 65 and older in the UK. Outcomes were ascertained using Read codes and censored at 10 years; 10-year CVD risk was assessed using the Framingham risk score. Both the RD (n=8,510) and the propensity score matched populations (n=10,164) demonstrated good balance of confounders. The unadjusted estimates for statin use on MI and motor vehicle accidents were HR = 1.36 (95% CI: 1.10, 1.68) and HR = 0.74 (0.44, 1.22), respectively. Using RD, the adjusted point estimate for statin use and MI was in the protective direction, although the confidence interval included the null (HR: 0.61, 95% CI: 0.31, 1.19). Conversely, using propensity score matching, the adjusted estimates for statin use and MI remained in the harmful direction: HR = 1.25 (95% CI: 0.96, 1.62). For the outcome of motor vehicle accidents, both RD and propensity score matching produced estimates near the null: 0.99 (95% CI: 0.31, 3.11) and 0.92 (95% CI: 0.49, 1.73), respectively. Unlike propensity score matching, RD estimates for statins on MI were similar to those from trials, although precision was limited. A strength of RD is that it can reduce bias in confounders by exploiting exogenous variation around the cutoff, which is of key importance in making causal inference in observational studies.

Iterative Causal Forest For Identifying Subgroups Tiansheng Wang* Tiansheng Wang Michael R. Kosorok Alexander P. Keil Richard Wyss Michele Jonsson Funk John B. Buse Til Stürmer

Heterogeneous treatment effects (HTE), i.e., treatment effects varying across subgroups (SGs), can be assessed by examining interaction (INT) terms between treatment (W) and variables (X) in an outcome model. Standard SG analyses examine one factor at a time and may fail to accurately detect heterogeneity across complex SGs. Wager et al. developed causal forests (CFs) for estimating HTE in observational data. However, precisely and efficiently identifying HTEs remains a challenge. Based on Wager’s method, we developed a multi-depth, iterative CFs (MiCFs) to identify HTEs in SGs defined by binary and continuous variables. MiCF involves 1) fitting a crude full CF in a training data with predicted propensity score and outcome (Y) values to identify important variables; 2) growing pruned, iterative causal forests (iCF) at multiple tree depths (D) (D4, D3, and D2 for 4-way, 3-way, and 2-way INT, respectively) by selected variables, respectively; 3) obtaining the tree structure that minimizes an HTE loss function in each pruned iCF; 4) selecting the “best” SG decision based on tree structures by simple majority vote; 5) identifying SGs of interest based on decisions from D4, D3, and D2 iCF by requiring different cutoff values (Theta) for a stability score defined as the occurrence of the voted decision divided by iteration number K. Finally, an SG-specific treatment effect can be computed by inverse probability of treatment weighting in testing data. To test miCF’s performance, we simulated 6 scenarios: 4-way, 3-way, 2-way, two 2-way, three 2-way INTs, and no INT. Using Theta of 0.3, 0.5, and 0.5 for D4, D3, and D2 iCF, respectively, the accuracy score (the frequency of accurate SG identification across simulations) for the 6 scenarios are 0.7, 1, 1, 1, 0.3, and 1, respectively. Using stability score with cutoffs allow us to control the risk of false discovery of SGs. MiCF is a promising method to identify SGs in large cohorts with known, sufficient confounders.



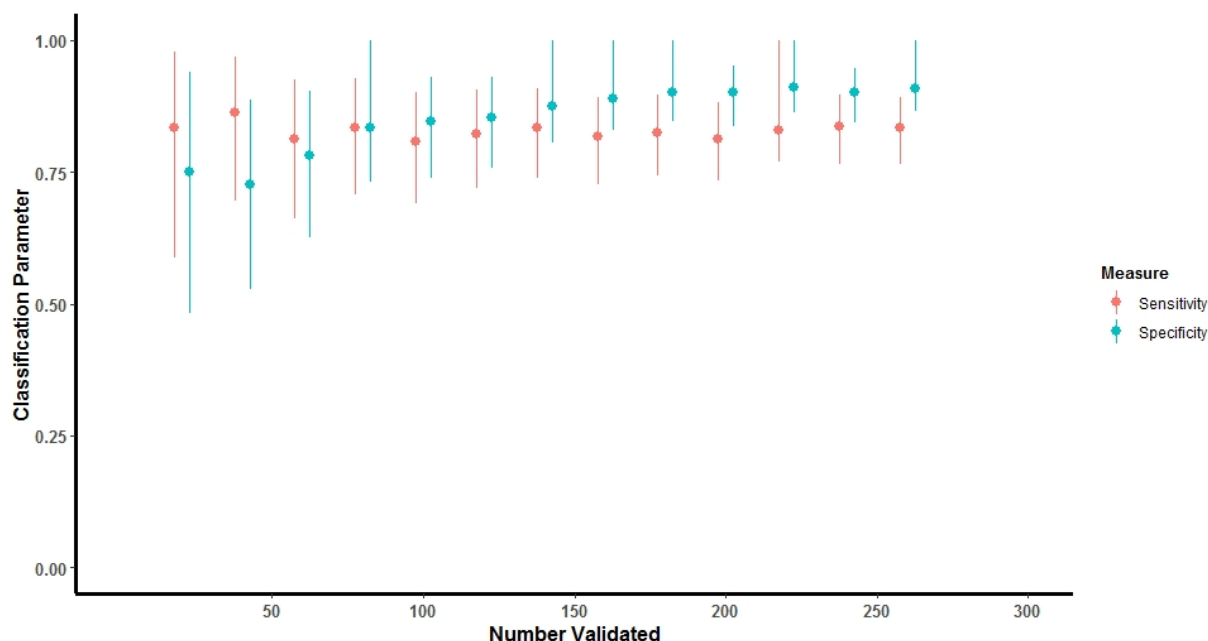
Sampling validation data based on the desired precision of the bias-adjusted estimate of association Lindsay Collin* Lindsay Collin Richard F MacLehose Thomas P Ahern Michael Goodman Darios Getahun Michael J. Silverberg Jaimie L. Gradus Timothy L. Lash

Background: Data collected from a validation substudy permit calculation of a bias-adjusted estimate of effect that is expected to equal the estimate of effect that would have been observed had the gold standard been available for the entire study population. We developed and applied a framework of Bayesian monitoring to determine when sufficient validation data have been collected to yield a bias-adjusted estimate of association with a prespecified level of precision.

Methods: We demonstrate the utility of this method using data from the Study of Transition, Outcomes and Gender—a cohort of transgender and gender non-conforming youths (n=1,331). Our interest is in the association between transmasculine/transfeminine status and self-inflicted injury. Transmasculine/transfeminine status were determined from gender code in the medical record at cohort enrollment, which is known to be misclassified as it can indicate gender identity or sex recorded at birth. To address exposure misclassification, we demonstrate the method’s ability to determine when sufficient validation data have been collected to calculate a bias-adjusted estimate of association with precision that is less than 1.8-times greater than the precision of the conventional estimate, which was decided *a priori* based on the conventional estimate.

Results: In the conventional age-adjusted analysis, we observed that transmasculine children and adolescents were 1.8-times more likely to inflict self-harm than transfeminine youths (95%CI 1.3, 2.6). Using the adaptive validation approach, 200 cohort members were required for validation to yield a bias-adjusted estimate of OR=3.0 (95%CI 1.8, 5.6), which was similar to the bias-adjusted estimate using complete validation data (OR=2.6, 95%CI 1.7, 4.2).

Conclusions: Our method provides a novel approach to effective and efficient estimation of classification parameters as validation data accrue, with emphasis on the precision of the bias-adjusted estimate of association.



A North American prospective cohort study of sugar-sweetened beverages consumption and semen quality

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Tanran R. Wang Michael L. Eisenberg Greg J. Sommer Kenneth J. Rothman Sherri O. Stuver
Elizabeth E. Hatch

Background: In the United States, the amount of sugar in the American diet increased by 19% between 1970 and 2005, mainly due to the consumption of sugar-sweetened beverages (SSB). Dietary factors, including high sugar intake from SSB, may have adverse effects on male reproductive health. Few studies have examined the consumption of SSB in relation to semen quality.

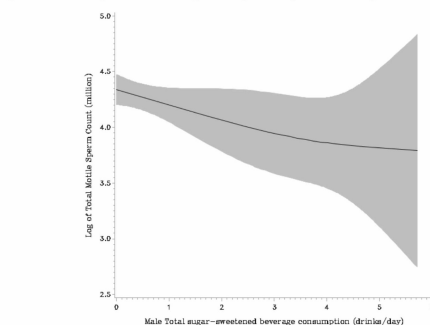
Objective: We prospectively evaluated the association between male SSB consumption and semen parameters.

Methods: We analyzed data from 375 men (654 samples) participating in a semen testing substudy of Pregnancy Online Study (PRESTO), a preconception cohort of North American couples. After enrollment, male participants aged ≥ 21 years were invited to perform at-home semen testing using the Trak™ system. SSB consumption and covariate data were obtained via baseline questionnaire. We estimated the percent difference in mean log-transformed semen parameter values (%D) and 95% confidence intervals (CI) for associations between SSB intake and semen volume (mL), total sperm count (TSC, million), sperm concentration (million/mL), motility (%) and total motile sperm count (TMSC, million), adjusting for potential confounders.

Results: Adjusted %Ds (CIs) comparing seven or more (7+) SSB per week vs. none were -1.8 (-12.5, 10.1), -32.1 (-51.1, -5.9), -33.3 (-51.5, -8.5), -10.2 (-23.0, -0.6) and -40.2 (-58.4, -14.1) for semen volume, sperm concentration, TSC, motility, and TMSC, respectively. Adjusted risk ratios (95% CIs) for the association between SSB consumption and World Health Organization low semen parameters cut-points, comparing 7+ SSB per week vs. none were 0.67 (0.35, 1.27), 1.72 (1.05, 2.80), 2.00 (0.96, 4.18), 1.67 (1.05, 2.64), and 2.06 (1.02, 4.31) for low semen volume (<1.5 ml), low sperm concentration (<15 million/ml), low TSC (<39 million), low motility (<40%), and low TMSC (<16 million), respectively.

Conclusion: Greater total SSB consumption was associated with reduced semen quality.

Figure 1: Male Total Sugar-sweetened Beverages Consumption vs Log of Total Motile Sperm Count Restricted Cubic Spline



Adjusted for abstinence time, age (years), current or occasional smoker (yes vs. no), current body mass index, hours of work per week, caffeine intake, alcohol intake (drinks/week), average hours of sleep per night, vigorous exercise (hrs/week), education (years), physician-diagnosed depression, physician-diagnosed anxiety and use of psychotropic medication.

Healthy eating patterns and epigenetic measures of biological age Jacob Kresovich* Jacob Kresovich Yong-Moon “Mark” Park Dale Jack

Background: Healthy eating has been associated with lower risk for chronic diseases and death, but mechanisms underlying this association are unclear. Biological age is strongly related to adverse health outcomes and can be estimated using the blood methylome.

Objective: To determine whether healthy eating patterns are associated with methylation-based measures of biological age.

Methods: Among 2,694 women in the Sister Study with blood genome-wide DNA methylation data from the HumanMethylation450 BeadChip, four healthy eating indexes (Dietary Approaches to Stop Hypertension [DASH], Healthy Eating Index [HEI-2015], Alternative Health Eating Index [AHEI-2010], and the Alternative Mediterranean [aMed]) were calculated using a validated 110-item Block food frequency questionnaire completed at enrollment. Four epigenetic measures of biological age (Hannum AgeAccel, Horvath AgeAccel, PhenoAgeAccel and GrimAgeAccel) were derived. Linear regression models, adjusted for covariates and sampling weights, examined cross-sectional associations between eating patterns and measures of biological age.

Results: All four healthy eating patterns were associated with lower biological age assessed by the PhenoAge and GrimAge epigenetic clocks. The strongest associations were for aHEI-2010 (per 1-SD increase in diet quality, PhenoAgeAccel: $\beta = -0.5$ years, 95% CI: -0.8, -0.2; GrimAgeAccel: $\beta = -0.4$ years, 95% CI: -0.6, -0.3). For the DASH and aMed diets, inverse associations with PhenoAgeAccel were only observed among women who did not meet physical activity guidelines (DASH, < 2.5 hours/week: $\beta = -0.7$, 95% CI: -1.1, -0.3, ≥ 2.5 hours/week: $\beta = 0.1$, 95% CI: -0.4, 0.6; aMed, < 2.5 hours/week: $\beta = -0.7$, 95% CI: -1.1, -0.2, ≥ 2.5 hours/week: $\beta = 0.2$, 95% CI: -0.4, 0.7).

Conclusions: Higher diet quality is inversely associated with methylation-based measures of biological age. Physical activity may be an important modifier of these associations.

Hypothetical interventions on diet quality and lifestyle factors, and their impact on breast cancer survival: the Pathways Study Isaac J. Ergas* Isaac Ergas Patrick T. Bradshaw Elizabeth M. Cespedes Feliciano Janise M. Roh Marilyn L. Kwan Lawrence H. Kushi

Background

Cancer survivors are motivated to make lifestyle changes after diagnosis, yet there is limited evidence to inform recommendations. We used a causal inference approach to estimate the impact of hypothetical diet and physical activity interventions on breast cancer survival.

Methods

A total of 3,660 women diagnosed with invasive breast cancer from 2005-2013 at Kaiser Permanente were included. Using food frequency and physical activity questionnaires completed on average 2.3 (range:0.7-18.7) months after diagnosis and at 6, 12, 24, and 72-month follow-ups, we estimated physical activity in MET hours (PA) and derived three diet quality indices: the American Cancer Society guidelines (ACS), the Plant-Based Index (PDI), and the 2015 Healthy Eating Index (HEI). Mortality follow-up continued through to the end of 2018, resulting in 655 deaths. We used the parametric g-formula to estimate 13-year risk ratios (RR) and 95% confidence intervals (CI) for all-cause mortality under hypothetical interventions on diet quality and physical activity compared to the natural course (no intervention).

Results

Risks were inversely associated with all-cause mortality [ACS RR: 0.95 (0.82-1.04), PDI RR: 0.90 (0.53-1.12), HEI RR: 0.95 (0.83-1.00), PA RR: (0.74 (0.66-0.84)] under hypothetical interventions where all participants separately maintained a score equal to the highest diet quality index score or the highest level of physical activity from the study population to the risk where all participants maintained their natural course. The strongest association was observed when comparing the risk where all participants maintained both the highest PDI and PA scores to the risk of all participants maintaining the natural course [0.70 (0.59-0.82)].

Conclusion

Our results suggest that an intervention designed to jointly increase diet quality and physical activity may convey the lowest risk of death among breast cancer survivors.

Longitudinal and Cross-sectional Associations between the Dietary Inflammatory Index and Objectively and Subjectively Measured Sleep among Police Officers

Michael Wirth* Michael Wirth Desta Fekedulegn Michael Andrew James Burch Alexander McLain Jean Davis James Hebert John Violanti

Background: Poor-quality diets and abnormal sleep patterns are common among police officers. Diet can affect chronic inflammation which may influence sleep quality and quantity. Associations were examined between the energy-density Dietary Inflammatory Index (E-DIITM) and sleep quality and quantity among police officers.

Methods: Data were from the Buffalo Cardio-Metabolic Occupational Police Stress Cohort with baseline in 2004-2009 (n=464) and first follow-up in 2010-2014 (n=281). A food frequency questionnaire assessed dietary intake from which the E-DII was calculated. Sleep was measured objectively (wrist actigraph) and subjectively (Pittsburgh Sleep Quality Index, PSQI). Standard repeated-measures linear regression models with time-varying E-DII and sleep were fit to examine cross-sectional associations. A second approach assessed longitudinal effects by computing changes (relative to baseline) in E-DII while adjusting for the baseline E-DII score. Effect modification by shift status (day, evening, or night shift) was examined.

Results: Cross-sectionally, a 1-unit increase (i.e., pro-inflammatory) in E-DII score was associated with a 1.5-minute increase in wake-after-sleep onset (WASO, p=0.02), a worsening of sleep fragmentation (p=0.04), a non-significant decrease in sleep quantity ($\beta=-0.03$, p=0.26) and an improvement in subjective sleep quality ($\beta=-0.14$, p=0.01). In models with both longitudinal and cross-sectional effects, with every 1-unit pro-inflammatory increase in E-DII score, WASO increased by 2 minutes (p=0.05) which was driven by those primarily working day shifts ($\beta=4.14$, p=0.01). Subjective sleep quality improved ($\beta=-0.45$, p=0.06) for every 1-unit increase in the change in E-DII score among those working night shifts.

Conclusion: More pro-inflammatory diets were associated with two objective measures of sleep quality, but not sleep duration. Reasons for diet-related discrepancies between qualitative and quantitative sleep measures will be discussed.

The impact of obesity on COVID-19 outcomes: the role of age and diabetes status Geetanjali Datta* Geetanjali Datta Qihan Yu Marie Lauzon Susan Cheng Jane C Figueiredo Joseph Ebinger Sarah-Jeanne Salvy

Background: Previous reports on the associations between obesity and COVID-19 have not fully accounted for age effects or the role of potential metabolic mediators, such as diabetes. These considerations are necessary to further our understanding of mechanistic pathways explaining COVID-19 outcomes. **Specific aim:** We aimed to examine the role of diabetes in mediating the association between obesity and COVID-19 outcomes stratifying by age. **Methods:** We conducted a retrospective cohort study of all COVID-19 patients treated at Cedars-Sinai Medical Center (CSMC) between March 11, and December 7, 2020 (N=1931). Data on sociodemographic characteristics and pre-existing conditions were extracted from electronic medical records and linkage to Census data. The main exposure of interest was body mass index (BMI). The outcomes of interest were mortality and disease severity, measured in four categories (not admitted, admitted to hospital, admitted to ICU, intubated). Covariates included age, sex, smoking status, zip code-level median household income, race, and ethnicity. We produced age-stratified (<65 and ≥65) descriptive statistics, bivariate and multivariate, and causal mediation models. **Results:** In adjusted models among those <65 years (N=1154), higher BMI was not associated with mortality, but was associated with disease severity (Intubation $OR_{\text{obese vs normal BMI}}=1.7$, 95% CI 1.2-2.2). Diabetes explained 25% (95% CL:11%-50%) of this association. Among those ≥65 (N=777), in relation to normal BMI, lower BMI was associated with higher risk of mortality (OR=2.4, 95% CI 1.3-4.4) and overweight was associated with a lower risk of mortality (OR=0.5, 95% CI 0.3-0.9). BMI was not associated with disease severity among those ≥65. **Conclusions:** Diabetes accounted for a meaningful proportion of the association between obesity and COVID-19 severity among those younger than 65. Conversely, among those older than 65, underweight was a greater risk factor than obesity for mortality.

Body mass index and C-reactive protein: time to revisit who has acute inflammation in population-based cohorts? Quaker Harmon* Quaker Harmon Greg Travlos Ralph Wilson Frankie LaPorte Donna Baird

C-reactive protein (CRP) is a hepatic protein that is elevated in response to inflammation. Very high levels of CRP are used clinically to identify patients with acute infections or inflammatory conditions. In non-hospitalized populations, higher CRP values in the non-inflammatory range are predictive of cardiovascular risk (CVD). In epidemiologic studies, individuals with CRP values ≥ 10 mg/L are often excluded from analysis due to the presumed presence of an acute infectious process. CRP cut points used in epidemiologic studies may not reflect the increasing prevalence of obesity. High body mass index (BMI) is associated with elevations in CRP which may be due to biological processes separate from infection. We used data from the Study of Environment, Lifestyle and Fibroids (SELF, 2010-2018) to examine the association between measured BMI and high sensitivity CRP from 1130 African American women age 23-41 each with 4 CRP measurements over 5 years. A clear pattern of higher CRP with higher BMI emerged (correlation coefficient = 0.62). As an example, we examined the usual clinical cut points of CRP for women with BMI 40- <50 kg/m² who had a median CRP of 7.8 mg/L (SD 9.5): 38% had CRP 3- <10 (high risk for CVD), and 41% would be classified as acute infection (CRP 10+). In contrast those with BMI 18.5- <25 kg/m² had a median CRP of 0.6 mg/L (SD 4.8), 10% were high risk for CVD and 3% would be classified as acute infection. Linear mixed models were used to assess the association between BMI and CRP concentrations. After adjustment for employment, recent birth, parity, use of contraception, and chronic medical conditions, a unit increase in BMI was associated with an 11.8% (95% confidence interval 11.1-12.4) increase in CRP. These results demonstrate that BMI is strongly associated with CRP concentrations and the widely used cut-point of 10 mg/L to identify those with acute infection may instead be capturing those with elevated BMI or chronic inflammation.

C-reactive protein (CRP) concentration by measured body mass index (BMI) in Study of Environment, Lifestyle and Fibroid (SELF) participants*, Detroit, MI 2010-2018

BMI kg/m ²	N visits	Continuous Median CRP mg/ml (SD)	Clinical categories			
			<1 mg/ml (CVD low risk)	1- <3 mg/ml (CVD average risk)	3- <10 mg/ml (CVD high risk)	10+ mg/ml (Acute infection)
<18.5	43	0.3 (1.2)	84%	9%	7%	0%
18.5- <25	769	0.6 (4.8)	66%	21%	10%	3%
25- <30	940	1.3 (5.0)	42%	31%	20%	6%
30- <35	937	2.7 (5.1)	22%	34%	34%	11%
35- <40	801	4.3 (7.6)	10%	30%	37%	24%
40- <50	882	7.8 (9.5)	4%	17%	38%	41%
50- <60	175	12.6 (10.8)	1%	9%	31%	59%

*SELF participants are self-identified African American or Black women ages 23-41

Associations of urban environment features with hypertension and blood pressure across 230 Latin American cities Ione Avila-Palencia* Ione Avila-Palencia J. Jaime Miranda Daniel A Rodríguez Kari Moore Nelson Gouveia Mika R Moran Waleska Teixeira Caiaffa Ana V Diez-Roux

Aim: We examined associations of built environment features with hypertension and blood pressure in adults across 230 Latin American cities.

Methods: In this cross-sectional study we used data from the SALURBAL project. The individual-level outcomes were hypertension and levels of systolic and diastolic blood pressure. The exposures were city and sub-city built environment, presence of mass transit infrastructure, and green space. Associations were estimated using logistic and linear multilevel regression models. Models were run as single and multiple exposure models and adjusted for individual-level age, sex, education, and sub-city educational attainment.

Results: A total of 109,176 participants were included in the hypertension analyses and 50,228 participants in the blood pressure analyses. In multiple exposure models, a higher city fragmentation was associated with higher odds of having hypertension [OR (95%CI): 1.10 (1.01, 1.21)] and higher levels of diastolic blood pressure [Mean difference (95%CI): 0.98 (0.30, 1.66)]; presence of mass transit in the city was associated with higher odds of having hypertension [OR (95%CI): 1.26 (1.07, 1.50)] and higher levels of diastolic blood pressure [Mean difference (95%CI): 1.27 (0.11, 2.42)]; and higher sub-city population density was associated with lower odds of having hypertension [OR (95%CI): 0.93 (0.88, 0.98)]. Higher levels of greenness were associated with lower levels of diastolic blood pressure [Mean difference (95%CI): -0.37 (-0.67, -0.08)] only in the model adjusted by country. Our analyses showed no evidence of an association between the exposures of interest and systolic blood pressure.

Discussion: Our results contribute evidence that integrated management of urban design, transport planning, and public health is needed to develop policies to improve cardiovascular health in cities in low- and middle-income countries.

Using deep learning to incorporate longitudinal health factors into 10-year atherosclerotic cardiovascular disease risk prediction in the Multi-Ethnic Study of Atherosclerosis (MESA)

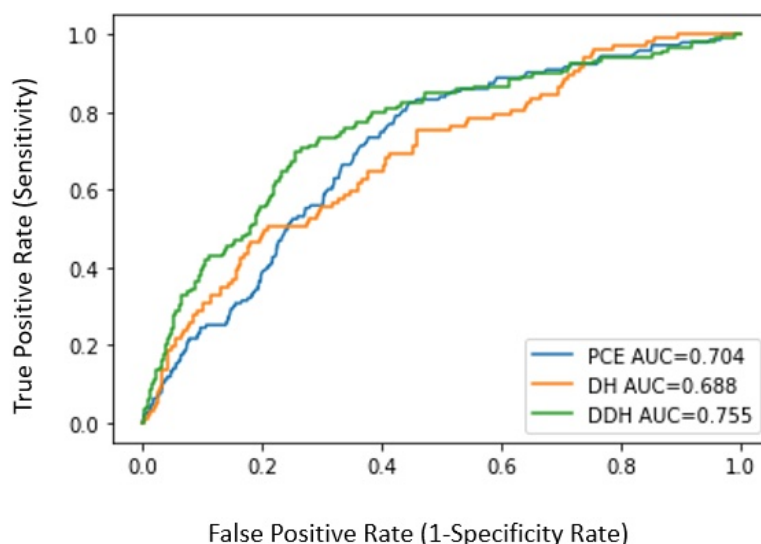
Norrina B. Allen* Jingzhi Yu Amy Elizabeth Krefman Xiaoyun Yang Lindsay Pool Lucia C. Petito Lihui Zhao Norrina B. Allen

The Pooled Cohort Equations (PCE) are used to guide clinical cardiovascular prevention strategies. The current tools are based on classical regression methods, which may smooth over more complex interactions between risk factors and do not incorporate longitudinal risk factors or account for competing risks. Increasingly sophisticated deep learning methods have been developed to incorporate longitudinal risk factor patterns to identify individuals more accurately at high risk for future atherosclerotic cardiovascular disease (ASCVD). Whether models created using these methods have greater discrimination than more traditional cross-sectional risk prediction models remain unknown.

Our study included 29560 records from 6755 participants of the Multi-Ethnic Study of Atherosclerosis without baseline ASCVD who were followed for adjudicated ASCVD or death. We split the dataset 70/30 into training and testing sets. Ten-year ASCVD risk was calculated in the training set using three methods: 1) the PCE (benchmark); 2) a non-longitudinal neural network, DeepHit (DH) and 3) a longitudinal neural network, Dynamic-DeepHit (DDH). Candidate predictors for DH and DDH included factors incorporated in the PCE: sex, race, age, total cholesterol, high density lipid cholesterol, systolic blood pressure, diabetes diagnosis, hypertension treatment and smoking status. The discriminative performance of all 3 models was determined in the testing set via AUC.

Our final analytic sample was 53% female with an average age of 62 at baseline. 1095 deaths and 737 ASCVD diagnoses occurred during 10 year study follow-up. The performance of the DDH model that incorporated 5 years of longitudinal risk factor data was modestly better than that of the PCE and the DH model that solely incorporate cross-sectional risk factor data (AUC of 0.76 versus 0.70) (Figure 1).

Incorporating longitudinal risk factors in ASCVD risk prediction may improve model performance. Validation in other cohorts is further needed.



Association of influenza vaccination with self-rated health and gender in Canadian adults with heart disease or stroke Na Zeng* Zeng Na Yue Chen Daniel J Corsi Dilan Patel Fenghao Ma Shi Wu Wen

Objectives

Seasonal influenza vaccination is highly recommended by the National Advisory Committee on Immunization for individuals with heart disease or stroke. Our study aimed to examine separate and joint associations of self-rated health (SRH) and gender with no seasonal influenza vaccination among Canadian adults affected by heart disease or stroke.

Methods

We used data from the Canadian Community Health Survey between 2015 and 2016. Multivariable modified Poisson regression model was used to quantify the separate and joint associations of interest. Additive interaction between SRH and gender was assessed by calculating relative excess risk due to interaction, attributable proportion due to interaction, synergy index. Sampling weight and average design effect were applied for all statistical analyses.

Results

Of 7,174 Canadians with heart disease or stroke aged 18 and above from surveyed population of 109,659, 42.7% did not receive seasonal influenza vaccination in the past year. No apparent additive interaction between gender and SRH associated with non-vaccination against seasonal influenza was found. Among individuals aged 65 to 75 years old, those with excellent SRH were about 77% more likely to be unvaccinated against seasonal influenza compared with individuals with poor SRH. For participants between 18 to 64 years, males were 13% more likely to have unvaccinated behaviour than females.

Conclusion

Our study suggests that the risk of un-vaccination against influenza increased for those who rated themselves in excellent health condition and being male in Canadian adults affected by heart disease or stroke in specific age groups.

Adolescent psychological assets and cardiovascular health maintenance in young

adulthood: A 22-year prospective study Farah Qureshi* Farah Qureshi Anne-Josée Guimond Sakurako S. Okuzono Scott Delaney Kelb Bousquet-Santos Julia K. Boehm Laura D. Kubzansky

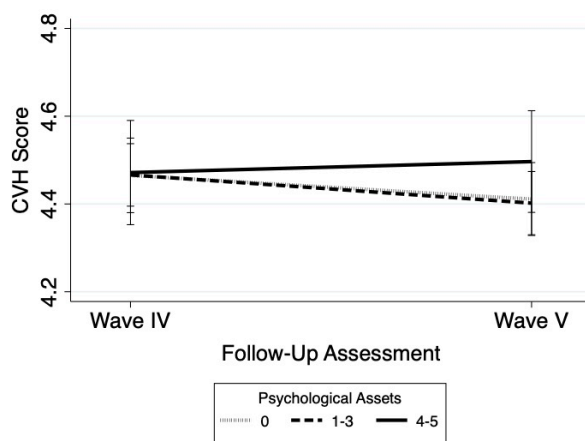
Background: Given prior work linking facets of positive psychological well-being (e.g., optimism, happiness) with better cardiovascular health (CVH), they are increasingly considered health assets. However, the potential effects of such assets on CVH early in life are poorly understood. This study investigates the long-term impact of adolescent psychological assets on CVH in young adulthood.

Methods: Data are from 3,374 youth in the National Longitudinal Study of Adolescent Health. We assessed psychological assets at Wave 1 (mean age=15 yrs) via an index (range=0-5) including measures of happiness, optimism, self-esteem, belongingness, and feeling loved. We defined composite CVH scores at Waves 4 (mean age=28 yrs) and 5 (mean age=38 yrs) using clinical recommendations for healthy levels of 7 biomarkers (range=0-7): high- and non-high density lipoprotein cholesterol, systolic and diastolic blood pressure, HbA1c, C-reactive protein, and body mass index (BMI). Participants with ≥ 6 healthy biomarkers at both waves were classified as maintaining optimal CVH in young adulthood. Logistic regression models evaluated associations of total assets with optimal CVH maintenance, adjusting for baseline covariates, including BMI and negative emotions. Linear mixed models also evaluated longitudinal associations with mean CVH scores over time.

Results: Only 7% of the sample maintained optimal CVH (mean score Wave 4=4.37, Wave 5=4.31). Findings indicated a dose-response relationship between assets and CVH, with each additional asset conferring a 16% greater likelihood optimal CVH maintenance ($OR_{\text{fully adjusted}}=1.16$, 95% CI=1.04, 1.29). No longitudinal associations were noted with CVH scores, but trends hinted at a possible divergence in CVH by Wave 5 (Figure 1).

Conclusion: Greater psychological assets in adolescence were associated with healthier CVH patterns decades later. Fostering the development of assets early in life may be a novel strategy for cardiovascular health promotion.

Figure 1. Cardiovascular health (CVH) scores from Wave 4 (mean age=28) to Wave 5 (mean age=38) by levels of adolescent psychological assets.*



* Unadjusted models found no associations between assets and CVH scores averaged across waves (95% $CI_{\text{per 1-SD assets}}=-0.02, 0.03$) or participants' annual change in CVH (95% $CI_{\text{per 1-SD assets}}=-0.001, 0.006$).

Systematic review and meta-analysis of the relationship between resilience resources and cardiovascular disease in the United States

Jee Won Park* Jee Won Park Rachel Mealy Ian J. Saldanha Eric B. Loucks Belinda L. Needham Mario Sims Joseph L. Fava Akilah J. Dulin Chanelle J. Howe

Background: Resilience resources (e.g., optimism, social support) may protect against adverse cardiovascular (CV) outcomes. The objective of our systematic review and meta-analysis was to summarize and quantify the relationship between resilience resources at the individual, interpersonal, or neighborhood level and CV disease among adults in the United States.

Methods: We systematically searched Medline, Embase, CINAHL, and PsycINFO through 9/25/2020 for peer-reviewed prospective cohort studies and randomized controlled trials published in English. We used the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I) tool for risk of bias assessment. We meta-analyzed data (i.e., adjusted point estimates and 95% CIs) across relevant studies using random-effects models.

Results: Our systematic review included 13 prospective cohort studies from 17 articles with a total of 310,906 participants. Six of these 13 studies were included in our meta-analyses. Studies were published between 1983 to 2019, and follow-up ranged from 2 to 16 years. Generally, studies had a moderate overall risk of bias. Most included studies reported a lower incidence of adverse CV outcomes with higher levels of individual-level resilience resources (point estimates: 0.46-1.18). Larger social networks (interpersonal-level resilience resource) was associated with a lower coronary heart disease risk (RR: 0.76, 95% CI: 0.56-1.02). Neighborhood-level resilience resources (i.e., perceived social cohesion and residential stability) were associated with a lower odds of stroke (OR: 0.92, 95% CI: 0.84-1.01).

Conclusions: Higher levels of resilience resources were associated with a lower risk or odds of adverse CV outcomes. Resilience-based interventions may be potential targets for reducing CV disease risk and improving CV health. However, studies should explore the relationship between resilience resources and CV outcomes in diverse populations.

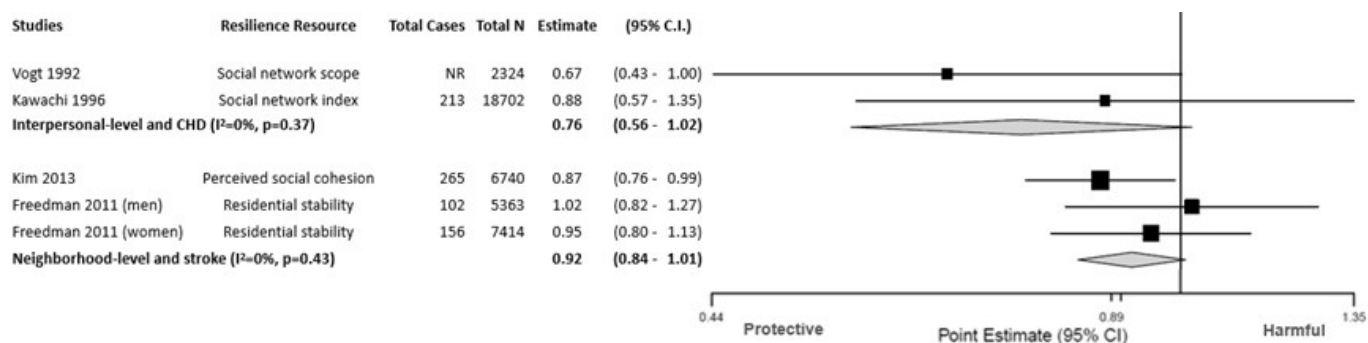


Figure. Forest plot of interpersonal- and neighborhood-level resilience resources and CHD and stroke, respectively. Abbreviations: CHD coronary heart disease; NR not reported.

Environment/Climate Change

Hyper-localized air pollution measures and preeclampsia in Oakland, California Dana Goin*

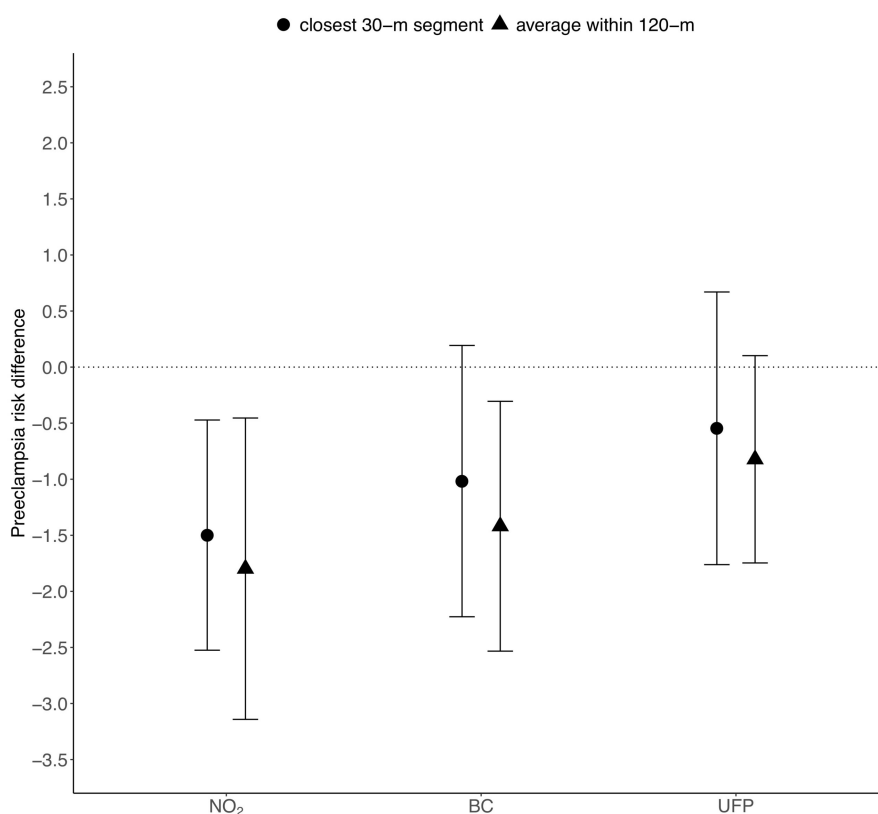
Dana Goin Sylvia Sudat Corinne Riddell Rachel Morello-Frosch Joshua Apte M. Maria Glymour
Deborah Karasek Joan Casey

Background: Exposure to nitrogen dioxide (NO₂), black carbon (BC), and ultrafine particles (UFP) during pregnancy may increase risk of preeclampsia, but previous studies have not assessed hyper-localized differences in pollutant levels which may cause exposure misclassification.

Methods: Google Street View cars with mobile air monitors repeatedly sampled NO₂, BC, and UFP every 30-meters in Downtown and West Oakland neighborhoods during 2015–2017. Data were linked to electronic health records of pregnant women in the 2014–2015 Sutter Health population who resided within 120-meters of monitoring data (N=1,095) to identify preeclampsia cases. We used G-computation with log-binomial regression to estimate risk differences (RD) associated with hypothetical interventions reducing pollutant levels to 25th percentiles observed in our sample on preeclampsia risk, overall and stratified by race/ethnicity.

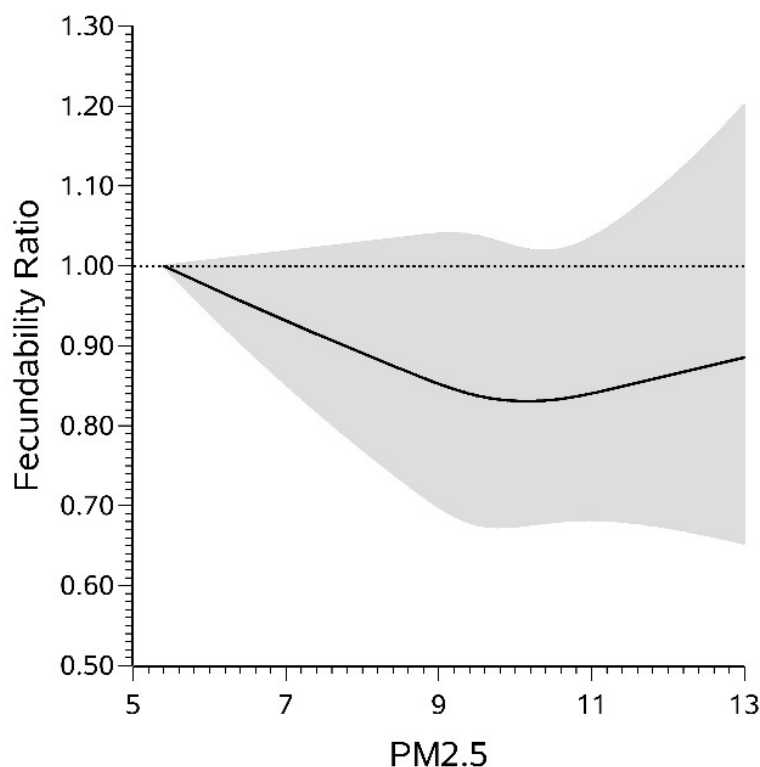
Results: Prevalence of preeclampsia was 6.8%. Median (IQR) levels of NO₂, BC, and UFP were 10.8 ppm (9.0, 13.0), 0.34 mg/m³ (0.27, 0.42), and 29.2 # ' 10/cm³ (26.6, 32.6), respectively. Changes in preeclampsia prevalence achievable by limiting each pollutant to the 25th percentile was NO₂ RD = -1.5 per 100 women (95% CI: -2.5, -0.5); BC RD = -1.0 (95% CI: -2.2, 0.02); and UFP RD = -0.5 (95% CI: -1.8, 0.7). Estimated effects were largest for non-Latina Black mothers: NO₂ RD = -2.8 (95% CI: -5.2, -0.3) and BC RD = -3.0 (95% CI: -6.4, 0.4).

Conclusion: BC and NO₂ are associated with risk of preeclampsia in Oakland, California, and may contribute to disparities by race/ethnicity.



Air pollution and fecundability: Results from a Danish preconception cohort study Amelia K. Wesselink* Amelia Wesselink Tanran R. Wang Matthias Ketzel Ellen M. Mikkelsen Jørgen Brandt Jibrán Khan Ole Hertel Lauren A. Wise Anne Sofie Dam Lauren Jonathan I. Levy Kenneth J. Rothman Henrik T. Sorensen Elizabeth E. Hatch

A growing literature indicates that air pollution may adversely influence human reproduction. Yet most existing epidemiologic studies on air pollution and fertility are small or restricted to infertile study populations. We examined the association between residential exposure to air pollution and fecundability – the per cycle probability of conception – in a preconception cohort of 10,183 Danish couples. During 2007-2019, women aged 18-45 years who were trying to conceive completed an online baseline questionnaire and bi-monthly follow-up questionnaires for up to 12 months. We geocoded time-varying residential addresses during the year before baseline and used the DEHM/UBM/AirGIS dispersion modelling system to estimate the annual mean concentrations of nitrogen dioxide, nitrogen oxides, carbon monoxide, ozone, sulfur dioxide, PM_{2.5} and PM₁₀ (particulate matter with diameters <2.5 µm and <10 µm, respectively). We used proportional probabilities regression models to estimate fecundability ratios (FRs) with 95% CIs, adjusting for potential confounders and co-pollutants. We followed women until pregnancy or censoring event (stopped trying, loss to follow-up, fertility treatment initiation, or 12 menstrual cycles). Individual pollutants were positively correlated with one another (Spearman correlations: 0.41-0.96), except for ozone, which was inversely correlated with other pollutants. Annual average PM_{2.5} concentrations were associated with slightly reduced fecundability (Figure 1): in comparison with the reference group (<8.0 µg/m³), FRs for PM_{2.5} concentrations of 8.0-9.9, 10.0-11.9, 12.0-12.9, and ≥13.0 µg/m³ were 0.89 (95% CI: 0.82, 0.97), 0.87 (95% CI: 0.78, 0.96), 0.89 (95% CI: 0.73, 1.08), and 0.84 (95% CI: 0.62, 1.14), respectively. Associations were stronger among nulliparous women. Other pollutants were not appreciably associated with fecundability. Our results indicate that long-term air pollution exposure may be related to reduced fertility.



Mid-term PM_{2.5} exposure and cardiovascular and thromboembolic hospitalizations in Medicare beneficiaries with high-risk chronic conditions Rachel Nethery* Rachel Nethery
Kevin Josey Benjamin Bates Poonam Gandhi Jung Hyun Kim Soko Setoguchi

Background

Numerous studies have reported associations between fine particulate matter (PM_{2.5}) exposure and cardiovascular hospitalizations in older populations. However, most of these studies focused on short-term PM_{2.5} exposure. No studies to date have investigated these associations in vulnerable older subjects at high risk for cardiovascular and thromboembolic events (CTE) nor adjusted for medication use or chronic conditions.

Methods

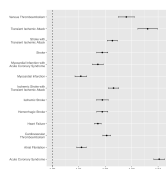
Among a 20% random sample of 2008-2017 Medicare Fee-for-Service population, we identified a cohort with high risk conditions for CTE. These conditions included cardiovascular disease, cancer, and prosthesis implantation and were defined as having inpatient diagnoses or procedures, which has been shown to have high positive predictive values. The cohort was linked with seasonal average PM_{2.5} concentrations from a well-validated, high-resolution predictive model by zipcode of residence. We assessed 13 CTE hospitalization outcomes (Figure) and fit a Cox proportional hazard model to assess associations between each outcome and PM_{2.5}. Cox models were inverse probability weighted to adjust for confounding (demographics, comorbidities, medication use, and neighborhood socio-economic features) and the competing risk of death.

Results

Among 2,092,183 individuals in the high-risk cohort (mean age 77, 60% female, 88% white), we found that PM_{2.5} exposure was significantly associated with increased risk of each of the 13 CTE hospitalization types (Figure for hazard ratios and 95% CIs). The strongest increases were observed for acute coronary syndrome (HR: 1.040), transient ischemic attack (HR: 1.036), and venous thromboembolism (HR: 1.028).

Conclusion

In a large cohort of individuals at high risk for CTE, after adjusting for comorbidities, medications, and SES factors, mid-term PM_{2.5} exposure was associated with increases in all 13 CTE hospitalization types. Future analyses will assess interactions between medications/conditions and PM_{2.5} exposure.



The impact of mobility on COVID-19 incidence and disparities at the sub-city level in 314

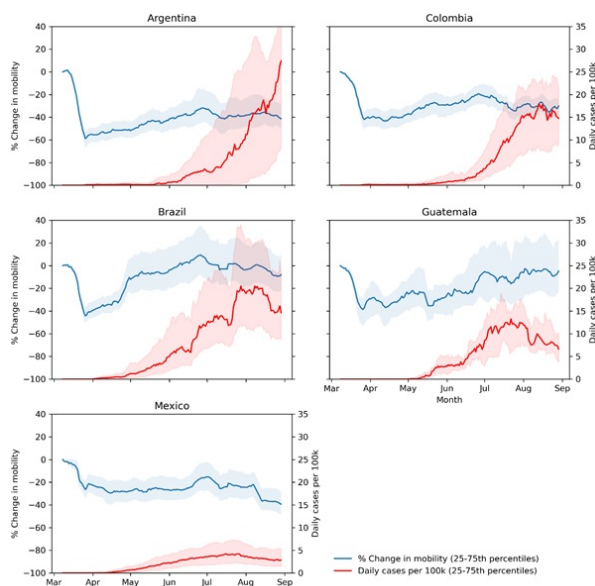
Latin American cities Josiah Kephart* Josiah L. Kephart Xavier Delclòs-Alió Daniel A. Rodríguez Usama Bilal Olga L Sarmiento Manuel Ramirez-Zea Alex Quistberg Tonatiuh Barrientos-Gutiérrez Ana V. Diez Roux

Background: Policies which reduce population mobility have been a core component of government efforts to reduce SARS-CoV-2 transmission. However, little is known about the impact of mobility at the sub-city level on subsequent COVID-19 incidence or the contribution of mobility to disparities in COVID-19 incidence by socioeconomic status.

Methods: We compiled aggregated mobile phone location data, COVID-19 confirmed cases, and features of the urban and social environments to analyze linkages between mobility, COVID-19 incidence, and community educational attainment at the sub-city level among cities with >100,000 inhabitants in Argentina, Brazil, Colombia, Guatemala, and Mexico. We used mixed effects negative binomial regression to explore longitudinal associations between changes in weekly mobility (lags 1-4 weeks) and subsequent COVID-19 incidence at the sub-city level, adjusting for urban environmental factors.

Results: Among 1,031 sub-cities representing 314 cities in five Latin American countries, 10% higher weekly mobility was associated with 7.5% higher weekly COVID-19 incidence the following week. This association gradually declined as the lag between mobility and COVID-19 incidence increased and was attenuated at a mobility lag of four weeks. The association between sub-city educational attainment and COVID-19 incidence varied between countries, and we found evidence that suggests differences in mobility contribute to COVID-19 incidence disparities by education at the sub-city level.

Conclusions: Lower population movement within a sub-city is associated with lower risk of subsequent COVID-19 incidence among residents of that sub-city and may contribute to COVID-19 socioeconomic disparities. More research is warranted to confirm the effectiveness of policies which target mobility at the sub-city or neighborhood level to limit city-wide disruption and mitigate COVID-19 socioeconomic disparities.



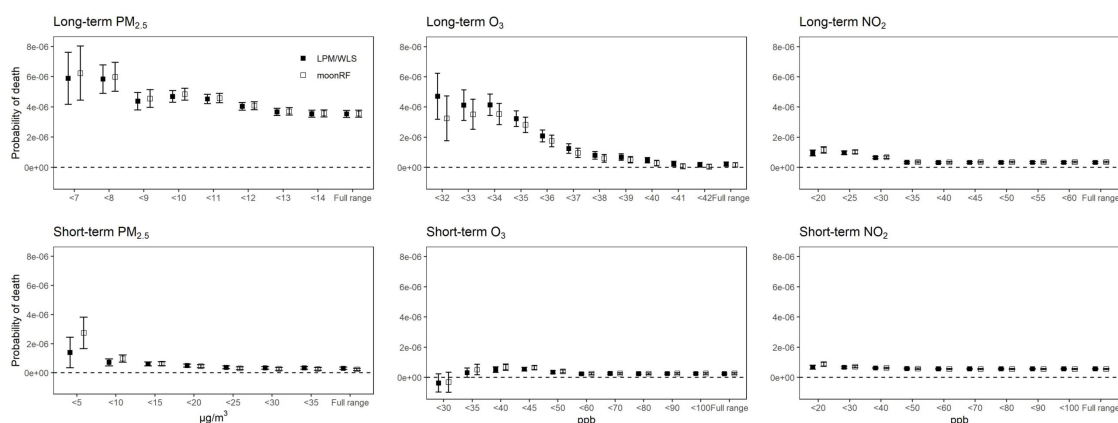
Assessing additive effects of air pollutants on mortality rate in Massachusetts Yaguang Wei*
Yaguang Wei Brent Coull Petros Koutrakis Jiabei Yang Longxiang Li Antonella Zanobetti Joel Schwartz

Background: We previously found additive effects of long- and short-term exposures to fine particulate matter (PM_{2.5}), ozone (O₃), and nitrogen dioxide (NO₂) on mortality rate among Medicare beneficiaries in Massachusetts during 2000–2012 using a generalized propensity score (GPS) adjustment approach. However, the study did not capture possible interactions and high-order nonlinearities, was computationally expensive, and omitted potential confounders.

Methods: We allowed for time-varying covariates by creating a counting process data structure that had 3.8 billion person-days of follow-up. We proposed two new methods to increase computational efficiency and flexibility. The first method, weighted least squares (WLS), leveraged large volume of data by aggregating person-days yet retained all the information after the aggregation, which gave equivalent results to the linear probability model (LPM) method in the previous analysis but significantly reduced computational burden. The second method, m-out-of-n random forests (moonRF), implemented a scaling random forests that captured interactions and nonlinearities in the GPS model. To minimize confounding bias, we additionally controlled potential confounders that were not included previously.

Results: We found consistent results between LPM/WLS and moonRF: all exposures were significantly associated with mortality rate, even at low levels. Long-term PM_{2.5} exposure posed the highest risk: 1 µg/m³ increase in long-term PM_{2.5} was associated with 1,053 (95% confidence interval [CI]: 984, 1,122) early deaths using LPM/WLS or 1,058 (95% CI: 988, 1,127) early deaths using moonRF in each year.

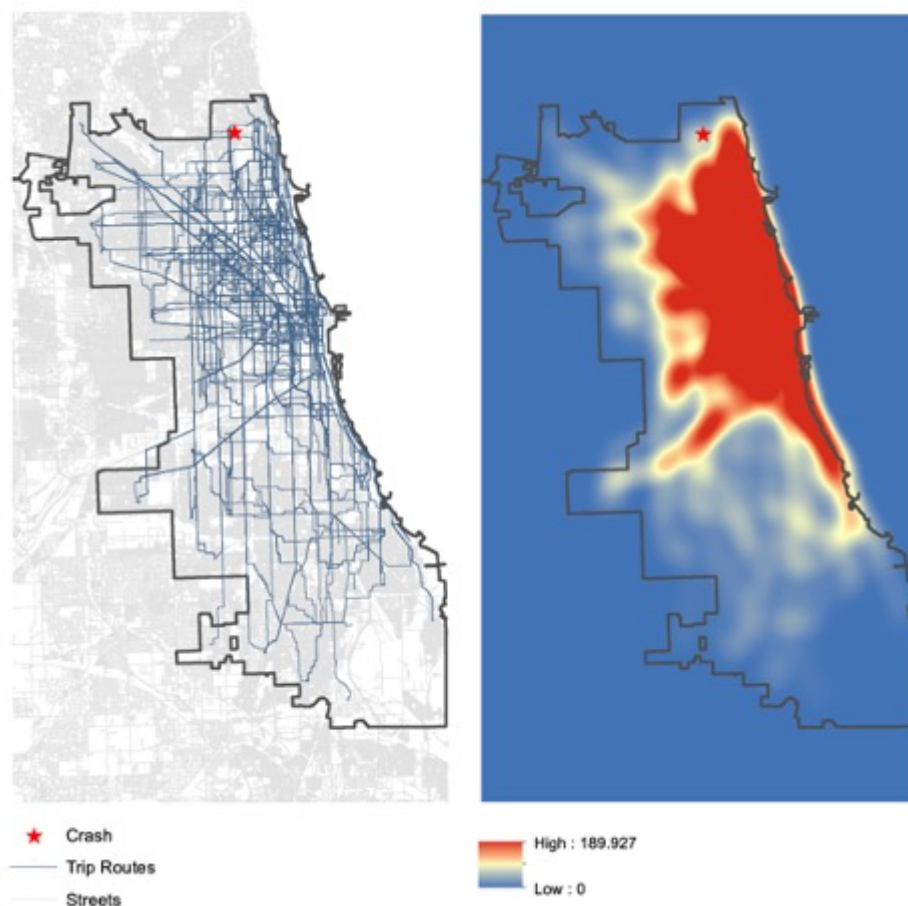
Conclusions: This study provides more rigorous evidence of causal links between PM_{2.5}, O₃, and NO₂ exposures and mortality. The consistency between LPM/WLS and moonRF suggests that there were not many interactions and high-order nonlinearities. In the big data context, the proposed methods will benefit future scientific work.



Associations between Rideshare Trips and Alcohol-Involved Motor Vehicle Crashes in Chicago

Ava Kamb* Ava Kamb Christopher N. Morrison Gabrielle D'Ambrosi Kytt MacManus Andrew G. Rundle David K. Humphreys

Objective. Rideshare companies such as Uber and Lyft have substantially changed transportation markets in the US and globally. The aim of this study is to examine whether ridesharing is associated with reductions in alcohol-involved crashes. **Method.** This case control study used highly spatially and temporally resolved trip-level rideshare data and motor vehicle crash data for Chicago from November 2018 to December 2019. The units of analysis were motor vehicle crashes in the city of Chicago. Cases were 962 crashes that police indicated were alcohol-involved. Controls were crashes in the same census tract, matched 1:1. The exposure of interest was the density per square mile of rideshare trips that were in progress at the time of the crash, calculated using a kernel density function around the estimated route paths of active trips. Control variables were taxi trip density, time of day, day of week, public holiday, temperature, precipitation, and month. A conditional logistic regression compared alcohol-involvement to rideshare trip density. **Results.** Rideshare trip density was 69.0 per square mile at the location of case crashes and 105.7 per square mile at the location of control crashes. After controlling for covariates, the conditional logistic regression model identified that an increase of 1 rideshare trip per square mile at the crash site was associated with 0.2% decreased odds that the crash was alcohol involved (OR = 0.998; 95%CI: 0.996, 0.999). There was no association for taxi trips. **Conclusions.** Increased ridesharing activity was associated with decreased odds that motor vehicle crashes were alcohol involved.



Effects of comprehensive background check policies on firearm fatalities in four states

Rose Kagawa* Rose Kagawa Amanda Charbonneau Christopher McCort Alexander McCort Jon Vernick Daniel Webster Garen Wintemute

Background: In 2018, 38,390 people were killed in firearm homicides and suicides. One approach to reducing firearm violence with wide public support in the US is the extension of background check requirements to private transfers (i.e., guns obtained from persons who are not licensed firearm dealers), referred to as comprehensive background check (CBC) policies. Recent research has failed to document protective state-level effects of this extension of background check requirements; however, these prior studies focused on CBC laws adopted in the 1990s. We estimate the effect of the enactment of CBC policies on state-level firearm homicide and suicide rates in states enacting CBC policies within the past ten years (Colorado, Delaware, Oregon, Washington).

Methods: We compare age-adjusted firearm homicide and suicide rates measured annually from 15 years prior to policy enactment until 2018 in each treated state to rates in control groups constructed using the synthetic control method. Analyses and results are currently blinded to treatment status.

Preliminary Results: In one state, the post intervention period difference between the average rate of firearm suicide in the treated and synthetic states was 1.85 per 100,000 (pre-intervention mean rate=5.0 per 100,000). This difference was larger in magnitude than the differences in 27 of 28 placebo tests. All other differences were smaller in magnitude (<0.8 per 100,000) and considered within the range of natural variation.

Conclusion: The enactment of CBC laws was associated with changes in firearm suicide in 1 out of 4 states that adopted a CBC law since 2013 and no change in firearm homicide rates. Coupled with previous null results from Indiana, California, Maryland, Pennsylvania, and Tennessee, these results suggest extending background check requirements to private transfers alone and as currently implemented is not sufficient to achieve significant state-level reductions in firearm fatalities.

The role of state-level household firearm ownership on 2001-2016 trends in firearm suicide rate in the United States: a hierarchical age-period-cohort analysis. Gonzalo Martínez-Alés*

Gonzalo Martínez-Alés Catherine A. Gimbrone Caroline Rutherford Mark Olfson Madelyn Gould Jeffrey Shaman Katherine M. Keyes

In the US, state-level household firearm ownership is strongly associated with firearm suicide mortality rates. The extent to which recent increases in firearm suicide are explained by between-state differences, and trends, in household firearm ownership remains unknown. Using firearm suicide mortality data from the US National Vital Statistics System, we conducted hierarchical age-period-cohort (random-effects) models of firearm suicide mortality rates between 2001-2016, adjusting for an estimate of state-level household firearm ownership. Variance in household firearm ownership was largely explained by between-state differences, and the proportion of households owning a firearm in each state remained relatively stable over time; we therefore categorized states in octiles according to their average ownership over the study period. Additional adjustment covariates included individual-level race/ethnicity and sex, and state-level annual poverty rate, annual unemployment rate, annual median household income in US dollars, and median elevation in feet. We found that recent increases in firearm suicide rates (from 5.6/100,000 in 2001 to 7.0/100,000 in 2016) were due to both period and cohort effects. A negative period effect between 2004-2010 was followed by a positive period effect beginning in 2011, at a random effect coefficient of around 0.1. Period effect variability, expressed as median odds ratio, decreased from 1.18 to 1.11 with inclusion of state-level household firearm ownership in the model. Individuals born between 1996-1999 had higher suicide rates than most cohorts born between 1930-1995, with random effect coefficients of around 0.2, except for baby-boomers. In conclusion, trends in state-level firearm ownership rates only partially explain recent increases in firearm suicide, yet firearms remain major determinants of suicide risk in the US. Broader approaches are required to understand and diminish recent increases in firearm suicide mortality.

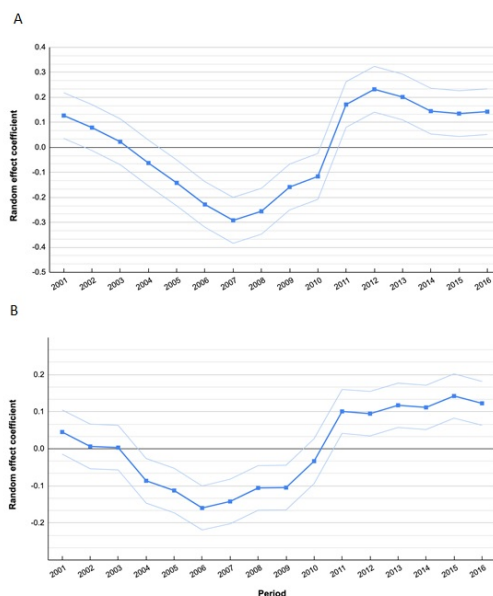


Figure: Period effect of firearm suicide in the United States between 2001-2016, obtained from a hierarchical age-period-cohort effects model, adjusted for (A): individual-level race/ethnicity and sex, and state-level annual poverty rate, annual unemployment rate, annual median household income in US dollars, and median elevation in feet; and (B): same as A and state-level firearm ownership rates.

Simulating the bounds of plausibility: estimating the impact of high-risk versus population-based approaches to prevent firearm injury Ava Hamilton* Ava Hamilton
Magdalena Cerdá Katherine M Keyes

Background. Firearm violence remains a persistent public health threat. Policy responses have included firearm ownership disqualifications among groups deemed high risk, but are unevenly enforced. Price increases have been successful population-based approaches to reduce harm for other products. We used agent-based modeling to simulate high-risk (ownership disqualification) and population-based (price increases for firearms) approaches in New York City to determine the maximum impact on firearm homicide.

Methods. We created a population of 260,000 agents reflecting a 5% sample of the NYC adult population. Agents were disqualified from firearm ownership in three categories: low (psychiatric hospitalization and alcohol-related misdemeanor and felony convictions), moderate (drug misdemeanor convictions and domestic violence restraining orders), and high prevalence (all felony and misdemeanor convictions) disqualifications.

Results. To reduce firearm homicide by 5% (95% CI -7.2%, 16.32%) in NYC, 22% of the moderate prevalence high-risk group or 3% of the high prevalence high-risk group would need to be effectively disqualified, or increasing the price by 8%. A combined intervention increasing price and effectively disqualifying high-risk groups achieved approximately double the reduction in homicide as any one intervention alone. Price increases coupled with increases in illegal firearm ownership by even 5% nullified the effects of the price increase.

Conclusion. Firearm ownership disqualification based on risk status needs to be almost perfectly implemented to achieve meaningful reductions in firearm homicide; high-risk interventions that are based on health services access and criminal justice convictions should be considered in light of social justice and stigma. Similar reductions can be achieved with modest firearm price increases, though the efficacy is substantially reduced if price increases move buyers to illicit markets.

Association of Unemployment and Violence and Crime in US Cities During the Coronavirus Pandemic Julia Schleimer* Julia Schleimer Aaron Shev Veronica Pear Christopher McCort Alaina De Biasi Elizabeth Tomsich Hannah Laqueur Shani Buggs Garen Wintemute

Background.

The coronavirus pandemic and efforts to contain it have created an economic crisis. At the same time, rates of violence, particularly firearm-involved crime, have surged across the United States (US). We examined whether unemployment was related to increased rates of violence and crime during the pandemic.

Methods.

We selected 16 major US cities and compiled monthly data from January 2018-July 2020. The primary exposure was excess unemployment beginning March 2020, measured as the difference between observed unemployment rates and those predicted by seasonal auto-regressive integrated moving average models. Outcomes included interpersonal firearm violence and all Uniform Crime Reporting Part I offenses (homicide, rape, robbery, aggravated assault, burglary, larceny-theft, motor vehicle theft, and arson). Data were obtained from the Bureau of Labor Statistics, Local Area Unemployment Statistics; the Gun Violence Archive; and city open data portals. Using separate models for each outcome, we estimated the association of excess unemployment with crime and violence using Poisson and negative binomial generalized linear models with clustered standard errors.

Results.

On average, the unemployment rate per 100 persons was 8.1 percentage points higher than expected across cities from March through July 2020. Conditional on measured confounders, an absolute increase of 1% in unemployment over expected levels was positively associated with firearm violence (RR: 1.04; 95% CI: 1.02-1.07), aggravated assault (1.01; 1.00-1.02), homicide (1.04; 1.02-1.06), and motor-vehicle theft (1.02; 1.01-1.03). The strength of these associations increased over time.

Conclusions.

Findings suggest that the pandemic-related economic shock contributed to an increase in violence and crime. Future research should examine whether policies to stem increases in unemployment reduce the burden of violence and related inequities.

Optimizing SARS-CoV-2 pooled testing strategies through incorporation of simple-to-implement symptom and exposure screening tools Lindsey M. Filiatreau* Lindsey Filiatreau Paul Zivich Grace Mulholland Ryan Max Jessie K. Edwards Daniel Westreich

Pooled testing for SARS-CoV-2 is an effective testing strategy with the potential to conserve testing resources, save personnel time, reduce turnaround time, and increase testing efficiency (i.e., the number of test kits used/result obtained). However, in high-prevalence settings, the efficiency gains of pooled testing are reduced because a large proportion of pools require further pooling or individual testing. We propose a differentiated pooled testing strategy that independently optimizes pool sizes for two groups to preserve efficiency gains in expected high-prevalence settings. Here we consider two readily distinguishable groups: individuals with and without symptoms consistent with COVID-19 or known/probable exposure to SARS-CoV-2.

We compare the efficiency of our novel strategy to a typical pooling strategy in which tests are processed in uniform pool sizes regardless of the prevalence of SARS-CoV-2 in the population. We calculate the efficiency of each strategy using a previously published web calculator that accounts for diagnostic test performance and the effect of pooling on test performance. We estimate the gain in efficiency (ΔE) under a range of scenarios, varying the prevalence of SARS-CoV-2 among symptomatic/exposed and asymptomatic/unexposed individuals, and the probability of being symptomatic/exposed in the overall population.

We found that ΔE increases as prevalence of SARS-CoV-2 among symptomatic/exposed and asymptomatic/unexposed individuals diverge and as the probability of being symptomatic/exposed increases. In a population where 10-25% of the general population is symptomatic/exposed, we expect a sizeable gain in efficiency under a large set of plausible conditions. When less than 10% of the population is symptomatic/exposed, ΔE may be negligible. These results can be used to identify settings where differentiated pooled testing presents a critical opportunity to conserve time and resources with a minimal increase in operational complexity.

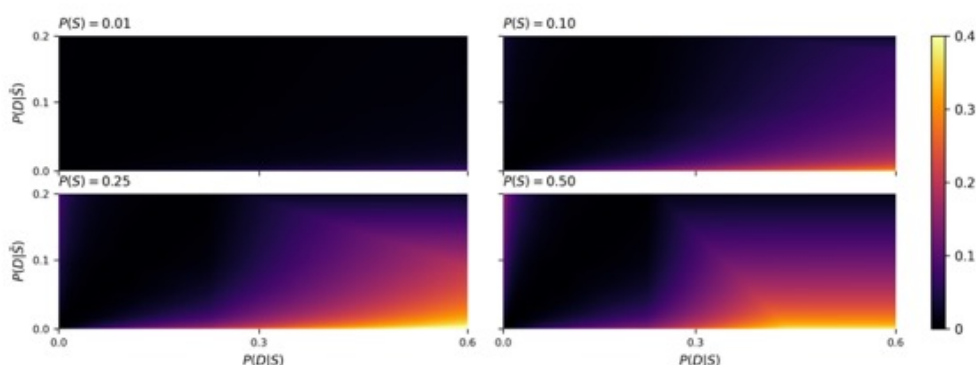


Figure. Gain in efficiency expected from implementation of a differentiated pooled testing strategy over a traditional two-stage hierarchal pooled testing strategy.

*Gain in efficiency is defined as the efficiency of a traditional two-stage strategy minus the efficiency of the differentiated pooled testing strategy. Comparisons consist of settings with prevalence of disease among symptomatic individuals ($P(D|S)$) ranging from 0-60%, a prevalence of disease among asymptomatic individuals ($P(D|\bar{S})$) ranging from 0-20%, and proportion of symptomatic individuals in the general population ($P(S)$) of 0.01, 0.10, 0.25, and 0.50.

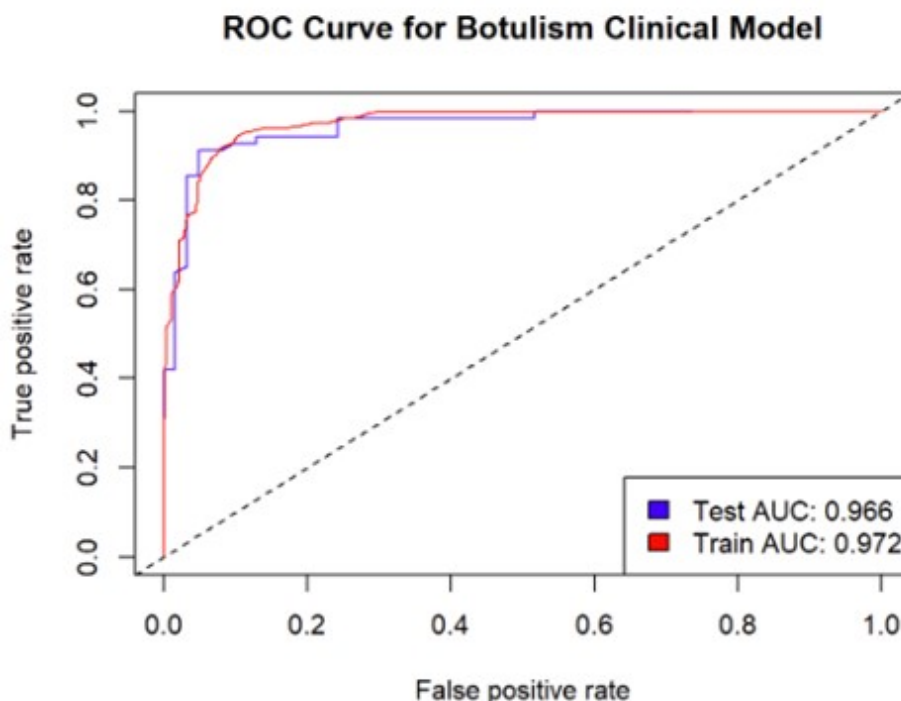
Predictive Model for Botulism Antitoxin Consultation Seth Edmunds* Seth Edmunds

Background: The Centers for Disease Control and Prevention (CDC) Botulism Consultation Service provides clinical consultations on suspected cases of all types of adult botulism. In 2017, CDC published a clinical criteria tool to trigger suspicion of botulism for clinicians. However, when the tool was applied to the CDC botulism surveillance database, its ability to accurately predict a botulism confirmation was poor. To allow for better prediction, an ensemble of multiple statistical models was developed.

Methods: Botulism case report and outcome data for cases reported to the CDC botulism surveillance database during 2000-2018 were pre-processed into numeric binary variables, and the assumption was made that if the value was unknown or not reported that it was not present/normal. The Botulism Clinical Criteria Tool prediction was generated based upon the signs, symptoms, and febrile status as indicated in the published Clinical Criteria Tool paper. The SuperLearner R package was utilized to build an ensemble model which used a negative binomial log-likelihood optimization. The ensemble was weighted with ranger accounting for 66%, biglasso 25%, and glm 8%.

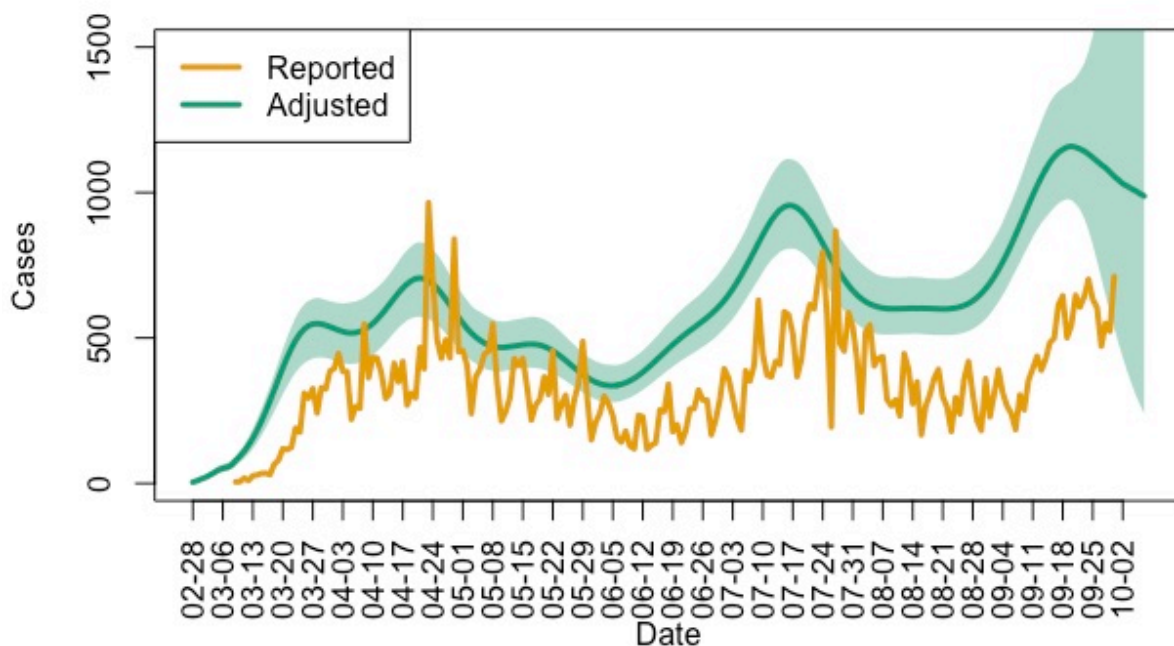
Results: The model using test data had an accuracy of 0.90 (0.84, 0.95), which was considerably higher than the Tool at 0.47 (0.44, 0.49). The test data AUC was 0.966 which compared well to the training data AUC at 0.972.

Discussion: A predictive ensemble model, trained and tested on data from the CDC botulism surveillance database, was shown to have a high accuracy versus the clinical criteria tool. A limitation of this ensemble approach is that there is a risk for overfitting, which does impose some limits on the model predictions. This model could be used to identify high probability suspect cases and expedite the release of antitoxin to state partners. This would free up limited consultation and reporting resources for both outbreak and sporadic botulism events.



Double adjustment in case ascertainment and uncertainty about date of infection in COVID-19 time series surveillance data Neal Goldstein* Neal Goldstein Harrison Quick Igor Burstyn

Surveillance data captured during the COVID-19 pandemic may not be optimal to inform a public health response, because it is biased by imperfect test accuracy, differential access to testing, and uncertainty in date of infection. We present a double adjustment approach to account for bias in surveillance and uncertainty in infection date. COVID-19 time series surveillance data were downloaded from the Colorado Department of Public Health & Environment by report and illness onset dates for 9-Mar-2020 to 30-Sep-2020. We used existing Bayesian methods to first adjust for misclassification in testing and surveillance, followed by deconvolution of date of infection. Uncertainty from each step was propagated forward corresponding to 10,000 posterior time-series of doubly adjusted epidemic curves. The effective reproduction number (R_t), a parameter of principal interest in tracking the pandemic, gauged the impact of the adjustment on inference. Observed period prevalence was 1.3%; median of the posterior of true (adjusted) prevalence was 1.7% (95% credible interval [CrI]: 1.4%, 1.8%). Sensitivity of surveillance declined over the course of the epidemic from a median of 88.8% (95% CrI: 86.3%, 89.8%) to a median of 60.8% (95% CrI: 60.1%, 62.6%). The Figure depicts the doubly adjusted posterior distribution of the epidemic curve accounting for the incubation period of SARS-CoV-2 and any delays in testing and reporting, as well as misclassification in case ascertainment. The mean (minimum, maximum) values of R_t were higher and more variable by report date, 1.12 (0.77, 4.13), compared to those following adjustment, 1.05 (0.89, 1.73). The epidemic curve by report date tended to overestimate R_t early on and be more susceptible to fluctuations in data. Adjusting for epidemic curves based on surveillance data is necessary if estimates of missed cases and the effective reproduction number play a role in management of the COVID-19 pandemic.



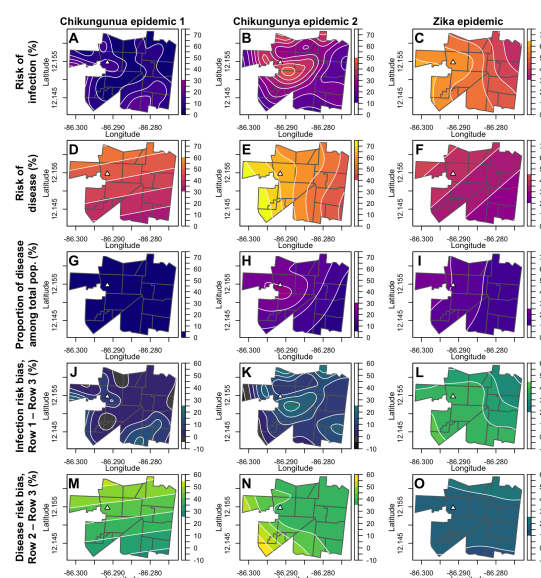
Spatial studies of infection and disease in explosive chikungunya and Zika epidemics in a prospective cohort study in Managua, Nicaragua, reveal bias of standard case-based infectious disease mapping Fausto Bustos Carrillo* Fausto Bustos Carrillo Brenda Lopez Mercado Jairo Carey Monterrey Damaris Collado Tatiana Miranda Sergio Ojeda Nery Sanchez Miguel Plazaola Harold Suazo Laguna Douglas Elizondo Sonia Arguello Saira Saborio Josefina Coloma Leah Katzelnick Aubree Gordon Hugh Sturrock Angel Balmaseda Guillermina Kuan Eva Harris

Widespread epidemics of chikungunya (CHIKV) and Zika virus (ZIKV) across the Americas recently caused millions of symptomatic and asymptomatic infections. We examined the non-spatial, spatial, and spatiotemporal epidemiology of two chikungunya epidemics (2014, 2015) and one Zika epidemic (2016) in a prospective pediatric cohort in Managua, Nicaragua.

We used generalized additive models, Kuldorff's spatial scan test, and geostatistics to analyze ~3,000 initially CHIKV- and ZIKV-naïve participants in each epidemic. We assessed the risk of infection (the proportion of the immunologically naïve population to become infected), the risk of disease (the proportion of disease in the infected population), and the traditional metric (the proportion of disease in the total population).

Across three major epidemics, the risks of infection and disease exhibited different spatial patterns, contrary to traditional assumptions. Only clusters of infection outcomes, not disease outcomes given infection, were large and identified. High infection risk by the cemetery and extensive month-to-month changes characterized the spatiotemporal infection dynamics of all three epidemics. Critically, assuming the total (rather than the infected) population was at risk for disease, as is common practice in spatial epidemiology, biased all analyses and substantially underestimated the burden of infection and disease for all epidemics.

Our results show that high-infection areas may not exhibit much disease. Similarities across the epidemics suggest that targeting interventions to the built, non-household environment may reduce epidemic potential. Importantly, our results highlight how spatial analyses of many infectious pathogens that cause asymptomatic infections (including SARS-CoV-2) distort identification of high-risk areas, overlook critical epidemiological principles of risk, and always underestimate epidemic burden, thereby weakening the rationale for stronger pandemic control measures.



Challenges in estimating effects of COVID-19 on preterm birth Louisa H. Smith* Louisa Smith
Camille Dollinger Diego Wyszynski Sonia Hernández-Díaz

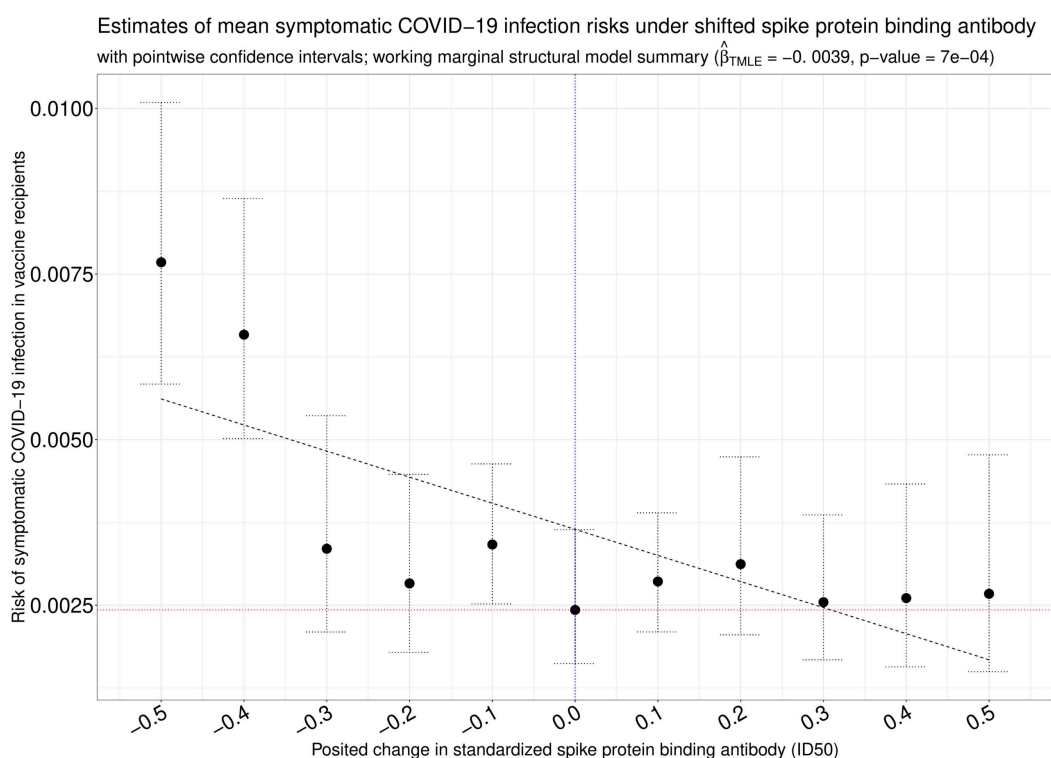
Concern about negative effects of SARS-CoV-2 infection during pregnancy is justified by evidence from other viruses, including influenza, SARS, and MERS. Preterm birth may be one such effect. Initial evidence from studies of severe COVID-19 late in pregnancy appeared to bear out this concern: estimates of upwards of 60% risk of preterm birth have been reported in the literature. However, other studies have reported lower risk of preterm birth among pregnancies with COVID-19 than in the general population, even as low as 0%. These extremes demonstrate the challenges of quantifying the risk of preterm birth in an exposed population when the exposure is acute, subject to temporal trends, likely varies in its effect over pregnancy, and whose severity is intrinsically tied, along with the length of gestation, to the sampling scheme and to clinical decisions about delivery.

We propose various descriptive and causal questions about COVID-19 and preterm birth in the context of the International Registry of Coronavirus Exposure in Pregnancy (IRCEP), a cohort of over 17,000 women tested for SARS-CoV-2 during pregnancy. We discuss study designs and analyses that address the biases that interfere with answering these questions. Specifically, we consider the following: a) longer pregnancies have more time to be exposed to the virus and to get tested (in our sample, 34% were tested after 37 weeks), b) SARS-CoV-2 testing is now routinely offered at delivery, but access earlier in pregnancy has varied by time and place (60% of those tested in March were symptomatic, compared to 25% in July), c) severe disease late in pregnancy often precludes prospective enrollment (of COVID-affected pregnancies, 1% of those who enrolled during pregnancy had severe disease, compared to 4% of those who enrolled soon after). These methodological considerations are likely applicable to other studies of preterm birth as well as studies in which having had a test is a prerequisite for enrollment.

Evaluation of causal vaccine efficacy under stochastic interventional shifts of an immunologic marker in COVID-19 vaccine efficacy trials Nima Hejazi* Nima Hejazi David Benkeser Peter Gilbert

Initial efficacy assessments of vaccine candidates for COVID-19 have made for a promising start to curbing the pandemic. A critical next step is identifying immune correlates of protection, that could be used in the development of next-generation protective vaccine candidates. Deploying the classical tools of causal inference in service of such goals is obstructed by the historical focus of the field on static interventions, which cannot be applied to *quantitative* immunologic marker measurements without simplifying assumptions. Stochastic interventions, which define the target parameter as the mean counterfactual outcome under shifted versions of the observed immunologic marker distribution, hold promise for circumventing such difficulties. Complicating analytic efforts further, vaccine efficacy trials regularly employ two-phase sampling of immunologic markers, necessitating careful adjustment for formal statistical inference.

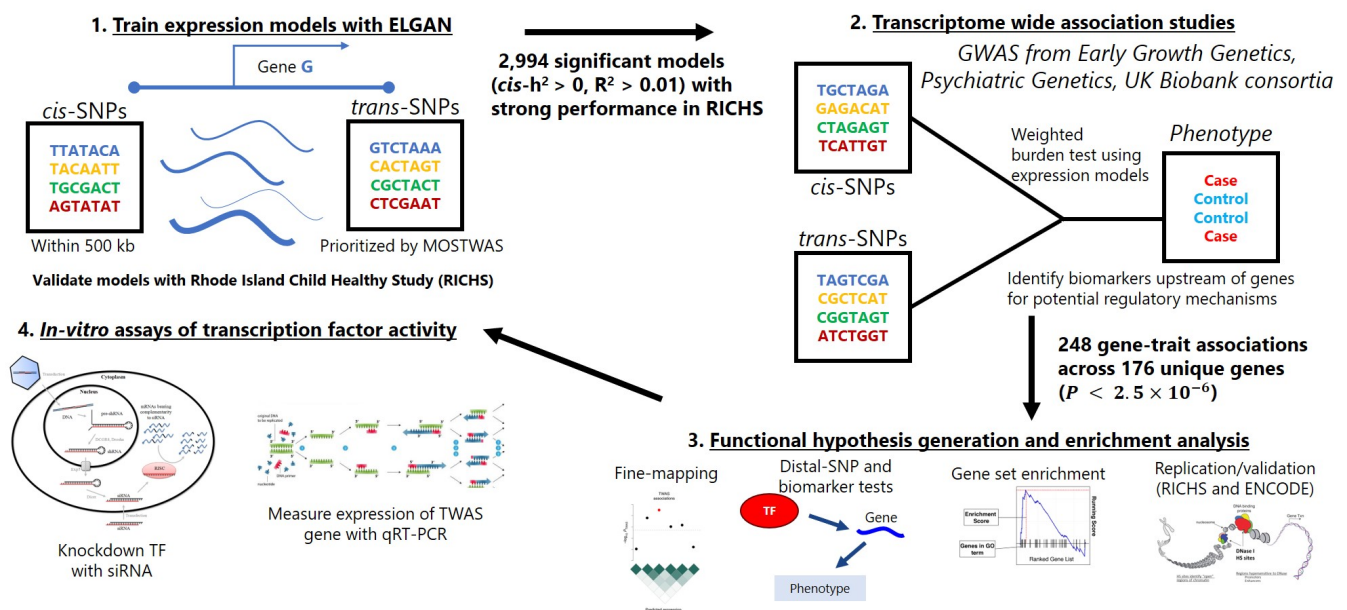
We present a novel framework for evaluating *causal* vaccine efficacy under stochastic interventional shifts of immunologic markers, with multiply robust, nonparametric-efficient estimators utilizing state-of-the-art machine learning in nuisance parameter estimation. Our effect definitions quantify how disease risk would change across counterfactual shifts of the observed immunogenicity of immunologic markers modulated by vaccination, similar to a dose-response analysis. Our framework readily incorporates corrections for two-phase sampling and right-censoring of disease endpoints, and defines vaccine efficacy by comparing counterfactual risks in vaccine and placebo arms. The approach, appearing in the correlates statistical analysis plan (<https://doi.org/10.6084/m9.figshare.13198595>) of the COVID-19 Prevention Network, is applied to mock data inspired by real-world vaccine efficacy trials to demonstrate how candidate correlates of protection may be evaluated by the impacts on disease risk of posited post-vaccination immunogenicity shifts.



Mediator-enriched placental transcriptome-wide analyses of 40 traits reveal genetic mechanisms that support the Developmental Origins of Health and Disease (DOHaD) hypothesis

Arjun Bhattacharya* Arjun Bhattacharya Vennela Avula Weifang Liu Yun Li Robert M. Joseph Lisa Smeester Karl CK Kuban T. Michael O'Shea Carmen J. Marsit Rebecca C. Fry Hudson P. Santos, Jr.

The placenta is the master regulator of the intrauterine environment and is central to the DOHaD hypothesis - that *in utero* experience has lifelong impacts on child health. Studies show that genetics and genomics of the placenta (i.e., genetic variants, epigenetic changes, gene expression) are associated with child health outcomes. An integrative analysis of genetics, placental genomics, and child health outcomes has not been done and would yield insight into the DOHaD hypothesis. Recently, we developed Multi-Omic Strategies for Transcriptome-Wide Association Studies (MOSTWAS), which uses mediation analysis to scan variants genome-wide, detect gene-trait associations (GTAs), and develop hypotheses for trait-associated gene regulation. Here, using genetic, transcriptomic, and methylomic data from the Extremely Low Gestational Age Newborn (ELGAN) Cohort Study (), we applied MOSTWAS (**Figure 1**) to train genetic models of expression of genes on the ELGAN RNA-seq panel, 2,994 of which showed strong in- and out-sample accuracy. With these models, we conducted TWAS for 40 traits from 5 categories (autoimmune, metabolic, cardiovascular, perinatal, neuropsychiatric) and identified 264 GTAs across 176 TWAS genes and potential transcription (TFs) or epigenomic factors regulating their expression. Of the 176 genes, 50 were associated with multiple traits, many not genetically correlated (e.g., *ID11* with BMI and schizophrenia). In addition, 91 GTAs showed significant associations through distal variants, with 8 TFs associated with multiple TWAS genes. For example, *RORA*, a TF involved in inflammatory signaling and positively associated with fetal birthweight (FBW), was negatively associated with *UBA3*, showing a negative TWAS association with FBW. We will functionally validate select TF-TWAS gene pairs *in vitro*. In sum, our study reveals complex and potentially shared placental genomic pathways associated with peri- and postnatal outcomes, motivating further study of DOHaD.



Robust Mendelian randomization in the presence of residual population stratification, batch effects and horizontal pleiotropy Carlos* Carlos Cinelli Nathan Brian Sriram Eleazar

Mendelian Randomization (MR) exploits genetic variants as instrumental variables to estimate the causal effect of an “exposure” trait on an “outcome” trait from observational data. However, the validity of such studies is threatened by population stratification, batch effects, and horizontal pleiotropy. Although a variety of methods have been proposed to partially mitigate those problems, residual biases may still remain, leading to highly statistically significant false positives in large genetic databases. Here, we describe a suite of sensitivity analysis tools for MR that enables investigators to properly quantify the robustness of their findings against these (and other) unobserved validity threats. Specifically, we propose the routine reporting of sensitivity statistics that can be used to readily quantify the robustness of a MR result: (i) the partial R^2 of the genetic instrument with the exposure and the outcome traits; and, (ii) the *robustness value* of both genetic associations. These statistics quantify the *minimal strength* of violations of the MR assumptions that would be necessary to explain away the MR causal effect estimate. We also provide intuitive displays to visualize the sensitivity of the MR estimate to any degree of violation, and formal methods to *bound the worst-case bias* caused by violations in terms of multiples of the observed strength of principal components, batch effects, as well as putative pleiotropic pathways. We demonstrate how these tools can aid researchers in distinguishing robust from fragile findings, by showing that the MR estimate of the causal effect of body mass index (BMI) on diastolic blood pressure is relatively robust, whereas the MR estimate of the causal effect of BMI on Townsend deprivation index is relatively fragile.

Proteomics identified novel proteins associated with genetic risk of abdominal aortic aneurysm: the Atherosclerosis Risk in Communities Study (ARIC) Brian T. Steffen* Brian Steffen James S. Pankow Pamela L. Lutsey Ryan T. Demmer Faye L. Norby Nathan Pankratz Kunihiro Matsushita Adrienne Tin Weihong Tang

Introduction: Abdominal aortic aneurysm (AAA) is a condition characterized by a weakened dilated vessel wall with the potential for lethal rupture. A recent genome-wide association study identified and replicated nine AAA-related variants (rs602633, rs4129267, rs3827066, rs1795061, rs10757274, rs10985349, rs9316871, rs6511720, and rs2836411), but pathways through which these loci may influence disease have not been elucidated.

Hypothesis: AAA risk variants were hypothesized to be associated with plasma proteins with numerous roles including, but not limited to, inflammation and extracellular matrix remodeling.

Methods: Data from participants of the community-based ARIC Study were used. Genomic DNA from whole blood was genotyped using the Affymetrix Genome-Wide Human SNP array 6.0. Concentrations of 4,870 proteins were determined using the SomaLogic aptamer-based capture array in plasma collected at visit 3 (1993-95). Outliers that were 6 standard deviations from the means were excluded. Race-specific multiple linear regression analysis evaluated associations between genetic variants and log base 2 transformed protein levels, with adjustment for age, sex, estimated glomerular filtration rate, field center, and ten principal components of ancestry. Identified proteins in whites (N=7,241) were then examined for replication in Black participants (N=1,671). Cox regression was used to evaluate the associations between identified proteins and incident AAA (n=454) over a median 21.2-year follow-up in all 11,064 participants.

Results: In white participants twenty-six protein associations were identified for rs602633 (*PSRC1-CELSR2-SORT1*), rs4129267 (*IL6R*), and rs3827066 (*PCIF1-ZNF335-MMP9*) following Bonferroni correction ($p \leq 5.13 \times 10^{-6}$). Associations were observed between rs4129267 and soluble interleukin-6 receptor subunit alpha ($\beta = -0.339$; $p < 1.0E-200$) and CRP ($\beta = 0.093$; $p = 2.24E-7$); rs602633 and granulins ($\beta = 0.184$; $p < 1.0E-200$), complement C1q TNF-related protein-1 ($\beta = 0.115$; $p = 2.17E-184$), and neogenin ($\beta = -0.031$; $p = 5.60E-13$); and rs3827066 and kit ligand ($\beta = -0.045$; $p = 2.41E-08$). Five associations were replicated in Black participants ($p \leq 1.9 \times 10^{-3}$). In the whole cohort, top quintiles of CRP (HR: 1.68; 95% CI: 1.22, 2.31), kit ligand (HR: 0.56; 95% CI: 0.40, 0.78) and neogenin (HR: 0.57 95% CI: 0.42, 0.78) were significantly related to incident AAA risk compared to corresponding bottom quintiles.

Conclusions: Three of the nine AAA risk variants were associated with plasma protein concentrations, with the strongest associations for those involved in inflammation, endothelial dysfunction, and extracellular matrix remodeling. Granulin, complement C1q tumor necrosis factor-related protein-1, kit ligand, and neogenin represent novel targets for genetic risk of AAA and may link genetic susceptibility to disease pathogenesis.

Risk of Hematopoietic Cancer in Congenital Heart Diseased Children with or without Genetic Syndromes Mohammad Sazzad Hasan* Mohammad Sazzad Hasan Aihua Liu Liming Guo Elie Ganni Jay S. Kaufman Ariane J. Marelli

Background: Individuals with genetic syndromes can manifest both congenital heart disease (CHD) and cancer due to possible common underlying pathways. However, reliable risk estimates of hematopoietic cancer (HC) among children with CHD based on large population-based data are scant. **Method:** We conducted a population-based analysis to estimate the cumulative incidence of HC in a cohort of children (0-18) born between 1999 and 2017, with at least one hospitalization records of CHD diagnosis. We merged the CIHI-Discharge Abstract Database, which regularly collects hospitalization and day surgery records in all Canadian provinces except Quebec, with Quebec's hospital discharge data, Med-Echo, to develop the Canadian Congenital Heart Disease Database. Hematopoietic cancer and syndromes were both identified by hospitalization diagnoses. We used a modified Kaplan-Meier curve analysis to estimate the cumulative incidences (with 95% confidence intervals) up to 18 years of age, with death as a competing risk and stratified by the genetic syndrome status. **Result:** We followed 143,881 CHD children from birth for 1,387,934 person-years. In this study population, 8.7% had genetic syndromes, and 911 HC cases were observed. The cumulative incidence of HC up to age 18 was 2.42% (95% CI: 2.10-2.73%) among children with a genetic syndrome and 0.83% (0.75-0.92%) without the syndrome. The incidence proportion was higher in the first six years of life than the subsequent 6-years intervals up to adulthood. Children with severe CHD lesions and genetic syndrome had a cumulative incidence of 2.95% (95% CI: 2.29-3.61%), whereas with non-severe CHD lesions and genetic syndrome had 2.23% (95% CI: 1.87-2.59%). **Conclusion:** This is the first population-based analysis documenting that genetic syndromes in CHD children are a powerful predictor of hematopoietic cancers. The finding is essential in informing risk-stratified policy recommendations to protect CHD children from cancer.

Type II error in large genome wide association studies - causes, consequences and amelioration CM Schooling* CM Schooling

Genome wide association studies (GWAS) of specific disease conditions are central to scientific discovery. GWAS are often used to identify risk factors for specific chronic diseases, which typically occur at older ages and may share etiology, such as physiological risk factors like blood pressure, smoking, diet and social determinants of health. GWAS of chronic diseases often recruit in middle- to old-age, and thereby inevitably recruit from the living, i.e., only recruit survivors of their genetic make-up, the disease condition in question and any competing risk of the disease condition. Effects of such sample selection on genetic estimates have rarely been considered, although they would be expected to attenuate estimate for associations of harmful genetic variants with late-onset diseases, because of selection on surviving the genetic variant, the disease in question and any competing risk of the disease in question. We use genetic summary statistics from the UK Biobank to demonstrate that conditions vulnerable to competing risk, such as stroke, have fewer strong genetic associations for genetic variants associated with survival than conditions with similar etiology, such as ischemic heart disease, that occur earlier in life. As such, we provide empirical evidence that typical GWAS of late onset diseases are open to systematic type 2 error from selection bias attenuating or reversing estimates. Such, selection bias could be addressed by adjusting for all common causes of survival to recruitment and the disease condition of interest, but such information is not usually available and is unlikely to be sufficiently comprehensive and well-measured to obviate bias. Investigating the role of selection bias in GWAS as well as the use of study designs less open to selection bias, such as longevity studies, is vital to investigating the genetics of late onset conditions.

Shared and population-specific associations of genetic variation in the 10q24.32/AS3MT region with arsenic metabolism efficiency Meytal Chernoff* Meytal Chernoff Lizeth Tamayo Dayana Delgado Lin Tong Matthew Stephens Farzana Jasmine Lei Huang Shelley A. Cole Karin Haack Jack Kent Jason G. Umans Lyle G. Best Joseph Graziano Ana Navas-Acien Margaret R. Kargas Muhammad G. Kibriya Habibul Ahsan Brandon L. Pierce

Background: Arsenic is a carcinogen affecting >56 million people in Bangladesh and >10 million in the U.S via drinking water. Consumed inorganic arsenic is converted to mono- and di-methylated (DMA) forms. DMA in urine, expressed as a percentage of total arsenic (DMA%), reflects arsenic metabolism efficiency (AME) with higher DMA% indicating increased AME and increased clearance of arsenic from the body. Genetic variation near the *AS3MT* (arsenic methyltransferase) gene, impacts AME. Prior studies identified two independent associations, but the causal variants and underlying mechanisms remain unknown. **Methods:** We performed targeted sequencing of the *AS3MT* region, genotyping 345 common SNPs with minor allele frequency (MAF) >0.005. This was followed by imputation to fill sequencing gaps for individuals in 3 cohorts: 2428 Bangladeshi individuals from the Health Effects of Arsenic Longitudinal Study (HEALS), 558 American Indians from the Strong Heart Study (SHS), and 706 European Americans from the New Hampshire (NH) Skin Cancer Study. Conditional, forward stepwise regressions in each population identified variants independently associated with DMA%. We identified candidate causal variants using a Bayesian method, the Sum of Single Effects Regression (SuSiE). **Results:** Mean total urinary arsenic in HEALS was 116.9 ug/g compared to 14.3 in SHS and 7.3 in NH reflecting differences in drinking water concentrations. Regression analyses identified 3 independent signals in HEALS (rs145537350, rs12573221, rs419687; MAF 0.007, 0.13, 0.12; p-values $\sim 10^{-15}$ to 10^{-9}), 2 in SHS (rs191177668 and rs4919688; MAF 0.14 and 0.27; p-values $\sim 10^{-26}$ to 10^{-19}), and 1 in NH (rs191177668; MAF 0.012; p-value $\sim 10^{-9}$). One of these signals was shared across populations, but with large differences in MAF across populations. We also identified population-specific association signals in SHS and HEALS, suggesting possible population-specific causal variants or biological mechanisms underlying AME.

Depression, Current Antidepressant Use, and Breast Cancer Risk: Findings from the Sister

Study Jihye Park* Jihye Park Mary V. Diaz-Santana Katie M. O'Brien Hazel B. Nichols Aimee A. D'Aloisio Deborah B. Bookwalter Clarice R. Weinberg Dale P. Sandler

Background: There is a strong biologic rationale linking depression and antidepressant use to breast cancer risk; however, epidemiologic findings are inconsistent. Prior research suggests that overweight is an effect-measure modifier of the association between antidepressant use and breast cancer risk.

Methods: We examined depression, antidepressant use, and breast cancer risk in a prospective cohort of women who had a sister with breast cancer (but were breast cancer free themselves) at enrollment. We restricted to 40,311 women who completed the first follow-up questionnaire, 2.8 years (range 1.2-5.4 years) after enrollment (2003-2009 at ages 35-74), where we assessed depression and antidepressant use. Depression was defined by a Center for Epidemiologic Studies Depression Scale scores ≥ 8 . Current antidepressant use was self-reported and compared to non-current use; medications were classified by drug class (selective-serotonin reuptake inhibitors [SSRIs], Tricyclic antidepressants [TCAs], and serotonin-norepinephrine reuptake inhibitors [SNRIs]). Cox proportional hazards models estimated multivariate adjusted hazard ratios (HRs) and 95% CIs for breast cancer risk.

Results: During follow-up (mean=7.7 years), 2,183 breast cancers cases were diagnosed. In multivariable analyses, depression was not associated with breast cancer risk (HR=0.97, 95% CI=0.89-1.07). Antidepressant use was associated with a possible reduction in risk (HR=0.92, 95% CI=0.82-1.02), but the association did not vary by body mass index. However, when considering drug classes, we observed stronger inverse associations with use of SSRIs alone among non-overweight women (HR=0.76, 95% CI=0.59-0.99) and with use of SNRIs alone among overweight women (HR=0.70, 95% CI=0.51, 0.97).

Conclusions: Depression was not associated with breast cancer risk. We observed a possible inverse association between antidepressant use and breast cancer risk with possible variations in associations by drug class.

Vitamin D supplement use and risk of breast cancer by race/ethnicity Katie O'Brien* Katie O'Brien Alexander Keil Quaker Harmon Chandra Jackson Alexandra White Mary Diaz Santana Jack Taylor Dale Sandler

Vitamin D has anti-carcinogenic properties, but a relationship between vitamin D supplement use and breast cancer is not established. Few studies have accounted for changes in supplement use over time or evaluated racial/ethnic differences. The Sister Study is a prospective cohort of 50,884 women aged 35-74 who had a sister with breast cancer, but no breast cancer themselves at enrollment (2003-2009). We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between vitamin D supplement use and incident breast cancer (3,502 cases over a median of 10.5 years of follow-up). Vitamin D supplement use was common, with 64% reporting use at baseline. Considering supplement use as a time-varying factor, ever use of vitamin D supplements was not strongly associated with breast cancer (HR=0.96, 95% CI: 0.89-1.04). However, after adjusting for prior use, recent use of vitamin D supplements was inversely associated with breast cancer (HR=0.88, 95% CI: 0.78-1.00). The inverse association was stronger for ductal carcinoma *in situ* (HR=0.68, 95% CI: 0.52-0.87), than invasive breast cancer (HR=0.94, 95% CI: 0.72-1.08, p-for-heterogeneity=0.02). Supplement use was less common among African American/Black (56% at baseline) and non-Black Hispanic/Latina (50%) women than non-Hispanic White women (66%), but there was limited evidence of racial/ethnic differences in HRs (p-for-heterogeneity=0.16 for ever use, p=0.51 for recent use). This research supports the hypothesis that recent vitamin D use may be inversely associated with breast cancer risk.

Early-life agricultural pesticide exposure as a risk factor for thyroid cancer in the Sister Study cohort Danielle A. Duarte* Danielle Duarte Danielle N. Medgyesi Catherine Lerro Cherrel Manley Srishti Shrestha Dale P. Sandler Laura Beane Freeman Mary H. Ward Rena R. Jones

Background: The thyroid gland may be particularly susceptible to carcinogenic exposures during childhood. No studies have evaluated childhood residential pesticide exposure and risk of adult thyroid cancer.

Methods: In the Sister Study cohort (n=50,884 women across the US, aged 35-75 years at enrollment in 2003-2009), we assessed childhood farm residences (≤ 18 years of age, >1 year) and whether the longest childhood residence (≤ 14 years of age) was on or near a farm. We evaluated the major crops grown and whether pesticides were applied. We evaluated incident malignant thyroid cancers from enrollment through 2018 (n=246) using Cox regression to estimate hazard ratios (HR) and 95% confidence intervals (CI). In secondary analyses, we expanded to include prevalent thyroid cancers diagnosed between age 18 and enrollment (n=502) and estimated odds ratios (OR) with logistic regression. Models were adjusted for age, race/ethnicity and smoking.

Results: Neither any childhood farm residence (n=44 exposed cases) or longest childhood residence on/near a farm (n=66) were associated with thyroid cancer risk. However, ever living on a farm with non-orchard fruit crops (e.g., berries, melons) was non-significantly associated with risk (HR=1.23, CI:0.92-1.64, n=54). Having the longest childhood farm residence regularly treated with pesticides was associated with thyroid cancer in analyses of prevalent cases, with borderline significance (OR=1.22, CI:0.98-1.52, n=110).

Conclusions: The finding for non-orchard fruit crops, most of which are treated with fungicides, supports prior studies suggesting a link between fungicides and thyroid cancer. We found limited evidence that early-life agricultural pesticide exposures are associated with increased risk. Future studies to evaluate residential use and proximity to pesticide applications are warranted.

Significance: Our study is the first to evaluate early life as a critical window of agricultural pesticide exposure for thyroid cancer.

History of gestational hypertensive disorders and breast cancer risk in the Sister Study

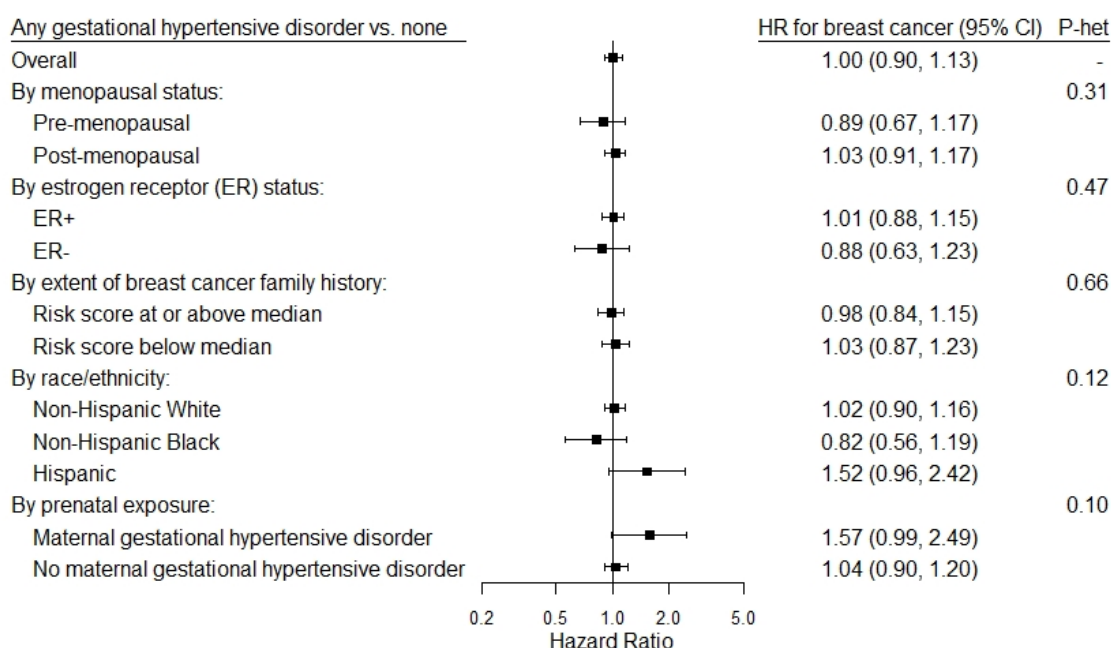
cohort Mandy Goldberg* Mandy Goldberg Mary V. Diaz-Santana Katie M. O'Brien Shanshan Zhao Clarice R. Weinberg Dale P. Sandler

Background: Pre-eclampsia and gestational hypertension are hypothesized to be associated with reduced maternal breast cancer risk, but the epidemiologic evidence is inconclusive. Our objective was to examine associations between history of gestational hypertensive disorders and breast cancer risk in a nationwide cohort of women with a family history of breast cancer.

Methods: Women ages 35-74 years without a history of breast cancer, but who had a sister previously diagnosed with breast cancer, were enrolled in the Sister Study from 2003-2009 (N=50,884). At enrollment, participants reported their pregnancy history, including any diagnoses of eclampsia, pre-eclampsia, or gestational hypertension in each pregnancy. We used Cox proportional hazards models to estimate HRs and 95% CIs for the association between history of any gestational hypertensive disorder and risk of invasive breast cancer or ductal carcinoma *in situ* among 40,721 parous women. We used age as the time scale and adjusted for reproductive, social and behavioral factors, along with birth cohort and race/ethnicity. We examined effect measure modification by menopausal status, estrogen receptor status, extent of breast cancer family history, race/ethnicity, and prenatal exposure to a maternal gestational hypertensive disorder.

Results: The prevalence of any gestational hypertensive disorder was 11.9%. During follow-up (mean=10.1 years), 2948 eligible parous women were diagnosed with breast cancer. History of any gestational hypertensive disorder was not associated with breast cancer risk (HR=1.00, 95% CI 0.90, 1.13). While stratified analyses suggested some differences by menopausal status, race/ethnicity and prenatal exposure to maternal hypertensive disorder, we did not see clear evidence of statistical heterogeneity (see figure).

Conclusions: History of a gestational hypertensive disorder was not associated with breast cancer risk in a cohort of women with a first-degree family history of breast cancer.



Evidence of Stage Shift in US Lung Cancer Diagnosis, 2009-2016 Paris Offor* Paris Offor
 Chelsea Obrochta MPH Benjamin Schumacher MPH Dr. Caroline Thompson PHD

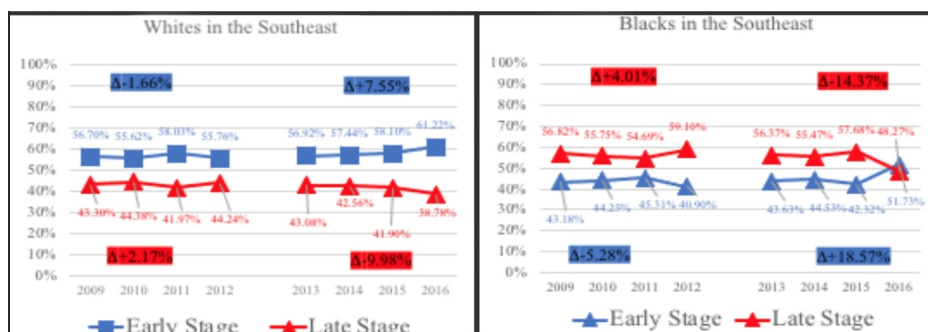
Paris Offor, Chelsea Obrochta MPH, Benjamin Schumacher MPH, Caroline Thompson MPH PHD

Purpose: In 2013, the U.S Preventive Services Task Force (USPSTF) began recommending lung cancer screening for current and past smokers with at least a 30 pack-years of smoking history. Screening can be shown as effective if a shift towards earlier stages of diagnosis are seen at the population level. We investigated if the implementation of the USPSTF guidelines produced a stage shift by race and/or geographical regions.

Methods: We used lung cancers diagnosed between 2009 and 2016 from Surveillance, Epidemiology, and End Results (SEER). We compared yearly trends in local/regional vs distant stage at diagnosis before and after 2013, and stratified by patient race (White vs Black) and SEER geographical region. Trends were illustrated by percent increase/decrease of early and late stage diagnoses after USPSTF guideline implementation.

Results: We observed small increases for early stage and decreases for late stage for both races overall for before and after 2013. When stratified for geographical regions, we observed different results per region. For example in the Southeast, before 2013, whites had a 1.66% decrease in early-stage and a 2.17% increase in late stage in comparison to Blacks who experienced a 4.01% increase in late stage and a 5.37% decrease in early stage before 2013. Whites experienced a 7.55% increase in early-stage and 9.98% decrease in late stage while Blacks experienced a 14.37% decrease in late-stage and 18.57% in early stage after 2013. Blacks also experienced higher proportions of late stage diagnoses compared to Whites who were mostly diagnosed in early stage.

Conclusions: Lung cancer diagnosis has been decreasing over time, and stage shift is evident in some populations, however not uniformly. Blacks are still more likely to be diagnosed at a later-stage compared to Whites.



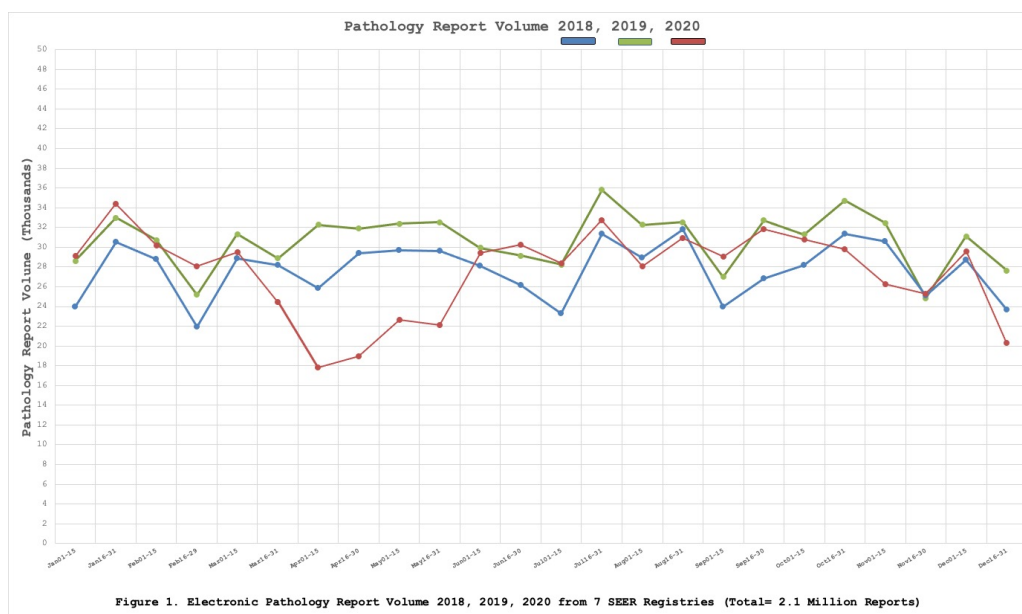
Assessing the impact of COVID-19 on cancer care: Longitudinal surveillance of pathology volume

Todd Golden* Todd Golden Linda Coyle Jennifer Stevens Serban Negoita

Pathology reporting volume was investigated as a proxy for cancer screening, diagnosis, and treatment to assess the impact of COVID-19 on oncology services. All electronic pathology reports 2018-2020 were included from 7 central registries (covering a population >45 million) in the National Cancer Institute Surveillance, Epidemiology, and End Results Program, and reviewed by site (breast, lung, colorectal, prostate, other), age (<50, 50-64, 65-74, ≥75 years), and registry. Only pathology laboratories reporting at least monthly to their registry throughout the study period were included.

While in 2019 there was a 10.8% increase in pathology volume over 2018, in 2020 there was an 10.4% decrease in reports (76,356 fewer) compared to 2019. 70.3% of this decrease occurred over 12 weeks, March - May 2020, with 28.4% fewer than expected (53,709 reports) during this initial peak of the pandemic. The maximum bi-weekly decrease was 44.8% (14,460 reports), in April 2020. In 2020 the greatest decrease by age was in 50-64-year-olds (12.3%), by site in lung cancer (17.3%), and by registry in New York (22.3%). Two additional periods of volume decrease, both of shorter duration and magnitude, occurred mid-July through August and mid-October through December.

Since the onset of the pandemic there remains a deficit in expected pathology volume compared to 2019, reflecting the continued impact of COVID-19, with the majority of the volume decrease occurring during the initial peak of the pandemic. This initial peak along with two smaller volume decreases align temporally with the 3 increasing peaks of U.S. COVID-19 new cases reported by the WHO COVID-19 Dashboard. Based on historical trends it was expected the 2020 volume would actually be greater than 2019, the comparison year, as seen at the start of the 2020; therefore, the volume decreases reported likely represent conservative estimates of the actual volume decrease. Continued surveillance and path report type analysis are planned.



Associations Between Race/Ethnicity and Mental Health Outcomes in 5 Southern U.S. Cities During the COVID-19 Pandemic Estelle El Khoury* Estelle El Khoury Daniel Hagen Emily Goldmann

Introduction: The COVID-19 pandemic has had a profound impact on mental health, particularly among those who have experienced greater pandemic-related stressors. Although these stressors have been more common among specific racial/ethnic groups, mental health disparities remain understudied.

Methods: Data were collected in 5 Southern U.S. cities (Atlanta-GA, Austin-TX, Dallas-TX, Houston-TX, New Orleans-LA) from May 26 to June 6, 2020 using random-digit-dial phone and Web-based (Dynata panel) surveys (n=1,727). Mental health outcomes included past-week psychological distress (Patient Health Questionnaire-4 score ≥ 6), trouble sleeping, physical reactions when thinking about the pandemic, and self-rated worsened mental health during the pandemic. Associations between race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, non-Hispanic Asian) and mental health were examined in separate multivariable logistic regression models.

Results: Approximately 21% reported psychological distress, 21% physical reactions, 25% trouble sleeping, and 33% worsened mental health. Pandemic-related stressors (money/food shortages, essential worker status, knowing people with COVID-19, physical isolation) were more prevalent among non-White compared to White respondents ($p < 0.05$). Adjusting for demographic factors and previous psychiatric diagnosis, there were no significant racial/ethnic differences in these outcomes. After further adjustment for stressors, Black respondents had 42% lower odds of worsened mental health compared to White respondents (OR=0.58; 95% CI: 0.36-0.92). Odds of other mental health outcomes did not differ significantly by race/ethnicity.

Conclusion: Despite greater pandemic-related stressor experience, odds of mental health outcomes were lower or no different among Black and Hispanic vs. White respondents in adjusted models. Additional research on the role of COVID-specific stressors and resilience factors for mental health is needed as the pandemic continues.

Age, period, and cohort trends in perceived mental health treatment gaps in the United States, 2002-2019 Melanie S Askari* Melanie S Askari Pia M Mauro Navdep Kaur Katherine M Keyes

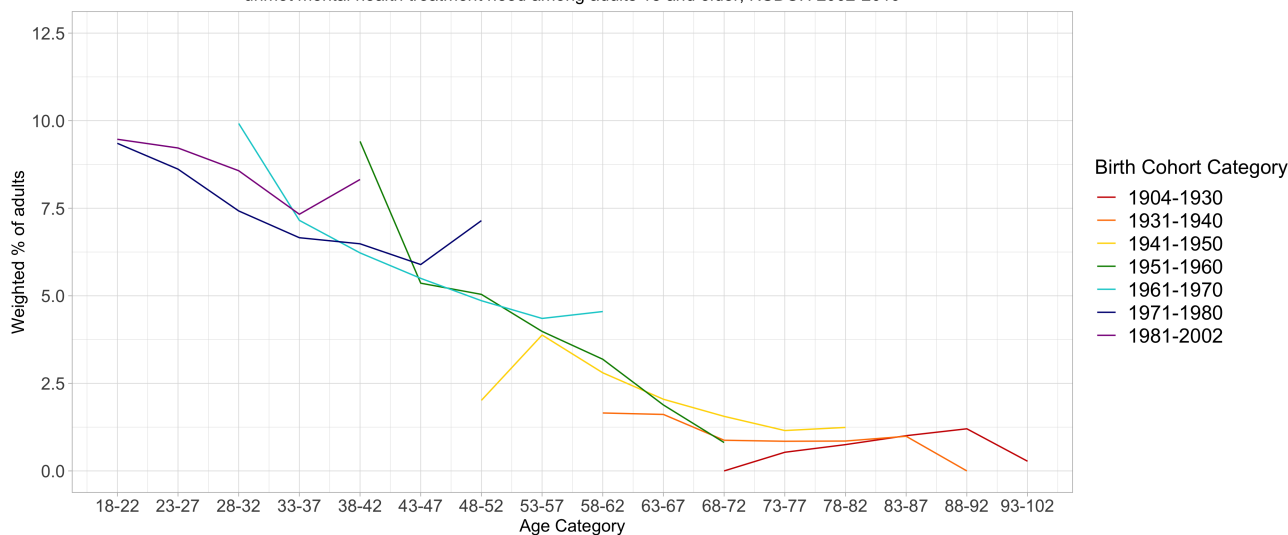
Background: Age, period, and cohort trends in the prevalence of psychiatric disorders have been identified in prior research. As perceived need for mental health treatment is associated with treatment utilization, identifying age, period, and cohort trends in perceived need for mental health treatment could focus attention on those with greatest burden of unmet mental health treatment need.

Methods: We included data from adults in the 2002-2019 National Survey on Drug Use and Health adults ages 18 and older (N=634,236). Hierarchical age-period-cohort models were used to assess age-period-cohort effects in perceived unmet mental health treatment need (i.e., perceived a need for mental health treatment but did not receive treatment). Level-1 covariates included age, race/ethnicity, household income, education, and gender; median odds ratio (MOR) estimated level-2 variance units.

Results: Perceived unmet adult mental health treatment need increased from 5.8% in 2002 to 7.1% in 2019 ($p < 0.0001$). Younger cohorts (i.e., 1993-2002 birth cohorts) and younger age groups (i.e., ages 18-22) reported higher perceived unmet mental health treatment need compared with older cohorts. Perceived unmet mental health treatment need peaked in the 1999 cohort. Cohort effects (MOR=1.26; covariance parameter: 0.34; 95% CI: [0.24, 0.51]) were observed with more disparate effects in ages 33-53. Period effects were null or modest over time (MOR=1.07; covariance parameter: 0.02; 95% CI: [0.01, 0.04]) with slight decreases in unmet mental health treatment need from 2011-2017.

Conclusion: Perceived mental health treatment gaps differed by age group, time period, and birth cohort. In the context of higher prevalence of psychiatric disorders in certain adult sub-groups, it is important to address structural barriers (e.g., financial or healthcare system barriers) and stigma that could be driving increases in perceived unmet mental health treatment need in younger adult age groups and birth cohorts.

Figure 1: Age- and birth cohort-specific prevalence of past-year unmet mental health treatment need among adults 18 and older, NSDUH 2002-2019



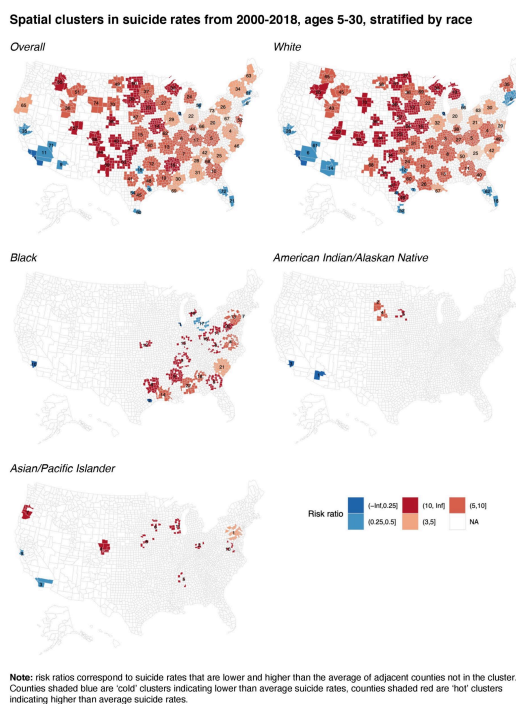
Racial disparities in adolescent suicide clusters: trends over time and space Jonathan Platt*
Jonathan Platt John Pamplin Katherine Keyes Sasikiran Kandula Catherine Gimbrone Caroline G.
Rutherford Jeffrey Shaman Gonzalo Martinez-Ales

Individual suicides correlate both spatially and temporally, leading to suicide clusters. Suicide clusters are especially prevalent among youth, and have become increasingly prevalent since 1999. Historically, suicide risk has been highest in non-Hispanic White and Native Americans, suicide rates among Black children ages 5-12 have recently increased, narrowing racial differences. These emergent trends suggest that patterns in suicide clusters may also be changing. This research aimed to estimate racial differences in spatiotemporal trends in youth suicide clusters.

ICD-coded suicide mortality rates from 2000-2018 were estimated from the CDC Wide-ranging Online Data for Epidemiologic Research (WONDER) data for ages 5-30. Race groups were: White, Black, Asian/Pacific Islander (API), and American Indian/Native Alaskan (AI/AN). Spatiotemporal clusters were identified using the space-time statistic (implemented in SaTScan), which identifies 'cold' and 'hot' clusters respectively as lower- and higher-than-expected suicide rates in a prespecified geographic radius (150 km) and time period (12 months) using likelihood ratio tests.

Throughout the study period, the temporal prevalence of suicide clusters increased for all groups, and the number of spatial clusters ranged from 5 to 68 among American Indian/Alaskan Native and White groups. Among Black youth, 'cold' clusters were identified in large urban counties, while 'hot' clusters were identified in Southeastern and mid-Atlantic counties (see figure). The proportion of all suicides included in clusters ranged from 0.6% to 5.7% among White and AI/AN groups.

We identified important temporal and spatial trends in youth suicide rates, with some evidence that the spatial patterning of clusters differed by race. Ongoing work seeks to identify determinants of patterns, including urban/rural risk factors, and the risk specific to the 'Stroke Belt' of the Southeastern US.



Epidemiologic evaluation of three depression screening tools among postpartum Kenyan women Anna Larsen* Anna Larsen Jillian Pintye Mary M. Marwa Salphine Watoyi John Kinuthia Felix Abuna Lauren Gomez Julia Dettinger Grace John-Stewart

Postpartum (PP) depression disproportionately affects women in low- and middle-income countries (LMICs) and is associated with maternal and infant adverse outcomes. Screening tools that effectively identify individuals for intervention will be important as LMICs adopt policies for maternal mental health. We compared 3 screening tools for diagnostic performance and epidemiologic associations.

Women participating in a cluster randomized trial (PrIMA) in 20 maternal child health clinics in Kenya were evaluated at 6 weeks PP with: Center for Epidemiologic Studies Depression Scale (CESD-10), Patient Health Questionnaire-9 (PHQ-9), Edinburgh Postnatal Depression Scale (EPDS). Symptoms of moderate-to-severe depression (MSD) were defined as CESD-10 \geq 10, EPDS \geq 13, or PHQ-2 \geq 3. We determined kappa agreement between tools and sensitivity, specificity, and area under the curve (AUC) for each scale against major depressive disorder (MDD)-assessed using PHQ-9 algorithm for DSM-IV MDD using receiver operating characteristics. We evaluated associations between MSD and intimate partner violence (IPV), a known predictor of PP MSD.

Among 3042 PP women assessed, median age was 24 years (IQR 21-28), 87% were married, and 8% experienced IPV. Prevalence of MSD varied by tool: 13% CESD-10, 9% EPDS, and 5% PHQ-2; 39 (1%) had MSD in all scales with modest agreement between tools (EPDS/PHQ-2 K=0.188, PHQ-2/CESD-10 K=0.268, CESD-10/EPDS K=0.373). In comparisons with MDD, PHQ-2 had the highest AUC (se:89%, sp:97%, AUC:0.98), followed by CESD-10 (se:63%, sp:88%, AUC:0.85), and EPDS (se:51%, sp:92%, AUC:0.79). IPV association with MSD was significant using all scales: EPDS (OR:2.3, 95%CI:1.4-3.9), CESD-10 (OR:1.9, 95%CI:1.1-3.3), PHQ-2 (OR:1.7, 95%CI:1.02-2.9).

Depression screening tools varied widely in detection of PP MSD and had moderate differences in strength of association with a known cofactor and in AUC for MDD. These differences have implications for tool selection in research and practice.

Latent Class Analysis to Determine Classes of Psychopathology Following Traumatic**Experiences in the Danish Population** Meghan L. Smith* Meghan Smith Anthony J. Rosellini

Péter Szentkúti Erzsébet Horváth-Puhó Timothy L. Lash Sandro Galea Paula P. Schnurr Henrik T.

Sorensen Jaimie L. Gradus

Introduction: It is well-established that psychopathology can follow traumatic events. However, most studies focus largely on posttraumatic stress disorder and depression. Trauma may be associated with additional forms of psychopathology, and unstudied combinations of disorders.

Methods: From Danish national registries, we identified residents of Denmark who experienced 1+ traumatic events (fire/explosion, transportation accident, toxic exposure, traumatic brain injury, physical assault, assault with weapon, pregnancy-related trauma, suicidal death of family member, or multiple traumas) between 1994-2016 and were diagnosed with one or more mental disorders within 5 years (N=166,539). We ascertained incident ICD-10 psychiatric diagnoses following an index trauma, and assigned persons with 1+ diagnoses to one or more of 11 diagnostic categories (e.g., stress, substance, depressive, psychosis, personality, etc.). We used latent class analysis (LCA) to assess profiles of posttraumatic psychopathology, and compared two- through 14-class solutions on model fit (e.g., Bayes Information Criteria, entropy) and consistency with past LCA studies.

Results: A 13-class solution was deemed optimal. Three of these classes were characterized by high comorbidity: broad high comorbidity (Mean # diagnoses = 4.3), depression with stress/substance use/personality/neurotic (Mean # diagnoses = 3.8), and substance use with personality/stress/psychosis (Mean # diagnoses = 3.1). The other 10 classes were characterized by distinct patterns of mild comorbidity (Mean # diagnoses = 1.6-2.0) or negligible comorbidity (Mean # diagnoses = 1.0-1.4).

Conclusion: Psychopathology following trauma is not limited to posttraumatic stress disorder and depression. Assessing the risk of a wide variety of psychiatric outcomes can help elucidate complex and varied reactions to trauma. Future research should assess whether characteristics of persons and/or traumatic experiences predict later psychopathological profiles.

Early childhood exposure to food insecurity and adolescent mental health in the United**States** Marine Azevedo Da Silva* Marine Azevedo Da Silva Marine Azevedo Da Silva Sara Mohammadi Frank Elgar

Background

Although evidence suggests that food insecurity has a detrimental impact on a range of psychosocial outcomes for children, it is unclear if early childhood food insecurity itself is associated with long-term mental health problems. Previous research has relied on measures of household food insecurity, which may not accurately reflect the degree of food insecurity experienced by a child. Indeed, children are often shielded from experiencing food insecurity by their parents. We investigated the association between child food insecurity and adolescent depression and anxiety symptoms.

Methods

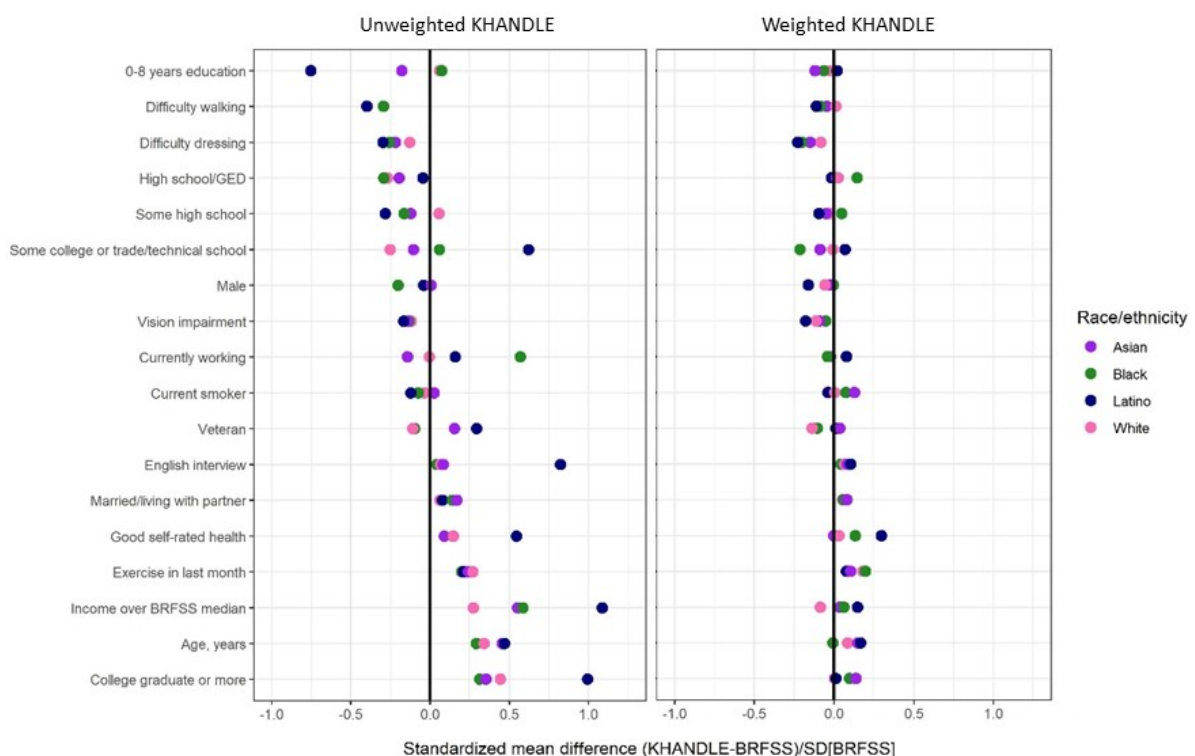
We used data from the Fragile Families and Child Wellbeing Study, a birth cohort study of 4898 children born in 20 large U.S. cities between 1998-2000. Household and child food insecurity measures were assessed at ages 3-5 using the 18-items US Department of Agriculture Food Security Module. Symptoms of depression and anxiety were respectively measured at age 15 by the Center for Epidemiologic Studies Depression Scale and the Brief Symptom Inventory. Negative binomial regression models were used to estimate the association between early childhood food insecurity and adolescent mental health.

Results

The final analytic samples were nearly 3000 children. After controlling for sociodemographic factors, health-related behaviors, and caregiver depression, household food insecurity at age 3-5 was associated with higher rates of depressive symptoms and anxiety at year 15. However, we found no association between child-specific food insecurity and depressive symptoms and anxiety. In a sensitivity analysis, disaggregating the household food security status in food-secure household, food-insecure household with shielded child, and food-insecure household with non-shielded child, we surprisingly found that only shielded children living in food-insecure households had higher rates of symptoms of depression and anxiety in adolescents compared to child living in a food-secure household.

Generalizability of a diverse cohort on cognitive aging to the target population of older adults in California without dementia: Findings from the KHANDLE study Eleanor Hayes-Larson* Eleanor Hayes-Larson Taylor M Mobley Dan Mungas M. Maria Glymour Paola Gilsanz Charles DeCarli Rachel Whitmer Marissa Seamans Elizabeth Rose Mayeda

Population-representative estimates of cognitive impairment are needed to understand the burden of disease and inform treatment and prevention. However, participants in studies on cognitive decline and dementia often differ from the general population on a variety of sociodemographic and clinical factors. There is a growing movement to enroll cohorts with more diverse life experiences, such as the Kaiser Healthy Aging and Life Experiences (KHANDLE) study, a recently recruited cohort study of dementia-free long-term Kaiser Permanente members in Northern California. Even in these cohorts, differences between participants and the general population may remain. Our analyses assessed the generalizability of the KHANDLE sample (n=1,708) to the general population of dementia-free adults ages 65+ in California, and developed weights in KHANDLE enabling estimation of race/ethnicity-specific prevalence of cognitive impairment in this target population. Our target population was represented by pooling California Behavioral Risk Factor Surveillance Study (BRFSS) participants from 2014 to 2018 (unweighted n=12,399). We assessed generalizability by comparing covariate balance (standardized mean difference) in harmonized sociodemographic, health, and behavioral measures between KHANDLE and BRFSS. Across racial/ethnic groups, KHANDLE participants were slightly older, had more education, higher income, and reported better health than BRFSS participants; differences were largest for Latinos (Figure, left panel). To improve generalizability, we developed stabilized inverse odds of selection weights in KHANDLE that yielded acceptable race/ethnicity-specific covariate balance for all harmonized variables, including variables not included in the weight development (Figure, right panel). Applying these weights to measures of cognitive impairment in KHANDLE will allow estimation of race/ethnicity-specific prevalence of cognitive impairment in the target population (work ongoing).



Quantifying the force of selection in Mexico to US migration: a first step towards understanding the effects of migration on cognitive aging

Audrey R. Murchland* Audrey Murchland Adina Zeki Al Hazzouri Scott C. Zimmerman Katrina Kezios Erika Meza Neal Jawadekar Jacqueline M. Torres Richard N. Jones M. Maria Glymour

Background: Estimates of the health effects of migration are likely biased by selection processes such that people with underlying health advantages are more likely to migrate. Restricting to never migrants born in Mexico, we estimated the association between the propensity to migrate to the US and later life cognitive test performance.

Methods: We merged data for Mexicans living in Mexico from the Mexican Health and Aging Study (N=18,302) with data for Mexican-born migrants living in the US from the Health and Retirement Study (N=924) and calculated the propensity to migrate from Mexico to the US at each year of life. Logistic regression models for migration propensity included time-constant variables (parental education) and age at life events (education, marital status, labor force entry, and smoking initiation). Then, among never migrants in MHAS (N=15,915), we estimated the association of predicted propensity to migrate (by specific lifecourse periods), on a harmonized global measure of cognition assessed in 2001, 2003, and 2012. Linear mixed effects models were adjusted for sex and practice effects.

Results: At baseline, mean cognitive score was -1.26 (0.9 SD), mean age was 61 years (9 SD), and mean lifetime migration propensity was 0.14 (0.09 SD). Every 10-percentage point higher lifetime migration propensity was associated with a -0.05 (95% CI: -0.13, 0.03) unit difference in cognitive score at age 70. Cognitive decline was also slower for people more likely to migrate (rate of change per decade associated with a 10-percentage point increase in migration propensity $b=0.004$; 95% CI: 0.002, 0.005). Migration propensity in early life increased the magnitude of the estimates (Table 1).

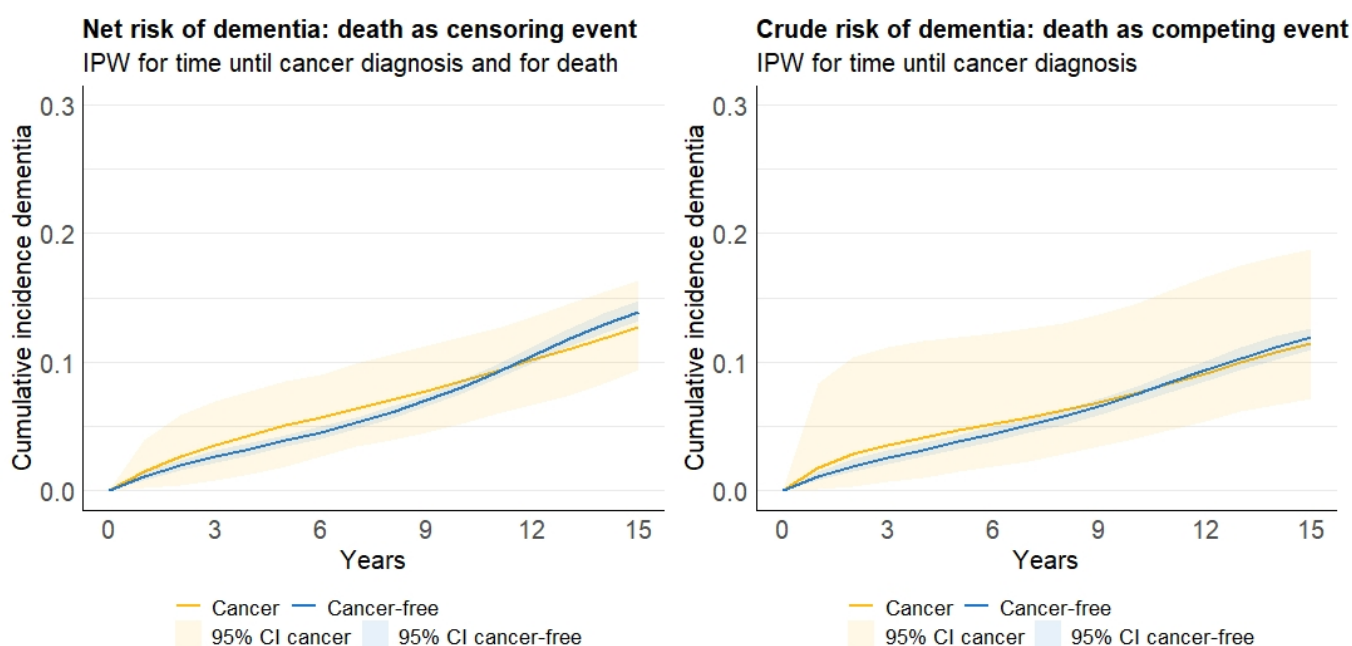
Conclusions: Increased propensity to migrate was associated with lower average global cognition but slower decline in late life among Mexican non-migrants. Selective migration, thus, may bias estimates of the health effects of migration.

Table 1. Estimated change in global memory score for ten-percentage point increase in propensity to migrate to the US among MHAS non-migrants (N=15,915)

	Beta (SE)
Propensity for Lifetime Migration	
Propensity	-0.0505 (0.0436)
Propensity*Decade	0.004 (0.0006)
Propensity for Migration by Age 50	
Propensity	-0.1266 (0.0450)
Propensity*Decade	0.005 (0.0006)
Propensity for Migration by Age 25	
Propensity	-0.1966 (0.0858)
Propensity*Decade	0.008 (0.001)
Propensity for Migration by Age 13	
Propensity	0.8640 (0.5745)
Propensity*Decade	0.061 (0.009)
Models adjusted for practice effects and sex	

Toward a clearer understanding of the inverse association between cancer and dementia L. Paloma Rojas-Saunero* L. Paloma Rojas-Saunero Kimberly D. van der Willik Sanne B. Schagen Sonja A. Swanson M. Arfan Ikram

Background: Previous observational studies have shown that cancer patients have a lower risk of dementia than persons without a history of cancer, though multiple sources of biases could affect the validity and interpretability of such results. **Aim:** To illustrate how selection bias can be amplified based on study design decisions, and present alternative estimands that treat the competing event of death differently, while accounting for immortal time bias. **Methods:** We selected participants without history of dementia at baseline from the Rotterdam Study. We replicated prior design and analytic strategies used in previous studies, by treating cancer as a (i) time-varying vs. (ii) “time-fixed” exposure and computing hazard ratios (HR) with Cox proportional hazard models, with death as a censoring event. Next, we compared the crude and net risk of dementia among participants with and without cancer, using inverse probability weighting to mitigate potential immortal time bias since participants may die before cancer diagnosis. **Results:** Out of 8899 participants, 1813 (20%) were diagnosed with cancer, of whom 68 (4%) had dementia, and 890 (49%) died. Among those without cancer, 781 (11%) were diagnosed with dementia, and 1341 (19%) died. When cancer was treated as time-varying, HR was 0.9 (0.7-1.2); when treated as a “time-fixed” exposure of ever developing cancer over follow-up, the HR was 0.4 (0.3-0.6). The crude and net risk of dementia in participants with cancer was similar to that in participants without cancer when immortal time bias was addressed (Figure). **Conclusions:** Several versions of selection bias can be present in different ways, from selecting individuals who survived to have a cancer diagnosis, relying on death as an independent censoring event, and conditioning on survival through hazard ratios. We will further delve into the meaning of the research questions with “cancer” as an exposure, clarifying what can be done about these and other sources of bias.



Examining the causal mediating role of cardiovascular factors on the relationship between physical activity and cognitive impairment via separable effects mediation analysis Ryan M Andrews* Ryan M Andrews Michelle C Carlson Vanessa Didelez

Delaying or preventing the onset of cognitive impairment will be a crucial goal for public health over the next 10-30 years. Accumulating epidemiologic evidence suggests that physical activity is protective against cognitive impairment; however, less is known about possible mechanisms underlying this relationship. In this study, we investigated whether there is a causal effect of physical activity on time-to-cognitive impairment, and whether this relationship is mediated by blood pressure or body mass index. Interpreting the results of prior studies in this area can be difficult because of their use of Cox proportional hazards models, nested counterfactuals, and/or use of a single static mediator measurement. Our study overcomes these difficulties via the use of a novel separable effects mediation method that is based on additive hazards models, avoids nested counterfactuals, and treats both direct and indirect effects as dynamic quantities that unfold over time to better match the intuitive meaning of mediation. Using longitudinal data from the Cardiovascular Health Cognition Study, we found that engaging in higher levels of physical activity does have a protective overall effect on time-to-cognitive impairment, as expected (Figure 1). Interestingly, this effect seems to be noticeable only after 2-3 years of follow-up. We also found that neither blood pressure nor body mass index mediates this effect, which undermines the hypothesis that physical activity delays or prevents cognitive impairment via improvements in cardiovascular health. However, we cannot fully rule out the possibility that our lack of an indirect effect is due to one or more violations of our causal assumptions. Overall, we believe our study is an important first step towards more interpretable and realistic causal mediation analyses in cognitive impairment and neuroepidemiologic research, and we encourage additional studies to replicate and refine our results.

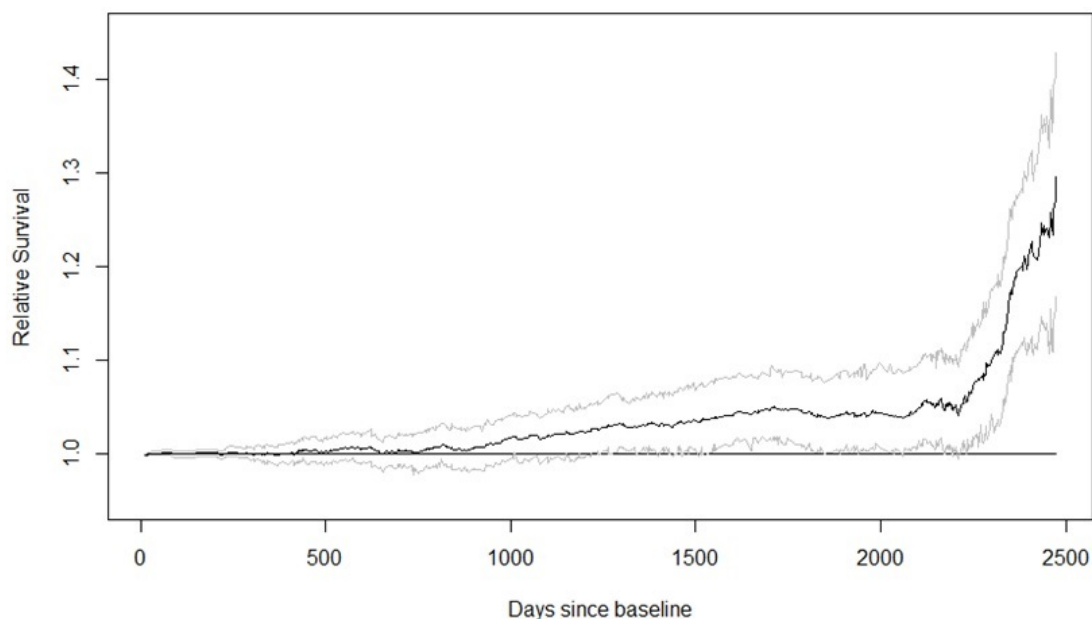


Figure 1: Plot on the relative survival scale of the overall effect of physical activity on cognitive impairment. The black line shows the effect estimate over time, and the gray lines correspond to a 95% confidence interval around the estimate. Estimates above 1.0 indicate that physical activity is protective against cognitive impairment.

Adult child education and older parents' cognitive decline: A longitudinal, cross-national study Jacqueline Torres* Jacqueline Torres Erika Meza Emilie Courtin

Background: Emerging research suggests that the socio-economic status (SES) of adult children may be a population-modifiable determinant of older parents' cognitive outcomes. Yet, no studies have evaluated cross-national comparisons. **Methods:** We evaluated the effect of adult child education on older parents' memory decline across 11 European countries using data from the Survey of Health, Aging and Retirement in Europe, a longitudinal study of adults ≥ 50 years. We included respondents with at least one living adult child (>25 years) at study baseline (2004), with follow-up through 2017 (N=16088). We regressed respondents' total verbal recall z-scores on the average years of educational attainment among their adult children overall and by gender using three-level (country, respondent, time) linear mixed models. We evaluated differences in associations across countries with similar policy contexts, proxied by a welfare regime classification. **Results:** At baseline, respondents were 65 years old and their adult children had completed an average of 12.5 years of education. Across countries, higher educational attainment among adult daughters - but not sons - was associated with a slower rate of decline in parents' verbal memory z-scores (b: 0.003 [95% CI: 0.001, 0.006]). In Southern European countries, higher education among adult sons - but not daughters - was associated with a faster decline in verbal memory z-scores (b: -0.003 [95% CI: -0.008, -0.002]) among older parents. For comparison, the analogous coefficient for the association between additional year of baseline age and decline in verbal memory z-scores was [b: - 0.005; 95% CI: -0.007, -0.003]). **Conclusion:** Higher education among adult daughters was associated with a slower rate of verbal memory decline among older parents in Europe. However, heterogeneity by national social policy characteristics suggests the broader context may shape how adult child education contributes to parents' cognitive aging.

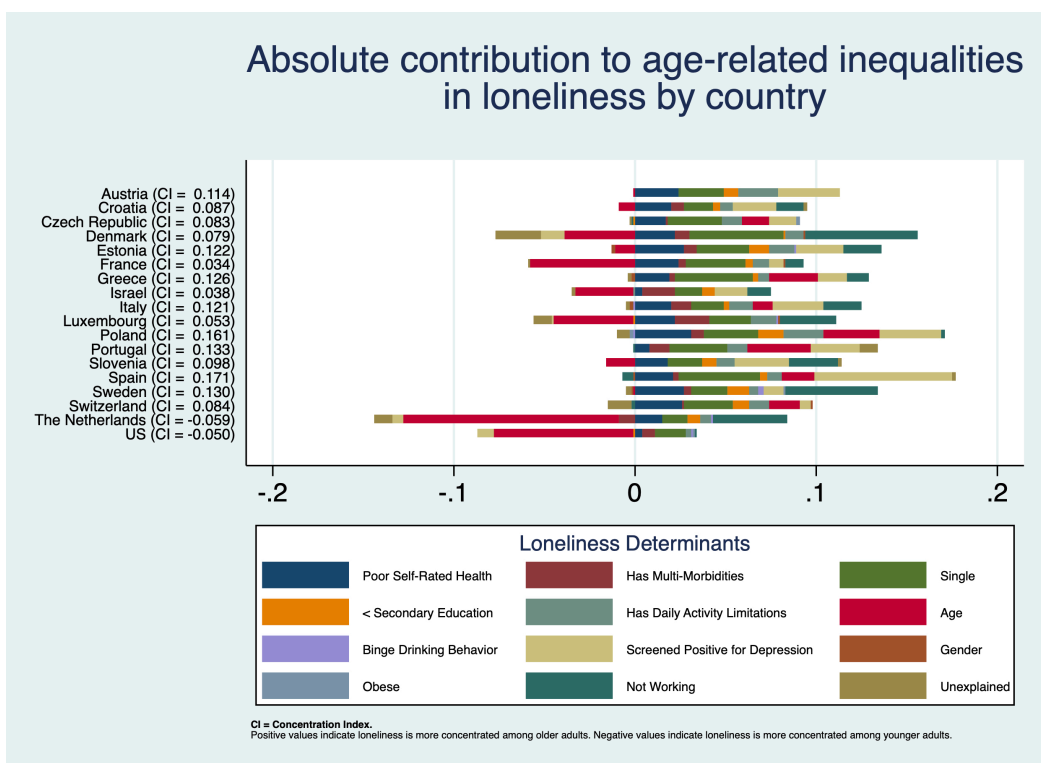
Determinants of loneliness in older adulthood: a decomposition of 20 countries Robin Richardson* Robin Richardson Christopher Crowe Katherine Keyes Esteban Calvo

Background: Loneliness is common in older age and can have negative effects on health. The determinants of loneliness, and potential differences across countries, remain poorly described.

Methods: We used nationally-representative data of older adults from 19 European countries and the US (N=81,993). Loneliness was measured with the 3-item UCLA loneliness scale. We investigated factors that correlate with loneliness, including age, gender, educational attainment, marital status, work status, limitations performing daily activities, depression, self-rated health, binge drinking behavior, obesity, and presence of multi-morbidities. We used Concentration Indices (CI) to quantify the degree of age-related inequalities in loneliness in each country (potential score range: -1 to 1; 0 indicates no inequality), and then decomposed country-specific CIs into a weighted sum of each potential determinant’s contribution to loneliness with a decomposition analysis. All analyses were stratified by country and restricted to adults aged 50 to 90 years.

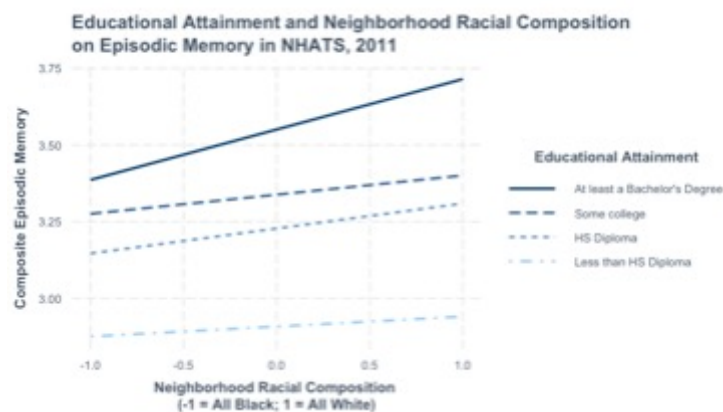
Results: Most countries had CIs greater than 0 (n = 15), indicating loneliness was more concentrated among older adults, with especially large age-related inequalities in Spain (CI = 0.17, 95% CI: 0.14, 0.20) and Poland (CI = 0.16, 95% CI: 0.12, 0.20). The decomposition found consistent contributors to age-related inequalities in loneliness across countries include being single (relative contribution = 15.1% in Italy to 98.8% in France), poor self-rated health (relative contribution = 6.1% in Portugal to 70.9% in France), and depression (relative contribution = 7.6% in Switzerland to 48.6% in Israel). Other factors, such as not working, were substantial contributors in some countries but not others (relative contribution = 0.1% in Austria vs. 78.7% in Denmark).

Conclusion: While both health and demographic factors contributed to age-related inequalities in loneliness, the magnitude of contribution varied substantially by country.



The association of education and neighborhood racial composition on cognitive function and decline in a nationally-representative sample Kristina Dang* Kristina Dang Mary Haan Maria Glymour Jennifer Weuve Isabel Allen

Background. Neighborhood racial composition, as a measure of structural racism, and individual socioeconomic position (educational attainment) are important areas for research in Alzheimer's disease. We sought to better understand the contributions of these two factors/exposures to cognition and cognitive decline in a sample of nationally representative older adults. **Methods.** The National Health and Aging Trends Study is a nationally representative sample of 8,245 participants aged 65+ at baseline (2011). We merged the census tract in which each participant resided with American Community Survey measures, both from 2011. For each census tract, we computed the Index of Concentration at the Extremes for our measure of neighborhood racial composition, defined as: [(the number in most privileged extreme, i.e., Whites) – (the number in most deprived extreme, i.e., Blacks)]/(total number of people). Annual scores from tests of delayed and immediate word list recall were standardized to the mean and standard deviation at baseline, and a composite measure of episodic memory was calculated as the average of the two tests' z-scores. We used linear mixed effects models to examine educational attainment (less than high school, high school diploma, some college, at least a bachelor's degree) and neighborhood racial composition [-1, 1] in predicting memory and memory decline over 6 years, adjusting for age, race/ethnicity (Black, Hispanic, White), gender, census division (NE, MW, S, W), and practice effects, with random effects for census tract and participant. **Results.** In the full sample, higher education predicted better episodic memory [difference=0.30 standard deviation units (0.21, 0.40); 0.41 (0.31, 0.50); 0.60 (0.49, 0.71) with less than HS as referent], but did not predict decline [-0.01 (-0.02, 0.01); 0.01 (-0.004, 0.03); 0.03 (0.01 0.05)]. Neighborhood composition was not associated with episodic memory [0.09 (-0.004, 0.18)], however, did predict decline (-0.03 (-0.05, -0.02)). **Conclusion.** Neighborhood racial composition was associated with the rate of memory decline.



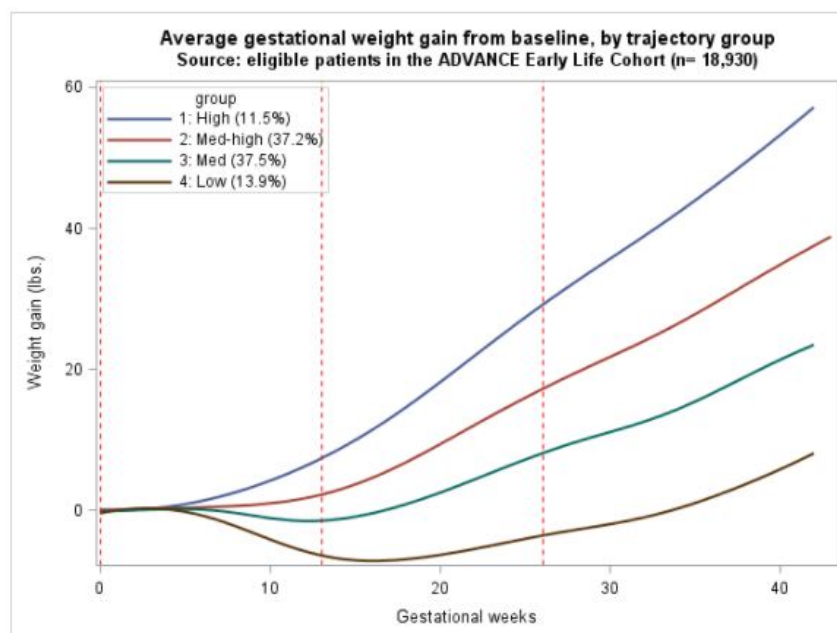
Using group-based latent-class trajectory modeling to identify distinct patterns of gestational weight gain in a safety-net population Sarah-Truclinh Tran* Sarah-Truclinh Tran Anna Booman Rachel Springer Jennifer Lucas Miguel Marino Jean O'Malley Amy Palma Teresa Schmidt Kristin Scott Kalera Stratton Jonathan Snowden Kimberly Vesco Janne Boone-Heinonen

Gestational weight gain (GWG) is a potentially modifiable risk factor that may influence birth outcomes and long-term maternal health. There is limited research describing the various pathways by which women experience GWG and if certain trajectories affect health risks. Our objective was to identify distinct temporal patterns of GWG within a large safety-net population.

We analyzed longitudinal clinical data from patients' first pregnancy in the ADVANCE Early Life Cohort during 2011 and 2020. The analytic sample included 18,930 patients with a singleton pregnancy who had a baseline weight measure and ≥ 2 weight measures in each trimester. We used group-based latent-class trajectory modeling to derive distinct GWG patterns and then compared the characteristics of patients exhibiting each pattern.

The best-fitting model identified 4 latent groups, labelled as "low," "medium," "medium-high," and "high" weight gain, and comprised 13.9%, 37.5%, 37.2%, and 11.5% of patients, respectively (see figure). Over the entire pregnancy, the lowest to highest groups gained an average 0.20, 0.67, 1.1, and 1.5 pounds/week, respectively. Variations existed by trimester and between groups. In the 1st trimester, the two lowest groups had average weight losses of -1.2 and -0.32 lbs/wk while the two highest groups had average gains of 0.37 and 1.2 lbs/wk. In the combined 2nd and 3rd trimesters, all groups had increased GWG rates, with the highest group gaining an average 1.7 lbs/wk compared to 0.48 lbs/wk in the lowest. The most important differentiating factor examined was maternal pre-pregnancy BMI. Women having severe obesity (class 2, 3) were 9-14 times more likely than normal-weight women to be in the lowest trajectory group than the medium one.

Conclusion: We identified 4 distinct GWG trajectories in a safety-net population that provides groundwork for future investigations of associations with maternal, perinatal outcomes, particularly for women with severe obesity who are underserved.

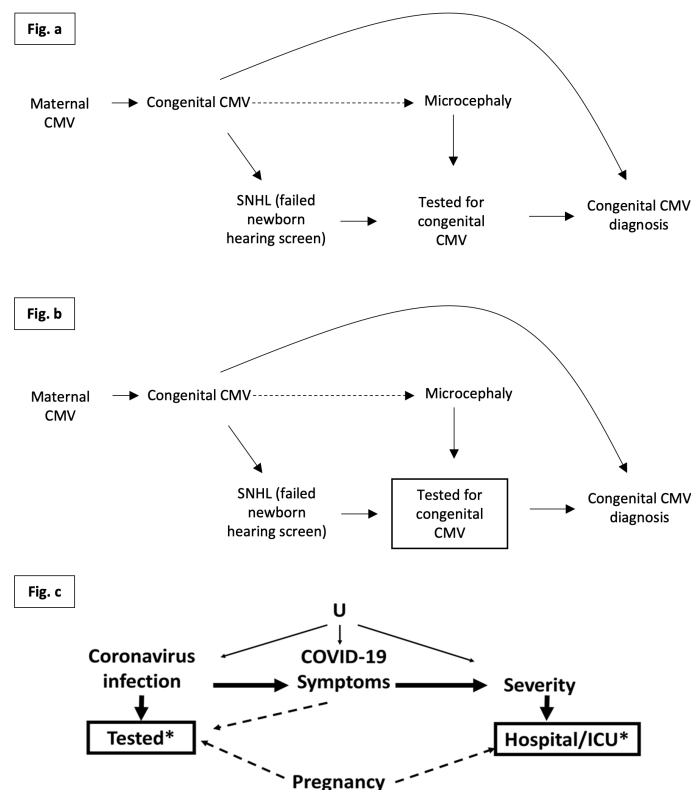


Can we use ensemble machine learning to accurately identify severe maternal morbidity in a perinatal database? Abigail Cartus* Abigil Cartus Ashley Naimi Katherine Himes Marian Jarlenski Sara Parisi Lisa Bodnar

Severe maternal morbidity (SMM) is an important maternal health indicator, but existing tools to identify SMM have substantial limitations. Our objective was to retrospectively identify true SMM cases and non-cases using ensemble machine learning in a hospital database and to compare machine learning algorithm performance with existing tools for SMM identification. We screened all deliveries occurring at Magee-Womens Hospital, Pittsburgh, PA (2010–2011 and 2013–2017) using the CDC list of diagnoses and procedures for SMM, intensive care unit (ICU) admission, and/or prolonged postpartum length of stay (PPLOS). We performed detailed medical record review to confirm case status. We trained ensemble machine learning (SuperLearner) algorithms, which “stack” predictions from multiple algorithms to obtain optimal predictions, on 171 SMM cases and 506 non-cases from 2010–2011, then evaluated the performance of these algorithms on 160 SMM cases and 337 non-cases from 2013–2017. SuperLearner algorithms performed better than the existing screening criteria in terms of positive predictive value (0.86 versus 0.64, respectively). However, SuperLearner algorithms did not perform as well as the screening criteria in terms of overall accuracy (0.79 versus 0.82), negative predictive value (0.77 versus 0.99), or true-positive detection rate (0.32 versus 0.13, respectively). The most important predictor variables were ICU admission and PPLOS. Ensemble machine learning did not globally improve the ascertainment of true SMM cases. Our results suggest that accurate identification of SMM likely will remain a challenge in the absence of a universal definition of SMM or national obstetric surveillance systems.

Collider stratification bias in the surveillance of outcomes related to infections in pregnancy: an example from cytomegalovirus and lessons for COVID-19 Chelsea Messinger*
Chelsea Messinger Sonia Hernández-Díaz

For infections that are not universally screened for in pregnancy or in infants, estimating the effect of prenatal infection on maternal and/or fetal outcomes may be complicated by surveillance bias. Preferential testing of patients with symptoms or risk factors can be conceptualized as conditioning on a collider. We have published an example of testing bias in estimating the effect of congenital cytomegalovirus (cCMV) infection on microcephaly. Here, we describe that testing bias in greater depth and discuss how similar testing bias may be present in studies attempting to estimate the effect of pregnancy on COVID-19. In our prior work, we identified a population-based pooled cohort of 2,338,580 pregnant women and their newborns in 2 insurance claims databases from the USA. Neither pregnant women nor infants are universally screened for CMV infection, and infants are generally only tested for CMV if they are symptomatic. The prevalence ratio (PR) for the association between cCMV and microcephaly in the full cohort (PR=232, 95% CI 154-350) was therefore upwardly biased because infants with microcephaly are more likely to be tested (Fig. a). However, conditioning on CMV testing (PR=15, 95% 5.6-41) introduced selection bias due to selective testing of infants with symptoms such as hearing loss (Fig. b). The issues presented by conditioning on testing in the cCMV example can be extended to estimation of the effect of pregnancy on COVID-19 outcomes. Since both pregnancy and symptoms trigger testing, conditioning on SARS-CoV-2 testing may bias the association between pregnancy and COVID-19 severity (Fig. c). In addition, pregnant women are more likely to be hospitalized/admitted to the ICU irrespective of coronavirus infection. Ignoring potential collider stratification bias due to selective testing for infections in pregnancy may result in incorrect conclusions about the strength of causal associations between pregnancy and COVID-19 clinical course.



Genomic study of early pregnancy maternal lipid traits revealed four known adult lipid loci

Marion Ouidir* Marion Ouidir Suvo Chatterjee Jing Wu Fasil Tekola-Ayele

Blood lipids during pregnancy are known risk factors for cardiovascular diseases and adverse pregnancy outcomes. Genome-wide association studies (GWAS) in predominantly male European ancestry populations have identified genetic loci associated with blood lipid levels. However, the genetic architecture of blood lipids in pregnant women remains poorly understood. Our goal was to identify genetic loci associated with blood lipid levels among pregnant women from diverse ethnic groups via trans-ethnic GWAS meta-analysis and to evaluate whether previously known lipid GWAS loci are transferable to pregnant women.

The trans-ethnic GWAS were conducted on serum level of cholesterol, HDL, LDL, triglycerides and total lipids during first trimester among pregnant women from four population groups (501 White-, 470 African-, 450 Hispanic- and 233 Asian-Americans) recruited in the NICHD Fetal Growth Studies cohort, adjusting for maternal age and population stratification. The four GWAS summary statistics were combined using trans-ethnic meta-analysis approaches based on random effects accounting for genetic heterogeneity among populations.

In the trans-ethnic GWAS meta-analyses, 13, 9, 33 and 1 SNPs were associated ($P < 5 \times 10^{-8}$) with cholesterol, HDL, LDL and total lipids, respectively. The lead SNPs annotated to *CELSR2*, *APOE*, *CETP* and *ABCA1* genes and overlapped with known lipids-related loci. Novel low-frequency loci (*GALNT7*, *SLAIN2*, *LOC101928274*, *NRXN3*, and *ANKRD27*) were associated with triglycerides, primarily driven by one population. 429 out of 454 known lipids-related loci in previous GWAS studies, were evaluated in our data and 143 (33%) loci were significant ($p < 0.05$).

This trans-ethnic GWAS meta-analysis in pregnant women of diverse populations identified four known lipid-loci. Replication of 1/3rd of the known loci from predominantly European study populations underlines the need for genome-wide lipids-related association studies in diverse populations.

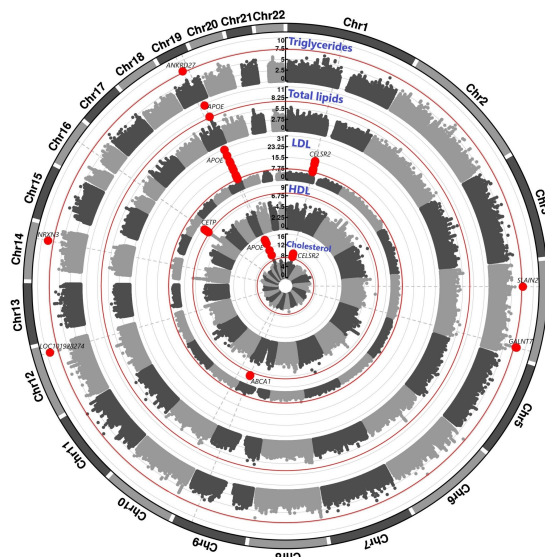


Figure 1. Circular Manhattan plot of genome-wide association \log_{10} p-values across 22 chromosomes for five lipid traits. SNPs surpassing genome-wide significant association ($p < 5 \times 10^{-8}$) are marked in red and their nearby genes are included.

Development of a predictive model to identify women with recent gestational diabetes at high risk for progression to postpartum impaired glucose intolerance Angela Bengtson*

Angela Bengtson Ana Lucia Espinosa Dice Melissa Clark Erika Werner

Women with gestational diabetes mellitus (GDM) are at high risk for impaired glucose metabolism (IGT) or diabetes mellitus (DM) postpartum. Glucose testing at 4-12 weeks postpartum is used to identify women at high-risk of progression, but has poor uptake and predictive ability. Predictive models that identify high-risk women around the time of delivery may improve outcomes. In a cohort of women with recent GDM who had glucose tolerance testing at 2 days postpartum and were followed until 1 year postpartum, we identified 27 clinical, obstetric, sociodemographic potential predictors of IGT at 1 year postpartum, defined as HbA1c \geq 5.7%. We used multivariable Lasso regression with 10-fold cross validation to identify a parsimonious set of predictors. We compared the area under the receiver operating curve (AUC) from the final multivariable model to bivariable logistic regression models for all predictors in the final model. We evaluated the sensitivity, specificity, positive and negative predictive values (PPV, NPV) of predicted probability cut-points to identify women with IGT at 1 year postpartum. Of 203 women with recent GDM, 35% (n=71) developed IGT by 1 year postpartum. Overall, 9 predictors were included in the final model (Table), including pre-pregnancy weight, insulin treatment, family history of DM, GDM diagnosis <24 weeks, and glucose values at 2 days postpartum. The AUC from the final multivariable model was 0.86 (95% CI 0.80-0.93), compared to 0.75 (95% CI 0.66-0.84) for the strongest bivariable predictor (weight at 2 days postpartum). A cut-point of 0.39 had sensitivity 80% (95% CI 66%-90%) specificity 79% (95% CI 69%-88%), PPV 71% (95% CI 57%-82%), and NPV 86% (95% CI 76%-93%) to identify women with IGT at 1 year postpartum. We developed a predictive model with improved predictive ability identify women at high-risk for IGT by 1 years postpartum around delivery. Additional work is needed to validate this model in other populations of women with GDM.

Table. Performance of models to predict Pre-DM or DM within 1 year postpartum		Individual Predictors		Combined Predictors		
Time period	Predictor	Bivariable Logistic Results		Multivariable Lasso Results		
		OR (95% CI)	AUC (95% CI)	Penalized OR*	Un-penalized OR*	AUC (95% CI)
Prenatal	Pre-pregnancy weight, continuous	1.02 (1.01, 1.03)	0.74 (0.66, 0.83)	1.00	1.01	0.86 (0.80, 0.93)
Prenatal	Family history of DM	2.06 (0.98, 4.34)	0.59 (0.50, 0.67)	1.59	2.97	
Prenatal	Race/ethnicity (ref. white)		0.63 (0.53, 0.72)			
		Black	1.37 (0.30, 6.27)	-	-	
		Hispanic	3.20 (1.38, 7.40)	2.77**	6.56**	
		Other	0.91 (0.26, 3.25)	-	-	
Prenatal	GDM diagnosis <24 weeks GA	6.00 (1.81, 19.89)	0.60 (0.53, 0.66)	1.93	3.47	
Prenatal	Hypertensive disorders in pregnancy	2.84 (0.65, 12.47)	0.53 (0.48, 0.58)	1.86	4.86	
Prenatal	Insulin/medication treatment for GDM management	3.58 (1.65, 7.79)	0.65 (0.57, 0.73)	1.25	1.34	
2 days pp	Weight 2 days pp, continuous	1.03 (1.01, 1.04)	0.75 (0.66, 0.84)	1.01	1.02	
2 days pp	Fasting Plasma Glucose, continuous	1.05 (1.02, 1.09)	0.63 (0.53, 0.74)	1.01	1.02	
2 days pp	2-hour Plasma Glucose, continuous	1.02 (1.01, 1.03)	0.64 (0.54, 0.75)	1.01	1.02	

pre-DM: pre diabetes mellitus; DM: diabetes mellitus; AUC: area under the receiver operating curve; GA: gestational age; BMI: body mass index; LGA: large for gestational age; GDM: gestational diabetes mellitus; OGTT: oral glucose tolerance test; pp: postpartum. All bivariable predictors included in the multivariable model.
 * 95% CIs not available for coefficients from Lasso model. **OR indexes Hispanic vs. white/Black/Other in Lasso model.

Examining the Moderating Role of Accredited Social Health Activists Home Visits and Accompanied Antenatal Care Visits on Preterm Birth and Low Birth Weight in Rural Mysore District, India Purnima Madhivanan* Sandra Kiplagat Kavitha Ravi Diana M. Sheehan Vijaya Srinivas Anisa Khan Mary Jo Trepka Zoran Bursac Dionne Stephens Karl Krupp

The Indian government established the Accredited Social Health Activists (ASHA) program in 2006, to connect marginalized individuals to the healthcare system. The objective of the study was to examine the moderating role of ASHA home visits and ASHA accompanied antenatal care (ANC) visits on the relationship between sociodemographic latent classes of pregnant women, and preterm birth and low birth weight infants in rural Mysore District, India.

Secondary analysis of data from a prospective cohort study conducted between 2011-2014 of 1,540 pregnant women was conducted. Latent class analysis was performed to identify distinct patterns based on sociodemographic factors. Multivariable logistic regression was conducted to examine the moderating effects of ASHA accompanied ANC visits (never/rarely vs. occasionally/regular) and ASHA home visits (never/rarely vs. occasionally/regular) on the association between the latent classes, and preterm birth and low birth weight infants adjusting for covariates.

Four latent classes were identified. Class 1 were "low socioeconomic status (SES)/early marriage/multigravida/1 child or more", Class 2 were "low SES/later marriage/primigravida/no children", Class 3 were "high SES/later marriage/multigravida/1 child or more", and Class 4 were "high SES,/later marriage/primigravida/no children". Women in Class 1 and Class 3 who never or rarely had ASHA accompanied ANC visits had higher odds of preterm birth (aOR: 2.62 95% CI: 1.12-6.12, aOR: 3.47 95% CI:1.31-9.15, respectively) when compared to Class 4. These effects were not observed among women with occasional or regular ASHA accompanied ANC visits. There were no moderating effects on ASHA home visits on low birth weight.

The findings demonstrate that accompanying women by ASHA to ANC moderates the risk of preterm birth among women at high risk. Targeted policies and interventions in improving and strengthening the ASHA are essential in reducing adverse birth outcomes in rural India.

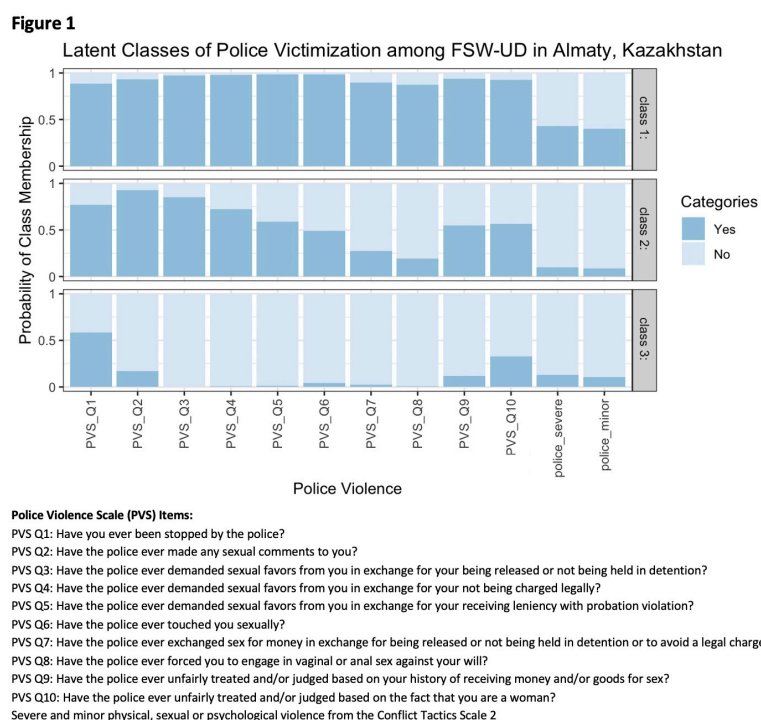
Patterns of Police Victimization among Women who use Drugs and Engage in Sex Work in Kazakhstan Trena Mukherjee* Trena Mukherjee Andrea Norcini Pala Alissa Davis Tara McCrimmon Gaukhar Mergenova Sholpan Primbetova Assel Terlikbayeva Nabila El-Bassel

Objective: Globally, nearly one-third of women who use drugs engage in sex work. Decriminalization of sex work substantially reduces the risk of police violence and HIV, however, drug use remains criminalized in many settings. Little is known about the heterogeneity of police violence against FSW who use drugs (FSW-UD) and its associated HIV risk.

Methods: Using data from a community-based sample of 255 FSW-UD enrolled in NOVA in Almaty, Kazakhstan (2015-2017), latent class analysis (LCA) was used to differentiate women into distinct classes of police victimization. Multinomial logistic regression was used to identify HIV risk factors.

Results: LCA identified three classes of police victimization: poly-victimization (class 1; 34%); extortion and discrimination (class 2; 15%); and low victimization (class 3; 51%) (*Figure 1*). Compared to FSW-UD in the low victimization class, poly-victimized FSW-UD had higher odds of arrest (OR: 3.04; [95% CI]:1.43-6.47), detention (2.87; 1.61-5.11) and poor police perceptions (7.47; 3.92-14.24), reporting greater number of clients (2.13; 1.22-3.70) and client violence (2.68; 1.53-4.68), injection drug use (1.91; 1.10, 3.33), including risky injection practices (1.27; 1.08-1.50), and stigma of drug use (1.22; 1.07-1.38) and sex work (1.21; 1.05-1.40). FSW-UD in extortion and discrimination class reported lower odds of exchanging sex for drugs/alcohol (0.50; 0.38-0.66), engaging in survival sex (0.53; 0.39-0.71), experiencing intimate partner violence (0.20; 0.07-0.55) and risky injection practices (0.61; 0.46-0.81), compared to FSW-UD in the low victimization class.

Conclusion: This study suggests that nearly half of FSW-UD report multiple counts of police violence, despite decriminalization of sex work. HIV risk vary by patterns of police victimization, with poly-victimized FSW-UD at greatest risk. Interventions to mitigate police violence and HIV in this subgroup are urgently needed to reduce the rising HIV epidemic in Kazakhstan.



Association of crack cocaine use frequency with HIV disease progression: A prospective cohort study Alexandria Macmadu* Alexandria Macmadu Hudson Reddon Brandon Marshall Nadia Fairbairn Seonaid Nolan Eugenia Socías Amy Justice M-J Milloy

Background: Prior evidence suggests that plasma HIV viral load is elevated during periods of crack cocaine use independent of antiretroviral therapy (ART) exposure. We sought to evaluate the effect of crack cocaine use frequency on HIV disease progression among HIV-positive people who use unregulated drugs (PWUD).

Methods: We analyzed data from the ACCESS study, an open prospective cohort of HIV-positive PWUD, including comprehensive HIV clinical monitoring in a setting with no-cost healthcare and ART. Multivariable generalized linear mixed-effects models were used to estimate the independent effect of time-updated crack cocaine use frequency on HIV disease severity, adjusting for ART exposure and relevant confounders. HIV disease severity was measured using the Veterans Aging Cohort Study (VACS) Index.

Findings: Between 2005 and 2018, 806 individuals were recruited and contributed 8,537 observations following ART initiation. At baseline, the frequencies of crack cocaine use in the previous 180 days were: none (187, 23%), less than weekly (150, 19%), weekly (229, 28%), and daily or greater (240, 30%). In multivariable models adjusted for ART exposure and other confounders, daily or greater frequency of crack cocaine use was significantly associated with higher VACS Index scores ($\beta = 0.9$, 95% confidence interval: 0.2, 1.6) as compared to none, and VACS Index score increased with crack cocaine use frequency in a dose-response manner (Figure 1).

Interpretation: Daily or greater frequency of crack cocaine use may exacerbate HIV disease progression among HIV-positive PWUD. Although the observed effect was small, it was also independent of ART exposure. As this finding has been supported by previous evidence, the observed difference may reflect an underlying biological mechanism or other factors linked with crack cocaine use that warrant further investigation.

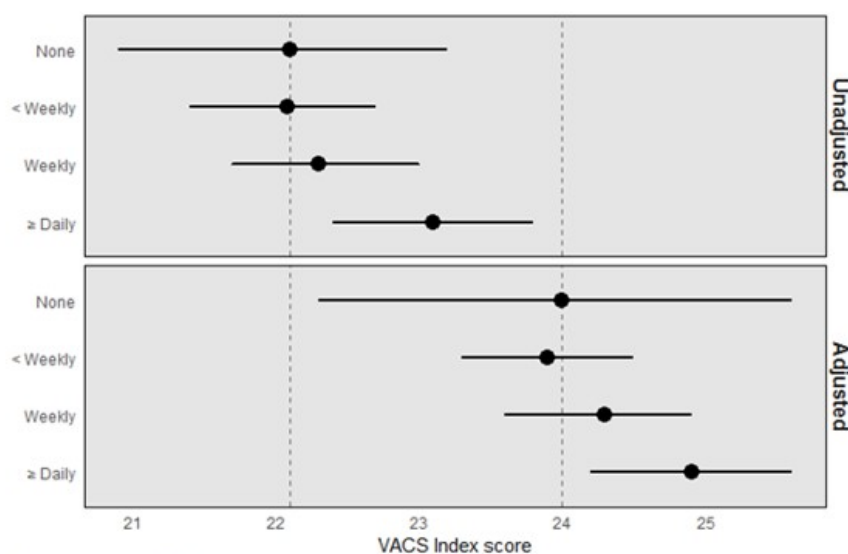


Figure 1. VACS Index by frequency of crack cocaine use in the prior 6 months

All adjusted models are adjusted for age, sex at birth, ethnicity, injection drug use, unstable housing, engaging in methadone maintenance therapy, recent incarceration, binge alcohol use, weeks since ART initiation, and adherence to ART.

Alcohol use disorder and recent alcohol use and HIV viral non-suppression among people engaged in HIV care in an urban clinic, 2013-2018 Catherine Lesko* Catherine Lesko Heidi Hutton Jessie Edwards Mary E. McCaul Anthony T. Fojo Richard Moore Geetanjali Chander

Objective: To estimate joint associations between having an alcohol use disorder (AUD) and recent alcohol use and viral non-suppression.

Design: Observational cohort study of patients enrolled in routine clinical care at the Johns Hopkins HIV Clinic between 2014 and 2018.

Methods: AUD was defined by history of a clinical diagnosis of alcohol abuse or dependence. Recent alcohol use was self-reported on a modified version of the US Alcohol Use Disorders Identification Test consumption questions; high-risk drinking was defined as reporting ≥ 7 drinks/week for women or ≥ 14 drinks/week for men or reporting any instances of binge drinking. Lack of durable viral suppression was defined as having ≥ 1 viral load measurement >20 copies/mL in the same calendar year as alcohol consumption was reported.

Results: Among 1690 patients who were majority male and Black race, 26% had ever been diagnosed with an AUD and 21% reported recent high-risk alcohol use. Prevalence of lack of durable viral suppression was 39%. Relative to non-drinkers without an AUD, high-risk drinking in the absence of an AUD and not drinking in the presence of an AUD were only weakly associated with viral non-suppression; any level of drinking among patients with an AUD was strongly associated with higher prevalence of viral non-suppression.

Conclusions: Subsequent analyses of the association between alcohol use and viral suppression should consider patients' history of AUD. No level of alcohol use may be "safe" for people with a prior AUD with regard to their probability of maintaining viral suppression.

The Relationship Between Hepatitis C Virus Rates and Office-Based Buprenorphine**Prescribing in Ohio** Daniel Brook* Daniel Brook Shibani Chettri Angela Hetrick Christine Schalkoff Adams Sibley Kathryn Lancaster Vivian Go William Miller David Kline

Introduction: The United States is experiencing an epidemic of hepatitis C virus (HCV) infections due to injection drug use, primarily of opioids and predominantly in rural areas. Buprenorphine, a medication for opioid use disorder, may indirectly prevent HCV transmission. While rural areas have limited access to buprenorphine, counties with higher rates of HCV may have more access. Thus, we assessed the urban versus rural relationship of HCV rates and office-based buprenorphine prescribing in Ohio.

Methods: We fit negative binomial models between the county-level acute and total (defined as acute and chronic) HCV incidence rates during 2013-2015 and 1) the number of patients in each county that could be served by office-based buprenorphine (prescribing *capacity*) and 2) the number served by office-based buprenorphine (prescribing *frequency*) from January 1-March 31, 2018. We adjusted for the 2015 county-level primary care physician prevalence and the 2010-2015 age-adjusted unintentional drug overdose death rate.

Results: For each 10% increase in acute HCV rate in 2013-2015, office-based buprenorphine prescribing capacity increased 0.01% (95% CI: -0.19%, 0.21%) in urban counties and 0.52% (95% CI: 0.23%, 0.82%) in rural counties in 2018. For each 10% increase in total HCV rate, prescribing capacity increased 0.52% (95% CI: 0.08%, 0.96%) in urban counties and 1.01% (95% CI: 0.66%, 1.35%) in rural counties. For each 10% increase in acute HCV rate, office-based buprenorphine prescribing frequency decreased 0.05% (95% CI: -0.24%, 0.14%) in urban counties and increased 0.54% (95% CI: 0.03%, 1.06%) in rural counties. For each 10% increase in total HCV rate, prescribing frequency increased 0.19% (95% CI: -0.18%, 0.57%) in urban counties and 1.21% (95% CI: 0.62%, 1.81%) in rural counties.

Conclusions: Rural counties in Ohio may have more office-based buprenorphine prescribing in counties with higher HCV rates, whereas urban counties may have more ubiquitous to buprenorphine.

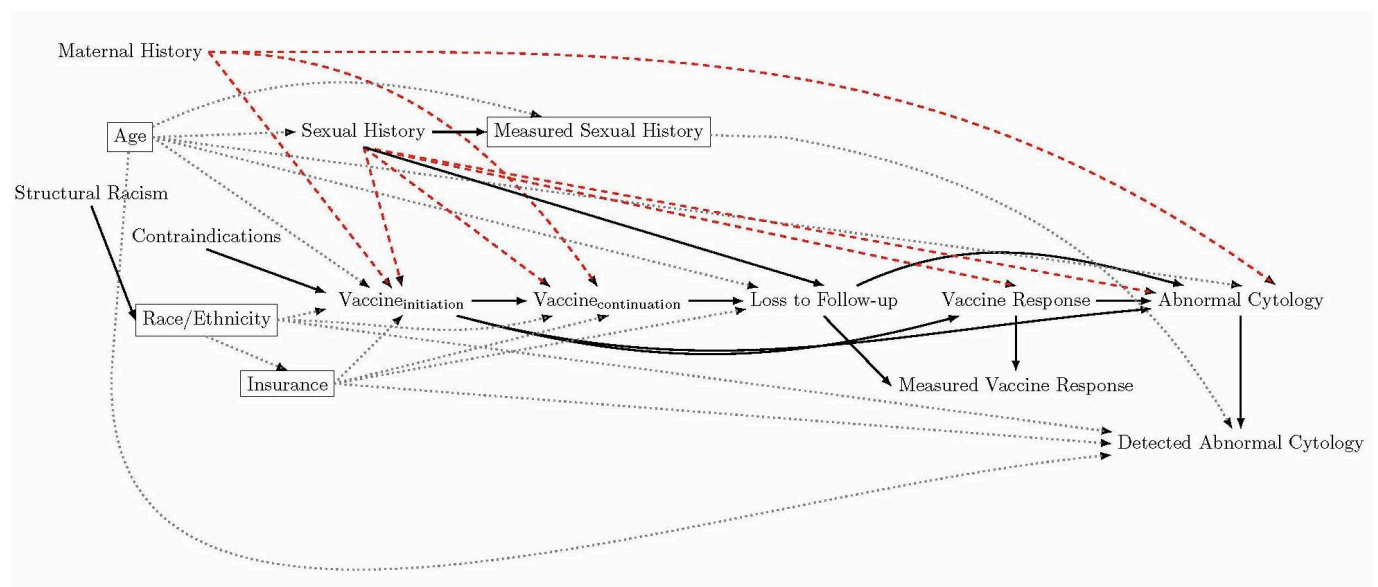
A case study and proposal for publishing pre-analytic directed acyclic graphs: The effectiveness of the quadrivalent HPV vaccine in perinatally HIV exposed girls

Ruby Barnard-Mayers* Ruby Barnard-Mayers Hiba Kouser Jamie Cohen Katherine Tassiopoulos Ellen Caniglia Anna-Barbara Moscicki Nicole G. Campos Michelle R. Caunca George R. Seage III Eleanor J Murray

Developing a causal graph is an important step in etiologic research planning and can be used to highlight data flaws and irreparable bias and confounding. However, there has been little guidance on how to build or report a causal graph for applied health research. Here, we present a step-by-step approach to constructing and reporting a causal graph, using as a case study the effectiveness of the quadrivalent human papillomavirus (HPV) vaccine in girls with perinatal HIV.

Recent findings have suggested that the human papillomavirus (HPV) vaccine is less effective in protection against HPV associated disease for people living with HIV. In order to understand the relationship between HIV status and HPV vaccine effectiveness, it is important to outline the key assumptions of the causal mechanisms before designing a study to either corroborate or challenge these findings.

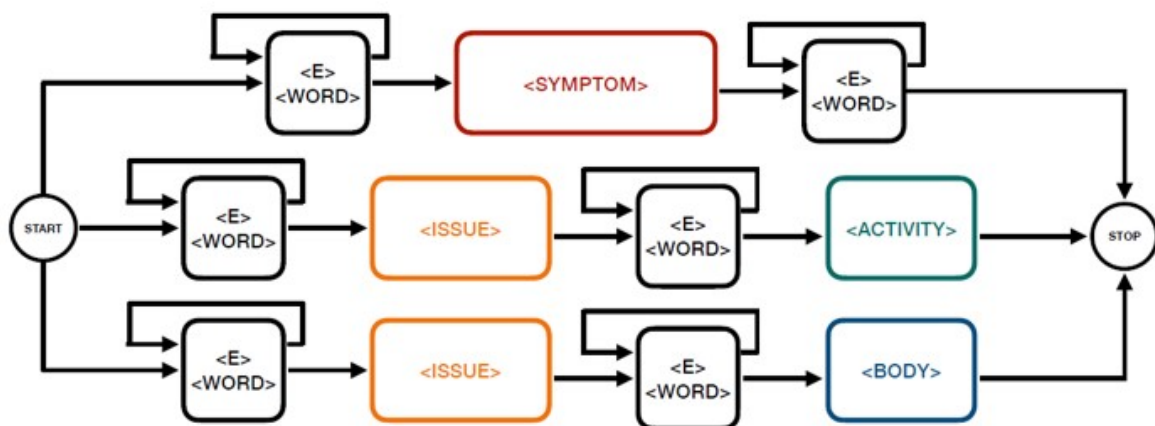
We describe the process of building a causal graph and determining the resulting analytic approach required to investigate this relationship. We outline a format for justifying the inclusion and omission of arrows and nodes from the causal graph and discuss the key assumptions made by the graph, as well as implications for the analysis. We differentiate between a causal graph based on general knowledge and one designed for our specific dataset of interest, which can introduce additional nodes and arrows to consider. Finally, we outline a process for requesting peer feedback on assumptions prior to conducting data analysis.



Identifying COVID-19 signs, symptoms, and health impacts using natural language processing on Twitter data Thu T Nguyen* Thu Nguyen Shayan Fazeli Anaelia Ovalle Davina Zamanzadeh Majid Sarrafzadeh Gilbert C. Gee

Background: For novel illnesses such as COVID-19, timely assessment about symptoms is extremely important. Increasingly, people have turned to social media to share their lives, which provides an opportunity to explore symptoms. Many problems are reported to physicians, but many are not due to factors such as recall bias and social desirability. Hence, many symptoms of COVID-19 may be unknown and thus, complicate diagnosis and treatment. **Objective:** Identify COVID-19 related topics, signs, symptoms, and health impacts using Twitter data. **Methods:** We collected 3,508,993 English language tweets from the U.S. containing at least one COVID-19 related term from January 2020 to September 2020 using Twitter’s Streaming Application Programming Interface (API). Latent Dirichlet Allocation (LDA), an unsupervised machine learning technique, was used for topic modeling. We also used Recursive Transition Networks (RTNs) and designed graphs that utilize linguistic and grammar characteristics to identify connections between words within text data, to uncover potential symptoms, impacts on specific parts of the body, and impacts on activities related to COVID-19. **Preliminary Results:** The COVID-19 topics clustered around various aspects such as politics, quarantine, social distancing, and health care. One topic included tweets with descriptions of symptoms and reported experiences and challenges with getting tested. Figure 1 presents our designed language graph. Mentions of symptoms such as pain, soreness, fatigue, swelling, and tremor are monitored to help uncover potential impacts on activities such as swallowing, hearing, and drinking. We focused on less-investigated impacts of the pandemic as well. In our data, depression is among the most frequently mentioned symptoms as alongside cough, fever, aches, weakness, and fatigue. **Conclusion:** Social media can be used to collect timely data on COVID-19 signs and symptoms for novel discovery and investigation.

Figure 1. Our Recursive Transition Network for Symptom Search



Tag	Description	Example
{Symptom}	Medical symptom	I have a <i>headache</i>
{Issue}	Issues in activity/body	I have <i>pain in my neck</i>
{Activity}	Physical activity	For me, it is <i>hard to breathe</i>
{Body}	Body part	I have <i>tremor in my hand</i>

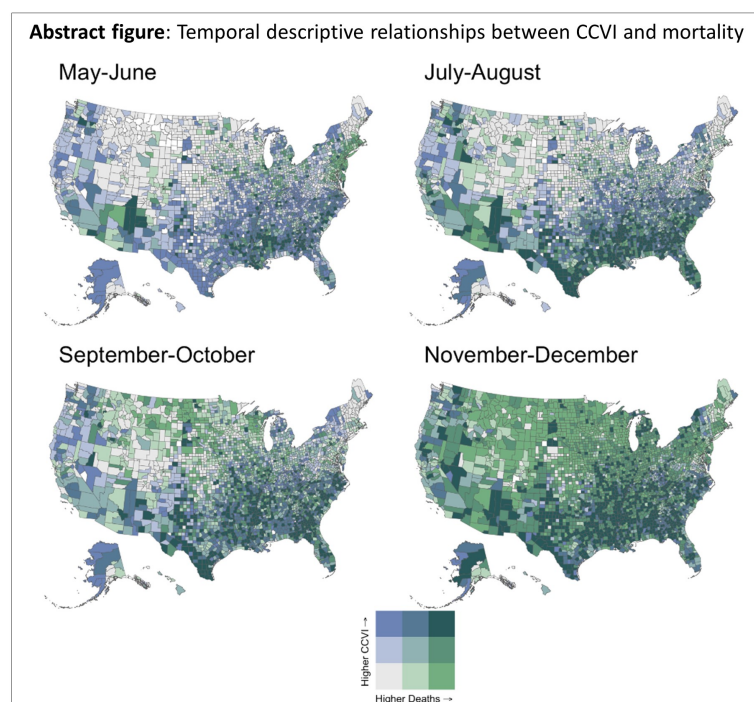
A national time series analysis of community vulnerability and COVID-19 mortality George Pro* George Pro Sean Young

COVID-19 is an ongoing public health challenge. Several cross-sectional studies have shown socio-economic and other disparities in COVID-19 outcomes, such as mortality. Over a year into the pandemic, there is a need for retrospective longitudinal studies to provide better context around disparities in order to cope with current problems and prepare for future disasters. This study aimed to identify relationships between county vulnerability and mortality over time.

We used the New York Times data repository and US census data to calculate the rate of COVID-19 deaths per 100,000 county residents over four time periods: early pandemic (May-Jun), early-mid (Jul-Aug), mid-recent (Sep-Oct), and recent (Nov-Dec). We used Surgo Venture's COVID Community Vulnerability Index (CCVI) as a multi-dimensional indicator of health, economic, and social environments (0=least vulnerable, 1=most vulnerable counties). We used a generalized linear model with an interaction to test whether the association between CCVI and death (log transformed) changed over time.

Death rates increased over time (May-Jun, 10.9; Nov-Dec, 59.3). High CCVI counties with the most drastic increase in deaths were clustered in the US South. CCVI was positively associated with death rates during the earlier pandemic months, and the strongest association was identified in the months of July and August ($B=1.74$, $p<0.0001$). By the end of 2020, death rates were exceedingly high for the majority of the US, but no longer dependent on CCVI.

Historically, health services and emergency preparedness have been strained in poorer areas. Our results are in line with other findings that disparities have exacerbated the toll of COVID-19, especially when coinciding with the summer's economic recession and the near-collapse of many smaller health systems. Health policies designed to strengthen responses to disease outbreaks must prioritize the timely treatment of chronic cases in the most vulnerable populations.



The Embodiment of Place: Neighborhood police-reported crime during pregnancy and DNA methylation in stress-related genes Chantel Martin* Chantel Martin Ai Ye Radhika Dhingra Evans Lodge Allison Aiello Cathrine Hoyo

Exposure to crime and violence is an often-cited psychosocial stressor associated with adverse pregnancy and birth outcomes, yet underlying biological mechanisms remain unclear. Using data from 191 mother-child pairs in the Newborn Epigenetics Study and geocoded exposure to police-reported crime from Durham Police Department, we examined the association between gestational exposure to neighborhood police-reported crime and umbilical cord DNA methylation (DNAm) in stress-related genes. Gestational exposure to police-reported crime (violent, drug-related, and burglary) was assessed using z-scores of exposures at the census block group level. Cord blood DNAm was measured using Illumina's HumanMethylation450k BeadChip and selected n=289 CpG sites mapping to 17 genes. Linear regression models were used to estimate associations between gestational exposure to police-reported crime and CpG sites for each gene, adjusting for race, maternal age, education, and smoking, offspring sex, sample plate location, and estimated cell counts. Given the impact of racial residential segregation on neighborhood police-reported crime exposure, the top hit within each gene were explored in race-stratified models. Police-reported crime during pregnancy was associated with increased DNAm in 2 CpGs annotated to *BDNF* and 1 CpG annotated to *KLRG1* (FDR <0.10). A 1-SD increase in police-reported crime was associated with 2% increase in methylation at cg08362738 and cg25328597 (*BDNF* gene), and 2% increase in methylation at cg19866422 (*KLRG1* gene). These CpG sites were all located within CpG islands, and no differences were observed based on maternal race. Our findings demonstrate potential epigenetic mechanisms of neighborhood police-reported crime exposure during pregnancy that potentially act as mediators of adverse birth outcomes, and suggests a role for stress-related immunosenescence and brain derived cellular changes in these pathways.

Association between neighborhood stigma and HIV risk behaviors among Black MSM in the Neighborhoods and Networks (N2) Cohort Study Jonathan S. Russell* Jonathan Russell John A. Schneider Yen-Tyng Chen Russell Brewer Basile Chaix Dustin T. Duncan

Background

Though neighborhoods are physical spaces, they can contribute to a sense of community and influence the behaviors, interactions, and identity of the individuals who reside in them. Negative views by outsiders or perceptions of danger can lead to socio-spatial or neighborhood stigmatization, which has been shown to decrease access to resources and can contribute to adverse health outcomes, especially in marginalized groups.

Methods

Data from the Neighborhoods and Networks (N2) Cohort Study in Chicago of Black men who have sex with men was analyzed (n=412). Participants were asked three questions regarding perceived neighborhood stigmatization. HIV risk behaviors were assessed via self-report (i.e., alcohol or drug use before or during sex, condomless anal sex with a casual partner, six or more casual male partners, not having asked the last casual partner's HIV status, and having participated in a sex party or orgy). Multivariable logistic regression models were constructed to determine the association between indicators of neighborhood stigma and HIV risk behaviors, adjusted for socio-demographic characteristics.

Results

Reporting living in a neighborhood with a bad reputation was associated with sex work (aOR=2.58, 95% CI 1.20, 5.55); reporting a negative view of the neighborhood by outsiders was associated with condomless anal intercourse (aOR=1.75, 95% CI 1.09, 2.81), and early age of sexual debut (aOR=1.88, 95% CI 1.11, 3.19); and reporting that neighborhood residents are judged was associated with condomless anal intercourse (aOR=2.04, 95% CI 1.27, 3.30), and early age of sexual debut (aOR=2.24, 95% CI 1.30, 3.83).

Conclusions

Perceptions of neighborhood stigmatization are associated with behaviors that increase the risk of HIV acquisition. Understanding the ways in which social and spatial factors contribute to increased risk in populations with a high HIV burden can contribute to the design and implementation of effective interventions.

Gestational Exposure to Fatal Police Violence and Pregnancy Loss in US Core Based Statistical Areas, 2013-2015 Jaquelyn Jahn* Jaquelyn Jahn Nancy Krieger Madina Agénor Michael Leung Brigette A. Davis Marc G. Weisskopf Jarvis T. Chen

Background: Fatal police violence in the United States disproportionately affects Black, Native American, and Hispanic people, and for these groups is a racially oppressive population-level stressor that we hypothesize to increase the risk of pregnancy loss. Focusing on core based statistical areas (CBSAs) surrounding small and large urban centers, we accordingly tested whether gestational exposure to fatal police violence decreased the number of live births, which is reflective of a rise in lost pregnancies.

Methods: We linked microdata for all births (N=7,709,300) in 520 CBSAs with at least one incident of fatal police violence in 2013-2015 to Fatal Encounters, a database that prospectively identified 2,594 police-related fatalities using online media reports and public records. We estimated the association between month-to-month fatal police violence and conceptions resulting in live births using distributed lag quasi-Poisson models with CBSA-level fixed effects, and adjusted for seasonality using harmonic splines. We additionally stratified models by maternal race/ethnicity.

Findings: For each additional police-related fatality that occurred in the first through sixth months of gestation, we observed a 0.14% decrease (95% confidence interval: 0.05%, 0.23%) in the total number of live births within CBSAs, and a 0.29% decrease in births to Black women (95% CI: 0.11%, 0.48%). In models stratified by maternal race/ethnicity, we observed a statistically significant association between fatal police violence and changes in live births in models among Black, Asian, and Hispanic women, but not among White women.

Interpretation: Our findings suggest fatal police violence may have population-level consequences for pregnancy loss and adds to the evidence regarding the importance of preventing these fatalities.

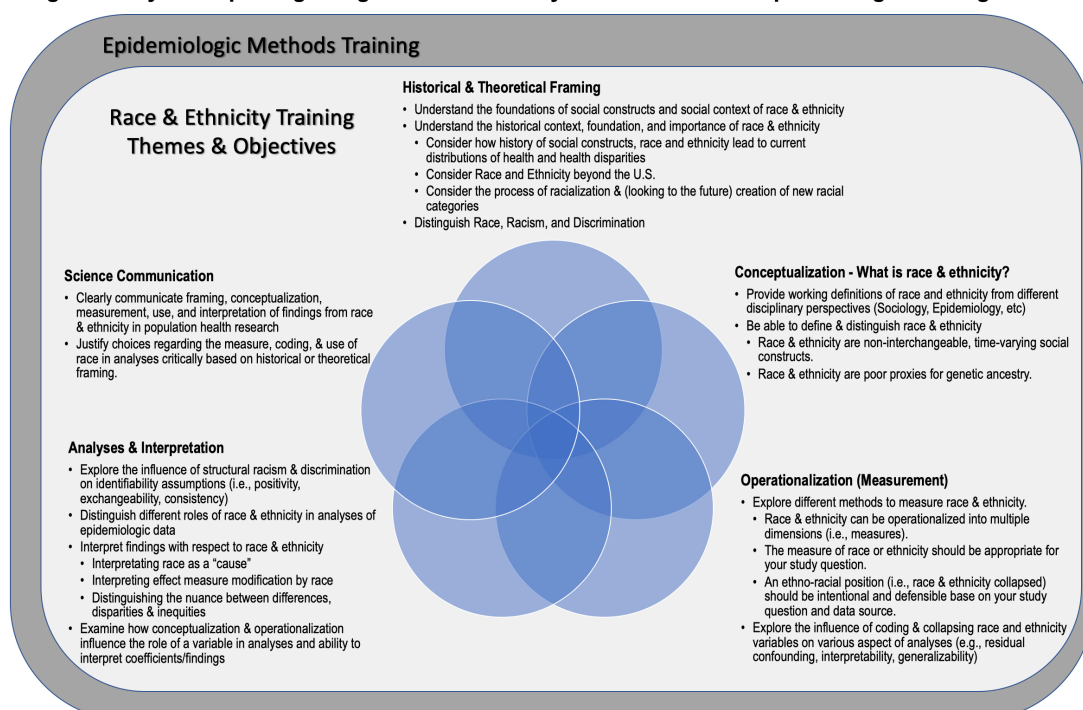
Improving pedagogy: A doctoral student initiative to integrate race and ethnicity into the epidemiology curriculum Evans Lodge* Evans Lodge Esther LáShauntá Katherine Rae Anne Brooke Maya

Race and ethnicity are ubiquitously incorporated in U.S. epidemiologic research, yet the history and theory of race and ethnicity are not adequately taught in graduate-level epidemiology coursework. Critical discussions regarding the conceptualization, operationalization, and utilization of race and ethnicity are often relegated to optional “social epidemiology” courses. This siloing of knowledge contributes to a public health literature that misunderstands race and ethnicity, often manifest as implicit or explicit endorsement of biological essentialism or the misguided exchanging of race and ethnicity with socioeconomic status. We argue that critical and consistent training in race and ethnicity is requisite across standard epidemiologic methods courses.

As epidemiology teaching assistants at the University of North Carolina, we identified gaps in our required two-year epidemiologic methods coursework, created course-specific learning objectives, and developed a matrix integrating relevant material throughout the required curriculum. We present key themes and objectives in Figure 1, including the history and modern definitions of race and ethnicity and a critical evaluation of different methods to measure, code, and interpret variables regarding race and ethnicity in epidemiologic models. These materials are being incorporated for all doctoral-level epidemiology trainees at the University of North Carolina.

The field of epidemiology risks sustaining a culture and science that misunderstands, minimizes, and jeopardizes the health of marginalized groups by not training all epidemiologists to critically understand race, ethnicity, and other important social constructs. To equip the next generation of epidemiologists with the required tools and understanding, epidemiology educators must integrate such training - rooted in critical thought on history, social construction, and identity - into their curricula.

Figure 1. Key Concepts Regarding Race and Ethnicity for Graduate-Level Epidemiologic Training



Does research on social policies typically evaluate heterogeneous treatment effects? A quantitative assessment of a contemporary sample of articles in epidemiology, medicine, and economics Dakota Cintron* Dakota Cintron Ellicott Matthay Maria Glymour Nancy Adler David Vlahov Laura Gottlieb Erin Hagan May Lynn Tan

Background. Evaluating heterogeneous treatment effects (HTEs) of social policies is critical for population health. HTEs can determine whether a policy exacerbates or reduces health disparities. Recognition of the importance of HTEs and new, data-driven methods for evaluating HTEs are growing. However, little is known about how often and by what methods HTEs are assessed in social policy and health research.

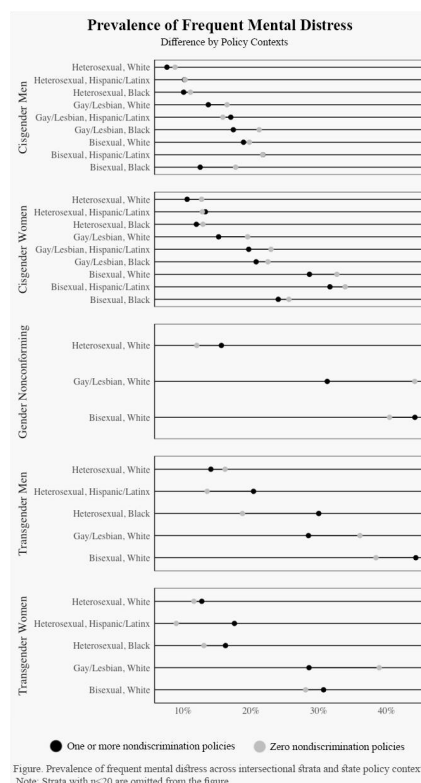
Method. Using 54 studies published in 2019 in 9 epidemiology, medical, or economics journals assessing the health effects of social policies, we evaluated: 1) how often were HTEs assessed?, 2) how often was the intent to assess HTEs specified a priori?, 3) were the methods to assess HTEs data-driven or theory-driven? 4) what methods for assessing HTEs were used (e.g., stratification, interactions)? 5) for what groups were HTEs assessed? Future work will assess the magnitudes of HTEs.

Results. HTEs were assessed in 52% (n=28) of the studies, and of those, 61% (n = 17) specified their intent to assess HTEs a priori. No studies used data-driven (machine learning) approaches to evaluate HTEs. Most (n=17, 61%) studies evaluated HTEs with descriptive methods, e.g., stratifying by groups, but not statistical tests; 7 studies (25%) assessed HTEs with statistical tests by including an interaction term in a regression framework; and 4 studies (14%) used both. HTEs were evaluated for diverse groups, including those based on sociodemographics (e.g., age, race, income, or marital status), geography (e.g., states), and study-specific characteristics (e.g., mental health status or exposure to war).

Discussion. Understanding HTEs can enhance policy and practice-based efforts to reduce inequities but will require attention to appropriate evaluation methods. Data-driven methods to identify subgroups that respond differentially to treatment are not commonly used in social policy research but should be considered among the range of tools available for evaluating HTEs.

Who benefits from nondiscrimination protections? A multilevel analysis of state-level LGBTQ+ nondiscrimination policies and frequent mental distress at the intersection of gender, sexual orientation, and race/ethnicity Ariel Beccia* Ariel Beccia Eric Ding Tubanji Walubita Katarina Ferrucci Esther Boama-Nyarko William Jesdale

State-level nondiscrimination policies are important social determinants of mental health for sexual and gender minorities (SGM), yet it is unknown whether these policies are equally protective across SGM subgroups. We thus assessed whether the prevalence of frequent mental distress differed by state policy context at the intersection of sexual orientation, gender identity, and race/ethnicity. Using data from the Behavioral Risk Factor Surveillance System 2014–2019 (N=1,106,924), we conducted a contextual intersectional Multilevel Analysis of Individual Heterogeneity & Discriminatory Accuracy (CI-MAIHDA). Participants were nested in 45 intersectional strata given by all combinations of 3 sexual orientation (gay/lesbian, bisexual, heterosexual), 5 gender identity (transgender women, transgender men, gender nonconforming, cisgender women, cisgender men), and 3 racial/ethnic (non-Hispanic Black, Hispanic/Latinx, non-Hispanic white) categories. These strata were interacted with 2 state policy context categories (≥ 1 , 0 nondiscrimination policies), resulting in 90 strata-policy groups. Multilevel logistic models with individuals at level 1 and strata-policy groups at level 2 were used to estimate prevalence ratios for frequent mental distress (defined as reporting 14–30 days of poor mental health) across state policy contexts for each stratum. There were large disparities in frequent mental distress prevalence across strata (range: 7.6–52.5%), with transgender/gender nonconforming sexual minorities having the highest prevalence on average. However, living in state with ≥ 1 nondiscrimination policy was only protective for strata including cisgender and/or non-Hispanic white people (Figure). Our findings suggest that state nondiscrimination policies may not confer equal mental health protections for all SGM subgroups. More broadly, CI-MAIHDA modeling is a promising approach to investigate the heterogeneity of policy effects across populations to promote health equity.



Heterogeneous Treatment Effects of Housing Vouchers on Long-term Neighborhood Opportunity for Children Huiyun Kim* Huiyun Kim Nicole M. Schmidt Theresa L. Osypuk Naomi Thyden David H. Rehkopf

Neighborhood effects study has provided a scientific rationale for neighborhood-level interventions to mitigate the negative impact of geographical concentration of poverty on health and developmental outcomes. The Moving to Opportunity (MTO, 1994-2010) demonstration is one exemplary poverty dispersal policy that promotes voucher-induced residential mobility of low-income families into low-poverty neighborhoods.

Using a child-specific index for neighborhood-based opportunity, this study revisits the MTO demonstration to examine heterogeneous treatment effects of housing vouchers on long-term neighborhood opportunities for children.

Results from model-based recursive partitioning suggest that MTO treatment effects on neighborhood opportunity over follow up were significantly modified by the following 8 characteristics: adult race, household member with a disability, sites, adult ethnicity (Hispanic origin), household youth expelled from school, household youth with a learning problem, adult enrollment in school, and household with adolescents in the home. Recursive partitioning identified 11 different subgroups, defined by the 8 variables, as displaying the most treatment heterogeneity. The largest, positive low-poverty treatment effect on neighborhood opportunity was found in the subgroup of non-Hispanic, non-Black adults living in either Baltimore, Boston, Chicago, or LA site. The largest, positive Section 8 treatment effect on overall COI was found in the subgroup of Black adults living in either Baltimore or Boston who had an adolescent in the home and had neither a household member with a disability nor youth expelled from school.

This study suggests that previously unidentified child and family health conditions could influence the extent to which housing voucher program benefits participants in terms of neighborhood opportunity.

Preventing NIMBY-ism in recreational cannabis: A geospatial analysis of the association of local alcohol and cannabis policies with alcohol and cannabis outlet co-location in**California** Ellicott C. Matthay* Ellicott Matthay Cynthia Fu Laurie M. Jacobs Leyla M. Mousli Catherine J. Mueller Mallie J. Paschall William R. Ponicki Laura D. Rambaran Serena Zhang Paul J. Gruenewald Dorie E. Apollonio Laura A. Schmidt

Background: Alcohol outlet density is associated with crime, injuries, and other public health concerns. Emerging evidence suggests potential harms of retail cannabis outlets as well. Local governments are responsible for regulating cannabis outlet locations but rarely consider geographic co-location with existing alcohol outlets, despite the potential for generating dual-burden harms associated with both substances, especially in low income communities and communities of color. Little is known about what local policies promote or deter alcohol and cannabis outlet co-location.

Methods: For 12 California counties and the cities within them (239 total jurisdictions), we collected and coded regulations pertaining to the density and locations of alcohol and cannabis outlets against public health best practices. Alcohol and cannabis outlet locations were identified and geocoded using established listings. We applied Bayesian geospatial analysis to evaluate the associations of alcohol and cannabis policy measures with census block group-level alcohol and cannabis outlet densities and alcohol-cannabis outlet co-location, controlling for relevant confounders and accounting for spatial autocorrelation.

Results: 79% of jurisdictions banned retail cannabis sales. No jurisdictions placed restrictions on where cannabis outlets could be located in relation to alcohol outlets. Among those that allowed retail cannabis, cities and counties that strictly regulated alcohol and cannabis outlet locations—for example, by limiting outlet density or discouraging over-concentration in low-income neighborhoods—were 3.4 times less likely to have high-density, highly-co-located cannabis and alcohol outlets (95% CI: 1.7, 6.6).

Conclusions: Local regulations can encourage or discourage high densities of co-located cannabis and alcohol outlets. Discouraging co-location may help protect vulnerable communities from disproportionate potential harms related to alcohol and cannabis use.

Aging into Medicare among a senior food pantry population: an assessment of food security, health, and food pantry use over time Erlene E. Martinez-Miller* Erlene Martinez-Miller Tammy Leonard Sandi L. Pruitt

Low-socioeconomic older adults are vulnerable to food insecurity, the inability to access/afford adequate food, and poor health. At age 65, US adults become Medicare eligible, providing sudden healthcare resources to low-socioeconomic individuals previously uninsured and potentially freeing up funds. Despite this advantage, the impact of Medicare eligibility on food security for low-income older adults is unknown. We examined the association of Medicare eligibility with food security and food pantry visits among older adult clients (aged ≥60 years) in Dallas, Texas with data from Crossroads Community Services, a food pantry, and linked electronic health records (EHR) from a safety net healthcare system (2015-2018). We used log-binomial regression to estimate prevalence ratios of food insecurity by Medicare eligibility overall and by chronic conditions. We examined the impact of Medicare eligibility on monthly food pantry visiting patterns among non-disabled clients using regression discontinuity. Models adjusted for sociodemographic characteristics. For food security, we assessed 604 households with 2,636 visits and for food pantry visits, 199 households with visits before and after age 65 with 457 total visits. Participants' mean age was 49 years, 63% were women, 39% had <high school education, and 60% were Black and 29% Latinx. Of those with EHRs, 75% had ≥1 chronic condition. Medicare eligibility was associated with worse food security, particularly among those with a chronic condition (Figure 1; any food insecurity PR[95%CI]: 0.87[0.77, 0.99]). Frequency of food pantry visits increased after becoming Medicare eligible (OR[95%CI]: 6.78[2.48, 18.53]). Overall, findings highlight how Medicare eligibility may improve food security among older adults, potentially attributable to increased food pantry use after Medicare eligibility. Future studies should examine underlying pathways of food pantry visiting patterns and their contributions to senior food security.

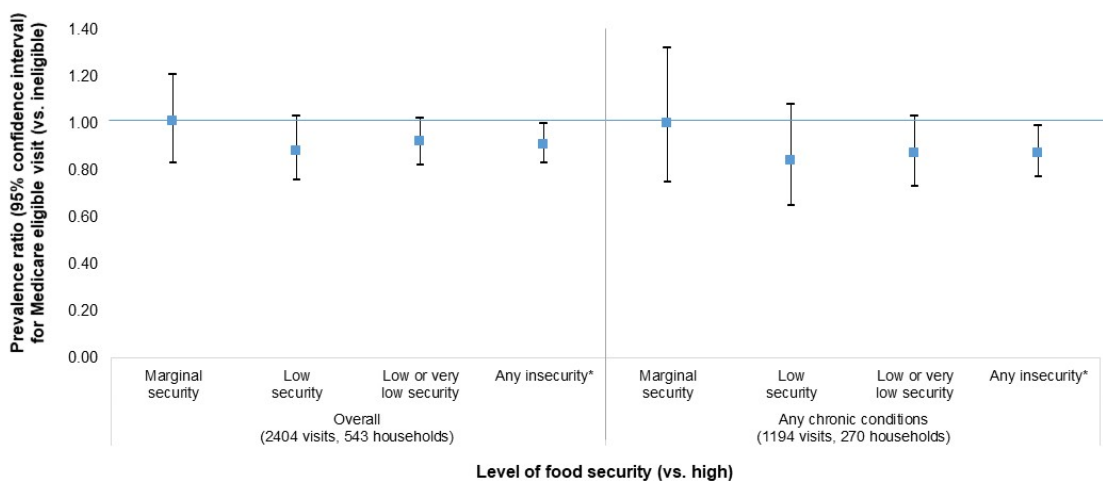


Table 1. Select adjusted^a prevalence ratios (95% confidence intervals)^b for food insecure visits^c among seniors by Medicare eligibility status at visit overall and among clients with any chronic condition^d (2015-2018).

*p<0.05
^aAdjusted for head of household gender, race/ethnicity, marital status, education, employment, monthly household income, household size, transportation use, Supplemental Nutrition Assistant Program (SNAP) receipt, official US identification, and census-level percentages of US citizen, Medicare eligibility, and foreign-born residents.
^bGeneral estimating equations used to cluster for household with an autoregressive correlation matrix.
^cAny insecurity=marginal, low, or very low security.
^dModels for clients without a chronic condition were unable to be completed due to small sample size.

Non-discriminatory allocation of limited health resources Mats Stensrud* Mats Stensrud

Health care systems are constantly faced with limited resources. Allocation of treatments — such as vaccines and ventilators during the current COVID-19 pandemic — is a major practical and ethical challenge.

A key problem is to ensure that the allocation policies are fair and non-discriminatory. Despite the growing literature on fairness, there is no consensus as to how notions of fairness should be formalized. To justify most practical decisions, however, we would include arguments about causal effects: we would assess *how* the decision is made (the causes of the decision) and *what would happen if* a different was made (the effects of the decision). Recently several causal definitions of fairness have been proposed. While these definitions are formally defined in counterfactual frameworks for causal inference, we argue that these definitions suffer from any of the following shortcomings: the definitions (i) require interventions that are ill-defined, (ii) demand identification conditions that are unfalsifiable and unreasonably strong, (iii) can be gamed by decision makers with malicious intentions, or (iv) fail to reflect what we consider to be reasonable human notions of fairness and discrimination. To illustrate our arguments, we present several examples from the fairness literature. Finally, we suggest new causal fairness criteria that mitigate some of the concerns. We describe strategies to evaluate these criteria in observed data and give conditions that allow identification of counterfactual outcomes under new decision rules.

Effectiveness of TNFi versus non-TNFi biologics on disease activity in patients with rheumatoid arthritis: data from the ACR's RISE registry

Milena Gianfrancesco* Milena Gianfrancesco Jing Li Clairissa Ja Michael Evans Maya Petersen Gabriela Schmajuk Jinoos Yazdany

Objective: Rheumatoid arthritis (RA) is a chronic disease characterized by heterogenous clinical response to various treatments. Our understanding of how medications, such as biologic disease modifying anti-rheumatic drugs (bDMARDs), influence disease activity is largely based on randomized controlled trials (RCTs). However, RCTs tend to be conducted in homogenous groups by age, sex, race, and ethnicity, and often are limited by small sample sizes. We examined differences in longitudinal disease activity using a national, representative population of RA patients, comparing various treatment assignments of bDMARDs that have been studied in RCTs: namely, TNF-inhibitors (TNFis) and non-TNFis.

Methods: We included 16,448 individuals with an RA diagnosis who were new users of bDMARDs using electronic health record data collected through a national rheumatology registry from 2008-2018. bDMARD use and disease activity were assessed at each quarter; covariates included sex, race, ethnicity, age, smoking, obesity, practice type, area deprivation index, and other DMARD use. Longitudinal targeted maximum likelihood estimation estimated the average treatment effect (ATE) of TNFi vs. non-TNFi use on disease activity at 12 months after the index date among the entire population, and across various subgroups based on demographic and clinical characteristics, accounting for censoring and time-varying confounding.

Results: TNFi were significantly associated with higher disease activity compared to non-TNFi over a 12-month period (ATE=1.00, 95% CI 0.99, 1.00). Analyses based on subgroups found a stronger benefit of non-TNFi compared to TNFi use among patients with high disease activity at baseline, of Black and Asian race, and under the age of 65.

Conclusion: Non-TNFi may be more beneficial than TNFi in certain patient populations as a first-line bDMARD therapy. These findings fill gaps where RCTs have not been conducted and have the potential to lead to a more personalized approach to care.

Probabilistic Bias Analyses Assessing Outcome Misclassification: An Illustration using Linked EHR and Claims Data to Evaluate Prolonged Opioid Use Following Surgery Jessica C Young* Jessica Young Nabarun Dasgupta Til Stürmer Virginia Pate Michele Jonsson Funk

Background: Linkage between insurance claims data and electronic health records (EHR) is becoming increasingly available offering granular data to leverage in epidemiologic studies. However, the measurement of key study constructs such as outcome classification may differ between insurance claims data and EHR.

Objective: In an ongoing study using EHR to evaluate preoperative gabapentinoids and prolonged opioid use following surgery, we linked a subset of patients to Medicare claims data. We illustrate how this linkage can be used to inform probabilistic bias analyses to quantify the potential bias from outcome misclassification.

Methods: Because neither the EHR nor claims data are a true “gold-standard”, we conducted two probabilistic bias analyses. The first assumed that patients with prolonged opioid use in either EHR or Medicare claims data were correctly classified as having prolonged opioid use (“gold-standard” was the combined EHR and claims data). The second treated the Medicare claims alone as the “gold-standard”. For both bias analyses, we calculated the positive predictive value and negative predictive value of prolonged opioid use measured by the EHR data, and conducted a probabilistic bias analysis with 1,000 iterations, reporting the bias-adjusted risk ratio and 95% CI.

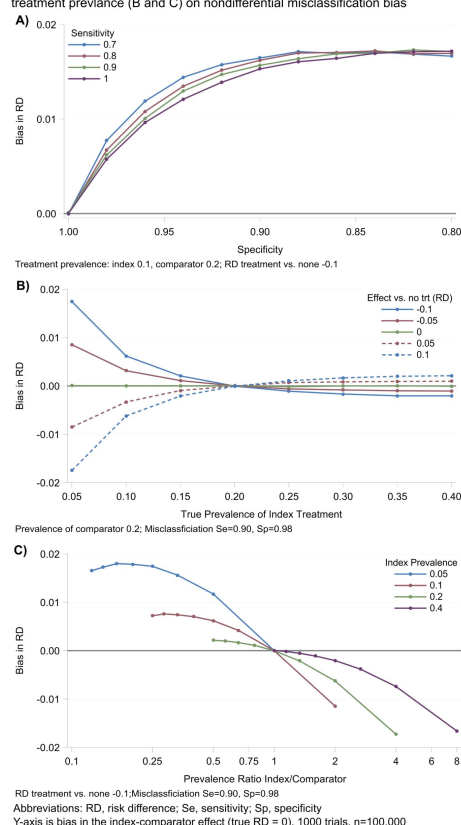
Results: The overall risk ratio of prolonged opioid use comparing patients who received gabapentinoids to those who did not was 1.67 (0.85, 3.23). Among the linked subset, 1.6% of patients had prolonged opioid use in the EHR data, compared to 5.0% in the Medicare claims data. Using the combined gold-standard, the bias-adjusted risk ratio and 95% CI was 1.51 (0.86, 2.35). Using Medicare as the gold-standard, the bias-adjusted risk ratio and 95% CI was 1.50 (0.79, 2.37).

Conclusions: Linkage can help inform probabilistic bias analyses. Because there is no true gold-standard, we conducted 2 bias analyses to better understand the potential impact of outcome misclassification.

Nondifferential exposure misclassification in active comparator studies: drivers of bias away from the null Rachael Ross* Rachael Ross I-Hsuan Su Michele Jonsson Funk

Active comparator studies have strengths over studies using an untreated comparator group such as reduced confounding by indication and healthy user bias. Independent nondifferential misclassification of a binary exposure produces bias towards the null; however, in active comparator studies there are at least three levels of exposure (index, comparator, none) so bias may be in any direction and present even when the index-comparator effect is null. Treatment misclassification may occur for a variety of reasons. Out-of-pocket payment, physician samples, or over the counter use results in reduced sensitivity (false negatives). Nonadherence results in reduced specificity (false positives). We conducted Monte Carlo simulation studies to identify drivers of the magnitude and direction of bias from nondifferential exposure misclassification in active comparator studies. We estimated bias of the index-comparator effect from 1000 trials of a cohort ($n=100000$) with a three-level treatment (index, comparator, none) and a binary outcome (untreated $p=0.2$). The true index-comparator risk difference (RD) was zero. Misclassification was uniform across treatments (index and comparator sensitivity and specificity were equal). The Figure depicts results from scenarios that varied specificity/sensitivity (A), effect of treatment vs. none (B), and treatment prevalence (B, C). There was no bias when specificity was perfect, prevalence of index and comparator were equal, or treatment had no effect. The amount of bias was driven by specificity, imbalance of index/comparator prevalence, and the strength of the treatment effect. The direction of bias was driven by the sign of the treatment effect and whether the index or comparator was more prevalent. Our simulation study identified factors that influence the direction and magnitude of bias to inform interpretation of study results and limitations in active comparator studies. Future work should explore their impact in a real-world setting.

Figure. The impact of sensitivity and specificity (A), the treatment effect (B), and treatment prevalence (B and C) on nondifferential misclassification bias



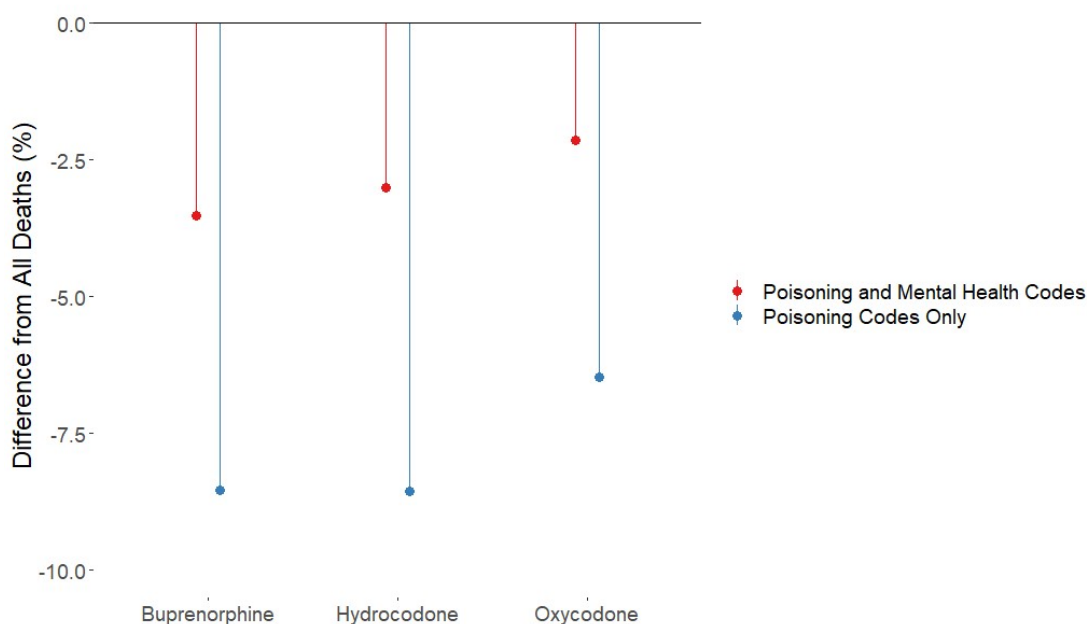
Difference in mortality assessment due to the definition of overdose when using death certificate text Joshua Black* Joshua Black Gabrielle Bau Richard McCoy Chelsey Thibodeaux Karilynn Rockhill Janetta Iwanicki Richard Dart

BACKGROUND: Drug overdose mortality is a key metric in evaluating the drug epidemic in the United States, often garnering attention from the popular media. It is used to evaluate policy and is a key metric in the Healthy People 2030 initiative. Our goal was to assess differences in drug-involved death counts utilizing two definitions from public health policy.

METHODS: Drug mentions on death certificates from 2010 to 2017 were analyzed from the Drug Involved Mortality database to identify buprenorphine-, hydrocodone-, and oxycodone-involved deaths. Drug mentions with contextual evidence indicating they were not involved were removed. Two common overdose definitions based on International Classification of Disease, Version 10 codes and one all-inclusive definition were used: 1) all codes involving poisoning and mental health disorder related harmful use or dependence from controlled substances and alcohol, and, 2) underlying cause of death poisoning codes from controlled substances only, and 3) all deaths.

RESULTS: Among all deaths, 3,359 involved buprenorphine, 27,095 involved hydrocodone, and 47,257 involved oxycodone. The poisoning and mental health code definition identified 118 fewer buprenorphine-involved deaths, 817 fewer hydrocodone-involved deaths, and 1,013 fewer oxycodone-involved deaths. The definition using only poisoning identified 287 fewer, 2,320 fewer, and 3,054 fewer deaths, respectively. Relative to all deaths, other definitions undercounted from 2.14% to 8.56% (Figure). Oxycodone death counts had smaller undercounts compared to the other two drugs.

CONCLUSIONS: Among likely drug-involved deaths, the different codes used to define overdose caused a substantial difference in the number of deaths counted. The definition using only poisoning is often used and failing to include deaths where alcohol poisoning or mental health disorders are the underlying cause underestimates the contributing factors harmful use or dependence has on drug mortality.



Quantification Of Medication-Mediated Effects On Pregnancy Outcome In Women With Rheumatic Conditions Gretchen Bandoli* Gretchen Bandoli Kristin Palmsten Christina Chambers

Background: Rheumatic disease in pregnancy is associated with an increased risk of preterm birth (PTB) and small for gestational age (SGA) offspring. It is unclear whether the excess risk is mediated through medications. The objective was to quantify the medication mediated effects of disease modifying antirheumatic drugs (DMARDs) and oral corticosteroids (OCS) on the risk of PTB and SGA among women with rheumatic conditions.

Methods: DMARDs or OCS used between last menstrual period and 37 weeks or delivery were assessed for risk of PTB and SGA, respectively. We performed a causal mediation analysis to identify the natural direct and natural indirect effects, and the proportion mediated by each medication according to methods described by Tchetgen Tchetgen and Phiri. Log-linear regression models for the total effect and direct effect were adjusted for maternal age, education, race/ethnicity, pre-pregnancy BMI, asthma, and tobacco use. Models for the direct effect were weighted for women with rheumatic conditions by computing the predicted probability from a log-linear regression of medication use during pregnancy on risk factors (education, planned pregnancy, tobacco use) and a disease severity measure, the Health Assessment Questionnaire.

Results: From 2,182 women, 975 had a rheumatic condition. PTB occurred more frequently in women with rheumatic conditions (12.9% vs 7.0%; aRR 1.8, 95% CI 1.4, 2.4). DMARDs mediated 32% of the total risk, OCS mediated 62%. Indirect effect estimates for DMARDs included the null. SGA offspring was increased in women with rheumatic conditions (9.7% vs. 5.8%, aRR 1.8, 95% CI 1.3, 2.5); 6% of the total effect was mediated through DMARDs, and 13% through OCS, although indirect effect estimates crossed the null for both agents.

Conclusions: Mediation through DMARDs and OCS were only notable for the risk of PTB. The strongest mediation was observed through OCS, although residual confounding by disease severity may remain.

Disinfection by-products and nitrate ingestion and risk of endometrial cancer in**postmenopausal women** Danielle N. Medgyesi* Danielle Medgyesi Britton Trabert Peter J. Weyer
Laura E. Beane Freeman Mary H. Ward Rena R. Jones Joshua N. Sampson

Background. Disinfection by-products (DBPs) and *N*-nitroso compounds, formed endogenously after nitrate/nitrite ingestion, are suspected endometrial carcinogens but epidemiologic studies are limited.

Methods. Among postmenopausal women in the Iowa Women's Health Study cohort, we evaluated total trihalomethanes (TTHM), the sum of five haloacetic acids (HAA5), and nitrate-nitrogen (NO₃-N) in public water supplies (PWS), and dietary nitrate/nitrite in relation to incident primary endometrial cancer (1986-2014). For women using their PWS ≥10 years at enrollment (N=10,501; cases=261), we computed historical averages of annual concentrations based on years of use and years of exposure above ½ the U.S. maximum contaminant level (>½-MCL; 5mg/L NO₃-N; 40µg/L TTHM; 30µg/L HAA5). We assessed dietary nitrate/nitrite intakes with a food frequency questionnaire (N=22,897; cases=566). We estimated hazard ratios (HR) and 95% confidence intervals (CI) via Cox models adjusted for age, BMI, menopausal age, oral contraceptive use, estrogen use, and parity, and used a competing risk model for associations with low- and high-grade Type I tumors.

Results. Average DBPs ≥95th percentile were associated with endometrial cancer risk (TTHM HR_{95vsQ1}=2.11;CI=1.36-3.28; HAA5 HR_{95vsQ1}=1.80;CI=1.17-2.78; *ptrends*½-MCL. We found a non-significantly stronger association for low- vs. high-grade tumors (*phet*=0.30). We found no associations with NO₃-N in drinking water or total dietary nitrate/nitrite. Risk was increased among women with the highest nitrite intake from processed meats and low vitamin C intake (HR_{Q4vsQ1}=1.48;CI=1.01-2.19; *ptrend*=0.05).

Conclusions. We report a novel association between relatively high DBP levels and endometrial cancer that warrants future evaluation. Increased risk was associated with dietary nitrite from processed meats and low antioxidant intake, a pattern that could result in endogenous nitrosation.

Exposure to particle radioactivity and breast cancer risk in a US-wide prospective cohort

Alexandra J White* Alexandra White Allyson Gregoire Jared Fisher Longxiang Li Petros Koutrakis Dale Sandler Rena Jones

Background. Outdoor air pollution has been associated with breast cancer risk but underlying biologic mechanisms are not well understood. No previous study has considered whether radioactive airborne particle exposure may contribute to the carcinogenicity of air pollution.

Methods. Annual average ambient particle radioactivity exposure, defined as gross beta particle radiation, was estimated for the enrollment address (2003-2009) of 48,184 Sister Study participants using a nationwide spatiotemporal ensemble model that incorporated data from the U.S. Environmental Protection Agency's RadNet monitoring network. Sister Study participants, who have a sister with breast cancer but no history of breast cancer themselves at enrollment, were followed for incident breast cancer. Cox regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between breast cancer risk (invasive and ductal carcinoma *in situ*) and beta particle radiation in quartiles and per interquartile range (IQR) increase (0.079 mBq/m³). Models were adjusted for age, race/ethnicity, and education. We evaluated whether associations varied by tumor estrogen receptor (ER) status and additionally adjusted for levels of outdoor residential air pollutants (NO₂, PM_{2.5}, PM₁₀).

Results. There were 3,796 incident breast cancer cases diagnosed over a median of 10 years of follow-up. Exposure to beta particle radiation was not associated with overall breast cancer risk. However, higher levels of beta particle radiation were associated with a higher risk of ER- breast cancer (HR_{Q4vsQ1}=1.35, 95% CI:1.04-1.74; HR_{IQR}=1.15, 95% CI: 1.03-1.28) but not ER+ breast cancer (HR_{IQR}=0.96, 95% CI: 0.91-1.02) (IQR heterogeneity p=0.003). Results were unchanged with adjustment for air pollution levels.

Conclusion. Our novel findings suggest that particle radioactivity may be a risk factor for ER- tumors, a more aggressive form of breast cancer, independent of air pollutant concentrations.

Up to date patterns for colorectal cancer screening: Low uptake in a population with no regular primary care provider Kamala* Kamala Adhikari Gary Teare

Objective: This study examined patterns of modality use for colorectal cancer screening (CRCS), and quantified the association between having a regular primary care provider (PCP) and being up-to-date for CRCS in a community-based representative population in Alberta, Canada.

Methods: This was a cross-sectional study using the Canadian Community Health Survey data (2015-2016) of adults between 50 and 74 years of age (N=4,600). Being up-to-date for CRCS was defined as having completed a fecal immunochemical test (FIT) within the last 2 years or colonoscopy/sigmoidoscopy in the last 5 years before the survey. Multivariable logistic regression analysis was used to assess the association between having a regular PCP and being up-to-date for CRCS, adjusting for age, marital status, education, and smoking.

Results: 60.9% (95% CI=58.6, 63.2) of surveyed adults were up-to-date for CRCS, using either FIT (45.0%) or colonoscopy/sigmoidoscopy (28.0%). Among those who had colonoscopy/sigmoidoscopy in the last 5 years, 41.1% had also completed the FIT in the last 2 years. The adjusted odds ratio of being up-to-date for CRCS was 0.24 (95% CI=0.17, 0.35) for those who did not have a regular PCP compared to those who did. This pattern was observed in male and female sub-groups and the sub-groups with and without a medical consultation in the last 12 months. Absolute probability of being up-to-date for CRCS was lower by 34.4% among those without a regular PCP (33.4%, 95% CI=25.4, 41.5) than those who had (67.8%, 95% CI=65.4, 70.3).

Conclusions: Findings suggest a suboptimal uptake of CRCS overall during the period of the study, with disproportionate use of screening modalities, prevalent overuse of screening among those who were up-to-date, and high disparity in CRCS uptake. The use of multicomponent intervention strategies that are shown to be useful to increase appropriate CRCS participation, with a customized approach for those without a regular PCP, may address the issues. Future studies that longitudinally assess the CRCS up-to-date status across screening modalities and risk groups can further improve our understanding of CRCS uptake and adherence to guide future improvement and interventions.

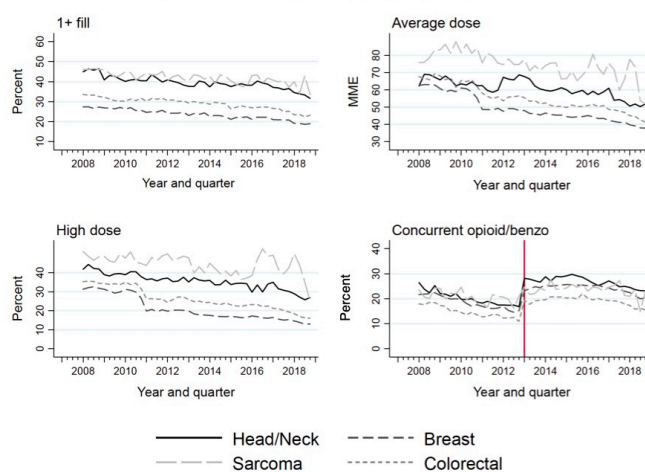
Cancer and the overdose crisis: Opioid prescribing in patients with cancer, 2008-2018

Tarlise Townsend* Tarlise Townsend Rebecca Haffajee Talya Salz Megan Caram Fumiko Chino Amy Bohnert

Opioids are often used to manage cancer-related pain, but the frequency and intensity of opioid prescribing to patients with cancer, and how these have changed over time, are not well characterized. Amid efforts to curb excessive opioid prescribing to the general population, there are growing concerns about a chilling effect on appropriate opioid prescribing for cancer-related pain. Efforts to minimize opioid-related harms without compromising management of cancer-related pain are critical, yet basic information about current levels and recent trends in opioid prescribing for cancer is lacking.

We used commercial healthcare claims data from all 50 states to characterize quarterly opioid receipt in patients receiving active treatment for one of four cancers, 3+ months from end of life (N=325,394). We examined unadjusted trends in six prescribing outcomes, 2008-2018, stratified by cancer type, age, race/ethnicity, and gender. We used generalized estimating equations to assess sociodemographic and clinical factors associated with prescribing. Across cancer types, the rate of at least one opioid fill per quarter fell 33%, or 9.9 percentage points, most sharply in adults under age 65 and Asian patients. This decline was concentrated in acute prescribing, while the percentage receiving 30+ days supplied remained stable before declining 2016-2018. Average daily dose fell 37.6%, or 24.5 MME, most sharply in patients ages 65 and over and Hispanic patients. Opioid receipt was substantially greater in patients with sarcoma or head/neck cancer, younger patients, and those with a history of substance use disorder and anxiety or depressive disorder. These findings raise key questions about the consequences of declining opioid prescribing for opioid-related harms and pain management in patients receiving cancer treatment. Research to discern the drivers of these changes and the mechanisms underlying sociodemographic and clinical predictors of prescribing is also needed.

Figure 1. National opioid prescribing trends by cancer type (unadjusted)



Notes: MME = morphine milligram equivalents. All outcomes measured at quarterly level. 1+ fill indicates receipt of at least one opioid fill in quarter. High dose indicates receipt of at least one day in quarter with effective daily dose of 90+ MME. Concurrent opioid/benzodiazepine prescribing refers to any overlapping days prescribed in quarter. The vertical line indicates the expansion of Medicare Part D to cover benzodiazepines.

Minority children experience higher risk of death from many central nervous system tumor types even after accounting for treatment received and socioeconomic status: An analysis of the National Cancer Database (NCDB) Kristin J Moore* Kristin Moore Lindsay A Williams

Christopher L Moertel

Background: Central nervous system (CNS) tumors are the most common solid childhood malignancy comprising 25% of cancers in individuals aged 0-19 years. Racial/ethnic minority have poorer outcomes than white children; however, whether these associations depend on treatment received is infrequently evaluated as available treatment data is often inadequate.

Methods: Using the National Cancer Database (NCDB; 2004-2016), we identified children (aged 0-19 years) diagnosed with CNS tumors. Kaplan-Meier survival curves (Log-rank p-values) were used to characterize survival differences by race/ethnicity for 17 histologic types. Hazard ratios (HR) and 95% CI were calculated by race/ethnicity defined as (non-Hispanic white [NHW; referent], non-Hispanic Black [NHB], Hispanic, Asian and Pacific Islander [API], and American Indian and Alaskan Natives [AI/AN]) using multivariable Cox proportional hazards model while adjusting for detailed treatment, age, sex, year of diagnosis, insurance status, urban/rural status, distance between hospital and home, and income.

Results: There were 23,031 cases identified. Differences in survival by race/ethnicity were present for all cases combined ($p < 0.001$) and among invasive cases ($p < 0.001$). Compared to NHW children, NHB and Hispanic children had a higher risk of death for any CNS tumor (NHB HR 1.26, 95% CI 1.16, 1.38; Hispanic HR 1.11, 95% CI 1.02, 1.21). When evaluated by histology, minority race/ethnic children had a higher risk of death for glioblastoma, oligodendroglioma, choroid plexus tumors, and hemangioma. In medulloblastoma, API children had better survival than NHW (HR 0.62, 95% CI 0.39, 0.99).

Conclusions: Even when accounting for detailed treatment received and socioeconomic measures, minority children had a higher risk of death from many types of brain tumors suggesting societal and biologic complexities experienced by minority children may contribute to the observed disparities.

Anti-Müllerian Hormone Levels and Breast Cancer Risk in the Study of Women's Health Across the Nation Nydjie Grimes* Nydjie Grimes Katherine Reeves

NP Grimes, EB Gold, S Crawford, N Avis, GA Greendale, N Santoro, L Habel, AS Karlamangla, KW Reeves

Anti-Müllerian hormone (AMH) is a dimeric glycoprotein and a member of the transforming growth factor family produced by the granulosa cells of primary follicles. Independent of age, higher AMH levels have been shown to predict later age at menopause, an established risk factor for breast cancer. The relation of premenopausal AMH with breast cancer risk has been evaluated in a few studies of reproductive-aged non-Hispanic white women, with most reporting a positive association. We assessed the association of AMH with breast cancer risk in SWAN, a multi-ethnic cohort of women who self-identified as Caucasian (46.9%), Black (28.3%), Japanese (8.5%), Chinese (7.6%), or Hispanic (8.7%). At enrollment, participants were women aged 42 - 52 years who had an intact uterus and at least 1 ovary, and at least 1 menstrual period in the last 3 months. AMH was assessed in women who had to experience a natural menopause transition, had a documented date of final menopause, and had at least 1 blood sample while pre- or perimenopausal (n=1536). AMH was measured by a high-sensitivity monoclonal ELISA assay and values were natural log transformed for analysis. Breast cancer diagnoses were assessed at enrollment and subsequent follow-up visits through 2018. In total, 90 women reported an incident breast cancer diagnosis. In multivariable linear regression models adjusting for age, race/ethnicity, smoking, body mass index, and other factors, higher AMH levels were associated with a non-significant increased breast cancer risk. Compared to women in the 1st quartile, the hazards ratio (95% confidence interval) for women in 2nd, 3rd, and 4th quartile were 1.38 (0.74 - 2.59), 1.33 (0.70 - 2.53), and 1.66 (0.87 - 3.66). Although results were not statistically significant, findings provide further evidence that AMH could potentially be a marker for breast cancer risk.

Infertility, infertility diagnoses, and risk of cardiovascular disease Leslie V. Farland* Leslie V. Farland Yixin Wang Audrey J. Gaskins Janet W. Rich-Edwards Siwen Wang Jorge E. Chavarro Kathy M. Rexrode Stacey A. Missmer

Background: Menstrual cycle irregularity, early menopause, and obesity are characteristics known to be associated with both cardiovascular disease and certain infertility diagnoses. However, few studies have investigated the association between infertility and cardiovascular disease. The objective of this study was to investigate the association between history of infertility, infertility diagnoses, and risk of cardiovascular outcomes.

Materials and Methods: Participants in the Nurses' Health Study II who were gravid or reported infertility (12 months of trying to conceive without success) were followed from 1989 until 2017 for development of incident, physician diagnosed coronary heart disease (myocardial infarction, coronary artery bypass grafting, or percutaneous transluminal coronary angioplasty) and stroke. Cox proportional hazard models were used to calculate hazard ratios (HR) and 95% confidence intervals (CI), with adjustment for potential demographic and lifestyle confounding variables.

Results: Among 103,730 participants, 27.6% reported having ever experienced infertility. Compared to gravid women, women with a history of infertility were at greater risk of CHD (HR:1.14; CI:1.02-1.27). We observed no association between infertility and risk of stroke (HR:0.94; CI:0.79-1.11). The association between history of infertility and CHD was strongest for infertility occurring at a younger age (P-trend:0.01; HR infertility first reported at age ≤ 25 :1.27; CI:1.09-1.47). When we investigated specific infertility diagnoses, women with infertility and a diagnosis of ovulatory disorders (HR:1.30; CI:1.07-1.58) or endometriosis (HR:1.40, CI:1.08-1.82) had the greatest risk of CHD compared to gravid women.

Conclusions: We observed that women with a history of infertility may be at greater risk of experiencing CHD later in life. Women who experienced infertility at younger ages and who had diagnoses of ovulation disorders or endometriosis were at the highest risk of CHD.

Long-term mortality in women with pregnancy loss and modification by race/ethnicity Sonia M. Grandi* Sonia M. Grandi Stefanie N. Hinkle Sunni L. Mumford Lindsey A. Sjaarda Katherine L. Grantz Pauline Mendola James L. Mills Anna Z. Pollack Edwina Yeung Cuilin Zhang Enrique F. Schisterman

Background: Pregnancy loss is a common reproductive complication but the association between pregnancy loss and long-term mortality and whether this association varies by maternal race/ethnicity is not well understood.

Methods: A racially diverse cohort of 48,188 pregnant women enrolled at 12 U.S. clinical sites in the Collaborative Perinatal Project (CPP) from 1959-1966 was used for this study. CPP records were linked to the National Death Index (NDI) and the Social Security Death Master File for deaths until 2016. Pregnancy loss was defined as the total number of self-reported losses, including ectopic pregnancies, abortions, and stillbirths/fetal deaths, that occurred prior to or during enrollment in the CPP. The outcomes were all-cause mortality and cause-specific mortality defined in the NDI. Stratified Weibull models with maternal age as the underlying time scale were used for all analyses.

Results: Analyses are based on 48,188 women (46.0% White, 45.8% Black, 8.2% Other) of whom 25.6% reported a history of ≥ 1 pregnancy loss. Over a median follow-up of 52 (IQR: 47, 54) years, 18,789 (39.0%) women died. Overall, women with a history of pregnancy loss had a higher relative risk of all-cause mortality (HR 1.07, 95% CI 1.04, 1.11; Figure), and coronary heart disease (CHD) (HR 1.14, 95% CI 1.05, 1.25) and cerebrovascular deaths (HR 1.15, 95% CI 0.98, 1.35) compared to women with no history of loss. Stratified by race/ethnicity, an increased risk of all-cause and CHD deaths associated with pregnancy loss was observed in White women (All-cause: HR 1.12, 95% CI 1.06, 1.19; CHD: HR 1.32, 95% CI 1.16, 1.52; Figure) but not in Black women (All-cause: HR 1.04, 95% CI 0.98, 1.09; CHD: HR 1.04, 95% CI 0.92, 1.17).

Conclusions: Pregnancy loss increases the risk of all-cause and cardiovascular mortality. These findings support pregnancy loss as a risk factor for long-term mortality and the need to assess reproductive history as part of routine screening in women.

Association of preterm birth with risk of early natural menopause Christine R Langton*
Christine Langton Brian Whitcomb Alexandra Purdue-Smithe Susan Hankinson JoAnn Manson
Bernard Rosner Elizabeth Bertone-Johnson

Early menopause, defined as the cessation of ovarian function before the age of 45 years, affects approximately 10% of women in Western populations. Current research suggests that women who experience early menopause are at increased risk of cardiovascular disease (CVD). Research examining maternal pregnancy outcomes and their relation to CVD has demonstrated a strong positive association between preterm birth and CVD risk. Preterm birth has a complex etiology, and underlying pregnancy-related vascular factors may contribute to, and thus influence, menopause timing. We evaluated the association of preterm birth with early natural menopause among 66,031 parous participants in the prospective Nurses' Health Study II.

Nurses were 25 to 42 years old at baseline (1989) and provided information on menopause status and age at menopause every 2 years through 2017. In 2009, participants reported their complete pregnancy history including the gestational age of each birth and type of delivery. Preterm birth was defined as a singleton gestation <37 weeks. We used logistic regression models to estimate risk via odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age at first birth (18 to 45 years), race/ethnicity, and prepregnancy lifestyle factors including smoking and body mass index.

During 28 years of follow-up, 1,664 women experienced early natural menopause. In multivariable models, women whose first pregnancy ended in preterm birth had a 13% higher risk of early menopause compared to women with a term pregnancy (OR=1.13, 95% CI, 0.95-1.34). Risk was higher for women whose first birth was preterm with spontaneous labor and vaginal delivery versus term (OR=1.21, 95% CI, 0.90-1.64).

In this large, prospective study, preterm birth was associated with a modestly but non-significant higher risk of early menopause. Further research is needed to evaluate this finding and determine if menopause timing contributes to the association of preterm birth with CVD risk.

Severe maternal morbidity and cardiovascular disease Ugochinyere Vivian Ukah* Ugochinyere Vivian Ukah Natalie Dayan Brian J Potter Aimina Ayoub Nathalie Auger

Introduction: The relationship between severe maternal morbidity and cardiovascular disease is not well studied. Severe maternal morbidity consists of life-threatening complications around pregnancy that may affect cardiac function. Our objective was to examine the long-term risks of cardiovascular disease after a pregnancy complicated by severe maternal morbidity.

Methods: We used a longitudinal cohort of women who delivered in the province of Quebec, Canada between 1989 and 2019. The exposure was severe maternal morbidity, defined according to the Canadian Perinatal Surveillance System, and included conditions such as acute renal failure, and severe preeclampsia. The outcome was hospitalization for cardiovascular disease beginning 42 days after delivery, with follow-up extending up to thirty years later. We used time-varying adjusted Cox regression models to estimate hazard ratios (HR) with 95% confidence intervals (CI) for cardiovascular outcomes, comparing severe maternal morbidity with no severe morbidity.

Results: In a total of 1,336,846 women, severe maternal morbidity occurred in 66,537 (5.0%) women. Severe maternal morbidity was associated with an increased risk of cardiovascular hospitalization during follow-up (HR 1.78, 95% CI 1.73-1.83), compared with no morbidity. The association was strongest the first year after delivery (HR 4.44, 95% CI 3.79-5.21), but persisted beyond 15 years (HR 1.45, 95% CI 1.38-1.52). The morbidities most strongly associated with cardiovascular hospitalization were cardiac conditions (HR 5.39, 95% CI 4.67-6.23), cerebrovascular accidents (HR 3.82, 95% CI 2.94-4.96), and acute renal failure (HR 2.64, 95% CI 2.19-3.18).

Conclusion: Severe maternal morbidity is associated with a greater risk of cardiovascular hospitalization after the postpartum period, compared with no morbidity. Women with severe maternal morbidity may benefit from clinical surveillance after delivery, to prevent the development of cardiovascular disease.

The human cost of inaction: A counterfactual analysis of the effect of lockdown timing on COVID-19 cases and deaths in England Kellyn Arnold* Kellyn Arnold Mark Gilthorpe Nisreen Alwan Alison Heppenstall Georgia Tomova Martin McKee Peter Tennant

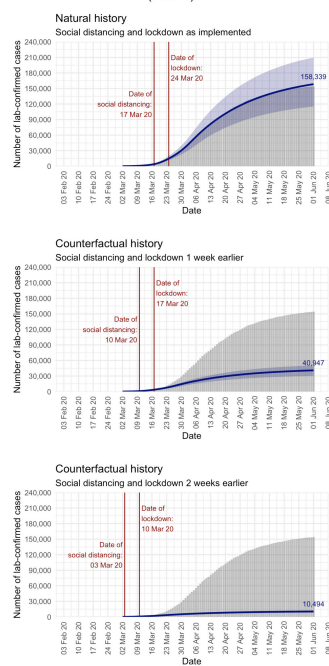
Background: The United Kingdom has experienced one of the highest per-capita death tolls from COVID-19 worldwide. It is debated whether this may partly be explained by the relatively late initiation of voluntary social distancing and mandatory lockdown measures during the pandemic's first wave. In this study, we estimated the number of cases and deaths that would have occurred in England by 1 June 2020 if these interventions had been implemented one or two weeks earlier, and the impact on the required duration of lockdown.

Methods: Using official data on the number of Pillar 1 lab-confirmed cases of COVID-19 and associated deaths occurring in England from 3 March to 1 June, we modelled: the *natural* (i.e. observed) growth of cases, and the *counterfactual* (i.e. hypothetical) growth of cases that would have occurred had measures been implemented one or two weeks earlier. Under each counterfactual condition, we estimated the expected number of deaths and the time required to reach the incidence observed under natural growth on 1 June.

Findings: Introducing measures one week earlier would have reduced by 74% the number of confirmed COVID-19 cases in England by 1 June [Figure 1], resulting in approximately 21,000 fewer hospital deaths and 34,000 fewer total deaths; the required time spent in full lockdown could also have been halved, from 69 to 35 days. Acting two weeks earlier would have reduced cases by 93% [Figure 1], resulting in between 26,000 and 43,000 fewer deaths.

Interpretation: The relatively late introduction of social distancing and lockdown measures is likely a key reason for the scale, severity, and duration of the first wave of COVID-19 in England. Our results highlight the importance of acting swiftly to minimise the spread of an infectious disease when case numbers are increasing exponentially.

Cumulative lab-confirmed cases of COVID-19 in England (Pillar 1)



An agent-based model for transmission and control of COVID-19 epidemic in Bangladesh

Ayesha Sania* Ayesha Sania S M Niaz Arifin Farhanaz Farheen

Background: Despite the high proportion (80%) of asymptomatic cases and low mortality due to COVID-19, the virus's spread remains a significant public health problem for densely populated Bangladesh. Understanding the disease dynamics in the unique Bangladesh context is essential to guide policy decisions.

Methods: We have developed a stochastic agent-based model (ABM) considering the key characteristics of COVID-19 in Bangladesh, which vastly differ from the developed countries. We have implemented the ABM extending the SIR model, where the infected population is sub-divided into asymptomatic, mildly symptomatic, and severe Symptomatic populations. Due to limited access to testing in Bangladesh, the official reported cases are a fraction of the actual symptomatic cases. Although not directly relevant to the epidemiological process, our model attempts to capture this while calibrating against official daily test-positive cases. We calibrated the ABM against the official data from six representative districts and subsequently simulated the effects of different intervention scenarios (or lack thereof).

Results: The MAPE (Mean Absolute Percentage Error) for the capital, Dhaka, is 0.7776%, and that for the commercial capital, Chittagong, is 2.7201% (Figure 1(a), (b)), indicating the accuracy of our model. The cumulative number of cases (asymptomatic, reported, and unreported symptomatic) and peak infection timing correspond with that reported in seroprevalence studies. Our model also reveals that no more than 50% of the symptomatic cases are reported as official test positive cases. Among the intervention scenarios simulated, a notable finding is that a large-scale outbreak is likely when schools are reopened, maintaining the status quo otherwise (Figure (c), (d)).

Conclusions: Our model forecasts the course of the COVID-19 pandemic in Bangladesh with high accuracy. This is a useful tool to simulate the impact of interventions to help policymakers plan appropriate COVID response.

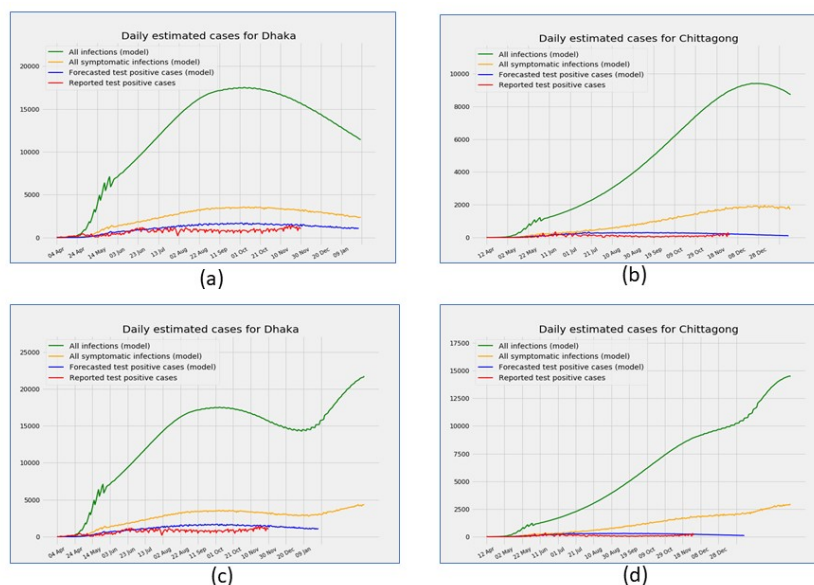


Figure 1: ABM output for Dhaka (a) and Chittagong (b) after calibration. Scenario if school was opened in December in Dhaka (c) and Chittagong (d).

Reported test positive cases have been considered for the period April to November 2020

A cross-sectional analysis of demographic and behavioral risk factors of SARS-CoV-2 antibody positivity among a sample of U.S. college students

Sina Kianersi* Sina Kianersi
Christina Ludema Jonathan T. Macy Edlin Garcia Chen Chen Maya Luetke Mason H. Lown Molly
Rosenberg

Background: Colleges and universities across the United States are developing and implementing data-driven prevention and containment measures against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Identifying risk factors for SARS-CoV-2 seropositivity could help to direct these efforts.

Objective: To estimate the associations between demographic factors and social behaviors and SARS-CoV-2 seropositivity and self-reported positive SARS-CoV-2 diagnostic test.

Methods: In September 2020, we randomly sampled Indiana University Bloomington (IUB) undergraduate students. Participants completed a cross-sectional, online survey about demographics, SARS-CoV-2 testing history, relationship status, and risk behaviors. Additionally, during a subsequent appointment, participants were tested for SARS-CoV-2 antibodies using a fingerstick procedure and SARS-CoV-2 IgM/IgG rapid assay kit. We used unadjusted modified Poisson regression models to evaluate the associations between predictors of both SARS-CoV-2 seropositivity and self-reported positive SARS-CoV-2 infection history.

Results: Overall, 1,076 students were included in the serological testing analysis, and 1,239 students were included in the SARS-CoV-2 infection history analysis. Current seroprevalence of SARS-CoV-2 was 4.6% (95% CI: 3.3%, 5.8%). Prevalence of self-reported SARS-CoV-2 infection history was 10.3% (95% CI: 8.6%, 12.0%). Greek membership, having multiple romantic partners, knowing someone in one's immediate environment with SARS-CoV-2 infection, drinking alcohol more than 1 day a week, and hanging out with more than 4 people when drinking alcohol increased both the likelihood of seropositivity and SARS-CoV-2 infection history.

Conclusion: Our findings have implications for American colleges and universities and could be used to inform SARS-CoV-2 prevention and control strategies on such campuses.

Machine Learning Algorithms to Predict COVID-19 Acute Respiratory Distress Syndrome in Patients with Rheumatic Diseases: Results from the Global Rheumatology Alliance Provider Registry

Zara Izadi* Zara Izadi Milena Gianfrancesco Kimme Hyrich Anja Strangfeld Laure Gossec Loreto Carmona Elsa Mateus Saskia Lawson-Tovey Laura Trupin Stephanie Rush Gabriela Schmajuk Patricia Katz Lindsay Jacobsohn Samar Al Emadi Leanna Wise Emily Gilbert Ali Duarte-Garcia Maria O Valenzuela-Almada Jeffrey A Sparks Tiffany Y Hsu Kristin M D'Silva Naomi Serling-Boyd Suleman Bhana Wendy Costello Rebecca Grainger Jonathan S. Hausmann Jean W Liew Emily Sirotych Paul Sufka Zachary S Wallace Pedro M Machado Philip C Robinson Jinoos Yazdany

Background: Acute Respiratory Distress Syndrome (ARDS) is a rare but life-threatening complication of COVID-19. We aimed to predict ARDS onset using a series of machine learning algorithms optimized for rare events and to identify risk factors associated with ARDS in patients with pre-existing rheumatic disease. **Methods:** We used data from the COVID-19 Global Rheumatology Alliance Registry: Mar 24 - Nov 1, 2020. ARDS diagnosis was indicated by the reporting clinician. Five machine learning algorithms predicted ARDS using a vector of 42 variables obtained at COVID-19 diagnosis, 10-fold cross-validation, and the synthetic minority oversampling technique to balance the distribution of events. Algorithms included penalized regression (GLMNET), gradient boosting (GBM), random forest (RF), support vector machines (SVM), and neural networks (NNET). Performance was assessed in the test set (random 25% of cases) using accuracy, area under curve (AUC), sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). The most influential predictors identified by the top performing model were reported. **Results:** A total of 5931 COVID-19 cases from 67 countries were included. ARDS was reported in 388 (6.5%) cases. Model accuracy ranged from 0.66 (GLMNET and NNET) to 0.79 (GBM). GBM had the highest AUC (0.75), followed closely by GLMNET and RF (0.74). PPV was ≥ 0.95 in all models while NPV was consistently low ranging from 0.09 (NNET) to 0.16 (GBM). GBM had the highest sensitivity (0.81) and was considered the top performing model. Hypertension, smoking, daily prednisone dose, age, interstitial lung disease, sulfasalazine use and tumor necrosis factor inhibitor use were the most influential predictors identified by GBM. **Conclusions:** GBM predicted ARDS with 81% sensitivity in this large cohort of patients with rheumatic disease. Further studies are needed to validate the proposed prediction model in external cohorts and to evaluate its clinical utility.

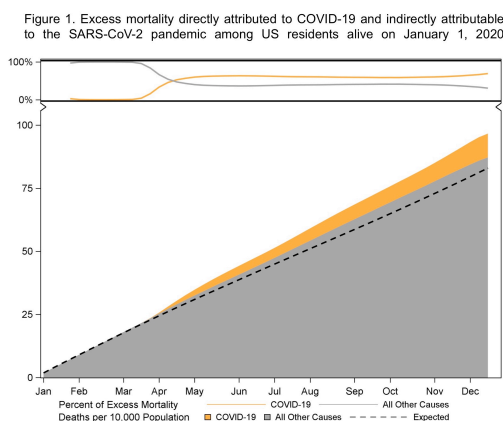
Direct and indirect effects of the SARS-CoV-2 pandemic on mortality in the US: Differences by age, sex, race/ethnicity and region Lauren Zalla* Lauren Zalla Grace Mulholland Lindsey Filiatreau Jessie Edwards

Despite the sweeping social and economic consequences of the SARS-CoV-2 pandemic in the US, few studies have quantified the indirect effects of the pandemic on mortality.

Using provisional death counts reported to the National Vital Statistics System and expected death counts estimated by the Centers for Disease Control and Prevention, we calculated the “excess” risk of mortality as the difference between actual and expected risks of mortality among US residents alive on January 1, 2020. Using cause of death data, we estimated the proportion of excess mortality that was directly attributed to COVID-19. The remainder represents the proportion indirectly attributable to the pandemic. To examine group differences, we stratified by age, sex, race/ethnicity and region.

Nationally, the one-year excess risk of mortality was 13.6 deaths per 10,000 people, with two thirds of excess mortality directly attributed to COVID-19. Indirect causes accounted for 33%. The proportion due to indirect causes varied widely by age, however, ranging from well over 80% among people ages 15-34 to as low as 1% among those ages 85+. Indirect causes accounted for a higher proportion of excess mortality among men (38%; an additional 6 deaths per 10,000) compared to women (27%; an additional 3 deaths per 10,000), and among Blacks (42%; an additional 9 deaths per 10,000) and other racial and ethnic minorities compared to Whites (23%; an additional 2.6 deaths per 10,000). The proportions of excess mortality attributable to direct and indirect causes have remained relatively stable since April.

The effect of the SARS-CoV-2 pandemic on mortality may be severely underestimated when only considering deaths attributed to COVID-19. The indirect effects of the pandemic on mortality are substantial in some groups, such as young people, men, and racialized minorities. These findings should inform a more tailored and equitable approach to addressing excess mortality due to the SARS-CoV-2 pandemic in the US.



Associations between disability and infertility among U.S. reproductive age women Sandie Ha* Sandie Ha Valerie Martinez

Background: Disability is increasingly common among U.S. reproductive age women. Although women with disabilities (WWD) report similar desires to give birth, reproductive health issues such as infertility in this population is understudied.

Objectives: We evaluate the association between self-reported disabilities and infertility in a U.S. representative sample of reproductive age women. Among those with infertility, we also assess whether disabilities were associated with decreased odds of seeking infertility-related medical attention.

Methods: Non-pregnant women ages 18-49 years without history of hysterectomy or oophorectomy ($N=3,789$) were identified from the National Health and Nutrition Examination Survey (NHANES, 2013-2018). Disabilities (any, physical, cognitive, or sensory disability) and infertility were self-reported through an in-person interview with trained interviewers. Logistic regression models estimated the odds ratio and 95% confidence intervals for the association between disabilities and infertility, and among those with infertility, disabilities and infertility-related care seeking. Models adjusted for potential confounders and complex probability sampling.

Results. Compared to unaffected women, WWD had significantly higher odds of reporting infertility [aOR: 1.49 (1.01-2.20)] after adjusting for covariates. The associations were consistent for sensory [aOR:1.97 (1.12 - 3.48)] and cognitive disabilities [aOR:1.53 (1.06-2.21)]. Among women with infertility, women with any disability appeared less likely to have a doctor's visit regarding this condition, but this association was not statistically significant [aOR 0.87 (0.36 - 2.12)].

Conclusion. WWD have increased odds of reporting infertility, and if affected, may be less likely to visit a health care provider for this condition. More research is needed to further understand reproductive health issues and needs among WWD, and to guide policy and clinical practice in this vulnerable population.

Assessment of geographic misclassification: Comparing block-, block group-, and county-level measures of abortion accessibility in the United States Jane Seymour* Jane Seymour
Dennis Milechin Ushma Upadhyay Abby Rudolph

In the literature, abortion accessibility is often operationalized as distance or drive time to an abortion-providing facility. Many studies use county or block group as the geographic unit of analysis, as client and provider survey data are commonly available only for these larger units. While informative, these studies may misclassify accessibility. Our analysis examined the magnitude of accessibility misclassification resulting from use of block groups or counties, as compared to blocks, the smallest geographic unit used by the Census.

Abortion accessibility was operationalized as the proportion of US women aged 15-44 living within a 30-minute drive time of an abortion-providing facility. We geocoded the 850 abortion-providing facilities in the 2018 Advancing New Standards in Reproductive Health facility database. With shapefiles for block, block-group, and county from the 2010 Census, and OpenStreetMap data, we computed 30-minute drive time isochrones for each facility and then the fraction of each geographic unit of interest that intersected these isochrones. Using these fractions and Census population estimates, we determined the proportion of US women within 30 minutes of an abortion-providing facility and compared differences across block, block group, and county measures.

With the block-based estimate, 65.3% of the 62,374,964 US women aged 15-44 lived within a 30-minute drive time of an abortion-providing facility. This estimate was 0.3 percentage points greater than the block group-based estimate (65.0%) and 24.2 percentage points greater than the county-based estimate (41.1%).

Our findings indicate that block group-based estimates approximate abortion accessibility well relative to the smallest Census unit, blocks, but county measures may dramatically underestimate accessibility. Given that block-based estimates are computationally intensive and fewer data are available at this level, block group-based measures may be an acceptability proxy.

Reproductive

Associations of opioid use with reproductive hormones and anovulation Kerry SJ Flannagan*
Kerry Flannagan Sunni L Mumford Lindsey A Sjaarda Joshua R Freeman Jeannie G Radoc Victoria C
Andriessen Neil J Perkins Jessica R Zolton Robert M Silver Enrique F Schisterman

Opioids are commonly prescribed to reproductive-age women for pain management after delivery or miscarriage. However, opioids have multiple endocrine effects, and may alter reproductive hormone function and ovulation. We have previously shown that limited opioid use while trying to conceive is associated with reduced fecundability, which may be related to these endocrine effects. Therefore, we examined associations of opioid use with hormone levels throughout the menstrual cycle and anovulation in a cohort of healthy women.

We followed 1211 women for up to 6 menstrual cycles attempting natural conception. We measured opioid use at baseline by urine immunoassay and classified women as exposed or unexposed to any opioid. We assessed urinary concentrations of pregnanediol glucuronide (PdG), follicle stimulating hormone (FSH), luteinizing hormone (LH), and estrone-3-glucuronide (E1G) during the first 2 cycles. Women used fertility monitors throughout follow-up. We estimated relative mean differences in hormone levels with linear mixed models and risk ratios (RR) for anovulation using Poisson regression, adjusting for sociodemographic characteristics, use of other drugs, time since a woman's last pregnancy, and typical severity of menstrual pain.

Eighty-seven (7%) women were positive for opioid use. During the luteal phase, mean PdG was 16% lower (95% CI -36%, 9%) and mean E1G was 18% lower (95% CI -34%, 1%) among opioid users, however, no associations were observed with hormones over the entire cycle, during the follicular phase, or at ovulation. Opioid use was associated with a higher risk of anovulation, but the association was attenuated and imprecise after adjustment (RR 1.54; 95% CI 0.96, 2.46).

Our results suggest that opioid use is related to slight disruptions in menstrual cycle hormones and potentially higher risk of anovulation. This may explain some of the association of opioid use with lower fecundability, even among non-opioid-dependent women.

Factors associated with enrollment and retention in a North American internet-based preconception cohort

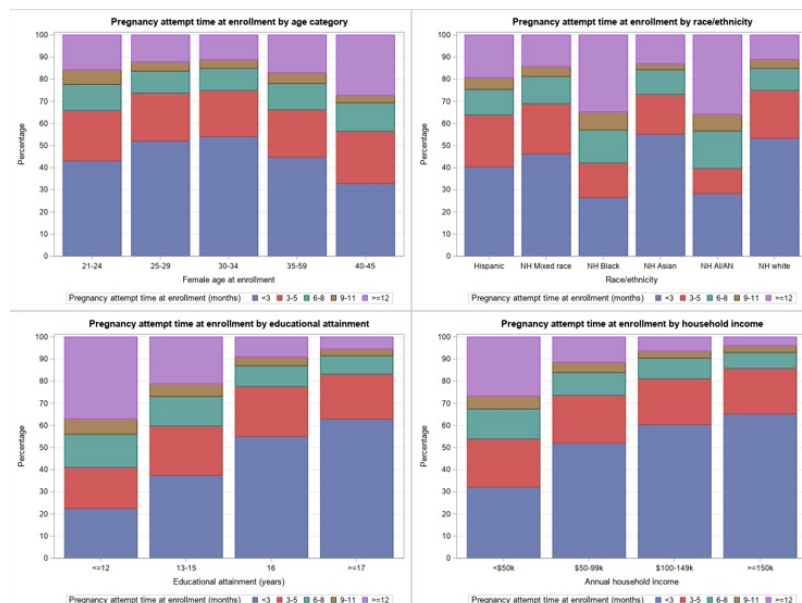
Ruth J. Geller* Ruth Geller Olivia R. Orta Renée Boynton-Jarrett Amelia K. Wesselink Tanran Wang Jessica Sara Levinson Maya Thirkill Martha Rose Koenig Marlon D. Joseph Sydney Willis Mary Willis Elizabeth E. Hatch Lauren A. Wise

Background: Racial and socioeconomic disparities in fertility exist in the US, yet most fertility research is conducted in high-socioeconomic status, majority-white cohorts. Internet-based studies provide an opportunity to recruit more diverse participants into preconception cohorts.

Methods: We analyzed data collected during 2013-2020 from Pregnancy Study Online (PRESTO), a North American internet-based prospective cohort study of women age 21-45 years who are not using contraception or fertility treatments. We examined demographic characteristics (age, race/ethnicity, educational attainment, and annual household income [HHI]) of female participants and tabulated them against factors related to enrollment and retention: pregnancy attempt time at enrollment, how the participant learned about the study, survey breakoff (starting but not completing the enrollment survey), and loss to follow-up.

Results: Among 13,470 women, the mean (SD) age at enrollment was 30 (4.2) years; 18% identified as women of color (e.g., Latina, 7%; non-Hispanic Black, 5%); 8% had ≤12 years of education, and 24% had HHI <\$50,000. Several demographic factors were related to pregnancy attempt time at enrollment (Figure). Recruitment via Facebook yielded the highest proportion of women with ≤12 years of education and HHI <\$50,000, compared with sources such as pregnancy-related websites, clinic-based recruitment, and other social media. Survey breakoff was highest among non-Hispanic Black women (36%, compared to 17-32% in other race/ethnicity groups). The majority (54%) of women with HHI <\$50,000 were lost to follow-up, compared with 16% of women with HHI ≥\$150,000.

Conclusions: Sustainable commitments from fertility researchers are needed to recruit and retain women of color and women across a wide range of educational backgrounds and income in order to advance reproductive health equity. Future qualitative work will examine factors related to study participation in depth.



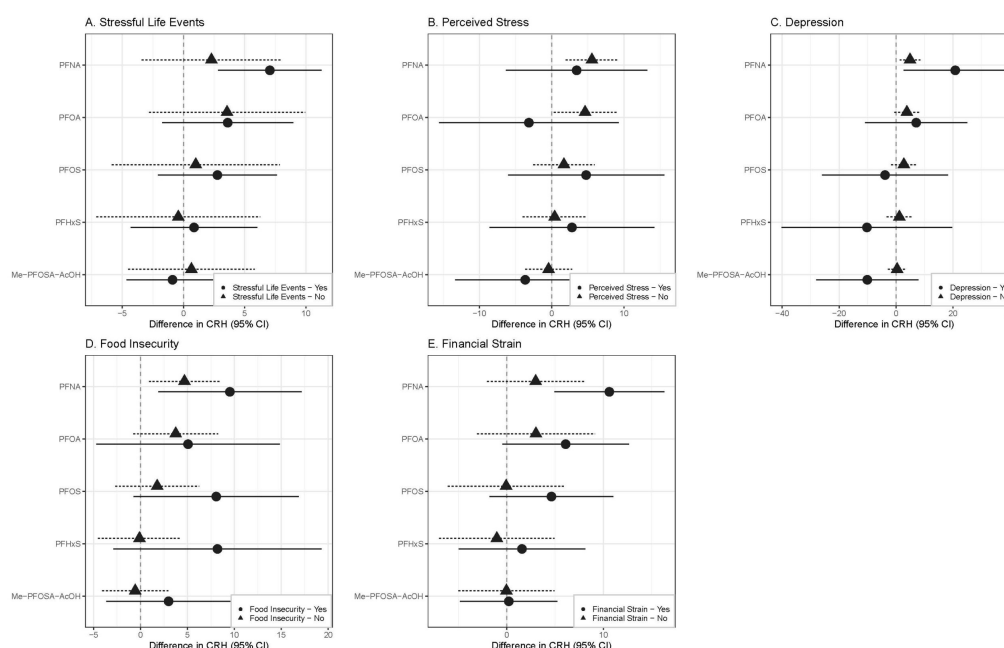
Joint effects of prenatal exposure to per- and poly-fluoroalkyl substances and psychosocial stressors on corticotropin releasing hormone during pregnancy Stephanie Eick* Stephanie Eick Dana Goin Lara Cushing Erin DeMicco Amy Padula Tracey Woodruff Rachel Morello-Frosch

Background: Prenatal exposure to per- and poly-fluoroalkyl substances (PFAS) and psychosocial stressors has been associated with adverse pregnancy outcomes, including preterm birth (PTB). Previous studies have suggested joint exposure to environmental chemical and social stressors may explain even greater differences in risk of PTB. Elevated corticotropin releasing hormone (CRH) during mid-gestation may represent one biologic mechanism linking chemical and non-chemical stress exposures to PTB.

Methods: Using data from a prospective birth cohort (N=497), we examined the associations between individual PFAS (ng/mL) and CRH (pg/mL) using linear regression. PFAS and CRH were measured during the second trimester in serum and plasma, respectively. Coefficients were standardized to reflect change in CRH associated with an interquartile range (IQR) increase in natural log transformed PFAS. We additionally examined if the relationship between PFAS and CRH was modified by psychosocial stress using stratified models. Self-reported depression, stressful life events, perceived stress, food insecurity, and financial strain were assessed using validated questionnaires during the second trimester and included as binary indicators of psychosocial stress.

Results: An IQR increase in PFNA was associated with elevated CRH ($\beta=5.17$, 95% CI=1.79, 8.55). Increased concentrations of PFOA were also moderately associated with CRH ($\beta=3.62$, 95% CI=-0.42, 7.66). The relationship between PFNA and CRH was stronger among women who experienced stressful life events, depression, food insecurity, and financial strain compared to women who did not experience these stressors (Figure).

Conclusions: This study is the first to examine the relationship between PFAS exposure and CRH levels in mid-gestation. We found these associations were stronger among women who experienced stress, which aligns with previous findings that chemical and non-chemical stressor exposures can have joint effects on health outcomes.



Herpes Simplex Virus Type 2 Seroprevalence and Incidence and Growth of Ultrasound-Diagnosed Uterine Fibroids in a Large Population of Young African-American Women

Kristen Moore* Kristen Moore Quaker Harmon Donna Baird

Reproductive tract infections (RTIs) have long been hypothesized risk factors for fibroid development, but few studies have investigated it. In our 2016 cross-sectional analysis from the Study of Environment, Lifestyle and Fibroids, a large Detroit-based cohort of 24-35 year-old African-American women with ultrasound fibroid screening, we found no evidence of a relationship between one of the most prevalent RTIs in the US, herpes simplex virus type-2 (HSV-2), and fibroids. With prospective data from the cohort (ultrasound exams at 20-month intervals over 5 years), we examined HSV-2's association with fibroid incidence and growth. We computed adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for incidence comparing HSV-2 seropositive vs negative using Cox proportional hazards models among 1,208 women fibroid-free at baseline. HSV-2's influence on fibroid growth was assessed based on the difference in a fibroid's size between consecutive ultrasounds (N = 1,323 growth measures) using a linear mixed model, estimating the adjusted relative growth rate, scaled to 18 months. HSV-2 seropositivity did not increase the risk of fibroid incidence (aHR: 0.85, 95% CI: 0.65, 1.13) or the average fibroid growth rate 3.1% (95% CI: -5.8, 13.0). Thus, women can be reassured that HSV-2 seropositivity is unlikely to increase fibroid incidence or growth, given these longitudinal measures.

Are we overcounting deaths attributable to secondhand smoke (SHS) exposure and underestimating disparities? An analysis of SHS-attributable lung cancer and ischemic heart disease deaths among U.S. adults Andrea R. Titus* Andrea Titus Rafael Meza James F.

Thrasher Kristi E. Gamarel Nancy L. Fleischer

Introduction: Ischemic heart disease (IHD) and lung cancer are causally linked to secondhand smoke (SHS) exposure, but existing estimates of SHS-attributable mortality in the U.S. do not account for declines in SHS exposure prevalence, differences by age, or disparities across population groups. We used detailed population and SHS exposure data to explore patterns of SHS-attributable mortality by sex and race/ethnicity between 2000 and 2018.

Methods: We compiled the following annual data by sex and race/ethnicity (non-Hispanic White, non-Hispanic Black, Hispanic, and other non-Hispanic): CDC WONDER mortality data, Census Bureau population estimates, and nationally representative survey data on smoking prevalence and SHS exposure prevalence. We estimated smoking and SHS exposure prevalence by age and year using predicted values from logistic regression. At the intersection of sex and race/ethnicity, we calculated attributable fractions and attributable deaths for both smoking and SHS exposure by age and year. We scaled estimates by the size of the nonsmoker population for each group to examine disparities over time.

Results: SHS-attributable IHD and lung cancer deaths declined from 30,500 in 2000 to 9,900 in 2018. While the absolute number of deaths declined in all groups, non-Hispanic Black males and females bore an increasingly disproportionate share of attributable deaths. In 2018, non-Hispanic Black males accounted for 5.5% of the total nonsmoking population, but 13.6% of SHS-attributable IHD deaths and 9.4% of attributable lung cancer deaths (up from 6.4% and 6.9% in 2000). Non-Hispanic Black females accounted for 6.7% of the nonsmoker population in 2018, but 9.7% of IHD deaths and 9.3% of lung cancer deaths (up from 6.8% and 4.9%).

Conclusions: While SHS-attributable deaths have decreased in recent decades, disparities may be increasing. Detailed demographic data and attributable fraction methods can shed light on changing patterns of attributable mortality.

These disparities are rubbish: a block-group spatial analysis on racial disparities of litter bins in New York City Nadav L. Sprague* Nadav L. Sprague Ahuva L. Jacobowitz Christina A. Mehranbod Ariana N. Gobaud Charles C. Branas

Background: Low-income and non-white communities in the United States, as well as New York City (NYC) specifically, face well-documented environmental health disparities. Recent media articles point to environmental disparities in access to street litter bins, notably regarding NYC removing litter bins from predominately low-income and Black neighborhoods. Decreased access to litter bins and proper trash removal are associated with vector-borne diseases, asthmatic/allergic reactions, and violent crimes. While many studies have examined the negative health impacts of improper trash removal, no studies to date have investigated the disparities in trash distribution. This exploratory study will examine the association of New York City litter baskets and neighborhood income and demographics.

Methods: This cross-sectional study used DSNY Litter Basket Inventory for 2020 aggregated within block groups (n = 5,789) for NYC. Multilevel Bayesian conditional autoregressive Poisson models estimated the prevalence rate ratio for counts of litter bins in each block group, accounting for spatial dependencies. Models adjusted for block group racial demographics, median household income, and percent land use.

Results: In an aspatial model, block groups with a higher percentage of Black or Asian residents and more retail space were independently associated with a lower prevalence of litter bins. After accounting for spatial autocorrelation, block groups with a higher percentage of Black or Asian residents and more retail space were independently associated with a higher prevalence of litter bins. In both models, median household income was not associated with prevalence of litter baskets after controlling for race.

Conclusion: Results suggest racial environmental disparities in access to litter bins in NYC. This study is the first step in establishing racial environmental health disparities in access to litter bins. Future multi-city and longitudinal studies are warranted.

Geographic differences in racial disparities in access to the kidney transplant waitlist Laura McPherson* Laura McPherson Rebecca Zhang Jason Wang Katie Ross-Driscoll Joel Adler Stephen O. Pastan Rachel E. Patzer

While kidney transplantation is the optimal treatment for patients with end-stage renal disease (ESRD), inequitable access to this treatment option persists, where non-Hispanic (NH) Black and Hispanic white patients historically have lower rates of waitlisting compared to NH white patients. Given the history of disparities in kidney transplant, we examined the interaction between race and geography by determining whether these racial disparities vary across the US Organ Procurement and Transplantation Network (OPTN) regions. Using the US Renal Data System, our cohort consisted of 1,225,580 adult, ESRD patients [NH white (58%), NH Black (29%), and Hispanic white (13%)] who initiated dialysis from 1/1/2006-6/30/2017 followed through 6/30/2018, with linkage to neighborhood-level data in the 2019 American Community Survey. Patients were assigned to one of 11 OPTN regions via residential zip code. Race and ethnicity was abstracted from the Centers for Medicare and Medicaid Services 2728 form completed at time of ESRD diagnosis. Multivariable Cox models were used to compare racial differences in kidney transplantation across OPTN regions. The cohort was majority male (57%) with a mean age of 63 years. Approximately 18% of patients were waitlisted, including 19% NH Black, 16% NH White, and 24% Hispanic over one-year median follow-up. Controlling for demographic, clinical, and socioeconomic characteristics, the overall hazard of waitlisting among NH Black patients was 0.81 (95% CI: 0.80-0.82) and Hispanic white patients was 0.65 (95% CI: 0.63-0.68) vs NH white patients. Disparities in access to the waitlist persisted across all OPTN regions, with consistently lower effect estimates among the Hispanic (HR range: 0.59-0.79) and NH Black (HR range: 0.77-0.89) patient populations. Regions with the largest racial disparities in waitlisting were the Southeast (3, 11) and Pacific Northwest (6), with the Southeast (3, 11) having a larger proportion of NH Black patients.

	All Patients	Non-Hispanic white patients	Non-Hispanic Black patients	Hispanic white patients	Hazard ratios for time from dialysis start to waitlisting by OPTN region ^a , 1/1/2006-6/30/2017 (followed through 6/30/2018)	
	(N=1,225,580)	N=710,775 (58.0%)	N=354,136 (28.9%)	N=160,669 (13.1%)	Non-Hispanic Black to Non-Hispanic white patient HRs	Hispanic white to Non-Hispanic white patient HRs
OPTN Region ^a	N (%)	N (%)	N (%)	N (%)	HR (95% CI) ^b	HR (95% CI) ^b
1	41,807 (3.4)	32,616 (2.7)	5,995 (0.5)	3,196 (0.3)	0.84 (0.76, 0.92)	0.70 (0.57, 0.85)
2	144,060 (11.8)	88,329 (7.2)	48,475 (4.0)	7,256 (0.6)	0.83 (0.80, 0.86)	0.69 (0.65, 0.73)
3	207,484 (16.9)	10,1634 (8.3)	91,699 (7.5)	14,151 (1.2)	0.78 (0.76, 0.81)	0.61 (0.58, 0.65)
4	124,991 (10.2)	50,383 (4.1)	29,087 (2.4)	45,521 (3.7)	0.82 (0.79, 0.84)	0.67 (0.63, 0.71)
5	173,896 (14.2)	87,513 (7.1)	23,726 (1.9)	62,657 (5.1)	0.89 (0.87, 0.91)	0.79 (0.76, 0.83)
6	33,016 (2.7)	28,205 (2.3)	2,321 (0.2)	2,490 (0.2)	0.79 (0.74, 0.84)	0.62 (0.55, 0.70)
7	91,442 (7.5)	61,633 (5.0)	22,453 (1.8)	7,356 (0.6)	0.85 (0.82, 0.88)	0.72 (0.68, 0.77)
8	66,271 (5.4)	49,374 (4.0)	12,460 (1.0)	4,437 (0.4)	0.82 (0.80, 0.85)	0.68 (0.63, 0.73)
9	76,550 (6.3)	43,718 (3.6)	23,608 (1.9)	9,224 (0.8)	0.81 (0.79, 0.83)	0.65 (0.62, 0.69)
10	123,048 (10.0)	88,450 (7.2)	32,025 (2.6)	2,573 (0.2)	0.80 (0.78, 0.82)	0.65 (0.62, 0.68)
11	143,015 (11.7)	78,920 (6.4)	62,287 (5.1)	1,808 (0.2)	0.77 (0.75, 0.78)	0.59 (0.57, 0.61)

Abbreviations: CI, confidence interval; HR, hazard ratio; OPTN, Organ Procurement Transplant Network
^aStates in each OPTN Region: 1 (CT, Eastern VT, MA, ME, NH, RH); 2 (DE, DC, MD, NJ, PA, WV); 3 (AL, AR, FL, GA, LA, MS); 4 (OK, TX); 5 (AZ, CA, NV, NM, UT); 6 (AK, HI, ID, MT, OR, WA); 7 (IL, MN, ND, SD, WI); 8 (CO, IA, KS, MO, NE, WY); 9 (NY, Western VT); 10 (IN, MI, OH); 11 (KY, NC, SC, TN, VA)
^bModels adjusted for age, sex, body mass index, cause of end-stage renal disease, cardiovascular disease, diabetes, hypertension, chronic obstructive pulmonary disease, cancer, tobacco usage, alcohol consumption, drug usage, receipt of pre-dialysis exogenous erythropoietin, hemoglobin level, albumin level, pre-end stage renal disease nephrology care, informed about transplant options at end-stage renal disease initiation, primary health insurance status, dialysis initiation before or on/after implementation of the Kidney Allocation System on 12/4/2014, and poverty level, education level, race level by zip code

School racial segregation and long-term cardiovascular health in the United States Min Hee Kim* Min Hee Kim Gabriel Schwartz Justin S. White M. Maria Glymour Kiarri N. Kershaw Daniel Collin Sean F. Reardon Scarlett Lin Gomez Rita Hamad

Background: Cardiovascular disease (CVD) and its risk factors disproportionately affect Black adults. Black youth attending highly racially segregated schools may explain black-white CVD disparities in young adulthood, with pathways including higher stress and lower economic opportunities, i.e., adverse social determinants of CVD.

Methods: We estimated the effects of school segregation on self-reported CVD and its risk factors in young adulthood by exploiting the random timing of court orders releasing school districts from *Brown v. Board* desegregation plans during 1991 and 2013. To do so, we linked school district data among Black (N = 1,557) and White (N = 870) children in the Panel Study of Income Dynamics with their health outcomes during adulthood through 2017. We first fitted ordinary least squares (OLS) regression models adjusting for individual, family, and area-level covariates and state and year fixed effects, stratified by race. We then carried out instrumental variables (IV) analysis, using the occurrence of court decisions that resulted in increased school segregation as an instrument for school segregation.

Results: OLS models show that, among Black adults, school segregation was associated with poorer self-rated health ($\beta = 0.48$, 95%CI: 0.02, 0.94) and the increased probability of heart disease ($\beta = 0.03$, 95%CI: 0.002, 0.053). School segregation was also associated with a lower likelihood of smoking among White adults ($\beta = -0.30$, 95%CI: -0.51, -0.09). In IV models, school segregation increased poorer self-rated health ($\beta = 1.85$, 95%CI: 0.12, 3.58) and drinking ($\beta = 2.26$, 95%CI: 0.43, 4.09), but also decreased the stroke probability ($\beta = -0.14$, 95%CI: -0.28, -0.01) for Black adults. School segregation did not influence White adults' CVD risk.

Discussion: School segregation can have wide-reaching longstanding impacts on Black adult's CVD risks. Future research can explore the mechanisms through which these effects occur.

Educational inequalities in all-cause mortality: the mediating role of epigenetic ageing in a multi-cohort study and meta-analysis Cristian Carmeli* Cristian Carmeli Giovanni Fiorito Paolo Vineis Lifepath Consortium

Epigenetic age acceleration (EAA), measured through patterns of DNA methylation in blood, is a potential social-to-biological mechanism by which social adversities get 'under the skin' leading to disease susceptibility, and ultimately early mortality. In this study we aimed to assess the portion of educational inequalities in mortality explained by EAA.

Data were from six prospective population-based cohort studies in Australia, Germany, Ireland, Italy, UK and USA, totalling 9,861 participants (49.2% women) and 2,362 deaths (37.8% women) from all causes. On average, age at baseline was 64 and follow-up lasted 11 years. Educational attainment was categorized as low for those not having attained a high school diploma or high otherwise. EAA was measured at baseline as residual of regressing GrimAge epigenetic clock on age. Sex was included as a potential effect modifier and age as time scale in Aalen additive hazard models. We estimated hazard rate differences (per 10,000 person-years) for total effect and indirect effect (portion of the total effect explained by EAA) parameters via the inverse odds ratio weighting mediation method. Estimates from each cohort were pooled through a random effect meta-analytic model.

Men whose education was low had 58 excess deaths [95% confidence interval (CI): 41 to 75] compared to their more advantaged counterparts (total effect). The indirect effect through EAA was 33 [95% CI: 23 to 42]. In women the total effect resulted in 11 excess deaths [95% CI: -2 to 23], and the indirect effect in -2 [95% CI: -9 to 4]. Sensitivity analyses assessing the impact of potential error in EAA measurement, age-variant hazard differences and confounding of the mediator-outcome association supported the results. Last, cell composition in blood did not explain the mediation by EAA.

Our results highlighted a substantive portion of educational inequalities in mortality is explained by EAA in men, and supported EAA as a social-to-biological mechanism.

Accounting for Survivor Bias in Transplant Benefit Models Erin M. Schnellinger* Erin Schnellinger Edward Cantu Michael O. Harhay Douglas E. Schaubel Stephen E. Kimmel Alisa J. Stephens-Shields

Background: The lung allocation system in the U.S. prioritizes lung transplant candidates based on estimated pre- and post-transplant survival. However, these models do not account for all waitlist candidates; rather, they only account for those who survive on the waitlist long enough to receive transplant. Transplanted candidates may differ from un-transplanted candidates, resulting in survivor bias and inaccurate predictions.

Methods: We propose a weighted estimation strategy to account for survivor bias in the pre- and post-transplant models used to calculate Lung Allocation Scores (LAS), the current basis for prioritizing lung transplant candidates in the U.S. We then created a modified LAS using these weights, and compared its performance to that of the existing LAS via time-dependent receiver operating characteristic (ROC) curves, calibration curves, and Bland-Altman plots.

Results: Overall, accounting for survivor bias improved discrimination and calibration over the existing LAS, and led to changes in patient prioritization. Individuals who received lower (worse) priority under the modified LAS tended to experience increases in their estimated waitlist urgency, whereas those who received higher (better) priority under the modified LAS tended to experience increases in their estimated transplant benefit.

Conclusions: Our approach to addressing survivor bias is intuitive and can be applied to any organ allocation system that prioritizes patients based on estimated post-transplant survival. This work is especially relevant to current debate about methods to ensure more equitable distribution of organs.

When Two Worlds Collide: The Convergence of Machine Learning and Epidemiologic Methods for Complex Survey Data

Lydia Feinstein* Lydia Feinstein Nathaniel MacNeill Jesse Wilkerson Paivi M Salo Christian Douglas Michael B. Fessler Peter S. Thorne Alison A. Motsinger-Reif Darryl C. Zeldin

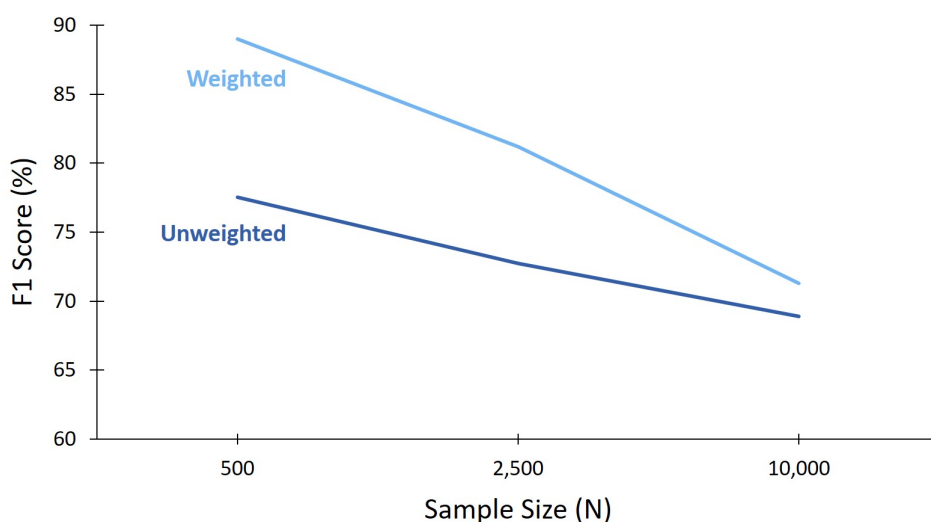
Introduction: One challenge impeding the incorporation of machine learning into epidemiologic research is a lack of precedence for analyzing complex survey data. Traditional analyses that fail to account for unequal probabilities of observation via weighting sacrifice generalizability to target populations, but it remains unclear how weighting affects machine learning algorithms. We determined whether weighting changes the performance of gradient boosting—an ensemble machine learning algorithm—and whether weighting is more important under various theoretical conditions.

Methods: We first conducted a case study using data from 15,820 participants in the 1988-1994 National Health and Nutrition Examination Survey (NHANES III). All-cause mortality status through 2015 was ascertained via linkage to the National Death Index. We developed a gradient boosting model for predicting mortality based on 27 predictor variables, and compared results before and after weighting. We conducted the same comparison in 35 datasets we simulated to vary (1) sample size; (2) predictor strength and dimensionality; and (3) weight variability. Models were evaluated using 5-fold cross validation and compared with the F1 score, the harmonic mean of sensitivity and positive predictive value.

Results: The weighted gradient boosting model performed better than the unweighted model in the NHANES III sample (F1 score 86% vs 80%). Simulations demonstrated that sample size was the most influential contributor to the superior performance of the weighted model, with weighting being more important the smaller the sample size (**Figure 1**). When holding sample size constant at 10,000, no other parameters influenced how weighting affected model performance.

Conclusions: Epidemiologic research may benefit from more readily available software options for weighting machine learning analyses of complex survey data. Future research should consider the impact of other survey design parameters (e.g., clustering).

Figure 1. F1 Score of a Weighted vs. Unweighted Gradient Boosting Model for Predicting All-cause Mortality Under Different Sample Size Scenarios



Using INLA-SPDE spatial modeling to Examine Associations Between Neighborhood

Characteristics and Alzheimer Disease and Related Dementia Dana M. Alhasan* W. Braxton Jackson II Nathaniel S. MacNell Christian Douglas Matthew C. Lohman Jana A. Hirsch Maggi C. Miller BOCAI@mailbox.sc.edu Frankie LaPorte W. Braxton Jackson II Chandra L. Jackson

Neighborhood environment has been associated with cognitive decline, yet few studies have examined the association with dementia. We investigated the ecologic relationship between census-tract neighborhood features and geographic distribution of diagnosed dementia case incidence from 2010-2014 in the South Carolina (SC) Alzheimer's Disease Registry (ADR). To combat the limitations of ecologic models, differences of geographic area reporting frequency, differences in measurement of exposures, and lack of data for geographic areas of interest, we used Inverse Nested Laplace Approximations and Stochastic Partial Differential Equations (INLA-SPDE) estimation to predict or approximate the incidence over a continuous spatial field at the census-tract level ($n=1,103$). We included all reported cases ($N=65,984$) of dementia in the SC ADR. Point addresses were available for 66% of cases; 34% only had zip codes. Neighborhood measures came from USDA Food Environment, Dartmouth Atlas of Health Care, Center for Air, Climate, and Energy Solutions, US Department of Agriculture, County Health Rankings, Decennial Census, and American Community Survey (2008-2012). We geocoded and validated all geographic data prior to applying INLA-SPDE. Preliminary INLA-SPDE models showed an estimated dementia IRR of 1.41 (95% CI 1.29-1.66) for a 10% increase in proportions of household in the census tract living below the federal poverty level and an IRR of 1.05 (95% CI 1.00-1.09) comparing urban vs. rural areas. We observed environmental disparities across multiple measures that corresponded to socioeconomic segregation statewide. Initial results show evidence for neighborhood effects on dementia incidence, compounding disparities observed across demographic strata. Future studies should consider all available neighborhood characteristics to accurately assess disparities. The INLA-SPDE method could have wide applicability to epidemiologic analyses of data collected across disparate spatial scales.

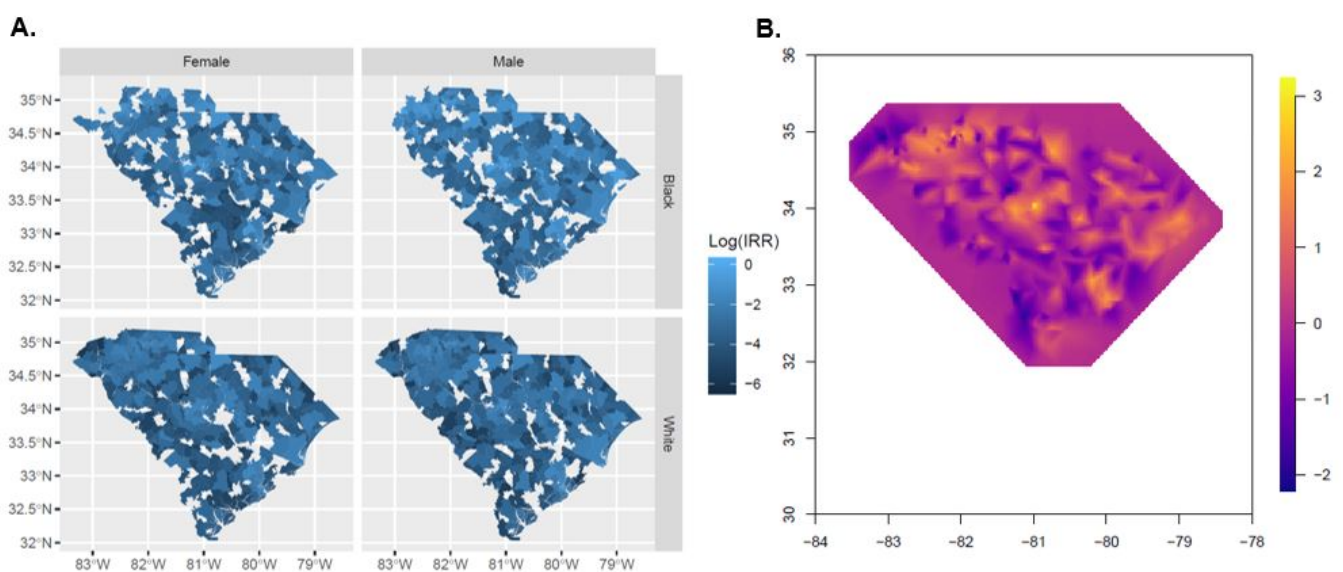


Figure 1: INLA-SPDE Model of Dementia Incidence in South Carolina

Dementia disease registry data (A) present methodological challenges due to variability in reporting units and apparent missing data resulting from the process of aggregating cases. The INLA-SPDE approach uses layered spatial fields (B) to represent data, providing estimates less limited by reporting units and zero-inflation.

Extending target validity when estimating the incidence of late sequelae of SARS-CoV-2

Grace E. Mulholland* Grace Mulholland Lauren C. Zalla Arti Virkud Jessie K. Edwards

In the coming years, the long-term health implications of SARS-CoV-2 infection are likely to be of great interest to patients, health care providers, public health practitioners, and policymakers. It is likely that many studies of late SARS-CoV-2 sequelae will be conducted in restricted subsets of people with prior SARS-CoV-2 infection, such as those who were hospitalized with COVID-19. Estimates derived from such restricted subsets cannot, however, be assumed to have target validity when the target population of interest is all people in a geographic area with prior SARS-CoV-2 infection. The risk of late sequelae may differ according between the source population for the restricted subset and the with respect to factors relevant to risk of late sequelae such as exposure characteristics, symptom presentation, or COVID-19 severity.

We describe an approach to efficiently recruit a probability-based sample of people with prior SARS-CoV-2 infection that, when re-weighted, is representative of a target population consisting of all people in a geographic area with prior SARS-CoV-2. Our approach relies on available or collected data from a sample of the target population selected without regard to symptoms or known SARS-CoV-2 exposure. These data are used to derive prevalence of prior SARS-CoV-2 across the joint distribution of measured characteristics and subsequently allocate targets for a probability-based recruitment strategy. Combining this probability-based sample with data from a restricted subset 1) increases the utility of data from the restricted subset, allowing valid inference among a broader target population of people with prior SARS-CoV-2 infection, and 2) improves precision of estimates relative to a probability-based sample alone, provided that the incidence of late sequelae is higher in the restricted subset than in the target population.

The Importance of Making Assumptions in Bias Analysis Richard MacLehose* Richard MacLehose Tom Ahern Tim Lash Charles Poole Sander Greenland

Quantitative bias analyses allow researchers to adjust for uncontrolled confounding, given specification of certain bias parameters. When researchers are concerned about unknown confounders, plausible values for these bias parameters will be difficult to specify. Ding and VanderWeele developed bounding factor and E-value approaches that require the user to specify only some of the bias parameters. We describe the mathematical meaning of bounding factors and E-values as well as the plausibility of these methods in an applied context. We encourage researchers to pay particular attention to the assumption made, when using E-values, that the prevalence of the uncontrolled confounder among the exposed is 100% (or, equivalently, the prevalence of the exposure among those without the confounder is 0%). We contrast methods that attempt to bound biases or effects with alternative approaches such as probabilistic bias analysis. We provide an example from the recent literature where failure to make this distinction led to erroneous statements. If the primary concern in an analysis is with known but unmeasured potential confounders, then E-values are not needed and may be misleading. In cases where the concern is with unknown confounders, the E-value assumption of an extreme possible prevalence of the confounder limits its practical utility.

Childhood Internalizing and Externalizing Behavior Problems and Cardiovascular and Diabetes Mellitus Risk in Adolescence Paula Bordelois* Paula Bordelois karestan C Koenen Mitchell S Elkind Shakira F Suglia Katherine M Keyes

Common psychopathological disorders, including depression and anxiety, are known risk factors of cardiovascular disease (CVD) and Type 2 Diabetes Mellitus (T2DM) in adults. Because CVD and T2DM have long latency periods and psychopathology tends to track from childhood into adulthood, it is possible that these relationships are established early in life. We examined, prospectively, the relationship of internalizing and externalizing behavior problems –the two overarching domains of common childhood psychopathology– with elevated CVD and T2DM risk in late adolescence in data from a large British birth-cohort, the Avon Longitudinal Study of Parents and Children (ALSPAC, N=7,730). Using parents' ratings of children's behavior at ages 4 and 7 (Strengths and Difficulties Questionnaire), we assessed whether hyperactivity and conduct problems (externalizing) and emotional problems (internalizing) predicted higher CVD and T2DM risk at age 17: triglycerides > 130 mg/dl, low density cholesterol > 130 mg/dl, and homeostasis model assessment of insulin resistance index > 2.9. After accounting for attrition bias and adjusting for demographics, socioeconomic and maternal factors, pregnancy and birth outcomes, and early childhood factors, we found positive associations of high triglyceridemia with both hyperactivity (RR= 1.61, 95% CI=1.24-2.09) and conduct problems (RR= 1.51, 95%CI= 1.20-1.90), and of insulin resistance with hyperactivity (RR= 1.28, 95% CI= 1.01-1.61); we also found an inverse association of high triglyceridemia with emotional problems (RR= 0.64, 95% CI= 0.42-0.97). This research suggests that childhood externalizing problems might be an early life risk factor for CVD and T2DM and also, that internalizing problems are either not a risk factor for early cardiovascular/diabetes risk or, that risk in these children does not increase until after adolescence. Future research should aim at confirming these findings and investigating the mechanisms involved.

Longitudinal changes in physical activity during pregnancy by race/ethnicity, body mass index, and parity: the NICHD Fetal Growth Studies-Singletons Susanna Mitro* Susanna Mitro

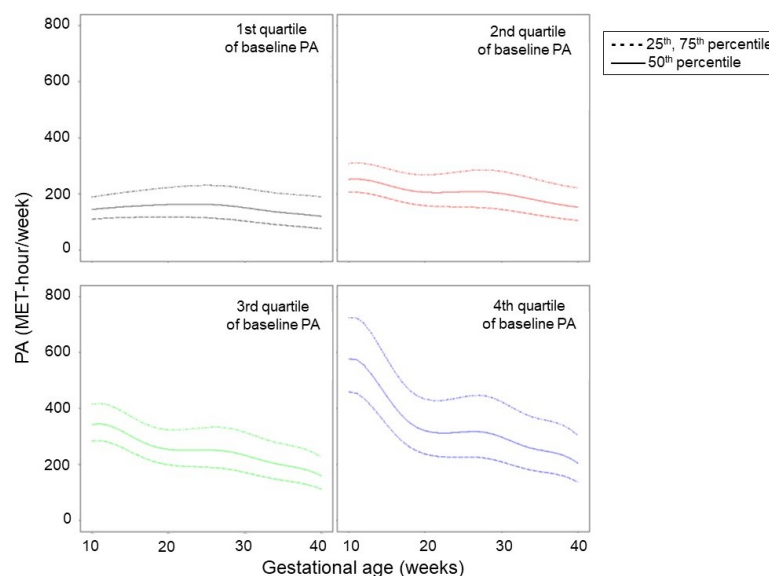
Shyamal Peddada Jessica L. Gleason Dian He Brian Whitcomb Lindsey Russo Jagteshwar Grewal Cuilin Zhang Samrawit F. Yisahak Stefanie N. Hinkle John Owen Germaine M. Buck Louis Roger Newman William Grobman Anthony C. Sciscione Angela Ranzini Sabrina Craig Edward Chien Daniel Skupski Deborah Wing Katherine L. Grantz

Background: Physical activity (PA) is associated with perinatal benefits such as lower risk of gestational diabetes and preterm birth. PA reportedly decreases in pregnancy, but most prior studies were limited to non-Hispanic (NH) white women with normal body mass index (BMI). We investigated PA variation by race/ethnicity, BMI, parity, and baseline PA over gestation.

Methods: Metabolic equivalent of task (MET)-hr/week of total PA (sum of domestic, occupational, exercise, transportation, inactive) was calculated from PA reported 6 times by 2778 women with singleton gestations on the Pregnancy PA Questionnaire. Linear mixed models were used to model MET-hr/week by race/ethnicity (NH white, NH Black, Hispanic, Asian/Pacific Islander (API)), BMI (<25, 25-<30, ≥ 30 kg/m²), parity (0, 1, >1), and baseline PA (quartiles). Baseline PA (collected at 10-13 weeks) represented PA over the past year. Models were adjusted for age, prior miscarriage, jobs, marital status, education, race/ethnicity, parity, and BMI.

Results: Total median PA declined 47%, from 297 MET-hr/week at 10 weeks to 157 MET-hr/week at 40 weeks gestation. NH Black women had significantly higher PA than NH white or Hispanic women at weeks 11-13, and NH white women had significantly higher PA than NH Black, Hispanic, or API women at weeks 35-39; mid-pregnancy PA was similar across groups. Nulliparas had significantly lower PA than primiparas or multiparas each week from 10-39. Total PA did not vary by pre-pregnancy BMI. Baseline PA was strongly associated with later PA (Figure): women in the highest quartile reduced their PA from a median of 576 to 204 MET-hr/week, while women in the lowest quartile had more stable PA (decreasing from median 145 to 120 MET-hr/wk) from weeks 10-40.

Conclusion: Understanding pregnancy PA by race/ethnicity and parity may help target interventions for groups with lower PA. Baseline PA was strongly associated with PA across gestation, suggesting PA should be discussed early.



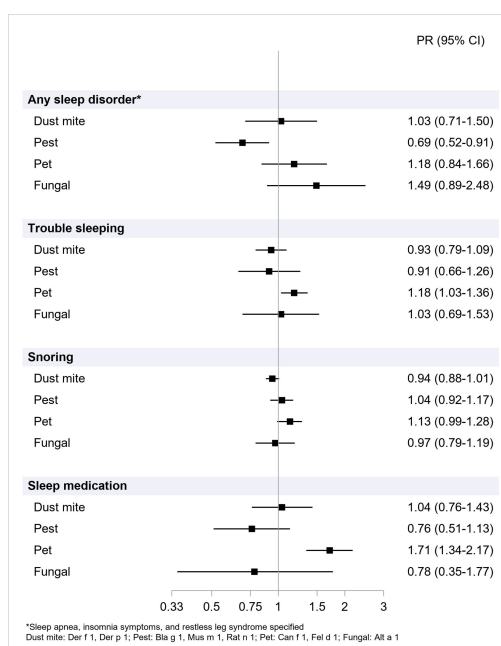
Exposure to allergens in the bedroom and sleep health Jesse Wilkerson* Jesse Wilkerson
Chandra L. Jackson Paivi M. Salo Lydia Feinstein Matthew Curry Michael B. Fessler Peter S. Thorne
Darryl C. Zeldin

Background: Exposure to allergens is common in U.S. bedrooms and can contribute to upper and lower respiratory problems/discomfort (e.g., congestion, sneezing, cough, wheezing, breathlessness), which may negatively impact sleep health. Few studies, however, have investigated allergen exposures and sleep health at the national level, especially using multiple sleep measures.

Methods: Among adult participants of the 2005-2006 National Health and Nutrition Examination Survey, we investigated associations between dust mite, pest, pet, and fungal allergen levels in the bedroom and self-reported sleep disorders, trouble sleeping, snoring, and frequent sleep medication use. Allergen levels were measured using vacuumed dust collected from bedroom beds or floors and were dichotomized at either the 75th or 90th percentile based on previously defined thresholds. Adjusting for sociodemographic, health behavior, and clinical characteristics, we used average marginal predictions from fitted logistic regression models to estimate prevalence ratios (PR) and 95% confidence intervals (CI) for each sleep measure, comparing participants above and below allergen thresholds.

Results: Among 3,403 participants, 7% reported a doctor-diagnosed sleep disorder, 25% told a doctor they have trouble sleeping, 51% reported being told they snore, and 10% used sleep medications ≥ 5 days/month. Most participants (72%) had ≥ 1 elevated allergen in the bedroom. Elevated pet allergens were associated with a higher prevalence of trouble sleeping (PR: 1.18; CI: 1.03-1.36), snoring (PR: 1.13; CI: 0.99-1.28), and frequent sleep medication use (PR: 1.71; CI: 1.34-2.17). Conversely, elevated pest allergen levels were associated with a lower prevalence of a sleep disorder (PR: 0.69; CI: 0.52-0.91). Elevated levels of dust mite and fungal allergens were not associated with sleep health.

Conclusions: Elevated allergen levels in the bedroom may influence sleep health in the U.S. population. More research is needed.



Plant-based dietary patterns and breast cancer recurrence and survival in the Pathways Study Ijeamaka Anyene* Ijeamaka Anyene Isaac Ergas Lawrence Kushi Marilyn Kwan Elizabeth M. Cespedes Feliciano

Background

Plant-based diets are recommended for cancer prevention and control, but some plant-based foods are associated with adverse health outcomes. For the first time, we evaluated whether an overall and a healthful plant-based dietary quality index were associated with the risk of breast cancer recurrence, all-cause and non-breast cancer death post diagnosis.

Methods

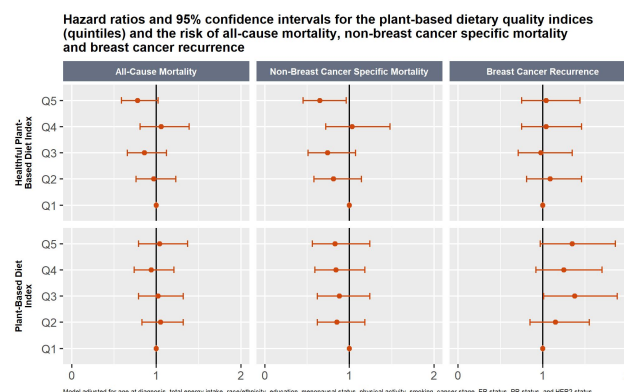
We included 3,660 women diagnosed with invasive breast cancer from 2005-2013 with an average age at diagnosis of 59.7. Food frequency questionnaires completed an average of 2.3 (range: 0.7-18.7) months after diagnosis were used to derive the healthful plant-based diet index (hPDI, which assigned positive scores to healthy plant foods, but reverse scores to animal foods and unhealthy plant foods) and overall plant-based diet index (PDI, which assigned positive scores to plant foods and reverse scores to animal foods). 461 breast cancer recurrences and 655 deaths occurred over 40,888 person-years of follow-up. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals, adjusting for total energy, demographic, health-related behaviors, and tumor characteristics.

Results

Women with the highest hPDI scores (quintile 5 vs 1) had a reduced hazard of all-cause mortality (HR: 0.78 (0.59-1.02)) and non-breast cancer mortality (HR: 0.65 (0.45-0.96)) but no association with breast cancer recurrence (HR: 1.04 (0.75-1.44)). Women with the highest PDI scores (quintile 5 vs 1) had no association with all-cause mortality (HR: 1.04 (0.79-1.37)) and a reduced hazard of non-breast cancer mortality (HR: 0.83 (0.56, 1.24)) and an increased hazard of breast cancer recurrence (HR: 1.35 (0.97-1.86)).

Conclusion

The two plant-based indices had differing associations with all-cause and non-breast cancer death and breast cancer recurrence. Therefore, it may be important to distinguish between healthful and unhealthy plant-based diets in lifestyle change recommendations.



Self-Efficacy's Influence on Outings and Contacts During the COVID-19 Pandemic Gillian A.M. Tarr* Gillian Tarr Keeley Morris Alyson Harding Sato Ashida Samuel Jacobs Kumi Smith Austin Rau Jesse Berman Timothy Church Marizen Ramirez

Background

Successful strategies for pandemic suppression require understanding what influences individual adherence to restrictions, such as stay at home orders or physical distancing. The objective of this study was to identify socio-behavioral factors (e.g. psychological distress, self-efficacy) associated with less frequent outings and fewer non-work, non-household contacts during the initial restrictions of the COVID-19 pandemic.

Methods

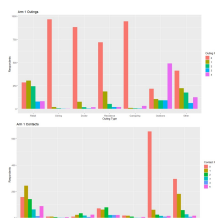
We surveyed 1,001 adults from families with children in April and May 2020. We used the Stress and Coping Model to understand the impacts of 1) stress in response to the pandemic measured by the Kessler-6 and 2) self-efficacy as a coping resource, on coping by reducing outings and contacts. Censored Poisson regression was used to convert right-censored outing and contact variables to continuous variables. We used multiple imputation by chained equations for missing data, principal components analysis to reduce the dimensionality of contextual variables, and negative binomial models to test the associations from our Stress and Coping Model.

Results

Outings and contacts are shown in the Figure. There was no association between stress and outings (OR 1.01; 95% CI 0.98, 1.03) or contacts (OR 1.00, 95% CI 0.96, 1.04). Self-efficacy for preventive behaviors (e.g., staying 6 feet away from others in public, quarantining when warranted) was consistently associated with both outings (OR 0.82, 95% CI 0.71, 0.96) and contacts (OR 0.60, 95% CI 0.47, 0.78). This effect was robust to removing outdoor outings and contacts from the total.

Conclusions

Confidence in one's ability to follow public health guidelines to prevent COVID-19 transmission was associated with fewer outings and substantially fewer non-household, non-work contacts among adults with children. In concert with understanding the determinants of self-efficacy, this can be leveraged to improve public health campaigns to reduce disease transmission.



Team diversity increases step counts in collaborative arms, and reduces them in competitive arms of a behavioral gamification intervention trial Jeffrey Rewley* Jeffrey Rewley

Background:

Team diversity is an important factor relating to productivity, but the evidence of its effects is mixed. In this study, we aim to examine how team diversity affects team performance vis-a-vis step counts in a setting where teams were randomly assigned.

Methods:

Participants were randomized into teams of three on enrollment and were assigned to either competitive or collaborative arms. The competitive teams received leaderboard information. The collaborative teams had one randomly-selected member selected each day to represent the team.

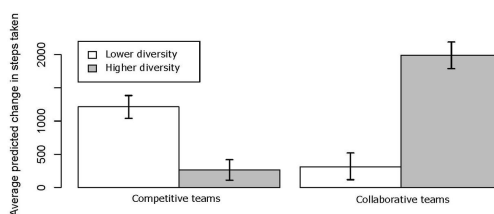
We fit generalized estimating equations clustered by teams using participant step counts as an outcome in the collaborative and competitive arms separately. We included individual and team characteristics as predictors. We created team characteristics of categorical variables via the number unique values which we observed in the team. For continuous characteristics, we calculated the range of values observed in the team.

Results:

In the collaborative arm, team diversity was positively-associated with step counts. Having 3 races present in a team increased step counts by 1,739 (95% CI: 427 to 3,051). In the competitive arm, team diversity was generally negatively-associated with step counts; having 3 races present in a team reduced step counts by 1,481 (95% CI: -2,947 to -16). Individual and team characteristics more-strongly predicted outcomes in the collaborative arm ($R^2 = 0.63$) vs the competitive arm ($R^2 = 0.44$).

Conclusions:

We found that increasing diversity was positively associated with step counts among collaborative teams, and negatively associated among competitive teams. This indicates people may be more willing to work with those less like them and more willing to compete with those who are more similar. As well, the total steps taken was more-accurately predicted by characteristics of those in collaborative teams as compared to competitive teams indicating a more homogeneous response to collaborative rather than competitive conditions.



Average predicted change in steps from baseline to the end of the study period for teams without diversity compared to teams with high diversity. For no diversity, all predictor variables of team diversity were set to the minimum possible value (e.g. an age range of 0). For high diversity, all team diversity independent variables were set to the maximum for categorical variables, or the inter-quartile range for continuous variables. Error bars represent 95% confidence intervals calculated from bootstrap sampling.

Residential Green Space and Fecundability in a North American Preconception Cohort

Study Mary Willis* Mary Willis Amelia K. Wesselink Perry Hystad Kirupto Kirwa Elizabeth E. Hatch Lauren A. Wise

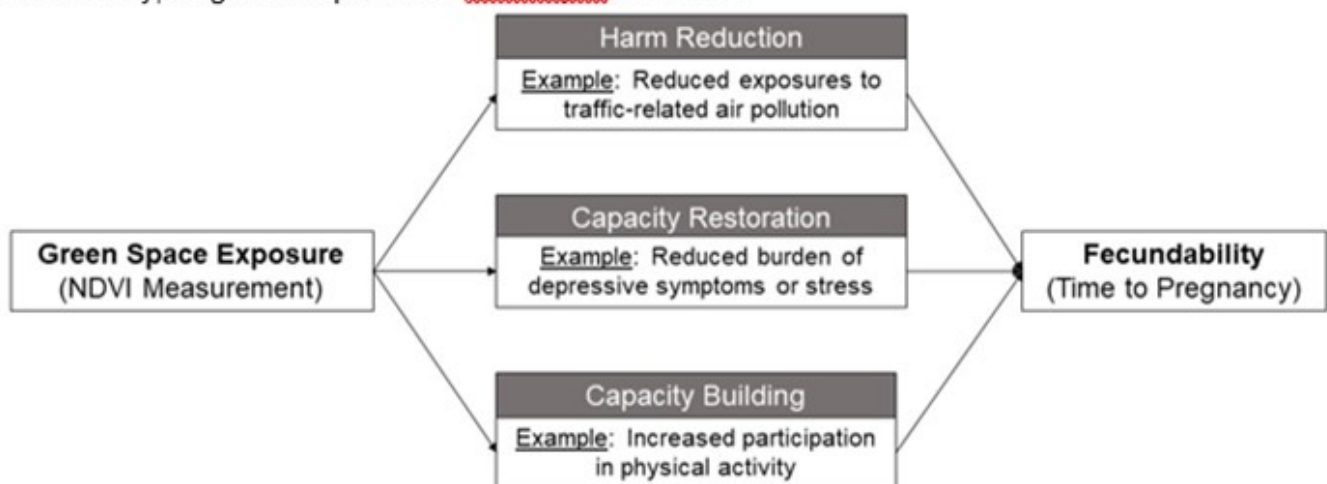
Background: A growing body of literature suggests that exposure to green space (natural vegetation) may have positive effects on human health, including reproductive health. Residential green space may improve health via reduced exposure to traffic-related air pollution, reduced depressive symptoms or stress levels, and increased physical activity (Figure 1). We hypothesize that increased exposure to green space may also promote fecundability, a sensitive marker of fertility.

Methods: In a large North American preconception cohort study (Pregnancy Study Online, PRESTO), we examined associations between residential green space (measured by satellite normalized difference vegetation index [NDVI] at a 30m resolution) and fecundability (per-cycle probability of conception). From 2013 through 2019, women aged 21-45 years who were trying to conceive without fertility treatment completed online questionnaires every 8 weeks for up to 12 months. We followed participants until reported pregnancy or a censoring event (end of pregnancy attempt, loss to follow-up, initiation of fertility treatment, or 12 menstrual cycles) whichever came first. Using geocoded residential addresses over follow-up, we calculated seasonal NDVI within 50-500 meter buffers around each residence to quantify green space exposure. We used proportional probabilities regression models to estimate fecundability ratios (FR), adjusting for sociodemographic and lifestyle characteristics.

Results: Among 7,644 pregnancy planners, adjusted models show a 7% (95% CI: 0.98, 1.13) increased when comparing the he top quintile (most green space) to the bottom quintile (least green space) within 250m of a residence. Results are similar for other distance buffers.

Conclusion: We present the first epidemiologic evidence that residential greenness is positively associated with fecundability. Future work will examine the role of key pathways that may mediate this relationship.

Figure 1: Conceptual overview of hypothesized pathways linking green space exposure to increased fecundability, diagram adapted from [Markevych et al. 2017](#)



NDVI: Normalized Difference Vegetation Index, a satellite-based metric of green space.

Environment/Climate Change

Associations of unconventional natural gas development activity with adolescent internalizing disorders Irena Gorski-Steiner* Irena Gorski-Steiner, MPH Brian S. Schwartz, MD

While UNGD has been of public concern for over a decade, no study yet has evaluated the relationship between UNGD and health outcomes in adolescents, despite recognition that young people may be the most vulnerable population for the adverse effects of environmental exposures. Identifying factors associated with depression and anxiety is of high importance because these disorders can decrease quality of life and require high expenditures for public health. Prior research implicates two primary pathways from UNGD activity, air quality and community impacts (e.g., truck traffic, noise, vibration, odors), both of which can impact the mental health of adolescents. We analyze associations of unconventional natural gas development activity (assigned at individual residential locations using metrics that incorporated spatial and temporal information on UNGD by the number and size of, and distance to, wells) with diagnosis and/or treatment of internalizing disorders (i.e., anxiety, adjustment, and depressive disorders) in adolescents in Pennsylvania using electronic health records from Geisinger from 2008-16. Our study design was a nested case-control with 7974 cases and 26,965 controls frequency-matched on sex, age, and year. We used logistic regression with generalized estimating equations, robust standard errors, an exchangeable correlation structure by administrative community type, and three levels of increasing covariate adjustment. When we evaluated associations using all years there were no associations, but in a sensitivity analysis, we restricted to years with high UNGD activity (2010-16; 33,294 adolescents). In this later subset of years, the fourth quartile (vs. first) of the UNGD activity composite was associated with higher odds of internalizing disorders (OR, 95% CI: 1.15, 1.06-1.25). In this first study of UNGD and adolescent health, we found that UNGD activity was associated with new-onset of internalizing disorders.

Environment/Climate Change

Assessing the Effect of Increasing Precipitation on Asthma Emergency Department Visits in New York State from 2005-2014 Arjita Rai* Arjita Rai Neil Muscatiello Temilayo Adeyeye Tabassum Insaf

Precipitation, through its effect on other seasonally varying factors (e.g., pollen), may impact the occurrence of asthma symptoms. Literature review shows some evidence of an association between precipitation and asthma. Previous ecological studies have relied on sparsely situated land-based monitors to estimate human exposure to spatially variable meteorological data. This analysis aims to explore the association between precipitation and risk of asthma emergency department (ED) visits in New York State (NYS) using a spatially contiguous 12 km gridded weather data.

Measures of daily total precipitation, maximum temperature, and heat index were obtained using NASA's North American Land Data Assimilation System data, which integrates satellite and ground based observations. Statewide data on ED visits for asthma (ICD-9 code 493) were obtained for 2005-2014 during non-winter months. A time-stratified, semi-symmetric, bi-directional, case-crossover study design was employed to assess the effect of precipitation on asthma. Piecewise linear splines were used to estimate thresholds, with adjustments for potential confounding by fine particulate matter and ozone.

The study period included 970,903 asthma ED cases, with the highest percentage of cases occurring in fall (39.4%). Daily precipitation totals ranged from 0-227.1mm, with a daily mean of 3.3mm and a 99th percentile at 35.4mm. We found a small, statistically significant risk of asthma ED visits when precipitation is above 60mm (RR=1.02, 95% CI:1.01,1.03). Seasonal differences exist, with spring showing a lower trigger point of 40mm (RR=1.02, 95% CI:1.01,1.03), as compared to summer (130mm; RR=1.05, 95% CI:1.003,1.09) and fall (60mm; RR=1.01, 95% CI:1.00; 1.03).

Extreme precipitation may be related to an increased risk of asthma ED visits in NYS. Although use of reanalysis data for precipitation estimates is still evolving, gridded estimates provide a means of addressing the gaps in exposure classification.

Environment/Climate Change

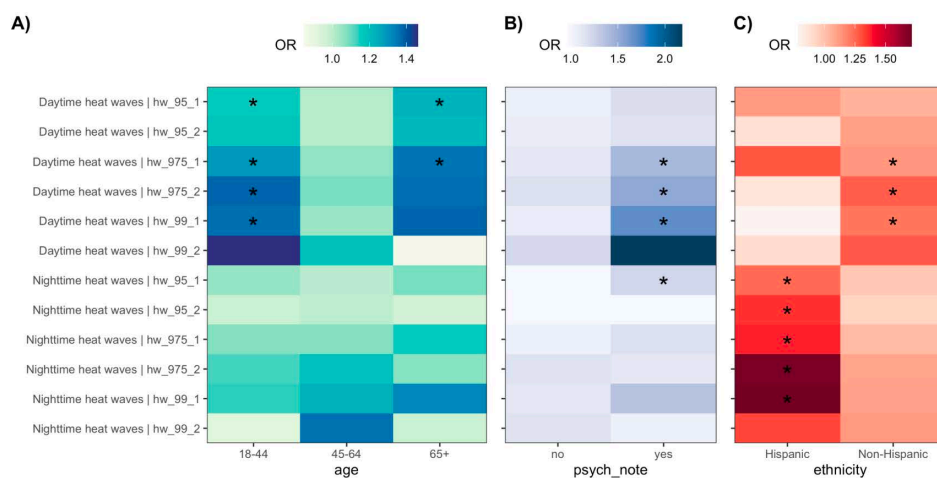
Heatwaves and Stillbirth in California and Oregon Megan Richards* Megan Richards Megjiao Huang Matthew Strickland Andrew Newman Joshua Warren Howard Chang Lyndsey Darrow

Background: It has been suggested that elevated ambient temperatures may be associated with an increased risk of stillbirth; however, the association is not well understood. Methods: We estimated the association between heatwaves and stillbirth using vital records from California (1996-2017) and Oregon (1991-2017). Stillbirths were matched 1:4 to live births based on maternal race, education and county of residence. Exposures were assigned at the county level using Daymet meteorological data, and days over the 97.5th percentile in each county were identified. Three heatwave definitions were used: (1) total number of days over the threshold in the previous week, (2) number of continuous days over the threshold in the previous week, and (3) the average degrees Celsius over the threshold over the previous week. Odds ratios and 95% confidence intervals (CI) were estimated using conditional logistic regression models adjusted for maternal age and time trends. Secondary models were stratified by stillbirth timing (before 28 weeks/after 28 weeks) or maternal race/ethnicity. Results: There were a total of 53,315 fetal deaths in California and 5,247 fetal deaths in Oregon during the study period. Across heatwave definitions, there was little evidence of association between heatwaves and risk of stillbirth. For California and Oregon, pregnant women who were exposed to at least two continuous days of heat were 1.01(CI: 0.97, 1.06) and 1.15(CI: 0.99, 1.34) times as likely to have a stillbirth compared to women who did not experience two continuous days of heat, respectively. As the heatwave duration became longer (2 continuous days, 3 continuous days, 4 continuous days), there was not a corresponding increase in the odds ratios. Stratified analyses were not meaningfully different than primary models. Sensitivity analyses using case-crossover and survival analyses yielded similar results. Conclusion: Heatwaves did not increase the risk of stillbirth in California or Oregon.

Heat waves and emergency department visits among the homeless Lara Schwarz* Lara Schwarz Edward M Castillo Theodore C Chan Jesse J Brennan Emily S Sbiroli Gabriel Carrasco-Escobar Alexander Gershunov Tarik Benmarhnia

Homelessness is a major social challenge in the United States and was projected to increase by 40-45% in 2020. People experiencing homelessness are believed to be particularly vulnerable to the health effects of heat waves, but epidemiological evidence to substantiate it is lacking. This study aims to determine the effect of heat waves on emergency department (ED) visits for individuals experiencing homelessness and explore vulnerability factors. A unique dataset was utilized with granularity on socio-demographics of ED visits in San Diego from 2012 to 2017. A time stratified case-crossover design was applied to study the association between various heat wave definitions and ED visits. Twelve measures of heat waves, considering three percentile thresholds (99, 97.5, 95) of varying durations (1, 2 days) based on maximum and minimum temperature were analyzed. Associations were compared to matched non-homeless population using coarsened exact matching based on age, gender and race/ethnicity. Of the 17,478 ED visits identified as homeless, most were under the age of 65 (94%), of non-Hispanic ethnicity (85%), and 14.8% included a psychiatric consultation. Results indicated a positive association, with the strongest risk of ED visits during daytime (ex: 97.5th percentile, 2 days) heat waves [odds ratio:1.21, 95% confidence interval:1.05, 1.40]. Homeless patients that were younger and elderly, of Hispanic ethnicity, and that required a psychiatric consultation were particularly vulnerable to heat waves. Odds of ED visits were higher for homeless visits after matching to non-homeless. These results demonstrate the importance of prioritizing homelessness in heat action plans and considering vulnerability factors to reduce this burden.

Figure: Odds ratios of heat wave impacts on emergency department visits among homeless patients, May to September, 2012 to 2017 by A) age group B) encounter with a psychiatric consult C) Hispanic ethnicity.



* indicates that the 95% confidence interval does not cross the null

What is the true prevalence of drug use in the general population? Simulating underreported and unknown use for more accurate national estimates Natalie S Levy*
 Natalie S Levy Joseph J Palamar Stephen J Mooney Charles M Cleland Katherine M Keyes

Background

National estimates of drug use are critical to public health surveillance. However, available estimates rely on self-report and suffer from misclassification due to underreported and unknown use. We outline a quantitative bias analysis-based approach that leverages data on the magnitude and correlates of misclassification to correct national data for observed sensitivity and specificity, providing more accurate estimates of drug use in the United States (US) general population.

Methods

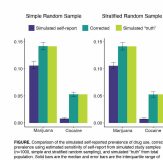
We simulated a population (n=100,000) reflecting the demographics of the US adult population based on the 2018 American Community Survey. Within this population, we simulated counts of self-reported past-month cannabis and cocaine use derived from National Survey on Drug Use and Health (NSDUH) 2018 data. We generated “true” counts by increasing self-reports by a probability of underreporting drawn from existing literature. We applied our algorithm to simple and stratified random samples of the simulated population to produce corrected prevalence estimates (calculated by dividing self-reported prevalence by estimated sensitivity) to recover the “true” population prevalence, validating our approach. We then applied this same method to 2018 NSDUH data to produce a range of misclassification-corrected estimates.

Results

Simulated self-report sensitivities varied by drug and sampling method (cannabis: 77.6-78.5%, cocaine: 14.3-22.1%.) Across repeated samples, median corrected prevalences closely approximated simulated “true” prevalences. Applying our algorithm substantially increased 2018 NSDUH estimates (*self-report*: cannabis=10.5%, cocaine=0.8%; *corrected*: cannabis=15.6-16.6%, cocaine=2.7-5.5%.)

Conclusion

National drug use prevalence estimates can be corrected for underreporting using a simple method. However, valid application of this method to correct existing estimates requires accurate data on the extent and correlates of misclassification in the general US population.

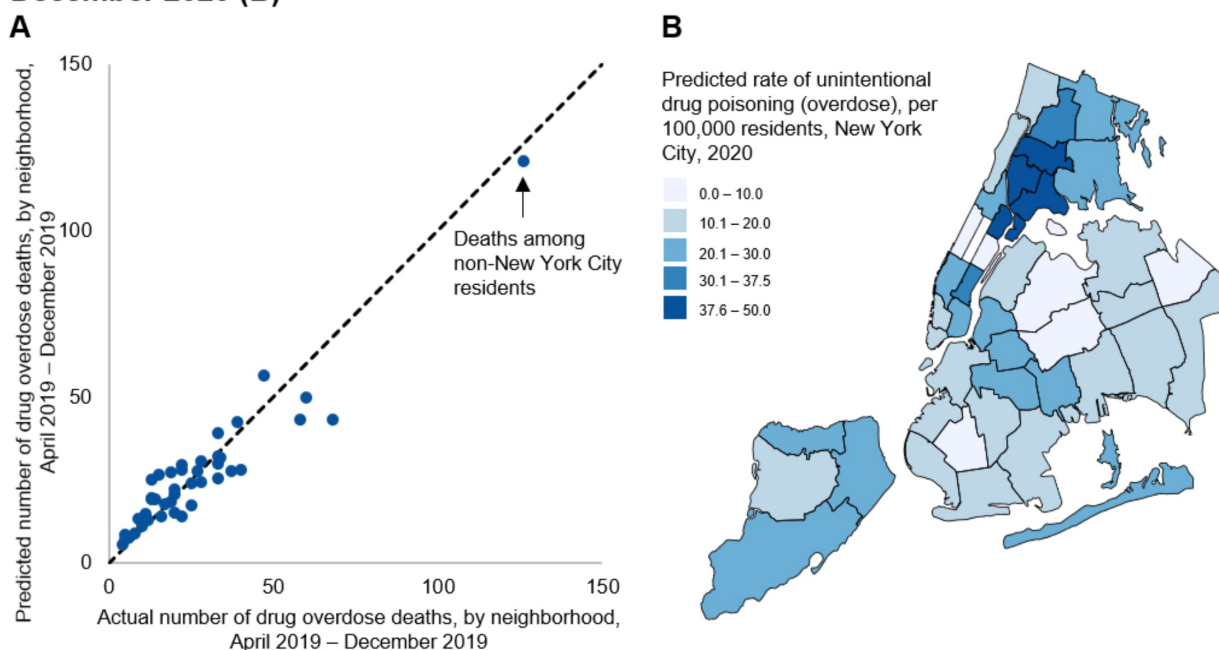


Nowcasting drug overdose deaths in New York City during the COVID-19 pandemic using emergency department syndromic surveillance data and machine learning methods

Michelle Nolan* Michelle Nolan Hillary V. Kunins Denise Paone

Background: During the COVID-19 pandemic, the number of deaths that required medical examiner investigation increased substantially; thus, the time to finalize the cause and manner of death increased, hindering timely surveillance. We used machine learning models to determine whether trends in drug overdose deaths could be predicted (“nowcasted”) using emergency department (ED) visits as measured by syndromic surveillance data. **Methods:** Using New York City (NYC) Department of Health and Mental Hygiene ED syndromic surveillance data, an automatic data feed from NYC hospitals, as predictor data, we calculated the number of ED visits from January 2017 – December 2020 by month and neighborhood for each of the following syndromes: overdose, opioid, drug, abuse/misuse, withdrawal, heroin, detoxification, and alcohol. We split data from January 2017 – March 2019 into a training dataset (75%, $n = 1,161$) and April 2019 – December 2019 into a testing dataset (25%, $n = 387$). We developed and tested models to predict the number of overdose deaths by month and neighborhood using linear regression and three machine learning models: least absolute shrinkage and selection operator-type regression, random forest, and gradient boosting machine. We used 10-fold cross-validation with three repeats and compared models using adjusted R^2 and Root Mean Square Error (RMSE). Using the best performing model, we compared the predicted number of overdose deaths to the actual number for April 2019 – December 2019 and predicted the number of overdose deaths through December 2020. **Results:** Random forest performed the best of the models tested (adjusted $R^2 = 0.61$, RMSE = 1.78). The three most influential variables, as measured by mean decrease in accuracy, were alcohol ED visits, overdose ED visits, and neighborhood. **Conclusion:** Machine learning models reliably nowcasted overdose mortality trends and can inform the implementation of place-based public health interventions to reduce overdose deaths.

Figure: Actual versus predicted drug overdose deaths, New York City, April 2019 – December 2019 (A) and predicted overdose deaths, New York City, January 2020 – December 2020 (B)



An Application of Marginal Structural Models to Evaluate Buprenorphine-Naloxone Effects on Opioid Overdose and Death among Patients with Opioid Use Disorder Tianyu Sun* Tianyu Sun Natallia Katenka Stephen Kogut Ashley Buchanan

Opioid use disorder (OUD) is a chronic disease requiring long-term treatment and is associated with opioid overdose and increased risk of mortality. However, no existing randomized clinical trial has assessed the efficacy of pharmacological treatment on subsequent overdose and mortality due to a limited duration of patient follow-up and ethical considerations. We aimed to emulate a target trial to assess the association between continuously receiving buprenorphine-naloxone during follow-up and opioid overdose and death using the Optum deidentified Clinformatics® Data Mart Database when the randomized clinical trial was unavailable or infeasible. The target patient population was insured adult patients with newly diagnosed OUD in the US during 2010-2017. The first eligible OUD diagnosis in the database was defined as the start of follow-up. Patients were required to be continuously enrolled during baseline (the one year before the first OUD diagnosis), had not received medications for OUD during the baseline, and had at least 30 days of follow-up. We identified 58,835 patients. A marginal structural model was fit using inverse probability weights to account for measured baseline and time-varying covariates, as well as possibly informative loss-to-follow-up. Continuous receipt of buprenorphine-naloxone was associated with a reduced risk of opioid overdose (hazard ratio (HR) = 0.66, 95% confidence interval (CI): 0.49, 0.91), all-cause death (HR= 0.24, 95% CI: 0.08, 0.75), and overdose or death (HR= 0.58, 95% CI: 0.40, 0.84). The E-value for the hazard ratio of death was 7.8. It was much larger than the upper 95% CI of the association between each measured baseline variable and all-cause death in the model. We can assume that the unmeasured confounding itself likely does not explain the observed estimate of the effect of treatment on the endpoint of all-cause mortality.

Cycles of chronic opioid therapy following prescription drug monitoring program mandatory use legislation: A retrospective cohort study Bennett Allen* Bennett Allen Victoria A. Jent Magdalena Cerdá

Background

Laws mandating prescriber use of prescription drug monitoring programs (PDMPs), state databases that track opioid analgesic (OA) and other controlled substance prescriptions, are associated with reductions in OA prescribing. Some research indicates prescribers may use mandates to terminate patients from chronic opioid therapy (COT), leading to COT cycles that may increase overdose risk through care discontinuity. We estimate risks of COT cycling in New York City (NYC) due to the PDMP mandate, compared to risks in neighboring New Jersey (NJ).

Methods

We used monthly, patient-level data on OA prescriptions dispensed in NYC and NJ between August 2011 and July 2015. We defined COT as three sequential months of prescriptions, permitting one-month gaps. Exposure was mandate enactment in NYC; NJ was unexposed. We estimated risks of COT cycling using Prentice, Williams, and Peterson gap-time models adjusted for age, sex, dose, and payment type. Failure time was duration between cycles. Drawing on methodological developments in demography, we fit models in a life-table difference-in-differences (DID) design to estimate causal risks using cohort data. Sub-group analysis estimated cycling risk among patients receiving high-dose prescriptions. Sensitivity analyses to test robustness to cycle volume considered only first cycles using Cox proportional hazard DID models.

Results

The cohort had 7,604 patients dispensed 12,695 prescriptions. The overall cycling risk in NYC post-mandate was HR 1.01 (0.94-1.08). For high-dose prescriptions, the risk was HR 1.17 (1.02-1.34). Sensitivity analyses identified an overall risk of HR 1.01 (0.94-1.11) and high-dose risk of 1.09 (0.91-1.31).

Conclusions

The PDMP mandate had no overall effect among patients in NYC, but increased cycling risk among high-dose patients by 17%, highlighting the potential for overdose through care discontinuity. As state mandates expand, provider education in the treatment of high-dose COT patients is necessary.

Association between statewide opioid prescribing interventions and opioid prescribing patterns in North Carolina, 2006-2018 Courtney Maierhofer* Courtney Maierhofer Shabbar I. Ranapurwala Bethany L. DiPrete Naoko Fulcher Christopher L. Ringwalt Paul R. Chelminski Timothy J. Ives Nabarun Dasgupta Vivian F. Go Brian W. Pence

Objective. To examine the impact of three sequential statewide policy and legislative interventions on opioid prescribing practices among privately insured individuals in North Carolina.

Methods. An interrupted time series approach was used to examine level and trajectory changes of new and prevalent opioid prescription rates, days' supply, and daily morphine milligram equivalents before and after implementation of a 1) prescription drug monitoring program, 2) state medical board initiative, and 3) legislative action. Analyses were conducted using individual-level claims data from a large private health insurance provider serving North Carolina residents, ages 18-64, from January 2006-August 2018.

Results. Rates of new and prevalent prescription opioid patients were relatively unaffected by the prescription monitoring program but sharply declined in the months immediately following both medical board (-3.7 new and -19.3 prevalent patients per 10,000 person months) and legislative (-14.1 new and -26.7 prevalent patients) actions. Among all opioid prescriptions, days' supply steadily increased on average over the study period, but declined after legislative action (-1.5 days' supply per year).

Conclusions. The voluntary prescription drug monitoring program launched in 2010 only marginally affected opioid prescribing patterns on its own, but its redeployment as an investigative and clinical tool in multifaceted public policy approaches by the state medical board and legislature later in the decade plausibly contributed to notable declines in prescription rates and days' supply. This study lends new emphasis to the importance of enforcement mechanisms for state and national policies seeking to reverse this critical public health crisis.

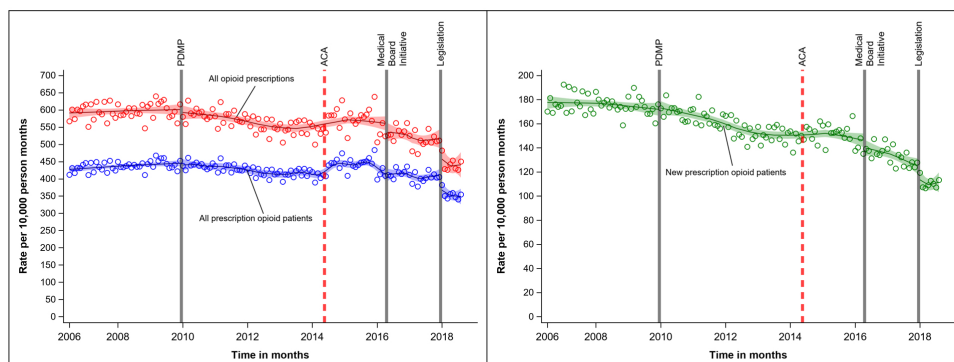


Figure 1. Prescription opioid rates, per 10,000 person-months, among privately insured North Carolina residents from July 2006 through August 2018.

Note. PDMP=Prescription Drug Monitoring Program; ACA=Affordable Care Act; Medical Board Initiative=Safe Opioid Prescribing Initiative; Legislation=Strengthen Opioid Misuse Prevention Act. New prescription opioid patient population includes person-months where the individual has been insured continuously for ≥ 6 months and has no opioid prescription in the prior 6 months. All prescription opioid patient population includes person-months where the individual has been insured continuously for ≥ 6 months regardless of prior opioid prescriptions.

Neighborhood Walkability and Mortality in a Prospective Cohort of Women Sandra India Aldana* Sandra India Aldana Andrew G. Rundle Anne Zeleniuch-Jacquotte James W. Quinn Byoungjun Kim Yelena Afanasyeva Tess Clendenen Karen L. Koenig Mengling Liu Kathryn M. Neckerman Lorna E. Thorpe Yu Chen

Background

There is paucity of long-term prospective studies evaluating community-level walkability characteristics in relation to risk of death.

Objective

To assess the association between baseline measures of neighborhood walkability (NW) and risk of death in a large prospective cohort of women (the New York University Women’s Health Study, or NYUWHS).

Methods

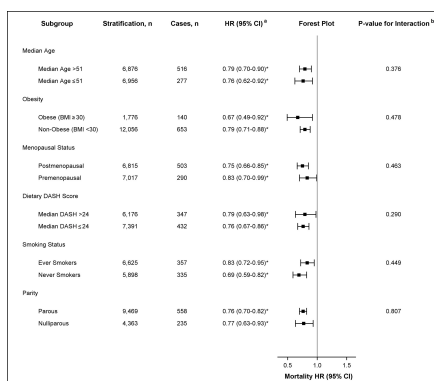
Baseline residential addresses of 13,832 women in the NYUWHS were geo-coded and the Built Environment and Health Neighborhood Walkability Index (BEH-NWI) was calculated for each participant’s neighborhood. The participants were recruited from 1985 to 1991 in NYC and followed up for an average of 27 years. We conducted survival analyses using Cox proportional hazards models to assess the association between BEH-NWI and the risk of all-cause mortality and mortality from obesity-related diseases, cardiometabolic diseases, and obesity-related cancers.

Results

Residing in a neighborhood with a higher BEH-NWI score was associated with a reduced risk of death. Compared to women in the bottom BEH-NWI tertile, those in the highest tertile were 0.96 times (95% CI: 0.93-0.99), 0.91 times (95% CI: 0.86-0.97), and 0.72 times (95% CI: 0.62-0.85) less likely to die from any cause, obesity-related diseases, and particularly, obesity-related cancers, respectively, adjusting for confounders. In stratified analyses, the protective associations with obesity-related cancers were consistent across potential risk factors (**Figure 1**). No association was found between BEH-NWI and risk of death from cardiometabolic diseases. Results were similar in analyses censoring women at moving time, and using propensity scores matching women with high and low BEH-NWI on potential confounders. Baseline BMI, outdoor walking, and/or history of diabetes mediated 6% to 40% of the association between NW and mortality.

Conclusion

Our findings suggest a protective role of NW in obesity-related mortality in women, particularly obesity-related cancer mortality.



The association between serum mercury concentration and cognitive impairment: the REasons for Geographic and Racial Differences in Stroke study Yijia Zhang* Yijia Zhang Cheng Chen Liping Lu Frederick Unverzagt Leslie A. McClure Marguerite R. Irvin Suzanne Judd Mary Cushman Ka Kahe

Objective: The objective of this study is to examine the association between serum mercury concentration and cognitive impairment.

Methods: A random sub-cohort of participants ($n=2064$) from the REasons for Geographic and Racial Differences in Stroke cohort (2003–present) were classified into quintiles based on serum mercury concentration (<0.02 , $0.02-0.03$, $0.03-0.04$, $0.04-0.07$, and >0.07 $\mu\text{g/dL}$). Cognitive impairment was defined as scoring below four on the Six-Item Screener (SIS) in the most recent assessment as of September 29, 2018. Multiple logistic regression was used with adjustment for age, sex, race, education level, household income, smoking status, alcohol consumption, physical activity, BMI, medical histories of dyslipidemia, hypertension, and diabetes, systolic blood pressure, total cholesterol, LDL-cholesterol, depression, long-chain omega-3 polyunsaturated fatty acid intake, and serum arsenic.

Results: Based on participants' most recent SIS score, a total of 255 cases of cognitive impairment were identified. After adjustment for potential confounders, compared to the lowest quintile (Q1) of serum mercury, participants in the higher quintiles were more likely to have cognitive impairment (odds ratio [95% confidence interval] = 1.85 (1.15–2.98) for Q2; 1.65 (0.98–2.78) for Q3; 2.00 (1.20–3.33) for Q4; 2.09 (1.22–3.59) for Q5; P for trend = .046).

Conclusions: This prospective study suggested that serum mercury was associated with cognitive impairment in US adults.

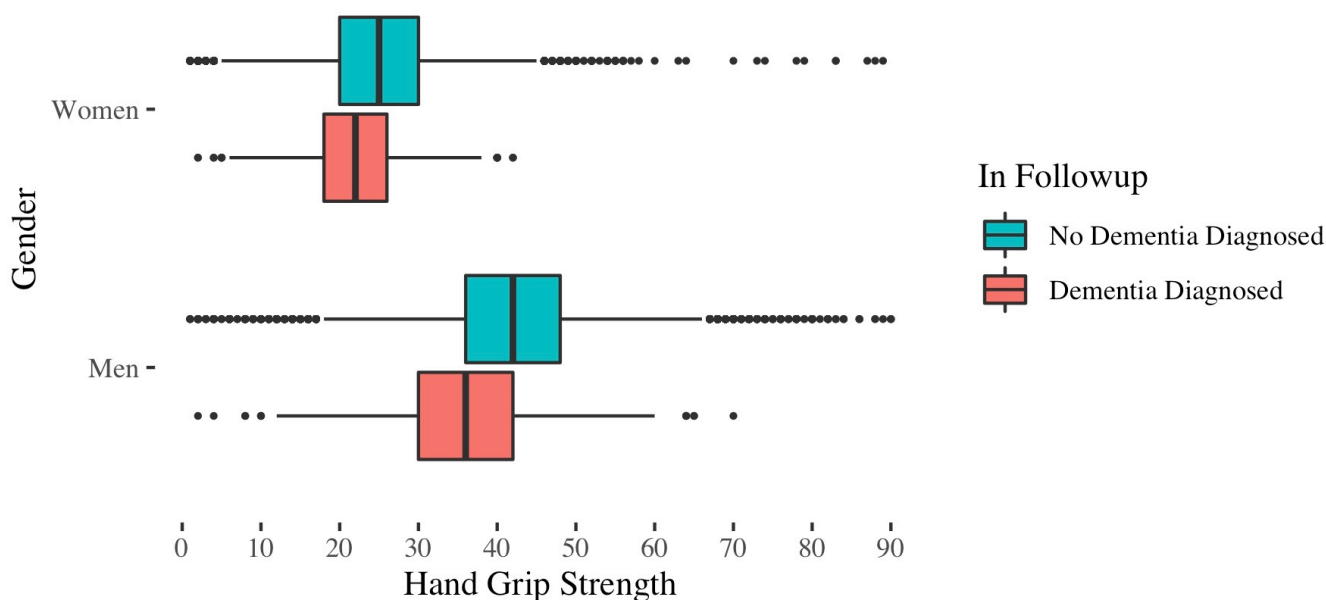
Handgrip strength is associated with dementia risk: Results from the UK Biobank Kate A. Duchowny* Sarah Ackley Kate A. Duchowny Scott C. Zimmerman Willa D. Brenowitz M. Maria Glymour

Introduction: Previous work indicates biological processes antecedent to neurodegeneration cause early changes in physical health well in advance of both cognitive impairment and dementia diagnosis. Handgrip strength (HGS), a simple, reliable surrogate measure of total body muscle strength, may be an important early marker of dementia risk.

Methods: Dementia-free UK Biobank participants aged 39-73 were enrolled during 2006-2010 (N=497,782) and completed HGS assessments via dynamometer. Fluid intelligence and prospective memory (N=163,835) were assessed with touch-screen tests and standardized by subtracting the mean and dividing by the standard deviation. Dementia diagnoses were obtained from primary care and hospital records over a median of 9.0 years (IQR:1.4) of followup. Linear and Cox proportional hazard models were used to assess the relationship between HGS, current cognitive status, and incident dementia diagnosis. All models were adjusted for gender, age, and age²; secondary models also adjusted for APOE-e4 allele status, race, education, and Townsend deprivation index.

Results: In minimally adjusted models, for every 1 kg lower in HGS, average standardized fluid intelligence was 0.012 (95% CI: 0.011, 0.013) points lower. This association was largely attenuated after full covariate adjustment (b=0.004, 95% CI: 0.004, 0.005). Full covariate adjustment also attenuated results for prospective memory. Each 1 kg lower in HGS was associated with a 4.5% (95% CI: 3.8%, 5.0%) higher hazard of incident dementia in minimally adjusted models, and 4.4% (95% CI: 3.8%, 5.0%) higher hazard in a fully adjusted model.

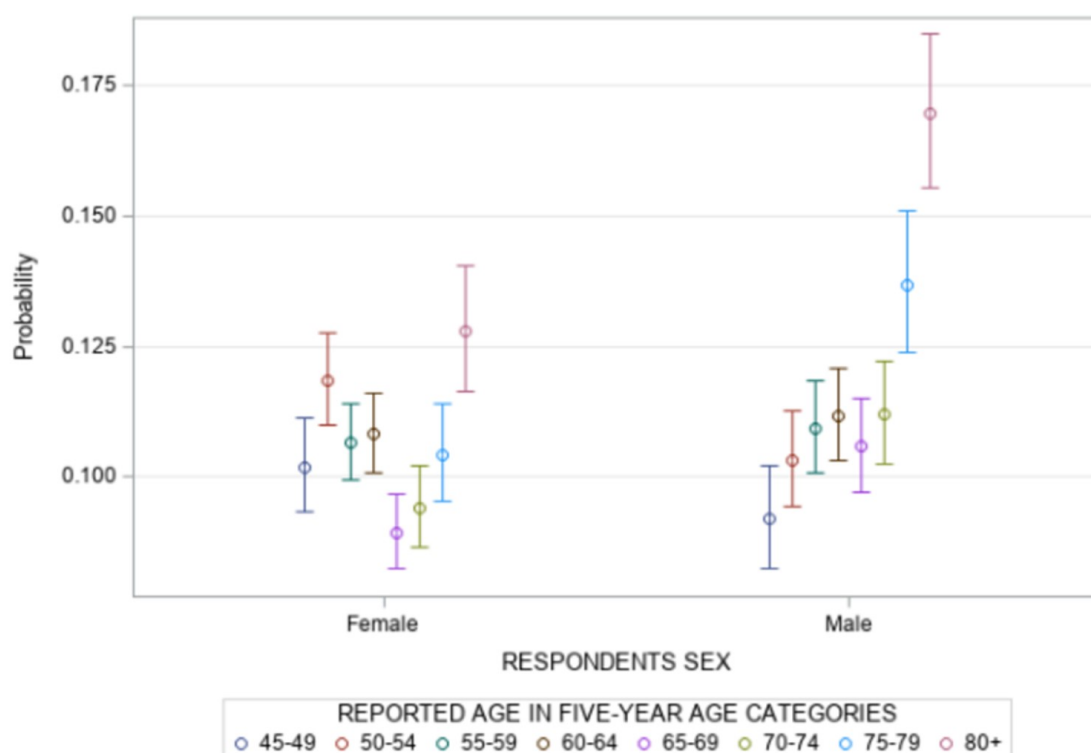
Discussion: HGS in middle aged and older adults is not strongly associated with contemporaneously measured cognition, but did predict incident dementia. Since prior research suggests a 2-4kg decrease in HGS is a clinically meaningful reduction in overall strength, our findings indicate handgrip strength may be an important marker of future dementia diagnosis.



Overall and sex-specific risk factors for subjective cognitive decline Karen Schliep* Karen Schliep Lily Gu Fares Qeadan Kristine Lynch Michelle Sorweid Michael Varner Norman Foster

Prior research using pooled results from meta-analyses has indicated that at least 35% of dementia risk may be amenable to prevention, but how modifiable factors impact subjective cognitive decline (SCD) in a single, nationally-representative sample and whether these factors differ between men and women has not been explored. Here, we estimate the population attributable fraction of potentially modifiable risk factors for SCD with a focus on sex differences. Data were collected from men and women (45 years and older) who completed the U.S. Behavioral Risk Factor Surveillance System Cognitive Decline Module (2015–2018), N=216,838. We calculated population attributable fractions for SCD, stratified by sex, of nine known modifiable risk factors, including limited education, deafness, social isolation, depression, smoking, physical inactivity, obesity, hypertension, and diabetes. Our models adjusted for age, race, income, employment, marital and Veteran status, and accounted for communality among risk factors. The final study sample included more women (53.7%) than men, but with similar prevalence of SCD (10.6% of women versus 10.9% of men). When examining association between age and SCD, women had a U-shaped relationship compared to men's positive linear relationship (Figure). After adjusting for demographics and communality, women and men had nearly equivalent overall population attributable fractions to explain SCD (39.7% for women versus 41.3% for men). Overall, the top three contributing risk factors were social isolation, depression, and hypertension, which explained three-quarters of the overall population attributable fraction, with minimal discrepancies between women and men. Future research assessing interplay between potentially early and mid-life modifiable factors, SCD, and risk for subsequent neurodegenerative disorders is warranted; as is further research on whether menopause may explain differential reporting of age of SCD in women versus men.

Age of Subjective Cognitive Decline



The longitudinal association between change in gait speed and incident falls in older adults Claire Adam* Claire Adam Erin Semmens Annette Fitzpatrick Cindy Leary Anjum Hajat Christina Park

Background Falls in older adults are a significant public health challenge, and screening for falls is important for prevention. Slower gait speed is associated with increased fall risk, and gait speed thresholds (e.g., 1 m/s) are often used to identify older adults with a higher fall risk. Change in gait speed, however, is an under-studied measure, potentially useful for characterizing individuals with increased fall risk, despite exceeding gait-speed thresholds. **Methods** We studied the association between gait speed and falls in 2,914 participants in the Ginkgo Evaluation of Memory Study, a randomized controlled trial conducted in four U.S. communities between 2000-2008. Gait speed was assessed annually with a 15-foot walk test, and falls were ascertained every 6 months by self or proxy report. We investigated the association between change in gait speed and risk of an incident fall using Cox proportional hazards models. Baseline change in gait speed was the difference between gait speed at the baseline visit and 0-6 months prior to a fall; annual change in gait speed was the difference between gait speed 12-18 months and 0-6 months prior to a fall. Models were adjusted for sex, race, study site, treatment, and mild cognitive impairment at baseline, with age as the time axis. **Results** Of the 830 participants with an incident fall, 35% (287) had a gait speed above 1 m/s prior to falling. Participants with decreasing gait speed, as measured by an annual change of $\geq 10\%$, had a significantly increased hazard of falling (HR: 1.20, 95% CI: 1.02-1.41), compared to participants whose gait speed increased over time. Decreased gait speed from baseline, a change of $\geq 10\%$, was not significantly associated with hazard of falling (HR: 1.13, 95% CI: 0.98-1.32). **Conclusions** These results provide evidence of an association between change in gait speed and fall risk, which has implications for how gait speed may be used to assess fall risk in a clinical setting.

One-year frailty state transitions among Medicare beneficiaries in the National Health and Aging Trends Study Emilie D Duchesneau* Emilie D Duchesneau Shahrar Shmuel Til Stürmer Allison Musty Jennifer L Lund

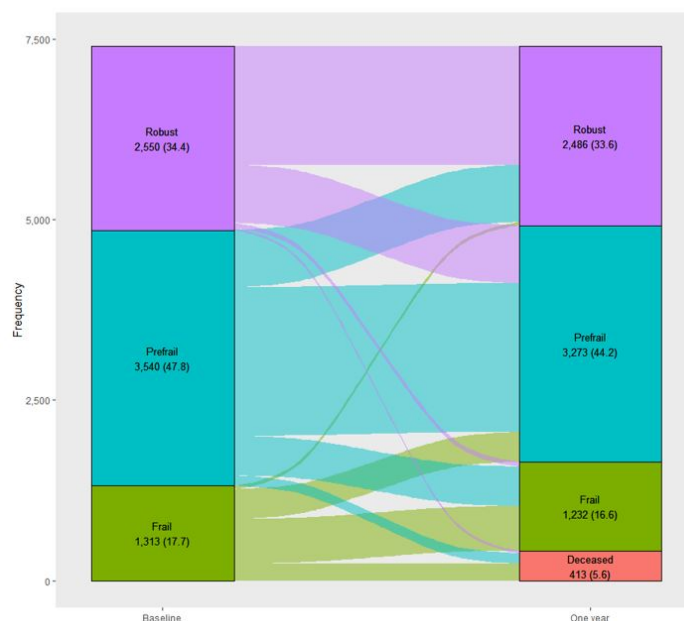
Introduction. Frailty, an age-related state of increased vulnerability to adverse outcomes, is common in older adults. Frailty is dynamic, but transitions are not well described. We described one-year frailty state transitions in a cohort of older adults and identified predictors of frailty progression.

Methods. This was a cohort study using baseline and one-year post-baseline data from the National Health and Aging Trends Study (2011 cohort). Community and non-nursing home residential care dwelling participants 65+ years were included. We assessed the five Fried frailty phenotype domains (exhaustion, low physical activity, shrinking, slowness, weakness) based on self-report and physical assessment. Missing domains were imputed. Frailty phenotype was categorized as robust: 0 domains; prefrail: 1-2, and frail: 3-5. Frailty state transitions were defined as movements between phenotype categories from baseline to one-year and were visualized using Sankey diagrams. Inverse probability weights were used to account for dropout. Frailty progression was defined as an increase in number of domains or death. Predictors of progression were identified using log-binomial regression that included demographic and clinical characteristics as independent variables.

Results. Our analytic sample included 7,404 adults. Baseline prevalence of prefrailty and frailty were 48% and 18%, respectively. The magnitude and direction of frailty state transitions are presented in the Figure. One, 4, and 18% of robust, prefrail, and frail individuals died during follow-up and 1,129 individuals dropped out. One-third of individuals experienced frailty progression or death. Older age, lung disease, dementia, and use of mobility devices were predictive of progression.

Conclusion. Frailty transitions and progression are common in older adults. Identifying individuals at risk of progression enables the development of targeted interventions that can delay frailty progression and improve quality of life.

Figure. One-year frailty state transitions in older adults in the National Health and Aging Trends Study



Sleep Medication Use and Increased Risk of Dementia in The Atherosclerosis Risk in Communities (ARIC) Study Kelsie M. Full* Kelsie M. Full Snigdha Pusalavidyasagar Priya Palta Kevin J. Sullivan Jung-Im Shin Adam P. Spira Pamela L. Lutsey

Background:

In the last two decades, the use of pharmaceutical sleep medications (sedative-hypnotics) has increased in the United States (US). Approximately 6% of older adults in the US report using sleep medications, with the prevalence of use increasing with age. Sleep medication use may be an indicator of sleep disturbances that are early markers of or contributors to neurologic disease. In this study, we tested the hypothesis that sleep medication use was associated with greater risk of incident dementia in a community-based cohort of aging adults.

Methods:

Participants in the Atherosclerosis Risk in Communities (ARIC) study (N=6,140; mean age=75.6 ± 5.2 years, 58.9% female, 22.4% black) were followed from 2011-2013 through 2017 for dementia diagnosis. Participants taking barbiturates, benzodiazepines, antidepressants, non-benzodiazepine receptor agonists(z-drugs), or other hypnotics in 2011-2013 were categorized as sleep medication users. Dementia cases were identified based on cognitive assessments and expert adjudication. Additional cases were identified through hospitalization discharge codes and diagnostic codes from death certificates. Cox proportional hazards regression models were used to estimate hazard ratios for time to dementia diagnosis.

Results:

Over a median 4.8 years of follow-up, 642 dementia cases were ascertained. After adjustment for demographics, sleep medication use was associated with incident dementia (Hazard Ratio (HR): 1.41; 95% Confidence Interval (CI): 1.19, 1.67). This association persisted after adjustment for lifestyle, physiological characteristics and APOE genotype (HR: 1.25, CI: 1.04, 1.49).

Conclusion:

In this study, we examined sleep medication use as a proxy for sleep disturbances. Study findings suggest a link between sleep medication use and incident dementia among older adults. Sleep medication use may be an important indicator to identify individuals with poor sleep who are high risk for dementia.

Table 1. Associations of Sleep Medication Use with Incident Dementia in the Atherosclerosis Risk in Communities (ARIC) Study (N=6,140)

Overall Sleep Medication Use	Non-users	Medication Users
Model 1	1.00 (reference)	1.26 (1.14, 1.39)
Model 2	1.00 (reference)	1.41 (1.19, 1.67)
Model 3	1.00 (reference)	1.23 (1.03, 1.47)
Model 4	1.00 (reference)	1.25 (1.04, 1.49)

Model 1: crude unadjusted results
 Model 2: Model 1 plus age, sex, education, education
 Model 3: Model 2 plus race/ethnicity (BMI, hypertension, current smoking status
 Model 4: Model 3 plus family history of dementia, hypertension, diabetes, prevalent dementia, prevalent
 *P<0.05, **P<0.01

Does the neighborhood social environment modify the effect of air pollution on incident dementia? Sindana Ilango* Sindana Ilango Christina Park Cindy Leary Erin Semmens Annette L Fitzpatrick Joel Kaufman Anjum Hajat

Background: Growing epidemiologic evidence suggests chronic exposure to air pollution increases risk of dementia in older adults. Cognitively stimulating activities and social interactions, made available through the social environment, may slow cognitive decline. Therefore, we examined whether the social environment offers resilience to the adverse effect of air pollution on dementia in a cohort of older adults.

Methods: This observational study draws from the Ginkgo Evaluation of Memory Study, a clinical trial aimed at understanding dementia prevention. Participants aged 75 years and older were enrolled between 2000 and 2002 and evaluated for dementia semi-annually through 2008. Long-term exposure (20 years before baseline) to fine particulate matter (PM_{2.5}) was assigned using annual averages from fine-scale spatiotemporal models. The effect of PM_{2.5} on incident dementia was examined with multi-level Cox proportional hazard models, with zip code as a random effect and adjusting for demographic and study visit characteristics. Census tract-level measures of the social environment at baseline (e.g., number of civic/social organizations and places of worship) from the National Neighborhood Data Archive were used to assess effect measure modification. Relative Excess Risk due to Interaction was estimated as a qualitative measure of additive interaction from the product term between air pollution and neighborhood social environment. Other measures of social environment, including neighborhood deprivation index, number of senior centers, and eateries will also be evaluated.

Results: This study included 2,587 individuals (mean age=78 years) free of mild cognitive impairment at baseline. For every interquartile range (IQR: 2.3 µg/m³) higher exposure to PM_{2.5}, risk of dementia was 22% higher (95% CI: 1.03, 1.43). We found no evidence of interaction between air pollution and neighborhood social environment on the additive scale. Additional analyses evaluating NDI and other metrics of the social environment are ongoing.

Conclusions: We found no evidence to suggest a synergistic effect between exposure to PM_{2.5} and measures of social environment on the additive scale. Given the many qualities of the social environment that may reduce dementia pathology, examination of other metrics are encouraged.

The intersectional impact of sex and social factors on subjective health: analysis of the Canadian Longitudinal Study on Aging (CLSA) Afshin Vafaei* Afshin Vafaei Susan Phillips Janelle Yu

OBJECTIVES: Self-rated health (SRH) is a widely validated measure of the general health of older adults. Our aim was to understand what factors shape individual perceptions of health and how those perceptions vary for men and women and across social locations.

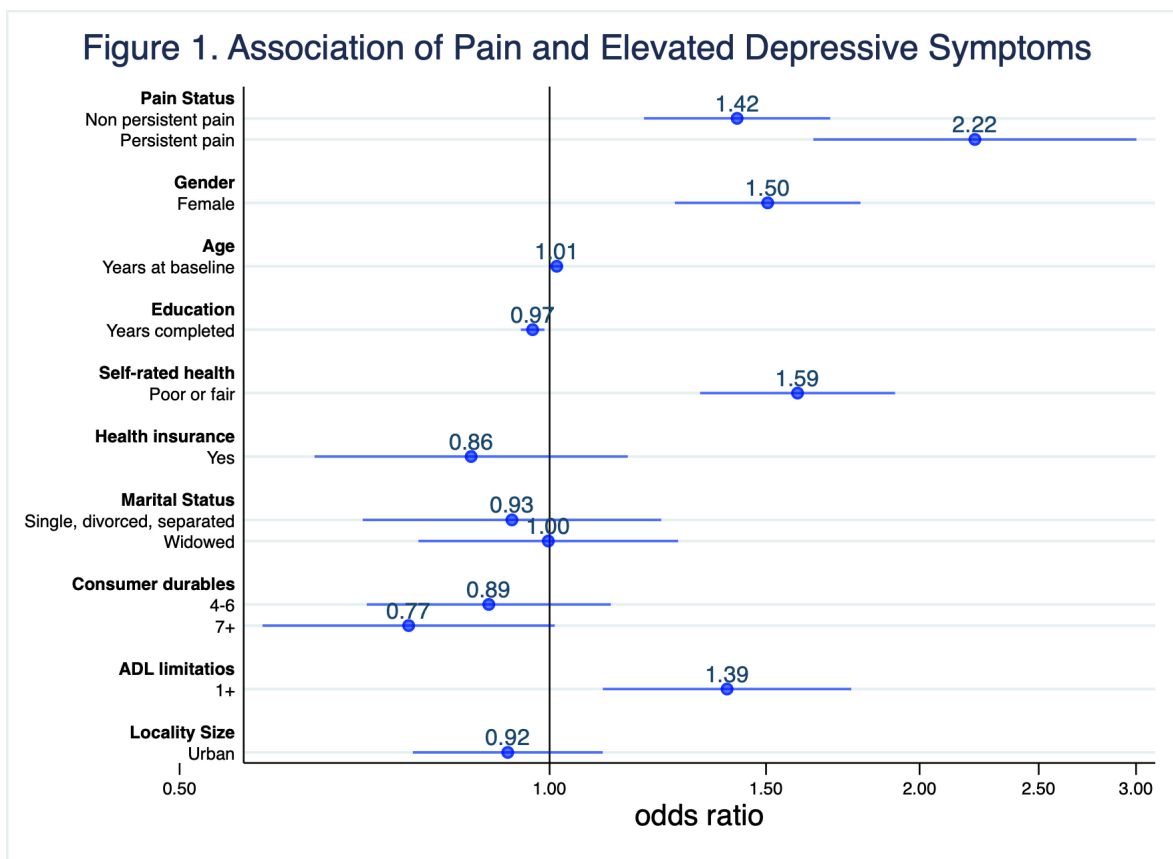
METHODS: We used data from the Canadian Longitudinal Study on Aging (CLSA) which included community-dwelling adults aged 45 to 85. SRH was measured via subjective questions. Multiple Poisson regression identified individual, behavioral, and social factors related to SRH. Intersections between sex, education, wealth, and rural/urban status, individual and joint cluster effects on SRH were quantified using multilevel models.

RESULTS: After adjustment for relevant confounders, women were 43% less likely to report poor SRH. The strongest cluster effect (21%) was for groupings by wealth. This effect reduced to 15 per cent after adding either of sex or education. The largest joint cluster effect (13.6%) was observed for strata that included sex, wealth, and rural/urban status, suggesting that almost 14 per cent of variation in SRH arises from this intersection. Interactions between sex and social factors were not significant, demonstrating that the complex interplay of sex and social location was only revealed when intersectional methods were employed.

DISCUSSION: Sex and social factors affected older adults' perceptions of health in complex ways that only became apparent when multilevel analyses were carried out. Utilizing intersectionality analysis is a novel and nuanced approach for disentangling etiologies of health outcomes.

The Association of Persistent Pain and Incident Elevated Depressive Symptoms Among Older Adults in Mexico Sirena Gutierrez* Sirena Gutierrez Sadaf Milani Jacqueline M. Torres

Background: Prior literature on the association between pain and depression is mixed and has not been evaluated in low- and middle-income countries (LMICs), which have a disproportionate burden of chronic pain compared to high-income countries. **Methods:** We used data from the Mexican Health and Aging Study, a national cohort study of adults ≥ 50 years in Mexico (2012, 2015, 2018). Analyses were limited to those with no prior history of elevated depressive symptoms at baseline ($n=4929$). Our primary exposure was a measure of persistent pain, (i.e. moderate or severe pain reported in both 2012 and 2015 waves) vs. non-persistent pain (i.e. moderate or severe pain at only one wave), and no pain (i.e. no pain at either wave). Our primary outcome was elevated depressive symptoms in 2018, defined as ≥ 5 symptoms on the 9-item CES-D. We estimated multivariable logistic regression models and controlled for respondent’s demographics, socioeconomic characteristics, and health characteristics. Final analyses will correct for attrition by applying inverse probability attrition weights. **Results:** At baseline, participants were an average of 63 years old and 50.2% female. Overall, 60.8% reported no pain, 33.6% reported non-persistent pain, and 5.5% reported persistent pain between baseline and two-year follow-up in 2018, and 14.9% of the participants reported incident elevated depressive symptoms by the final wave. Reporting persistent pain (OR: 2.22, 95% CI: 1.64, 3.00) or non-persistent pain (OR: 1.42, 95% CI: 1.19, 1.69) was associated with higher odds of incident elevated depressive symptoms compared to reporting no pain at prior waves. There was no statistically significant additive or multiplicative interaction by gender. **Discussion:** Pain and depression are both debilitating yet preventable and treatable conditions. Interventions to reduce pain may have population-level benefits for mental health among older adults in LMICs.



Metabolic Syndrome predicts the incidence of functional disability in elderly community dwellers in Japan A prospective cohort study of the Iwate-KENCO study Naomi Takahashi*
Shuko Takahashi Naomi Takahashi Kozo Tanno Megumi Tsubota Kiyomi Sakata

Objectives: Previous study have demonstrated the association between functional disability and cardiovascular risk factors. However, there have been a few studies in which the association between metabolic syndrome (MetS) and functional disability was investigated in Japanese community elderly dwellers. The aim of this study is to compare the incidence of functional disability, defined as certification of the long-term care insurance (LTCI) system, between the people with MetS and the people with non-MetS.

Methods: A total of 11,686 individuals (40.6% men, mean age of 71.4 years) who were 65 years of age or more who did not have a history of LTCI certification were followed in prospective study for 10.4 years (the Iwate-KENCO study). We defined MetS as having at least three factors (overweight, low high-density lipoprotein, elevated blood pressure, and diabetes mellitus) based on modified criteria primarily according to the joint interim statement. A Cox proportional-hazards model was used to determine the hazard ratios (HRs) for the incidence of functional disability.

Results: The number of individuals with functional disability was 3,713. MetS group scored significantly higher HR for functional disability (HR [95% CI]: MetS= 1.22 [1.10, 1.35]). After excluding sub-clinical cases, a significant association between MetS and functional disability remained significant. But the significantly higher HR for functional disability disappeared in the MetS group in an analysis of severe functional disability.

Conclusions: MetS, therefore, was a risk factor for later incidence of functional disability in the elderly people. We might intervene the people who have MetS appropriately in order to prevent those high-risk individuals from suffering functional disability.

LATEBREAKER

Aging

Racial/Ethnic Disparities in Childhood Sexual Abuse and Subjective Cognitive Decline in the US Monique J. Brown* Monique Brown

Introduction: Subjective cognitive decline (SCD), a potential precursor for Alzheimer's disease, is one's perception of worsening cognitive function or more frequent confusion or memory loss. Racial disparities have been seen in the association between environmental adverse childhood experiences (ACEs) such as parental separation and objective cognition. However, research is lacking on assessing racial disparities in the relationship between direct ACEs (such as abuse) and SCD. Therefore, the aim of this study was to examine racial/ethnic disparities in the relationship between CSA and SCD among a representative sample of the US population.

Methods: Data were obtained from the 2019 Behavioral Risk Factor Surveillance System survey (N=82,688; age = ≥ 45 years). The interaction between CSA and race/ethnicity on SCD was tested. Weighted multivariable logistic regression models, adjusting for age, gender, income, education, employment, diabetes and depression were used to determine the associations CSA and SCD among Black, White, Other and Hispanic populations.

Results: Approximately 11% of respondents reported SCD in the past year while 26% of respondents reported some form of CSA. The interaction between CSA and SCD was statistically significant in the fully adjusted model ($p=0.046$). Among all populations, CSA was positively associated with SCD [Black: (adjusted OR (aOR): 3.58; 95% CI: 2.32 - 5.53); White: aOR: 2.56; 95% CI: 2.20 - 2.97); Other: aOR: 2.65; 95% CI: 1.27 - 5.55); Hispanic: aOR: 7.55 (2.75 - 20.8).

Conclusion: Regardless of racial/ethnic group, CSA was associated with SCD in later life. Nevertheless, racial/ethnic minority groups had greater effect estimates. Cognition interventions should consider addressing CSA among affected populations and the racial/ethnic disparities that exist. Future research should address the potential racial/ethnic disparities in the relationship between other direct ACEs, such as physical/psychological abuse, and SCD.

Electronic nicotine delivery systems (ENDS) use and academic achievement among 9th - 12th graders in the US - Findings from the 2017 Youth Risk Behavior Survey (YRBS) Vijaya Kancherla* Vijaya Kancherla Olivia Russell

Objective: Epidemiological evidence suggests that cigarette smoking lowers academic achievement among adolescents; however, contemporary evidence is lacking on the association between electronic nicotine delivery systems (ENDS) alone, and dual use of ENDS and cigarette smoking, with academic achievement in high school students in the United States.

Methods: We used 2017 Youth Risk Behavior Survey (YRBS), a nationally-representative, population-based cross-sectional survey of 14,765 US high school adolescents (9th-12th grade). Low academic achievement was defined as receiving mostly Cs, Ds, and Fs during the year prior to the survey. Current ENDS use was self-reported in the survey, and assessed in combination with cigarette use. Multiple logistic regression was performed to estimate crude and adjusted prevalence odds ratios and associated 95% confidence intervals (CI). We examined effect modification by gender.

Results: Overall, 575 (6.5%) adolescents reported ENDS use in the past 30 days of survey, while 330 (3.5%) reported cigarette use, and 519 (6.3%) reported dual use. Stratified adjusted analysis showed that among females, current ENDS users had 2-fold (95% CI=1.3, 3.1) increased prevalence odds for low academic achievement, and among males, current ENDS users had 1.7-times (95% CI=1.2, 2.3) higher prevalence odds of low academic achievement, relative to those who reported no tobacco use. Current dual use of ENDS and cigarettes was also significantly associated with low academic achievement in both genders, relative to their counterparts.

Conclusions: Our study showed a significant association between ENDS use and low academic achievement among high school students in the US. Pathways of gender differential should be further examined. Findings guide translational research on ENDS use and its prevention programs. Prevention strategies for ENDS use in adolescents should be implemented immediately.

Longitudinal changes in five domains of physical activity across gestation: the NICHD Fetal Growth Studies-Singletons

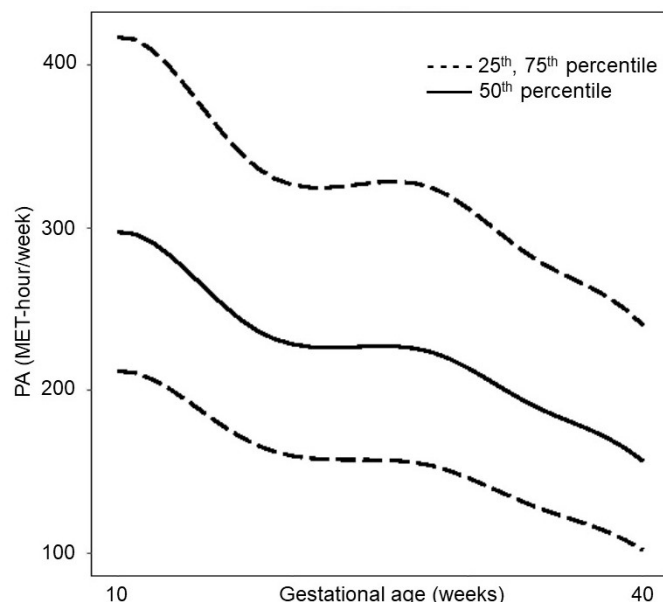
Susanna Mitro* Susanna Mitro Shyamal Peddada Jessica L. Gleason Dian He Brian Whitcomb Lindsey Russo Jagteshwar Grewal Cuilin Zhang Samrawit F. Yisahak Stefanie N. Hinkle John Owen Germaine M. Buck Louis Roger Newman William Grobman Anthony C. Sciscione Angela Ranzini Sabrina Craigo Edward Chien Daniel Skupski Deborah Wing Katherine L. Grantz

Background: Physical activity (PA) in pregnancy, especially leisure-time PA (i.e., exercise) is associated with healthy outcomes such as lower risk of gestational diabetes and preterm birth. Although non-leisure-time activities likely account for a greater share of total pregnancy PA than exercise, patterns of activity at home, work, and commuting are not well described.

Methods: PA was self-reported 6 times over pregnancy (between 10-41 weeks) by 2778 women using the Pregnancy PA Questionnaire. Reported time spent on 32 activities in 5 domains (sports/exercise [e.g. walking for fun, jogging, prenatal exercise], domestic [e.g., cooking, cleaning, childcare], occupational [e.g., sitting, walking, carrying things at work], transportation [e.g., walking, driving, riding in a car], and inactive [e.g., reading, watching TV]) was used to calculate metabolic equivalent of task (MET)-hours/week. Linear mixed effects models with cubic splines were used to model trajectories of MET-hours/week across pregnancy for each domain.

Results: Total PA (sum of domains) declined 47% from week 10 to 40 (Figure). This decrease was largely driven by changes in domestic PA, which declined 43%, and occupational PA, which declined 72% (including women who stopped working in pregnancy). Domestic PA made up the largest share of total PA in early pregnancy (42%), followed by occupational PA (28%). Exercise PA declined around 60% over pregnancy but constituted <5% of total PA. Inactive PA (14% of early pregnancy PA) and transportation PA (11% of early pregnancy PA) declined 19% and 23% respectively. Exercise PA was poorly correlated with other domains ($r = 0.02-0.38$, varying by domain and gestational age).

Conclusion: Studies of pregnancy PA often focus on exercise PA, which is only a small proportion of total PA in pregnancy and is not highly correlated with other types of PA. Future studies of PA-associated pregnancy outcomes should include domains other than exercise.



Who's really smoking at home? Transporting prevalence estimates of in-home cannabis smoking from the 2020 Global Drug Survey (GDS) to the 2018 National Survey on Drug Use and Health (NSDUH) survey population Osika Tripathi* Osika Tripathi Caroline A. Thompson Jason Ferris John Bellettiere

Objective: To increase external validity of in-home cannabis smoking prevalence from a convenience sample of GDS cannabis users, by transporting estimates to NSDUH respondents.

Methods: The study was conducted among past-year cannabis users: 6,580 U.S. respondents from GDS and 10,565 from NSDUH. A question about in-home cannabis smoking was added to the GDS, which is an anonymous web-based survey of more involved drug users. The NSDUH is a population-based survey of U.S. adolescents and adults that included many of the same questions as GDS on drug use, but no question about in-home smoking.

Multivariable logistic regression modeled GDS participation on demographic and drug use variables in a pooled GDS-NSDUH dataset. We used multiple imputation to address missing survey data. Inverse odds of probability weights (IOPW) were computed from resulting predicted values and used to reweight the GDS study sample to the NSDUH target population.

The prevalence and frequency (%; 95% CI) of GDS cannabis users who smoke in their home (ever or daily) was estimated with and without IOPWs using weighted logistic regression to output predicted probabilities, by age and sex.

Results: In the GDS, 65% (63%-66%) of male cannabis users smoked in their home compared to 69% (64%-70%) of females. After transporting to NSDUH, the prevalence estimates were 50% (41%-58%) and 61% (47%-74%), respectively. Among 25-34 year-old GDS cannabis users, 69% smoked in their home, which decreased to 42% after transporting. GDS respondents 35+ years old had the highest *daily* smoking in their homes (38% (35%-40%)) which decreased to 22% (16%-29%) after transporting.

Conclusion: While not representative of U.S. cannabis users, GDS estimates describe behaviors for highly involved drug users, giving us insight into trendsetter's behaviors. Assuming a correct transport model, we used this convenience sample to estimate in-home smoking for a more representative sample of US cannabis users through transportation.

Assessing Stage of Change among African American Smokers Who Qualify for Low Dose Computed Tomography Screening Yu-Hsiang Kao* Yu-Hsiang Kao Tyra Gross Michael D. Celestin Lucretia Young Mirandy Li David L. Smith Leonard R. Bok Jyotsna Fuloria Jennifer Hart Sarah Moody-Thomas Tung-Sung Tseng

Background: African Americans have higher incidence and mortality of lung cancer compared to other racial/ethnic groups. Low dose computed tomography (LDCT) screening can detect lung cancer early and help prevent lung cancer-specific mortality for smokers at high-risk, but remains under-utilized with this population. Furthermore, while LDCT screening and smoking cessation combined may result in higher quit rates, we know little about the readiness to quit of African American smokers who qualify for LDCT screening.

Objective: To investigate the stage of change among African American smokers who qualify for LDCT screening.

Methods: We recruited 60 African American daily smokers seen in primary care clinics in a New Orleans, LA hospital who qualified to receive LDCT screening. Enrollees completed a paper-based, anonymous cross-sectional survey that collected demographic, tobacco use and smoking cessation behaviors. Descriptive statistics were used to provide summary information on demographic, tobacco use, lung cancer risk perception and stage of change.

Results: Of 59 smokers responded their quit intention, majority were older (61.1 [SD=5.5]), female (61%), earned annual income less than \$20,000 (91.5%), had Medicaid (71.2%), overweight/obesity (71.2%), and considered long-time smokers (mean years=40.5 [SD=11.3]). Regarding lung cancer risk perception, half of smokers thought they will develop lung cancer in the future; and, 60.3% reported they are more likely to be ill with lung cancer compared to the same age population. Most smokers reported being in the contemplation (45.8% planned to quit in 6-months or longer than 6-months) and preparation (42.3% planned to quit in 1 month) stages, with a few (11.9%) reported being in the pre-contemplative stage.

Conclusion: To improve smoking cessation for African American smokers eligible for LDCT screening, programs should develop interventions to promote progression from contemplation and preparation stages to action.

Associations between childhood maltreatment, binge eating, and binge drinking in young adult women Jessica Friedman* Jessica Friedman Cynthia Yoon Rebecca L. Emery

Background

Binge drinking and binge eating are prevalent, high-risk behaviors among young adult women, each with serious physical and psychological health consequences. The current study assesses the relative magnitude of associations between childhood maltreatment subtypes and the individual and co-occurrence of these binge behaviors.

Methods

Data were collected from a diverse sample of emerging adult women participating in the population-based study EAT 2018: Eating and Activity over Time (N=788; aged 18-30; 19% Asian, 22% Black, 19% Latino, and 36% White). Multinomial logistic regression was used to estimate the associations among childhood maltreatment subtypes (i.e., familial sexual abuse, non-familial sexual abuse, physical abuse, emotional abuse, household dysfunction), and binge drinking, binge eating, and co-occurring binge drinking and eating.

Results

Approximately two-thirds (62%) of the young women reported at least one type of childhood maltreatment. In models mutually adjusted for childhood maltreatment and household dysfunction, physical and emotional abuse showed strong associations with binge behaviors. Physical abuse had the strongest association with both binge drinking only (aOR = 1.84, 95%CI [1.10, 3.06]) and co-occurring binge eating and drinking (aOR = 3.08 95% CI [1.42, 6.70]) compared to the referent group of women with no reported binge eating or drinking behaviors. Emotional abuse had the strongest association with binge eating only (aOR = 2.19 95% CI [1.12, 4.31]) compared to the referent group with no binge behaviors.

Conclusions

The assessment of the associations among subtypes of childhood maltreatment and binge eating and drinking revealed different patterns of binge behavior by maltreatment type. This study identifies childhood physical and emotional abuse as particularly relevant factors contributing to different manifestations of binge behaviors in emerging adulthood.

The impact of muscle-strengthening exercise on mortality risk in a large screening trial

Jessica Gorzelitz* Jessica Gorzelitz Charles Matthews Britton Trabert

Both aerobic physical activity and muscle-strengthening exercise (MSE) is recommended for adults, including specific recommendations of ≥ 2 days per week of MSE. However, the epidemiologic evidence on the mortality benefits of MSE is limited. Using data from the Prostate, Lung, Colorectal and Ovarian (PLCO) cancer screening trial, we examined the association between MSE (self-reported weightlifting sessions/week) and all-cause mortality. Cox proportional hazards regression, with age as the time scale, was used to examine the associations between MSE (any vs. none and meeting recommendations ≥ 2 sessions/week vs. not) and mortality. Models were adjusted for demographic, lifestyle, and behavioral risk factors. The analytic sample was 104,002 adults enrolled in the original trial who subsequently completed the follow up questionnaires about health behaviors including MSE. Mortality risk was estimated from the time of the follow-up questionnaire (median 9 years follow-up) through 2016. Mean age at follow up questionnaire was 71.3 (standard deviation (SD) 5.9) years, with mean body mass index (BMI) of 27.8 (SD 4.9) kg/m². Sixteen percent (n=17,389) were meeting public health guidelines of ≥ 2 MSE sessions/week. Participation in any MSE was associated with an 8% reduction in all-cause mortality (HR 0.92, 95% confidence interval (CI): 0.88-0.96). Meeting public health MSE recommendations had similar associations (0.93, 0.88-0.98). After further adjusting for participation in aerobic exercise, associations for any MSE (0.93, 0.89-0.97) and meeting MSE recommendations (0.94, 0.89-0.99) remained. Similar results were noted for men and women, participants with healthy BMI and with obesity, and by race (non-Hispanic black and white). Participation in MSE was associated with a lower risk of death. Our study provides support for MSE as a health behavior to increase longevity for older Americans, and future research should focus on increasing participation in MSE.

Spinal Cord Injury Research Participant's Views on Data Sharing Freda Warner* Freda Warner Jessica McDougall Kathleen Ginis Jacquelyn Cragg John Kramer

The objective of the proposed study is **to determine the perspective of individuals with spinal cord injury on the topic of open data sharing**. Open data sharing comprises the act of making data from research studies widely available for researchers unrelated to the original study to perform their own analyses. To achieve our objective, we will: 1) develop a patient-centered survey addressing key issues related to open data sharing, 2) disseminate the survey to individuals with spinal cord injury in Canada and the United States, and 3) perform a comprehensive statistical analysis of responses. **Our hypothesis is that open data sharing will have widespread support but depend on participant characteristics (e.g., age), medical complications, and the type of data shared**. This work is urgently needed to guide the development of an open access data repository for studies involving research participants with spinal cord injury.

LATEBREAKER

Big Data

Today is not tomorrow's yesterday: combining data sources can mitigate delays in EHR data availability Elise Gatsby* Kristine Lynch Elise Gatsby Patrick R Alba Benjamin Viernes Scott L DuVall Kristine E Lynch

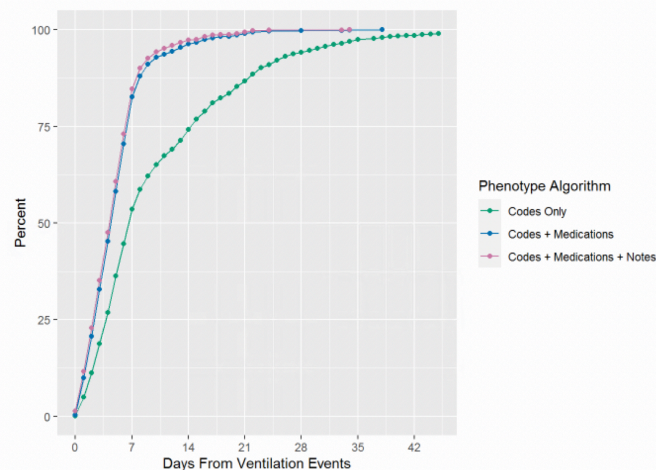
It is common for phenotype algorithms using electronic health records (EHRs) to incorporate multiple sources of data to improve validity. However, data from one source may be provisionally incomplete owing to temporal delays between reality and when the data are observable for research access. Procedure codes, for example, may have near perfect sensitivity but not appear in the data until after hospital discharge, sometimes weeks after the event occurred. We evaluated the lag time from event to data availability for mechanical ventilation procedures within records of the Veterans Health Administration (VA).

The COVID-Shared Data Resource (CSDR) is a new VA data source for COVID-19 research. It includes data from the EHR and is updated weekly. We examined the time between the day ventilation occurred and when the record appeared in the CSDR. Ventilations were considered beginning 11/25/20-1/27/21 having both structured (ventilation procedure codes and medications) and unstructured data (documentation of ventilation in notes). The numerator was defined as a count of total observed events by week across the 9-week period, with the denominator consisting of total actual events by week. Mean weekly percentages of data availability were calculated had the ventilation algorithm used data from codes, codes+medications, and codes+medications+notes. Daily percentages were also calculated.

1147 ventilation events were evaluated. Using codes, 54% of the events existed in the EHR by 1-week post ventilation, 74% by 2 weeks, 87% by 3 weeks, 94% by 4 weeks. Adding medications to the algorithm improved weekly availability to 83%, 96%, 99%, 99%, respectively, with slight improvements from notes (85%, 97%, 99%, 99%).

Data delays are especially important for time-sensitive surveillance research, such as COVID-19. Researchers should evaluate the extent to which missing data due to delayed data availability can bias results and consider how different data types can mitigate this issue.

Figure. Mechanical ventilation data availability by phenotype algorithm expressed as mean daily percentages (n=1,147 ventilation events)



The effect of travel distance on overall survival for HPV-associated cancers, Oklahoma, 2005-2019 Hanh Dao* Sameer Gopalani Hanh Dao Lance Ford Sameer Gopalani Nancy Etzold Janis Campbell Amanda Janitz

Objective

As travel burden can influence cancer diagnosis and treatment, we evaluated the association between travel distance to an NCI-Designated Cancer Center and overall survival for HPV-associated cancer patients.

Methods

We included HPV-associated (cervical, vulvar, vaginal, penile, anal, and oropharyngeal) cancer patients at the University of Oklahoma Medical Center (OUMC) diagnosed from January 1, 2005 through June 30, 2019. We calculated unidirectional distance from each patient's address at diagnosis to OUMC using network analysis (ArcGIS; v10.8) and categorized distance as short (<25 miles), intermediate (25-74.9 miles), and long (75+ miles). We defined our outcome, overall survival, as the time from the date of initial diagnosis to the date of last contact. We used Kaplan-Meier estimation and Cox proportional hazard models to evaluate the association between travel distance and overall survival (SAS; v9.4).

Results

Overall, 1,146 (46%) of the patients traveled a short distance for treatment; 687 (22%), an intermediate distance; and 974 (32%), a long distance. Cancer type, ethnicity, insurance type, and age at diagnosis were all univariately associated with survival ($p < 0.05$). In the multivariable analysis, cancer type and race did not modify the relationship between survival and travel distance (interaction p -values > 0.05).

The adjusted 5-year survival rates were 68% (95% CI: 65-71%), 62% (95% CI: 59-66%), and 63% (95% CI: 60-67%) in the short-, intermediate-, and long-distance groups, respectively. After adjusting for cancer type, ethnicity, insurance type, race, and age at diagnosis, relative to the short distance group, both intermediate distance (HR: 1.18; 95% CI: 1.02-1.37) and long distance (HR: 1.17; 95% CI: 1.02-1.34) were associated with poorer overall survival.

Discussion

Travel distance to a cancer center was associated with overall survival for HPV-associated cancers. The findings of our study are limited due to relatively high censoring (63%).

Frailty is associated with a higher mortality in older people with cancer history: evidence from the 1999-2014 National Health and Nutrition Examination Survey Dongyu Zhang*

Dongyu Zhang Erin Mobley Caretia Washington Todd Manini Christiaan Leeuwenburgh Paul Okunieff Daohong Zhou Marco Pahor Alexander Parker Dejana Braithwaite

Purpose: To investigate if frailty was associated with mortality in older people with cancer history.

Methods: We identified 2,148 older people (≥ 60 years at interview) with cancer history from the 1999-2014 cohorts of the National Health and Nutrition Examination Survey. A comprehensive 45-item frailty index (FI) was the exposure and categorized based on validated cutoffs ($FI \leq 0.21$: not frail, $0.21 < FI \leq 0.45$: moderately frail, $FI > 0.45$: severely frail). Outcomes included all-cause, cancer-specific, and cardiovascular disease (CVD)-specific mortality. Multivariable Cox proportional hazards models estimated adjusted hazard ratio (aHR) and 95% confidence interval (CI) of FI, adjusting for age, sex, race, education, marital status, body mass index (BMI), smoking and alcohol use, protein and energy intake, survival time, history of more than 1 cancer, and survey year. To explore if effect measures of FI were heterogeneous between cancer and CVD-specific mortality, a joint-Cox model was applied. Subgroup analyses were conducted by relevant sociodemographic and lifestyle factors.

Results: The mean age of participants was 72.9 years ($SD=7.2$), 52.6% of them were male, 76.0% were white, and 61.4% were frail ($0.21 < FI \leq 0.45$: 1,143, $FI > 0.45$: 176). During the follow-up (median: 6.0 years), 758 people died (cancer-specific: 219, CVD-specific: 146). The multivariable model suggested that frailty was associated with a higher all-cause mortality ($FI > 0.45$ vs. ≤ 0.21 : aHR=3.76, 95% CI=2.90-4.89, p-trend<0.01). In subgroup analyses, effect measures were larger in people younger than 75 years or with $BMI \geq 30$ kg/m². Positive and significant associations were also observed for cancer and CVD-specific mortality, but the joint-Cox model suggested aHR of frailty was larger for the latter (cancer: 2.30, CVD: 5.61).

Conclusions: In older people with cancer history, frailty is associated with a higher mortality, and it may have a stronger impact on CVD-specific death compared to cancer-specific death.

Cancer incidence and risk in a combined cohort of World Trade Center rescue and recovery workers, 2002-2015 Jiehui Li* Jiehui Li Janette Yung Baozhen Qiao Erin Takemoto David G Goldfarb Rachel Zeig-Owens James E Cone Robert M Brackbill Mark R Farfel Amy R Kahn Maria J Schymura Moshe Z. Shapiro Christopher R Dasaro Andrew C Todd Dana Kristjansson David J Prezant Paolo Boffetta Charles B Hall

Increased cancer incidence has been reported from 3 individual cohorts of World Trade Center (WTC) disaster rescue/recovery and clean-up workers (responders). To better assess cancer incidence and risk associated with specific WTC exposures, we analyzed a combined cohort of 56,259 responders pooled from those 3 WTC cohorts. Invasive cancers including in-situ bladder tumors diagnosed during 2002-2015, were identified via linkages with 13 state cancer registries. WTC-related exposures were defined as site arrival date, work on the WTC pile, and dust exposure on 9/11. Follow-up was from 6 months after 9/11/2001 or enrollment date, through 12/31/2015 or death. We used standardized incidence ratios (SIR) to assess cancer incidence, with rates from the New York state population as referent; Cox regression, adjusted for age, sex, race, and smoking, to examine associations between WTC exposure and cancer risk. A total of 3236 first primary incident cancers were identified, with an accumulated 624,620 person-year of follow-up. The SIR for all cancers combined was slightly lower than expected (0.96; 95% CI 0.93-0.99). However, significantly elevated SIRs were observed for prostate (1.19; 95% CI 1.11-1.26), skin melanoma (1.43; 95% CI 1.24-1.64), thyroid (1.81; 95% CI 1.57-2.09) and tonsil cancer (1.40; 95% CI 1.00-1.91). Adjusted HRs were significantly higher in those arriving on 9/11 than those arriving after 9/17/2001 for prostate (1.61; 95% CI 1.33-1.95) and thyroid cancers (1.77; 95% CI 1.11-2.81), with a significant exposure-response trend for both sites. Dust exposure was also significantly associated with an increased risk of prostate cancer, but not with other sites. Our combined cohort findings are generally consistent with previous studies; a greater-than-expected rate of tonsil cancer is reported for the first time. Higher levels of WTC-specific exposures are associated with increased cancer risk for specific cancer sites, warranting further investigation.

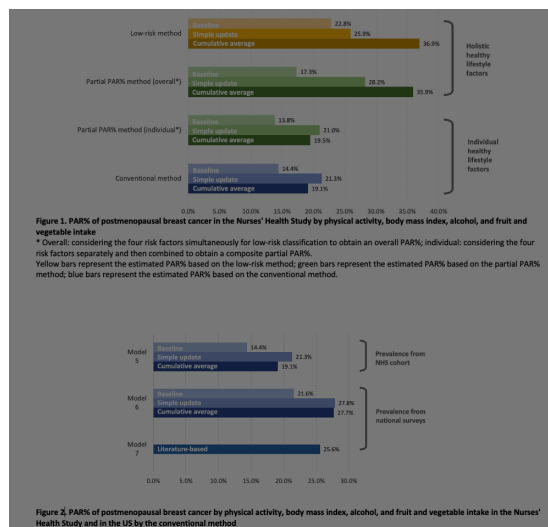
Assessing preventability of post-menopausal breast cancer by lifestyle risk factors: influence by method, data source, and timing of exposure measurement You Wu* You Wu Hanseul Kim Kai Wang Mingyang Song Molin Wang Rulla Tamimi Heather Eliassen Stephanie Smith-Warner Walter Willett Edward Giovannucci

Background: A substantial proportion of cancer incidence may be prevented by primary intervention through lifestyle changes. One way to quantify the preventable fraction associated with risk factors for a specific outcome is the population attributable risk (PAR%); however, PAR% estimates have shown large variation across target populations, methods, and data sources.

Methods: We evaluated the degree to which the PAR% for alcohol consumption, body mass index, fruit and vegetable intake, and physical activity and postmenopausal breast cancer in the Nurses' Health Study (NHS) varied by different methods and data sources. For the low-risk method, the age-standardized incidence rate in a low-risk group in the NHS was compared with the cohort average as well as the US rate. The partial PAR% method estimated the PAR% by the four risk factors while holding other covariates constant in the NHS. The conventional method estimated the PAR% based on the exposure distribution and the relative risk data in the NHS, from US national surveys, or from meta-analyses. Within each model, we used repeated measurements to compare the results using baseline data, simple updates, or cumulative average.

Results: When considering the contribution of each risk factor individually then combined, within the NHS, the PAR% estimated by the partial PAR% method for the baseline, simple update, and cumulative average models were 13.8%, 21.0%, 19.5%; while the conventional method gave corresponding PAR% of 14.4%, 21.3%, 19.1%. The estimations were higher based on meta-analyses and US national surveys at 25.6%. When considering the preventable fraction for all four risk factors simultaneously, within the NHS, the low-risk method yielded PAR% for the three timings: 22.8%, 25.9%, 36.9%; while the partial PAR% method yielded PAR% estimates at 17.3%, 28.2%, 35.9%.

Conclusions: The three methods provided similar PAR% results based on the same data sources and target populations. However, sizable increases in the PAR% were observed for repeated measures over a single measure and for calculations based on achieving all four recommendations rather than considering them individually and then combining the results. Most of the published PAR% estimates likely underestimated the potential of long-term healthy lifestyle to lower breast cancer risk.



Ethnic enclaves and incidence of cancer among ethnic minorities in the Multi-Ethnic Study of Atherosclerosis Jinhee Cha* Jinhee Cha Gabriela Bustamante Felice Lê-Scherban Daniel Duprez James S. Pankow Theresa Osypuk

Residence in ethnic enclaves, defined as neighborhoods with high proportions of co-ethnic minorities, may influence risk of chronic disease. However, evidence is mixed, and past research has not focused on cancer incidence or mortality using prospective designs. We examined the association between residency in ethnic enclaves and total cancer events (incidence and mortality; prostate, breast, lung, colon, non-melanoma skin, blood and other cancer) among ethnic minorities in the Multi-Ethnic Study of Atherosclerosis (MESA), a prospective cohort study that enrolled participants ages 45-84 in six U.S. communities. Using MESA's baseline 2000 survey, we included participants without a history of cancer who identified as Hispanic (n=1496) or Chinese (n=804). Ethnic enclaves were operationalized as the percentage of residents in each participant's census tract of the same ethnicity as reported in the 2000 Census. A four-level compound variable was created based on the tract's % poverty and % co-ethnic residency. Using the median for each variable as the cut point, neighborhoods were categorized as low/high poverty and low/high enclaves. Cancer events included deaths and hospitalization for any cancer diagnosis. The association between ethnic enclaves and time to first cancer event was estimated using Cox proportional hazards regression, adjusting for age, gender, smoking, individual income and tract clustering. Hispanics living in low-poverty, high-enclave neighborhoods had 54% lower cancer events compared to residents of low-poverty, low-enclave neighborhoods (HR: 0.46, 95%CI: 0.21, 1.01). High-enclave, high % poverty neighborhoods were associated with reduction in cancer risk among Hispanics. We did not find significant differences in cancer risk by ethnic enclaves among Chinese participants. Hispanic participants in MESA residing in ethnic enclaves had lower cancer events, which may be explained by contexts, and/or long-term migration or adaptations to such contexts.

Perinatal exposures and breast cancer risk Mary V Diaz Santana* Mary V Diaz Santana Clarice R. Weinberg Mandy Goldberg Katie M. O'Brien Dale P. Sandler

Background:

Perinatal factors may play a role on breast cancer (BC) risk, but findings from epidemiological studies have been mixed. This study aimed to prospectively assess the relationship between perinatal exposures and daughter's BC risk, overall, and by estrogen receptor and menopausal status.

Methods:

Associations between self-reported perinatal factors and BC risk were assessed using nationwide data from the Sister Study (2003-2009), a cohort study of 50,884 women aged 35-74 at enrollment. In utero exposures considered included maternal preeclampsia or gestational hypertension, gestational diabetes, maternal smoking, and use of diethylstilbestrol. Other perinatal factors were low birthweight, high birthweight, multiple birth membership, short gestational age, having been breastfed, or being fed soy formula. We estimated hazard ratios (HRs) and 95% CIs using Cox proportional hazards models, with age as the primary time scale. The analyses related to hypertensive disorders were adjusted for whether the participant was their mother's first birth and excluded women who themselves had a preeclamptic pregnancy.

Results: Women whose mothers experienced preeclampsia (adjusted HR = 0.74, CI 0.54-1.01) or any hypertension during their pregnancy (adjusted HR = 0.80, CI 0.65-0.99) were less likely to develop breast cancer later in life. Multiple birth membership was associated with increased BC risk (HR = 1.20, CI 1.01-1.42). No differences by menopausal status were observed. High birthweight was associated with an increase in ER-negative BC risk (HR = 1.43, CI 1.01-2.03).

Conclusion:

We observed an inverse association between in utero exposure to preeclampsia or any hypertension during pregnancy and BC risk. Multiple birth membership was associated with increased BC risk. Being heavy at birth may be associated with an increased risk of ER-negative BC.

Associations Between MICA and MICB Genetic Variants, Protein Levels, and Colorectal Cancer (CRC): Atherosclerosis Risk in Communities (ARIC) Shuo Wang* Shuo Wang Guillaume Onyeaghala Nathan Pankratz Heather Nelson Bharat Thyagarajan Weihong Tang Faye Norby Chinenye Ugoji Corinne E. Joshi Christian R. Gomez David Couper Joseph Coresh Elizabeth A. Platz Anna Prizment

Introduction: Major histocompatibility complex class I-like proteins (MICA and MICB) are ligands for natural killer (NK) cells. Colorectal tumor cells can release MICA/MICB into tumor microenvironment neutralizing NK anti-tumor response. We hypothesized that MICA/MICB polymorphisms are associated with higher circulating MICA/MICB levels and increased CRC risk in the ARIC study.

Methods: MICA/MICB levels were measured in frozen plasma samples from Visit 3 (V3, 1993-95) and Visit 5 (V5, 2011-13) by SomaScan® assays. SNPs were genotyped by the Affymetrix Genome-Wide Human SNP Array. We examined: 1) the associations of pre-selected functional MICA (rs1051792, rs1063635, rs2516448, rs3763288, rs1131896) and MICB (rs2395029) SNPs with log-transformed V3 MICA/MICB levels in general linear regression model; 2) the associations of MICA/MICB SNPs and V3 MICA/MICB levels with CRC risk using Cox proportional hazards model; and 3) in a nested case-control study, compared relative changes in MICA/MICB levels in CRC cases and cancer-free controls (matched by age, sex, and race; 1:5) using median test (Figure 1).

Results: In 1993-2015, 287 CRC cases were identified in 10,397 cancer-free participants (white and black). All MICA/MICB SNPs, but rs1131896, were associated with corresponding protein levels ($p < 0.02$). Only rs2395029 was associated with CRC risk: HR (95% CI): 2.28 (1.18-4.42). MICA/MICB levels were not associated with CRC. For Q4 vs. Q1: multivariable-adjusted HRs (95% CIs): 0.82 (0.62-1.09) for MICA, 1.01 (0.76-1.36) for MICB. From V3 to V5, MICA levels increased by 14% in cases and by 4% in controls ($p = 0.03$). MICB levels increased by 6% in cases but decreased by 2% in controls ($p < 0.01$).

Conclusions: Several MICA/MICB SNPs were associated with corresponding protein levels and CRC risk. During 20-year follow up, MICA/MICB levels changed more in CRC cases than controls. This warrants further study of the MICA/MICB variants and changes in protein levels in relation to CRC.

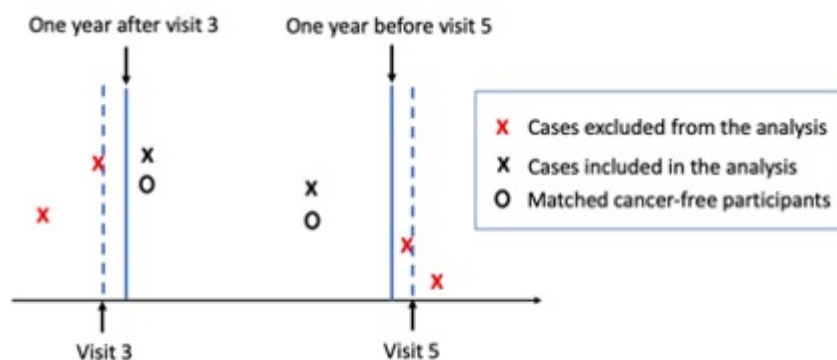


Figure 1. Inclusion and exclusion criteria for comparison in V3 to V5 changes in MICA/MICB protein levels.

The survival impact of second primary lung cancer in patients with lung cancer Eunji Choi*
Eunji Choi Sophia Luo Jacqueline Aredo Lynne R. Wilkens Ann Leung Loic Le Marchand Iona Cheng
Heather Wakelee Summer Han

Introduction: Lung cancer (LC) survivors have high risk of developing second primary lung cancer (SPLC), but little is known about survival impact of SPLC. We compared overall survival between patients with single primary LC versus SPLC using data from SEER and the Multiethnic Cohort Study (MEC).

Methods: In SEER, we identified 144,101 patients who were diagnosed with initial primary lung cancer (IPLC) and underwent surgery for IPLC between 1998 and 2013, who had a potentially curable disease. Each patient was followed from the date of IPLC diagnosis to SPLC diagnosis (for those with SPLC) and death or last vital status through 2016. We performed multivariable Cox regression to evaluate the association between overall survival and SPLC diagnosis (versus single primary LC) as a time-varying predictor. To investigate potential effect modification, we tested interaction between SPLC and stage at initial diagnosis using a likelihood ratio test and assessed overall survival stratified by stage. Using MEC data (n=1,567 IPLC patients who underwent surgery), we evaluated survival impact of SPLC by smoking status at IPLC diagnosis.

Results: Over 743,957 person-years (mean: 5.13 years), 12,140 patients (8.4%) developed SPLC versus 131,941 patients diagnosed with single primary LC in SEER. Compared to patients with single primary LC, those with SPLC had significantly reduced overall survival (hazard ratio, HR=2.09; $P < 1 \times 10^{-6}$). The effect of SPLC on reduced survival was more pronounced among patients with early-stage (I-III) IPLC versus advanced-stage (IV) IPLC (HR 2.14 vs. 1.19; Interaction $P < 1 \times 10^{-6}$). Analysis using MEC showed that the effect of SPLC diagnosis on reduced survival was larger among persons who actively smoked at initial diagnosis versus those who formerly or never smoked (HR=2.31 vs. 1.41; Interaction $P = 0.04$), implying that the potential impact of SPLC prevention could be higher among patients with early-stage IPLC and actively smoking at IPLC diagnosis.

Conclusions: SPLC diagnosis is significantly associated with a decreased survival compared to patients with single primary LC. More intensive surveillance and follow-up strategies are warranted for patients with high-risk of SPLC.

Immune-related conditions and survival after cancer diagnosis Jeanny Wang* Jeanny Wang
Eric Engels Ruth Pfeiffer

Background: Immune surveillance may play a role in preventing cancer progression. We studied associations of immune-related conditions with cancer-specific mortality among elderly Americans.

Methods: We identified a cohort of 1,229,443 patients diagnosed with 20 common cancer types (age 67-99, years 1993-2013) using Surveillance Epidemiology and End Results (SEER)-Medicare data. With Medicare claims, we ascertained 39 conditions (4 immunosuppressive [N=3380 affected cases], 32 autoimmune [N=155,766], 3 allergic [N=101,366]) during the 2 years prior to cancer diagnosis. For each cancer type, we estimated adjusted hazard ratios (aHRs) for cancer-specific mortality associated with each condition, applying a Bonferroni cutoff ($p < 6 \times 10^{-5}$).

Results: We observed 17 associations with cancer-specific mortality at the Bonferroni threshold for autoimmune (3 positive, 5 inverse) and allergic conditions (9 inverse). Among autoimmune conditions, scleritis was associated with decreased cancer-specific mortality for cancers of the bladder, prostate, breast, colorectum, and lung (aHR range: 0.85-0.93). Increased risk was observed with rheumatoid arthritis for patients with melanoma (aHR: 1.44, 95%CI: 1.25-1.67) or lung cancer (1.08, 1.05-1.11), and with hemolytic anemia for bladder cancer (2.38, 1.58-3.59). Among allergic conditions, inverse associations with cancer-specific mortality were seen for colorectal, lung, breast and prostate cancers, and for chronic lymphocytic leukemia, for allergic rhinitis (aHR range: 0.76-0.91) and asthma (0.78-0.94). Although less significant (p range: 6×10^{-4} - 4×10^{-2}), cancer-specific mortality appeared elevated in patients with immunosuppressive conditions for 11 (55%) cancer types (aHR range: 1.25-4.85).

Conclusions: For patients with several cancer types, certain immune-related conditions were associated with cancer-specific mortality. Protective associations with allergic conditions appeared notable and may reflect enhanced immunosurveillance.

Predicting breast cancer risk in a community-based sample of high-risk survey respondents

Rachel J. Meadows* Rachel Meadows Wilson S. Figueroa Kate P. Shane-Carson Tasleem J. Padamsee

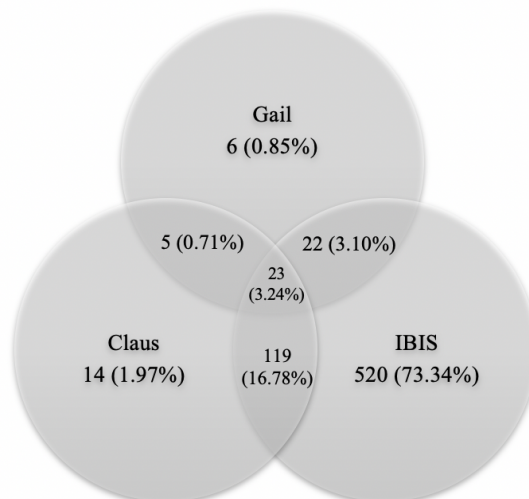
Introduction: Identifying women with high risk of breast cancer is necessary for clinicians to deliver guideline-recommended cancer risk management care. Risk prediction models estimate individuals' lifetime risk of breast cancer but are mainly used in clinical settings. Therefore, we aimed to (1) apply three breast cancer risk models - Gail, Claus, IBISv7- to a community-based sample of racially diverse women and (2) assess the feasibility and results of risk estimates from self-reported information.

Methods: N= 4,502 women from mainly non-clinical settings self-identified as high risk for breast cancer and were screened for eligibility; 1,053 women (23%) were initially eligible & completed an online survey. Risk models were used to estimate lifetime risk of breast cancer for each participant as applicable (e.g., Gail only applies to women ≥ 35 years old). Final eligibility required meeting a threshold of $\geq 20\%$ lifetime risk by ≥ 1 model. Descriptive statistics were used to assess the feasibility of applying each model and the results for lifetime risk estimates.

Results: N= 717 women (68% of those initially eligible) met final eligibility criteria of $\geq 20\%$ lifetime risk. Participants were 18-74 years old, 65% White, and 35% African American. All women reported the information necessary to run at least one model; $>90\%$ had necessary information to run >1 model. Most participants (76%) were identified as high risk by one model only; 73% of these were identified by IBISv7, 2% by Claus, 0.85% by Gail. Twenty percent were identified by 2 models; 3.2% were identified by all 3 models.

Conclusions: Risk prediction modeling is feasible using self-reported data in non-clinical settings. Gail, Claus, and IBISv7 models have low levels of agreement in identifying high-risk women. The IBISv7 model identifies high-risk women most often. Researchers and clinicians should consider the use of multiple models to avoid misidentifying potentially high-risk women.

Figure 1. Participants meeting 20% risk threshold according to Gail, Claus, and IBISv7 risk prediction models (n=709)



Note. 8 participants reported BRCA mutations and therefore were included in the full high-risk sample (resulting in a total n=717), despite not meeting the 20% risk threshold on Gail, Claus, or IBIS model.

Temporal trends in the population attributable risk (PAR) for endometrial cancer Elyse Llamocca* Elyse Llamocca Jennifer Sinnott Jordyn Brown Ashley Felix

Background: Endometrial cancer (EC) incidence rates peaked in 1975, remained steady, and have increased without signs of slowing from 2002. To investigate the role of established EC risk factor prevalence on incidence changes, we calculated PARs, estimates of the proportion of EC cases caused by a risk factor. Methods: We abstracted cohort study-specific RRs from recent meta-analyses and population-based cohort studies and historical and recent prevalence estimates in the following hierarchy: published national survey estimates, calculated national survey estimates, or prevalence in population-based case-control study controls. Results: From 1970s-80 to 2010s, prevalence of ever smoking cigarettes (CS) decreased; diabetes (D), hypertension (H), and obesity (OB) prevalence increased; and overweight (OW) prevalence stayed steady. From 1980s-90s to 2010s, metabolic syndrome (M) prevalence increased. From 1980s-90s to 2000s, estrogen only (E) menopausal hormone therapy (MHT) prevalence decreased and continuous-combined (CC) and sequential-combined (S) MHT prevalence increased. Historic to recent PAR changes were: CS: -0.09 (95% CI -0.13-0.06), -0.07 (95% CI -0.10-0.04); D: 0.06 (95% CI 0.03-0.10), 0.10 (95% CI 0.05-0.15); H: 0.08 (95% CI 0.03-0.13), 0.09 (95% CI 0.04-0.15); OB: 0.21 (95% CI 0.17-0.25), 0.39 (95% CI 0.35-0.44); OW: 0.08 (95% CI 0.05-0.12), 0.09 (95% CI 0.05-0.12); M: 0.12 (95% CI 0.05-0.20), 0.25 (95% CI 0.11-0.38); E: 0.19 (95% CI 0.10-0.28), 0.08 (95% CI 0.04-0.13); CC: -0.03 (95% CI -0.04-0.01), -0.04 (95% CI -0.07-0.02); S: 0.01 (95% CI 0.00-0.03), 0.02 (95% CI 0.00-0.05). Conclusion: OB and M PARs doubled. Risk factor prevalence changes may shape EC incidence temporal trends. Limitations: exposure definitions or age group changes over time and between studies and limited prevalence data, particularly on MHT. We will expand this preliminary analysis by exploring more risk factors, such as contraceptives, parity, and menarche/menopause age.

Disparities in mastectomy use for early invasive breast cancer between safety-net and general population breast cancer patients Rachel J. Meadows* Rachel Meadows Yan Lu Aaron Gehr Kalyani Narra Anuradha Lingam Bassam Ghabach Rohit Ojha

Background: Despite advantages of breast conserving therapy for early invasive breast cancer, mastectomy use is higher in safety-net than other cancer care settings. Patient (e.g., sociodemographic and insurance) and health system (e.g., care process) factors are proposed explanations for this disparity, but little evidence is available to disentangle the contribution of these factors. We aimed to assess the magnitude of disparity in mastectomy use explained by differences in patient characteristics between safety-net and general population breast cancer patients.

Methods: We used data from JPS Oncology and Infusion Center, the only safety-net cancer center in Tarrant County, TX. We used data from the Texas Cancer Registry to identify patients in Tarrant County as the general population comparison. Eligible patients in both populations included women aged ≥ 18 years diagnosed with stage I or II first primary breast tumors ≤ 5 cm between 2011 and 2017. We estimated crude and adjusted risk differences (RD) and 95% confidence limits (CL) for mastectomy use between populations. Adjustment was based on standardizing the distribution of age, race/ethnicity, and insurance status of the safety-net population to the general population.

Results: Our study comprised 367 safety-net and 5,133 general population breast cancer patients. Safety-net had higher frequency aged ≤ 65 years (85% vs. 66%), racial/ethnic minorities (63% vs. 29% minorities), and uninsured (56% vs. 5.5%) compared with the general population. Mastectomy use in the safety-net population was higher than the general population (RD=7.8%, 95% CL: 2.5%, 13%). Adjustment for sociodemographic factors reduced the disparity in safety-net patients (RD=-2.5%, 95% CL: -14%, 9.2%).

Conclusions: Our results suggest that sociodemographic and insurance differences explain higher use of mastectomy among safety-net breast cancer patients, which may be useful evidence for deliberating interventions to reduce mastectomy use.

Power Lines and Cancer Risk Mia Ye* Mia Ye

Background: Studies have reported an increased cancer risk associated with living near high-voltage electric power transmission lines. Power lines produce low-to mid-frequency magnetic fields (EMFs). These types of EMFs are in the non-ionizing radiation part of the electromagnetic spectrum and could be a potential cancer risk. The results from previous epidemiologic studies were mixed and most of them were from case-control studies. Most of these studies found less than 2-fold increase with less than an overall sample size of 500. We evaluated statistical power for case-control studies regarding power lines and cancer risk and provided guidance for future studies.

Methods: We calculated statistical power for case-control study regarding power lines and cancer risk. Based on the general scenario for power line exposure and cancer risk from historic data, we assumed the cancer incidence rate at 0.00001, relative risk at 1.5, 1.7 and 2.0, and power line exposure rate at 0.001 and 0.005. The statistical power was estimated by exact method based on R simulation.

Results: The study power was very low in current key study results from case control studies and ranged from 9% - 64%. Assuming the exposure rate is 1 per 100,000, a case control study with 500 per group has less than a 1% power to detect relative risk at 2.0. With larger sample size, a study with 10,000 per group only has 12.20%, 21.03, and 38.30% power to detect relative risk at 1.5, 1.7 and 2.0 respectively.

Conclusions: Our results indicated that current findings from case-control studies did not support a possible cancer risk associated with power line exposure. Most of the results could be false positives due to inappropriate statistical power. In the future, appropriate sample size is important for evaluating the cancer risk associated with power line exposure to avoid false positive results. In addition, the case control study design may have limits for detecting increased risk related to power lines.

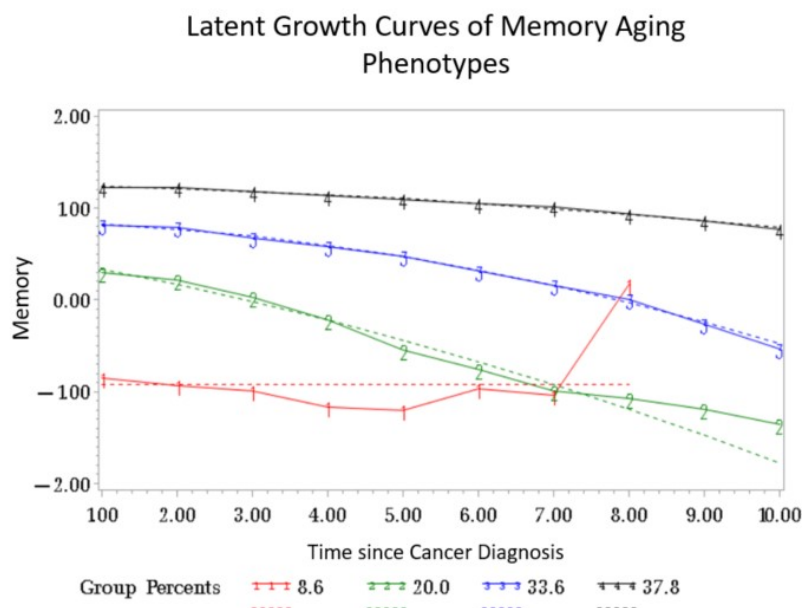
Memory aging phenotypes among older cancer survivors: A latent growth curve analysis of the Health and Retirement Study Ashly C. Westrick* Ashly Westrick Kenneth M. Langa Lindsay C. Kobayashi

While cancer survivors experience many long-term health effects, there is limited evidence on the potentially heterogeneous memory aging of older cancer survivors. Few cancer survivorship studies have access to pre-diagnostic data on potential determinants of memory aging, limiting knowledge of etiology and interventions to improve memory aging in this growing population. We aimed to identify memory aging phenotypes of older US cancer survivors, and determine sociodemographic and health-related predictors of membership.

Data were from 2,755 survivors aged ≥ 50 in the U.S. Health and Retirement Study (1998 - 2016). Self-reported first incident cancer diagnosis (except non-melanoma skin cancer) and memory (composite immediate and delayed word-list recall score, combined with proxy-reported cognition) were assessed at biennial interviews. Memory aging phenotypes were identified using latent growth curve (LGC) models, with baseline being time of cancer diagnosis. Logistic regression was used to evaluate predictors of group membership.

4 distinct memory aging groups were identified: low memory (n=234, 8.49%); medium-low memory (n=537, 19.5%); medium-high memory (n=935, 33.9%); and high memory (n=1049, 38.1%) (Figure 1). The low memory group received less chemotherapy compared to the other groups (22.2% vs. 28.1%, 31.4%, 39.3%, respectively), and had the shortest mean survival time after diagnosis (1.98 vs 3.55, 4.21, 4.29 years, respectively). Older age at diagnosis (OR: 1.36, 95%CI: 1.33-1.40), being male (OR: 4.29, 95%CI: 2.82-6.51), having a history of stroke (OR: 2.63, 95%CI: 1.65-4.18), and depression both prior to diagnosis (OR: 1.16, 95%CI: 1.08-1.24) were independently associated with being in the low memory group vs. the high memory group.

We identified distinct memory aging phenotypes among older cancer survivors. Further research should evaluate the influence of pre-cancer memory and how cancer survivor phenotypes differ from the general population.



The effect modifying role of race and obesity on the relationship between cancer diagnosis and heavy drinking: results from the 2018 BRFSS study Rachel Guyer* Rachel Guyer S. Cristina Oancea Ursula Running Bear

In January 2020, the American Cancer society estimated that over 1.8 million new cancer diagnoses would be made that year. A cancer diagnosis presents a significant burden on patients. Heavy alcohol consumption is a known risk factor for several types of cancer. Additionally, alcohol consumption is associated with a 3-fold increase in the likelihood of smoking cigarettes, which also increases cancer risk. The relationship between alcohol consumption and cancer has been well-characterized, however little research exists describing the impact of cancer diagnosis on heavy drinking. The BRFSS 2018 data was used to test for the association between cancer diagnosis and heavy drinking in US adults ages 18-80 years. The association was investigated using weighted and adjusted multivariable logistic regression models while testing the effect-modifying role of race and obesity. The weighted and adjusted odds (WAO) of current heavy drinking in American Indian/Alaska Native obese individuals and White non-obese individuals who have been diagnosed with cancer were significantly lower than the WAO of current heavy drinking among their counterparts who have not been diagnosed with cancer ((WAOR=0.21;95%CI:(0.11,0.42);N=2966) and (WAOR=0.85;95%CI:(0.75,0.96);N=165832), respectively). Marginally significant decreases in heavy drinking were seen among White obese and Black obese individuals who have been diagnosed with cancer ((WAOR=0.80;95%CI:(0.62,1.02);N=81658) and (WAOR=0.58;95%CI:(0.31,1.10);N=11732), respectively). The study results indicate that race and obesity modify the association between cancer diagnosis and heavy drinking. This suggests that there may be a difference in how different races or those with high BMI perceive health risks after cancer diagnosis. Further studies are needed to determine these perceived health risks following a cancer diagnosis to explain the decreased odds of heavy drinking in those diagnosed with cancer.

Is the use of a seat belt associated with screening for cancer? Results from the BRFSS 2018 survey Rachel Guyer* Rachel Guyer S. Cristina Oancea

Cancer is the second leading cause of death in the United States, and the American Cancer Society estimated that over 1.8 million new cancer diagnoses would be made in 2020. Adherence to screening recommendations is important for detecting cancer in the early stages when treatments are more likely to be successful. The current study examines the relationship between seat belt use and adherence to several cancer screening recommendations. The BRFSS 2018 data was used to test for the association between the use of a seat belt (SB) when driving or riding a car and a history of screening for cancer (SC). The association was investigated using weighted and adjusted multivariable logistic regression models on multiple age-based groups chosen according to cancer screening recommendations. The weighted and adjusted odds (WAO) of screening for cancer were significantly greater among individuals who were always or almost always wearing a SB compared to their counterparts who only sometimes, seldom or never used a SB, in females screened for cervical and colorectal cancer, and males screened for prostate and colorectal cancer, after adjusting for confounders of interest. It is notable that no significant association was found between wearing a SB and screening for breast cancer among females 40-65 YO (WAOR=1.28; 95%CI:(0.96,1.72)), while this association became significant among females 50-65 YO (WAOR=1.82; 95%CI:(1.21,2.72)). The results of this study indicate that individuals who wear a seat belt are more likely to participate in recommended screening for breast, cervical, prostate, and colorectal cancer. This suggests that those who do not wear seat belts may be at a greater risk of diagnosis with late-stage cancer and thus are a potential target for public health campaigns meant to increase adherence to cancer screening. Further studies are needed to determine whether seat belt use is associated with late-stage cancer diagnosis.

Exploring Global Cohort Resources for Studying Early Life Factors in Cancer Development

Rachel Hanisch* Rachel Hanisch Clare Rauche Dana Buckholz Somdat Mahabir

Background

Cancer research in human populations has primarily focused on exposures in the middle to later years of the lifespan. While this narrow age range yields the highest number of cancer cases, cancer prevention efforts are more difficult and perhaps less effective in this phase of life. Emerging evidence that early life factors affect cancer development later in life calls for a refocusing of efforts targeting the early life spectrum of modifiable exposures. This paradigm shift in cancer research could translate into substantial gains in cancer prevention and control. The goal of this study is to document key information available from existing prospective cohorts worldwide that can be leveraged for cancer research.

Methods

Cohort studies with 5,000 or more total participants at enrollment with relevant early life exposures (environmental, geographic, socio-demographic, genetic, social or chemical) were included for analysis. In addition to the types of exposures, we assessed sample size, geographical location of the cohorts, and types of biological samples collected. Information was abstracted and verified for each cohort selected.

Results

We assessed the information from 83 eligible cohorts from 25 countries worldwide. These included 9 cohorts in Asia/Middle East, 1 in Africa, 12 in North America, 52 in Europe, and 9 in Australia/Pacific. These 83 collective cohorts represent a sample size of 3,861,307 participants (2,464,170 children, 1,191,162 mothers and 205,975 fathers). The year of enrollment commencement ranged from 1934 to 2014. A total of 52 (62.7%) cohorts reportedly collected biological samples from participants.

Conclusions

The results of our investigation demonstrate that existing cohort resources can potentially be leveraged to advance research on early life exposures and events in cancer development. Leveraging these resources could advance innovative efforts to investigate the association between early life factors and cancer risk later in life.

LATEBREAKER

Cancer

Changes in dietary methionine intake and survival in postmenopausal women with breast cancer: results from the Women's Health Initiative Yangbo Sun* Yangbo Sun Jay H. Fowke Wei bao Buyun Liu Linda G. Snetselaar Robert B. Wallace Aladdin H. Shadyab Nazmus Saquib Lihong Qi Ting-Yuan David Cheng Karen C. Johnson

Background: Previous experimental studies have shown that limiting methionine (Met) in the diet of animals or in cell culture media suppresses mammary cancer cell proliferation or metastasis. However, no previous study has investigated the associations of changes in Met intake among women with breast cancer on survival. We examined associations of changes in dietary intake of Met (i.e., post- compared with pre-diagnosis of breast cancer), as well as changes in folate/folic acid and vitamin B12 (two important factors to promote Met synthesis in the body), with death from any cause and breast cancer death among breast cancer survivors.

Methods: Our study included 2096 postmenopausal women from the Women's Health Initiative who were diagnosed with invasive breast cancer and completed a food frequency questionnaire both before and after diagnosis. Multivariable Cox proportional hazards regression models were used to estimate adjusted HRs and 95% CIs of death from any cause and breast cancer.

Results: Relative to pre-diagnosis, 28% of women decreased Met intake by $\geq 20\%$, and 29% increased Met intake by $\geq 20\%$, and 43% had a relatively stable Met intake ($\pm 19.9\%$), following breast cancer diagnosis. During a mean 14.5 years of follow up, there were 1025 deaths from any cause, including 245 due to breast cancer. Compared with women with relatively stable Met intake, women with decreased Met intake had a lower risk of death from any cause (HR 0.81, 95% CI 0.68-0.98), and a lower risk of death from breast cancer (HR 0.63, 95% CI 0.44-0.91) in fully adjusted models. Increased Met intake, or changes in dietary folate/folic acid or vitamin B12 intake, were not associated with death from any cause or breast cancer death.

Conclusion: Among women with breast cancer, decreased dietary Met intake after breast cancer diagnosis was associated with lower risk of death from any cause and breast cancer death, while increased dietary Met intake was not associated with death.

LATEBREAKER

Cancer

Examining The Impact of a Cancer Diagnosis on the Rate of Non-Fatal Self-Injury: a Matched Cohort Study Using Population-Based Administrative Databases in Ontario Lena Nguyen* Lena Nguyen Alyson Mahar Tony Eskander Julie Hallet Wing C. Chan Rinku Sutradhar

Background: Psychological distress following a cancer diagnosis potentially increases the risk for intentional, non-fatal self-injury (NFSI). Little is known about NFSI rate among patients with cancer and how it compares to the cancer-free population.

Objectives: This study aims to evaluate and compare NFSI rates among individuals in Ontario diagnosed with cancer against matched controls with no history of cancer, taking into account pre-existing differences in NFSI rate.

Methods: Adults diagnosed with cancer from 2007-2019 were age and sex matched to 2 cancer-free individuals. The absolute and relative difference in NFSI rates were calculated in the 5 years prior to and after index, where index was the date of cancer diagnosis. Comparisons were made using a difference in difference approach. Poisson regression was used to examine if the change in NFSI rates before and after index differed between cancer patients and controls. Covariates included socio-demographic characteristics, clinical characteristics, prior self-injury and pre-existing psychiatric illness.

Results: The cohort included 803,740 persons with cancer and 1,607,480 matched controls. Prior to index, the cancer group had 0.95 NFSI events per 1000 person years and controls had 0.88 events per 1000 person years; after index these rates were 0.91 events per 1000 person years and 0.77 events per 1000 person years, respectively. The adjusted rate among individuals with cancer was 1.06 (95% CI: 0.97-1.15) times higher in the pre-period and 1.15 (95% CI: 1.05-1.27) times higher in the post period, corresponding to a ratio of relative rates of 1.09 (95% CI: 0.99-1.21).

Implications: A cancer diagnosis was associated with increased NFSI after accounting for pre-existing differences in self-injury rates prior to diagnosis. Although rare, NFSI are a strong risk factor for death by suicide. Robust and accessible psychosocial oncology programs are needed to support mental health along the cancer journey.

LATEBREAKER

Cancer

Factors Affecting Malignant Peripheral Nerve Sheath Tumor Survival: An Analysis Using Data from the Surveillance, Epidemiology, and End Results Program Allison Domingues*

Allison Domingues Erin Marcotte

Malignant peripheral nerve sheath tumors (MPNSTs) are rare soft tissue sarcomas that generally arise from the Schwann cells of the peripheral nervous system and can occur throughout the body. Though MPNSTs are rare in the general population, individuals with Neurofibromatosis-1 (NF1)—an autosomal dominant genetic disorder—are at substantially increased risk and are typically diagnosed at earlier ages. MPNSTs have poor prognosis, with a 5-year survival estimated at just over 50%. This study aimed to characterize the factors associated with cause-specific MPNST survival including information related to treatment and census-tract level socioeconomic status (CT-SES). We identified 2370 primary MPNSTs using the SEER 18 (2000-2016) database. We used Cox proportional hazards modeling to estimate hazard ratios (HR) and 95% confidence intervals for the association between survival and sex, race/ethnicity, CT-SES quintile, metastasis at diagnosis, tumor site, age at diagnosis, and treatment by surgery. Models were fit in both all cases as well as stratified into those diagnosed before and after age 30 in order to assess what differences may exist between the general population and those with a higher probability of NF1. Among all cases and cases diagnosed at ages 30 and above, we observed statistically significant associations between age at diagnosis, CT-SES, and metastasis at diagnosis and lower survival. However, among cases diagnosed before age 30, only CT-SES was significantly associated with survival. These findings suggest that there may be differences in the factors affecting survival between the general population and those with NF1.

Characteristic	Overall HR (95% CI)	<30 Years HR (95% CI)	>=30 Years HR (95% CI)
Sex			
Male	0.9715 (0.8428, 1.1199)	1.0702 (0.80138, 1.4291)	0.9422 (0.7970, 1.1140)
Female	ref	ref	ref
Race			
White	ref	ref	ref
Black	1.0510 (0.8441, 1.3087)	1.0360 (0.66237, 1.6205)	1.0760 (0.8302, 1.3946)
API	0.9514 (0.7351, 1.2313)	0.9511 (0.51864, 1.7509)	0.9529 (0.7114, 1.2765)
AI/AN	0.7964 (0.3226, 1.9660)	0.9498 (0.22262, 4.0518)	0.7706 (0.2357, 2.5196)
Hispanic	1.0031 (0.8128, 1.2380)	0.9206 (0.63119, 1.3426)	1.0597 (0.8170, 1.3746)
Non Hispanic Unknown	0.8009 (0.3278, 1.9569)	0.3578 (0.04826, 2.6530)	0.9874 (0.3594, 2.7126)
SES (Yost Quintile)			
Quintile 1	ref	ref	ref
Quintile 2	0.7070 (0.5597, 0.8931)	0.6127 (0.38810, 0.9672)	0.7729 (0.5827, 1.0251)
Quintile 3	0.8338 (0.6642, 1.0468)	0.7192 (0.46638, 1.1091)	0.8830 (0.6701, 1.1635)
Quintile 4	0.7020 (0.5516, 0.8933)	0.7117 (0.44084, 1.1491)	0.7218 (0.5418, 0.9617)
Quintile 5	0.7893 (0.6175, 1.0089)	1.0660 (0.67336, 1.6875)	0.7525 (0.5588, 1.0132)
Surgery			
Yes	1.1746 (0.9114, 1.5138)	0.9376 (0.50980, 1.7244)	1.2273 (0.9198, 1.6376)
No	ref	ref	ref
Metastasis at Diagnosis			
Yes	1.6075 (1.1788, 2.1923)	1.8047 (0.98900, 3.2930)	1.4799 (1.0156, 2.1565)
No	ref	ref	ref
Site			
CNS	ref	ref	ref
Head/Neck	0.7991 (0.5661, 1.1280)	0.8972 (0.46490, 1.7315)	0.8141 (0.5357, 1.2372)
Trunk/Core	0.9354 (0.6780, 1.2905)	1.0226 (0.55039, 1.8999)	0.9649 (0.6501, 1.4320)
Limb	0.8675 (0.6290, 1.1965)	0.9776 (0.53279, 1.7938)	0.8810 (0.5948, 1.3048)
Other/Unknown	0.9645 (0.6030, 1.5426)	1.2209 (0.47043, 3.1684)	0.9786 (0.5617, 1.7051)
Age at Diagnosis			
	1.0054 (1.0016, 1.0093)	1.0059 (0.98440, 1.0279)	1.0094 (1.0031, 1.0158)
Number in situ tumors			
One	ref	ref	ref
Two+	0.8585 (0.6797, 1.0845)	0.7249 (0.36153, 1.4534)	0.8624 (0.6700, 1.1102)

API=Asian and Pacific Islander; AI/AN=American Indian/Alaska Native; CNS=Central Nervous System

LATEBREAKER

Cancer

Stomach Cancer Incidence in the UAW-GM Autoworkers Cohort Hilary Colbeth* Hilary Colbeth Sally Picciotto Sadie Costello Ellen Eisen

Objective The United Auto Workers-General Motors (UAW-GM) Cohort was jointly funded by labor and management (1985) as a cancer mortality study, motivated by worker concerns regarding digestive cancers due to occupational metalworking fluid (MWF) exposure. Previously, we found little evidence of increased stomach cancer risk; however, we recently reported an elevated risk of stomach cancer mortality with increasing straight fluid exposure after extending follow up to 2015. Here we present an investigation of MWF exposure and stomach cancer incidence among 39,520 autoworkers.

Methods Over a follow-up period of up to 42 years (1973-2015), adjusted hazard ratios (HR) for incident stomach cancer were estimated using a Cox proportional hazards model with categorical levels of lagged cumulative exposure. Three MWF (straight, soluble, synthetic) exposures were categorized with a pre-determined reference group. Potential healthy worker survivor effect (HWSE) bias was assessed by estimating the following pathway-specific adjusted HRs: (1) cumulative exposure and leaving work; and (2) employment status and incident stomach cancer.

Results In total, 214 incident stomach cancer cases occurred throughout the follow-up. The estimated exposure-response pattern for each MWF exposure was non-monotonic and rose to 1.68 (95% CI: 1.05-2.67) for straight fluids. All HRs within the soluble and synthetic exposure categories displayed wide 95% CIs which included the null. Pathway-specific analyses suggested that higher cumulative exposure was associated with a greater risk of leaving work and that the hazard of incident stomach cancer was higher among those who left work, hallmark associations of the HWSE.

Conclusions Stomach cancer incidence was strongly associated with cumulative exposure to straight MWFs. Further, the pathway-specific analysis suggests bias due to the HWSE, which may result in attenuation of the true effect. Causal inference methods, such as g-methods may be appropriate.

LATEBREAKER

Cancer

Exploring disparities in pediatric acute lymphoblastic leukemia outcomes Amanda Janitz*
Amanda Janitz Janis Campbell Chao Xu Rene McNall-Knapp Hanumantha Pokala Jessica Blanchard

Background: Childhood cancer is the leading cause of disease-related death among children aged 5-19 years in the US. While there have been great successes in the treatment of cancer, little information is available on disparities in access to treatment and survival among underrepresented populations, especially American Indian (AI) children.

Methods: We partnered with a children's hospital at an academic medical center to abstract data from electronic medical records and the institution's cancer registry on cancer diagnosis, treatment, and outcomes for children with acute lymphoblastic leukemia (ALL) (n=371). We evaluated the relation between 1) race/ethnicity and 2) distance to care from residence at diagnosis to the children's hospital and event-free survival diagnosed prior to age 20 from 1994-2019. We evaluated the difference in survival times from diagnosis to date of first recurrence, death, or end of the study period by race using Kaplan-Meier analysis with the log-rank test. We used the Cox Proportional Hazards Model for multivariable survival analyses of race/ethnicity and distance to care (<25, 25-74, and ≥75 miles).

Results: The median age of ALL diagnosis was 5.4 years, with 48% being female, the most common insurance types were Medicaid (51%) and private insurance (45%). We observed an increased, though imprecise, hazard rate of cancer recurrence among non-Hispanic (NH) AI children compared to NH white children after adjusting for year of diagnosis (HR: 1.10, 95% CI: 0.76, 1.58), with HRs below the null for NH Asian, NH Black, and Hispanic children. We observed no association between distance to the children's hospital and cancer recurrence.

Conclusion: As a next step, we will obtain electronic medical record data from the other children's hospital in the state and link our dataset with the state cancer registry to allow for a more comprehensive, population-based evaluation of cancer disparities in Oklahoma.

LATEBREAKER

Cancer

Nonsteroidal Anti-Inflammatory Drug Use and Skin Cancer Risk: A Prospective Cohort**Study** Marie Al-Rahmoun* Marie Al-Rahmoun Reza Ghiasvand Manon Cairat Yahya Mahamat-Saleh Gianluca Severi Marie-Christine Boutron-Ruault Trude Eid Robsahm Marina Kvaskoff Agnès Fournier

Background: Skin cancer incidence has increased over the past decades. Nonsteroidal anti-inflammatory drugs (NSAIDs), which are among the most commonly used drugs, may have photosensitizing but also chemopreventive effects. Whether they influence skin cancer risk is not clarified. We aimed to analyze the relationship between the use of NSAIDs and the risk of skin cancers in the E3N cohort.

Methods: E3N is a prospective cohort of French women born in 1925-1950. Health and lifestyle data were self-reported biennially by participants and matched with drug reimbursement data allowing identifying participants' NSAID use since 2004. We used Cox models adjusted for skin cancer risk factors to estimate hazard ratios (HRs) with 95% confidence intervals (CIs).

Results: Over 2004-2014, 455 cutaneous melanoma, 1,743 basal cell carcinoma, and 268 squamous cell carcinoma cases were ascertained among 62,486 women with a mean age of 62.1 (\pm 6.3) years at the start of the follow-up. There were no associations between ever use of NSAIDs and risk of basal cell carcinoma (HR=1.08, 95%CI=0.96-1.22) or squamous cell carcinoma (HR=1.02, 95%CI=0.75-1.37), compared with never use. However, for squamous cell carcinoma risk, we observed significant variation across NSAID classes ($P_{\text{homogeneity}}=0.001$), with a lower risk of squamous cell carcinoma with ever use of propionic acid derivatives (HR=0.63, 95%CI=0.48-0.83). We found a higher risk of melanoma with ever use of non-aspirin NSAIDs (HR=1.44, 95%CI=1.12-1.84) but not with ever use of high-dose aspirin (HR=0.94, 95%CI=0.71-1.25, $P_{\text{homogeneity}}=0.03$).

Conclusion: Our findings of a higher melanoma risk in non-aspirin NSAID users and a lower squamous cell carcinoma risk in propionic acid derivative users deserve further investigation in other settings.

LATEBREAKER

Cancer

Nighttime fasting duration, time of breakfast and breast cancer risk Anna Palomar-Cros*
 Anna Palomar-Cros Barbara Harding Ana Espinosa Kyriaki Papantoniou Kurt Straif Beatriz Pérez-Gómez Inés Gómez-Acebo Ana Molina-Barceló Juan Alguacil Pilar Amiano Eva Ardanaz Rafael Marcos Vicente Martín Victor Moreno Adoninda Tardón Yolanda Benavente Gemma Castaño-Viñals Dora Romaguera Manolis Kogevinas

Introduction

Prolonged nighttime fasting has been linked with a reduction in breast cancer incidence and progression; while some studies suggest that skipping breakfast is associated with poor metabolic outcomes such as impaired glucose homeostasis and low-grade inflammation. This study evaluates the effects of nighttime fasting duration and time of breakfast on breast cancer risk.

Methods

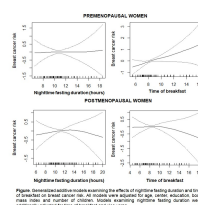
We analyzed data from 1,181 breast cancer cases and 1,326 population matched controls from the Spanish multi-case control study, enrolled from 2008-2013. We collected circadian nutritional habits at mid-age via a telephonic interview. We defined nighttime fasting as the period between the last meal and the first meal the following day. We examined the effects of nighttime fasting duration and time of breakfast on breast cancer risk applying generalized additive models, separately for premenopausal and postmenopausal women (see figure). We estimated OR and 95% CI using logistic regression. We adjusted models for age, center, education, time of breakfast, number of children and body mass index.

Results

In both premenopausal and postmenopausal women, fasting for more than 11 hours overnight (the median duration among controls) was not associated with breast cancer risk compared to a shorter fasting period (OR= 1.02, 95% CI 0.70-1.48 and OR= 1.00, 95% CI 0.78-1.28, respectively). Menopausal status modified the association between time of breakfast and breast cancer risk (p -value <0.01). Among premenopausal women, each hour delay in the time of breakfast was associated with a 19% increase in breast cancer risk (OR=1.19, 95% CI 1.05-1.36). In postmenopausal women, time of breakfast was not associated with breast cancer risk (OR = 1.01, 95% CI 0.92-1.10).

Conclusion

Our results suggest that late breakfast is associated with an increased risk of breast cancer in premenopausal women. We did not observe an association between nighttime fasting duration and breast cancer risk.



LATEBREAKER

Cancer

Exposure to Particulate Matter Air Pollution and Risk of Gastrointestinal Cancers: A Systematic Review and Meta-Analysis Natalie Pritchett (Haley, married name)* Natalie Pritchett (Haley, married name) Emily C. Spangler George M. Gray Alicia A. Livinski Joshua N. Sampson Sanford M. Dawsey Rena R. Jones

Background: Outdoor air pollution, especially particulate matter (PM), is a known lung carcinogen, but research investigating other cancer types such as gastrointestinal (GI) cancers is limited.

Objective: We conducted a systematic review and meta-analysis to investigate the association between exposure to PM and GI cancers in adults.

Methods: We searched five databases for original research published from 1980 - 2019 in English that quantified exposure to PM in relation to GI cancer incidence or mortality. We evaluated the risk of bias of individual studies and the overall quality and strength of the evidence according to the Navigation Guide methodology.

Results: Fifteen studies met the inclusion criteria and included participants from 13 countries. We rated most studies with “probably low” risk of bias and rated the overall body of evidence as “moderate” quality with “limited” evidence for an association with PM and GI cancers. We based this determination on the generally positive, but inconsistently statistically significant effect estimates reported by a small number of studies and the fact that chance, bias, and confounding could not be ruled out with reasonable confidence.

Discussion: We conducted a systematic review and meta-analysis of epidemiologic studies of exposure to PM air pollution and GI cancer and concluded that currently there is limited evidence of associations based on a small number of studies. Future researchers should strive to conduct more studies in the geographic areas with highest GI cancer burden, evaluate the impact of different PM exposure assessment approaches on observed associations, and include investigation of cancer subtypes and specific chemical components of PM.

LATEBREAKER

Cancer

Socioeconomic Patterns and Environmental Greenness in Relation to Census Tract-Level Colorectal Cancer Rates in Kentucky. Johnnie D Newton* Felicia Pugh Madeline M Tomlinson Matthew Ruther Tyler Ellis Natalie DuPre1

Background: Kentucky has the third-highest rate of colorectal cancer (CRC) in the United States. Normalized Difference Vegetation Index (NDVI) is a commonly used measure of greenness that has been associated with health benefits like CRC risk reduction behaviors. Associations between greenness exposure and CRC have not been fully studied and are confounded by complex correlations with socio-economic (SES) determinants. We examined the relationship between census tract-level NDVI and CRC in Kentucky, controlling for SES patterns and separately for individual SES markers.

Methods: 1996-2014 annual average NDVI within Kentucky census tracts were linked to census tract-level SES, demographic, and housing factors averaged from 2010-2018 American Community Surveys. Principal components analysis was used to identify factor loadings of 11 SES variables. Poisson regression was used to estimate relative risks (RR) and 95% confidence intervals (CI) of census-tract level sex-specific CRC case rates for a 0.1 unit increase in NDVI, adjusting for SES patterns, population density, race, age, physical inactivity, and obesity. We also considered models with single SES markers: percent below poverty, education, and household income.

Results: Three principal components explained 75% of SES variation in census-tracts. NDVI was not associated with CRC rates when adjusting for SES patterns (female RR = 0.96 95%CI 0.91-1.02; male RR= 1.04 95%CI 0.98-1.11); however, associations were stronger among females when adjusting for individual SES variables (female RR = 0.89 95%CI 0.85-0.95; male RR= 0.99 95%CI 0.94-1.05).

Conclusions: Census-tract level greenness was generally not associated with Kentucky CRC rates when considering confounding by SES patterns; however, associations were more strongly inverse for greenness and female CRC rates when adjusting for individual SES markers. Future work should consider the complexities of SES confounding in ecological analyses of greenness and health.

LATEBREAKER

Cancer

Comparisons of age-adjusted incidence of myeloid malignancies by subtype in Hong Kong and the United States Bryan Bassig* Bryan Bassig Bu-Tian Ji Yok-Lam Kwong Nathaniel Rothman Kit-fai Wong Qing Lan

Myeloid malignancies typically arise in the bone marrow and consist of many disease subtypes. Data on incidence rates and patterns of myeloid malignancies for subtypes based on the World Health Organization (WHO) classification are lacking in Asian populations. We calculated and compared age-adjusted incidence rates for 28 myeloid malignancy WHO-defined subtypes in Hong Kong (HK) with those for Asians and whites living in the United States (U.S.). Data on myeloid malignancy diagnoses were collected from four hospitals in HK between 2014 and 2016 that represent nearly all of the cases diagnosed in HK over this time period, and from the U.S. Surveillance, Epidemiology, and End Results (SEER) Program between 2010 and 2016. With the exception of acute myeloid leukemia (AML) (2.23 cases per 100,000 person-years) and myeloproliferative neoplasms (MPN) (2.10 cases per 100,000 person-years), rates of all subtypes in HK were <1 case per 100,000 person-years including for myelodysplastic syndrome (MDS) overall (0.85 cases per 100,000 person-years). Overall rates of AML, MDS, and MDS/MPN (neoplasms with characteristics that overlap between MDS and MPN) were lower in HK compared to both white and Asian individuals in the U.S, but the patterns by specific subtypes within these broader categories varied. For these three broad groups of myeloid malignancies, rates in U.S. Asians were intermediate to those in HK and white individuals in the U.S. Overall rates of MPN were also lower in HK compared to white individuals in the U.S. (standardized rate ratio (SRR)=0.8, 95% CI=0.7-0.8), but were similar in HK and Asians in the U.S. (SRR=1.1, 95% CI=0.97-1.2 for HK vs. U.S. Asians). These patterns were similar in analyses stratified by sex, although rates for major subtypes were lower in women compared to men across all three populations. These results suggest a multifactorial etiology involving both genetic and environmental factors for specific myeloid malignancy subtypes.

Young adult males experience worse survival from many CNS tumor types compared to females: An analysis of the National Cancer Database (NCDB) Kristin J Moore* Kristin Moore
Lindsay A Williams Christopher L Moertel

Background: Central nervous system (CNS) tumors are the leading cause of male cancer-related death and the fourth-leading cause of female cancer-related death among young adults (20-39 years). Few studies have evaluated whether the observed associations depend on treatment received and socioeconomic status.

Methods: Using the National Cancer Database (NCDB; 2004-2016) we identified individuals aged 20-39 years at diagnosis with a CNS tumor defined by one of 17 histologic types. Kaplan-Meier survival curves (Log-rank p-values) were used to characterize survival differences by sex for each histology. Hazard ratios (HR) and 95% CI were calculated using multivariable Cox proportional hazards models for male sex (female referent) and death while accounting for age, race, year of diagnosis, insurance status, urban/rural status, distance between hospital and home, and income.

Results: A total of 49,614 cases were included (46.9% male). Males had significantly worse long-term survival overall ($p < 0.001$) and had a higher risk of death following any CNS tumor diagnosis (HR 1.47, 95% CI 1.41-1.54). A statistically significant increased risk of death for males compared to females was observed for diffuse astrocytoma, anaplastic astrocytoma, glioblastoma, oligodendroglioma, oligoastrocytic tumors, other malignant glioma, neuronal and mixed neuronal-glial tumors, meningioma, and hemangioma even after adjustment for confounders. The largest risk of death for males was observed in hemangioma (HR 2.58, 95% CI 1.41-4.71), meningioma (HR 2.01, 95% CI 1.71-2.35), and neuronal/mixed neural-glial tumors (HR 1.52, 95% CI 1.07-2.17).

Conclusions: Among young adults, males had a higher risk of death overall and among many histologies, even after accounting for detailed treatment received and socioeconomic measures. These findings suggest lifestyle risk factors or biologic processes may underlie the observed sex disparities in CNS tumor survival among young adults.

LATEBREAKER

Cancer

Extracting features from mammograms in addition to breast density improves risk prediction for breast cancer: preliminary application Graham Colditz* Graham Colditz Shu (Joy) Jiang

Growing emphasis is being placed on the clinical use of breast cancer risk (BC) prediction tools to more appropriately stratify risk for women undergoing routine mammographic screening. We evaluate a novel method to add to the information obtained from routine mammography typically summarized as breast density (BD).

To refine risk stratification for precision prevention, we developed a model to better capture the between-patient heterogeneity in the breast tissue. We extract features that are highly correlated with the onset time of BC from baseline mammograms defined by ~13 million pixels.

The proposed method, supervised functional principal component analysis (sFPCA), is accompanied with an eigenvalue decomposition algorithm that is computationally efficient and performs well in simulation studies. The proposed method is applied to the motivating dataset from the Joanne Knight Breast Health cohort at Siteman Cancer Center. This cohort of 10,092 women, with mammograms (BIRADs breast density, BD) and well-studied BC risk factors, has been followed for 10 years and includes pathology confirmed incident BC. We selected a random sample of 785 women from 347 incident cases and 681 controls matched on age and year of cohort entry.

The extracted features using the proposed sFPCA method provide complementary and independent information from BD. The added value of these extracted features is then confirmed by estimating the 5-year risk of breast cancer. The predictive performance, under a 10-fold cross-validation show that the model with age + BD + weight + height achieved AUC of 0.59 (sd=0.13), while the model with additional features + age + BD + weight + height achieved AUC of 0.73 (sd=0.12).

These emerging results suggest that the additional supervised image-based features provide complimentary information to breast density, and better discriminate risk of breast cancer. This new method opens novel data integration for risk prediction from routine screening mammograms.

Association of serum carbohydrate antigen 125 levels with all-cause and cause-specific mortality among US women Yangbo Sun* Yangbo Sun Buyun Liu Robert B Wallace Jay H Fowke Karen C Johnson Wei Bao

Background Carbohydrate antigen 125 (CA-125), also known as cancer antigen 125, is a tumor biomarker initially related to ovarian cancer. However, recent studies have frequently observed increased levels of serum CA-125 both in patients affected by malignancies other than ovarian cancer and in patients affected by non-malignant cardiovascular diseases (CVD) such as systolic heart failure and new-onset atrial fibrillation. Nevertheless, the association of CA-125 levels with mortality and the underlying causes of death in the general population remain unclear.

Methods We included 1985 women (≥ 20 years) free of CVD or cancer and not currently pregnant who participated in the National Health and Nutrition Examination Survey (NHANES) 2001-2002. Serum CA-125 levels were measured among women using electrochemiluminescence immunoassay. All-cause and cause-specific mortality were ascertained by linkage to mortality records through December 31, 2015. Cox proportional hazards regression models were used to estimate the HRs and 95% CIs of mortality associated with serum CA-125 levels.

Results During 25,683 person-years of observation, 329 deaths occurred, including 58 deaths from CVD and 70 deaths from cancer. After adjustment for a variety of potential confounders, the HRs and 95% CIs for all-cause mortality, CVD mortality and cancer mortality comparing the highest with the lowest tertile of CA-125 levels were 1.19 (0.85-1.66), 2.86 (1.11-7.37) and 0.65 (0.26-1.60), respectively. In the fully adjusted model, compared with women with normal CA-125 levels (≤ 35 U/mL), the HRs and 95% CIs for all-cause mortality, CVD mortality and cancer mortality among women with high serum CA-125 levels (> 35 U/mL) were 1.70 (0.89-3.24), 4.63 (1.63-13.2) and 1.09 (0.21-5.59), respectively.

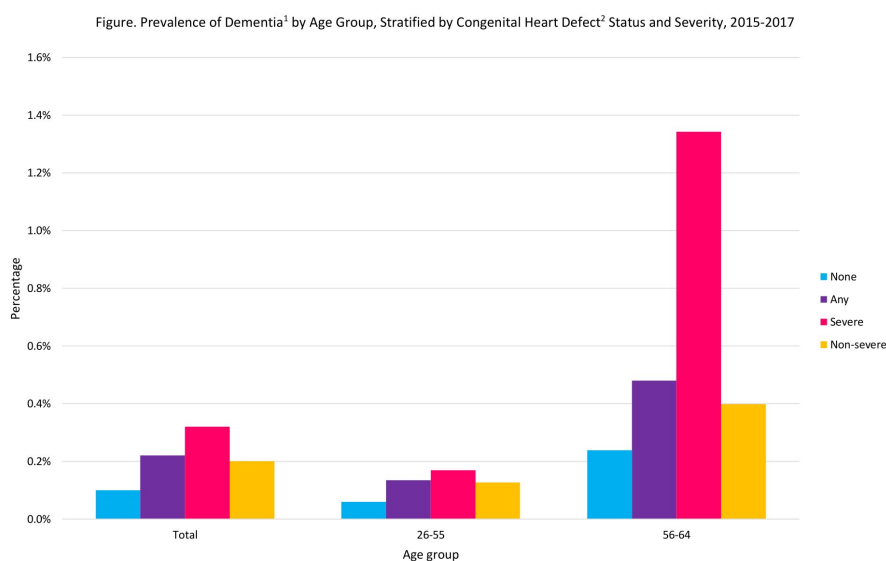
Conclusions Higher serum levels of CA-125 were associated with higher CVD mortality.

Further investigation is needed to replicate our findings and determine the underlying mechanisms and clinical implications.

Prevalence of dementia by age among privately-insured adults with and without congenital heart defects, 2015-2017

Karrie F. Downing* Karrie Downing Matthew E. Oster Sherry L. Farr

Neurocognitive issues are common among individuals with congenital heart defects (CHD). However, less is known about prevalence and onset of dementia among adults with CHD. Our objectives were to determine if prevalence of diagnosed dementia among adults ages 26-64 years differs by presence and severity of CHD and if these relationships are modified by age group (26-55, 56-64 years). Using IBM MarketScan Commercial claims databases, we identified adults with CHD (defined as ≥ 2 outpatient CHD diagnosis codes >30 days apart or ≥ 1 inpatient code documented in 2007-2017) continuously enrolled from 2015-2017 in employer-sponsored health insurance. Those with Down syndrome diagnosis codes documented from 2007-2017 were excluded. Severe CHDs were those typically requiring intervention in the first year of life. Dementia was defined as ≥ 2 outpatient dementia diagnosis codes ≥ 1 day apart or ≥ 1 inpatient code and identified between 2015 and 2017. Log-binomial regression models estimated adjusted prevalence ratios (aPRs) and 95% confidence intervals (CIs) for associations between presence and severity of CHD and dementia. All models included sex, region, age as of January 2015, and an interaction term for age and CHD presence or severity, respectively. There were 20,072 adults with CHD diagnoses and 7,121,951 adults with no CHD diagnosis. Overall, 0.2% of adults with CHD and 0.1% without were diagnosed with dementia [aPR=2.2 (CI: 1.6-2.9)]. Stratifying by age, the aPR among 26-55 year-olds was 2.3 (CI:1.5-3.6) and among 56-64 year-olds was 2.0 (CI: 1.4-3.0). For CHD severity, the overall aPR comparing severe CHD to no CHD was 4.0 (CI: 2.2-7.3); comparing non-severe CHD to no CHD was 1.9 (CI:1.4-2.7); and comparing severe to non-severe CHD was 2.3 (CI:1.1-4.5). Across all age groups, dementia is more prevalent among adults with both severe and non-severe CHD compared to those without CHD and also among adults with severe CHD compared to those with non-severe CHD.



¹Defined as ≥ 2 outpatient dementia diagnosis codes ≥ 1 day apart or ≥ 1 inpatient code identified between 2015 and 2017. Dementia diagnosis codes were identified from the Center for Medicare & Medicaid Services Chronic Conditions Data Warehouse.

²Defined as ≥ 2 outpatient congenital heart defect diagnosis codes ≥ 30 day apart or ≥ 1 inpatient code identified between 2007 and 2017. Congenital heart defect diagnosis codes include ICD-9-CM codes between 745-747 and ICD-10-CM codes between Q20-Q26, excluding non-specific codes and ostium secundum type atrial septal defect.

Associations between APOL1 genetic variants and blood pressure and modifications by air pollutants in African American mother-child dyads Yu Ni* Yu Ni Claire Simpson Robert Davis Adam Szpiro Catherine Karr Csaba P Kovesdy Rebecca Hjorten Frances A. Tylavsky Nicole R. Bush Kaja Z. LeWinn Cheryl A. Winkler Jeffrey B. Kopp

Background: Carriage of two *APOL1* genetic variants is associated with increased risk for chronic kidney diseases in people of African descent. Less is known about the variants' associations with blood pressure and interactions with air pollution.

Methods: We investigated the association of *APOL1* variants with blood pressure in a prospective cohort of 556 African American mothers and 493 of their children. Participants with two *APOL1* risk alleles were classified as having the high-risk genotype. Blood pressure was measured at the child age 4-6 years visit. Mothers with SBP 130 mmHg and/or DBP 80 mmHg were defined as hypertensive, and children with SBP and/or DBP 90th percentile were characterized as having high blood pressure (HBP). We fit multivariate linear and Poisson regressions and further adjusted for population stratification. Several effect modifiers were examined using interaction models, including air pollution exposures (PM_{2.5}, NO₂ and proximity to road) in both populations; hypertensive disorder, obesity and smoking in mothers; sex, preterm birth, obesity and prenatal smoking exposure in children.

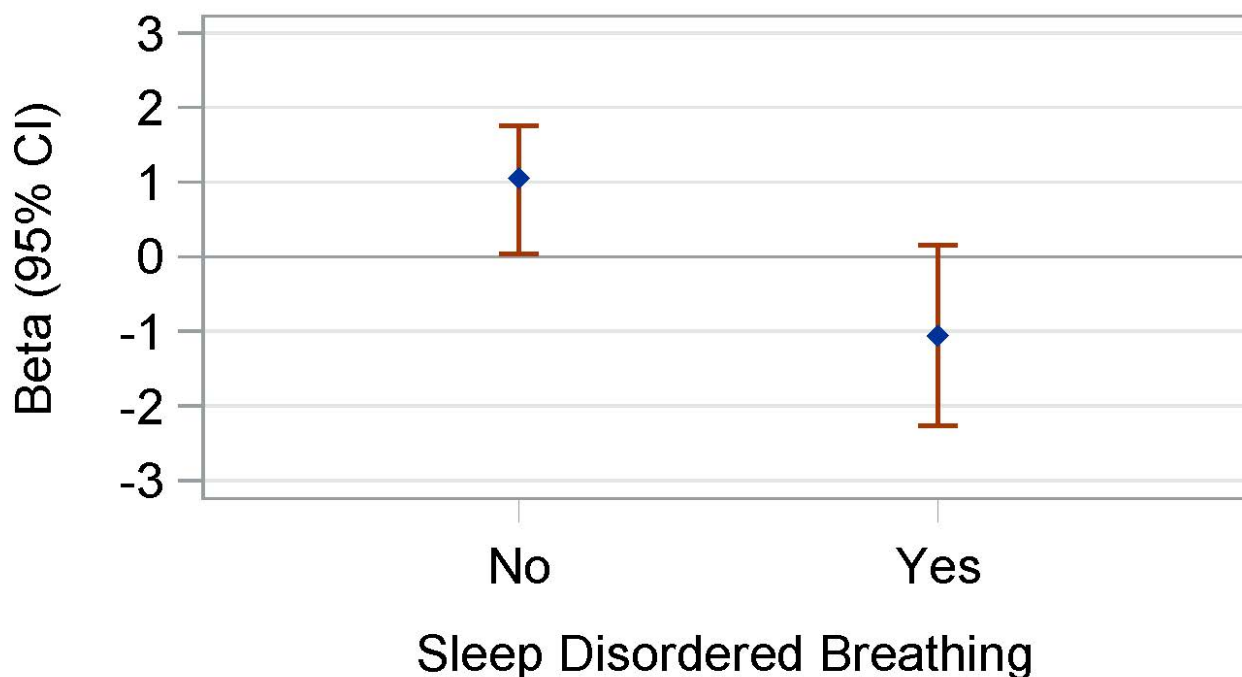
Results: 10% of the mothers and 15% of the children had two *APOL1* risk alleles. 231 (42%) of the mothers and 154 (31%) of the children were categorized as hypertensive and HBP, respectively. We found no association of *APOL1* alleles or *APOL1* risk genotypes with blood pressure in either population. Each 2- $\mu\text{g}/\text{m}^3$ increase of 4-year average PM_{2.5} was related to a 16.3 (95%CI: 5.7, 26.9) mmHg and a 2.9 (95%CI: -3.1, 8.8) mmHg higher DBP in mothers with the *APOL1* high-risk and low-risk genotype, respectively ($P_{\text{interaction}}$: 0.01). Girls with *APOL1* risk alleles or high-risk genotype had a higher risk of HBP than boys with the same genetic variants (*APOL1* alleles: IRR_{girl}: 1.3, 95%CI: 0.95,1.7; IRR_{boy}: 0.8, 95%CI: 0.7, 1.04; $P_{\text{interaction}}$: 0.02; High-risk genotype: IRR_{girl}: 1.9, 95%CI: 1.2,3.03; IRR_{boy}: 0.7, 95%CI: 0.4,1.1; $P_{\text{interaction}}$: 0.005).

Conclusions: We found no evidence for effects of *APOL1* variants on blood pressure but detected potential interactions with PM_{2.5} in mothers and sex-specific associations in children. Our study suggests novel areas of investigation into population health disparities and highlights the adverse response to air pollution in subgroups.

Sleep may modify associations between poly- and per-fluoroalkyl substances and blood pressure: A nationally representative study of U.S. adults Symielle A. Gaston* Symielle Gaston
Chandra L. Jackson

Poly- and per-fluoroalkyl substances (PFAS) are persistent organic pollutants that have been associated with elevated blood pressure. Sleep has been shown to both affect blood pressure and contribute to the clearance of toxins. Yet, studies have not examined sleep as a potential effect modifier of associations between PFAS and blood pressure. To investigate the PFAS-blood pressure association as well as sleep as a potential modifier, we pooled cross-sectional 2005-2016 National Health Nutrition Examination Survey data from 7,906 U.S. adults. Serum PFAS measured over all survey years and summed included perfluorodecanoic acid, perfluorohexane sulfonic acid, 2-(N-methylperfluorooctanesulfonamido) acetic acid, perfluorononanoic acid, perfluoroundecanoic acid, and perfluorododecanoic acid. At least 3 systolic blood pressure (SBP) and diastolic blood pressure (DBP) measurements were collected and averaged. Sleep comprised self-reported short sleep duration (<7 hours), sleep disordered breathing (SDB), sleep apnea, and trouble sleeping. Adjusting for age, other sociodemographic characteristics, and health behaviors, linear regression was used to estimate changes in SBP and DPB associated with each \log_2 -fold increase in total PFAS. PFAS by sleep interaction terms were added to models that were stratified when interactions were significant. Mean age \pm SE was 47 ± 0.32 years, mean \pm SE SBP was 118 ± 0.31 mmHg, and mean \pm SE DPB was 71 ± 0.29 mmHg. Each \log_2 -fold increase in total PFAS was associated with a 0.84 mmHg increase in SBP (95% CI: 0.20,1.47). Although total PFAS was not associated with DBP among adults with SDB, total PFAS was positively associated with DBP among adults without SDB (beta [95% CI]:1.05 [0.35,1.75]). The remaining sleep measures did not modify associations. PFAS was associated with higher blood pressure among U.S. adults, and this association appears to vary by SDB status. Prospective studies with objective sleep measures are warranted.

Adjusted Associations between Total PFAS and Diastolic Blood Pressure, Stratified by Sleep Disordered Breathing



Difficulty of falling asleep and non-HDL cholesterol level among Canadian elderly - a cross-sectional analysis of the CLSA baseline data Jian Liu* Jian Liu Surim Son Michael Giancaterino

To examine whether difficulty of falling asleep (DoFA) is associated with non-HDL cholesterol (nHDL-c), 26,954 individuals aged 45-85 from Canadian Longitudinal Study for Aging (CLSA) at baseline were included in this study. DoFA was categorized into five groups by the answer to question "Over the last month, how often did it take you >30 minutes to fall asleep?" ie, never, <1/wk, 1 - 2 times/wk, 3 - 5 times/wk, or 6 - 7 times/wk. nHDL-c was the difference of total-c and HDL-c. The following cut-offs were used to create five nHDL-c categories, ie, <2.6, 2.6 to <3.7, 3.7 to < 4.8, 4.8 to 5.7, and ≥ 5.7 mmol/L. Ordinal logistic regression (logit link) continuation ratio models were used to estimate the odds of higher nHDL-c levels for DoFA status. Adjusted means of nHDL-c by DoFA status were estimated by general linear models (GLMs). All analyses were sex separately using analytic weight to ensure generalizability. The proportions of DoFA in five categories were 41.6%, 25.7%, 13.6%, 9.4%, 9.7% for women, and 52.9%, 24.9%, 10.5%, 6.1%, 5.6% for men, respectively. After adjustment of demographical and lifestyle variables, and other covariates such as depression, waist circumference, SBP, comorbidity, and sleeping hour, compared to those who reported never having DoFA, the ORs (95% CIs) of higher levels of nHDL-c for those whose DoFA status in 1 - 2 times/wk, 3 - 5 times/wk, or 6 - 7 times/wk were 1.10 (1.02, 1.17), 1.08 (0.99, 1.18), 1.12 (1.01, 1.25), 1.32 (1.19, 1.47) in women, and 1.00 (0.93, 1.07), 0.98 (0.89, 1.07), 1.16 (1.02, 1.31), 1.01 (0.88, 1.16) in men, respectively. The adjusted means of nHDL-c among the five DoFA status were 3.68, 3.73, 3.71, 3.78, 3.86 mmol/L for women, and 3.52, 3.52, 3.50, 3.65, 3.58 mmol/L for men, respectively. The results of this study have identified a risk association pattern between DoFA status and nHDL-c levels in women but not in men. Further research are need to confirm these findings.

Exploring pleiotropic effects of lipid modifiers on coagulation and hemostasis with genetics CM Schooling* CM Schooling Ryan Au Yeung JV Zhao

Statins have long been suspected to have pleiotropic effects via hemostatic or thrombotic factors. Randomized controlled trials have been too small to be definitive, and have rarely differentiated between effects of lipid modifiers. We examined the effect of genetically mimicking statins, PCSK9 inhibitors and alternative lipid targets (in genes *LDLR*, *APOC3*, and *LPL*) on key indicators of coagulation system function, i.e., prothrombin time (PT) and activated partial thromboplastin time (aPTT). We assessed the effect of established genetic mimics of lipid modifiers and of alternative lipid treatment targetson PT (n=58,110) and aPTT (n=37,767) using Mendelian randomization taking advantage of Biobank Japan. We used ischemic heart disease (IHD) in Japanese as a control outcome. Genetically mimicked statins increased PT (0.31 per effect size of LDL, 95% confidence interval (CI) 0.10 to 0.51) based on rs12916 but did not affect aPTT. Genetically mimicking targeting *LDLR* also increased PT based on rs688 (0.33, 95% CI 0.03 to 0.63) but did not affect aPTT. Genetically mimicking PCSK9 inhibitors or targeting *APOC3*, or *LPL* had no effect on PT or aPTT. Genetically mimicking statins, PCSK9 inhibitors and alternative lipid targets all reduced the risk of IHD in Japanese. Statins, and possibly targeting *LDLR*, may also act via a factor on the coagulation cascade, likely specific to the extrinsic or common pathway. Further elucidation of the mechanistic pathway may facilitate the development of new interventions and inform the use of statins particularly in relation to the use of other anti-coagulants.

Testosterone and survival in men and women: A Mendelian randomization study in the UK Biobank CM schooling* CM Schooling JV Zhao

Life expectancy in the developed West is currently stagnated and remains shorter in men than women. Well-established evolutionary biology theory suggests that lifespan trades off against reproductive success, possibly sex-specifically. We examined whether a key driver of reproductive success, testosterone, affected survival using a Mendelian randomization longevity study in the UK Biobank to obtain unbiased estimates, along with control exposures. We applied published genetic instruments for testosterone to obtain inverse variance weighted estimates of associations with survival to (i.e., age at) recruitment, in 167020 men and 194174 women. We similarly obtained estimates for smoking initiation, and absorbate, a marker of vitamin C metabolism. Testosterone was associated with poorer survival (0.10 years younger at recruitment per effect size of testosterone, 95% confidence interval (CI) 0.004 to 0.20). As expected, smoking initiation was also associated with poorer survival (0.37 years younger, 95% CI 0.25 to 0.50), but not absorbate (0.01 years younger, 95% CI -0.09 to 0.11). Several aspects of a healthy lifestyle (low animal fat diet) and several widely used medications (statins, metformin, dexamethasone and possibly aspirin) may modulate testosterone. Explicitly designing interventions sex-specifically based on these insights might help address stagnating life expectancy and sexual disparities in life expectancy.

Hypertension associated with oil spill clean-up following the 2010 Deepwater Horizon

disaster: Results from the GuLF Study W. Braxton Jackson II* W. Braxton Jackson II Richard K. Kwok Patricia A. Stewart Lawrence S. Engel John A. McGrath Matthew D. Curry Mark Stenzel Tran B. Huynh Caroline P. Groth Gurumurthy Ramachandran Sudipto Banerjee Gregory C. Pratt Aaron Blair Aubrey K. Miller Xian Zhang Dale P. Sandler

Background: Oil spill response and clean-up (OSRC) workers from the 2010 *Deepwater Horizon* (DWH) disaster were exposed to crude oil hydrocarbons, fine particulate matter (PM_{2.5}), and other chemicals that may lead to adverse cardiovascular health outcomes.

Methods: We analyzed data from 8,351 Gulf Long-Term Follow-up Study participants who were free of physician diagnosed hypertension at the time of the oil spill. Blood pressure was measured at a home visit, 0-2 years following enrollment. We examined hypertension risk in relation to worker status (yes/no), hierarchical job classes representing potential for exposure to total hydrocarbons (THC), quintiles of cumulative THC exposure, and potential exposure to PM_{2.5}. Hypertension was defined by either antihypertensive medication use or elevated blood pressure (systolic \geq 140 mmHg and/or diastolic \geq 90 mmHg). We used multivariable log binomial regression to calculate prevalence ratios (PR) and 95% confidence intervals (CI) for the association between oil spill exposures and hypertension. We also used multivariate linear regression to estimate exposure effects on continuous blood pressure measurements.

Results: Prevalence ratios were elevated for OSRC job classes involving clean up on water, (PR=1.34; 95% CI: 1.08-1.66), operations (PR=1.31; 95% CI: 1.06-1.61) and response (PR=1.51; 95% CI: 1.20-1.90). Increasing cumulative exposure to THC was associated with increased hypertension risk [quintile 3: PR=1.29 (95% CI: 1.13-1.46); quintile 4: PR=1.25 (95% CI: 1.10-1.43); quintile 5 PR=1.31 (95% CI: 1.15-1.50)] as well as increased blood pressure. Elevated hypertension risk was also associated with PM_{2.5} exposure for workers in the hot zone PR=1.26 (95% CI:1.05-1.52).

Conclusions: Oil spill exposures were associated with hypertension and increased blood pressure 1 to 3 years after the DWH disaster. Additional research is needed to determine the persistence of effects and other adverse cardiovascular outcomes.

The role of atrial fibrillation in ischemic heart disease, stroke, other cardiovascular disease subtypes, type 2 diabetes and Alzheimer's disease: a Mendelian randomization study Kwok

Man Ki* Man Ki Kwok C Mary Schooling

Background: Atrial fibrillation (AF) has been associated with numerous diseases. However, whether AF is a cause or consequence of these diseases is uncertain. To clarify, we assessed the causal role of AF on ischemic heart disease (IHD), stroke, other cardiovascular disease subtypes, type 2 diabetes, and late-onset Alzheimer's disease using bi-directional two-sample Mendelian randomization (MR).

Methods: Single nucleotide polymorphisms (SNPs) strongly ($P < 5 \times 10^{-8}$) and independently ($r^2 < 0.001$) associated with AF (n=60,620 cases and 970,216 controls) were applied to the largest genome-wide association studies (GWAS) of the aforementioned outcomes in people of European descent. Inverse variance weighting (IVW) with multiplicative random effects were used to meta-analyze SNP-specific Wald estimates, with sensitivity analyses including MR-Egger, weighted median, and MR-PRESSO.

Results: Genetically predicted log odds of AF was associated with any stroke (IVW odds ratio (OR) 1.22, 95% CI 1.18 to 1.27), particularly cardioembolic stroke and subdural hemorrhage, with sensitivity analyses showing similar positive findings. Genetically predicted AF was also associated with arterial thromboembolism (1.32, 1.13 to 1.53), and heart failure (1.26, 1.21 to 1.30). Conversely, genetically predicted IHD and ischemic stroke, particularly cardioembolic stroke, were positively associated with AF.

Conclusions: Atrial fibrillation plays a role in any stroke, arterial thromboembolism, and heart failure. In addition, patients with IHD or ischemic stroke might be predisposed to developing AF.

LATEBREAKER

Cardiovascular

Multiple Dietary Quality Indexes and the Risk of Heart Failure in the Health Professionals**Follow-up Study** Xiao Gu* Xiao Gu Dong Wang Teresa T. Fung Dariush Mozaffaria Luc Djousse Bernard Rosner Frank M. Sacks Walter C. Willett

Background: Due to the increasing disease burden and the limited effectiveness of pharmacological therapies, strategies to predict and prevent heart failure (HF) are urgently needed. Healthy eating has been shown associated with lower risks of multiple cardiovascular diseases, while studies of dietary quality and HF incidence are still sparse. The Prime Diet Quality Score (PDQS) was developed to overcome the limitations of applying the well-established Alternative Healthy Eating Index (AHEI) in clinical settings. In this study, we aimed to investigate whether the AHEI, as well as the PDQS, is associated with the risk of HF and its subtypes, heart failure with preserved ejection fraction (HFpEF) and heart failure with reduced ejection fraction (HFrEF).

Methods: Our study included 41,520 men who were free from cardiovascular disease and cancer at baseline from the Health Professionals Follow-up Study (HPFS). The AHEI and PDQS were computed based on dietary data that were collected every 4 years beginning in 1986 using semi-quantitative food frequency questionnaires (FFQs). Heart failure, as well as HFpEF and HFrEF, were first self-reported and then adjudicated based on the review of medical records. Data were analyzed from 1986 through 2008. Associations between the exposures and outcomes were estimated with multivariate-adjusted Cox proportional hazards models.

Findings: During 930,597 person-years of follow up, 803 HF cases were documented. Among those with ejection fraction data, 184 participants were identified as HFpEF and 181 were identified as HFrEF. A higher AHEI was significantly associated with a lower risk of HFrEF after adjusting for potential confounders ($HR_{\text{comparing extreme quintiles}} = 0.60$, 95% CI: 0.38-0.93, P -linear = 0.01). Similar inverse associations with incident HFrEF were also observed for the PDQS ($HR_{\text{comparing extreme quintiles}} = 0.54$, 95% CI: 0.34-0.85, P -linear = 0.009). We did not observe significant associations of the dietary indexes with HFpEF, while the two dietary indexes were inversely, but non-significantly associated with total HF.

Conclusion: A healthy overall diet was associated with lower risk of HFpEF. Both AHEI and PDQS showed similar predictability of the HF outcomes. Moreover, the food-based PDQS can be readily computed with wider clinical applicability.

LATEBREAKER

Cardiovascular

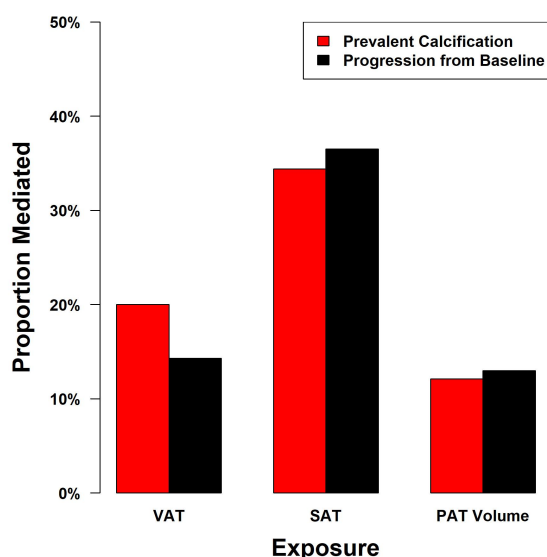
Assessment of the Mediatory Effect of Inflammation on the Association between Pericardial Adipose Tissue and Coronary Artery Calcification: An Ancillary Study in the Coronary Artery Calcification in Type 1 Diabetes (CACTI) Cohort Nathan Cohen* Nathan Cohen Brant R. Burkhardt Janet K. Snell-Bergeon Robert H. Eckel John E. Hokanson Amy C. Alman

Background - The present study investigated the mediatory effects of nine inflammatory markers on the association between adipose tissue (AT) and coronary artery calcification (CAC).

Methods - Data on 1,416 participants in the Coronary Artery Calcification in Type 1 Diabetes (CACTI) study were used in the analysis. Bootstrapping was utilized to assess mediation. Composite mediation across all nine inflammatory markers was assessed via a summation.

Results - The composite inflammation metric significantly mediated the association between AT and CAC. This result held regardless of the metric used to measure AT or CAC. For example, when visceral adipose tissue (VAT) was the exposure and prevalent calcification was the outcome, the average causal mediation effect (ACME) and average direct effect (ADE) were 0.028 (95% CI 0.016 to 0.04) and 0.115 (95% CI 0.075 to 0.15), respectively. These observed associations were largely driven by the mediatory effects of fibrinogen, tumor necrosis factor (TNF) receptor type 2, and MMP-3 based on analyses of individual markers. A greater proportion of mediation occurred in women than men. Stratified analyses by T1D status demonstrated significant mediation of the effect of VAT (ACME = 0.035; 95% CI 0.017 to 0.06) and subcutaneous adipose tissue (SAT) (ACME = 0.028; 95% CI 0.013 to 0.04) on prevalent calcification among individuals with T1D. Among individuals without T1D, the composite inflammation metric mediated the effect of SAT on prevalent calcification (ACME = 0.023; 95% CI 0.006 to 0.04), but no effect was observed for VAT (ACME = 0.013; 95% CI -0.006 to 0.03).

Conclusions - The composite inflammation metric mediated the association between AT and CAC in the entire cohort, but the mediatory effects were sensitive to the exposure, mediator, and outcome used in subgroup analyses. Mediation primarily occurred in individuals with T1D. Future studies should investigate the mediatory effects of other inflammatory markers.



The Association between Parental Diabetes Diagnosis and Major Osteoporotic Fracture Risk in Offspring: A Population-based Cohort StudyAmani Hamad* Amani Hamad Lin Yan
William D. Leslie Suzanne N. Morin Randy Walld Leslie L. Roos Shuman Yang Lisa M. Lix

Objectives: Previous research suggests an intergenerational influence of diabetes on bone health. We examined the association between parental diabetes diagnosis and major osteoporotic fracture (MOF) risk in offspring.

Methods: This population-based cohort study used de-identified administrative health data from Manitoba, Canada, which capture population-level records of hospitalizations, physician visits and drug dispensations. The cohort consisted of individuals 40+ years linked to at least one parent between 1997 and 2015. The exposure was a parental diagnosis of diabetes since 1970; the outcome was offspring incident MOF diagnosis in hip, forearm, spine, or humerus. Both measures were identified from hospital and physician visit records using validated case definitions. Multivariable Cox proportional hazards regression models tested the association of parental diabetes and offspring MOF risk.

Results: The cohort included 279,085 offspring; 89.4% were linked to both parents, 36.7% had a parental diabetes diagnosis. During a median follow-up of 12.0 years (IQR 6.0 – 18.0 years), 8762 offspring had a MOF diagnosis. After adjusting for fracture risk factors, parental diabetes diagnosis was not associated with MOF risk in offspring whether diagnosed in fathers (adjusted hazard ratio [aHR] 1.02, 95% confidence interval [CI] 0.97 – 1.08), mothers (aHR 1.02, 95% CI 0.97 – 1.07) or both parents (aHR 1.01, 95% CI 0.93 – 1.11). The results remained consistent in a stratified analysis by offspring sex, a secondary analysis based on MOF site, and planned sensitivity analyses.

Conclusions: The results indicate that parental diabetes is not associated with the risk of offspring MOF.

Outdoor physical activity modifies the influence of ozone on type 2 diabetes among older Mexican-Americans Yu Yu* Yu Yu Michael Jerrett Kimberley C. Paul Jason Su I-Fan Shih Jun Wu Eunice Lee Kosuke Inoue Mary Haan Beate Ritz

Outdoor physical activity modifies the influence of ozone on type 2 diabetes among older Mexican-Americans

Type 2 diabetes is a leading contributor to the global burden of morbidity and mortality. Ozone exposure has previously been linked to diabetes. Although physical activity is well-known for its protective effect against cardio-metabolic diseases, it is still unknown whether outdoor physical activity benefits would be outweighed by the detrimental impacts of air pollution exposure. Thus, we studied the modification of the effect of ozone exposure on incident diabetes risk in elderly Mexican-Americans by outdoor physical activity.

We selected 1,090 Mexican-American participants from the Sacramento Area Latino Study on Aging (SALSA) conducted from 1998 to 2007. Ambient ozone exposure levels were modeled with a land use regression model we built based on saturation monitoring data collected at 49 sites across the Sacramento metro area. Using Cox proportional hazard models, we estimated the risk of developing incident diabetes due to average ozone exposure we modeled for the 5-years prior to onset of an incident type 2 diabetes diagnosis or censoring; furthermore, we assessed whether outdoor physical activity modifies the association between ozone and diabetes.

During 10-years of follow-up, 186 incident diabetes cases were identified. The risk of developing diabetes was 1.14 (95% CI: 1.01, 1.29) per inter-quantile range (9.5 part per billion [ppb]) increment of average ozone exposure during 5 years prior to diabetes diagnosis or censoring. Among participants reporting high levels of outdoor physical activity, the estimated hazard ratio estimate for incident diabetes was 1.59 (95% CI: 1.23, 2.07) per 9.5 ppb increase in 5-year average ozone exposure.

Our findings suggest that ambient ozone exposure contributes to the development of type 2 diabetes, and that the impact of exposure seems to be exacerbated by outdoor physical activity. Policies and strategies are needed to reduce ozone exposure to guarantee that the health benefits of physical activity are not diminished or outweighed by high levels of air pollution exposure in susceptible populations such as older Hispanics.

Associations between the dietary inflammatory index and undiagnosed hyperglycemia by age, gender, race/ethnicity, and socioeconomic status: NHANES 1999-2014 Rachel

Meadows* Rachel Meadows Julie Bower Electra Paskett Gail Kaye Stanley Lemeshow Randall Harris

Background: Chronic inflammation contributes to hyperglycemia, which in many cases can be modified by diet. The energy-adjusted dietary inflammatory index (E-DII) was developed to assess the inflammatory potential of diet, but previous studies report conflicting evidence for an association between E-DII and hyperglycemia. **Objective:** To quantify overall and subgroup associations for E-DII and undiagnosed hyperglycemia by sociodemographic factors including age, gender, race/ethnicity, income, education, and occupation. **Methods:** Data included adults from the 1999-2014 National Health and Nutrition Examination Survey ($n = 33,571$). Undiagnosed hyperglycemia was defined as glycosylated hemoglobin (HbA1c) $\geq 5.7\%$ and no self-reported prediabetes or diabetes diagnosis. Logistic regression was used to estimate associations for E-DII and undiagnosed hyperglycemia adjusted for survey year, age, gender, race/ethnicity, body mass index, food security, family history of diabetes, smoking, and alcohol use. **Results:** Higher E-DII score (i.e., more pro-inflammatory) was associated with higher adjusted odds of undiagnosed hyperglycemia among females (OR=1.52 [95% CI: 1.25, 1.85]) and males (OR=1.49 [95% CI: 1.22, 1.82]). In further subgroup analyses, higher E-DII score was significantly associated with higher adjusted odds of undiagnosed hyperglycemia among non-Hispanic white males only and males aged 30-39 years, 50-59 years, and 60-69 years ($p < 0.05$). By socioeconomic indicators, higher E-DII score was significantly associated with higher odds of undiagnosed hyperglycemia mainly among males with higher levels of education, income, and occupation ($p < 0.05$). **Conclusions:** E-DII is associated with undiagnosed hyperglycemia in a large nationally representative sample of U.S. adults with differences in associations by sociodemographic groups. Conflicting results from previous work may be partially due to participants' sociodemographic characteristics.

Differential returns of education on diabetes by race-by-sex subgroup: results from the US Health and Retirement Study Michelle A DeVost* Michelle A DeVost M Maria Glymour Elbert S Huang Anusha M Vable

Background

Prior work suggests that more education is protective against diabetes and that this relationship may vary by demographic subgroup, but the heterogeneity of this relationship across race-by-sex subgroups is not well understood. We evaluated the relationship between education and diabetes among older adults in the US and whether this relationship varied by the interaction of race/ethnicity and sex.

Methods

Data from the Health and Retirement Study (n=34,493; 1992 to 2016) were used to assess the differential effects of education on ever-self-report of diabetes among adults age 50 and older. The base model included years of education, race-by-sex, birth year, and mother's education. To test for differential relationships by demographic subgroup, we used an interaction term between education and race-by-sex (ref=White men).

Results

In the base model, each additional year of education was associated with 5% lower odds of self-reported diabetes (aOR=0.95, 95% CI: 0.94, 0.96). In the interaction model, White women had lower odds of diabetes than White men, while Black women, Latina women, Black men, and Latino men had higher odds of diabetes than White men. The relationship between education and diabetes varied by demographic subgroup such that each additional year of education was associated with lower odds of diabetes for Black women (aOR=0.98, 95% CI: 0.95, 1.00), White women (aOR=0.95, 95% CI: 0.93, 0.98), and Latina women (aOR=0.95, 95% CI: 0.92, 0.99), while each additional year of education was associated with higher odds of diabetes for Black men (aOR=1.06, 95% CI: 1.02, 1.09).

Conclusions

The finding of poorer health with higher education for Black men is supported by prior research, but little work has evaluated diabetes as an outcome. If causal, increases in educational attainment may reduce social inequities in diabetes for Black and Latina women but increase social inequities for Black men.

Associations of neonicotinoids with insulin resistance and glucose homeostasis parameters in US adults: NHANES 2015-2016 Ann Vuong* Ann Vuong Cai Zhang Aimin Chen

Neonicotinoids are replacement insecticides increasingly used for organophosphates, methylcarbamates, and pyrethroids. Experimental evidence suggests neonicotinoids may affect glucose metabolism and insulin secretion through pancreatic β cell dysfunction, oxidative stress, and inflammation. However, no epidemiologic study has investigated neonicotinoids as potential diabetogens. We examined associations between neonicotinoids with insulin and glucose homeostasis parameters among 1381 non-diabetic adults in the National Health and Nutrition Examination Survey (2015-2016). Urinary concentrations of acetamiprid, clothianidin, imidacloprid, N-desmethyl-acetamiprid, and 5-hydroxy-imidacloprid were quantified. Fasting plasma glucose, insulin, and hemoglobin A1c (HbA1c) were assessed. Insulin resistance was defined as a homeostatic model assessment of insulin resistance ≥ 2.5 . We used weighted linear and logistic regression to estimate associations between detectable neonicotinoids with insulin and glucose homeostasis parameters. Weighted detection frequencies for imidacloprid, 5-hydroxy-imidacloprid, and N-desmethyl-acetamiprid were 4.4%, 21.5%, and 32.8%, respectively. Detectable imidacloprid ($\beta = -4.7 \mu\text{IU/mL}$, 95% CI -8.5, -0.8) and 5-hydroxy-IU/mL, 95% CI -8.5, -0.8) and 5-hydroxyimidacloprid ($\beta = -2.4 \mu\text{IU/mL}$, 95% CI -8.5, -0.8) and 5-hydroxy-IU/mL, 95% CI -4.6, -0.2) were associated with lower fasting plasma insulin levels. Individuals with detectable 5-hydroxy-imidacloprid had lower odds of insulin resistance (OR=0.3, 95% CI 0.2, 0.7). We observed evidence of sexually dimorphic associations between N-desmethyl-acetamiprid with glucose (pint=0.079) and 5-hydroxyimidacloprid with HbA1c (pint=0.038), with patterns suggesting positive associations in males and negative associations in females. Associations between 5-hydroxy-imidacloprid and insulin were modified by BMI (pint=0.013). We additionally observed age modified associations between 5-hydroxy-imidacloprid and glucose (pint=0.048). Results suggest neonicotinoids may be associated with insulin and glucose homeostasis indices and call for prospective studies to examine the metabolic impact of these replacement insecticides in humans.

The Effect of the National Health Program in Japan on the Development of Diabetes among Men with Prediabetes: Regression Discontinuity Evidence from the Minimum Target Age of the Program Akihiko Narisada* Akihiko Narisada Eiji Shibata Rei Wakayama Kohta Suzuki

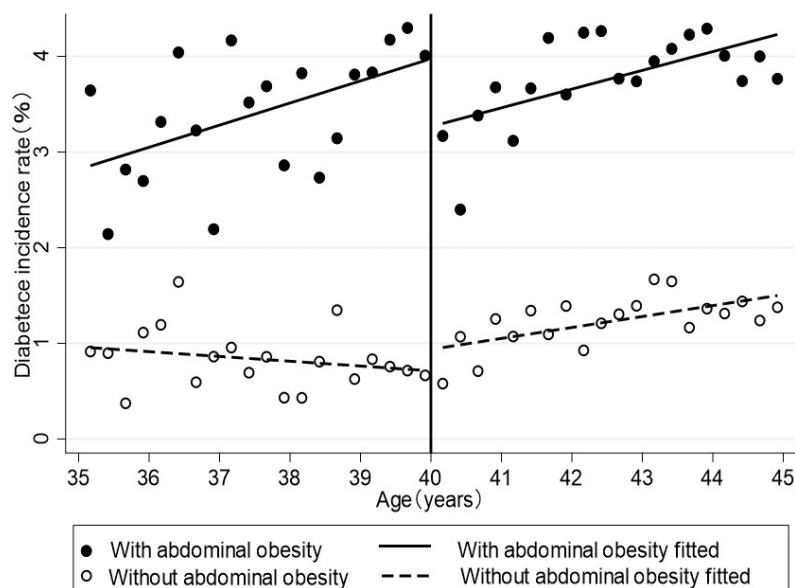
Background: Although diabetes prevention for prediabetes is a major public health challenge, there is limited evidence of the effectiveness of population-level interventions for prediabetes. The national health program (“Specific Health Checkups and Specific Health Guidance”), started in 2008 in Japan, identifies individuals aged over 40 years with abdominal obesity and lifestyle-related diseases risks (including prediabetes), and provides interventions to reduce disease risks (including diabetes). Despite the 10-year implementation, there is little empirical evidence as to whether this nationwide program has prevented diabetes. This study aimed to examine the effect of the national health program in Japan on diabetes prevention among men with prediabetes.

Methods: Using large health checkups database in Japan from 2009 to 2018, we calculated the incidence of diabetes in the following year by age in men with prediabetes (fasting plasma glucose ≥ 100 mg/dl) aged 35 - 44 years. We estimated the effect of the national health program on the development of diabetes using the age at which the program begins (40 years old) in a regression discontinuity design, according to the presence or absence of abdominal obesity (waist circumference ≥ 85 cm).

Results: Of the 178,145 men with prediabetes aged 35 - 44 years, 4,866 developed diabetes in the following year (incidence rate: 2.7%). We found a discrete 0.7 % decrease in the diabetes incidence at age 40 among men with prediabetes with abdominal obesity, who are eligible for intervention in this program (-0.7%; 95%CI -1.2-0.1). On the other hand, we found no significant changes in the diabetes incidence at age 40 among those without abdominal obesity, who are not subject to the intervention $\square 0.2 \square \square 95\% \text{CI} -1.2 \square - 0.6 \square \square$.

Conclusions: Our results indicated that the national health program in Japan prevents diabetes among men with abdominal obesity and prediabetes.

Figure. Age Profile for Diabetes Incidence Rate



Temporal trends in urinary phenol and phthalate metabolite concentrations in couples from a fertility clinic between 2000 and 2017. Lidia Minguez Alarcon* Lidia Minguez Alarcon
Paige L Williams Jorge E Chavarro Jennifer B Ford Russ Hauser

Background: Studies in the US, EU and other regions have shown temporal trends (both increasing and decreasing) for phenols and phthalates. Utilizing data from a large cohort followed over almost two decades we sought to examine temporal trends in urinary phenol and phthalate concentrations as well as chemicals more recently introduced to the market.

Methods: This prospective study included 1,815 men and women seeking infertility treatment who contributed 6,483 urines (median=2, range=1-30 sample per person). Urinary concentrations of twelve phenols and eighteen phthalate metabolites were quantified by the CDC using isotope-dilution tandem mass spectrometry. We estimated the changes in phenol and phthalates over time by fitting generalized linear mixed models with random intercepts to account for repeated samples while adjusting for age, BMI, gender and specific gravity.

Results: Over the study period, we observed significantly decreased (% per year) urinary concentrations of bisphenol A (-6.3), benzophenone-3 (-6.6), parabens (range=-5.4 to -14.2) triclosan (-18.1), dichlorophenols (-6.4 and -13.7), DEHP metabolites (range=-11.9 to -22.0), and metabolites of di-isosonyl, di-isodecyl, di-methyl and di-isobutyl phthalate (range=-0.3 to -5.8). In contrast, we found significantly increased (% per year) urinary concentrations of bisphenol S (3.9), isononyl ester phthalate (20.0), mono-ethyl, 3-carboxypropyl and benzyl phthalate metabolites (range=0.2 to 1.4), over time. Mono-n-butyl, hydroxybutyl and 2-ethyl-5-carboxypentyl terephthalate did not differ over time. Bisphenol F, triclocarban and monocarboxyisooctyl ester phthalate were mostly non-detected.

Conclusions: While exposure to the majority of these chemicals declined over time, some of them have increased, including replacements whose safety has not been fully evaluated. Further studies are needed to explore health effects of these new phenols and phthalates.

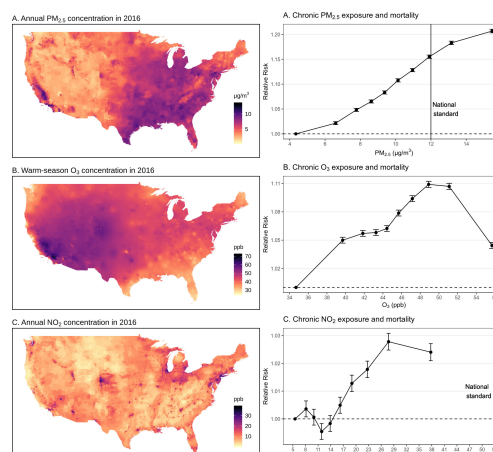
Emulating causal dose-response relations between air pollutants and mortality in the Medicare population Yaguang Wei* Yaguang Wei Mahdiah Danesh Yazdi Qian Di Weeberb J. Requia Francesca Dominici Antonella Zanobetti Joel Schwartz

Background: Fine particulate matter (PM_{2.5}), ozone (O₃), and nitrogen dioxide (NO₂) are major air pollutants that pose considerable threats to human health. However, what has been mostly missing in air pollution epidemiology is causal dose-response (D-R) relations between those exposures and mortality.

Methods: Using national Medicare cohort during 2000–2016, we emulated causal D-R relations between chronic exposures to PM_{2.5}, O₃, and NO₂ and all-cause mortality. To relax the contentious assumptions of inverse probability weighting for continuous exposures, including distributional form of the exposure and heteroscedasticity, we proposed a decile binning approach which divided each exposure into ten equal-sized groups by deciles, treated the lowest decile group as reference, and estimated the effects for the other groups. Binning continuous exposures also makes the inverse probability weights robust against outliers.

Results: Assuming the causal framework was valid, we found that higher levels of PM_{2.5}, O₃, and NO₂ were causally associated with greater risk of mortality and that PM_{2.5} posed the greatest risk. For PM_{2.5}, the RR of mortality monotonically increased from the 2nd (RR, 1.022; 95% CI, 1.018-1.025) to the 10th decile group (RR, 1.207; 95% CI, 1.203-1.210); for O₃, the RR increased from the 2nd (RR, 1.050; 95% CI, 1.047-1.053) to the 9th decile group (RR, 1.107; 95% CI, 1.104-1.110); for NO₂, the DR curve wiggled at low levels and started rising from the 6th (RR, 1.005; 95% CI, 1.002-1.018) till the highest decile group (RR, 1.024; 95% CI, 1.021-1.027).

Conclusions: The emulated causal D-R relations provided significant implications for reviewing the national air quality standards, as they inferred the number of potential early deaths prevented if air pollutants were reduced to specific levels; for example, lowering each air pollutant concentration from the 70th to 60th percentiles would prevent 65,935 early deaths per year.



Prenatal exposure to per- and polyfluoroalkyl substances and BMI growth trajectories in early childhood: the Healthy Start study Elizabeth M. Litkowski* Elizabeth M. Litkowski Lizan D. Bloemsma Deborah H. Glueck John L. Adgate Richard F. Hamman Dana Dabelea Anne P. Starling

Background: Prenatal exposures to certain per- and polyfluoroalkyl substances (PFAS) have been associated with lower birth weight but greater body weight in childhood and adulthood. Few studies have explored early-life trajectories of adiposity among children exposed prenatally to PFAS.

Methods: Among 535 mother-child pairs in the Colorado-based (US) Healthy Start study, we analyzed associations of maternal pregnancy serum concentrations of four PFAS detected at typical US background concentrations with trajectories of child body mass index (BMI). We obtained a median of 3 BMI measurements per child (range: 1 to 12) from age two to seven years from medical records. PFAS concentrations were categorized into tertiles to examine possible non-linear or non-monotonic associations. Confounder-adjusted mixed linear models with random slope and intercept were fitted to assess whether PFAS concentrations were associated with the rate of change in child BMI. Modification by child sex was assessed.

Results: Maternal PFAS concentrations predicted the rate of change in child BMI for three of the chemicals: perfluorononanoate (PFNA, $p=0.0332$) perfluorooctanoate (PFOA, $p=0.0389$) and perfluorooctane sulfonate (PFOS, $p=0.0173$). We did not detect effect modification by sex. We found non-monotonic associations between maternal PFAS concentrations and BMI. For PFNA and PFOS, the upper tertiles were associated with less rapid growth (PFNA: $p=0.0497$; PFOS: $p=0.0035$) compared to the lower two tertiles; while for PFOA, the middle tertile was associated with more rapid growth ($p=0.0099$) compared to the upper and lower tertiles.

Conclusion: In this background-exposed population, maternal concentrations of PFAS during pregnancy predicted child BMI growth trajectories, in some cases with non-monotonic dose-response functions.

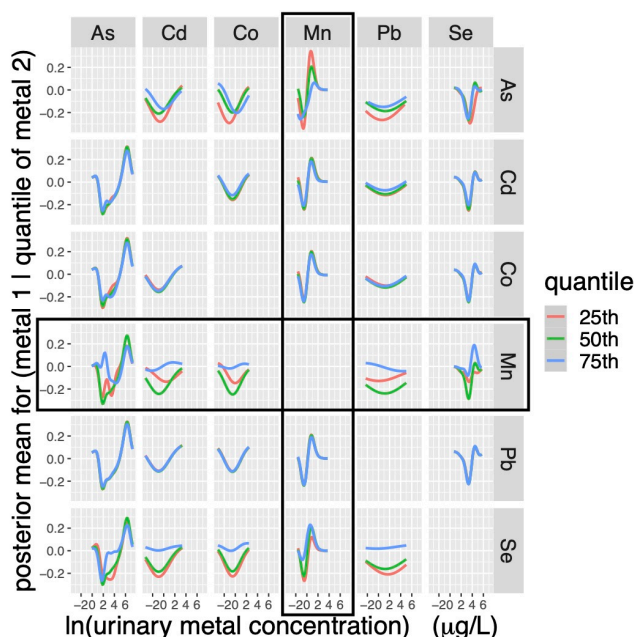
A longitudinal study of exposure to manganese and incidence of metabolic syndrome Emily Riseberg* Emily Riseberg Kenneth Chui Katherine A James Rachel Melamed Tanya L Alderete Laura Corlin

Background: Manganese (Mn) is an essential metal found naturally in rocks and soil. It has been proposed that Mn could be associated with metabolic syndrome (MetS).

Methods: We used data from 1463 adult residents of rural Colorado participating in the San Luis Valley Diabetes Study (SLVDS), a longitudinal cohort study with data collected between one and seven time points from 1984-1998. Metal concentrations ($\mu\text{g/L}$) were natural log transformed. Metabolic syndrome was defined as having three or more of the following outcomes: obesity (waist-hip ratio >0.9 for males, >0.85 for females, or body mass index $>30 \text{ kg/m}^2$), low high-density lipoprotein ($<40 \text{ mg/dL}$ for males, $<50 \text{ mg/dL}$ for females), high triglycerides ($\geq 150 \text{ mg/dL}$), high fasting glucose ($\geq 100 \text{ mg/dL}$ or diabetes), or hypertension (systolic blood pressure $\geq 130 \text{ mmHg}$ or diastolic blood pressure $\geq 85 \text{ mmHg}$). We assessed the association between $\ln\text{Mn}$ and MetS cross-sectionally using logistic regression and longitudinally using Fine and Gray competing risks regression models. Models were adjusted for urinary creatinine (g/L), age, alcohol intake (g/week), caloric intake (kcal/day), ethnicity (Hispanic/non-Hispanic), education ($<12/12/ >12$ years), household income, and smoking status (current/former/never). To assess interaction in the association of odds of MetS with other metals (cadmium [Cd], cobalt [Co], lead [Pb], and selenium [Se]), we used Bayesian kernel machine regression.

Results: The median (range) and geometric mean (95% CI) of Mn at baseline was 0.63 (0.2, 42.5) and 0.67 (0.64, 0.70) $\mu\text{g/L}$, respectively. The mean (standard deviation) of study failure time was 8.35 (5.09) years. $\ln\text{Mn}$ was not associated with MetS at baseline (OR=0.97, 95% CI=0.84, 1.12) or longitudinally (SHR=1.05, 95% CI=0.90, 1.23). There was evidence of interaction with As, Cd, Co, Pb, and Se in the cross-sectional association (Figure).

Conclusions: $\ln\text{Mn}$ was not associated with MetS cross-sectionally or longitudinally in this rural population.



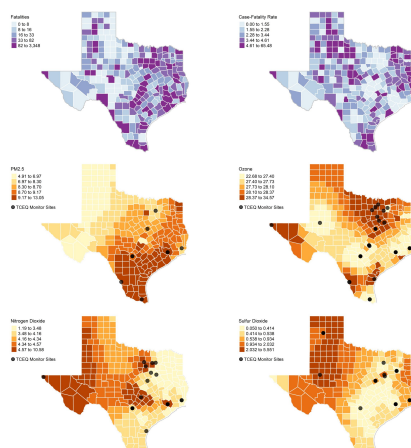
Ambient Air Pollution Exposure and COVID-19 Case Fatalities in Texas Vixey Fang* Vixey Fang Xiaohui Xu

Background: The ongoing COVID-19 pandemic has affected more than 20 million individuals and led to over 300,000 deaths within the U.S. Previous studies suggest that air pollution may affect disease severity but evidence remains inconclusive. This research explores the effects of air pollution on COVID-19 severity measured by case-fatality in Texas, which has the highest counts of COVID-19 deaths in the U.S.

Methods: Annual average air pollution levels including fine particles (PM_{2.5}), ozone (O₃), nitrogen dioxide (NO₂), and sulfur dioxide (SO₂) were calculated, while inverse distance weight was conducted to interpolate for counties without Texas Commission on Environmental Quality (TCEQ) air monitor stations. Zero-inflated negative binomial models were used to estimate the effects of air pollutants on COVID-19 severity at the county level in both single- and multiple-pollutant models while adjusting for covariates selected using backward elimination and comparing Akaike Information Criterion (AIC).

Results: Between Mar. 7 to Dec. 28, 2020, a total of 1,490,479 COVID-19 cases (Incidence=51.4 per 1,000 individuals) and 26,748 COVID-19 deaths (case-fatality rate=1.79%) have occurred in Texas. County-level PM_{2.5} was positively associated with COVID-19 case fatalities in both the single- and multiple-pollutant models. Under the best fitted tri-pollutant model, an IQR increase in PM_{2.5} (~1.78 ug/m³) resulted in an increase of 1.32% (95% CI 1.19% - 1.48%) in COVID-19 case fatalities (O₃: 1.16% (95% CI 1.06% - 1.27%); NO₂: 1.18% (95% CI 1.07% - 1.31%). Counties with higher percentage of females and African Americans have significantly higher COVID-19 case fatalities.

Conclusions: This study suggested that exposure to high levels of air pollutants may lead to severe COVID-19 disease outcomes. Public health efforts to lower air pollution levels, especially in counties with high percentages of females or African Americans, may assist in decreasing COVID-19 case fatalities.



Air pollution and metabolic disorders: dynamic versus static measures of exposure among Hispanics/Latinos and non-Hispanics Noemie Letellier* Noemie Letellier Tarik Benmarhnia
Marta Jankowska

Introduction

Environmental exposure to air pollution disproportionately affects racial/ethnic minorities that could contribute to health inequalities including metabolic disorders. However, most existing studies used a static assessment of air pollution exposure (mostly using the residential address) and did not account for activity space when modelling exposure to air pollution. The aim of this study is to understand how exposure to air pollution impacts metabolic disorders biomarkers and how this effect differs according to ethnicity, and for the first time compared these findings with two methods of exposure assessment: GPS-based Dynamic and Static measures.

Methods

Among the Community of Mine study, a cross-sectional study conducted in San Diego County, biomarkers were measured including insulin resistance (fasting plasma insulin and glucose levels), hypertension and metabolic syndrome (MetS). Exposure to air pollution (PM_{2.5}, NO₂) was calculated using static measures around the home and work, and dynamic measures of mobility derived from GPS traces. Associations of air pollution with metabolic disorders were measured using generalized estimating equation models.

Results

Among 565 participants (mean age: 58.8, Hispanic: 42%), Hispanics were most exposed to PM_{2.5} compared to non-Hispanics using static measures. In contrast they were least exposed to PM_{2.5} using dynamic measures. For all participants, higher dynamic exposure to PM_{2.5} and NO₂ was associated with increased insulin resistance (β 0.06, 95%CI: 0.00-0.12; β 0.10, 95%CI: 0.04-0.15, respectively) and MetS (OR 1.40, 95%CI: 1.14-1.71; OR 1.54, 95%CI: 1.26-1.88, respectively). The association between dynamic PM_{2.5} exposure and MetS differed by ethnicity status.

Conclusion

These results highlight the importance of considering daily mobility in the evaluation of ethnic inequalities in health-relevant exposures.

Association of air quality reduction with incident dementia: effects of natural course and hypothetical air pollutant interventions using g-computation Noemie Letellier* Noemie Letellier Laure-Anne Gutierrez Claudine Berr Marion Mortamais Tarik Benmarhnia

Introduction

The benefits of air quality improvement on the burden of neurological disorders could be substantial given the emerging evidence regarding the role of air pollution on dementia incidence. However, none evidence exists about the impact of air pollution reduction on incidence of dementia. The aim of this study is to quantify how observed reduction in PM_{2.5} concentration leads to dementia-incidence benefits and simulate the benefits of hypothetical air quality improvement interventions on the reduction of dementia incidence.

Methods

Among the French Three-City Cohort (12 years of follow-up), dementia diagnoses were made using DSM-IV criteria and validated by an adjudication committee. Exposure to PM_{2.5} was estimated using Land Use Regression models. We performed multi-level Cox proportional and Aalen additive hazard regression models to assess the effect of observed PM_{2.5} reduction on dementia risk. Then, we used a parametric g-computation approach to quantify the effects of various hypothetical interventions to reduce PM_{2.5} exposure on dementia risk.

Results

Among 7051 participants (median age: 73), the median PM_{2.5} reduction between 1990 and 2000, 10 years prior to inclusion, was 12.2 (µg/m³). Such reduction reduced the risk of all-type of dementia (hazard ratio (HR) 0.85, 95% confidence interval (CI):0.76-0.95) and Alzheimer's disease (HR 0.83, 95%CI:0.72-0.94). Approximately 197 less cases of all type of dementia per 100 000 persons and year could be attributed to PM_{2.5} reduction. Using g-computation, we quantified the expected number of prevented dementia cases under different hypothetical interventions. For example, for compliance with a hypothetical reduction of more than 13.10 µg/m³ (reduction observed in the city of Montpellier), the rate difference was -0.40 (95%CI, -0.67 to -0.14).

Conclusion

These findings highlight the possible substantial benefits of reducing air pollution in the prevention of dementia.

Mixture effects of prenatal exposure to per- and polyfluoroalkyl substances and polybrominated diphenyl ethers on maternal and newborn telomere length Stephanie Eick*
Stephanie Eick Dana Goin Lara Cushing Erin DeMicco Amy Padula Tracey Woodruff Rachel Morello-Frosch

Background: Per- and polyfluoroalkyl substances (PFAS) and polybrominated diphenyl ethers (PBDEs) are endocrine disrupting chemicals that are widespread in the U.S. given their abundance in consumer products. PFAS and PBDEs have been associated with reproductive toxicity and adverse health outcomes, including certain cancers. It is possible that PFAS and PBDEs influence adverse health outcomes through alternations in telomere length. We examined joint associations between prenatal exposure to PFAS, PBDEs, and maternal and newborn telomere length using mixture analyses, to better reflect cumulative exposures.

Methods: Study participants were enrolled a demographically diverse cohort of pregnant women and children in San Francisco, CA. PFAS (ng/mL) and PBDEs (ng/g lipid) were measured in maternal serum samples obtained during the 2nd trimester. Newborn and maternal telomere length (T/S ratio) were measured in delivery cord blood of 292 newborns and 110 second trimester maternal whole blood samples, respectively. Quantile g-computation was used to assess the joint association between groups of PFAS and PBDEs and newborn and maternal telomere length. Groups considered were: (1) all PFAS and PBDEs combined, (2) PFAS and (3) PBDEs. Maternal and newborn telomere length were treated as separate outcomes and modeled separately.

Results: In mixtures analyses, a simultaneous one quartile increase in all PFAS and PBDEs was associated with a small increase in newborn (mean change per quartile increase =0.03, 95% CI=-0.03, 0.08) and maternal telomere length (mean change per quartile increase =0.03 (95% CI=-0.03, 0.09). When restricted to maternal-fetal paired samples (N=76), increasing all PFAS and PBDEs in the mixture was associated with a strong, positive increase in newborn telomere length (mean change per quartile increase=0.12, 95% CI=0.02, 0.27). PFAS were assigned the largest positive weights (figure) in the overall model.

Conclusions: Our findings suggest that PFAS and PBDEs may be positively associated with newborn telomere length.

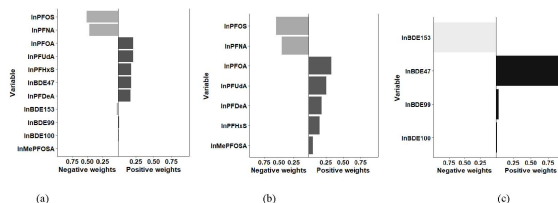


Figure. Weights representing the proportion of the positive and negative effects in the (a) overall mixture, (b) PFAS and (c) PBDEs in relation to newborn telomere length among paired samples (N=76).

Note: Negative and positive weights both sum to 1 and correspond to the effect size relative to other effects in the same direction and should not be directly compared

Examining modification of associations between air pollution exposure and low birth weight status by pre-pregnancy BMI in a North Carolina live birth cohort for 2011-2015

Kristen M Rappazzo* Kristen Rappazzo Joshua L Warren Chantel L Martin Breanna L Alman Thomas J Luben

Low birth weight (LBW) is an indicator of fetal underdevelopment and a risk factor for future health issues. Researchers using animal models have identified interactions between gestational dietary intake and air pollutant exposures and birth weight. We utilized North Carolina birth certificate data (n = 465,797) to examine potential modification of the association between air pollution and term low birth weight (LBW, <2500g at gestational age 37+ weeks) by prepregnancy body mass index (BMI); recognizing that BMI is an imperfect metric of metabolic health but may indicate the potential for metabolic stress. Geocoded residential locations from birth records were linked to daily air pollutant concentration estimates provided at the census tract centroids by the EPA’s CMAQ downscaler model and averaged over pregnancy trimesters. Risk differences (RD) and 95% CI were estimated for LBW with exposures at each trimester with interaction terms for BMI below 20 (underweight) or BMI above 30 (obese). Stratified RDs were estimated for all BMI categories. There was little evidence for interaction with BMI, except for 1st trimester ozone exposure with the lowest BMI category (RD per 10,000 births (95%CI): 10 ppb ozone increase: 2 (-4, 9), BMI <20: 33 (-73, 140), both ozone and BMI <20: 70 (-13, 152), interaction p-value = 0.012). This was repeated in stratified analyses with a RD of 26 (2, 50) for 1st trimester ozone exposure. We also observed positive associations for a 5 µg/m³ increase in 2nd trimester fine particulate matter (PM_{2.5}) in the <20, 25-30, and >30 BMI strata (RD 26-50), while the 20-25 BMI stratum was null (0 (-24, 25)). Prepregnancy BMI may be an effect measure modifier for ozone-LBW associations with 1st trimester exposures. Among gestational parents within specific BMI categories, associations were largely null for ozone and PM_{2.5} in the first trimester. This abstract does not reflect EPA policy.

Risk differences (95%CI) for air pollutant exposure and low birth weight, with interaction terms for underweight (BMI <=20) or obese (BMI >30) status. All models adjusted for co-pollutant, gestational parent marital status, medicaid payer status, race/ethnicity, and education level. Increase in PM_{2.5} is 5 µg/m³, and ozone is 10 ppb, BMI is dichotomized.

BMI	Exposure	1 st trimester	2 nd trimester	3 rd trimester
Underweight	PM _{2.5}	12 (-4, 29)	15 (-1, 32)	10 (-6, 26)
	BMI	168 (45, 291)	142 (27, 257)	178 (66, 289)
	Interaction	181 (115, 246)	171 (109, 233)	183 (123, 243)
Obese	PM _{2.5}	14 (-6, 34)	15 (-4, 35)	5 (-14, 24)
	BMI	-31 (-95, 32)	-75 (-135, -14)	-74 (-132, -16)
	Interaction	-31 (-76, 13)	-50 (-93, -8)	-60 (-102, -19)
Underweight	Ozone	2 (-4, 9)	2 (-5, 8)	-1 (-7, 6)
	BMI	33 (-73, 140)	189 (83, 296)	181 (74, 288)
	Interaction	70 (-13, 152)*	186 (102, 269)	177 (94, 261)
Obese	Ozone	9 (1, 17)	2 (-6, 10)	-4 (-12, 4)
	BMI	-20 (-75, 34)	-54 (-108, 0)	-96 (-151, -41)
	Interaction	-21 (-67, 25)	-53 (-99, -7)	-91 (-137, -44)

*interaction term significant at α<0.1 level

Risk differences (95%CI) for air pollutant exposure and low birth weight, stratified by BMI category. All models adjusted for co-pollutant, gestational parent marital status, medicaid payer status, race/ethnicity, and education level. Increase in PM_{2.5} is 5 µg/m³, and ozone is 10 ppb.

BMI	Timing	PM _{2.5}	Ozone
<=20	1 st trimester	7 (-52, 65)	26 (2, 50)
	2 nd trimester	50 (-3, 104)	-6 (-31, 18)
	3 rd trimester	10 (-44, 64)	-5 (-29, 20)
20< - 25	1 st trimester	9 (-16, 34)	3 (-7, 14)
	2 nd trimester	0 (-24, 25)	1 (-9, 12)
	3 rd trimester	4 (-19, 28)	-6 (-16, 5)
25< - 30	1 st trimester	23 (-11, 57)	2 (-13, 16)
	2 nd trimester	26 (-9, 61)	-2 (-17, 13)
	3 rd trimester	14 (-21, 50)	-4 (-20, 11)
>30	1 st trimester	9 (-23, 42)	-3 (-16, 10)
	2 nd trimester	31 (0, 62)	1 (-12, 14)
	3 rd trimester	16 (-15, 47)	4 (-9, 17)

Ambient particulate matter, ozone, and neurologic symptoms in Gulf states adults Emily Werder* Emily Werder Dale Sandler Lawrence Engel Kaitlyn Lawrence

Background: Studies of neurologic effects of air pollution often focus on neurodevelopment or later-life neurodegeneration, but effects throughout adulthood have received less attention. We examined environmental air pollution exposure and neurologic symptoms among adult U.S. Gulf coast residents.

Methods: We used United States Environmental Protection Agency estimates of daily ambient $PM_{2.5}$ and ozone to assign exposure for 21,467 adults in the Gulf Long-term Follow-up Study. Participants reported neurologic symptoms in the past 30 days at enrollment. We used log-binomial regression to estimate cross-sectional associations between each air pollutant and any neurologic, central (CNS), or peripheral nervous system (PNS) symptoms. We evaluated heterogeneity by social and demographic factors.

Results: 30% of participants reported neurologic symptoms. Ambient $PM_{2.5}$ was consistently associated with neurologic symptoms, whereas the relationship with ozone exposure was less clear. The highest quartile of 30-day average $PM_{2.5}$ was associated with any neurologic symptom (PR=1.16, 95% CI: 1.09-1.23) and there were increasing monotonic relationships between 30-day $PM_{2.5}$ and each outcome (p-trend<.0001). Associations with $PM_{2.5}$ were subtly stronger among nonsmokers and during colder seasons. The highest quartile of 7-day ozone was associated with increased PNS symptoms (PR=1.10, 95% CI: 1.02-1.18, p-trend=0.04), but not with other outcomes. Ozone concentrations above regulatory levels were suggestively associated with neurologic symptoms (PR=1.06, 95% CI: 0.99-1.14).

Discussion: $PM_{2.5}$ exposure was associated with modest increases in neurologic symptoms. We did not detect effect measure modification by socioeconomic status or other demographic factors. Mutual adjustment in co-pollutant models suggests that $PM_{2.5}$ is a more relevant exposure than ozone in the relationship with neurologic symptoms.

A mixed methods study examining neighborhood disadvantage and childhood behavior problems in Montevideo, Uruguay Seth Frndak* Seth Frndak Yanina Gallo Elena I. Queirolo Gabriel Barg Nelly Mañay Katarzyna Kordas

Background:

Neighborhood disadvantage (ND) is a risk factor for child behavior problems (CBPs), but is understudied outside the United States and Europe. Our mixed methods study aims to (1) create a culturally meaningful measure of ND, (2) test cross-sectional associations between ND and CBPs and (3) qualitatively explore life in the neighborhoods of families participating in the Salud Ambiental Montevideo study.

Methods:

Quantitative study comprised 272, ~7-year-old children with geolocation and twelve behavioral outcomes (Conner's Teachers Rating Scale and Behavioral Rating Inventory of Executive Functioning). ND factor was created at the census segment level (n=1,055) with 19 potential indicators of ND from the Municipality of Montevideo. Children assigned ND scores based on location within census segment. Multilevel models tested associations between ND and all CBP scales, controlling for confounders. The qualitative study comprised 10 caregivers. Photovoice and semi-structured interviews used to foster conversations about neighborhood quality, activities, and raising children. Thematic analysis with inductive coding was used to summarize qualitative study findings.

Results:

ND factor consisted of 11 census-based indicators related to education, employment, ethnicity, and housing quality characteristics, but unrelated to home ownership or some ethnicity variables. In multivariable models, ND was associated with greater conduct problems ($\beta=1.37$, $p<.05$), poor shifting ($\beta=1.56$, $p<.01$) and emotional control problems ($\beta=2.36$, $p<.001$). Photovoice and semi-structured interviews yielded four themes: physical disorder, recreation, safety/crime, and community resources. Residents discussed improving waste management/transportation, updating playgrounds, and ensuring neighborhood safety.

Conclusions:

ND in Montevideo comprised a unique set of indicators. ND was primarily related to behavioral regulation problems. Hypothesized pathways whereby ND affects CBPs are discussed.

Development of an Environmental Quality Index: Can state water data improve the water domain? Jyotsna Jagai* Jyotsna Jagai Alison Krajewski Monica Jimenez Danelle Lobdell

We developed a county-level Environmental Quality Index (EQI), which represents 5 domains of environment (air, water, land, built and sociodemographic) for 2006-2010 for the U.S. utilizing publicly available datasets. However, additional data, particularly on drinking water quality, that is only available at the state level may prove to strengthen the water domain. Domain specific indices, which are developed by reducing domain specific variables using principal components analysis (PCA), are reduced using PCA to create an overall EQI. We reconstructed the EQI specific to Illinois (IL) to test the utility of adding state-level drinking water quality data to the water domain; all other domains remained the same. We constructed the water quality index for IL for all counties (n=102) using nationally available data for 51 variables representing water quality. We then incorporated data on the 12 most sampled contaminants in IL from state Drinking Water Watch to construct a comparison water index. The PCA loadings for the additional variables were very low (range: -0.07 to 0.09), suggesting little added variability. To assess utility of the comparison index, both water indices were used in regression models as exposure metrics while adjusting for all other domains. IL hospitalization data for gastrointestinal illness (GI) was used as an outcome variable. Results are risk ratios (RR) and 95% confidence intervals (CI) comparing worst to best (referent) tertile of water quality. Counties with the poorest water quality were more likely to have hospitalizations for GI (RR 1.27; 95% CI: 1.26, 1.27) using the original water quality index. The exact same results were seen using the comparison water quality index. Our results suggest that the original data used to represent water quality accounts for most of the variation in water quality. Therefore, the incorporation of additional state-level data on water quality may not be necessary. This abstract does not reflect EPA policy.

Associations of prenatal chemical and non-chemical stressors with anxiety and depressive symptoms in early-adulthood in the New Bedford Cohort

Lisa B Rokoff* Lisa B Rokoff Brent A Coull Michelle Bosquet Enlow Susan A Korrick

Background: Environmental chemical exposures are understudied risk factors for mental health problems. We evaluated associations of early-adulthood anxiety and depressive symptoms with prenatal organochlorine and metal exposures, considering effect modification by non-chemical stressors.

Methods: Of 788 participants recruited into a sociodemographically diverse prospective birth cohort (1993-1998) in New Bedford, Massachusetts, 240 completed symptom assessments at 19-25 years. Hexachlorobenzene, p,p'-dichlorobiphenyl dichloroethylene (DDE), polychlorinated biphenyls (PCB₄), lead (Pb), and manganese levels were analyzed in cord blood. Anxiety and depressive symptoms were assessed by the Generalized Anxiety Disorder (GAD-7) and Patient Health Questionnaire (PHQ-8), respectively; scores were dichotomized at moderate severity. Using complete case and inverse probability weighting (IPW), we estimated covariate-adjusted RRs with modified Poisson regression, overall and in strata of a prenatal social disadvantage (PNSD) index based on maternal age, marital status, parental education, and household income.

Results: In multi-chemical complete case models (N=172), higher cord blood Pb levels were associated with increased risk of elevated symptoms, particularly in those with fewer non-chemical stressors. For PHQ-8, RRs (95% CI) per doubling Pb were 1.90 (1.22, 2.96) and 0.87 (0.53, 1.42) in low and high PNSD strata, respectively (interaction p=0.01). RRs with other chemicals were imprecise or null, except PCB₄ was associated with lower risk in the high PNSD stratum. With IPW, prenatal DDE was associated with greater risk of elevated GAD-7 symptoms; other estimates did not appreciably change for IPW vs. complete case.

Conclusion: Prenatal Pb and DDE exposure may increase susceptibility to anxiety and depression in young adults. Varying risk was observed in different PNSD strata, highlighting the importance of considering interactions between chemical and non-chemical stressors.

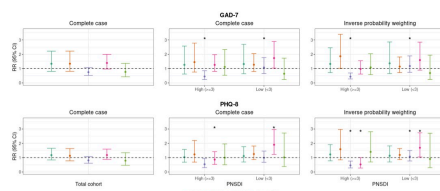


Figure 1. Overall and prenatal social disadvantage (PNSD)-strata specific RRs (95% CI) for early-adulthood moderately elevated anxiety (seven-item Generalized Anxiety Disorder (GAD-7)) and depressive symptoms (eight-item Patient Health Questionnaire (PHQ-8)) associated with a doubling of cord blood hexachlorobenzene (HCB), p,p'-dichlorobiphenyl dichloroethylene (DDE), the sum of four polychlorinated biphenyl congeners (PCB₄), lead (Pb), and manganese (Mn), from multi-chemical modified Poisson regression models adjusted for parental (PNSD index score, maternal smoking, maternal age) and participant (sex, race/ethnicity, age at assessment, Home Observation Measurement of the Environment score in adolescence) characteristics. For each outcome, RRs were estimated from 1) a complete case model with just the main effect of each chemical and 2) complete case and 3) inverse probability weighting models also including product interaction terms between each chemical and PNSD; asterisk indicates interaction p-value < 0.05.

Road traffic density and recurrent asthma emergency department visits among Medicaid enrollees in New York State 2005-2015 Temilayo Adeyeye* Temilayo Adeyeye Catherine Wargo Victoria Wagner Anisa Proj Susan McCauley Jacqueline Matson Tabassum Insaf

Background: Environmental exposures such as pollutants from traffic may contribute to asthma morbidity and recurrent emergency department (ED) visits. However, these associations are often confounded by socioeconomic status and health care access.

Objective: This study aims to assess the association between traffic density and recurrence of asthma ED visits in the New York State (NYS) Medicaid population between 2005 and 2015.

Methods: The primary outcome of interest was at least one recurrent asthma ED visit within 1-year of the index visit. Traffic densities (weighted for truck traffic) were spatially linked to home addresses. Bivariate and multivariate ordered logistic regression analyses were conducted to identify factors predicting recurrent asthma ED visits.

Results: In the multivariate model, Medicaid enrollees living within 300-meters of a high traffic density area were at a statistically significant risk of a recurrent asthma ED visit compared to those in a low traffic density area (RR=1.31; 95% CI:1.24 - 1.38). Additionally, being male (RR=1.24; 95% CI:1.20 - 1.27), being on cash assistance (RR=1.27; 95% CI:1.24 - 1.31) and receiving supplemental security income (RR=1.23; 95% CI:1.18 - 1.27) were associated with a higher risk of recurrent asthma ED visit. Black non-Hispanics (RR=1.20; 95% CI:1.10 - 1.31), Hispanics (RR=1.52; 95% CI:1.46 - 1.59) and those with race listed as "Other" (RR=1.58; 95% CI:1.48 - 1.68) had higher risk of recurrent asthma ED visits as compared to White non-Hispanics.

Conclusion: We observed significant persistent disparities in recurrent asthma ED visits related to traffic density and race/ethnicity among Medicaid enrollees in NYS.

Personal Exposure to Benzene, Toluene, Ethylbenzene, and Xylenes (BTEX) Mixture and Telomere Length: A Cross-Sectional Study of the General US Adult Population Zhongzheng Niu* Zhongzheng Niu Xiaozhong Wen Meng Wang Lili Tian Lina Mu

Background: Benzene, Toluene, Ethylbenzene, and Xylenes (BTEX) are a group of aromatic air pollutants from fossil fuels. There is no research on associations of BTEX mixture with telomere length (TL), a marker of cellular aging, in the general population.

Objectives: To examine the association of personal exposure to BTEX mixture with leukocyte TL.

Methods: We analyzed a subsample of 549 adults aged 20-59 years from the National Health and Nutrition Examination Survey 1999-2000. BTEX samples were collected by passive exposure badges worn by participants for a period of 48-72 hours. Levels of BTEX were measured with gas chromatography/mass spectrometry. Leukocyte TL was measured with qPCR. We used Bayesian Kernel Machine Regression (BKMR) to examine the mixture effect of BTEX on TL adjusting for potential confounders. Analyses were stratified by tobacco smoke exposure status.

Results: Levels of personal exposure to BTEX were mostly detectable and relatively higher in the group of 150 tobacco smoke-exposed (cotinine \geq 10ng/mL) participants than in the smoke non-exposed group (n=399, cotinine<10ng/mL). The BTEX chemicals were well intercorrelated ($0.5 < r \leq 0.9$, $P < 0.05$). All chemicals had weak, inverse correlations with TL ($r > -0.1$, $P > 0.05$). From BKMR models among the smoke non-exposed group, BTEX mixture was significantly, inversely associated with TL at low levels of BTEX (<40th percentile), but was not associated with TL at higher levels (>50th percentile). Also, we found a U-shape association of benzene and a positive association of ethylbenzene with TL independent of other BTEX chemicals. Among the tobacco smoke-exposed group, neither the BTEX mixture nor any particular chemicals were significantly associated with TL.

Discussion: Low-level exposure to BTEX mixture may be associated with shorter telomere length in the general population without tobacco smoke exposure.

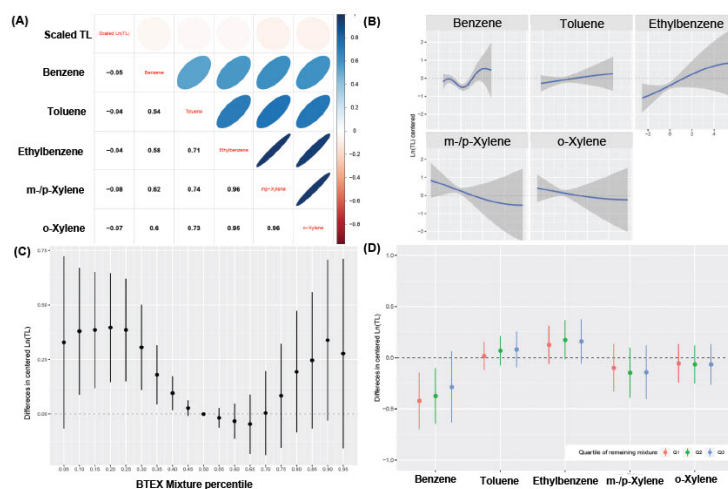


Figure 1. Association of BTEX with scaled, log-transformed telomere length (TL) estimated by Bayesian Kernel Machine Regression (BKMR) among 349 tobacco smoke non-exposed from NHANES 1999-2000. Model adjusted for age, sex, race, education level, family income, marital status, foreign-born status, BMI, and white blood cell count. (A) Pearson correlation matrix for TL and BTEX. (B) Univariate exposure-response function and 95% confidence bands for each BTEX chemical with the other pollutants fixed at the median. (C) BTEX mixture effect on TL, comparing various percentiles of the mixture to the median (50th percentile). (D) Single BTEX chemical effect on TL comparing the median (50th percentile) to the 20th, 50th, and 75th percentile.

County-level Environmental Quality and Gastroschisis in the National Birth Defects

Prevention Study Danelle Lobdell* Alison Krajewski Achal Patel Christine L. Gray Lynne C. Messer Peter H. Langlois Jennita Reefhuis Suzanne M. Gilboa Martha M. Werler Gary M. Shaw Suzan Carmichael Wendy Nembhard Tabassum Z. Insaf Marcia L. Feldkamp Danelle T. Lobdell Tania A. Desrosiers

The etiology of gastroschisis is not well understood. Genetic factors, young maternal age, low BMI, and isolated environmental exposures have been linked to this birth defect of the abdominal wall, but the contribution of combined exposures across socio-environmental domains has not been comprehensively examined. We used the Environmental Quality Index (EQI), a county-level estimate of cumulative exposures in five domains - air, water, land, sociodemographic, and built environment - developed by the US Environmental Protection Agency (EPA), to assess the association between environmental quality and gastroschisis in the National Birth Defects Prevention Study, a population-based case-control study conducted in multiple US states. We analyzed data for 594 infants with gastroschisis and 4105 non-malformed controls delivered between 2006 and 2011. Maternal residence at conception was geocoded and linked to the EQI, yielding exposure data for 369 counties. We used logistic regression to estimate adjusted odds ratios (aOR) and 95% confidence intervals (CI) for gastroschisis and EQI tertiles (referent = T1 = "best" environmental quality), adjusted for maternal age at conception (<20 or ≥20 years), race/ethnicity, periconceptional cigarette smoking, alcohol use, and maternal country of birth (US or non-US). Overall, the aORs for T2 and T3 were 1.11 (95% CI: 0.88,1.40) and 1.02 (0.80,1.29), respectively. For the individual domains, the aORs for the "worst" environmental quality (T3) were: air 1.04 (0.82,1.33); water 1.31 (0.99,1.73); land 0.99 (0.75,1.30); sociodemographic 1.20 (0.86,1.67); and built environment 1.28 (0.96,1.70). While some socio-environmental factors have previously been associated with gastroschisis, we did not observe strong associations with cumulative county-level exposures across environmental domains. These findings and conclusions are those of the authors and do not necessarily represent the official position of the EPA or the CDC.

Prenatal Exposure to Organophosphorus Pesticides and ADHD in the Norwegian Mother, Father and Child Cohort Amber M. Hall* Amber M. Hall Jake Thistle Cherrel Manley Gro Villanger Ted Reichborn-Kjennerud Pal Zeiner Amrit Sakhi Cathrine Thomsen Heidi Aase Stephanie M. Engel

Background: Organophosphorus pesticides (OPPs) are a common insecticide used worldwide. Although some studies have found an increased risk of attention-deficit/hyperactivity disorder (ADHD) and/or ADHD-related symptoms associated with prenatal OPP exposure, findings have been inconsistent. Furthermore, some prior studies were conducted in high exposure populations that may not reflect contemporary background exposures. As such, we aimed to investigate prenatal OPP exposure in relation to clinically diagnosed childhood ADHD in a population exposed primarily through diet.

Methods: We utilized the Norwegian Mother, Father and Child Birth Cohort (MoBa), comparing a random sample (N=552) to ADHD cases obtained through linkage with the Norwegian Patient Registry (N=297). Molar sums of diethylphosphate (DEP) and dimethylphosphate (DMP) metabolites were measured in maternal urine collected at 17 weeks' gestation. Values below the limit of detection and missing covariate data were imputed. We employed logistic regression to calculate ORs adjusted for season, birth year, child sex, maternal education, prenatal vegetable and fruit intake, maternal ADHD symptoms, and financial status. All models were also co-adjusted for both metabolite classes. We additionally examined effect measure modification (EMM) by child sex.

Results/Conclusions: We observed no associations between OPP metabolites and ADHD; ORs (95% CI) comparing the lowest to the highest quartile were 0.76 (0.45, 1.24) for the molar sum of DEP and 0.62 (0.38, 0.99) for the molar sum of DMP. We did not observe EMM by child sex. Our findings suggest that background exposure to prenatal OPP does not increase risk of childhood ADHD in this population of Norwegian women, primarily exposed through diet. Our study advances the literature in this area by accounting for maternal ADHD symptoms, and dietary intake of fruits and vegetables that may confound prior studies.

Gender differences in risk of post-traumatic stress symptoms after disaster: Differential exposure or differential vulnerability? Aki Yazawa* Aki Yazawa Ichiro Kawachi

Background. Women have been consistently observed to have a higher risk of developing post-traumatic stress disorder after disaster compared to men. In a study of survivors of the 2011 Great East Japan Earthquake and Tsunami, we sought to investigate: (a) whether there was differential exposure to disaster-related trauma by gender; (b) whether women and men have differential vulnerability to trauma; and (c) what factors could explain the gender difference in post-traumatic stress symptoms (PTSS).

Methods. We used data from a cohort of community-dwelling older adults who experienced the 2011 Great East Japan Earthquake and Tsunami. Survey data were obtained before the disaster (2010) and 2.5 years after the disaster.

Results. Women suffered 1.6 times higher prevalence of moderate PTSS than males (31.0% vs. 19.4%). We found evidence of differential exposure to disaster-related trauma by gender. Women were more likely to experience loss of relatives, while men were more likely to report loss of friends as well as separation from work. We did not find evidence for gender-based differential vulnerability to disaster-related trauma. Indeed, the gender gap in PTSS was larger among individuals who did not experience disaster-related trauma. Mediation analysis suggested that women experienced greater deterioration of non-kin social support (comparing pre- versus post-disaster), which significantly mediated the association between gender and PTSS.

Conclusion. Women experienced loss of relatives more often than men, which explained about a quarter of the gender gap in PTSS prevalence after disaster. Women reported more emotional support compared to men prior to the disaster, but they also experienced greater deterioration of instrumental support from non-kin relationships following the disaster, which explained about 20% of the gender gap in PTSS.

Associations between blood lead levels and mortality in the National Health and Nutrition Examination Survey, and effect modification by dietary inflammatory index Nasser Laouali*
Nasser Laouali Tarik Benmarhnia Youssef Oulhote

Background: Previous studies in the US reported a high mortality risk associated with higher blood lead levels (BLLs). Although the mechanisms of lead toxicity are not completely understood, increasing oxidative stress and inflammation are suspected major pathways. In parallel, diet with a high anti-inflammatory potential may prevent from chronic inflammation. **Objective:** To extend the follow-up of previous analyses to 2015 and to evaluate the potential modifying effect of the dietary inflammatory index (DII) in the associations between BLLs and all-cause and specific causes of mortality. **Methods:** We used data on 15,598 adults aged ≥ 20 years enrolled in the NHANES-III between 1988 and 1994 and followed up through Dec 31, 2015. BLLs were measured in samples collected via venipuncture. The DII was computed from baseline dietary intake of 28 components assessed using 24-hour dietary recalls. Mortality was determined from individual linkage to the National Death Index records. Associations between BLLs and mortality were assessed using Cox regression models while controlling for confounding. An interaction term between BLLs and DII was included in the models and estimates across the DII tertile groups are presented. **Results:** Over the follow-up, 1398 participants died (1398 from heart diseases, 399 from cerebrovascular diseases, 1247 from cancers). A doubling in BLLs was associated with higher all cause-mortality (HR: 1.50, 95% CI: 1.46-1.55), and mortality from heart diseases (HR: 1.64, 95% CI: 1.55-1.74), cerebrovascular diseases (HR: 1.44, 95% CI: 1.30-1.60), and from cancers (1.46, 95% CI: 1.38-1.56). DII modified these associations with weaker associations in participants with lower DII (more anti-inflammatory diet). For instance, a doubling in BLLs was associated with 58% (95% CI: 1.51, 1.65) higher hazard of all cause-mortality in the highest tertile of DII, whereas the association was weaker in the lowest tertile of DII 39% (95% CI: 1.2, 1.46). **Conclusion:** Our findings suggest that a higher anti-inflammatory diet may help prevent blood Pb adverse effects in adults.

The association between environmental quality and mental health using electronic health**records in North Carolina**

Christine L. Gray* Christine Gray Anne M. Weaver Cavin Ward-Caviness Joshua Moyer Kristen M. Rappazzo Lynne C. Messer Jyotsna S. Jagai Alison K. Krajewski Monica P. Jimenez Danelle T. Lobdell

Depression and anxiety are common disorders that contribute to diminished quality of life, worse cardiovascular outcomes, and high suicide rates in United States (US) adults. Poor mental health arises from complex factors including genetics, psychology, and lived experiences. Increasingly, environmental exposures are thought to impact mental health. We used electronic health records from a random sample of 14,685 adult (≥ 18 years old) patients seen at University of North Carolina-affiliated hospitals across the state's 100 counties, from 2006 to 2018. We linked those geocoded data to the US Environmental Protection Agency's 2006-2010 county-level environmental quality index (EQI), consisting of 5 unique domain indices (air, water, land, built, and sociodemographic) and an overall EQI for the US. We used log-binomial regression to estimate the association between North Carolina-specific tertiles of environmental quality (domain-specific and overall EQI) and diagnosis of a major depressive episode or generalized anxiety disorder (ICD-9 296.2, 296.3, 300.2; ICD-10 F32, F33, F42.1), controlling for sex, age, and race. Resulting prevalence ratios (PR) and 95% confidence intervals (CI) compared worst to best (referent) tertile of environmental quality. Residents of counties with the worst air and built environments were more likely to have anxiety or depression (PR 1.46; 95% CI 1.30, 1.64 and PR 1.17; 95% CI 1.06, 1.28, respectively). We observed inverse associations between anxiety or depression and land (PR 0.65; 95% CI 0.58, 0.73), sociodemographic (PR 0.59; 95% CI 0.48, 0.71), and water (PR 0.83, 95% CI 0.75, 0.91) domains. Associations with the overall EQI and anxiety or depression diagnoses were null (PR 1.01; 95% CI 0.92, 1.11). Our results suggest variation in how different domains of environmental quality may impact mental health disorders; worse air quality and built environment disamenities may be especially harmful. This abstract does not reflect EPA policy.

Rethinking Measurement of Air Pollution and Asthma in NHANES: Incorporating Multiple Dilution Adjustment Methods of Urinary Polycyclic Aromatic Hydrocarbons and Rescue Asthma Medication Use Stephen Uong* Stephen Uong Stephanie Lovinsky-Desir Jeanette Stingone

Previous studies within the U.S. National Health and Nutritional Examination Survey (NHANES) examined the relationship between polycyclic aromatic hydrocarbon (PAH) metabolites, a marker for recent air pollution exposure, and prior asthma diagnosis. Within cross-sectional studies, the recent use of rescue asthma medication is a more temporally appropriate indicator of asthma exacerbations than previous asthma diagnosis. Our study aimed to examine the relationship between PAH exposure and rescue asthma medication use, while also comparing multiple urinary dilution adjustment methods. Across multiple waves of NHANES (2005-2016), 16,550 study participants were included. PAH exposure was measured by urinary 1-hydroxypyrene concentration with creatinine dilution adjustment. The use of rescue asthma medication within one month prior to the survey date was determined through self-report. Prevalence ratios of the association between PAH metabolite concentration and rescue asthma medication use were generated using multivariable regression models accounting for the complex survey design. Results were compared between different urine dilution adjustment methods and evaluated among those with a previous asthma diagnosis. Additionally, effect measure modification was evaluated by age and controller asthma medication use. All models were adjusted for age, gender, race, poverty income ratio, and smoking status. The prevalence of rescue medication use was 1.39 times greater (95% CI 0.98-1.97) among those in the highest compared to the lowest quartile of PAH exposure. Results differed by urine dilution adjustment method and in a subset of those with a previous asthma diagnosis. Recent PAH exposure is associated with rescue asthma medication use, but results differ by the choice of urinary dilution adjustment method. In cross-sectional studies, rescue asthma medication use may be a more appropriate outcome measurement compared to previous asthma diagnosis.

Estimating the effect of long-term exposure to fine particulate matter on mortality in Canadian Community Health Survey Cohort using parametric g-computation Chen Chen*
Chen Chen Tarik Benmarhnia Hong Chen Megan Kirby-McGregor Jay Kaufman

Background

Numerous epidemiological studies reported the adverse health impact of long-term exposure to fine particulate matter (PM_{2.5}) on mortality across populations. However, previous studies mostly utilized traditional outcome regression approaches, which may fail under certain circumstances (e.g., if exposure-confounder feedback exists). We aim to explore this health impact using g-computation, which could validate traditional regression approaches and refine the effect estimates by considering more complex circumstances in the identification.

Method

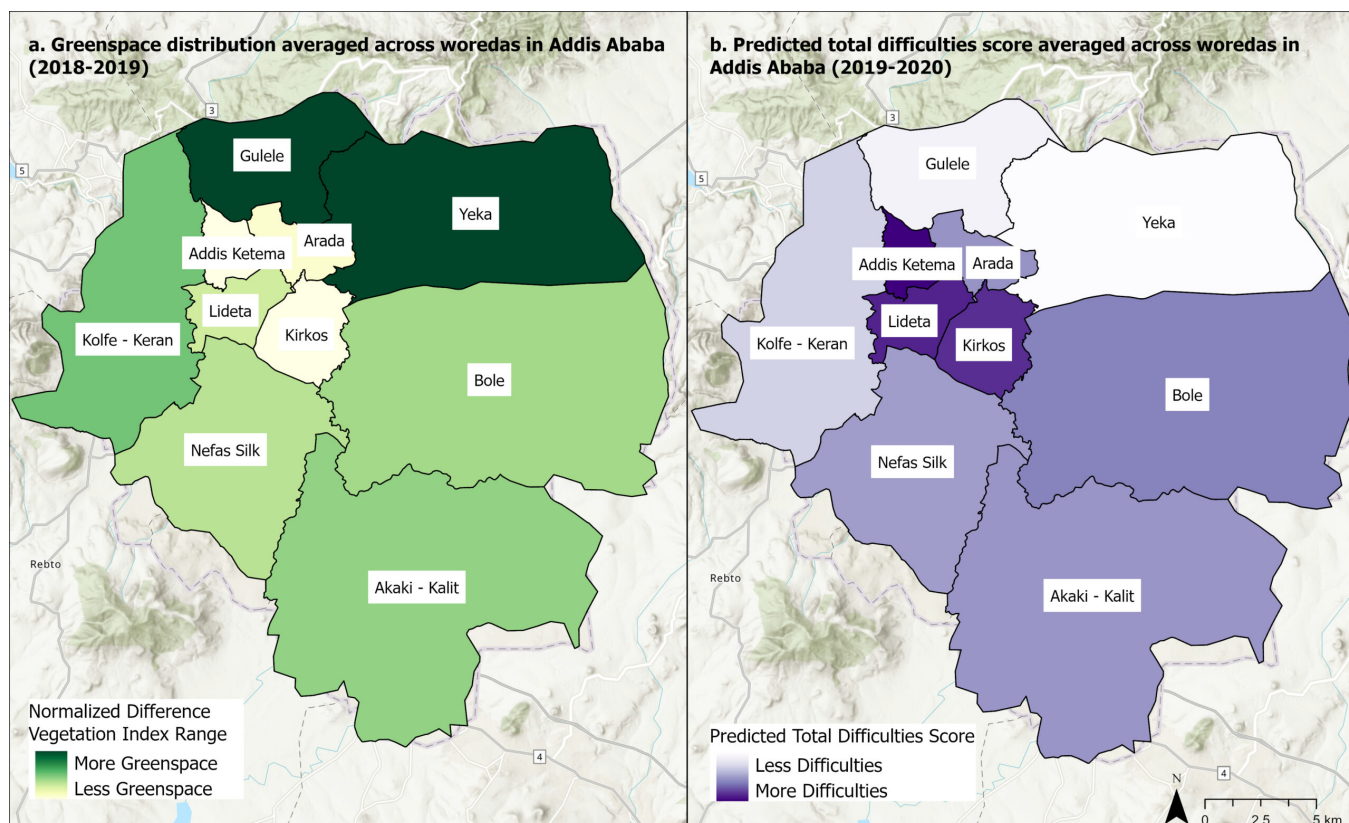
We utilize a cohort of ~540,000 respondents to the Canadian Community Health Survey from 2001 to 2012, whose death records and residential history were ascertained till 2016. Annual postal code specific three-year average PM_{2.5} concentration with one-year lag was derived from satellite measurements and linked to cohort respondents, with quintiles of exposure calculated for each calendar year. We apply parametric g-computation with pooled logistic regression adjusted for socio-economic, behavioral, and time-varying covariates to estimate 1) the effect on mortality by changing the long-term PM_{2.5} exposure level from the higher quintiles to the lowest quintile; and 2) the effect on mortality by reducing the long-term PM_{2.5} exposure levels from the observed values to below the national standard. We also evaluate the influence of exposure-confounder feedback and discuss whether other identification assumptions hold in assessing health impacts of air pollution.

Results and conclusion

Our preliminary results confirm an increase in the risk of premature mortality in relation to long-term exposure to PM_{2.5}. These results provide evidence on the effect of long-term exposure to PM_{2.5} on mortality in the presence of time-varying exposures and confounders. It also provides an alternative analytical strategy highly useful to air pollution epidemiological research, especially for evaluating specific intervention strategies.

The association between greenspace and emotional wellbeing among young adults in Addis Ababa, Ethiopia Hiwot Zewdie* Hiwot Zewdie Christine L Gray Misganaw E Dubie Berhanu Kenea Tolesa Bekele Wesene Molla Chimdi Temesgen Amy M Hobbie Jan Ostermann Kathryn Whetten

Greenspace is increasingly thought to be associated with improved mental health and wellbeing. Yet, there is a dearth of greenspace research in many places experiencing rapid growth and urbanization, particularly in sub-Saharan Africa, including Ethiopia. We used geocoded cross-sectional data from the current (12th) round of the Positive Outcomes for Orphans (POFO) study, a cohort of orphaned children who are now young adults, to examine greenspace and emotional wellbeing in Addis Ababa, Ethiopia. Greenspace exposure was calculated using the normalized difference vegetation index (NDVI), a validated measure for neighborhood greenness. The values were derived from publicly available satellite imagery (US Geological Survey, Landsat 8) from 2018-2019, averaged over administrative units, woredas (n=10), and subunits, kebeles (n=99), and linked to residing POFO participants. NDVI values are continuous from -1 to 1; values close to 1 represent high vegetation density and values close to or below 0 represent barren land or water. We assessed wellbeing as a continuous score of total difficulties (possible range: 0 to 40) using the Strengths and Difficulties Questionnaire (SDQ); higher scores indicate poorer wellbeing. We used linear regression, weighted for the complex sampling design and controlling for age, gender, income, childhood setting (residential or family care), and parental death (single, double orphan), to estimate the association between NDVI and wellbeing. Among the 158 participants with available data, the mean difficulties score was 6.86 (SD:4.27) and mean NDVI was 0.14 (SD:0.05). The adjusted model indicates increased greenspace was associated with decreased difficulties ($\beta = -14.50$, 95% CI: -30.53, 1.53). The figure reflects greenspace distribution (panel a) and model-predicted total difficulties (panel b) averaged across woredas. Though estimates are imprecise, preliminarily available data suggest greenspace may positively influence emotional wellbeing.



LATEBREAKER

Environment/Climate Change

Differential exposure misclassification in environmental epidemiology: an illustration in air pollution exposure and lung cancer survival Paige Sheridan* Paige Sheridan Chen Chen Caroline Thompson Tarik Benmarhnia

When measuring the impact of time-varying environmental exposures on time-to-event outcomes it is necessary to account for both the time-varying nature of the exposure and for differences in length of follow-up when comparing cases and controls at each event time. However, studies often overlook this necessity and attempt to simplify the analysis by averaging the exposure over follow-up in order to treat the exposure as time fixed. While this may initially appear to be an appropriate simplification, it may result in differential misclassification of the exposure when there are differences in the length of follow-up by outcome status. In this study, we use the target trial framework to identify how averaging a time-varying environmental exposure in a time-to-event context can introduce differential exposure misclassification into an observational study and propose a solution to avoid this error. Using data from the California Cancer Registry from 2000 - 2010 we estimate the impact of time-varying air pollution after a lung cancer diagnosis on five-year survival using pooled logistic regression and compare our estimates to those obtained using the previously applied naïve approach using an averaged exposure in a single Cox model. We find that the effect estimates under the pooled logistic approach are substantially attenuated (HR 1.01, 95% CI 1.00 - 1.02) when compared with the naïve approach (HR 1.17, 95% CI 1.15 - 1.19). After appropriately considering the time-varying nature of air pollution we find that the effect sizes found under the naïve approach are likely driven by differential exposure misclassification. Our findings highlight the importance of appropriately considering time-varying exposures in a time-to-event context to prevent this avoidable error.

LATEBREAKER

Environment/Climate Change

Examining modification of associations between air pollution exposure and low birth weight status by pre-pregnancy BMI in a North Carolina live birth cohort for 2011-2015

Kristen M Rappazzo* Kristen Rappazzo Joshua L Warren Chantel L Martin Breanna L Alman Thomas J Luben

Low birth weight (LBW) is an indicator of fetal underdevelopment and a risk factor for future health issues. Researchers using animal models have identified interactions between gestational dietary intake and air pollutant exposures and birth weight. We utilized North Carolina birth certificate data (n = 465,797) to examine potential modification of the association between air pollution and term low birth weight (LBW, <2500g at gestational age 37+ weeks) by prepregnancy body mass index (BMI); recognizing that BMI is an imperfect metric of metabolic health but may indicate the potential for metabolic stress. Geocoded residential locations from birth records were linked to daily air pollutant concentration estimates provided at the census tract centroids by the EPA’s CMAQ downscaler model and averaged over pregnancy trimesters. Risk differences (RD) and 95% CI were estimated for LBW with exposures at each trimester with interaction terms for BMI below 20 (underweight) or BMI above 30 (obese). Stratified RDs were estimated for all BMI categories. There was little evidence for interaction with BMI, except for 1st trimester ozone exposure with the lowest BMI category (RD per 10,000 births (95%CI): 10 ppb ozone increase: 2 (-4, 9), BMI <20: 33 (-73, 140), both ozone and BMI <20: 70 (-13, 152), interaction p-value = 0.012). This was repeated in stratified analyses with a RD of 26 (2, 50) for 1st trimester ozone exposure. We also observed positive associations for a 5 µg/m³ increase in 2nd trimester fine particulate matter (PM_{2.5}) in the <20, 25-30, and >30 BMI strata (RD 26-50), while the 20-25 BMI stratum was null (0 (-24, 25)). Prepregnancy BMI may be an effect measure modifier for ozone-LBW associations with 1st trimester exposures. Among gestational parents within specific BMI categories, associations were largely null for ozone and PM_{2.5} in the first trimester. This abstract does not reflect EPA policy.

Risk differences (95%CI) for air pollutant exposure and low birth weight, with interaction terms for underweight (BMI <=20) or obese (BMI >30) status. All models adjusted for co-pollutant, gestational parent marital status, medicaid payer status, race/ethnicity, and education level. Increase in PM_{2.5} is 5 µg/m³, and ozone is 10 ppb, BMI is dichotomized.

BMI	Exposure	1 st trimester	2 nd trimester	3 rd trimester
Underweight	PM _{2.5}	12 (-4, 29)	15 (-1, 32)	10 (-6, 26)
	BMI	168 (45, 291)	142 (27, 257)	178 (66, 289)
	Interaction	181 (115, 246)	171 (109, 233)	183 (123, 243)
Obese	PM _{2.5}	14 (-6, 34)	15 (-4, 35)	5 (-14, 24)
	BMI	-31 (-95, 32)	-75 (-135, -14)	-74 (-132, -16)
	Interaction	-31 (-76, 13)	-50 (-93, -8)	-60 (-102, -19)
Underweight	Ozone	2 (-4, 9)	2 (-5, 8)	-1 (-7, 6)
	BMI	33 (-73, 140)	189 (83, 296)	181 (74, 288)
	Interaction	70 (-13, 152)*	186 (102, 269)	177 (94, 261)
Obese	Ozone	9 (1, 17)	2 (-6, 10)	-4 (-12, 4)
	BMI	-20 (-75, 34)	-54 (-108, 0)	-96 (-151, -41)
	Interaction	-21 (-67, 25)	-53 (-99, -7)	-91 (-137, -44)

*interaction term significant at α<0.1 level

Risk differences (95%CI) for air pollutant exposure and low birth weight, stratified by BMI category. All models adjusted for co-pollutant, gestational parent marital status, medicaid payer status, race/ethnicity, and education level. Increase in PM_{2.5} is 5 µg/m³, and ozone is 10 ppb.

BMI	Timing	PM _{2.5}	Ozone
<=20	1 st trimester	7 (-52, 65)	26 (2, 50)
	2 nd trimester	50 (-3, 104)	-6 (-31, 18)
	3 rd trimester	10 (-44, 64)	-5 (-29, 20)
20< - 25	1 st trimester	9 (-16, 34)	3 (-7, 14)
	2 nd trimester	0 (-24, 25)	1 (-9, 12)
	3 rd trimester	4 (-19, 28)	-6 (-16, 5)
25< - 30	1 st trimester	23 (-11, 57)	2 (-13, 16)
	2 nd trimester	26 (-9, 61)	-2 (-17, 13)
	3 rd trimester	14 (-21, 50)	-4 (-20, 11)
>30	1 st trimester	9 (-23, 42)	-3 (-16, 10)
	2 nd trimester	31 (0, 62)	1 (-12, 14)
	3 rd trimester	16 (-15, 47)	4 (-9, 17)

LATEBREAKER

Environment/Climate Change

Association of phthalate replacement DINCH metabolite concentrations with demographic and environmental factors in a multi-site, multi-racial cohort of children Pamela L. Ferguson* Pamela Ferguson Michael S. Bloom Brian Neelon Sarah Commodore Roger B. Newman John L. Pearce John E. Vena Kelly J. Hunt

Background. 1,2-cyclohexane dicarboxylic acid diisononyl ester (DINCH) is a plasticizer used to replace high molecular weight phthalate diesters in items such as toys, medical devices, and food packaging. Little is known concerning DINCH levels in children.

Methods. Analysis included 590 children ages 4 to 8 in the Environmental Contributors to Child Health Outcomes (ECHO) study, a follow-up of the NICHD Fetal Growth Studies. There were 10 sites across the US. Urinary oxidative metabolites of DINCH, cyclohexane-1,2-dicarboxylic acid mono carboxyisooctyl (MCOCH) and cyclohexane-1,2-dicarboxylic acid mono hydroxyisononyl (MHNCH) esters, were determined at a National Institutes of Health-supported Human Health Exposure Analysis Resource lab. Values were adjusted for specific gravity and divided by molecular weight and summed to obtain a composite DINCH value. Multivariable linear regression was used to identify predictors of DINCH levels.

Results. Covariate-adjusted DINCH levels were 24% (95% CI 5%, 47%) higher in girls than boys, 45% (95% CI 9%, 93%) and 34% (95% CI 1%, 76%) higher in non-Hispanic (NH) Black and Hispanic children than NH white, 11% (95% CI 1%, 19%) lower per year older, and 47% (95% CI 8%, 102%) higher in children who ate fast food $\geq 1x/week$ versus never. DINCH levels were 55% (95% CI 14%, 111%) and 71% (95% CI 24%, 137%) higher in summer and winter, versus autumn. Northeast, west coast, and middle west sites had 29% (95% CI 9%, 44%), 32% (95% CI 3%, 52%) and 34% (95% CI 9%, 52%) lower DINCH values than southeastern sites. Ever receiving food assistance, mother's education and efforts to use BPA-free containers were unrelated to DINCH levels after adjustment for covariates.

Conclusions. Gender, age, race, diet, season, and geography were risk factors for children's DINCH exposure. Further research is imperative to determine if these differences are related to environmental inequities, as well as the long-term developmental consequences of these exposures.

LATEBREAKER

Environment/Climate Change

Street-View Greenspace Exposure and Childhood Cognition Marcia P Jimenez* Marcia P Jimenez Esra Suel Sheryl L. Rifas-Shiman Perry Hystad Andrew Larkin Steve Hankey Allan C. Just Marie-France Hivert Emily Oken Peter James

Background: Greenspace has been associated with diverse positive health benefits, with emerging evidence for children's cognition. Most studies, however, rely on satellite-derived measures of greenspace, which do not capture ground-level exposures or specific features such as trees. Google Street View (GSV) images offer the opportunity to measure greenspace from a street-based view and capture visible greenspace that may be most relevant for cognition.

Aim: Examine cross-sectional associations of GSV-based greenspace metrics with children's cognition in Project Viva, a highly-phenotyped eastern MA cohort in the Environmental influences on Child Health Outcomes (ECHO) consortium.

Methods: We applied the PSPNET deep learning segmentation algorithm to GSV images from 2007-2010 (when mid-childhood visit was conducted) to derive novel metrics of greenspace (% trees, %grass, %plants, etc.) at a 250m radius around participant's residential addresses (N=500). At the mid-childhood visit (median age 7.7y), children completed assessments of verbal and nonverbal intelligence, visual motor abilities, and visual memory using validated instruments. We used linear regression to examine associations between each GSV-based measure and cognition, adjusting for child's sex, race, and age, mother's characteristics (education, IQ, and marital status), father's education, household income, neighborhood median income, and urbanicity (population density).

Results: Higher percentage of GSV-based greenspace was associated with lower verbal (-7.5, 95%CI:-15.8,0.7) and non-verbal IQ (-12.2, 95%CI:-23.2,-1.2). This negative association was mostly driven by trees and strongest in less urban areas. The relationship between street-level greenspace and cognition was stronger compared to traditional satellite-based greenness measures.

Conclusion: Contrary to what we observed with traditional measures, we observed an inverse relationship between GSV measures of green space and children's cognition.

Association of placental weight and placental-to-fetal weight ratio with DNA methylation in placenta Suvo Chatterjee* Suvo Chatterjee Jing Wu Marion Ouidir Katherine Grantz Fasil Tekola-Ayele

Background: Placenta, a transient organ during pregnancy between the maternal and fetal interface, is central to fetal development. Placental weight (PW) and placental-to-fetal weight ratio (P/F) are markers of placental function linked to fetal and maternal adverse outcomes such as fetal growth restriction, preeclampsia, gestational diabetes, and cardiovascular diseases. Identifying genetic loci where DNA methylation in placenta is associated with PW and P/F can unravel molecular pathways that are dysregulated in aberrant fetal growth and diseases in later life.

Methods: We performed placental epigenome-wide association study (EWAS) of PW and P/F in an ethnic diverse cohort of pregnant women (n = 301). Then, DNA placental methylation at loci related to maternal adverse outcome were evaluated over PW and P/F.

Results: At 5% false discovery rate (FDR), methylation at 25 cytosine-(phosphate)-guanine sites (CpGs) was associated with PW and methylation at two CpGs was associated with both P/F and PW. At 92.6% of the 27 associated CpGs, higher methylation was associated with higher PW or P/F. Out of the 27 CpGs, higher methylation at three CpGs (which were associated with higher PW and P/W) was associated (FDR < 0.05) with decreased placental expression of *LTBP2*, *PIGV*, *LEPR* and *RPS6KA1* genes and methylation at two CpGs was associated with increased expression of *COX5A* and *SCAMP2* genes. Several associated loci, notably *LTBP2*, *RPS6KA1*, *COX5A*, and *LEPR*, have known roles in early development, cellular growth, oxidative stress, and body mass regulation. The set of 27 CpGs was significantly enriched for DNase 1 hypersensitivity sites and histone marks in placenta, skin, and blood (FDR<0.01).

Conclusion: We identified novel placental DNA methylation changes associated with PW and P/F. The findings suggest that epigenetic mechanisms at these loci may regulate placental function/efficiency, thereby mediating fetal development and early origins of diseases in later life.

Increased menopausal age decreases the risk of Parkinson's disease: a Mendelian randomization approach

Cynthia Diana Johanna Kusters* Cynthia Kusters Kimberly Paul Aline Duarte Folle Adrienne Keener Jeff Bronstein Lars Bertram Johnni Hansen Steve Horvath Janet Sinsheimer Christina Lill

Background: Sex hormones may protect dopaminergic neurons, possibly preventing or delaying the onset of Parkinson's disease (PD). Studies of PD and age of menarche or menopause as indicators of lifelong hormone exposure reported inconsistent findings, possibly due to difficulties reporting these life events accurately.

Objective: We employed Mendelian Randomization to assess the association between age at menopause and age at menarche with PD risk.

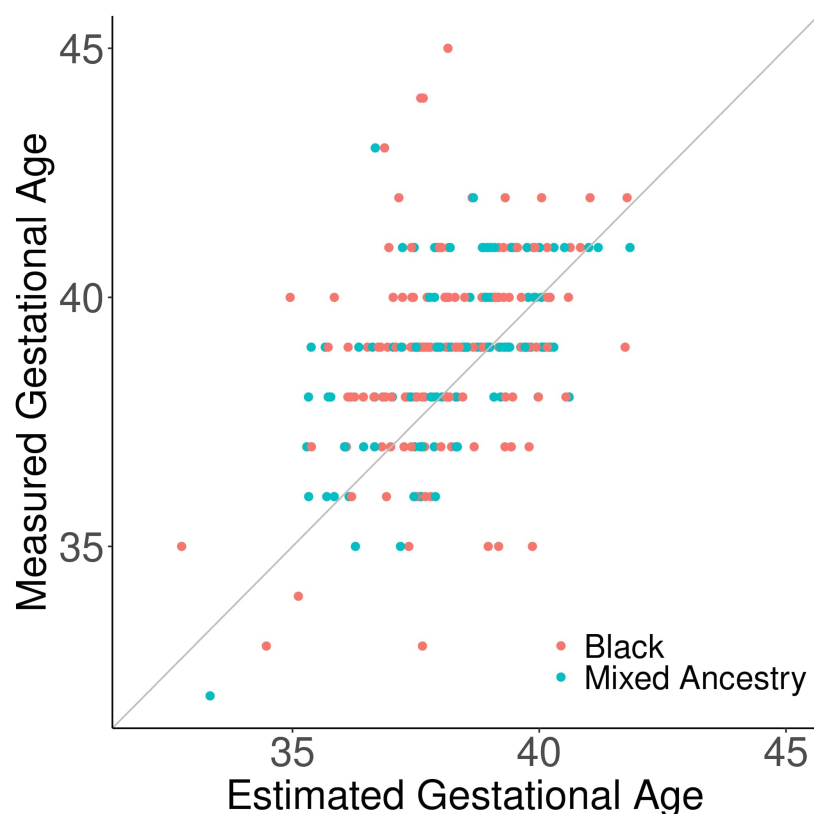
Methods: We performed MR-Egger analysis using external GWAS summary data from the UK biobank to assess the association between genetic variants and age of menopause and age of menarche, respectively. The association between genetic variants and PD was assessed using data from two population-based studies (PASIDA, Denmark, and PEG, USA) that enrolled 1,737 female subjects (825 cases (CA), 912 controls (CO)), and 2,430 male subjects (1,218 CA, 1,212 CO) of European ancestry. We adjusted for ancestry, study, and age at the interview. We included independent variants (linkage disequilibrium R-square < 0.1) and a P-value of 5×10^{-8} , 79 SNPs for the age of menopause and 307 for the age at menarche.

Results: There was no indication for directional pleiotropic effects based on the MR intercept. For each year increase in age of menopause the risk for PD decreases (OR: 0.80, 95%CI: 0.64-0.99, P:0.04) among women with a natural menopause, while there was no association among men (OR: 1.03, 95%CI: 0.88-1.22, P:0.68). Sensitivity analysis among various subgroups, using different subsets (P-value thresholds) and standard inverse variant weighting method for MR show the same association among women with slight variation. However, there was no indication for an association between the age at menarche and PD (OR: 1.34, 95%CI: 0.68-2.64, P:0.40).

Conclusions: A later age at menopause was associated with a decreased risk of PD in women, supporting the hypothesis that sex hormones may be neuroprotective in PD.

Methylation risk score performance and transferability in population of multi-ethnic ancestries Junyu Chen* Junyu Chen Evan Gatev Karen N. Conneely Nastassja Koen Michael P. Epstein Michael S. Kobor Heather J. Zar Dan J. Stein Anke Huels

Polygenic risk scores (PRS) are widely used in association studies and risk prediction. Recently, interest has been growing in generating methylation risk scores (MRS) by transferring PRS to DNA methylation data. One of the biggest challenges for MRS can be its limited applicability across ancestries. Here, we conducted a simulation study and real data analyses to evaluate the performance of MRS in multi-ethnic population. We adopted the Clumping and Thresholding (C+T) method, a well-established PRS method, by first using the Co-Methylation with genomic CpG Background (CoMeBack) approach to define Co-methylated Regions and then selecting one CpG site from each region based on its association with outcome. MRS was calculated as a sum of the remaining beta values weighted by the corresponding coefficients. By simulation studies based on publicly available data from 1199 samples with African, European and Indian ancestry and varying sets of causal CpG sites and variance explained by methylation, we showed that MRS have a similar distribution and prediction accuracy across different ancestries. We then calculated MRS for gestational age and smoking in the South African Drakenstein cohort (145 black infants and 115 admixed infants) using European-derived summary statistics. Both MRS have similar distribution and are significantly associated with the corresponding phenotypes across both ancestries. The prediction accuracy (R^2) of the MRS for gestational age is 0.19 (0.08, 0.30) among black infants and 0.30 (0.16, 0.43) among admixed infants. MRS for smoking have a prediction accuracy of 0.06 (0.00, 0.13) and 0.18 (0.06, 0.30) among black infants and admixed infants respectively. The observed differences are likely due to differences in phenotype distributions across different ancestries. In conclusion, our findings suggest a trans-ethnic transferability of MRS, which indicates their broad applicability for non-European and ethnically heterogeneous study populations.



Design of a Study to Assess the Impact of Returning Genetic Results within a Bangladeshi Population Lizeth I Tamayo* Lizeth Tamayo Brandon L Pierce Habibul Ahsan

In human genetics research, it is now common for researchers to consider returning genetic results to participants who want it. Genetic information has the potential to change individuals' perceived disease risk and motivate lifestyle modification. In the Health Effects of Arsenic Longitudinal Study (HEALS), a rural cohort in Bangladesh with substantial arsenic (As) exposure through drinking water, participants report strong interest in receiving genetic results. Participants may be more receptive to behavior changes that reduce exposure if aware of their genetic risk for As toxicity. In HEALS, we have identified genetic variants associated with reduced arsenic metabolism efficiency (AME) and increased risk for As-induced skin lesions (a common As toxicity) using genome-wide association (GWA) methods. Recent GWA analyses ($n > 4,700$) identified 3 variants in AS3MT and 1 in FTCD that show independent association with AME. These SNPs allow us to identify inefficient (vs. efficient) metabolizers using a polygenic risk score (PRS). We designed a study to enroll HEALS participants with (1) high urine As ($\geq 200 \mu\text{g/g}$ creatinine) based on >15 years of follow-up and (2) existing AS3MT and FTCD genetic data. The return of results arms (intervention groups 1 and 2) will consist of 100 "inefficient" (high-risk) and 100 "efficient" (low-risk) metabolizers (based on PRS), randomly selected from HEALS. A control arm of 100 participants will not receive genetic results until the end of the study. All participants will receive information reminding them of the effects of arsenic and strategies to reduce exposure. Urine samples will be collected at baseline and at 6-months to assess changes in arsenic exposure. We hypothesize that the intervention 1 group (low efficiency) will have a larger decrease in As levels compared to the control arm due to heightened awareness of their susceptibility. If successful, returning genetic information could be expanded within public health contexts.

Genome-wide association study (GWAS) of circulating vitamin D binding protein in African Americans Lisa Parlato* Lisa Parlato Rene Welch Irene Ong Jirong Long Qiuyin Cai Mark Steinwandel William J Blot Wei Zheng Shaneda Warren Andersen

Purpose of Study: Low vitamin D status is more common among African Americans and is linked to a number of health conditions including osteoporosis and cancer. Vitamin D binding protein (VDBP) regulates levels of biologically-active vitamin D. We conducted the first GWAS of VDBP among African Americans.

Methods: Data comprise 2,531 African American adults from the Southern Community Cohort Study. Serum VDBP levels were measured using the Polyclonal Human VDBP ELISA kit (Genway Biotech Inc). Participants were genotyped for SNPs with genome-wide coverage using multiple Illumina platforms. Genetic imputation was conducted using Minimac4. Associations between genetic variants and VDBP were evaluated using single-SNP statistical models adjusted for sex, BMI, and top principal components for ancestry. Significant SNPs (p -value $< 10^{-8}$) were selected and fine-mapping was conducted with forward stepwise linear regression models including all significant variants within 250 kbps.

Results: We identified two loci associated with lower VDBP levels: rs1979537 (per allele $\beta = -0.23$ nmol/L, $p = 3.51 \times 10^{-9}$) in *SLC4A4*, and rs13142062 (per allele $\beta = -0.47$ nmol/L, $p = 4.46 \times 10^{-32}$) in *GC*. In joint-analyses rs13142062 remained significant ($p = 4.46 \times 10^{-22}$); rs13142062 is in linkage disequilibrium with rs7041 ($r^2 = 0.85$), a SNP identified in a previous GWAS conducted in European-ancestry individuals, and with known influence on VDBP isotypes.

Conclusions: In this GWAS of African Americans, associations were found in *GC*, the gene that directly encodes for VDBP, and *SLC4A4*, a neighboring gene to *GC*. Our results replicate associations found in previous studies conducted in European-ancestry populations, and extend our knowledge of VDBP genetics in diverse populations.

Caregiver and household predictors of stunted child growth in the Asenze cohort, South

Africa Rachel Gruver* Rachel Gruver Nonhlanhla P. Myeza Claude A. Mellins Jane D. Kvalsvig Shuaib Kauchali Silvia S. Martins Saloshni Naidoo Myra Taylor Chris Desmond Jeremy C. Kane Leslie L. Davidson

Background:

Stunted growth (low height for age) indicates chronic undernutrition or illness, and has irreversible effects on child development, health and cognition. In South Africa, prevalence of stunting in children under 6 is 27%, well above national/WHO targets. Here we identify factors associated with stunting at age 7 in a peri-urban area with high HIV prevalence.

Methods:

The community-based Asenze cohort study measured child growth at average ages 5 and 7 years (n=1404). At age 5, HIV status was assessed for the child and their primary caregiver using rapid test or caregiver report, and caregivers completed measures of depression and anxiety (Client Diagnostic Questionnaire); experience of intimate partner violence (IPV); alcohol use (AUDIT scale); household food insecurity, measured as running out of food on one or more days in the past month; and the CHAOS scale measuring disorganization of home environment. We calculated stunting, defined as height-for-age <-2 SD of the WHO Child Growth Standards median. We used chi-squared tests to identify factors associated with stunting at age 7. Multivariable analysis and analysis of stunting trajectories from ages 5-7 will also be presented.

Results:

Caregiver HIV infection, major depression, and experience of IPV each predicted stunted child growth 2 years later (11% of children whose caregiver had HIV were stunted, vs. 8% with HIV-negative caregiver; 14% whose caregiver had major depression were stunted, vs. 8% without; 10% with caregiver IPV were stunted, vs. 6% without), as did child HIV infection (35% with HIV were stunted, vs. 8% of those HIV-negative); all significant at $p < 0.05$. Notably, household food insecurity did *not* predict stunting, nor did caregiver anxiety, caregiver alcohol misuse, caregiver mild/moderate depression, or household chaos.

Conclusions:

Further research should investigate the hypothesized roles of caregiver factors (major depression, IPV and HIV) in stunting to inform potential interventions.

Access to community services and psychiatric disorders among adolescents and young adults in the Nepal Chitwan Valley Family Study, 2016-2018 Melanie Askari* Melanie Askari Taylor Marks Sabrina Hermosilla

Background: Access to community services, such as schools and health services, can mitigate the negative consequences of psychiatric disorders among adolescents and young adults. Little research has assessed the relationship between distance to community services and youth prevalence of psychiatric disorders in Nepal.

Methods: Data from the 2016-2018 individual World Mental Health version of the Composite International Diagnostic Interview (WMH-CIDI 3.0) interview component of the Nepal Chitwan Valley Family Study included 3,221 youths ages 15-24. The relationships between distance to either schools or health services (neither, either, or both health services and schools <15-minute walk) and a) any past-year psychiatric disorder (PD), and b) any lifetime PD were assessed utilizing generalized linear models using a logit link, accounting for neighborhood clustering and adjusting for individual-level variables (age, gender, ethnicity, marital status, self-rated health).

Results: Among the 3,221 youths in our study, 7.1% had access to neither health services nor schools, 36.5% had access to either, and 56.4% had access to both <15-minute walk. Of those in our sample, 5.0% had a past-year PD and 22.7% had a lifetime PD. Those with access to either schools or health services had 0.46 times the odds of past-year PD than those with access to neither service in <15-minute walk (95% CI= 0.23-0.94). The association was attenuated with lifetime PD (aOR= 0.86, 95% CI= 0.51-1.43). Access to schools alone was protective of past-year PD (aOR= 0.44, 95% CI= 0.25-0.78), while access to health services was not (aOR= 1.27, 95% CI= 0.81-1.98).

Conclusion: Access to community services, such as schools and health services, was protective against past-year PD but not lifetime PD in our sample of Nepali youth. Public health interventions should address structural barriers, such as access to schools and health services, to mitigate the mental health burden for youth populations in Nepal.

LATEBREAKER

Global Health

The impact of migration on accuracy of self-reported HIV status in South Africa Rachel R Yorlets* Rachel Yorlets Mark N Lurie Carren Ginsburg Mark A Collinson F Xavier Gomez-Olive Michael J White

Background

Accurate self-report of HIV is a critical to achieving the United Nations' goal to end HIV by 2030, particularly in South Africa, the epicentre of the pandemic. Migration is a driver of HIV in South Africa, where 60% of men and 30% of women are circular migrants. Migrants face barriers to HIV care engagement, but could be more readily linked to care if self-report of HIV proved a valid surrogate for confirmatory biomarker testing.

Methods

This analysis utilises data from the first wave (n=3103) of The Migration and Health Follow-Up Study, a longitudinal cohort of circular migrants and residents aged 18–40 years randomly sampled from the Agincourt Health and Demographic Surveillance System in the Agincourt sub-district, Mpumalanga Province. Interviews collected sociodemographic data, self-reported HIV status, and blood for HIV testing. We evaluated sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) of self-report (n=1911) and created a multivariable log-binomial regression model (n=485).

Results

Sensitivity of HIV self-report was 44.1% (95% CI: 39.7–48.7), PPV was 93.5% (95% CI: 89.5–96.0), specificity was 99.0% (95% CI: 98.3–99.4), and NPV was 83.9% (95% CI: 82.8–84.9). Among persons with HIV (PWH), migrants were more likely than residents to accurately self-report (RR: 1.33, 95% CI: 1.09–1.62), and respondents who utilised formal health care for any reason were more than twice as likely to accurately self-report (RR: 2.40, 95% CI: 1.70–3.37), adjusting for confounding.

Discussion

Self-report of HIV-positive status was predictive of true HIV status, but most PWH do not report as HIV-positive. Migrants are more likely to accurately self-report than non-migrants. Findings support policies to link migrants who report as HIV-positive directly to care without confirmatory biomarker testing or medical documentation of status, which are often unavailable to migrants.

Income inequality and depression among Canadian secondary students: Are self-esteem and social cohesion mediating factors? Claire Benny* Claire Benny Karen Patte Scott
Leatherdale Roman Pabayo

Background. Nearly one-third of secondary school students report experiencing depressive symptoms in the past year. Existing research suggests that increasing rates of depression are a result of increasing social inequities, such as income inequality. The aim of this current study is to identify mechanisms by which income inequality may contribute to depression among Canadian secondary school students.

Methods. We used cross-sectional data from the 2017/18 wave of the Cannabis, Obesity, Mental health, Physical activity, Alcohol use, Smoking, and Sedentary behaviour (COMPASS) study among a large sample of Canadian secondary school students. The sample included 61,642 students attending schools across 43 Census divisions (CDs). We used multilevel path analysis to determine if the relationship between CD-level income inequality and adolescent depression was mediated by student's self-esteem and/or social cohesion.

Results. Attending schools in areas with higher levels of income inequality was related to higher self-reported depression scores among Canadian secondary students [unstandardized β (β) = 5.36; 95% CI = 0.74, 9.99] and lower self-esteem (β = -14.83, 95% CI = -25.05, -4.60). Income inequality was not significantly associated with social cohesion (β = -2.86; 95% CI = -8.29, 2.57), although social cohesion was associated with depression scores among students (β = -0.31; 95% CI = -0.34, -0.28).

Discussion. Findings from this study indicate that income inequality is associated with adolescent depression and that this relationship is mediated by self-esteem. Most students typically spend the majority of their waking hours in schools, but no school-based studies have evaluated this relationship in Canada. The current study is the first of its kind to assess the mechanisms by which area-level income inequality contributes to adolescent mental health. The findings of this research are applicable to school-level programs addressing adolescent mental health.

Travel Time to Treatment Facilities and Socioeconomic Disparities in Treatment for Early Stage Lung Cancer in California Chelsea Obrochta* Chelsea Obrochta Atsushi Nara James Murphy Caroline Thompson

Disparities in lung cancer treatment have been observed in underserved rural populations with increased travel requirements. The objective of this study is to investigate the relative contribution of travel time to patients' treatment facilities on socioeconomic disparities in timely receipt of appropriate treatment in early stage lung cancer patients.

We studied 22,833 patients diagnosed with early stage lung cancer (2006-2015) in the California Cancer Registry. The outcome was timely receipt of appropriate treatment. The exposure was mean-centered travel minutes (driving and public transit) to a patient's treatment facility, from their residence (centroid of their block group). Multivariable logistic regression models were used to estimate the effect of travel time on undertreatment and treatment delay, overall, and jointly with neighborhood socioeconomic status (nSES).

Overall, a 15-minute increase (from the mean) in driving time was significantly associated with a 5.44% and 3.13% decreased relative risk for undertreatment and treatment delay, respectively, and a 15-minute increase in public transit time was significantly associated with a 2.07% and 0.7% decreased relative risk for undertreatment and treatment delay, respectively. However, longer travel times did not translate to improved care for all socioeconomic groups. For example, considering a joint exposure with both travel time and nSES, a 15-minute increase in driving time for patients living in the lowest SES neighborhoods increased their relative risk of undertreatment to 37% higher than patients living in the highest SES neighborhoods.

Undertreatment and delayed treatment for cancer disproportionately affect underrepresented groups. The protective effect we observed from increased travel times was unexpected and may be a 'Travel Time Paradox'. This paradox effect was not uniform across groups; increased travel time resulted in lower care quality for lower socioeconomic groups.

The associations of household food insecurity with depression and weight status in a diverse sample of adolescents Mikayla Barry* Mikayla Barry Julia Wolfson Cindy Leung

Household food insecurity occurs when households lack the financial resources needed to purchase enough quality food. Worry about getting food, and low quality and/or insufficient dietary intake, may negatively impact the health of household members. However, the physical and psychological health consequences of food insecurity are understudied, particularly in adolescents. Therefore, this study examined the associations of food insecurity with depression and body mass index percentile (BMI%) in adolescents. Cross-sectional data came from electronic health records of 528 adolescents aged 12-17 years who attended well-child visits at a pediatric clinic in a diverse southeastern Michigan community. Adult caregivers reported household food security status using a validated 2-item screener. Adolescents self-reported depressive symptoms using the 9-item Patient Health Questionnaire (PHQ-9). BMI% was calculated using measured weight and height and was age- and sex-standardized based on national reference data. Multinomial logistic regression was used to model the odds of mild or moderate-to-severe depression by food security status. Linear regression was used to model BMI% by food security status. Models were adjusted for age, gender, race/ethnicity, and use of government insurance. Overall, 19.9% of adolescents lived in food-insecure households, 23.7% reported mild depression (PHQ-9 score of 5-9), and 15.7% reported moderate-to-severe depression (PHQ-9 score ≥ 10). Median BMI% was 81.0. Household food insecurity was associated with greater odds of mild (OR=2.35, 95% CI: 1.33, 4.16) and moderate-to-severe (OR=2.28, 95% CI: 1.16, 4.48) depression, relative to minimal or no depression (PHQ-9 score of 0-4). The association between food insecurity and BMI% was not statistically significant ($\beta=4.6$, 95% CI: -1.6, 10.7). To conclude, household food insecurity was associated with mild and moderate-to-severe depression, but not weight status, in adolescents.

Racial/ethnic disparities in adverse birth outcomes among women living in public housing in New York City

Melanie Baker* Melanie Baker Lorna Thorpe

Racial/ethnic disparities in adverse birth outcomes among women living in public housing in New York City

Melanie Baker, MPH; Lorna Thorpe, PhD, MPH

NYU Langone Health

New York City (NYC) is home to the largest public housing authority in the United States. More than 400,000 residents live in approximately 370 public housing developments; median household income is \$20,000 and approximately 90% of residents are non-Hispanic Black or Hispanic. We examined within-public housing racial/ethnic disparities in preterm birth and low birthweight among a population of women giving birth while living in NYC public housing between the years of 2013-2016 (n=45,890). Data for analysis were obtained from birth records provided by the NYC Office of Vital Records. Adjusted odds ratios and 95% confidence intervals were reported. Among women residents, there was a higher proportion of low birthweight and preterm birth among non-Hispanic Black women (10% and 11%) than Hispanic (7% and 9%) and non-Hispanic White (4% and 6%) women. Non-Hispanic Black women were 50% more likely to deliver a low birthweight infant [AOR=1.5, 95% CI (1.3, 1.6)] and 20% more likely to deliver a preterm infant [AOR=1.2, 95% CI (1.2, 1.3)] compared to Hispanic women. Non-Hispanic White women were 30% and 40% less likely to deliver a low birthweight and preterm infant, [AOR=0.7, 95% CI (0.5, 0.8); AOR=0.6, 95% CI (0.5, 0.8)] respectively, compared to Hispanic women. When stratified by maternal age, non-Hispanic Black women had elevated odds ratios of low birthweight and preterm birth for all age groups compared to Hispanic women but declined from 2013-2016 in women older than 35 years. Our findings show profound differences in adverse birth outcomes by race/ethnicity and maternal age, even when analyses were restricted to the public housing resident population. Further studies are warranted to identify important contributors to disparities in birth outcomes among women living in public housing.

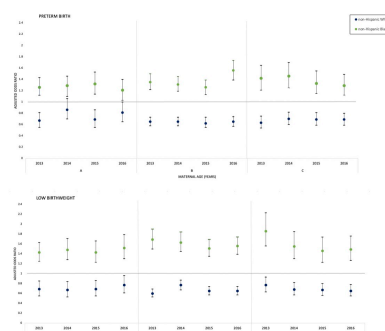


Figure 1. Odds ratios of preterm birth and low birthweight among women living in public housing whose age at delivery was A) younger than 25 years B) older than 25 years and less than 35 years and C) older than 35 years.
 *Models adjusted for marital status, insurance status, alcohol use, drug use, smoking 3 months prior or during pregnancy, previous low birthweight or preterm delivery.
 †Reference group is Hispanic women public housing residents.

Association of neighborhood level socioeconomic deprivation with preoperative health status in total joint arthroplasty patients: Analysis from a large, tertiary care hospital. Hilal Maradit Kremers* Celia Kamath Thomas O'Byrne Nilay Shah David Lewallen Daniel Berry Hilal Maradit Kremers

Research objective: Individual socioeconomic status (SES) are associated with baseline disparities in health status, access to care and clinical outcomes in total joint arthroplasty surgery. Neighborhood-level SES measures are sometimes used as a proxy for individual-level SES, but the validity of this approach is unknown in this setting. We examined the effect of neighborhood level SES and rurality on preoperative health status and clinical characteristics. **Study design:** This was a cross-sectional study of primary and revision TKA and THA surgeries performed at a large tertiary care hospital between 2000 and 2019. Demographic and clinical characteristics were ascertained through the institutional total joint registry. Patients' neighborhood area deprivation index (ADI) were derived from the American Census Survey (2015); rurality index was defined by census-tract level 2010 Rural-Urban Commuting Area (RUCA) codes. Logistic regression models were used to estimate association of ADI and RUCA scores and selected demographic and preoperative characteristics. **Principal Findings:** At the time of surgery, there were 22,406 THA and 24,422 TKA surgeries with a mean±SD age 67±13 years, 55% women and 95% white. 5.5% of patients lived in the most deprived neighborhoods (census block ADI quintile >80%) and 23% lived in small towns/rural areas. Patients from the most deprived neighborhoods were more likely to be female (OR 1.25, 95% CI: 1.15-1.36), non-white race (OR 1.78, 95% CI: 1.51-2.08), had higher BMI (OR 1.01, 95% CI: 1.00-1.01), and lower education levels (when compared to Bachelor's completion, middle school: OR 2.24, 95% CI: 1.77-2.83). These patients also had significantly worse health status on almost all clinical and functional measures. They had significantly higher comorbidity burden (e.g., myocardial infarction, heart failure, diabetes pulmonary and renal diseases) and more restrictions on basic (OR 1.16, 95% CI: 1.05-1.27) and instrumental (OR 1.70, 95% CI: 1.55-1.87) activities of daily living. Similar patterns were observed in terms of rurality. **Conclusions:** Neighborhood-level SES and rurality are of value in understanding SES and related preoperative health status in THA and TKA populations.

Association between neighborhood-level socioeconomic deprivation and long term outcomes following total joint arthroplasty. Hilal Maradit Kremers* Celia Kamath Thomas O'Byrne Nilay Shah David Lewallen Daniel Berry

Research objective: While individual level socioeconomic (SES) disparities in outcomes of total knee (TKA) and total hip (THA) arthroplasty are well documented, neighborhood SES factors and their interaction with individual level determinants (e.g., education) on outcomes are poorly understood. The magnitude of association between neighborhood deprivation may differ for more and less educated patients. We determined the contribution of neighborhood SES and rurality on long-term outcomes following TKA and THA surgery, accounting for individual-level education.

Study design: This retrospective cohort study utilized longitudinal registry data (2000-2019) from TKA and THA surgeries performed at a large tertiary care hospital. Patients' neighborhood area deprivation index (ADI) were derived from the American Census Survey (2015). Patients' rurality index was defined by census-tract level 2010 Rural-Urban Commuting Area (RUCA) codes. We used multivariable Cox regression analyses to examine the relationship between ADI and RUCA percentile scores and the risk of periprosthetic infections (PJI), revision surgery and mortality, adjusting for age, sex, race, calendar year of surgery and education. **Principal Findings:** 22,406 THA and 24,422 TKA surgeries with a mean±SD age 67±13 years, 55% women and 95% white. At time of surgery, 5.5% of patients lived in the most deprived neighborhoods (census block quintile >80%) and 23% lived in small rural towns. A total of 1022 (2.2%) patients suffered a PJI, 2647 (5.7%) had at least one revision surgery and 10,425 (22.3%) died during follow-up. Compared to patients from first quintile, the risk of PJI (HR 1.44, 95% CI:1.03-2.03) and revisions (HR 1.42; 95% CI:1.13-1.78) were significantly higher for patients living in fifth quintile. Relative to urban areas, the risk of revisions was higher for patients from small rural towns (HR 1.15, 95% CI:1.01-1.30); risk of PJI was higher for patients from larger rural towns (HR 1.28, 95% CI:1.06-1.55). Mortality increased with decreasing neighborhood SES advantage. Compared to first quintile, mortality was higher for those living in third (HR 1.12, 95% CI: 1.00-1.25), fourth (HR 1.19, 95% CI: 1.05-1.34) and fifth quintile (HR 1.30, 95% CI: 1.12-1.52). The education gradient in the least deprived neighborhoods was steeper than in the most deprived neighborhoods. **Conclusions:** In TKA and THA patients, neighborhood disadvantage and degree of rurality are negatively correlated with surgical outcomes and mortality independent of individual education level.

Socioeconomic inequalities in multi-drug resistant urinary tract infection in two large

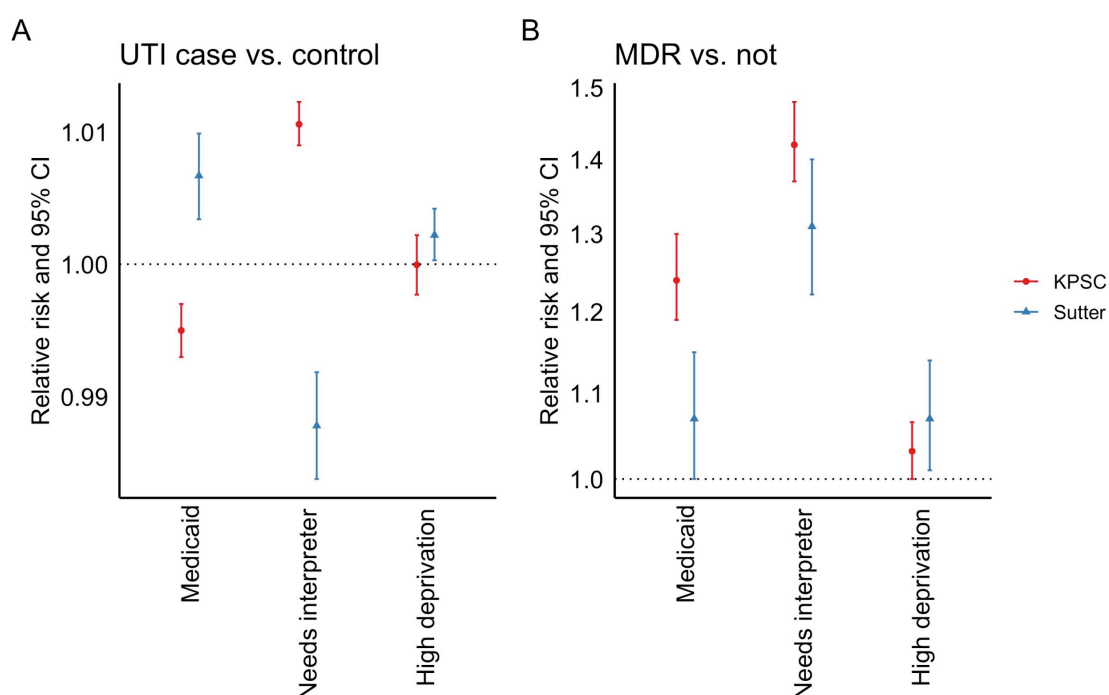
California health systems Joan Casey* Joan Casey Kara E. Rudolph Sarah Robinson Katia Bruxvoort Vennis Hong Alice Pressman Eva Raphael Rachel Morello-Frosch Sara Y. Tartof

Background: Urinary tract infections (UTIs) account for a substantial portion of outpatient visits and antibiotic prescriptions in the United States. Few studies, however, have considered low socioeconomic status (SES)-which may increase residential crowding, inappropriate antibiotic prescribing, or co-morbidities-as a risk factor for UTI or multi-drug resistant (MDR) UTI.

Methods: We used electronic health record data from two large California healthcare systems from 2015-2017 to identify cases of UTI, as well as urinary *E. coli*, isolate resistance patterns. UTIs resistant to 3 or more antibiotic classes were considered multi-drug resistant (MDR). We included three measures of SES: individual-level use of Medicaid, use of an interpreter, and a census tract-level deprivation index. We used targeted maximum likelihood estimation to estimate the association between SES and (1) risk of UTI; and (2) risk of an MDR UTI among cultured UTIs.

Results: Analyses included 601,352 UTI cases, 1,303,455 controls, and 425,035 urinary *E. coli* isolates from Kaiser Permanente Southern California (KPSC) and Sutter Health in Northern California. MDR prevalence among urinary *E. coli* isolates was 10.4% at KPSC and 12.8% at Sutter Health. Lower SES (i.e., use of Medicaid, using an interpreter, and community deprivation) was associated with increased risk of MDR UTI. As an example, using an interpreter was associated with 42% (RR = 1.42, 95% CI: 1.37, 1.48) and 29% (RR = 1.29, 95% CI: 1.21, 1.38) increased risk of MDR UTI at KPSC and Sutter Health, respectively, adjusted for potential confounding variables. Measures of SES were only weakly associated with UTI overall.

Conclusions: While minimal associations were observed between SES factors and risk of UTI, we estimated a social gradient in the risk of MDR UTI.



Racial-ethnic differences in the association between comorbidity burden and health-related quality of life among older women with breast cancer before diagnosis Eunkyung Lee* Eunkyung Lee Eunji Nam Jianbin Zhu Kirk Dourvetakis Robert B. Hines Michael Rovito

Background

This study examined the association between comorbidity burden and health-related quality of life (HRQOL) among older women with breast cancer before diagnosis and racial-ethnic differences in such associations.

Methods

This cross-sectional analysis included 3,340 women diagnosed with breast cancer at age ≥ 65 years between 1998-2015 from the SEER-MHOS database. Women completed a MHOS survey within 24 months before diagnosis. The distinct comorbidity burden classes (CBCs) were identified using latent class analysis based on self-reported comorbid conditions, functional status, and symptom indicators. Pre-diagnosis HRQOL was assessed using SF-36/VR-12 and summarized to the physical component summary (PCS) and mental component summary (MCS) scores. The adjusted least-squares mean and 95% confidence intervals (CI) for PCS and MCS were obtained according to CBCs and race-ethnicity.

Results

The latent class analysis identified four distinct comorbidity burden classes: class 1 being the most healthy and having the least burden and class 4 being least healthy and having the most burden. African American (AA) and Hispanic women were more likely to belong to class 4 than white women (13.8%, 16.3%, 12.1%, respectively). The mean PCS score for all women was 39.2 (95%CI: 38.8-39.6). The mean PCS score in class 1 was 45.56, and that in class 2, 3, and 4 was 35.11, 28.61, and 25.36, respectively. Although stepwise downward trends across the severity of CBC were observed for all racial-ethnic groups, a more considerable difference between class 1 and class 4 was observed for white women. The mean MCS score for all women was 51.3 (95%CI: 50.9-51.7). The mean MCS score in class 1 was 54.82, and that in class 2, 3, and 4 was 49.52, 47.90, and 39.12, respectively. A stepwise downward trend of MCS score according to the CBC severity was not observed for AA women. The difference of MCS score between class 1 and class 4 was small for white and Asian women but large for AA and Hispanic women.

Conclusion

The comorbidity burden affected HRQOL differently for racial-ethnicity groups: most considerably for white women's PCS and AA and Hispanic women's MCS scores. Future studies are warranted to examine how these racial-ethnic differences in pre-diagnosis comorbidity burden contribute to breast cancer treatment decisions and outcomes.

Employment quality as a mediator in the relationship between educational attainment and mental health: a novel use of the parametric mediational g-formula Kieran Blaikie* Kieran Blaikie Jerzy Eisenberg-Guyot Sarah B. Andrea Anjum Hajat

Background: In the US, considerable mental health inequities exist across the socioeconomic gradient, with those less educated disproportionately burdened by poor mental health. In recent years, employment quality (EQ), the relational features of the employee-employer relationship, has been identified as a modifiable mediator through which these inequities arise and could be alleviated. Research on this topic has been limited, however, with most studies cross-sectional, focused on Europe, or conducted using methods which cannot quantify time-varying mediation effects. This study aimed to address these limitations through using the parametric mediational g-formula, a novel approach for estimating mediation effects in the presence of time-varying mediation and confounding, with 2001-2017 data from the Panel Study of Income Dynamics (PSID), a nationally representative US cohort study. **Objective:** To 1) quantify the effect of educational attainment on mental health status mediated through EQ over the working years, and 2) determine the extent to which there are racial/ethnic or gender-based inequities in this relationship. **Methods:** Using longitudinal data on employment stability, working-time arrangements, material rewards, interpersonal power relations, and collective organisation, principal component analysis was used to construct a continuous employment quality (EQ) score. The randomised natural indirect effect of educational attainment (high school or more: no/yes) on moderate mental illness (Kessler K-6 score: $<5/\geq 5$) mediated through EQ was then estimated using the parametric mediational g-formula. **Results:** Preliminary results suggest a moderate amount of the educational inequity in mental health can be explained by differences in EQ. **Conclusions:** Improvements in EQ could be effective at reducing educational inequities in mental health.

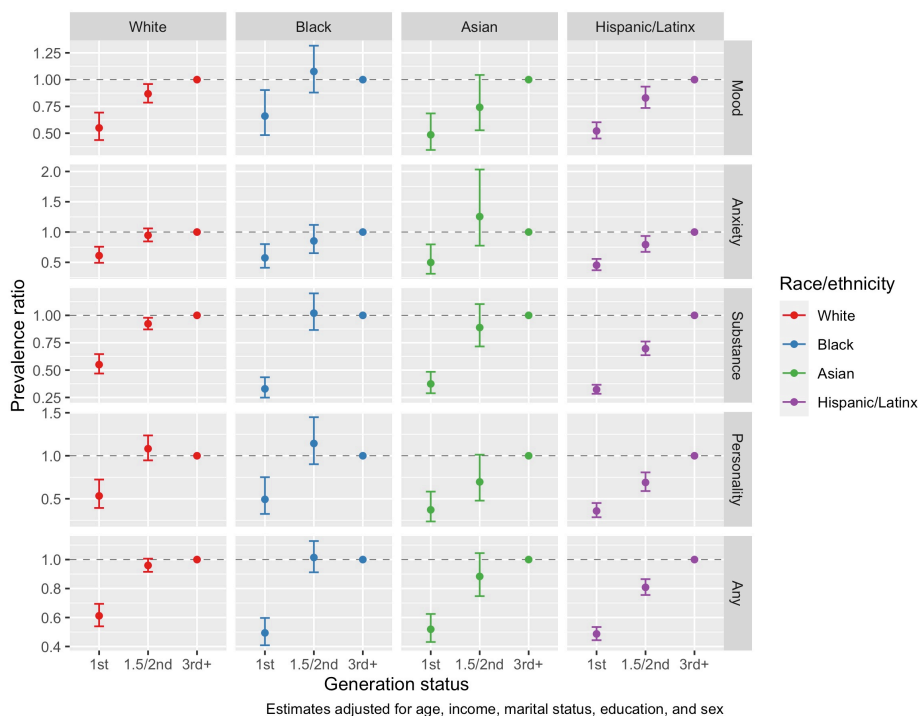
Generation status, race/ethnicity, and the prevalence of psychiatric disorders Precious Esie*
Precious Esie Lisa Bates

Previous research shows foreign-born immigrants have a lower prevalence of psychiatric outcomes relative to native-born counterparts. Yet, less is known about how this pattern varies by race/ethnicity, disaggregated generation status, or outcome. Furthermore, most U.S. studies comparing immigration-related patterns in health outcomes have excluded Black immigrants.

Data were drawn from the 2012-2013 NESARC-III. Outcomes of interest were lifetime DSM-IV mood, anxiety, substance use, and personality disorders, examined by immigrant generation among racial/ethnic groups (white, Black, Asian, Hispanic/Latinx). Using a lifecourse approach, we disaggregated generation status to differentiate those foreign-born who immigrated to the US at age ≥ 13 years (“first generation”), those either foreign-born who immigrated to the US at age < 13 years or born in the US to at least one first-generation parent (“1.5/second generation”), and those born in the US to US-born parents (“third+ generation”).

Across all racial/ethnic groups and relative to the third+ generation, the first-generation had a significantly lower prevalence of all outcomes under study (prevalence ratios ranged from 0.32-0.66). Among Hispanic/Latinx individuals, the 1.5/second-generation also had a lower prevalence of outcomes relative to the third+ generation. Among whites, results followed a similar pattern for mood and substance disorders. However, there were no significant differences between the 1.5/second-generation and third+ generation among Black and Asian subgroups; for some outcomes, the unadjusted prevalence among the 1.5/second-generation exceeded that of the third+ generation — e.g., lifetime mood disorders among Black individuals (20.1% vs. 18.8%), and lifetime anxiety disorders among Asian individuals (15.1% vs 12.7%).

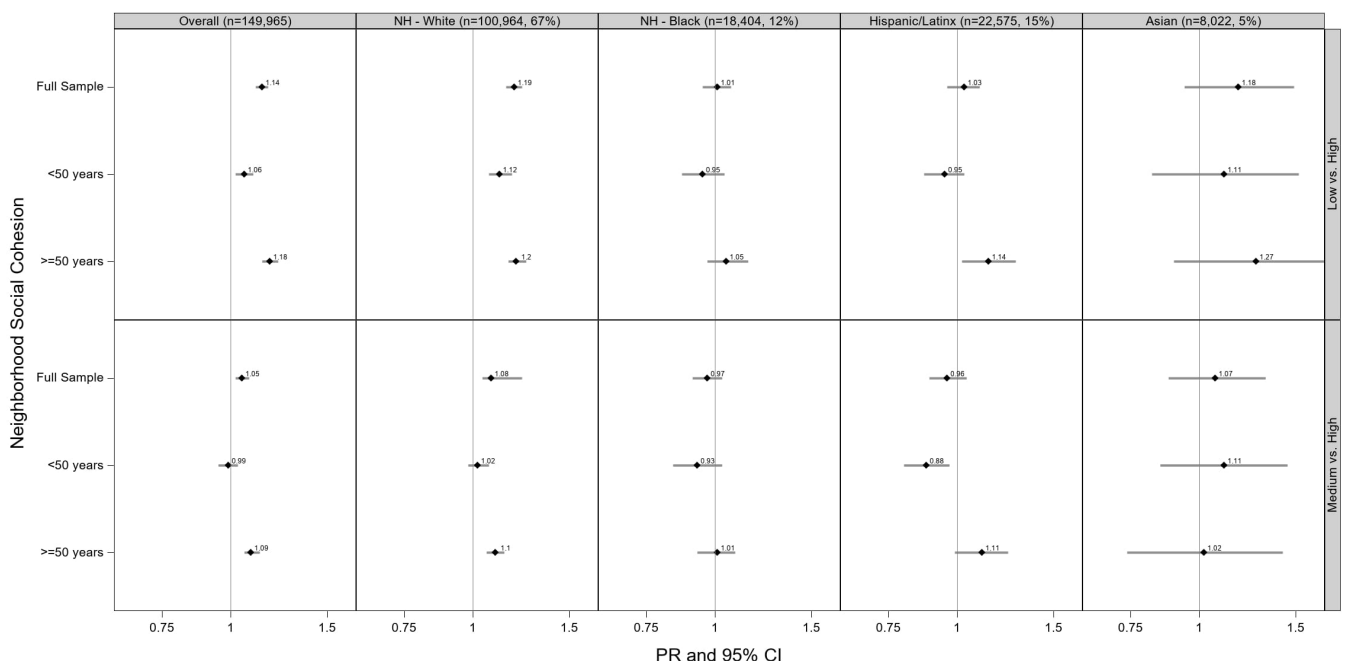
These findings suggest variability by race/ethnicity in the durability across generation status of the protective association between generation status and mental health.



Neighborhood social cohesion and obesity across racial/ethnic groups in the United States

Dana Alhasan* Dana Alhasan Symbielle A. Gaston W. Braxton Jackson II Patrice C. Williams Chandra L. Jackson

Prior research has shown that low neighborhood social cohesion (nSC) is associated with obesity, but few studies have assessed the nSC-obesity relationship among a large, racially/ethnically diverse, and nationally representative sample of the United States population. We examined overall and race/ethnic-specific cross-sectional associations by age among 149,965 participants of the National Health Interview Survey from 2013-2018. Based on a 4-item scale from the Project on Human Development in Chicago Neighborhoods Community Survey, we categorized nSC as low, medium, and high. We categorized obesity as a body mass index ≥ 30 kg/m² vs. non-obese (< 30 kg/m²). We used Poisson regression with robust variance to estimate PRs and 95% CIs while adjusting for sociodemographics (e.g., annual household income, educational attainment and marital status) and other confounders. Mean age \pm standard error of study participants was 47.1 ± 0.1 years, most (69.2%) self-identified as Non-Hispanic (NH)-White and 51.0% were women. Among NH-Whites, a lower percent lived in low (61.8%) vs. high (77.0%) nSC. A higher percent of NH-Black and Hispanic/Latinx participants reported low (14.0%; 19.1%) vs. high nSC (7.7%; 10.4%), respectively. Low vs. high nSC was associated with a 14% higher prevalence of obesity (PR=1.14 [95% CI: 1.11-1.17]), and the magnitude of the association was stronger among NH-White (PR=1.19 [95% CI: 1.15-1.23]) than Hispanic/Latinx (PR=1.03 [95% CI: 0.96-1.10]) and NH-Black (PR=1.01 [95% CI: 0.95-1.07]) adults. Among NH-White adults, low vs. high nSC was associated with a 20% higher prevalence of obesity among adults ≥ 50 years old (PR=1.20 [95% CI: 1.16-1.25]) compared to < 50 years old (PR=1.12 [95% CI: 1.07-1.18]). Among Hispanic/Latinx adults, low vs. high nSC was associated with obesity among ≥ 50 years old (PR=1.14 [95% CI: 1.02-1.28]) but not < 50 years old (PR=0.95 [95% CI: 0.87-1.03]) adults. Enhancing nSC may improve health and address health disparities.



Inequalities of Experiences for Multigenerational Families Due to COVID-19 in Marin County, California Michaela George* Michaela George Alanna Williams Chandra Alexandre

Background: The coronavirus disease 2019 (COVID-19) has disproportionately affected low income communities of color across the country. However, the impact the virus has brought upon low-income families in Marin County, California, who have experienced unexpected financial emergencies due to COVID-19, is still unknown.

Methods: A cross sectional study was conducted using Community Action Marin's database, which includes families experiencing financial emergencies and times of crisis, parents seeking affordable early childhood care, and supporting the food needs of low-income households. Participants took part in a 27 question questionnaire that focused on COVID-19 and the effects surrounding low income communities in Marin County due to state mandated guidelines.

Results: Preliminary results have shown that in the last month, about 50% of participants self reported financial negative impacts due to COVID-19. Over 40% reported that they have worried about how they will pay for housing/rent, how they will buy groceries, and how they will pay for household utilities and necessities. When asked about the importance of services needed for their personal living situations during these times, over 30% of participants believe financial support, mental health support, and healthcare support are extremely important, while more than 50% of participants believe food/grocery and housing support are extremely important.

Conclusion: These findings aims to contribute in the efforts to not only acknowledge the inequities low income families and communities of color face due to the current COVID-19 pandemic, but also understand how local non-profit organizations can better support their communities in times of need and areas that still need improvement such as financial and food assistance, childcare services, and job opportunities.

Disparities in Congenital Heart Disease Burden by Maternal Socioeconomic Status and Race/ethnicity in Canada Qun (Grace) Miao* Qun (Grace) Miao Sandra Dunn Shi-Wu Wen Jane Lougheed Mark Walker

Purpose: The purpose of this study was to investigate the interrelationships between maternal socioeconomic status (SES), ethnicity/race, and congenital heart diseases (CHD) among infants.

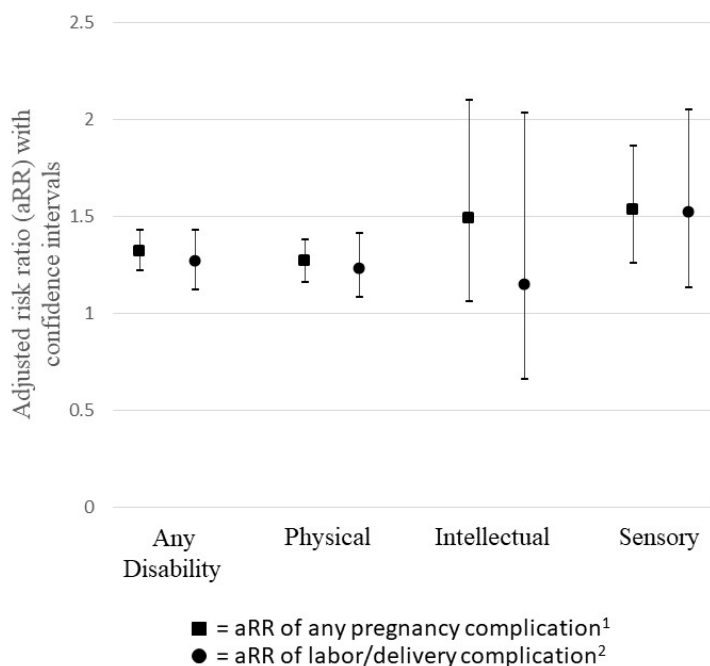
Methods: A retrospective cohort study was conducted including all singleton stillbirths and live births born in hospitals between April 1, 2012 and March 31, 2018 in Ontario, Canada. We analyzed data using multivariable logistic regression models. Associations between maternal neighbourhood household income, education level, ethnicity/race and CHD were assessed while adjusting for maternal age at birth, assisted reproductive technology, obesity, pre-existing health conditions, substance use during pregnancy, maternal rural residence, and infant's sex.

Results: Compared to infants whose mothers lived in the highest median household income neighbourhoods, infants whose mothers lived in the lowest median income neighbourhoods had a higher likelihood of having CHD (adjusted OR: 1.15, 95% CI: 1.06-1.24). Compared to infants whose mothers lived in neighbourhoods with more people with a university or higher degree, those infants whose mothers lived in neighbourhoods with less people with a university or higher degree had a higher chance of developing CHD (adjusted OR: 1.26, 95% CI: 1.16-1.36). Compared to White mothers, Black mothers had higher odds of giving birth to a child with CHD (adjusted OR: 1.10, 95% CI: 1.06-1.24). No association was detected between White and Asian mothers and CHD among infants.

Conclusion: Our study indicates that there are disparities in CHD burden by maternal SES and race/ethnicity in Ontario Canada. Further investigation is needed to examine racial variation in CHD using more detailed ethnic data.

Risk of obstetric intervention, severe maternal morbidity and mortality among pregnant women with disabilities in the Consortium on Safe Labor Jessica L. Gleason* Jessica Gleason Jagteshwar Grewal Zhen Chen Alison Cernich Katherine Grantz

Women with disabilities have been reported to have higher risk of preterm birth, gestational diabetes, preeclampsia and delivery via cesarean, but whether they are at risk for other obstetric interventions or adverse outcomes and the reason for increased cesarean are unknown. We performed a comprehensive analysis of obstetric interventions and adverse maternal outcomes from a retrospective medical record study among singleton deliveries, using ICD-9 codes to define disability. Adjusted relative risk (RR) of 21 maternal and obstetric outcomes were estimated, including composite variables for pregnancy and labor and delivery complications (Figure) among women with any disability (n=2,142) and each category (physical, sensory, or intellectual) compared to no disability (n=221,252). Compared to women with no disability, women with disabilities were at higher risk of both composites of pregnancy and labor/delivery complications (Figure). Specifically, women with disabilities were at higher risk for gestational diabetes, placenta previa, PROM, PPRM, and postpartum fever, as well as maternal death (RR 9.99; 95% CI 2.17, 45.6) and severe maternal morbidity: hypertensive disorders (RR=1.49; 95% CI 1.33, 1.67), hemorrhage (RR=1.27; 95% CI 1.09-1.49), and thromboembolism (RR 5.77; 95% CI 3.83-8.69). Heightened risk varied but was generally consistent across all disability categories. Women with any disability also had higher risk of interventions, including oxytocin augmentation, operative vaginal delivery, and cesarean delivery (RR 1.33; 95% CI: 1.25, 1.42) with the indication less likely to be a medically-indicated cesarean (RR 0.79; 95% CI 0.70, 0.89). Risk for interventions remained consistent across categories of disability. In conclusion, women with physical, intellectual and sensory disability during pregnancy are at higher risk for adverse outcomes, including a broad range of severe maternal morbidity and maternal mortality.



¹ Includes hypertension, GDM, placental abruption, placenta previa, PROM, or PPRM
² Includes chorioamnionitis, hemorrhage, blood transfusion, thromboembolism, maternal fever, and maternal death

Inequalities in exposure to ambient fine particulate matter in Canada Megan Kirby-McGregor* Megan Kirby-McGregor Chen Chen Jay Kaufman Tarik Benmarhnia Hong Chen**Background**

Exposure to fine particulate matter (PM_{2.5}) is associated with various adverse health outcomes. Previous cross-sectional analyses of environmental injustice in Canada found inequitable exposure to PM_{2.5} in low-income populations, visible minorities and immigrants. We expand on this literature by investigating if individuals belonging to different demographic groups benefit equally from improvements in ambient concentrations of PM_{2.5} from 2001 to 2016 in Canada.

Methods

We use census tract level estimates of average annual PM_{2.5} derived from satellite-based observations to investigate how the spatial distribution of PM_{2.5} has evolved over time. We use decennial census data to determine if demographic characteristics are associated with changes in exposure to PM_{2.5}, accounting for geographic boundary changes between census periods.

Results

Ambient PM_{2.5} concentrations have decreased from 2001 (median of 9.1 µg/m³ across tracts) to 2016 (median of 6.4 µg/m³ across tracts), with varying provincial patterns. Across census tracts, ranked estimates of fine particulate matter in 2001 and in 2016 are correlated (Spearman correlation coefficient = 0.75). Tracts with higher concentrations of PM_{2.5} in 2001 tend to remain among the most polluted tracts in 2016. Accounting for provincial differences, census tracts with greater proportions of immigrants, visible minorities, individuals who do not speak either official language, who have lower education, who work in mining or manufacturing, who are unemployed, or who are low income, experience larger relative decreases in PM_{2.5} over time, suggesting diminishing environmental injustice in Canada.

Conclusions

Identifying demographic groups that benefit least from improvements in ambient concentrations of PM_{2.5} can help guide policy for reducing environmental injustice due to differential exposure.

Using latent class analysis to identify asthma risk profiles among sexual minority adults

Charlotte Talham* Charlotte Talham Francisco Alejandro Montiel Ishino Faustine Williams

Background. Linear associations between social determinants of health and asthma are well established in the literature. However, the interactive effect of these factors is largely understudied. Sexual minorities have higher prevalence of asthma than their heterosexual counterparts. As such, our objective was to build a syndemic model of asthma to identify profiles of sexual minorities at highest risk.

Methods. We conducted a latent class analysis on 2001-2016 National Health and Nutrition Examination Survey data for US adults ≥ 18 years ($N=82,097$) with the distal outcome of current asthma. Indicators included gender, sexual identity, nativity, poverty income ratio, education, serum cotinine level, and BMI. We then conducted an LCA on a subpopulation of sexual minorities ($N=1,097$) using the same indicators and distal outcome. Covariates in both analyses were age group, race/ethnicity, marital status, US citizenship, ever-smoker, mental health care seeking, and access to healthcare. Model fit comparison was based on the following: (1) Bayesian information criterion (BIC); (2) sample-size-adjusted BIC (ssa-BIC); and (3) entropy.

Results. Our best fitting model for the subpopulation analysis was a four-class solution. The highest risk profile (10.4% of sample) had the highest conditional probabilities of being female, bisexual, and being vocationally trained, as well as had the highest average BMI at 42.3. They also had a high likelihood of being above poverty level and having high levels of serum cotinine. This profile had over 400% odds of seeking mental health care and almost 600% odds of being Black when compared to the lowest asthma risk profile.

Conclusions. Among sexual minorities, we found bisexual women were at highest risk of asthma. Person-centered subpopulation analyses provide a methodological extension to better understand and further examine the dynamic interactions of the determinants of health affecting medically underserved and underrepresented groups.

Quantifying within-city inequalities in child mortality across neighbourhoods in Accra, Ghana Honor Bixby* Honor Bixby James E Bennett Majid Ezzati Ayaga Agula Bawah Alexandra M Schmidt Samuel Agyei-Mensah George Owusu Brian E Robinson Jill Baumgartner Raphael E Arku

Countries in sub-Saharan Africa suffer the highest rates of child mortality worldwide, despite improvements over recent decades. While urban areas tend to have more favourable rates than rural areas, these comparisons likely mask large within-city inequalities, observed for mortality in high-income settings. Our aim was to empirically quantify variation in child mortality across neighbourhoods of Accra – Ghana’s capital and largest city.

We accessed data on over 700,000 women aged 25 to 49 years living in the Greater Accra Metropolitan Area (GAMA) recorded in the most recent Ghana census (2010). We summarised counts of child births and deaths by five-year age group of women and neighbourhood (n=406). We applied indirect methods to convert the summaries to population probabilities of death under-five years of age and assign a reference year to each probability. We fitted a Bayesian spatio-temporal model to the neighbourhood child mortality probabilities to obtain estimates for the year 2010, accounting for the spatial structure in the data and uncertainty arising from small number of births in some neighbourhoods and age groups of women.

Child mortality varied almost five-fold across neighbourhoods in the GAMA in 2010, ranging from 28 (95% credible interval (CrI): 8-63) to 138 (95% CrI: 111-167) deaths per 1000 live births. We found substantial variation between and within the GAMA’s twelve districts. Child mortality was highest in the urban core and industrial districts, with 95 deaths per 1000 live births on average across neighbourhoods. Outer rural or peri-urban neighbourhoods were, on average, the best performing but had greater within-district variation (up to 3.8-fold).

Child mortality rates in Accra’s inner-city neighbourhoods were equivalent to rates in the lowest performing countries worldwide. Child deaths are largely due to preventable and treatable causes. Here, we have highlighted specific communities being left behind in child mortality reductions.

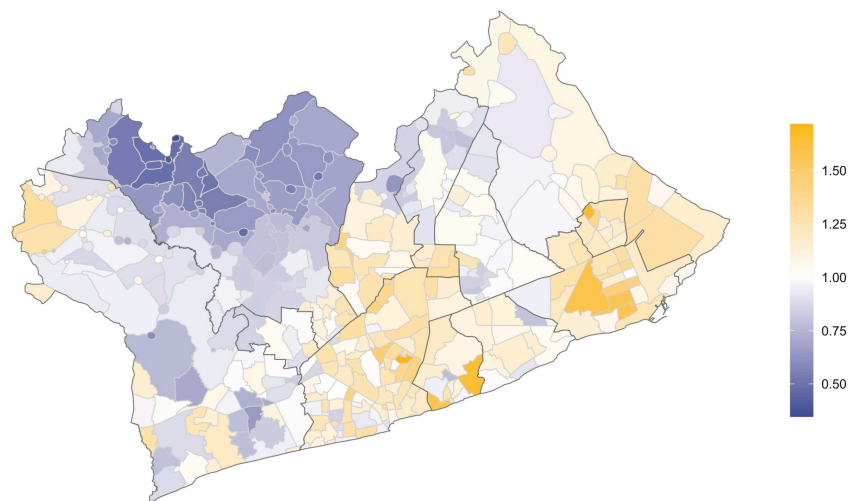


Figure 1: Neighbourhood child mortality relative to the mean across all neighbourhoods in the Greater Accra Metropolitan Area.

To control or not control while using a distal continuous outcome: Latent class analyses of complex survey data to identify profiles of acculturation and telomere length among US Hispanics/Latinxs Francisco Alejandro Montiel Ishino* Francisco Montiel Ishino Charlotte Talham Bradley Faustine

Objective: To identify profiles of acculturation and telomere length among US Hispanics/Latinxs. Purpose: Studies examining the relationship of acculturation and telomere length are limited. While findings have indicated a negative association with higher the levels of acculturation on telomere length, population level analyses and subpopulation profiles are scant. Methods: We used latent class analysis (LCA) on the 1999-2002 National Health and Nutrition Examination Survey on adults ≥ 18 years and older with acculturation and mean telomere length data (N=2,292). Acculturation was assessed by length of time in the US and language: used as a child; read and spoken; usually spoken at home; used to think; and used with friends. Telomere length assessed from leukocytes was used as the distal continuous outcome. Covariates included gender/sex (e.g., male and female), US citizenship (i.e., no or yes), less than a High School education (i.e., no or yes), ever-smoker status, and moderate physical activity. To account for the distal continuous outcome and covariates/controls we employed and compared an automatic BCH, manual BCH, and latent class regression approach. Results: Our best fitting model was a five-class solution: low acculturated [33.2% of sample]; (2) partially integrated [18.6%]; (3) integrated [19.4%]; (4) partially assimilated [15.1%]; and (5) assimilated [13.7%]. No significant telomere length differences were found. Acculturation profiles revealed nuanced differences in conditional probabilities with language use despite the length of time spent in the US. While telomere length did vary, there were no significant differences between profiles. Conclusion: Our study was among the first to identify profiles within the US Hispanic/Latinx population by acculturative process and telomere length. Approaches to understand telomere length differences while accounting for covariates/controls do not change the profiles identified but are accounted for in nuanced ways.

LATEBREAKER

Health Disparities

The Association between Racial Salience and COVID-19 Vaccine Hesitancy CHRISTINE JOSEPH* CHRISTINE JOSEPH Sandra Crouse Quinn Karen Kippen Sara Santarossa Ken Resnicow Denise White-Perkins Mei Lu Lamont Jones Christine Cole Johnson

The SARS-CoV-2 experience for Black/African Americans (BAA) in the US consisted of conflicting communication, reports of patients turned away from emergency departments, a seemingly disregard for exposure risks faced by residents of poor communities, and high COVID-19 related mortality. Parallel events accentuating the public health threat of police violence to this group, fueled conspiracy theories and created a “racialized” climate, contributing to current hesitancy on the part of many BAA to receive the SARS-CoV-2 vaccine. Few investigators, however, incorporate “race” into interventions addressing vaccine hesitancy (VH). We assessed the association between race-based concepts and self-report of VH in a convenience sample of BAA in metropolitan Detroit. An incentivized questionnaire was administered online via REDCap to members of community organizations and patient advisers of Henry Ford Health System. Included were several measures of racial salience (relevance of race to self-concept at a specific point in time or situation), as well as items on perceived risk of infection, perceived vaccine safety, conspiracy theories and others. VH was defined as self-report of being “Moderately” or “Very” hesitant to receive the SARS-CoV-2 vaccine. RESULTS: Of the 544 questionnaires completed, 496 (91%) had data sufficient for analysis. Mean age of the sample was 33.3 years and 42% were male. Scales/items measuring Race Consciousness ($p < 0.0001$), Race-related Descriptive Norms ($p < 0.0001$), Race Centrality ($p = 0.0126$), and Racial Fairness ($p = 0.0307$), were all significantly related to VH in a multivariate model, as were concerns around vaccine risks/side effects ($p < 0.0001$) and vaccine safety ($p < 0.0001$). A belief in conspiracy theories ($p < 0.001$) and low confidence in the ability to seek accurate health information ($p = 0.0009$) was also associated with VH. CONCLUSIONS: “Race” has been central to the social climate in which SARS-CoV-2 emerged and flourished in the US. Racial salience could increase effectiveness of interventions addressing VH, by linking to those factors most important to individuals.

LATEBREAKER

Health Disparities

Testing DNA methylation and blood-chemistry measures of biological aging in models of Black-White disparities in healthspan characteristics Gloria Huei-Jong Graf* Gloria Huei-Jong Graf

BACKGROUND. The weathering hypothesis proposes that health disparities are caused in part by social factors that accelerate biological processes of aging. We conducted proof-of-concept testing of eight DNA-methylation and blood-chemistry quantifications of biological aging as mediators of Black-white disparities in healthspan in older adults.

METHODS. We analyzed data from 2016 Health and Retirement Study (HRS), including blood chemistry and DNA methylation data from the Venous Blood Study (n=8231). We quantified biological aging from four DNA methylation “clocks” (Horvath, Hannum, PhenoAge, and GrimAge), a DNA methylation measure of the Pace of Aging (DunedinPoAm), and three blood-chemistry algorithms. We quantified Black-White disparities in healthspan from a battery of physical-function tests, self-reported limitations to activities of daily living (ADLs), and counts of chronic disease diagnoses. We tested if measures of biological aging mediated Black-White disparities in healthspan using Poisson regression models and causal mediation analysis.

RESULTS. DNA methylation and blood-chemistry quantifications of biological aging were moderately correlated (Pearson r range 0.1-0.4). Correlations with blood chemistry measures were higher for the PhenoAge and GrimAge clocks and DunedinPoAm as compared to the Horvath and Hannum clocks. GrimAge, DunedinPoAm and all three blood-chemistry measures were (a) associated with healthspan characteristics (IRR range 1.04-1.23); and (b) showed evidence of more advanced/faster biological aging in Black as compared to White participants (Cohen’s D 0.31-0.48). In mediation analysis, these measures accounted for about 1/3 of Black-White differences in healthspan-related characteristics (range 19-48%).

CONCLUSIONS. Several methods for quantification of biological aging from blood-chemistry and DNA methylation data show promise for application in health-disparities research.

LATEBREAKER

Health Disparities

Broadband access disparities persist across geography, language, and age MK Schiaffino*

MK Schiaffino Bradley Richardson Nishal Mohan Vinit Nalawade

A digital divide in access to the internet persists across both urban and rural geographies affecting the ability of Americans to work, study, or access health services and information effectively and efficiently. Evidence supports tailored interventions and accessible digital information, though little is found on the key underlying structure that makes access possible - broadband availability. The Federal Communications Commission (FCC) has dedicated substantial resources to improving rural access, but access disparities continue. Despite this knowledge and investment, families and individuals in both urban and rural geographies are struggling for minimum broadband access (25 Mbps Download | 3 Mbps Upload) to work from home, educate children remotely, seek telemedicine, or schedule COVID-19 vaccine appointments as we reach a grim anniversary in the pandemic. In our study we demonstrate the fine-scale download/upload speeds at the tract-level in California, one of the most populous and language diverse U.S. states. Fixed broadband deployment data from the FCC were linked to the 2019 American Community Survey using spatial identifiers. We fit mixed models for down/up outcomes with fixed effect for households in the tracts and random effects for LEP to account for variation. We adjusted for proportion of limited English proficient (LEP) in the tract as well as average household size, children under 18 and adults over 60. CA median download speeds were 25Mbps with significant variation at the tract-level. We found an increase in the proportion of LEP persons resulted in a significant drop of 35% in median download speed (Estimate=-.3568, p=.0037). A similar inverse relationship was observed when the proportion of persons over 60 increased, a significant 36.9% decrease in download speeds (p=.0008). Conversely, a significant increase in download speed was observed if the proportion of children under 18 increased. We observed access disparities among LEP and older adults, we need more research to understand academic outcomes.

LATEBREAKER

Health Disparities

Recruitment strategies of minority populations for research on Covid-19 and seasonal influenza vaccination intention in Pima County. Sara Ruiz* Sara Ruiz Kerry Johnson Ava Nidermeyer Maiya Block Mary Kinkade Domo Jordan Cori Cantin Lady Avila Gloria Villa-Barbosa Beatrice Krauss Carlos Perez-Velez Purnima Madhivanan

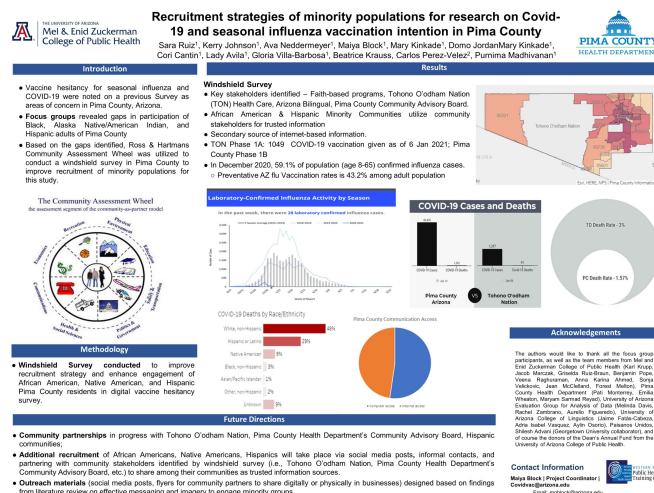
Arizona’s flu vaccine coverage for recommended at-risk groups remains at 42.6%, below the national average. The COVID-19 pandemic has impacted Pima County with 359 new cases as of 2 February, 2021. University of Arizona and Pima County Health Department are investigating recruitment methods of minority communities in Pima County to understand barriers to vaccine acceptance for COVID-19/ Flu vaccinations.

Methods: In Fall 2020, 56 Pima County adult residents participated in 11 focus group discussions (FDGs). Gaps in participation of minority population (African-American, Hispanic, and Native American) led to a Windshield survey to determine best recruitment practices.

Results: The survey highlighted concerns of racial and minority disparities in COVID-19 morbidity and mortality and lack of access to COVID-19 vaccine information via community trusted sources. The survey identified that minority communities are more likely to trust someone within their community. Several key stakeholders were identified to enhance recruitment in minority populations. Best practices for minority populations was to build community partnerships with key stakeholders and local institutions identified to distribute COVID-19 kits and flyers. Second best practice was to utilize digital recruitment methods as on average 91% of households had computer access and 83.1% had access to broadband internet.

Conclusion: COVID-19 has disproportionately impacted minority communities in Pima County. This has led to increased concerns about COVID-19 vaccine access and education resources. Since access to social media and communication platforms are often distributed to minority communities by stakeholders, the research team will engage them in future recruitment efforts.

Late breaking reason: The abstract can be considered a “late breaking” entry due to continued data analysis based on gaps in minority population recruitment in Pima County for COVID-19/Influenza vaccine intention study.



LATEBREAKER

Health Disparities

The Association Between Polycystic Ovary Syndrome and Metabolic Syndrome in the HCHS/SOL study: Common Genetic Architecture Hridya Rao* Hridya Rao Lindsay Fernandez-Rhodes Michelle L. Meyer Martha L. Daviglius Michelle A. Kominiarek Krista M. Perreira Raven Syan Christina Cordero

The relationship between Polycystic Ovary Syndrome (PCOS) and Metabolic Syndrome (MetS), and their common genetic architecture have not been studied in Hispanic/Latino populations, which are disproportionately burdened by cardiovascular disease and have diverse genetic ancestry. We analyzed the association between PCOS and MetS in women from Hispanic Community Health Study/Study of Latinos (HCHS/SOL), a population-based cohort-study. We identified common Single Nucleotide Polymorphisms (SNPs) associated with both conditions. We used information from reproductive and socioeconomic questionnaires, anthropometric and venous lab measurements, and genetic data for our analyses. PCOS was operationalized based on self-report or > 35 day or irregular menstrual cycles (between 20-40 years, not using hormone medications, and not pregnant or breast feeding). Postmenopausal women with self-reported PCOS were also included in the study for interaction analyses. MetS was defined as having ≥ 3 elevated subcomponents of MetS (waist circumference, hypertension, insulin resistance, lipid profile, and triglycerides). There were 793 women with PCOS, 2475 women with MetS, and 4121 were post-menopausal (menopause status was self-reported). We found that two previously-reported PCOS SNPs-rs10993397 (*AOPEP*) and rs9696009 (*DENND1A*) were positively associated with both PCOS & MetS in our population. These two SNPs were used as covariates in our models, along with other demographic and ancestry variables. The odds of having MetS was higher in women with PCOS vs women without PCOS (OR=1.32; 95% CI= 1.04, 1.68). The association did not change with adjustment for menopause status but did after adjusting for body mass index (OR=1.27; 95% CI=0.98, 1.64). Our study replicates the association between PCOS and MetS in Hispanic/Latina women. Future research will include conducting fine mapping analyses to identify SNPs in this diverse population that could be effect modifiers of the association between MetS and PCOS. Understanding the effect modification by SNPs will more precisely inform the genetic differences in metabolic phenotype of women with PCOS.

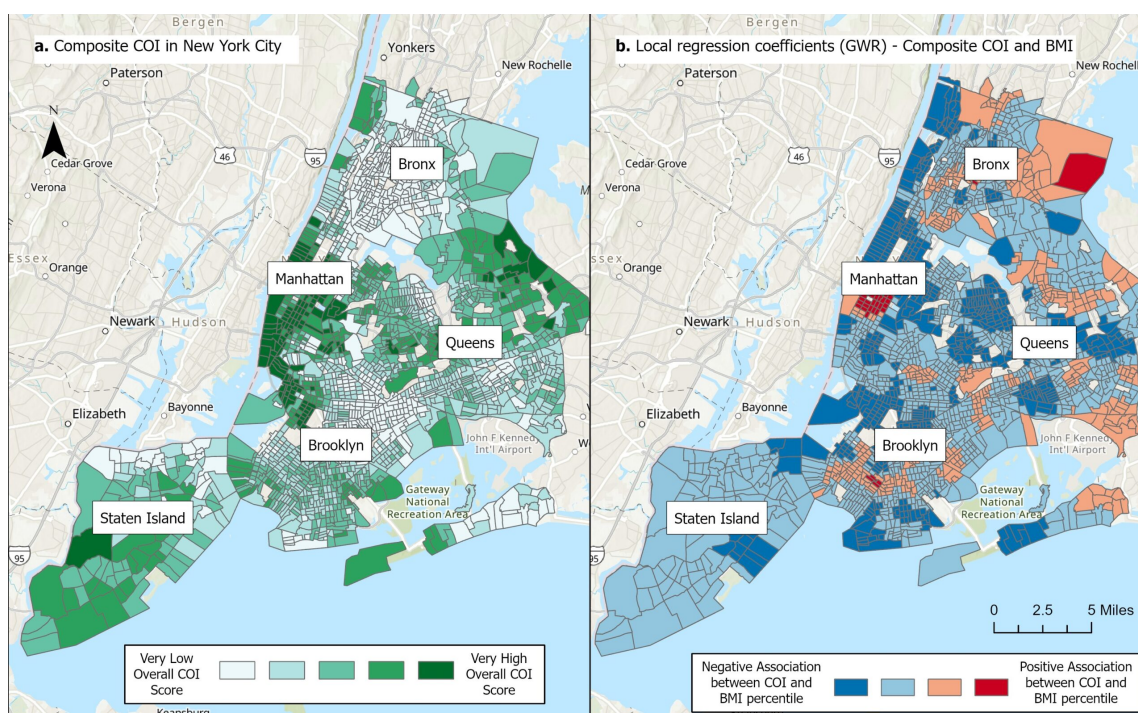
LATEBREAKER

Health Disparities

Novel epidemiologic and geospatial integration methods to examine neighborhood

opportunity and youth fitness associations Amy Zhao* Hiwot Zewdie Amy Y. Zhao Hiwot Zewdie Scott Ogletree Sarah E. Messiah Sarah C. Armstrong Asheley C. Skinner Cody D. Neshteruk J. Aaron Hipp Sophia E. Day Kevin J. Konty Emily M. D'Agostino

Introduction: Less than 25% of youth meet recommended physical activity (PA) guidelines. Low PA corresponds to poor fitness, which predicts health outcomes such as obesity, hypertension, diabetes, and cardiovascular disease. Neighborhood factors may serve as vital modifiable risk factors that foster youth PA and fitness. **Methods:** Data were drawn from the NYC FITNESSGRAM, which include fitness tests and demographic data from New York City public school youth. Two-level generalized liner mixed models, nested by census tract, estimated the association between neighborhood factors (greenspace, healthy food, walkability, and commuting time; drawn from the Child Opportunity Index [COI]) and fitness (body mass index [BMI] percentiles, curl-ups, push-ups, PACER, and sit and reach), overall and across sex. Geographically weighted regression models (GWR) explored spatial variation of the composite COI-fitness association. **Results:** Participants (n=300,000), ages 5-17, were 26% Black and 37% Hispanic. The highest magnitude of effects was observed for associations between greenspace-muscular endurance (curl-ups: β : 1.13, 95% CI: 0.76, 1.50; push-ups: β : 1.53, 95% CI: 1.21, 1.84), walkability-PACER (β : 2.11, 95% CI: 1.72, 2.50), and commuting time-PACER (β : 2.03, 95% CI: 1.87, 2.19). Stratified models showed strengthened COI-fitness associations among girls vs. boys. GWR models showed high spatial variation in the composite COI-BMI association; direction and magnitude of association varied across space. Generally, composite COI was inversely associated with BMI in high opportunity areas (more opportunity, lower BMI), whereas in low opportunity areas, COI was positively associated with BMI (more opportunity, higher BMI; **Figure 1**). **Conclusion:** Neighborhood factors were associated with better fitness, though in systemically deprived areas this relationship may be driven by factors not measured by the COI, highlighting priority areas for population health research.



Medicaid Expansion’s impact on emergency department use by state and payer Fan Zhao*
 Fan Zhao Roch Nianogo

Background States optionally implemented the Affordable Care Act’s Medicaid Expansion Program in 2014; however, studies on the effect of Medicaid Expansion on emergency department (ED) visits have inconsistent results.

Methods We used a recently developed flexible and stronger quasi-experimental design, the generalized synthetic control method (GSCM), a weighting method that is less prone to bias compared to the classic difference-in-difference method in the presence of a violation of the parallel trend assumption, and usually more efficient compared to the original synthetic control method. Quarterly ED data were from the Healthcare Cost Utilization Project (HCUP) Fast Stats, covering 33 states from 2010 to 2017. This is the largest dataset so far and can help depict the longer-term effects of the expansion program. We evaluated and disentangled the individual and pooled impact of the expansion on ED use by states that have adopted the Medicaid Expansion, something that is seldom done in the literature. Outcomes included total ED visits per 1,000 population and share of payer-specific ED visits (Medicaid, private insurance, and uninsured) among adults aged 19 to 64 years. We included race, age, marriage status, education attainment, income, employment status, health insurance status and comorbidity characteristics at the state level as covariates.

Results Total ED visits increased in some expansion states but decreased in others. There was an increase in Medicaid share of ED visits (Average Treatment Effect on the Treated, ATT=13.50, 95%CI 9.29, 17.71; percentage) and a decrease in private insurance and uninsured share (ATT=-5.67, 95%CI -7.29, -4.05; ATT=-8.23, 95%CI -13.43, -3.02; percentage).

Conclusions Medicaid Expansion shifted ED payer mix to Medicaid from private insurance and uninsured ED visits for adults aged 19 to 64 years old. The expansion could lead to a net increase of total ED visits in some expansion states but a decrease in others.

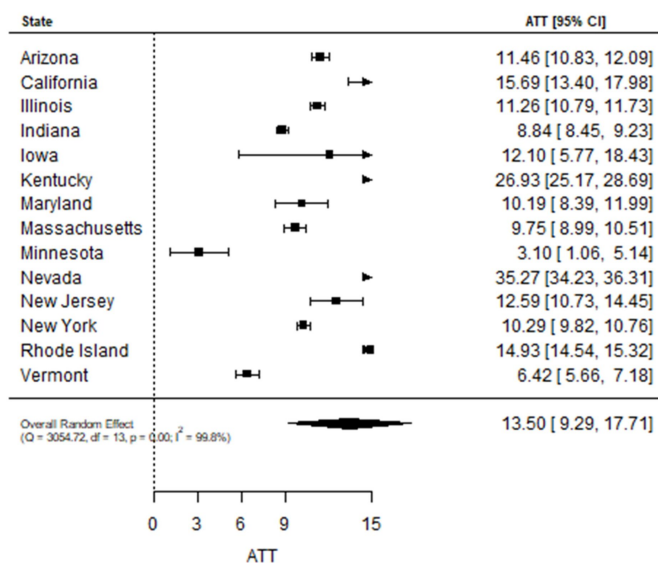


Figure 2 Average treatment effect (ATT) of Medicaid Expansion Program on Medicaid share of ED visits (%) in 14 expansion states, calculated with generalized synthetic control method (GSCM). The overall effect was summarized with a random-effect model.

The joint effects between low back pain and mental health conditions on health care utilization and costs in Ontario, Canada: A population-based cohort study Jessica Wong*
Jessica Wong Pierre Côté Andrea Tricco Tristan Watson Laura Rosella

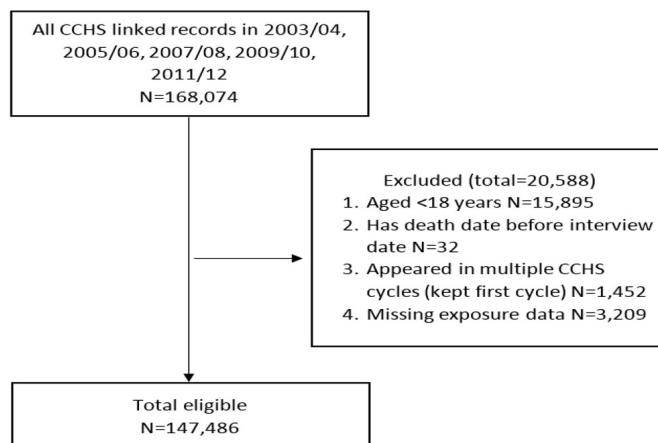
Background: Low back pain (LBP) and mental health conditions are key contributors to disability and health system burden. We assessed joint effects of LBP and mental health conditions on healthcare utilization and costs in a population-based sample of adults in a single-payer health system.

Methods: We included Ontario respondents aged ≥ 18 years of Canadian Community Health Survey (CCHS) from 2003-2012 linked to administrative data up to 2018 ($n=147,486$). Exposures were LBP, mood, and anxiety disorder (self-reported diagnoses), and fair/poor self-rated mental health. We assessed LBP-specific and all-cause utilization and costs with negative binomial and linear (log-transformed) models, adjusted for sociodemographic, health, and behavioural factors. We assessed additive and multiplicative interaction with relative excess risk due to interaction (RERI) and ratio of rate ratios (RR).

Results: Mean age of the cohort was 46 years ($SD=17$) with 51% female. Compared to the respective double unexposed group, the rate ratio of LBP-specific utilization was: a) 1.10 (95% CI 0.98-1.22) for fair/poor mental health, 2.20 (95% CI 2.10-2.30) for LBP, and 2.70 (95% CI 2.39-3.05) for LBP with fair/poor mental health; b) 1.26 (95% CI 1.15-1.38) for mood disorder, 2.19 (95% CI 2.09-2.30) for LBP, and 2.86 (95% CI 2.58-3.16) for LBP with mood disorder; and c) 1.18 (95% CI 1.06-1.31) for anxiety, 2.22 (95% CI 2.12-2.33) for LBP, and 2.47 (95% CI 2.25-2.72) for LBP with anxiety. We found positive additive and multiplicative interaction for LBP and fair/poor mental health ($RERI=0.40$, ratio of $RR=1.12$) and mood disorder ($RERI=0.41$, ratio of $RR=1.04$), but not anxiety for LBP-specific utilization, and no joint effects (no positive additive/multiplicative) for all-cause utilization or costs.

Conclusion: Comorbid LBP with fair/poor mental health or mood disorder had joint effects on LBP-specific healthcare utilization. Results will inform healthcare planning and interventions for priority groups.

Figure. Flow diagram for population-based cohort study of Canadian Community Health Survey (CCHS) Ontario respondents from 2003 to 2012 individually linked to provincial health administrative data up to 2018



Can the adverse childhood experiences (ACEs) checklist be utilized to predict emergency department visits among Canadian children and youth? Asmita Bhattarai* Asmita Bhattarai
Scott Patten

Background:

An extensive literature has shown an association of adverse childhood experiences (ACEs) with various adverse health outcomes, but their ability to predict events, or stratify risks is still less known. The study examined the ability of the ACEs checklist to predict emergency department (ED) visits within the subsequent year among children and youth presenting to mental health clinics with pre-existing mental health issues.

Methods:

The study analyzed linked data (n=6,100); the Regional Access and Information System (2016-2018) database, provided the ACEs items, clinical and demographic information related to children and youth (aged 0-17 years) accessing mental health services within Calgary, and the National Ambulatory Care Reporting System (2016-2019) database provided prospective follow-up data on ED visits. 25% of the data was reserved for validation purposes. Two different least absolute shrinkage and selection operator (LASSO) logistic models, each employing a different method to select tuning parameter lambda (namely Cross-validated and Adaptive) and performing 10-fold cross validation with 100 lambdas; were examined for their predictive performance.

Results:

The adaptive lasso model had a better fit than the cross-validated model. However, the predictive performance was not promising; as evident from poor discrimination (Area Under Receiver Operating Characteristics curve 0.60, sensitivity 37.8%, Positive Predictive Value 49.6%), poor calibration (over-triaged in low-risk and under-triaged in high-risk subgroups), and a poor out-of-sample deviance ratio of -0.04.

Conclusion:

The ACEs checklist did not demonstrate good performance in predicting ED visits within a year of enrolment in outpatient mental health service program and hence is not sufficient for application in clinical practice. Future studies exploring other machine learning approaches and including additional important variables may be able to produce better performing prediction models.

The medical home and use of mental health care in children with special health care needs

Jessica Rast* Jessica Rast Anne Roux Gabrielle Connor Tobechukwu Ezeh Lindsay Shea Paul Shattuck

Introduction. Children with special health care needs (CHSCN) commonly experience mental health concerns, but symptoms are often not identified or treated within primary care. Mental health care is not a primary focus of medically-oriented pediatric primary care, but the medical home has potential to address these concerns more adequately. The objective of this study is to examine the relationship between the medical home and use of mental health services in CHSCN.

Methods. We compared the use of mental health services, expenditures, and psychotropic medications for CHSCN ages 6-17 who did and did not receive care within a medical home using the Medical Expenditure Panel Survey years 2015-2017, a nationally representative survey of health and healthcare in US families. Use of mental health services was compared across CHSCN using multivariable regression.

Results. Forty seven percent of CHSCN received care within a medical home. CHSCN with and without a medical home were similar in office-based mental health visits (21.5% vs 25.1%), average expenditures for visits (\$146 vs \$128), and psychotropic medications (11.4% vs 13.8%). While medical home was associated with increased odds of healthcare satisfaction in multivariable regression (OR 2.93, 95% CI 2.33-3.69), it was not associated with measures of mental health care.

Conclusions. CHSCN with more significant mental health care needs face barriers to care that meets their needs, supports optimal long-term outcomes, improves quality of life, and reduces costs of care that could be addressed by integrated care. However, findings suggest that integration of mental health into the medical home isn't occurring; there was no difference in mental health visits or medication use, which may be markers of comprehensive mental health care. There are monetary and policy impediments to fully integrating mental health care and primary care, and further research into the medical home as a route to integrated care is needed.

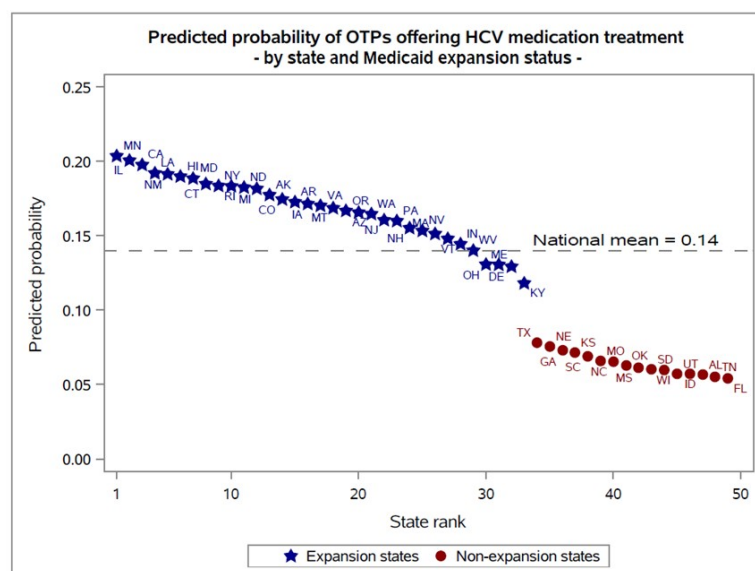
National trends in the integration of hepatitis C virus treatment into opioid treatment programs: Variation by state and Medicaid expansion decisions George Pro* George Pro D. Andrew Tompkins Soraya Azari Nickolas Zaller

The opioid epidemic poses multiple and intersecting public health challenges. Rising injection drug use has been paralleled closely by increasing rates of hepatitis C virus (HCV) infections, often leading to chronic liver disorders. HCV screening in opioid treatment programs (OTPs) is an important step in identifying cases, but connection to HCV treatment and direct-acting antiviral medication (DAA) remains low. State Medicaid expansions have broadly improved health services for vulnerable populations, but little research has addressed the role of expansions in supporting DAA services within OTPs.

We used the 2019 National Survey of Substance Abuse Treatment Services to identify OTPs in the US (n=1,680) that provide HCV screening services (n=1,111). Among this subgroup of OTPs, we used logistic regression to model the association between offering in-house HCV treatment and location in a Medicaid expansion state, adjusted for state HCV and opioid use disorder rates. To visualize differences, we plotted the predicted probability of OTPs offering HCV treatment by state and expansion status.

Nationally, among OTPs that offer HCV screening, 14% (n=162) also offered HCV treatment. Compared to OTPs in non-expansion states, those in expansion states had more than three times higher odds of offering HCV treatment (adjusted odds ratio = 3.05, $p < 0.0001$). The state-level predicted probability of OTPs offering HCV treatment was lower than the national mean in all non-expansion states.

Although Medicaid expansions were positively associated with OTPs offering HCV treatment in addition to screening, overall the probability of offering HCV treatment was low. Co-located treatment likely reduces barriers to DAA uptake following screening, but challenges to implementing HCV treatment in OTPs remain. Interventions that complement Medicaid may help promote healthcare utilization among OTP patients with co-occurring HCV.



Health literacy and self-management behaviors among individuals with type II diabetes

Amanda Ng* Amanda Ng Vivekanand Tatineni Basilica Arockiaraj Natalie Slopen

Control of diabetes—the seventh leading cause of death in the U.S. in 2019—requires that individuals engage in a variety of disease management behaviors. Health literacy may lead to better engagement in care; however, few studies have examined detailed measures of health literacy in relation to diabetes self-management, and most have used small and non-generalizable samples. We investigated associations between health literacy and self-management of type II diabetes among 4,816 diabetic adults from the 2016 Behavioral Risk Factor Surveillance System. We also tested for effect modification by sex, informed by prior research on sex differences in healthcare utilization. The study outcome, self-management behaviors included checking blood glucose, checking feet for sores, going to see a healthcare provider about diabetes, going to a healthcare provider to check A1C levels, ever taking a class on managing diabetes, and retinopathy screening. The outcome was treated as a nominal variable based on the number of behaviors (0-2, 3-4, 5-6). In bivariate multinomial logistic regressions all three self-reported measures of health literacy were associated with increased odds of more self-management behaviors (i.e., proficiency in finding health information, OR: 2.514, 95% CI: 1.455, 4.345; understanding oral health information, OR: 1.941, 95% CI: 1.215, 3.103; and, understanding written health information, OR: 1.604, 95% CI: 1.021, 2.521). Analyses adjusted for demographics and health conditions showed that proficiency in finding health information was associated with self-management among females but not males (OR: 2.398, 95% CI: 1.114, 5.165). This association was attenuated after controlling for healthcare access. These results provide evidence that proficiency in finding health information may be important for self-management of diabetes, especially in females, and that health care access is important to consider for both health literacy and self-management behaviors.

Multinomial Logistic Regression estimating the odds of higher self-management of diabetes predicted by an individual's proficiency in health literacy (BRFSS 2016).*

	Model 1: Bivariate		Model 2: +Demographics		Model 3: +Health Conditions		Model 4: +Health Care Access	
Finding Health Information	OR	95% CI	AOR	95% CI	AOR	95% CI	AOR	95% CI
<i>Among Females (N = 2815)</i>								
0 - 2	ref	1.000	ref	1.000	ref	1.000	ref	1.000
3 - 4	1.253	(0.668, 2.350)	1.422	(0.728, 2.780)	1.078	(0.586, 1.980)	0.961	(0.518, 1.783)
5 - 6	3.935	(1.785, 8.676)	3.423	(1.503, 7.799)	2.398	(1.114, 5.165)	2.081	(0.962, 3.500)
<i>Among Males (N = 1778)</i>								
0 - 2	ref	1.000	ref	1.000	ref	1.000	ref	1.000
3 - 4	1.501	(0.733, 3.071)	1.620	(0.760, 3.452)	1.759	(0.812, 3.813)	1.598	(0.718, 3.555)
5 - 6	1.739	(0.803, 3.769)	1.553	(0.687, 3.509)	1.784	(0.770, 4.137)	1.602	(0.676, 3.793)
Understanding Oral Health Information								
<i>Full Sample (N = 4816)</i>								
0 - 2	ref	1.000	ref	1.000	ref	1.000	ref	1.000
3 - 4	1.071	(0.718, 1.597)	1.084	(0.701, 1.676)	1.023	(0.653, 1.602)	0.874	(0.541, 1.412)
5 - 6	1.941	(1.215, 3.103)	1.684	(1.022, 2.775)	1.645	(0.984, 2.750)	1.553	(0.924, 2.612)
Understanding Written Health Information								
<i>Full Sample (N = 4543)</i>								
0 - 2	ref	1.000	ref	1.000	ref	1.000	ref	1.000
3 - 4	0.804	(0.539, 1.199)	0.823	(0.530, 1.278)	0.742	(0.470, 1.170)	0.694	(0.441, 1.092)
5 - 6	1.604	(1.021, 2.521)	1.372	(0.843, 2.234)	1.203	(0.726, 1.995)	1.116	(0.675, 1.844)

Note: Reported self-management behaviors include: (1) checking blood glucose at least four times per day, (2) checking feet for sores at least once per day, (3) going to see a healthcare provider about diabetes at least twice per year, (4) going to a healthcare provider to check A1C levels once per year, (5) ever taking a class on managing diabetes, and (6) retinopathy screening at least every two years. Survey weights have been applied to account for complex survey design.

Model 1 includes bivariate associations for predicting self-management of diabetes.

Model 2 adds potential demographic confounders (age, sex, education, race/ethnicity).

Model 3 adds comorbid health conditions (obesity (BMI), kidney disease) to Model 2.

Model 4 includes health care access (having insurance, having a regular physician) in addition to Model 3.

*Sample sizes for models vary based on availability of covariate data.

Medicaid Expansion Improved Dental Clinical Outcomes Among Low-income Adults

Hawazin Elani* Hawazin Elani Benjamin Sommers Ichiro Kawachi

Objectives: To examine the effect of the Medicaid expansion under the Affordable Care Act on clinical dental outcomes and utilization of dental services.

Methods: We analyzed data from the National Health and Nutrition Examination Survey from 2009 to 2018. We used a differences-in-differences linear regression to examine the effect of the Medicaid expansion in expansion states relative to control states. We examined changes in the full sample and separately in states that do and do not provide Medicaid adult dental benefits. Clinically examined outcomes included untreated dental caries, filled, and missing teeth. Self-reported outcomes were health coverage, access to dental care in the past year, and affordability of dental care. Our analysis included adults aged 19 to 64 years with income up to 138% below the federal poverty level (n=7,637).

Results: In the full sample, compared with non-expansion states, Medicaid expansion was associated with significant gains in Medicaid coverage (9.0 percentage points, 95% CI 0.9, 17.1), reduction in the uninsured rate (-12.8 percentage points, 95% CI -22.2, -3.4), increase in having a dental visit in the past year (7.3 percentage points, 95% CI 0.7, 13.9), and a decline in the inability to afford dental care (-10.6 percentage points, 95% CI -18.7, -2.5). In expansion states that provide dental benefits, the expansion was associated with reduced rate of untreated dental caries (-18.9 percentage points, 95% CI -32.5, -5.4), reduced number of missing teeth (-1.9 percentage points, 95% CI -3.4, -0.4), and increased number of filled teeth (10.9 percentage points, 95% CI 2.3, 19.5).

Conclusions: Though adult dental benefits remain optional in Medicaid, we find that the combination of Medicaid expansion and coverage of Medicaid dental benefits can improve oral health for low-income adults.

The findings and conclusions in this research are those of the author(s) and do not necessarily represent the views of the Research Data Center, the National Center for Health Statistics, or the Centers for Disease Control and Prevention.

LATEBREAKER

Health Services/Policy

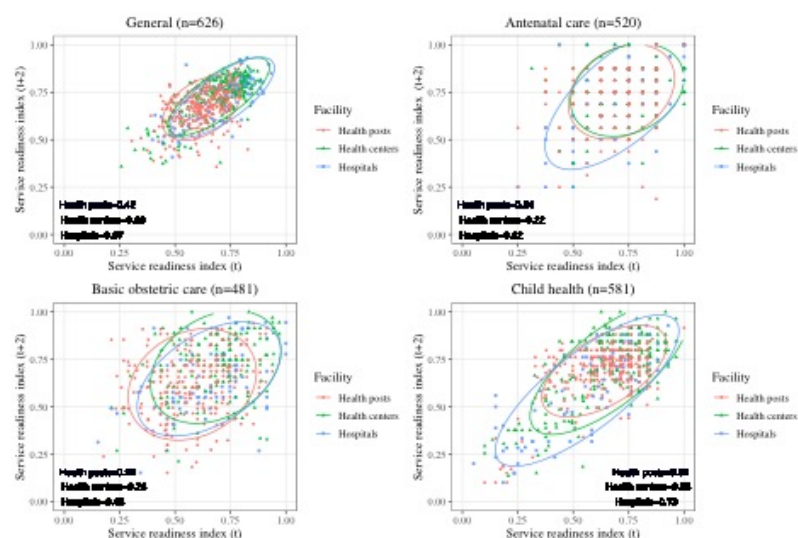
Stability of health care quality for maternal and child services: analysis of the continuous Service Provision Assessment of health facilities in Senegal, 2012 - 2018 Hannah Leslie*
 Hannah Leslie Celestin Hategeka Ibrahim Pape Ndour Kojo Nimako Mamadou Dieng Abdoulaye Diallo Youssoupha Ndiaye

High-quality healthcare is essential to ensuring maternal and newborn survival and to fulfilling the promise of universal health coverage. Measuring quality of care can be cumbersome; for current assessment methods to yield value in research and policymaking, it is important to know their reliability over time.

We use a unique dataset of health facilities in Senegal assessed at a 2-year interval to calculate measures of structural and process quality for antenatal care, basic obstetric care, and curative care for children. We test correlation and interrater reliability of quality measures within facility and for summary scores within 14 sub-national regions. We calculate quality-adjusted coverage measures using the same set of facilities at 2 points in time to quantify the impact of instability on metrics of health system performance.

Over 6 waves of continuous surveys, 2208 assessments were completed in hospitals, health centers, and health posts, including 626 paired assessments of the same facilities 2 years apart. At the facility level, correlation of structural quality was modest, ranging from 38% for inputs to antenatal care to 70% for curative care for children; correlation was highest for hospitals. Correlation of process measures was weaker. Quality measures summarized to sub-national region were not consistent over time. Differences in quality-adjusted coverage metrics using assessment of the same facilities at 2 time points were relatively small, with only 1% difference nationally and up to 5% for sub-national region.

Health facility assessment data in Senegal yielded inconsistent measures of quality over a 2-year span at both the facility and the sub-national level, particularly for processes of care. This suggests such assessments should be used cautiously and for a limited time to benchmark the level of quality or identify better vs. worse facilities. However, instability in quality measures had only modest impact on quality-adjusted coverage metrics.



Regional Differences in Risk of Falls Among Older U.S. Women and Men with HIV in the HIV Infection, Aging, and Immune Function Long-Term Observational Study (HAILO) Mona Abdo* Mona Abdo Xingye (Shirley) Wu Anjali Sharma Katherine Tassiopoulos Todd Brown Susan Koletar Michael Yin Kristine Erlandson

Background: Persons with HIV (PWH) experience a fall frequency in middle-age similar to people aged ≥ 65 without HIV. In a prior study of women with and without HIV from 4 sites, geographic location was a strong predictor of fall risk. The goal of this study was to determine regional variation of falls in a more geographically diverse cohort of older PWH, and examine if physical activity or age modify these associations.

Methods: We analyzed data from PWH enrolled in ACTG A5322 HAILO (HIV Infection, Aging and Immune Function Long-term Observational Study), who reported falls in the 6 months prior to each semiannual study visit, and had ≥ 1 consecutive pair of falls assessments. We examined associations between geographic region of study site [Northeast, Midwest, South (including Puerto Rico), and West] with recurrent falls (≥ 2) over each 12-month period using repeated measures multinomial logistic regression models, and assessed effect modification by adding an interaction term between geographic region and each potential effect modifier.

Results: A total of 788 men and 192 women with median age at entry of 51 (IQR:46-56) contributed to 240 weeks of data. U.S. region included 22% Northeast, 29% Midwest, 20% South, and 28% West. The West had the lowest incidence of falls. In multivariable analyses, compared to Westerners, greater risk for recurrent falls was seen among Midwesterners (OR 2.35[95%CI 1.29,4.28]) and Southerners (2.09[1.09,4.01]) but not among Northeasterners (1.37[0.73,2.57]). Associations between the Midwest and recurrent falls were strongest for those < 50 years (4.4[1.2,15.7]) or 50-59(2.3[1.1,4.8]). Among those with higher physical activity (moderate/vigorous exercise ≥ 3 days/week), Midwesterners had higher odds of recurrent falls (3.5[1.5,8.3]) than Westerners.

Conclusion: Among older PWH, risk of fall varies by geographic region and is modified by age and physical activity. This may identify subgroups of PWH for targeted falls screening/interventions.

External validation of the Data-collection on Adverse Effects of Anti-HIV Drugs (D:A:D) model for predicting cardiovascular events among people living with HIV

Ifedioranma Anikpo* Ifedioranma Anikpo Afiba Manza-A. Agovi Matthew J. Cvitanovich Frank Lonergan Rohit P. Ojha

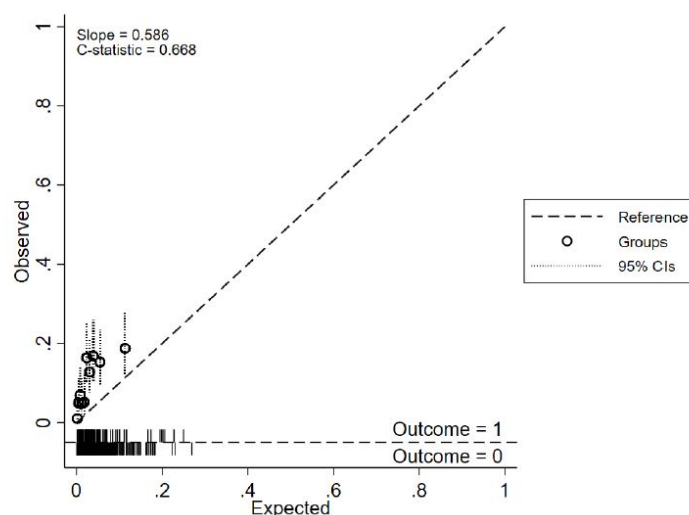
Background: Cardiovascular disease (CVD) risk stratification may inform care decisions for people living with HIV (PLWH). The most prominent CVD risk prediction model for PLWH is the Data-collection on Adverse Effects of Anti-HIV Drugs (D:A:D) model, which was developed using data from HIV cohorts across several countries. The performance of this model in external populations is unknown and should be tested before implementation. We aimed to evaluate the performance of the updated D:A:D model for 3- and 5-year CVD risk in a demographically diverse group of PLWH engaged in HIV care.

Methods: We used data from the HIV Care and Outcomes Registry (HIVCOR), which includes PLWH engaged in care at an urban safety-net health system in North Texas. Eligible individuals had a baseline clinical encounter between January 1, 2013 and December 31, 2014, with follow-up through December 31, 2019. The outcome was a composite variable of CVD events as defined in the D:A:D model. We estimated 3-year and 5-year predicted risks as a function of the prognostic index and baseline survival of the D:A:D model. We used predicted risks to assess model discrimination based on Harrell's C-index, and calibration in the large (expected/observed ratio).

Results: Our evaluable population comprised 1,086 PLWH, of whom 70% were male, 50% were non-Hispanic Black, and median age was 46 years. The C-index of the D:A:D model was 0.67 (95% confidence limits [CL]: 0.62, 0.72). The expected 3-year CVD risk was 1.8%, whereas the observed 3-year CVD risk was 5.9% (expected/observed ratio=0.30, 95% CL: 0.20, 0.44). The expected 5-year CVD risk was 3.1%, whereas the observed 5-year CVD risk was 10.3% (expected/observed ratio=0.30, 95% CL: 0.22, 0.40).

Conclusions: The D:A:D model was poorly calibrated for CVD risk among PLWH engaged in HIV care at an urban safety-net health system, which may be related to differences in case-mix and baseline CVD risk between our population and the D:A:D population.

Figure, Calibration plot for 5-year cardiovascular disease (CVD) risk for people living with HIV based on the D:A:D model



A Comparison of Two Methods of Analysis for National HIV Behavioral Surveillance Survey Data Collected through Respondent Driven Sampling

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Meredith R. Brantley Peter F. Rebeiro Bryan E. Shepherd Samantha A. Mathieson Jack Marr April C. Pettit

Introduction: Mistrust of research among people at high risk of HIV acquisition has led to study recruitment difficulties. These may be overcome by respondent driven sampling (RDS), where participants recruit others within their own networks. Generalized estimating equations (GEE) and RDS analysis tool (RDSAT) weighting can account for lack of independence between subjects due to RDS, but results from these methods have not been compared. Using RDS data from the National HIV Behavioral Surveillance (NHBS), we compared GEE and RDSAT weighted model results assessing the relationship between intimate partner violence (IPV) and psychological distress (PD).

Methods: NHBS surveyed cisgender heterosexual adults at high risk for HIV acquisition in Memphis, Tennessee in 2016. Participants self-reported IPV (physical or sexual violence) and PD (measured by the Kessler Scale). We used modified Poisson regression to compare results found using GEE and RDSAT weighting. These methods were used to estimate adjusted risk ratios (aRR) and 95% confidence intervals (CI) of PD by IPV status, controlling for gender, age, housing, education, and marital status.

Results: Among 543 participants, the median age was 34 years (interquartile range: 25, 47), 303 (55.8%) were female, and 528 (97.2%) were Black non-Hispanic. IPV was reported by 69 (12.7%) individuals, and PD by 63 (11.6%) individuals. The GEE model results (aRR=3.89; 95% CI: 2.44-6.20) and RDSAT weighted results (aRR=4.33; 95% CI: 2.29-8.18) both demonstrated a higher risk of PD among those who experienced IPV. RDSAT weighting led to a wider 95% CI which included the upper and lower 95% CI bounds of the GEE model.

Conclusions: While PD risk estimates using GEE and RDSAT weighing in this study sample were similar, GEE provided a narrower 95% CI demonstrating more precise population estimates. Future work will compare the stability and accuracy of these estimates and their estimated variance using the bootstrap and data simulations.

Are male couples reducing their HIV risk behaviors during the COVID-19 pandemic? Alison Walsh* Alison Walsh Rob Stepheson

There is evidence the 2020 COVID19 pandemic has altered intimate relationships. Sexual agreements (e.g., monogamy, non-monogamy) are an important element of HIV prevention for many partnered gay, bisexual, and other men who have sex with men (GBMSM); changing sexual agreements and behavior in this population may also impact HIV risk. This study described self-reported sexual behavior and agreements during and prior to the COVID19 pandemic among a sample of 215 GBMSM in long-term relationship (>6 months) in the United States. Participants were recruited from previous GBMSM HIV testing/prevention studies and were surveyed July-September 2020 on their individual and relationship characteristics and behaviors. Most participants did not report changes in their sexual relationships. 15% of respondents developed, ended, or changed their agreement during the pandemic. Agreements and outside partnerships appear to have shifted slightly towards monogamy (monogamous: 23% pre-pandemic vs. 31% during pandemic; non-monogamous: 45% pre-pandemic vs. 38% during pandemic). The pandemic factored into 85% of reported changes (N=28), primarily in response to social distancing. Reported reasons for changing agreements were: reducing COVID19 risk (93%), lower opportunities to see other partners (36%), and/or increased commitment to primary relationship (18%). Moreover, regardless of reported agreement, fewer individuals reported outside partners during the pandemic, and those that did have outside partners during the pandemic reported fewer numbers of partners (mean \pm standard deviation number of partners: 2.5 ± 2.0 during pandemic (N=53) vs. 3.9 ± 4.0 pre-pandemic (N=73)), regardless of their sexual agreement. More research is needed to investigate shifting behavior and associated HIV risk in coupled GBMSM in order to adapt HIV services during the pandemic.

Sexual Networks to Inform Allocation of Biomedical HIV Prevention Interventions M. Kumi Smith* M. Kumi Smith Matthew Graham Katherine Qiuying Zhu Guanghua Lan Zhiyong Shen

Background: Mixing matrices quantify how people with similar or different characteristics make contact with each other, creating potential for disease transmission. Information about sexual contact patterns in populations with high HIV incidence can greatly inform optimal allocation of effective yet costly interventions such as preexposure prophylaxis (PrEP) or treatment as prevention (TasP).

Methods: Egocentric network data was collected from men who have sex with men (MSM) who were HIV negative or unaware of their status recruited in a high prevalence setting in southern China. Matrices characterizing mixing by age and age-specific HIV prevalence were combined with published estimates of the probability of HIV transmission per male-male partnership to estimate expected number of new infections in each age combination. Confidence intervals were bootstrapped using resampling of partnerships over 1000 iterations.

Results: 832 MSM were retained for analysis after removing those reporting no partners (N=160; 10%) or who did not response to network questions due to study implementation issues (N=1301; 19%). We found evidence of assortative mixing by age, particularly in younger MS. 20-24 year olds were identified as the subgroup most vulnerable to acquiring HIV, making them strong candidates for PrEP which reduces susceptibility to HIV. Likewise 25-29 year olds had the highest HIV transmission rate, making them likely targets for TasP which reduces infectiousness in infected people.

Discussion: Collection and analysis of contact patterns in MSM is feasible and can greatly inform our understanding of infectious disease dynamics. It can also guide targeting of epidemiologically appropriate interventions such as PrEP and TasP. Findings provide much needed empirical data to inform key parameters used in mathematical models of HIV transmission in MSM, particularly in non-Western settings.

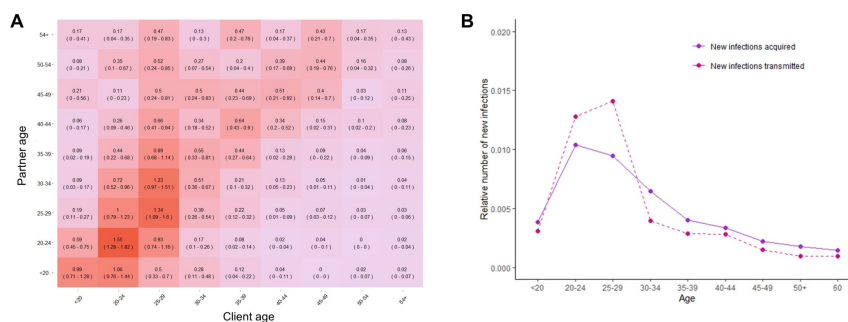


Figure 1, Panel A: Age-dependent mixing. Values are ratios of expected numbers of partnerships between MSM of ages i and j versus the observed patterns versus the number of partnerships under the proportionate mixing assumption. Lighter shades indicate ratio values whose 95% bootstrapped confidence intervals include the null value. Figure 1, Panel B: Plots of the number of new infections expected given baseline age-specific HIV prevalence and age-dependent mixing patterns. The solid line indicates the expected number of newly acquired infections; the dotted line indicates the expected number of transmitted infections.

LATEBREAKER

HIV / STI

Individual and neighborhood predictors of sustained HIV viral suppression: Analysis of health records from an academic health system in Chicago Adovich S. Rivera* Adovich Rivera Lauren Beach Donald Lloyd-Jones Juned Siddique Matthew J. Feinstein

Background: Sustained viral suppression is necessary to ensure the health of people with HIV. While reports show that more people with HIV are achieving viral suppression, routine measures of suppression often do not consider long-term trends, making it difficult to identify variables associated with sustained suppression. To overcome this, we used a data-driven approach to identify people with HIV who achieved sustained suppression.

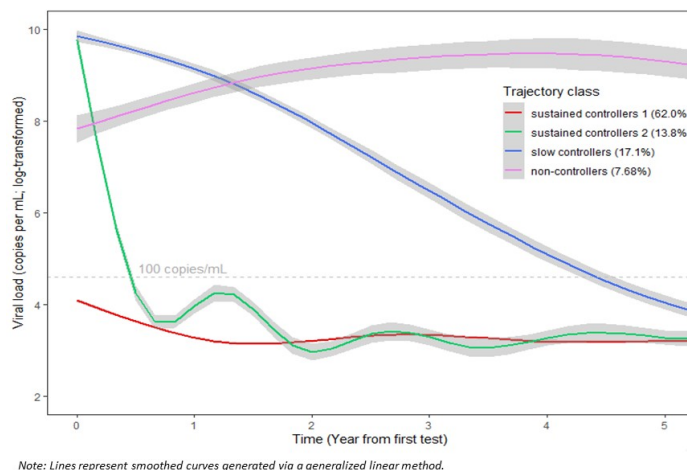
Methods: We analyzed data of people with HIV seen at a large training hospital in Chicago from 2004-2018 with ≥ 3 viral loads. We used latent trajectory analysis (LTA) to classify people with HIV into groups based on the trajectory of their viral loads. We then used multinomial regression to test the association of individual and neighborhood variables with the patterns. Neighborhood variables were derived from the Social Deprivation Index (SDI).

Results: LTA showed four patterns (n=2397): sustained controllers 1 (62%), sustained controllers 2 (13%), slow controllers (17%), and non-controllers (8%) (Figure 1). While, on average, 18% of viral loads for a non-controller was ≥ 100 copies, 92% of viral loads for a sustained controller 1 was ≤ 100 copies. Sustained controllers achieved viral suppression (≤ 100 copies) in less than a year on average, whereas the mean time to viral suppression for slow controllers was five years.

Multinomial regression focused on individuals living in Chicago (n=1631) demonstrated that individuals who have younger age, identify as Black, and/or have first visits after 2012 were more likely to be slow or non-controllers than sustained controllers 1. People who had diabetes or resided in neighborhoods with higher Black populations were more likely to be non-controllers. The composite SDI was not associated with trajectory patterns.

Conclusion: Using LTA, we identified unique trajectories of HIV viral suppression that were associated with different concomitant comorbidities, race-ethnicity, and neighborhood racial composition.

Figure 1. Latent Trajectories of People with HIV seen at an Academic center in Chicago



LATEBREAKER

HIV / STI

Optimizing identification of people living with hiv from electronic medical records Yiyang Liu* Yiyang Liu Khairul A Siddiqi Robert L Cook Patrick J Squires Jiang Bian Elizabeth A Shenkman Mattia Prosperi

Electronic health record (EHR)-based identification of people with HIV (PWH) can complement existing HIV cohorts and be a useful surrogate for regions that are not well represented in HIV studies to provide real-world evidence to assess gaps in the HIV care continuum and comorbidity burdens. Using a large EHR database (the OneFlorida consortium), we developed an improved computable phenotype algorithm to identify a virtual cohort of PLW. We assessed the potential of this virtual cohort in examining longitudinal trajectories of engagement through routine care and gaps in HIV care continuum.

OneFlorida covers over 15 million patients across all 67 counties in Florida. Our computable phenotype sequentially examined information from multiple EHR domains, including Diagnosis, Condition, Laboratory, Prescription, and Encounter. To identify a confirmed HIV case, the algorithm requires the patient to have at least one diagnosis code for HIV and meet one of the following inclusion criteria: had at least one positive HIV lab, have been prescribed with HIV indicated medications, or had 3+ HIV-related encounters.

Among the 15+ million patients from OneFlorida, we identified 60,673 PWH. Among them, 7.8% met all four inclusion criteria, 72.6% met the 3+ HIV encounters criteria plus having HIV diagnosis code, and 10.18% met all criteria except for having positive labs. Most of the sample (58.0%) were males, half were Black, and the mean age was 42.7 years. Patients' average follow-up period (the duration between the first and last encounter in the EHRs) for the virtual cohort was 1,692 days (~4.6 years). The median number of all encounters and HIV-related encounters were 80 and 21, respectively.

In conclusion, our computational phenotyping approach in conjunction with statewide EHR integration can be used to complement existing surveillance, standing limitations on missing data and selection bias (e.g. people who are enrolled in certain healthcare providers).

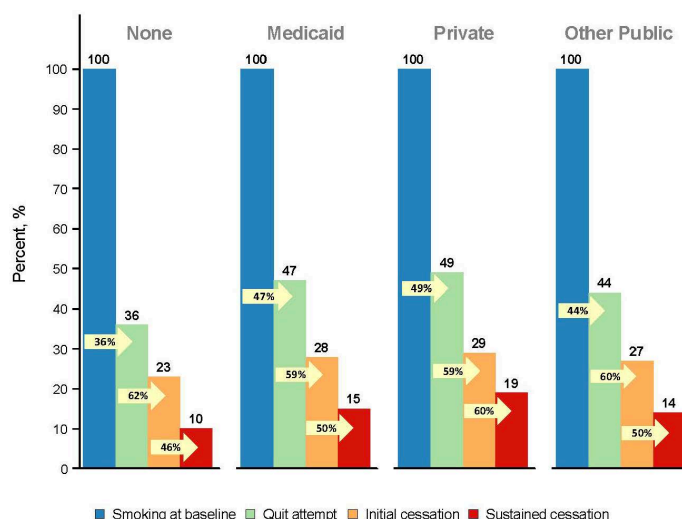
LATEBREAKER

HIV / STI

A new smoking cessation “cascade” among women with or at risk for HIV infection in the United States Tiffany L. Breger* Tiffany Breger Daniel Westreich Andrew Edmonds Jessie Edwards Lauren Zalla Stephen Cole Catalina Ramirez Igho Ofotokun Seble Kassaye Todd Brown Deborah Konkle-Parker Deborah Jones Weiss Gypsyamber D’Souza Mardge Cohen Phyllis Tien Tonya Taylor Kathryn Anastos Adaora Adimora

To decrease smoking, it is critical to understand points at which individuals face the greatest barriers to cessation. We define a smoking cessation cascade among participants in the Women’s Interagency HIV Study and examine differences along the cascade, stratifying by clinical and sociodemographic factors. We followed 1165 women smokers with or at risk for HIV infection from their first study visit in 2014 or 2015 until 1) an attempt to quit smoking within approximately three years of follow-up, 2) initial cessation (i.e., no relapse within approximately six months of quitting), and 3) sustained cessation (i.e., no relapse within approximately 12 months of quitting). Using the Aalen-Johansen estimator, we estimated the cumulative probability of achieving each step, accounting for the competing risk of death. We also estimated conditional probabilities of transitioning to the next cascade step among those who achieved the prior step. Less than half of women attempted to quit smoking, a quarter achieved initial cessation, and 14% achieved sustained cessation with no differences in the cascade by HIV status. Women under 40 years were most likely to achieve each step of the cascade and had a higher probability of transitioning from quitting to initial cessation (0.71; 95% CI: 0.58, 0.83) than women aged 40-50 (0.51; 95% CI: 0.38, 0.63) and over 50 (0.56; 95% CI: 0.44, 0.68). Women reporting at least some college education were more likely to achieve each step compared to those reporting no college education. Outcomes did not differ by race. Only 36% of uninsured women attempted to quit compared to 47% with Medicaid and 49% with private insurance (Figure). However, probabilities of achieving initial cessation among those who attempted to quit were similar for all insurance categories. To decrease smoking among women with or at risk for HIV infection in the United States, targeted, multi-stage interventions are needed to address multiple shortfalls along this cascade.

Smoking cessation cascade by type of health insurance among 1165 smokers participating in the Women’s Interagency HIV Study between 2014 and 2019.



LATEBREAKER

HIV / STI

The Effects of Non-Hazardous Alcohol Use on Viral Load Among HIV+ Stimulant-Using MSM Chika C. Chuku* Chika Chuku

Background: Stimulants use has been linked with increases in HIV diagnoses, making sexual minority groups especially vulnerable. ARTEMIS was a multi-component intervention aimed at improving positive affect, and also achieved significant reductions in viral load (VL) among HIV-positive stimulants-using MSM (SUMSM). **Objective:** The current analysis aims to examine the association between alcohol and stimulants use, stress, depression, and detectable VL. **Methods:** Data was obtained from a sample of 110 HIV+ SUMSM who provided self-report measures, urine samples for toxicology screening, and peripheral venous blood samples to measure CD4+ count and VL. The current analysis included race, age, depression, unprotected insertive anal sex while, alcohol consumption, frequency of stimulant use, minority stress, and detectable VL. Simple and multiple logistic regressions were performed using SAS software v9.4. **Results:** Stimulant use within the past 30 days ($B = 0.07$, $SE = 0.03$, $p = 0.03$) and non-hazardous drinking ($B = 1.14$, $SE = 5.94$, $p = 0.010$) were significantly associated with detectable viral load. Similarly, non-hazardous drinking was significantly associated with depression ($B = -0.92$, $SE = 0.42$, $p = 0.03$). Minority stress was significantly associated with depression ($B = 0.16$, $SE = 0.08$, $p = 0.04$). **Conclusion:** The findings support existing research that minority stress can contribute to depression. Additionally, the findings suggest that more recent stimulant use may impact an individual's HIV care regimen, leading to reduced VL suppression. The association between non-hazardous drinking and VL suggest that alcohol use may also impact an individual's HIV care regimen. Conversely, non-hazardous drinking was associated with a decrease in depression, which implies that depression and detectable VL are not necessarily related. These findings may inform future studies interested in examining HIV disease management among stimulant-using HIV+ MSM.

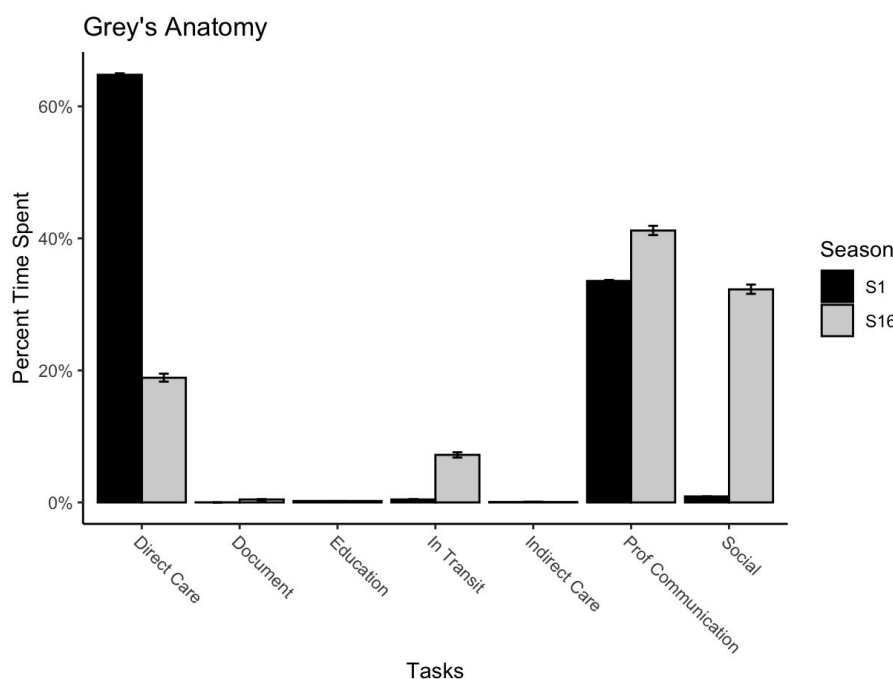
Charting is Never Exciting: Measuring Physician Time Use in Medical Dramas Katelin C. Jackson* Katelin Jackson Kayla A. Miller Samantha M. Hill Laila A. Reimanis Eric T. Lofgren

Background: Activity patterns of healthcare workers can affect hospitals' patient-care mission and patient outcomes. We can assess time use with direct observation, recording what activities were performed, and how often. However, these observations are time-intensive and require direct contact, which is impossible due to COVID-19. We explore the use of medical dramas as a means of training observers when patient contact is infeasible and assessing how the medical profession is portrayed in media.

Methods: Student observers used the WOMBAT (Work Observation Method By Activity Timing) platform to record the time use patterns of medical residents and physicians, recording what they were doing, if they were interrupted, etc. The main characters of the first and latest season of Grey's Anatomy were chosen for observation.

Results: We found higher proportions of time spent (64.8%, 95% CI [64.6, 65.0]) on medical tasks in Season 1. Compared to the latest season, which revealed little time spent on medical tasks but had higher proportions of time spent on social tasks. Professional Communication varied slightly but was the most consistent medical task completed for the seasons compared to other activities. Compared to existing observations, both seasons dramatically overrepresent the time physicians spend directly caring for patients and underrepresent their administrative duties. Critically, for a training tool, interrater reliability was excellent.

Conclusion: These findings suggest that medical dramas can serve as training tools in circumstances where clinical observation is impossible. There are notable inaccuracies in physician time use and considerable inter-season heterogeneity that should be considered if particular aspects of time use are of specific interest.



Association Between Sampling Method and Covid-19 Test Positivity Among Undergraduate Students: Testing Friendship Paradox in Covid-19 Network of Transmission Sina Kianersi*

Sina Kianersi Yong-Yeol Ahn Molly Rosenberg

Introduction: Coronavirus Disease 2019 (COVID-19) has largely affected colleges. Identifying students with higher probability of COVID-19 positivity could enhance mitigation and prevention efforts. Acquaintance sampling, a technique that samples the friends or acquaintances of randomly sampled individuals, could potentially identify students who are more likely to get COVID-19. It has been shown that those sampled in this way are at higher risk for some infectious diseases, due to a network phenomenon called 'the friendship paradox'. Yet, it is unclear whether the technique would be effective for COVID-19, where preventive measures such as social distancing disrupts social contact structure. The aim of the current study was to implement and test the method of acquaintance sampling in detecting students with higher probability of COVID-19 positivity.

Methods: In November 2020, we conducted a cross sectional study among randomly sampled Indiana University undergraduates. In an online survey, the randomly sampled participants nominated a friend, and reported their own and their nominated friend's COVID-19 status.

Results: Overall, 879 students were randomly sampled and participated in this study. Nominated friends were about 1.64 (95% CI: 1.33, 2.00) times more likely to have ever been infected with COVID-19, compared to randomly sampled students.

Conclusions: Our study suggests that acquaintance sampling is effective for identifying members of networks with higher COVID-19 risk. These findings could be useful for university policy makers when developing mitigation testing programs and intervention strategies against COVID-19 spread.

COVID-19 risk factors and symptom presentation in The Arizona CoVHORT Sana Khan* Sana Khan Leslie Farland Kristen Pogreba-Brown Kacey Ernst Yann Klimentidis Pamela Garcia-Filion Kelly Heslin Erika Austhof Collin Catalfamo Elizabeth Jacobs

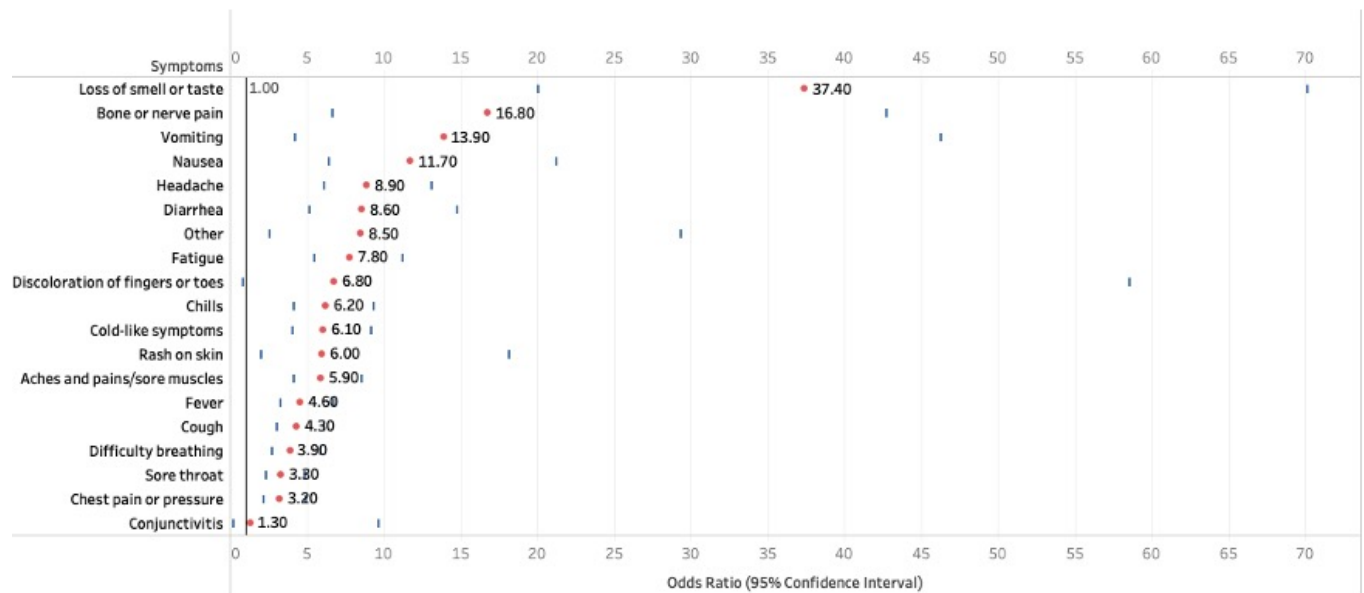
Background: The Arizona CoVHORT study is a population-based prospective cohort investigating acute and long-term risk factors of COVID-19 across the diverse Arizona population. Few studies have examined the symptom profile of non-hospitalized patients and characterized factors associated with different presentations. Identifying patterns related to symptom profiles in the general population helps identify possible triggers for COVID-19 testing.

Methods: Recruitment for this study was conducted through partnerships with the Arizona Department of Health Services and county health departments as well as phased mailing of recruitment postcards to a random sample of residences. Surveys were available in English and Spanish and all Arizona residents were eligible to participate. Odds ratios compared reported symptoms between laboratory-confirmed COVID-19 positive and negative participants.

Results: As of November 2020, CoVHORT had enrolled a total of 1,527 participants; of these, 16.6% had COVID-19, 22.2% had a negative test result, and 61.7% had not been tested. The majority of participants were female (62.9%) and White (86.5%), with 18.5% reporting Hispanic ethnicity, and with a mean (SD) age of 47.8 years (1.7). A greater percentage of COVID-19 positive participants reported a co-morbid condition (37.8%) as compared to negative (26.6%) and untested participants (25.5%). Among positive participants (n=254), 85.0% reported the presence of 1 or more symptoms, while the remaining 15% were asymptomatic. The most commonly reported first symptom among positive participants was sore throat (19.0%) and headache (14.8%). COVID-19 positive participants had greater odds of specific symptoms compared to those who tested negative (Figure 1).

Conclusion: Symptom presentation varied by COVID-19 status and may help inform the general population when testing is limited. Continued recruitment of a diverse sample is necessary to evaluate heterogeneity of the COVID-19 disease course.

Symptom Presentation in COVID-19 positive participants as compared to negative participants in The Arizona CoVHORT (n=1527)



Proteomics analysis suggests suppression of IL-15 among individuals at greater genetic risk of COVID-19-related respiratory failure: the Atherosclerosis Risk in Communities Study (ARIC) Brian T. Steffen* Brian Steffen James S. Pankow Pamela L. Lutsey Ryan T. Demmer Faye L. Norby Logan T. Cowan Weihua Guan Josef Coresh Weihong Tang

Title: Proteomics analysis suggests suppression of IL-15 among individuals at greater genetic risk of COVID-19-related respiratory failure: the Atherosclerosis Risk in Communities Study (ARIC)

Introduction: A genome-wide association study recently showed that two variants were independently associated with risk of developing COVID-19-related respiratory failure—rs657152, proximal to *ABO* on chromosome 9, and rs11385942, proximal to *SLC6A20*, *LZTFL1*, *CCR9*, *FYCO1*, *CXCR6*, *XCR1* on chromosome 3. Identification of these variants provides an opportunity to elucidate the underlying mechanisms of genetic risk of COVID-19 respiratory failure. Using an untargeted proteomics approach in a sample of 8,912 ARIC participants, we examined associations of these risk variants with circulating protein concentrations and then identified pathways that may be biologically relevant to COVID-19 severity.

Hypothesis: Risk variants related to severe COVID-19 were hypothesized to be associated with plasma proteins involved in the acute immune response.

Methods: DNA from whole blood was genotyped using the Affymetrix Genome-Wide Human SNP array 6.0. EDTA-plasma was collected at visit 3 (1993-95) and analyzed using an aptamer-based capture array of 4,870 protein analytes. Protein values that were 6 standard deviations from their respective means were excluded. We used race-specific multiple linear regression analysis to evaluate associations between each risk variant and log base 2 transformed protein levels, with adjustment for age, sex, estimated glomerular filtration rate, field center, and ten principal components of ancestry. A Bonferroni correction was applied to account for the numbers of proteins tested in white participants ($p \leq 5.13 \times 10^{-6}$; $N=7,241$). Identified associations were then replicated in Black participants ($N=1,671$). Ingenuity pathway analyses were conducted.

Results: This ARIC sample was a mean 60 (6) years old and 55% female. Among white participants, rs11385942 was significantly associated with teratocarcinoma-derived growth factor-1 (TDGF-1). This finding was not replicated in Black participants. The *ABO* variant rs657152 was associated with 85 proteins, many of which are directly or peripherally involved in the acute phase response, inflammation, and coagulation. Of these 85, 24 associations were replicated in Black participants ($p \leq 1.9 \times 10^{-3}$). Pathway analyses suggested suppressions of IL-15 production, signal transducer and activator of transcription 3 (STAT3) signaling, and NF- κ B signaling based on rs657152-protein associations.

Conclusions: Carriers of the *ABO* risk variant may have suppressed IL-15 production and impaired STAT3 and NF- κ B signaling, which may have implications for COVID-19 progression, severity, and efficacious pharmacotherapies. Replication in other cohorts and in COVID-19 cases are warranted to further characterize the relevance of these proteins to severe COVID-19 respiratory failure.

Patient delay and unsuccessful TB treatment outcomes in the Lake Victoria region of East Africa Grace E. Mulholland* Grace Mulholland Milissa Markiewicz Jessie K. Edwards

Tuberculosis (TB) is among the ten leading causes of death worldwide and is the leading cause of death from a single infectious agent. Timely diagnosis and treatment of TB disease has epidemiological and clinical benefits. Many countries with high TB incidence rely heavily on passive case finding; in such settings, understanding how often and why patients do not seek care sooner can inform interventions to reduce time to treatment initiation.

In 2019, we conducted an innovative two-stage study in which data were abstracted from TB registers for a cohort comprising all 776 adult patients initiating TB treatment over 6 months at 12 public sector health facilities in the Lake Victoria region of Kenya, Tanzania, and Uganda. We assessed patient delay, which was defined as seeking care more than 6 weeks beyond TB symptom onset, among a non-selected consecutive sample of 301 cohort members during routine care visits. At study end, we ascertained patient outcomes, where available, for the full cohort. We describe the cohort and survey sample, assess correlates of patient delay, and report reasons for delay. To reduce selection bias and improve precision, we use fractional imputation with variables abstracted from TB registers for the full cohort to impute values for patient delay among cohort members who did not participate in the survey. Using survival methods, we model the risk of unsuccessful TB treatment outcome (defined as treatment failure, death, or loss to follow-up) over the course of TB treatment.

Among survey participants, 54% reported seeking care more than 6 weeks after onset of TB symptoms. In the full cohort, 103 unfavorable TB treatment outcomes were recorded. The risks of unsuccessful TB treatment outcome at 100 and 200 days since treatment initiation were 0.09 and 0.16, respectively, among those who sought care within 6 weeks, and 0.10 and 0.15, respectively, among those sought care later.

Characteristics and outcomes of pregnant women with SARS-CoV-2 infection and other severe acute respiratory infections (SARI) in Brazil from January to November 2020. Lisiane Leal* Lisiane Leal Joanna Merckx Deshayne B. Fell Ricardo Kuchenbecker Angelica E. Miranda Wanderson K. de Oliveira Robert William Platt Livia Antunes Mariângela F. Silveira Natália Bordin Barbieri

Background: Knowledge about COVID-19 in pregnancy is limited, and evidence on the impact of the infection during pregnancy and postpartum is still emerging.

Aim: To analyze maternal morbidity and mortality due to severe acute respiratory infections (SARI), including COVID-19, in Brazil.

Methods: This population-based study used surveillance data from the SIVEP-Gripe (*Sistema de Informação de Vigilância Epidemiológica da Gripe*). Currently and recently pregnant women aged 10-49 years hospitalized for severe acute respiratory infection (SARI) from January through November, 2020 were selected. SARI cases were grouped into: COVID-19; influenza or other detected agent SARI; and SARI of unknown etiology. Characteristics, symptoms and outcomes were presented by SARI type and region. We used descriptive statistics to profile the study population. Binomial proportion and 95% confidence intervals (95% CI) for outcomes were obtained using the Clopper-Pearson method.

Results: Of 945,460 hospitalized SARI cases in the SIVEP-Gripe, we selected 11,074 women aged 10-49 who were pregnant (7,964) or recently pregnant (3,110). COVID-19 was confirmed in 49.4% cases; 1.7% had influenza or another etiological agent; and 48.9% had SARI of unknown etiology. The *pardo* race/ethnic group accounted for 50% of SARI cases. Hypertension/Other cardiovascular diseases, chronic respiratory diseases, diabetes, and obesity were the most common comorbidities. A total of 362 women with COVID-19 (6.6%; 95%CI 6.0-7.3) died. Mortality was 4.7% (2.2-8.8) among influenza patients, and 3.3% (2.9-3.8) among those with SARI of unknown etiology. The South-East, Northeast and North regions recorded the highest frequencies of mortality among COVID-19 patients.

Conclusion: Mortality among pregnant and recently pregnant women with SARIs was elevated among those with COVID-19, particularly in regions where maternal mortality is already high.

Risk Factors for Severe COVID-19 during Pregnancy Camille Dollinger* Sonia Hernandez-Diaz
Louisa Hills Smith Diego Wyszynski

Background: The risk for severe COVID-19 in pregnant women with SARS-CoV-2 infection is at least as high as in non-pregnant women. Comorbidities can further increase that risk. We describe characteristics associated with a severe clinical course of COVID-19 during pregnancy.

Methods: Since June 2020, the International Registry of Coronavirus Exposure in Pregnancy (IRCEP) follows up pregnant women 18 years of age and older tested for COVID-19 or clinically diagnosed with COVID-19. Participants self-enroll and administer online questionnaires on, among others, demographics, COVID-19 diagnosis, and clinical course. We classified participants as having mild, moderate, or severe COVID-19 according to their symptoms and compared their demographic and clinical characteristics.

Results: Of 6976 enrolled pregnant participants with COVID-19, 1438 (20.6%) were asymptomatic, 2249 (32.2%) were mild, 3135 (44.9%) were moderate, and 154 (2.2%) were severe. Among the moderate cases, 8.5% were hospitalized for an average of 5 days. Among the severe cases, 73.0% were hospitalized for an average of 9 days and 71.0% required ECMO. The highest proportion of moderate and severe cases were reported from Brazil (22.5%). Moderate and severe cases had higher average pre-pregnancy BMI (28.9 and 25.9 kg/m², respectively) compared with mild cases (24.5 kg/m²). Black women had a higher frequency of moderate or severe cases (54.3%) than Hispanic (50.1 %) or White (48.1%) women. The frequency of moderate or severe COVID-19 was higher in smokers (47.9%), with underlying hypertension (53.5%), diabetes (43.3%), asthma (59.6%), and thyroid disease (45.1%). Maternal age was not associated with the clinical course of COVID-19.

Conclusion: Certain demographics or health metrics are associated with increased risk of severe COVID-19 disease in pregnant women. This subpopulation could benefit from closer clinical observation.

Temporal changes in the serial interval distributions of COVID-19 in Hong Kong Wey Wen Lim* Benjamin Cowling Ben Cowling Amy Yeung Dillon Adam Mario Martin-Sanchez Eric Lau Peng Wu Sheikh Taslim Ali

Serial intervals represent the time delay between illness onset in successive cases in chains of transmission. The serial interval distribution is often used as a proxy for the generation time distribution, representing the time delay between successive infections in transmission chains, since infections are generally unobservable while illness onset dates are observable. The serial interval distribution is a key input into common approaches to estimate the time-varying reproductive rate. In this study, we examined detailed contact tracing data on laboratory-confirmed cases of COVID-19 in Hong Kong between 1 January and 30 September 2020, and identified 860 pairs of cases with clear epidemiological links between infector and infectee, representing approximately 30% of all confirmed cases. Analysis of these 860 pairs identified a mean serial interval of 4.2 days and standard deviation of 5.0 days, with 102 (11%) observed serial intervals being negative. We found clear changes over time in serial intervals, with longer serial intervals of mean 6 days during the rising phase of a community epidemic, declining to a low mean of 2 days when incidence fell due to effective control measures. We were able to correlate the changes in serial intervals with more timely isolation of potential infectors, consistent with our hypothesis that this would reduce post-symptomatic transmission but not necessarily pre-symptomatic transmission. Methodological developments are now needed to account for changing serial interval distributions when estimating reproductive rates.

Assessing COVID-19-related Knowledge, Attitudes, and Practices among Primary Care Patients in Southern California: A cross-sectional survey during the COVID-19 Pandemic

Shivani Mehta* Shivani N. Mehta Zoe C. Burger Dr. Stephanie A. Meyers-Pantele Dayanna Ortiz Pavan Mudhar Sekboppa Sor Yvonne Lam Jigna Kothari Dr. Meena Meka Dr. Timothy Rodwell

Background: Minority groups experience higher rates of infection, hospitalization, and death due to SARS-CoV-2 (COVID-19). In this study we sought to assess COVID-19-related knowledge, attitudes, and practices (KAP) among a predominantly Hispanic/Latinx cohort in Southern California to identify risk factors contributing to increased vulnerability to COVID-19.

Methods: Participants 18 years and older were recruited in a primary-care clinic in Southern CA and asked to self-report sociodemographic characteristics, vaccine acceptance, and KAP. KAP items were summed to create composite scores, with higher scores reflecting increased COVID-19 knowledge, positive attitude towards COVID-19, and disease prevention practices. Bivariate and multivariable regression models were fit to test associations between sociodemographic characteristics and KAP scores.

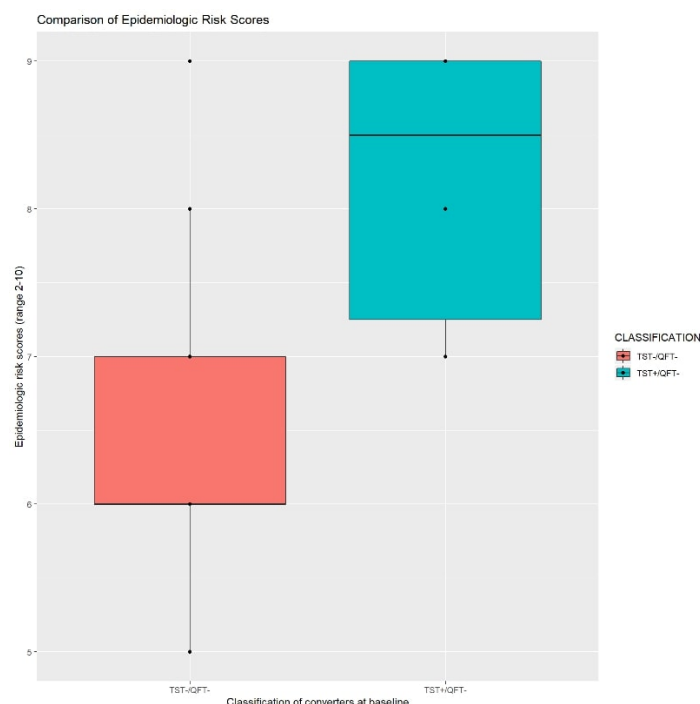
Results: We interviewed 323 patients, with mean age of 49 years (IQR 38.5-59), 69% were female, 82% were Hispanic/Latinx, 77% had at most a high school degree, 55% had an annual income \leq \$100,000 ($\beta = -.350$, 95% CI -1.67- -0.47, $p < 0.01$) were negatively associated with COVID-19 preventative practices when controlling for covariates. Within a subset of 241 patients, 21% indicated that they would not take a COVID-19 vaccine and 18% were unsure.

Conclusion: Our study showed there is high symptom awareness, moderate vaccine acceptance, and high association between demographic characteristics and COVID-19 KAP. These results could help tailor COVID-19 education, prevention, and intervention efforts for Hispanic/Latinx populations.

Characterization of conversion to *Mtb* infection in Uganda

Jesus Gutierrez* Jesus Gutierrez
Catherine Stein LaShaunda Malone Harriet Mayanja-Kizza W Henry Boom

Background: Household contact studies of tuberculosis (TB) index cases provide the opportunity to observe characteristics associated with development of *Mtb* infection. Most TB studies have transitioned to defining conversion to *Mtb* infection using interferon-gamma release assay (IGRA) alone, however there may be value in incorporating the tuberculin skin test (TST) into this definition. Our goal is to epidemiologically characterize conversion to *Mtb* infection using both the IGRA and TST in household contacts (HHCs) of TB cases. **Methods:** During our ongoing TB HHC study in Kampala, Uganda, we enrolled 281 HHCs and followed them for one year. Each individual received a TST and IGRA test at baseline, followed by sequential IGRA testing every 3-6 months. A final TST was performed at the end of the follow-up. We also gathered epidemiological and clinical characteristics and we computed a risk score to quantify risk for *Mtb* infection. Comparisons were done using Wilcoxon rank sum test. **Results:** We identified 130 individuals who were IGRA-negative at baseline. Among these, 41 converted to IGRA-positive sometime during the follow-up. We examined whether there were differences between the subjects who would eventually convert their IGRA by TST status at baseline. There were no differences in age, sex, HIV status or BCG vaccination between these two groups. Among individuals who would eventually convert to IGRA-positive, individuals who were TST-positive at baseline had higher epidemiologic risk scores than TST-negative ones [median 8.5 vs. 6.0; $p=0.001$]. Individuals who had positive TSTs had higher quantitative IGRA values at month 12 than did those with negative TSTs, though this did not attain significance [median 1.6 vs. 2.3; $p=0.44$]. **Conclusions:** Our results indicate that IGRA converters are not a homogeneous group. The difference in risk scores suggests more intense exposure to the index TB case, while the difference in interferon-gamma levels, although not statistically significant, may suggest a difference in the immunological response to *Mtb*. Since many studies use IGRA-conversion as an endpoint, our results suggest that the TST may add additional information about heterogeneity among IGRA converters, which will help inform studies looking at other immunological and genomic correlates of the TB immune response.



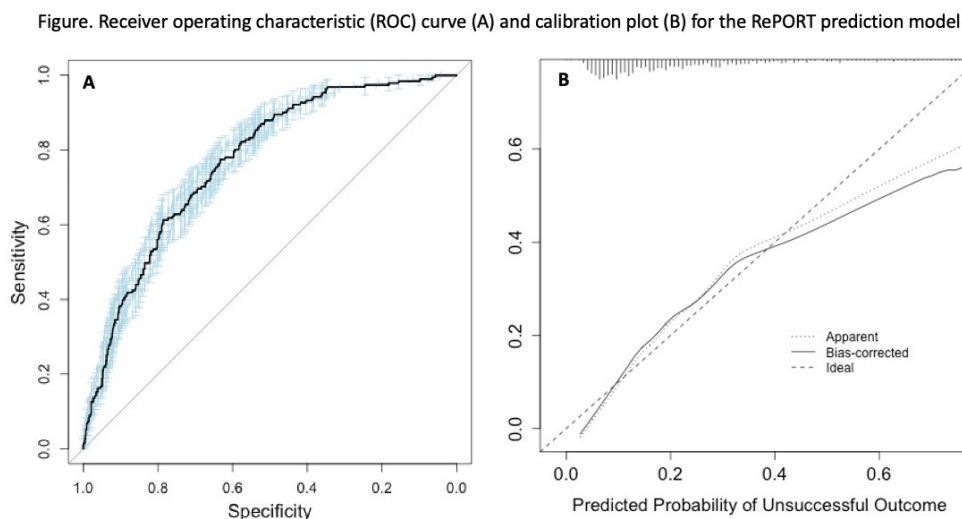
Development and validation of a prediction model for unsuccessful pulmonary tuberculosis treatment outcomes in a prospective cohort in Brazil Lauren Peetluk* Lauren Peetluk Peter F. Rebeiro Felipe Ridolfi Bruno Andrade Marcelo Cordeiro-Santos Afranio Kritski Betina Durovni Solange Calvacante Marina Figueiredo David Haas Valeria Rolla Dandan Liu Timothy Sterling

Introduction: Despite widespread availability of curative therapy, tuberculosis (TB) treatment outcomes remain suboptimal. Clinical prediction models can inform treatment strategies to improve outcomes. Using clinical data at treatment initiation, we developed a prediction model to identify patients at high risk of unsuccessful TB treatment outcome. We also evaluated the incremental value of considering HIV-related severity and isoniazid acetylase status.

Methods: Data were obtained from the Regional Prospective Observational Research for Tuberculosis (RePORT) Brazil cohort, which enrolled newly diagnosed pulmonary TB patients in Brazil from 2015-2019. This analysis included participants with culture-confirmed, drug-susceptible pulmonary TB who started first-line anti-TB therapy, and had ≥ 12 months of follow-up. The outcome was unsuccessful TB treatment outcome: a composite of death, treatment failure, regimen switch, incomplete treatment, and not evaluated. Missing predictors were imputed. Predictors were selected via bootstrapped backward selection. Discrimination and calibration were evaluated with c-statistics and calibration plots, respectively. Bootstrap internal validation estimated overfitting, and a shrinkage factor was applied to improve out-of-sample prediction. Incremental value was evaluated with likelihood ratio-based measures.

Interpretation: Of 944 participants, 191 (20%) had unsuccessful treatment outcomes. The final model included seven baseline predictors - hemoglobin, HIV-infection, drug use, diabetes, age, education, and tobacco use. The model demonstrated good discrimination (c-statistic=0.77; 95% confidence interval (CI): 0.73-0.80) and was well-calibrated (optimism-corrected intercept and slope: -0.12 and 0.89, respectively).

Conclusions: The prediction model performed well in the study population. It used information readily available at treatment initiation. The findings may be helpful in future studies to allocate resources or inform targeted interventions for high- and low-risk patients.



Social network diversity, social network size and Staphylococcus aureus colonization in an Arizona border community Steven D. Barger* Steven Barger Talima Pearson Monica R. Lininger Robert T. Trotter Mimi Mbegbu

Substantial evidence shows that social relationship resources are inversely associated with chronic disease risk. However, less is known about their association with infectious agents. In this study we examined colonization with *Staphylococcus aureus* as a function of social network diversity and social network size. *S. aureus* is a common bacteria that exists on skin as a commensal and can cause both skin and serious blood borne infections. Transmission of *S. aureus* occurs in part through physical contact with colonized persons and asymptomatic carriage of *S. aureus* may represent an important community reservoir for staph infection. However, no studies have examined staph colonization in the context of social relationships. We recruited naturally occurring social groups in public settings in Yuma County, AZ. Participants (N = 443 adults; 191 groups) completed measures of social network diversity and size. Hand, throat and nares swabs were obtained and cultured to detect *S. aureus*. Using a GLM with a Poisson family, log link and clustered robust standard errors we regressed staph colonization (yes/no; 42.9% positive) on network diversity and network size separately. In each model we subsequently adjusted for age, sex and ethnicity. Network diversity (incidence rate ratio [IRR] = 1.03 95% CI 0.97, 1.09) and network size (IRR = 1.03 95% CI 0.95, 1.10) were unrelated to staph colonization. These patterns persisted in adjusted models and when using categorical definitions of networks. Although previous research links infectious disease susceptibility to network diversity we found no association of network diversity with *S. aureus* colonization. Similarly, network size represents the number of people seen regularly face to face and thus broadly represents *S. aureus* exposure potential. Partitioning *S. aureus* into drug resistant and susceptible strains may further illuminate the clinical relevance of social relationships for bacterial colonization.

Trends in prevalence of extended-spectrum beta-lactamase-producing *Escherichia coli* isolated from patients with community- and healthcare-associated bacteriuria: results from 2014 to 2020 in an urban safety-net healthcare system Eva Raphael* Eva Raphael Maria

Glymour Henry Chambers

Background

The prevalence of infections caused by extended-spectrum beta-lactamase producing *Escherichia coli* (ESBL-*E. coli*) is increasing worldwide, but the setting in which this increase is occurring is not well defined. We compared trends and risk factors for ESBL-*E. coli* bacteriuria in community vs healthcare settings.

Methods

We collected electronic health record data on all patients with *E. coli* isolated from urine cultures in a safety-net public healthcare system from January 2014 to March 2020. All analyses were stratified by healthcare-onset/associated (bacteriuria diagnosed > 48 hours after hospital admission or in an individual hospitalized in the past 90 days or in a skilled nursing facility resident, N=1,277) or community-onset bacteriuria (all other, N=7,751). We estimated marginal trends from logistic regressions to evaluate annual change in prevalence of ESBL-*E. coli* bacteriuria among all bacteriuria. We evaluated risk factors using logistic regression models.

Results

ESBL-*E. coli* prevalence increased in both community-onset (0.91% per year, 95% CI: 0.56%, 1.26%) and healthcare-onset/associated (2.31% per year, CI: 1.01%, 3.62%) bacteriuria. In multivariate analyses, age >65 (RR 1.88, CI: 1.17, 3.05), male gender (RR 2.12, CI: 1.65, 2.73), and Latinx race/ethnicity (RR 1.52, CI: 0.99, 2.33) were associated with community-onset ESBL-*E. coli*. Only male gender (RR 1.53, CI: 1.03, 2.26) was associated with healthcare-onset/associated ESBL-*E. coli*.

Conclusions

ESBL-*E. coli* bacteriuria frequency increased at a faster rate in healthcare-associated settings than in the community between 2004 to 2020. Male gender was associated with ESBL-*E. coli* bacteriuria in both settings, but additional risks—age >65 and Latinx race/ethnicity—were observed only in the community

Protective factor of the school setting in Marin County amidst the Coronavirus Infectious Disease-19 (COVID-19) pandemic Michaela George* Michaela George Karina Arambula Charis Baz Sandra Rosenblum Alana McGrath Mike Grant

Background: After the initial school closure by the COVID-19 pandemic, school reopening in Marin County, California on 8 September 2020 was made possible by strict implementation of safety measures to mitigate widespread disease transmission. Since the reopening of schools, members of the community, school administration, staff and teachers became concerned about the contagion spreading in the classroom at a higher rate than in the community. We conducted an analysis to compare in-school versus community-based transmission events in children grades K-8th.

Methods: Data used in the analysis was made available in collaboration with Marin County Office of Education (MCOE) and Marin County Department of Health and Human Services (Marin HHS) Epidemiology COVID-19 Surveillance and the Contact Tracing teams. A descriptive analysis was performed to determine whether there was a correlation between increases in the in-person school student days and in-school COVID-19 transmission in children K-8th in Marin County over the fall 2020 term.

Results: Since 8 September 2020 through 18 December 2020, there were 8,443 in-person school students, on average per day, which is 52% of the overall 16, 339 student enrollment. A total of 573,051 student days and 72 in-person school days have been recorded during this period. Since school reopening, the cumulative number of cases of suspected in-school transmission was 6, as compared to 88 suspected community-based transmission among children K-8th through 18 December 2020. Overall percent positivity in Marin County declined as low as 0.80% during the same time period.

Discussion: The in-person school setting may be a protective factor for students, given stringent implementation of safety measures to mitigate the widespread transmission of COVID-19 while on school grounds. We plan to further investigate this difference and attempt to explain the stark contrast.

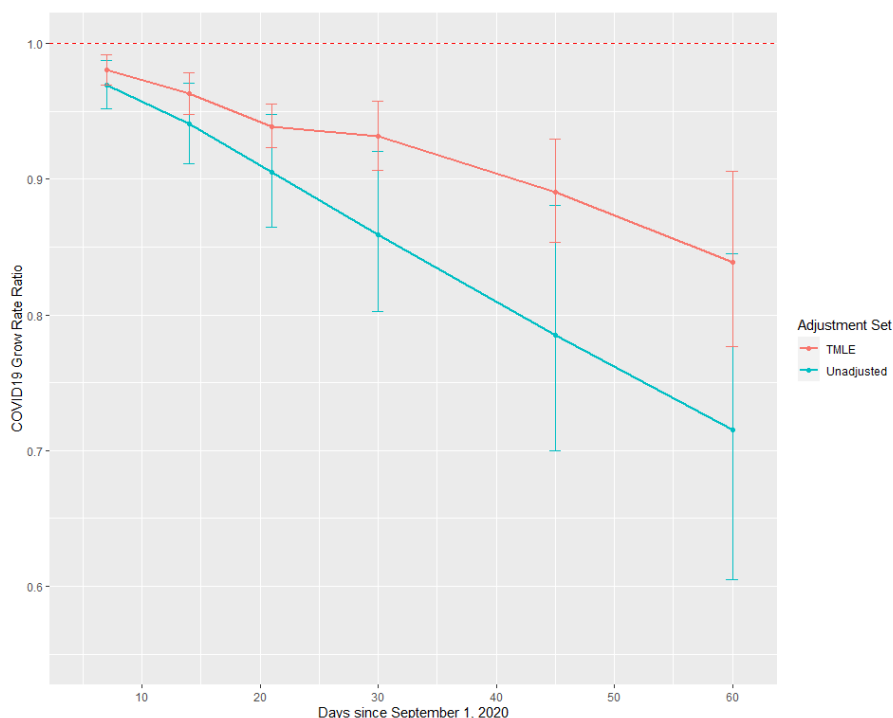
Evaluating public masking mandates on COVID-19 growth rates in U.S. states Angus Wong* Angus Wong Laura Balzer

Background: U.S state governments have implemented numerous policies to help mitigate the spread of COVID19. While there is strong biological evidence supporting the wearing of face masks or coverings in public spaces, the impact of public masking policies remains unclear.

Methods: We aimed to evaluate how early versus delayed implementation of state-level public masking orders impacted subsequent COVID19 growth rates. We defined “early” implementation as having a state-level mandate in place before September 1, 2020, the approximate start of the school year. We defined COVID19 growth rates as the relative increase in confirmed cases {7, 14, 21, 30, 45, 60}-days after September 1. Primary analyses used targeted maximum likelihood estimation (TMLE) with Super Learner and considered a wide range of potential confounders to account for differences between states. In secondary analyses, we took an unadjusted approach and calculated the average COVID19 growth rate among early-implementing states divided by the average COVID19 growth rate among late-implementing states.

Results: At a national level, the expected growth rate after 14-days was 4% lower with early vs. delayed implementation (aRR: 0.96; 95%CI: 0.95-0.98). Associations did not plateau over time, but instead grew linearly (Figure). After 60-days, the expected growth rate was 16% lower with early vs. delayed implementation (aRR: 0.84; 95%CI: 0.78-0.91). Unadjusted estimates were exaggerated (e.g. 60-day RR: 0.72; 95%CI: 0.60-0.84). Sensitivity analyses varying the timing of the masking order yielded similar results.

Conclusions: In both the short and longer term, state-level public masking mandates were associated with lower COVID19 growth rates. Given their low cost and minimal (if any) impact on the economy, masking policies are promising public health strategies to mitigate further spread of COVID19.



Awareness and personal preventive measures toward COVID-19 among the general public in Japan: A population-based postal survey Kohta Suzuki* Kohta Suzuki Rei Wakayama Aya Goto Chihaya Koriyama

The coronavirus disease 2019 (COVID-19) pandemic caused by the severe acute respiratory syndrome coronavirus 2 has changed people's lives globally. This study aimed to describe the results of a population-based postal survey about the general awareness and personal preventive measures before and during COVID-19 outbreak in Japan. This survey was carried out in April and May 2020. The number of target population was 5450 who lived in 4 prefectures (Fukushima, Tokyo, Aichi and Kagoshima). Given the situation that many internet-based surveys on COVID-19 were conducted, and this postal survey aimed to target the general public by minimize a selection bias and to collect information from the elderly. As a result, the number of participants was 3554 (65.2%). Of these, 1614 (45.4%) were men and 803 (22.6%) were and older than 70 years. A response rate in Tokyo was higher than 70%. Firstly, almost all people felt anxiety about COVID-19 and 1037 (29.2%) had the feeling of not only anxiety but also fear. Secondly, in terms of hand washing, the total of "quite a lot" and "always" was 2237 (63.0%) in 2019 which increased to 3419 (96.2%) in 2020. Thirdly, regarding wearing a face mask, the total of "quite a lot" and "always" also increased from 980 (27.5%) to 3341 (94.8%) during the same period. The results of other preventive actions such as event participation, eating out, and going to a private trip, their frequencies of "decreased" and "almost not as before" were more than 90%. After excluding those who answered "almost not as before", 2918 (93.1%) and 2423 (96.5%) answered "decreased" about eating out and going to a private trip, respectively. Finally, regarding influenza vaccination, 1944 (54.7%) were not vaccinated in the winter of 2019 to 2020. In conclusion, almost all people performed personal preventive measures, such as hand washing and wearing a face mask, although the vaccination rate for influenza in 2019-20 was lower than 50%.

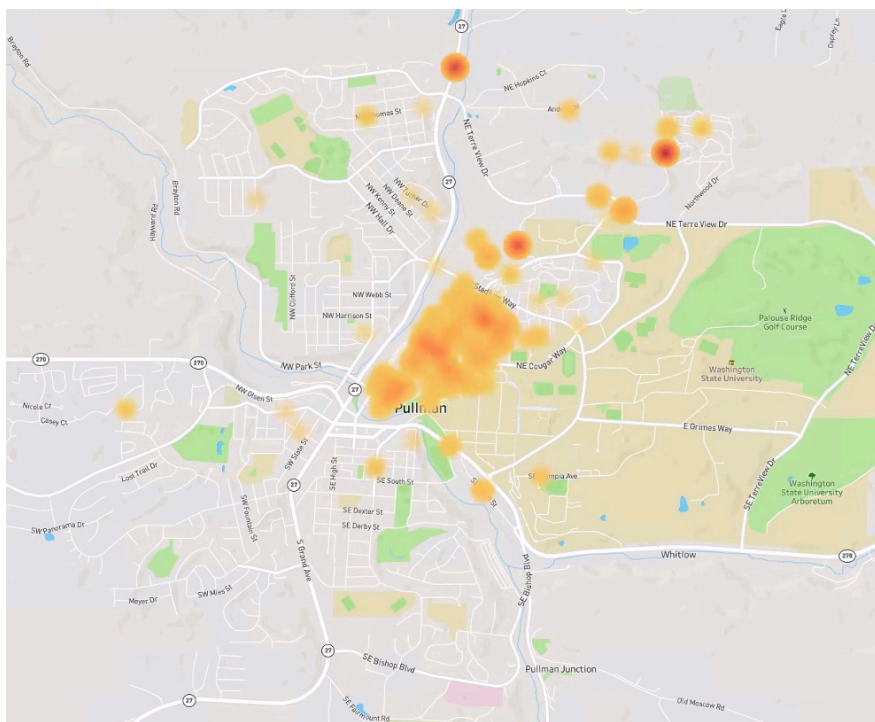
A Tale of One City: Geographic and Social Meta-Populations and COVID-19 Matthew Mietchen* Eric Lofgren Katelin Jackson Stephanie Johnson

Background: The COVID-19 pandemic is often described using national or state-level figures, but these can obfuscate distinct, local epidemics. Here, we examine the course of the COVID-19 outbreak in a rural community with a large land-grant university.

Methods: Using a timeseries of reported COVID-19 cases in Whitman County, WA from 8/1/2020 to 11/29/2020, we examine three selected groups - students within and outside the Greek system, and cases in the broader community. We estimate the peak of the epidemic in each group, as well as the number of days from the first reported case to the peak as a measure of the sharpness of the epidemic.

Results: Cases in the Greek system showed a sharp spike in cases, peaking 12 days before cases within the non-Greek community. This peak occurred 13 days after the first reported cases within the Greek system, suggesting rapid spread through this community, and 55% of cases occurred within two weeks of the initial case. The non-Greek peak occurred 32 days after the initial reported case, and only 24% of cases occurred within the first two weeks. These early cases also showed distinct geographic clustering in an area of town with high densities of off-campus student housing (see Figure). The broader community experienced a slower epidemic with a peak over 90 days from the peak in the Greek community, and only 7% of cases occurring within two weeks of the initial case.

Conclusions: Despite the small size of this community, both in terms of population and geography, there appears to be at least two distinct COVID-19 epidemics. We suggest that the social organization of the town, with students largely sequestered to one of four “hills”, may have formed largely non-interacting meta-populations. These distinct groups have implications both the control of COVID-19 and the utility of aggregate metrics.



Re-estimating prevalence of adult Hepatitis B Virus immunity in the United States Daniel Vader* Daniel Vader Neal D Goldstein Chari A Cohen Harrison Quick Alison A Evans

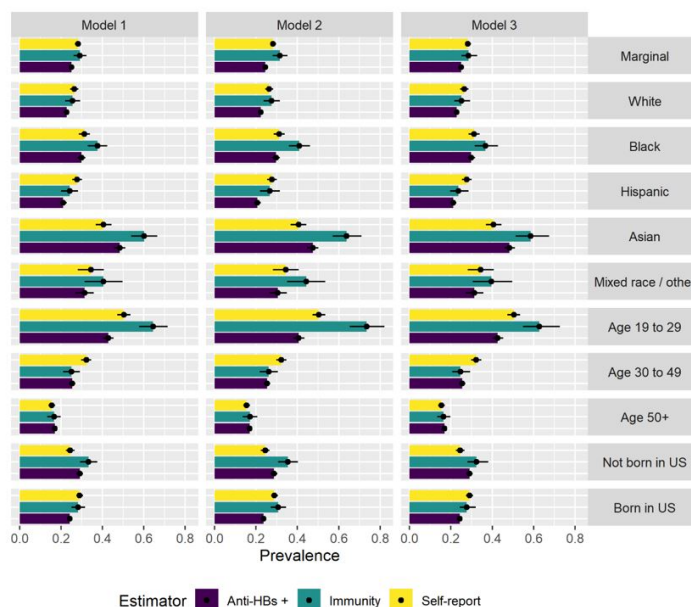
Background: Two primary instruments used to measure adult hepatitis B vaccination coverage in the United States are self-report and antibody to hepatitis B surface antigen. Estimates based on either of these measures are subject to misclassification when used to determine immunity to hepatitis B. This study quantifies this bias and presents misclassification-corrected estimates of hepatitis B immune prevalence in the U.S.

Methods: We used cross-sectional data from the 2015-2016 NHANES cycle on 5,151 subjects age 19 and older. We investigated existing literature on long-term immunity after vaccination to assess the sensitivity of anti-HBs as a measure of immunity and based specificity on the specificity of the anti-HBs testing system. Our model used a Bayesian approach to correct for misclassification of true immune status by anti-HBs, and compares corrected estimates of immune prevalence to uncorrected estimates based on anti-HBs and self-report.

Results: After correcting for misclassification, estimated marginal immune prevalence was 29.2% (26.0 to 32.3). Prevalence of immunity was highest among 19 to 29-year-olds (64.5%) and Asian Americans (60.1%). When treated as direct measures of immunity, anti-HBs based measures underestimated immune prevalence by 4.1% (95% CrI 1.2 to 7.0) and self-report by 1.0% (-2.5 to 4.4). Anti-HBs underestimated immunity by 11.7% (6.4 to 17.3) among Asian Americans and by 21.7% (15.9 to 27.7) among 19 to 29-year-olds. Self-report underestimated immunity by 19.5% (12.2 to 27.0) among Asian Americans and 14.1% (6.7 to 21.7) among 19 to 29-year-olds.

Conclusions: Misclassification results in minimal underestimation of overall hepatitis B immune prevalence in the U.S., but the impact of misclassification may have a major impact on some demographic subgroups. Researchers and policymakers should pay particular attention to how misclassification can affect estimates of HBV immunity among young adults and in communities that are at high risk of HBV infection.

Estimated prevalence of immunity, anti-HBs, and self-reported vaccination by model and demographic group.



Excess Risk of COVID-19 to University Populations Resulting from In-Person Sporting**Events** Stephanie Sikavitsas Johnson* Stephanie Johnson Katelin C Jackson Matthew S Mietchen Samir Sbai Elissa J Schwartz Eric T Lofgren

Background: One of the consequences of COVID-19 was the cancellation of in-person collegiate sporting events. We explored the impact of having in-person sports on COVID-19 transmission on a small, remote hypothetical college campus. We specifically explore the excess cases and outbreaks within the campus community that can be anticipated, reflecting the duty of universities to protect this population.

Methods: Using a stochastic compartmental model representing the interactions between the university community, we modeled the impact of transient influxes of visitors attending sporting events and ancillary activities (bars, dining out, etc.). We considered a number of scenarios, varying the extent to which visitors interact with the campus, the number of infectious visitors, and the extent to which the campus has controlled COVID-19 absent events. We also conducted a sensitivity analysis, exploring the model's outcomes over a wide range of uncertainty.

Results: Events caused an increase in the number of cases among the campus community. Cases increased 25% in a scenario where the campus already had an uncontrolled COVID-19 outbreak ($R_0 > 1$) and visitors had a low prevalence of COVID-19 and mixed lightly with the campus community. Cases increased 822% where the campus had controlled their COVID-19 outbreak ($R_0 < 1$) and visitors had both a high prevalence of COVID-19 and mixed heavily with the campus community. The model was insensitive to parameter uncertainty, save for the duration a symptomatic individual was infectious.

Conclusion: In-person sporting events represent a threat to the health of the campus community. This is the case even in circumstances where COVID-19 seems controlled both on-campus and among the larger population visitors are drawn from.

Genetic liability to COVID-19, independent of SARS-CoV-2 infection, in cardiovascular diseases and type 2 diabetes: A Mendelian randomization investigation Shiu Lun Au Yeung*
Shiu Lun Au Yeung C Mary Schooling

COVID-19 is increasingly recognized as having potentially long-term cardiovascular effects. Whether people who were more vulnerable to COVID-19 are also more likely to have subsequent adverse cardiovascular events regardless of the SARS-CoV-2 infection is unclear. To explore this question, we assessed the impact of genetic liability to COVID-19 on cardiovascular diseases, type 2 diabetes and their risk factors using a Mendelian randomization study of pre COVID-19 GWAS, to obtain effects independent of SARS-CoV-2 infection. We found a positive relation of liability to COVID-19 with large artery stroke (odds ratio (OR): 1.25 per log odds, 95% confidence interval (CI) 1.03 to 1.53) and type 2 diabetes (OR: 1.17, 95% CI 1.07 to 1.28), and reduced monocyte count, but not other cardiovascular diseases or risk factors. These findings indirectly suggest that any observed effects of COVID-19 on cardiovascular-related outcomes are likely a sequela of the virus, highlighting the importance of prevention policies.

Assessing the super learner as a tool for predicting seasonal influenza hospitalizations: a simulation study Jason R. Gantenberg* Jason R. Gantenberg Kevin W. McConeghy Chanelle J. Howe Jon Steingrimsson Robertus van Aalst Ayman Chit Andrew R. Zullo

Background

The importance of accurately forecasting infectious diseases has increased interest in ensemble machine-learning methods. One such method, the super learner, combines predictions from multiple algorithms/models, weighting them by their individual accuracy. Most research on predicting seasonal influenza in the United States has focused on influenza-like illnesses rather than influenza-related hospitalizations. We evaluated a super learner's predictions of three measures of national-level seasonal influenza hospitalization: peak rate, peak week, and cumulative rate.

Methods

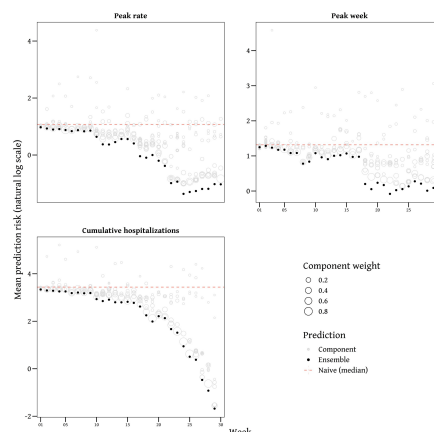
We used a super learner with 72 unique component learners (e.g., random forests, penalized regression) and trained it on a distribution of 15,000 influenza hospitalization curves simulated using surveillance data. For each prediction target, we generated predictions at all 30 weeks of the flu season and compared the average absolute prediction error of the ensemble super learner (weighted combination of component learner predictions), the discrete super learner (best-performing component learner), and a naive prediction (e.g., median simulated peak rate).

Results

The ensemble super learner performed comparably to the discrete super learner and better than the naive median across all seasonal targets. The discrete super learner's class varied by week (e.g., random forest, penalized regression). Ensemble predictions generally exhibited prediction errors similar to the naive prediction early in the season but improved upon the naive prediction as the season progressed.

Conclusions

Future work should examine the super learner's performance in empirical data, incorporating influenza-related variables (e.g., viral activity) that may improve predictive performance. Better predicting the influenza hospitalization peak and its timing could provide more lead time to allocate critical resources ahead of surges in hospital admission.



LATEBREAKER

Infectious Disease

Validity of electronic medical records for measuring COVID-19 infection Annette Regan*

Annette Regan Sheena Sullivan Onyebuchi

Validity of electronic medical records for measuring COVID-19 infectionAnnette K Regan;^{1,2,3} Sheena G Sullivan;^{3,4} Onyebuchi Arah⁴¹ University of San Francisco, San Francisco CA² OptumLabs Visiting Fellow, Eden Prairie, MN³ WHO Collaborating Centre for Reference and Research on Influenza, Melbourne VIC⁴ UCLA Fielding School of Public Health, Los Angeles CA

Background: Large-scale evaluation of SARS-CoV-2 infection and COVID-19 vaccination based on electronic medical information will rely on the quality of ICD coding. However, little is known about the validity of ICD-coded COVID-19 diagnoses.

Methods: We used data from a national cohort of pregnant women with a date of delivery since 1 January 2020 in the OptumLabs® Data Warehouse (OLDW). OLDW is a longitudinal, real-world data asset with de-identified administrative claims and electronic health record data. We identified all services with an ICD-10-CM diagnostic code of U07.1. For comparison, laboratory claim records were extracted to identify SARS-CoV-2 diagnostic testing within 3 days of the COVID-19 diagnosis. We compared ICD-coded diagnoses to SARS-CoV-2 test results (“gold standard”) to calculate sensitivity, specificity and predictive values.

Results: Of 81,210 pregnancies identified, 1,391 pregnant women had an ICD-10-CM diagnosis of COVID-19 and 3,247 women had a record of a laboratory test for SARS-CoV-2. Agreement between ICD-coded diagnosis and laboratory testing records was high 92% (95% CI 91, 93%), as was the specificity (95%; 95% CI 94, 96%). However, sensitivity of ICD-code diagnosis was low (22%; 95% CI 15, 30%) and the positive predictive value was 16% (95% CI 12, 21%).

Conclusions: Results from a national cohort of pregnant women suggest that the use of diagnostic coding alone would miss 78% of COVID-19 infections. Rather than relying exclusively on diagnostic coding, epidemiological research and surveillance should draw from multiple sources of COVID-19 diagnostic information.

LATEBREAKER

Infectious Disease

Using Voluntary Contact Diaries to Understand University Campus Employee Contact**Patterns** Stephanie Sikavitsas Johnson* Stephanie Sikvaitas Johnson Katelin C Jackson Matthew S Meitchen Eric T Lofgren

The COVID-19 pandemic has proven a difficult challenge for colleges and universities across the country. While students might be learning virtually, employees -faculty, staff, graduate students, etc.-might still have to be on campus. Student transmission has been found to be mostly off-campus and is the focus for many testing programs, leaving employee contact networks and transmission understudied. We conducted an anonymous, voluntary online contact diary survey study for faculty and staff of a PAC-12 school on their contact patterns with those both within and outside the university during the pandemic. Participants were asked in general terms about the individuals they encountered in one day, the type and location of the interactions, and what COVID-19 precautions were taken - if any. Participants were then asked if they were ever tested and diagnosed with COVID-19 or experienced symptoms of COVID-19, as well as their vaccination status. Finally, participants were asked to try and recall the same type of questions on a similar day from a year ago. Of the 413 responses, 72% worked primarily on the main campus. The mean number of contacts during the survey period was 2, with 33 respondents having 6 or more contacts. Of the 699 contacts identified, most were a partner/spouse (25%) followed by colleagues and students (19%). Of the 679 locations mentioned, 261 (38%) were at their own home and 87 (12.8%) made a direct mention of being on one of the college campuses. These results suggest that, even while effectively social distancing, there is substantial out of home contact for university faculty and staff.

LATEBREAKER

Infectious Disease

Investigating Lagged Associations Between Mobility to Retail Stores, Grocery Stores, and Workplaces and COVID-19 Case Count Kaelah Wilson* Kaelah Wilson Elsa Ghebrendrias Tabatha Page Joseph Gibbons Eyal Oren Caroline A. Thompson

The COVID-19 pandemic has caused an unprecedented number of infections and deaths. Human mobility is a significant factor in driving viral spread as people congregate at places of work, grocery and retail. The aim of this study is to quantify the impact of increased mobility using GPS smartphone data for three specific location types on COVID-19 case count, with a 4-week lag period between exposure and outcome.

County-level data was analyzed from 1,562 US state counties from February to August 2020. Google mobility data reports phone-based movement trends calculated as a percent change from pre-pandemic levels and averaged into a weekly score. Our outcome, case count, was also averaged into a weekly variable and rounded up to the nearest integer. Separate repeated measures adjusted Poisson regression models were used to examine the relationship between increased mobility to retail stores, grocery stores and workplaces and case counts. We also stratified regressions by census-defined poverty to measure effect modification by county-level socioeconomic deprivation.

We found that a 1% increase in mobility to retail stores or grocery stores was associated with a 2.1% increase COVID-19 cases 4 weeks later and a 1% increase in mobility to workplaces was associated with a 3.6% increase in COVID-19 cases 4 weeks later. Poverty was not found to modify this relationship for any location type. However, we were unable to account for county-wide testing rates over time, which could confound this association.

The study findings suggest that increased mobility is an important factor in the spread of COVID-19. While some essential businesses are realistically unable to close, public health policies can be adapted to limit viral spread. Social distancing and mask adherence can be mandated in places where human contact is unavoidable. Policies that limit mobility to settings with fewer mitigation guidelines may allow essential businesses to operate with a lower risk of transmission.

LATEBREAKER

Infectious Disease

Characteristics and healthcare utilization among drug use-associated infective endocarditis patients in an Appalachian state Ruchi Bhandari* Ruchi Bhandari Talia Alexander Frank Annie Umar Kaleem R. Constance Wiener Mark Bates Aravinda Nanjundappa Affan Irfan Chris Cook Sudarshan Balla Ellen Thompson Melanie Fisher

Background: The high prevalence of drug use in West Virginia (WV) is accompanied by sharp increases in life-threatening infections, such as infective endocarditis (IE). Despite the severity of the problem, there is lack of an empirically driven strategy to collect and analyze needed statewide data.

Methods: We developed a statewide database of adult IE patients hospitalized at the three largest tertiary cardiovascular centers in WV between January 2014 and December 2018. Data were abstracted from electronic medical records into a standardized dataset and compared between drug use-associated IE (DU-IE) and non-DU-IE patients on demographic, clinical, and substance-use behavior characteristics. Descriptive summary statistics are presented as counts, percentages, mean, and standard deviation. Groups are compared using chi-square or Fisher's exact test, or independent samples t-test.

Results: There were 808 IE patients admitted at the three study sites, with numbers rising significantly over the 5-year study period ($p=.002$). Majority of the patients (70.92%) had used drugs prior to hospital admission; almost all had injected drugs; polydrug use was common; and 37.13% patients had psychiatric disorders. Compared with non DU-IE patients, DU-IE patients were significantly younger (mean age: 35.49 vs. 61.03 years) with longer length of stay (mean: 18.98 vs. 28.57 days), higher proportion of discharges against medical advice (20.2% vs. 1.4%); and surgeries (42.06% vs. 26.70%); $p<.001$.

Discussion: The high proportion of DU-IE cases can be attributed to the disproportionately high level of opioid use in WV. Poorer outcomes among DU-IE patients can be explained by the unique operative and management complexities in DU-IE.

Conclusion: Registries like ours can provide epidemiological evidence for understanding the implications of DU-IE, identify specific risk groups, and form the basis for developing strategies for earlier diagnosis and more focused treatment.

LATEBREAKER

Infectious Disease

Inclusion of total days above flood stage improved seasonal influenza forecasting in Iowans

Eric Kontowicz* Eric Kontowicz Christine Petersen Jim Torner Kelly Baker Margaret Carrel Grant Brown

Influenza annually is a leading cause of respiratory infection, estimated to infect between nine and 49 million individuals within the U.S. Seasonal influenza occurs due to host susceptibility, climatic factors, and viral evolution. Iowa experiences large amounts of flooding each year, which was shown through Bayesian statistical modeling to increase population susceptibility to influenza. To date, no forecasting model approaches have been implemented including flooding. We hypothesize that seasonal influenza forecasting models using environmental factors and days above flood stage will accurately mimic the timing of seasonal influenza and outperform similar forecasting models that do not include flooding variables. Data was collected on influenza diagnoses from a large, de-identified, private insurance claims data base and Iowa State Hygienic Lab. Environmental feature data was obtained from weather stations and stream gauges across Iowa. Penalized regression and random forest models were used to make forecasting models predicting monthly influenza rates and categorized influenza burden two months in advance. All models developed produced predictions that accurately mimicked the timing of seasonal influenza but consistently underestimated influenza rates. When including flooding feature data, seasonal influenza rate prediction accuracy was increased by 1.11-fold (range: 0.99 - 1.23) and error was reduced by 0.96-fold (range: 0.88 - 1.12). We found that Random forest models produced the most accurate predictions of seasonal influenza rates ($R^2 = 0.72$, $RMSE = 10.59$, $MAE = 8.21$). When including flooding feature data for seasonal influenza burden category predictions, ROC was improved by 1.09-fold (1.01-1.16). Elastic net regression produced the most accurate predictions of seasonal influenza burden (sensitivity = 0.80, specificity = 0.74). Implementation of environmental features did predict seasonal influenza timing. Including feature data for flooding variables consistently reduced error and increased accuracy of predictions. Due to the complex relationship between influenza and environmental drivers, flexible modeling approaches like random forest and elastic net regression should be considered.

LATEBREAKER

Infectious Disease

Spatially Refined Time-Varying Reproduction Numbers of SARS-CoV-2 in Arkansas and Kentucky, March - November, 2020 Maria D. Politis* Maria D. Politis Xinyi Isaac Chun-Hai

Purpose: To examine and compare the time-varying reproduction number, R_t , for COVID-19 in Arkansas and Kentucky, how it differed among rural and urban counties, and to investigate the impact of policies and preventative measures on the R_t .

Methods: Arkansas and Kentucky county-level COVID-19 cumulative case count data (March 6-November 7, 2020) were obtained from the New York Times GitHub data repository. R_t was estimated using the R package 'EpiEstim' version 2.2-3, by county, region (Delta, non-Delta, Appalachian, non-Appalachian), and policy measures.

Results: In both states, counties with high populations had more cases, however, there were no clear patterns for per capita cumulative case count. The R_t was high for each region, falling below 1 in May or June depending on the region, before stabilizing around 1 in the later months. The R_t remained above 1 for the non-Appalachian region. The direction of the R_t estimates were reflected by the implementation of preventative and relaxation measures.

Conclusions: Both Arkansas and Kentucky have had an extensive spread of COVID-19 since both states maintained a median R_t above 1. We found that policy impact, especially mandated facial coverings, decreased the transmission of COVID-19, allowing for a more quantitative measure of the pandemic.

LATEBREAKER

Infectious Disease

Shigella and rotavirus are leading causes of antibiotic treatment among children in low-resource settings Elizabeth T. Rogawski McQuade* Elizabeth Rogawski McQuade Stephanie A. Brennhofer James A. Platts-Mills Joseph A. Lewnard

Enteric vaccines and other pathogen-specific interventions may reduce selection for antimicrobial resistance (AMR) by preventing diarrhea that prompts antibiotic treatment. We quantified the frequency of treatment that is attributable to specific enteric pathogens to describe the preventable burden of antibiotic use. We included 9392 diarrhea episodes and 38085 stools that were collected and validly tested in 1715 children from the 8-site MAL-ED birth cohort study. We identified etiologies for antibiotic-treated diarrhea episodes by calculating pathogen attributable fractions from a mixed-effects model associating pathogen quantity with detection in diarrheal vs. non-diarrheal stools. We estimated incidence rates and the proportions of antibiotic use for diarrhea and of all antibiotic use attributable to the top 10 causes of diarrhea (Figure 1). Adjusting for age, sex, and socioeconomic status, we estimated associations between specific etiologies and antibiotic treatment, and quantified whether severe diarrhea/dysentery mediated the relationship between pathogens and treatment. *Shigella* and rotavirus were the leading causes of antibiotic treatment, responsible for 11.7% and 8.6% of diarrhea treatments, and 14.8 and 10.9 courses per 100 child-years, respectively. *Shigella* and rotavirus-attributable diarrheal episodes were 47% (RR:1.47; CI:1.34-1.61), and 19% (RR:1.19; CI:1.09-1.31) more likely to be treated, respectively, compared to other episodes. While these two pathogens accounted for only 5.5% of antibiotic courses overall, they were responsible for 19.4% of all fluoroquinolone and 9.6% of all macrolide use. Diarrhea severity and dysentery (*Shigella* only) mediated 48% and 46% of the antibiotic treatment associations with *Shigella* and rotavirus, respectively. The evidence that *Shigella* and rotavirus were disproportionately responsible for antibiotic use due to their high burden and severity strengthens the value proposition for rotavirus and *Shigella* vaccines.

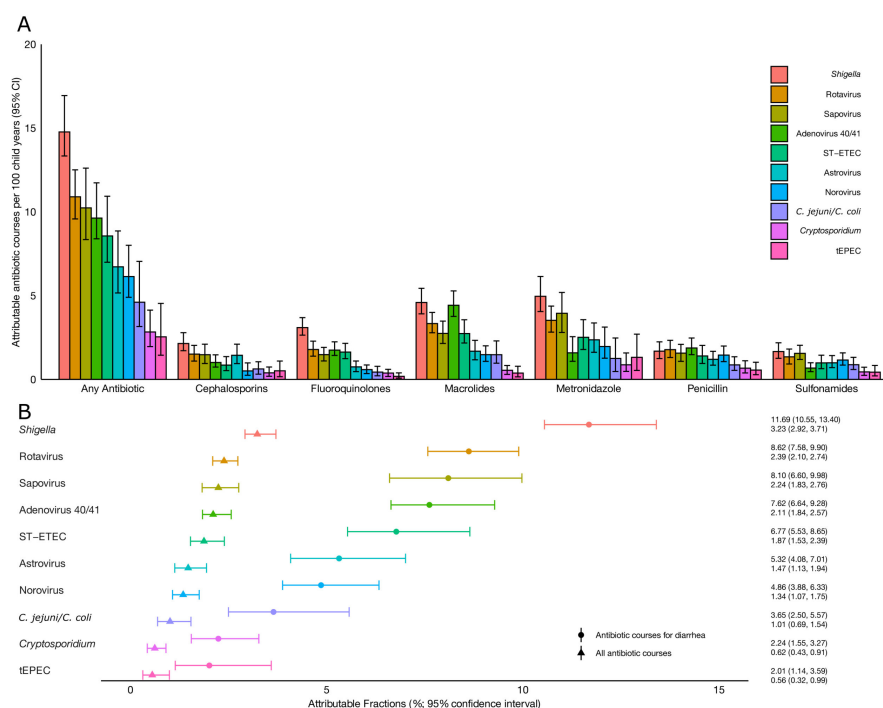


Figure 1. Incidence of class-specific antibiotic use attributable to specific enteric pathogens for the leading 10 causes of diarrhea (A) and the proportions of antibiotic courses that were attributable to each pathogen (B) among 1715 children in the MAL-ED birth cohort.
Note: C. jejuni/C. coli = *Campylobacter jejuni/Campylobacter coli*; ST-EPEC = heat-stable enterotoxigenic *Escherichia coli*; IEPEC = typical enteropathogenic *Escherichia coli*

LATEBREAKER

Infectious Disease

Use of Neighborhood Infection Prevalence to Identify Disparities of COVID-19 and HIV Co-occurrence in Philadelphia, Pennsylvania Jessica Webster* Jessica Webster Neal Goldstein Seth Wells

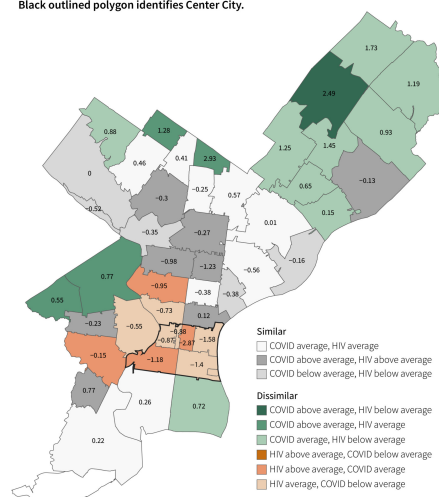
Introduction: The COVID-19 pandemic has highlighted how heightened rates of communicable diseases are often observed in marginalized and underserved communities. Akin to the HIV epidemic, the social and economic disparities associated with race and ethnicity are structural factors fueling the COVID-19 epidemic. This analysis aims to evaluate the co-occurrence of HIV and COVID-19 infections in Philadelphia, Pennsylvania, and to identify ecological correlates driving racial disparities in infection prevalence.

Methods: We designed a cross-sectional, ecological period prevalence study of COVID-19 and HIV cases at the level of zip code tabulation area in Philadelphia, Pennsylvania. For each zip code tabulation area, we created citywide comparison Z-score measures of COVID-19 cases, people living with HIV, and the difference between the scores. Choropleth maps were used to identify areas that were similar or dissimilar in terms of disease patterning, and linear regression models aided to identify independent ecological predictors of these patterns.

Results: The preponderance of zip code tabulation areas had similar burdens of disease relative to the citywide means: these tended to be clustered in the East, North Central, and Southwest areas. Relative to COVID-19, HIV represented a greater burden in Center City Philadelphia, while relative to HIV, COVID-19 was more apparent in Northeast Philadelphia. Areas with a greater proportion of Black or African American residents were overrepresented for both diseases.

Conclusions: While race is a shared nominal upstream factor that conveys increased risk for both infections, there are distinct, separate risk factors driving the overrepresentation of COVID-19 cases across Philadelphia. Difference-based measures of disease occurrence are useful for identifying areas that are under- or over-represented for diseases and may be able to elucidate effective or ineffective mitigation strategies.

Figure 1. Zip code tabulation area choropleth map depicting the difference between the COVID-19 Z-score and PLWH Z-score in Philadelphia, Pennsylvania as of July 27, 2020. Black outlined polygon identifies Center City.



COVID-19: coronavirus disease 2019; PLWH: people living with HIV
 * Z-scores may be interpreted relative to the citywide mean of 3,849 cases per 100,000 people (standard deviation: 570 per 100,000)
 † Z-scores may be interpreted relative to the citywide mean of mean of 1,417 per 100,000 people (standard deviation: 849 per 100,000)

LATEBREAKER

Infectious Disease

Use of Principal Component Analysis to predict COVID-19 vaccine behaviors in University Students Pallavi* Pallavi Aytha Swathi Marie-Claude Couture Kelly L'Engle Annette Regan**Use of Principal Component Analysis to predict COVID-19 vaccine behaviors in University Students**Pallavi Aytha Swathi;¹ Marie-Claude Couture;¹ Kelly L'Engle;¹ Annette K Regan^{1,2}¹ University of San Francisco, San Francisco CA² UCLA Fielding School of Public Health, Los Angeles CA

Background: Through the course of the COVID-19 pandemic, young adults have been identified as an important population group for spreading SARS-CoV-2. With emergency use authorization granted to three COVID-19 vaccines in the US since December 2020, immunization of young adults could prevent future spread of SARS-CoV-2.

Methods: We recently conducted a university-wide survey of perceptions and experiences with COVID-19 vaccines in undergraduate and graduate students aged 18 years and older. Students were asked to self-report whether they had received ≥ 1 dose of COVID-19 vaccine, and if unvaccinated, their intentions to receive COVID-19 vaccine in future. Based on these responses, we performed a decision tree analysis to classify intention to receive COVID-19 vaccine based on their experiences during the pandemic. Principal Component Analysis was used to extract features and reduce the dimensionality of the dataset.

Results: Preliminary survey data included responses from 1,084 students. Our training data included 75.5 % (n = 491) students expressed intention to get vaccinated soon, and 24.4 % (n = 159) students who were already vaccinated. Using the decision tree classifier, we developed a model that predicted if a student will receive the vaccine with a F1 score of 0.93. The outcomes of our test data indicated that 22 % of students would get vaccinated soon. The most influential factor for this outcome was if the students' experience with quarantine or isolation was classified as "hard."

Conclusions: Our analysis shows that a significant percentage of students definitely intend to receive the COVID-19 vaccination, and students' experiences with the pandemic are influential factors contributing to vaccine behaviors. These results are informative for vaccine campaigns which target university students and college-aged adults.

LATEBREAKER

Infectious Disease

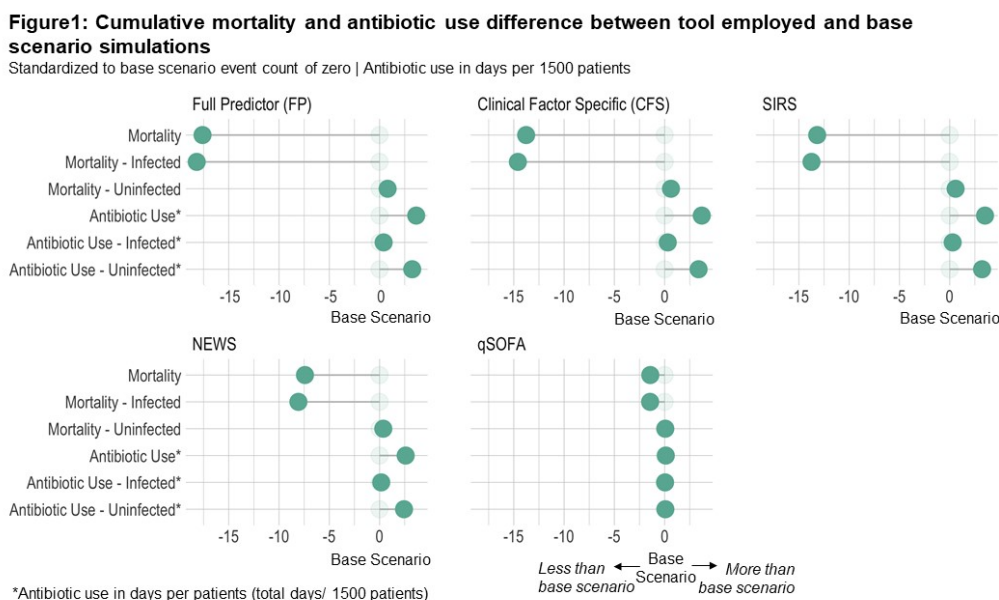
Modeling the impact of novel bacterial sepsis prediction tools on mortality and antibiotic use among immunocompromised patients Margaret Lind* Margaret Lind Benjamin Althouse Stephen J Mooney Marco Carone Amanda Phipps Steven Pergam

Background: We previously developed two sepsis prediction tools (full predictor [FP] and clinical factor specific [CFS]) with greater predictive validity in relation to high sepsis risk bacteremia than existing tools among allogeneic hematopoietic cell transplant (aHCT) recipients. To quantify potential benefits of tool implementation, we compared the estimated mortality and antibiotic use resulting from our tools to those resulting from existing tools (Systemic Inflammatory Response Syndrome-SIRS, quick Sequential Organ Failure System-qSOFA, and National Early Warning Score-NEWS).

Methods: Using a Markov model, we followed a simulated population of 1500 aHCT recipients for the first 100 days post-aHCT. Each day, a proportion of the population was cultured, positive for high-risk bacteremia, recovered from infection, considered tool positive/negative, received antibiotics, and died based on observed and literature-derived proportions. For each tool, mortality and antibiotic use were summarized. We evaluated the mortality/antibiotic use trade-off by comparing the deaths and antibiotic days to those estimated in the absence of a tool (base scenario).

Results: Our FP tool led to the fewest deaths (187, 95% prediction intervals, 163-211) and qSOFA led to the most (203, 177-229). qSOFA led to the fewest antibiotic days (1793, 1510-2081) and CFS led to the most (7157, 6690-7632). Relative to 1500 antibiotic days beyond the base scenario, FP led to fewer deaths than CFS (difference: 0.96, 0.02-2.60), SIRS (difference: 0.98, 0.03-2.52) and NEWS (difference: 1.70, 0.20-3.95, Figure1).

Conclusion: FP led to fewer simulated deaths than other examined tools and did so with relatively few additional days of antibiotics. These findings support the use of our FP tool as an alternative bacterial sepsis prediction tool among aHCT recipients.



Childhood Family Violence Exposure and Later Antisocial Behavior: Moderating Roles of Inflammatory Markers and Gender Melissa Tracy* Li Shen Chong Elana Gordis Kate Strully

Childhood family violence exposure, such as childhood maltreatment, harsh parenting, domestic violence, and psychological aggression, have been linked to later antisocial behaviors. Recent studies suggest that this link may be influenced by other factors. Childhood family violence is associated with inflammatory markers as measured by C-reactive protein (CRP) and interleukin-6 (IL-6), but limited studies have investigated the relationship between inflammatory markers and antisocial behavior. Moreover, significant gender differences have been found in the prevalence of antisocial behavior and inflammatory markers. We aimed to examine whether CRP and IL-6 at age 9 and gender moderate the link between family violence exposure from ages 0-9 and later antisocial behaviors (physical aggression, rule-breaking behavior, and psychological aggression) at ages 13-18, using prospectively collected data from the Avon Longitudinal Study of Parents and Children (n = 5072). Logistic regression analyses suggested that childhood family violence was significantly associated with later physical aggression (adjusted Odds Ratio [aOR]=1.27, 95% Confidence Interval [CI] = 1.15-1.41) and total antisocial behaviors (aOR=1.21, 95% CI = 1.08-1.35), when adjusting for socio-demographic characteristics and mother's prenatal depression, anxiety and substance use. Higher levels of IL-6 at age 9 were significantly associated with higher odds of physical aggression at ages 13-18 (aOR=1.13, 95% CI = 1.01 - 1.25), but not with rule-breaking, psychological aggression, and total antisocial behaviors. No significant 2- or 3-way interactions were found between childhood family violence, inflammatory markers, and gender in predicting antisocial behavior. Further longitudinal research is needed to understand the biological mechanisms underlying antisocial behaviors and the significant implications of childhood family violence exposure for youth antisocial behavior prevention.

Childhood exposure to violence as a predictor of co-occurring suicidal ideation and violent behavior Melissa Tracy* Melissa Tracy Jennifer Amoh Laura Hunter

The co-occurrence of self-harm and harm towards others is under-recognized yet associated with adverse long-term outcomes and specific treatment needs. We used prospectively collected data from the Avon Longitudinal Study of Parents and Children (ALSPAC) to examine co-occurring self-reported suicidal ideation (i.e., thoughts of self-harm) and physical fighting (i.e., hitting, kicking, or punching someone with the intention of hurting them) at age 18. Among 3,159 young adults, 10.6% and 7.3% reported suicidal ideation and physical fighting, respectively, and 1.0% reported both. Overall, 9.6% of boys and 21.3% of girls who reported physical fighting also reported suicidal ideation. We used multinomial logistic regression to evaluate relations between childhood exposure to maltreatment, intimate partner violence (IPV), and pro-violence attitudes and suicidal ideation alone, physical fighting alone, or both (compared to neither and adjusted for child sex and race). Maternal physical or emotional IPV at ages 0-9 years was associated with suicidal ideation alone (OR=1.52, 95% CI=1.12-2.05). Pro-violence attitudes (assessed at age 12 years) were associated with suicidal ideation alone (OR=1.04, 95% CI=1.02-1.06), physical fighting alone (OR=1.10, 95% CI=1.07-1.13), and co-occurring suicidal ideation and physical fighting (OR=1.06, 95% CI=1.00-1.13). Non-white young adults had considerably higher odds than whites of reporting both suicidal ideation and physical fighting (OR=4.46, 95% CI=1.66-12.01). Child physical or emotional abuse, reported by mothers at ages 0-9 years, was not associated with the outcome. These results indicate that the development of pro-violence attitudes by age 12 may reflect increased risk for suicidal ideation and interpersonal violence in early adulthood. Further, suicidal ideation is fairly common among young adults who are engaging in interpersonal violence, representing an opportunity for intervention, particularly among racial minority girls.

Adverse childhood experiences and sleep quality trajectories from adolescence to adulthood Chighaf Bakour* Chighaf Bakour Jill Desch Fahad Mansuri Skai W Schwartz

Introduction Adverse childhood experiences (ACEs) are traumatic events that occur prior to the 18th birthday, and are associated with negative health outcomes across the lifespan. This study examines the association between specific ACEs and the number of ACEs and sleep quality trajectories from adolescence to adulthood.

Methods: Using data from the National Longitudinal Study of Adolescent to Adult Health, we constructed trajectories of average sleep quality scores, measured by reported trouble falling asleep or staying asleep (0=rarely or never, 1=sometimes, 2=frequently) in waves 1 (age 12-18), 2 (age 13-18), 4 (age 24-32), and 5 (age 33-43). We used weighted logistic regression to calculate odds ratios and confidence intervals for each of ten ACEs and the number of ACEs, and trajectories of sleep quality scores after adjusting for relevant confounders.

Results: The analysis included 12,768 participants, 75.3% of whom experienced at least one ACE, including 14.7% who experienced 4 or more. We identified three distinct sleep quality trajectory groups from Wave 1-5: consistently good (Group 1), worsening (Group 2), and consistently poor (Group 3). Abuse (physical, emotional, or sexual), neglect, parental divorce, and foster home placement were significantly associated with trajectory Groups 2 and 3 versus Group 1. Additionally, parental incarceration, parental alcoholism, and community violence were associated with Group 3 vs Group 1. The number of ACEs showed a dose-response association with Group 3 vs 1 [aORs for 1 ACE=1.32 (1.05 , 1.66); 2-3 ACEs= 2.21 (1.74 , 2.81); 4+ ACEs= 3.92 (2.72 , 5.65)], and Group 2 vs 1 [aORs for 1 ACE= 0.98 (0.81 , 1.18); 2-3 ACEs =1.27 (1.08 , 1.48); 4+ ACEs=1.60 (1.27 , 2.01)].

Conclusion: ACEs can have a lasting impact on sleep quality from adolescence to adulthood, highlighting the need to mitigate their impact to prevent negative health outcomes associated with sleep disturbances.

Positive associations between IPV victimization in male couples and outside sexual partnerships during the COVID-19 pandemic Alison Walsh* Alison Walsh Rob

Social distancing measures during the 2020 COVID19 pandemic have the potential to increase intimate partner violence (IPV). However, it is unknown if gay, bisexual, and other men who have sex with men (GBMSM) have experienced increased intimate partner violence (IPV) risk at this time. This study explored and analyzed IPV experiences during the COVID-19 pandemic in a sample of coupled GBMSM in the United States (US). We hypothesized that pandemic-related stressors would be associated with increased IPV prevalence and severity. A sample of 214 coupled men in long-term partnerships (>6 months) in the US were surveyed July-September 2020. Participants reported demographic, sexual activity, substance use, relationship characteristics, and pandemic-related life changes (employment, COVID19 illness). IPV victimization and perpetration were measured with the IPV-GBM scale, which assesses individually experienced or perpetrated violence, sexual, emotional, monitoring, or controlling behaviors, and if behaviors were new and/or had changed in frequency during the pandemic. Reported prevalence and pandemic-related changes in victimization and perpetration were described. New or more frequent IPV victimization was modeled using logistic regression against employment, substance use changes, COVID19 illness, and changes in numbers of outside sexual partners during the pandemic. IPV perpetration prevalence was 15.13%, 34.44% of which was new or more frequent. Victimization prevalence was 14.95%, of which 46.88% was new or more frequent. After adjustment for sociodemographics, only changes in outside sexual partners was associated with IPV; for each additional outside sexual partner the odds of new or more frequent victimization increased by 94% (Odds ratio (95% CI): 1.94 (1.08, 3.47)). Additional research into IPV predictors, interventions, and support strategies during the pandemic in these populations are warranted.

Violence Victimization Impacts Experiences of Suicidal Ideation Among Adolescents with Depression -A Retrospective Cohort Study Jing Wang* Jing Wang Shannon Harrer Marissa L Zwald Ruth W Leemis Kristin Holland Deborah Stone Kathleen McDavid Harrison Elizabeth Swedo

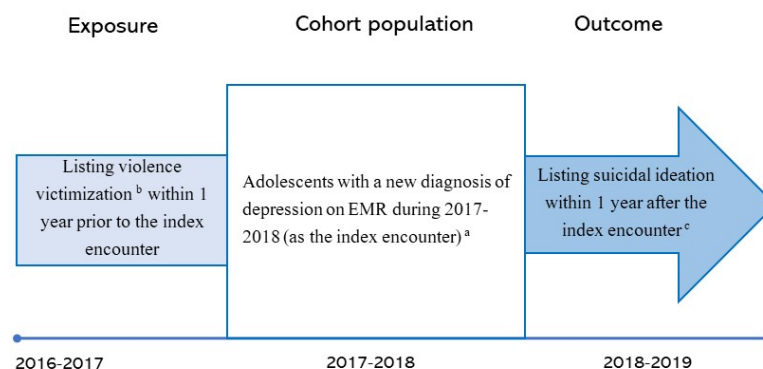
Research suggests that patients who experience childhood violence have a distinct course of depression (i.e., earlier onset, more episodes) compared to those without this exposure, but less is known about how this violence influences risk of suicidal ideation among persons with depression.

Using the IBM® Explorys® Electronic Health Record Database, which covers 18% of the U.S. population, we followed a cohort of adolescents up to one year after first listing a diagnosis of depression during 2017-2018 (n= 24,363), to identify a diagnosis of suicidal ideation. The exposure group comprised patients with documented violence victimization including child maltreatment or physical assault in the year prior to depression diagnosis (n=400) (Figure). We conducted logistic regression, adjusting for demographic characteristics, insurance type, substance use, and other mental illness, to assess the risk of suicidal ideation associated with violence victimization among adolescents with depression.

Overall, following a depression diagnosis, 14.8% of adolescents had documented suicidal ideation within a year—70% of whom experienced the outcome within 1-month post-depression diagnosis. Suicidal ideation was more common among individuals with documented victimization (31.5%) compared to those without (14.5%). After adjusting for covariates, adolescents with depression who had experienced violence in the year prior compared to those who had not had two times the odds of suicidal ideation (adjusted OR: 2.2, 95% CI: 1.7, 2.8).

Our study demonstrates that a history of victimization is associated with greatly increased odds for suicidal ideation among adolescents with depression. Accounting for past experiences of violence is a critical component of depression management in adolescents with implications for treatment and suicide risk assessment. Ultimately, primary violence prevention strategies have the potential to prevent later excessive morbidity from depression and suicidal ideation.

Figure. The Study Design of the Cohort



Data source: IBM® Explorys® Electronic Health Record Database

All conditions were defined by ICD-10-CM codes

^a: As depression can be recurrent, a new diagnosis of depression was defined as without listing depression during 1 year prior to 2017-2018, which might indicate a new incidence or new episode of depression.

^b: Violence victimization included child maltreatment (i.e. child physical, sexual, or mental abuse or neglect) or physical assault

^c: Patients listing suicidal ideation during 1 year prior to depression diagnosis were excluded from the cohort

The joint role of firearm and alcohol availability in intention firearm injury Veronica Pear*
Veronica Pear Garen Wintemute Jennifer Ahern

Individual and ecologic studies have found firearm access and alcohol use to be important risk factors for firearm homicide and suicide. We examined the association of community-level firearm and alcohol availability with individual-level risk of firearm injury and explored additive interactions between these exposures.

We conducted 2 nested case-control studies of California residents, 2005-2015; one of all firearm assaults and the other of all self-directed firearm injuries. Controls were randomly sampled from the remaining state population at each month at a 4:1 ratio with cases. We used case-control weighted G-computation to estimate individual and joint associations of firearm availability (measured as county firearm dealer density or sales density) and alcohol availability (ZIP code alcohol outlet density) with risk of firearm injury. We estimated the overall risk difference (RD) comparing outcomes when the exposures were set to high vs. low density. Models were adjusted for potential confounders and included splines and interactions, as appropriate.

Our final N was 335,972 in the assault study and 84,356 in the self-harm study. The RD for the joint association of firearm dealer and alcohol outlet density with risk of firearm assault was 0.06 injuries per 100,000 (95% CI: 0.02, 0.10), driven primarily by non-pawn dealers and off-premise alcohol outlets. The corresponding estimate for firearm self-harm was more modest (RD: 0.02; 95% CI: 0.01, 0.03) and was driven by non-pawn dealers and bars/pubs. Measuring firearm availability with sales yielded similar results for assault (RD: 0.05; 95% CI: 0.01, 0.10) but stronger results for self-harm (RD: 0.06; 95% CI: 0.03, 0.09). We did not find evidence of additive interactions.

Community-level firearm and alcohol availability are jointly associated with individual risk of firearm injury, but there is not synergy between them. Communities may consider reducing firearm and alcohol availability through zoning or other means.

Association between Autism Spectrum Disorder and Intentional Self-Harm in Children

Guohua Li* Guohua Li Stanford Chihuri Ashley Blanchard Carolyn DiGuseppi

Autism spectrum disorder (ASD) is a neurodevelopmental condition characterized by persistent challenges in social interactions and restricted, repetitive patterns of behavior and interests. The reported prevalence of ASD in the United States has more than doubled in the past two decades. Recent studies indicate that ASD is associated with increased morbidity and mortality from certain types of injuries, such as drowning, suffocation and asphyxiation. There is also mounting evidence that people with ASD are at heightened risk of intentional self-harm (ISH). We assessed the association of ASD with ISH treated in emergency departments among children aged 1-20 years, using data from the 2018 Nationwide Emergency Department Sample (NEDS). NEDS is the largest all-payer emergency department (ED) database in the United States. ISH cases were identified according to the ICD-10-CM external cause-of-injury matrix. The 2018 NEDS recorded a total of 129,400 ED visits for ISH in children aged 1-20 years. ISH accounted for 3.12% (1570 out of 50,334) of the visits made by children with ASD and 1.71% (127,830 out of 7,458,827) of the visits made by those without ASD, yielding a crude odds ratio (OR) of 1.85 [95% confidence interval (CI): 1.76, 1.94]. Compared to children without ASD, intellectual disability and attention deficit hyperactivity disorder (ID/ADHD), the estimated ORs of being treated for ISH were 1.69 (95% CI: 1.60, 1.79) for children with ASD and without ID/ADHD, 3.34 (95% CI: 3.25, 3.43) for children with ID/ADHD and without ASD, and 2.99 (95% CI: 2.70, 3.30) for children with ASD and ID/ADHD. The estimated ORs of ISH associated with ASD were similar across age groups and between sexes. Results from weighted analysis were consistent with those from unweighted analysis. These findings suggest that ASD is associated with a significantly increased risk of ISH and that comorbid ID/ADHD can explain only part of the excess risk of ISH in children with ASD.

Stretching for rehabilitation of muscle injuries: a systematic review Chinchin Wang* Chinchin Wang Nikki Rommers Ian Shrier

Background: Although stretching is common in injury rehabilitation programs, it is unclear if the benefits of stretching injured muscle outweigh the risks. Stretching increases range of motion, which might promote healing and protect against subsequent injury (injury to the same or different body part). However, it also reduces pain, which could mask symptoms resulting in new or further damage. Excessive stretching might prevent muscle regeneration or cause further damage.

Objective: The objective of this study is to summarise the evidence on whether stretching an injured muscle within a rehabilitation program alters risk of subsequent injury and time for return to full activity in adult and youth athletes.

Methods: We searched the MEDLINE, EMBASE, Cochrane Library, CINAHL, SPORTdiscus databases using terms related to muscle, injury, stretching, and rehabilitation. Inclusion criteria were: participants with muscle injury; intervention program that focused on stretching; and assessed subsequent injury or return to full activity as an outcome. Since only randomized trials were found, risk of bias was assessed using the Cochrane RoB-2 tool.

Results: We identified 4 randomized trials with 24 to 80 participants (total 235 participants). Interventions were heterogenous, and studies only assessed injuries to the same body part. All studies were of some concern or high risk of bias. In 2 of 3 studies that assessed subsequent injury, there were only 1-2 injuries in the entire study. In the third study, 7 injuries occurred in 11 stretching participants and 1 in 13 non-stretching participants. Of the studies that measured time for return to activity, participants who stretched returned sooner in 3 studies (2, 23 and 37 days), and later in 1 study (15 days).

Conclusion: There is limited evidence examining the role of stretching in injury rehabilitation. Future studies should compare stretching within a rehabilitation program against the same program without stretching.

Clinician-diagnosed injury risk increases minimally with increases in activity Chinchin

Wang* Chinchin Wang Tyrel Stokes Russell Steele Jay Kaufman Ian Shrier

Background: Limited research exists on the association between changes in activity levels and injury in children. The relationship between changes in activity and injury has been evaluated in adults using the acute:chronic workload ratio (ACWR), a ratio of recent to past activity. ACWR-based analyses in adults have generally predicted higher injury risks as $ACWR > 1$ (increasing activity) relative to $ACWR = 1$ (no change in activity), and varying relationships as $ACWR < 1$ (decreasing activity). Most of these analyses employed generalized linear models. Using generalized additive models, we previously predicted minimal increases in risk of self-reported musculoskeletal pain in children over a large range of ACWR. This relationship may vary depending on how injury is defined.

Objective: To assess the predictive relationship between the ACWR and clinician-diagnosed injury in children.

Methods: Using prospective data from 1670 Danish children collected over 5.5 years, we calculated ACWRs as a ratio of activity frequency in the index week to the weekly average activity frequency in the previous 4 weeks. We modelled the relationship between ACWR and clinician-diagnosed injury in the index week using generalized linear and additive mixed models (GLMM and GAMM) with a random intercept for individuals and assessed model fit using Akaike information criteria (AIC).

Results: The GAMM fit slightly better than the GLMM (AIC: 24,548 vs. 24,578). While the GLMM predicted exponentially increasing injury risk as $ACWR > 1$ and minimal differences in injury risk as $ACWR < 1$, the GAMM predicted minimal increases in injury risk as $ACWR > 1$ and few events.

Conclusion: Increases in activity of up to 2-fold predict modest increases in injury risk in children, while decreases in activity predict decreases in injury risk.

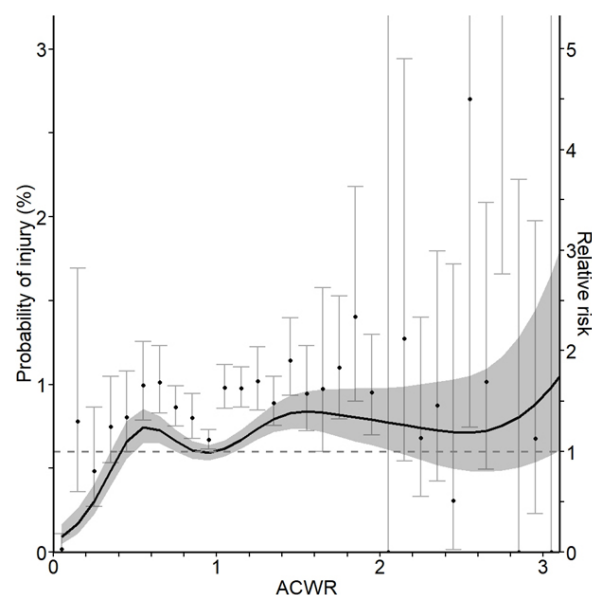


Figure 1. Generalized additive mixed model for the relationship between the acute:chronic workload ratio (ACWR) and clinician-diagnosed injury in children. Line represent model with 95% CI in shaded areas. Horizontal dashed line represents risk of injury at $ACWR = 1$, with relative risk versus $ACWR = 1$ shown on right y-axis. Points represent observed probability of injury with 95% CI at ACWRs discretized to 0.1, not accounting for repeated measures. The ACWR range (x-axis) is restricted to ≤ 3 for clarity.

COVID-19 Pandemic and Violence: Rising risks and decreasing urgent care-seeking for sexual assault and domestic violence survivors Katherine Muldoon* Katherine Muldoon Kathryn Denize Robert Talarico Deshayne Fell Agnes Sobiesiak Melissa Heimerl Kari Sampsel

Background: There is little information on care-seeking patterns for sexual assault and domestic violence during the COVID-19 pandemic. The objective of this study was to examine the changes in emergency departments (ED) admissions for sexual assault and domestic violence since the COVID-19 pandemic was declared.

Methods: Observational ED admissions data from The Ottawa Hospital were analyzed from March 4th to May 5th (62 days) in 2020 (COVID-19 period) and compared to the same period in 2018 (pre-COVID-19). Total and mean weekly admissions were calculated for all-cause ED admissions and for sexual and domestic violence cases. A Poisson regression (without offset term) was used to calculate the weekly case count ratio and 95% CI between the two time periods. Case characteristics were compared using Chi-square tests and percent differences were calculated

Results: Compared to pre-COVID-19, total ED admissions dropped by 1111.22 cases per week (32.9% reduction), and the Sexual Assault and Domestic Violence Program cases dropped 4.66 cases per week. The weekly case count ratio for sexual assault cases was 0.47 (95% CI:0.79-0.27), equivalent of 53.49% reduction in cases, and 0.52 (95% CI:0.93-0.29), equivalent to a 48.45% reduction in physical assault cases. The characteristics of presenting cases were similar by age (median 25 years), and sex (88.57% female), assault type (57.14% sexual assault, 48.57% physical assault) and location (31.43% patient's home, 40.00% assailant's home). There was a significant increase in psychological abuse (11.69% vs 28.57%) and assaults occurring outdoors (5.19% vs 22.86%).

Conclusion: This study found a decrease in ED admissions for sexual assault and domestic violence during COVID-19, despite societal conditions that elevate risk of violence. Trends in care-seeking and assault patterns will require ongoing monitoring to inform the provision of optimal support, particularly as countries begin to re-open or lock-down again.

COVID-19 and Perinatal Intimate Partner Violence: A cross-sectional survey of pregnant and post-partum individuals in the early stages of the COVID-19 pandemic Katherine Muldoon* Katherine Muldoon Kathryn Denize Robert Talarico Carlie Boisvert Olivia Frank Alysha Harvey Ruth Rennicks-White Deshayne Fell Meagan-Ann O'Hare-Gordon Yanfang Guo Malia Murphy Daniel Corsi Kari Sampsel Shi-Wu Wen Mark Walker Darine El-Chaâr

Background: The COVID-19 pandemic has caused extreme societal stress and concern for rising risk of intimate partner violence (IPV). This study was designed to investigate the prevalence, patterns and risk factors for perinatal IPV among those who gave birth since COVID-19 began.

Methods: We conducted a cross-sectional survey of patients who gave birth at The Ottawa Hospital and were >20 days post-partum between March 17th-June 16th 2020. Perinatal IPV was defined as psychological, physical, and/or sexual abuse in the 12 months pre-pregnancy, during pregnancy or post-partum. Log-binomial multivariable regression models were used to compute adjusted risk ratios (aRR) and 95% CI to quantify relationships with potential risk factors for IPV: maternal age, parity, household income, post-partum depression, and increase in partner substance use.

Results: Of 1568 patients who gave birth during the study period, 572 were contacted, 261 completed the survey and 216 had complete data for analyses. Median maternal age was 33 years (IQR: 30-36) and median infant age was 76 days (IQR: 66-90). In total, 52 (24.1%) reported perinatal IPV: 37 (17.1%) had controlling partners; 13 (6.0%) reported abuse in the 12 months pre-pregnancy, 11 (5.1%) during pregnancy, and 15 (6.9%) post-partum. Household income below the municipal median was the strongest risk factor for any IPV (aRR: 3.24, 95% CI: 1.87-5.59). There was no apparent association between maternal age (aRR: 0.99, 95% CI: 0.94-1.04), nulliparity (aRR: 1.18, 95% CI: 0.71-1.97), post-partum depression (aRR: 1.03, 95% CI: 1.00-1.07), or partner substance use increase since COVID-19 began (aRR: 0.73, 95% CI: 0.42-1.25) with IPV.

Conclusion: A quarter of our study population experienced perinatal IPV. Household income was the strongest risk factor for perinatal IPV, and surprisingly, many hypothesized risk factors (e.g., mental health, increased partner substance use etc.) were not associated with perinatal IPV in this sample.

Criminal offense importance for predicting violent crime among handgun purchasers in California. Aaron Shev* Aaron Shev Rose Kagawa Mona Wright Garen Wintemute

Firearm violence is a serious public health and safety concern in the United States causing nearly 40,000 deaths in 2018 alone. Previous studies have identified handgun owners with arrests and convictions for misdemeanors as being associated with an increased risk for committing future violent crimes. Prohibiting the purchase of firearms by those with a particularly high risk of future criminal activity is a widely accepted policy for reducing rates of violent crime. In this retrospective longitudinal cohort study, we conduct a variable importance analysis to determine the relative importance of classes of offenses in predicting an outcome of future violence. The data comprises the criminal histories of 79,678 adults, between the ages of 21 and 49, from their first handgun purchase in California in 2001 through 2013. All offenses were classified according to the Uniform Crime Reporting (UCR) Handbook. We used boosted cox proportional hazards regression trees to carry out the analysis. Our preliminary model determined assaults, weapon crimes, theft and drug abuse to be among the most important UCR classes for predicting future violence for handgun purchasers in California. Identifying specific UCR classes associated with a high risk of violence may provide candidates for firearm purchasing prohibitions effective at reducing violent crime.

Associations between adverse experiences and eating behaviors: Findings from EAT 2018

Cynthia Yoon* Cynthia Yoon Rebecca L. Emery Vivienne M. Hazzard Susan M. Mason Dianne Neumark-Sztainer

Background

Adverse experiences include childhood abuse, intimate partner violence, being attacked, beaten, or mugged, and other victimization experiences. However, the extent to which distinct adverse experiences are associated with adaptive and maladaptive eating behaviors remains unclear.

Purpose

This study aimed to examine the extent to which adverse experiences are associated with adaptive eating (i.e., intuitive and mindful eating) and maladaptive eating (i.e., overeating and binge eating) by gender.

Methods

The data were derived from a population-based study, EAT-2018: Eating and Activity over Time (N=1411, aged 18-30 years in 2017-2018). Linear regressions were used to examine the associations between adverse experiences and adaptive eating (intuitive and mindful eating). Modified Poisson regressions were used to estimate prevalence ratios (PRs) for associations between adverse experiences and maladaptive eating (overeating and binge eating).

Results

Depending on the type of adverse experience, prevalence ranged from 2.6% to 29.4%. Each adverse experience was negatively associated with adaptive eating and positively associated with maladaptive eating. The strongest correlate of lower intuitive eating score was intimate partner physical violence among men ($\beta=-0.57$, [95% CI= -0.90, -0.24]) and being attacked, beaten, or mugged among women ($\beta=-0.50$, [95% CI=-0.77, -0.23]). Regarding lower mindful eating score, the strongest correlate was childhood emotional abuse ($\beta=-0.75$, [95% CI=-1.04, -0.46]) among men and intimate partner sexual violence ($\beta=-0.58$, [95% CI=-0.82, -0.34]) among women. Regarding overeating and binge eating, the strongest correlate was being attacked, beaten, or mugged among men (PRs=2.05 and 3.22, respectively) and intimate partner sexual violence among women (PRs=2.08 and 2.43, respectively).

Conclusion

To adopt adaptive eating and prevent maladaptive eating, public health efforts should consider the contribution of adverse experiences.

LATEBREAKER

Injuries/Violence

Risk of falls and injuries among low and high functioning people with lower limb loss

Christopher Wong* Stanford Chihuri Christopher Wong Gregory Youdan

People with lower limb loss are at high risk for low function. Most never reach the independent community walking level, annual fall incidence is >50%, and injury risk is higher compared to other at-risk populations. However, low functioning people with limb loss paradoxically fall less often and incur fewer injuries than higher functioning people. Low functioning people may be physically inactive and thus exposed to less risk. In the present longitudinal study, we assessed whether fall and injury incidence per step-count varied by functional status in a small cohort of people with unilateral lower limb loss. Self-reported fall and injury data were collected at baseline and at 4 monthly follow-up periods. Functional status was operationalized as high if a participant was an independent community walker defined by Houghton prosthetic use scale scores ≥ 9 and low if a participant was a limited community walker defined by scores ≤ 8 . Step count data were collected from StepWatch4 monitors attached to each participant's prosthesis during the study. Generalized estimating equations using the Poisson distribution and the log of step count as an offset were used to assess the incidence rate ratio for falls and injuries by functional status. Overall, 10 participants aged 26-63 years (mean=49.9) were included. At baseline, 7 were high- and 3 were low-functioning, 3 were female, 7 had transtibial amputations, and 8 had vascular etiology. The high functional group had 4 falls and 5 injuries while the low functioning group had 3 falls and 3 injuries. Compared to high functional status, low functional status was associated with increased risk of falls (estimated incidence rate ratio (IRR) 6.10, 95% confidence interval (CI) 1.06-35.19), and injuries (IRR=27.23, 95%CI=8.91-83.17). Results of this study show that although low functioning people fall less and incur fewer injuries, they are at an increased risk of falls and injuries when exposure to risk is considered.

LATEBREAKER

Injuries/Violence

Homicide during pregnancy and the postpartum period in the United States, 2018 Maeve Wallace* Maeve Wallace Veronica Gillispie-Bell Kelly Davis Dovile Vilda Kiara Cruz

Objective: Despite evidence from sub-national geographies repeatedly finding that homicide is a leading cause of death during pregnancy and the postpartum period, national prevalence of pregnancy-associated homicide has never been reported. Our objectives were to report, for the first time, a national pregnancy-associated homicide mortality ratio, characterize victims, and compare risk of homicide between women and girls in the perinatal period (pregnancy and up to 1 year postpartum) and non-pregnant, non-postpartum women and girls of reproductive age.

Design: This study is a retrospective analysis of the National Center for Health Statistics 2018 maternal mortality file, which includes death records for all persons in the United States. Cases of pregnancy-associated homicide, were those with an underlying cause of death International Classification of Diseases, 10th revision code for assault (X85-Y09) or a manner of death indicating homicide.

Results: There were 3.3 homicides per 100,000 live births among women who were pregnant or within 1 year postpartum in 2018. Maternal homicide exceeded all of the leading causes of pregnancy-related mortality by more than two-fold. Prevalence was highest among non-Hispanic Black women (11.94 deaths per 100,000 live births) and women under age 25 (6.05 deaths per 100,000 live births). Homicide risk was heightened among non-Hispanic Black women and women under age 25 who were pregnant or within 1 year postpartum compared to their non-pregnant, non-postpartum counterparts (RR among non-Hispanic Black women=1.42, 95% CI=1.11, 1.82, P<0.05; RR among women under age 25=2.52, 95% CI=1.92, 3.32, P<0.05).

Conclusions: Homicide is a leading cause of death during pregnancy and the postpartum period in the United States. Black women and women under age 25 in the perinatal period are especially at risk. Research is needed to identify effective practice and policy interventions to prevent future deaths.

Genetically predicted sex hormone binding globulin and ischemic heart disease in men and women: a Mendelian randomization study Jie Zhao* Jie Zhao C Mary Schooling

Background: Ischemic heart disease (IHD) is a leading contributor to global burden of disease. Men are more vulnerable to IHD than women, which could be partly due to testosterone. Correspondingly, sex hormone binding globulin (SHBG) which lowers circulating testosterone might protect men against IHD. SHBG may also affect IHD independent of testosterone.

Objectives: To assess the sex-specific role of SHBG in IHD and its role independent of testosterone.

Methods: In univariable Mendelian randomization (MR), we used sex-specific, genome-wide significant genetic variants (343 for men and 328 for women) to predict SHBG, and examined their association with IHD (25,409 cases in men and 12,511 cases in women) in the UK Biobank. We also replicated using genetic instruments from Japanese men and applied to Biobank Japan. To assess the role of SHBG independent of testosterone in men, we used multivariable MR controlling for testosterone, additionally including 125 SNPs for bioavailable testosterone.

Results: Genetically predicted SHBG was associated with lower IHD risk in men (odds ratio (OR) 0.77 per standard deviation, 95% confidence interval (CI) 0.69 to 0.87), but not in women. The estimates were robust to different genetic instruments and similar in Japanese. The inverse association remained after controlling for testosterone in men (OR 0.78, 95% CI 0.70 to 0.87).

Conclusions: SHBG might lower the risk of IHD in men, with a role independent of testosterone. Exploring intervention strategies that increase SHBG and understanding the underlying pathways is important for targeting IHD treatments to take account of sex disparity.

Does having positive coping skills mediate the relationship between sense of community belonging and positive mental health among youth? Findings from a Canadian population-based Survey Salima Kerai* Salima Kerai Mohammad Ehsanul Karim Eva Oberle

Sense of community belonging and positive coping skills are two distinct assets known to contribute to positive mental health in youth. Still, the causal mechanisms by which these two assets may shape youth mental health are not well investigated in the literature. This research aimed to assess the mediating role of positive coping skills in the relationship between community belonging and youth mental health and whether race/cultural group moderates this relationship. Using the 2012 Canadian Community Health—Mental Health survey, we analyzed data on youth (15-29 years, n = 5338) to investigate the above questions. We used the causal mediation analysis based on the counterfactual framework via a weighting approach. We decomposed the total effect of community belonging on youth mental health into natural direct and natural indirect effects through positive coping skills. After controlling for potential confounders, we reported the adjusted odds ratio (OR), 95% bootstrap confidence interval, and the proportion mediated. The natural direct effect from community belonging to youth mental health was OR 2.5 (95% CI 2.1-3.2), and the natural indirect effect through positive coping was OR 1.2 (95% CI 1.1-1.3) – mediating 13.9% (95% CI 6.1-23.8%) of the total effect. There was evidence of effect modification by race/cultural grouping: for youth identifying as Aboriginal or as a visible minority, there was a higher natural direct effect (OR 3.8 3.8; 95% 2.6-6.3) compared to youth identifying as European Canadians (OR 2.1; 95% 1.7-2.9), but a smaller proportion mediated through positive coping skills (9.5% versus 16.9% respectively). Our findings suggest that part of the association between community belonging on positive mental health in youth can be explained through enhanced positive coping skills, with results differing across race/cultural groups. The present findings can inform interventions and programs for youth's mental health promotion.

The politics of depression: Diverging trends in internalizing symptoms among US adolescents by political beliefs Catherine Gimbrone* Catherine Gimbrone Lisa M. Bates Seth J. Prins Katherine M. Keyes

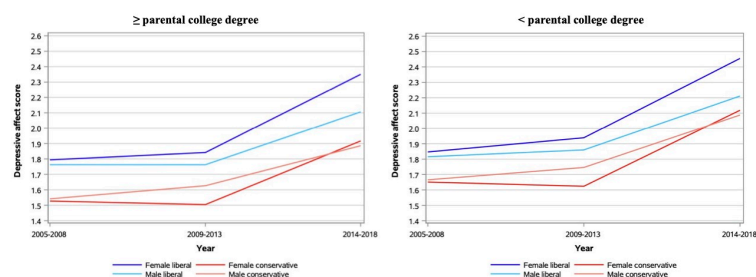
Background. Adolescent internalizing symptoms (e.g. depressive affect) have increased over the past decade in the US, particularly among girls. The reasons for these increases are unclear. We hypothesize that increasing political polarization has contributed to these trends in adolescent internalizing symptoms, and that the impact of the overall political climate may be differential by adolescent political beliefs and sociodemographic characteristics.

Methods. We analyzed nationally-representative data from 2005-2018 Monitoring the Future annual cross-sectional samples of 12th-graders (N = 86,138). We examined self-reported political beliefs, sex, and parental education as predictors of four internalizing symptom scales over time, including depressive affect.

Results. From 2005-2018, 19.8% of students identified as liberal and 18.1% identified as conservative, with little change in prevalence over time. Depressive affect (DA) scores increased for all adolescents after 2010, but increases were most pronounced for female liberals (β for interaction = 0.17, 95% CI: 0.01, 0.32), and scores were highest overall for female liberals with low parental education (Mean DA 2010: 2.02, SD 0.81 / 2018: 2.75, SD 0.92). Findings were consistent across multiple internalizing symptoms outcomes.

Conclusions. Trends in adolescent internalizing symptoms diverged by political beliefs, sex, and parental education over time, with female liberals experiencing the largest increases in depressive symptoms, especially in the context of demographic risk factors including parental education. These findings indicate a growing mental health disparity between adolescents who identify with certain political beliefs. It is therefore possible that the increasingly polarized political climate over the study period differentially affected adolescent wellbeing.

Figure. Linear regression predicted mean main effects of political beliefs on depressive affect by sex and parental education: Conservative and liberal 12th-graders from 2005 - 2018



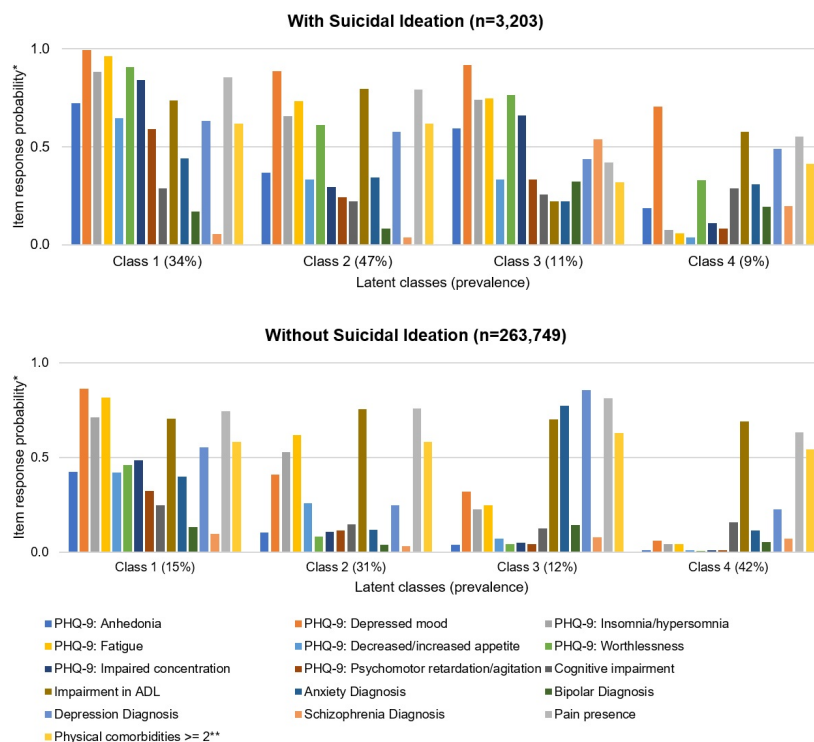
Linear regression predictions graphed. All models were adjusted for geographic region, urbanicity, race, and GPA.

Working-age adults at nursing home admission and suicidal ideation: a latent class

analysis Yiyang Yuan* Yiyang Yuan Julie Hugunin Anthony J. Rothschild Kate L. Lapane Christine M. Ulbricht

Working-age adults (22-64 years) comprise 16% of the U.S. nursing home (NH) population. Despite having many suicide risk factors, little is known about suicidal ideation among these residents. We conducted a latent class analysis (LCA) to describe patterns of well-being indicators and examined if patterns differed by the presence of ideation at admission. Using the national Minimum Data Set 3.0, we identified 266,952 working-age adults newly admitted to NHs in 2015. At admission, 1.2% had ideation, defined by a positive 9th item of the Patient Health Questionnaire (PHQ-9). LCA was conducted with binary indicators of the first 8 PHQ-9 items, dependency in activities of daily living, cognitive impairment, psychiatric diagnoses, pain presence, and ≥ 2 physical comorbidities. LCA models of 4 classes were determined for both groups but classes differed within and between those with and without ideation primarily by PHQ-9 items and diagnoses (Figure 1). For residents with ideation, those in Class 1 (34% of residents with ideation) had high probabilities of all PHQ-9 items while those in Class 2 (47%) had high probabilities of depressed mood, sleep problems, fatigue and feeling worthless. Class 3 (11%) members had high probabilities of having schizophrenia and all PHQ-9 items except the appetite item. For those without ideation, Class 3 members (12% of residents without ideation) had high probabilities of depression and anxiety disorder diagnoses but low probabilities of any PHQ-9 item. Those in Class 4 (42%) were unlikely to endorse any PHQ-9 item. These findings highlight differences in patterns of well-being indicators between working-age residents with and without ideation and emphasize the importance of not relying solely on psychiatric symptoms and diagnoses for identifying suicidal ideation. Additional research is needed to examine demographic and clinical characteristics associated with these classes and validate models to improve suicide prevention in this setting.

Figure 1. Latent class prevalence and item response probabilities in working-age adults in U.S. nursing homes, by suicidal ideation



Note.
 * Probability of endorsing the given binary item based on the latent class model. An item response probability >0.5 would indicate that residents belonging to this class would have higher probability to experience the given item.
 ** Included diagnosis of arthritis, diabetes mellitus, hypertension, cancer, cerebrovascular accident/transient ischemic attack/stroke, heart failure, asthma, hip fracture, other fracture, pneumonia, seizure disorder/epilepsy, and traumatic brain injury.

Polytrauma typologies: exploring general population and trauma-exposed population profiles Sabrina Hermosilla* Sabrina Hermosilla Karmel Choi Melanie Askari Taylor Marks

Background: Exposure to potentially traumatic events (PTE) is highly prevalent. Individuals may experience specific profiles of PTE exposure that could influence the onset and development of psychiatric disorders, and profiles may differ between population-based studies and trauma-exposed populations.

Methods: We conducted latent class analyses (LCA) on self-reported PTE data from 10,714 adult individuals from the Chitwan Valley Family Study, interviewed with the Nepali World Mental Health version of the Composite International Diagnostic Interview (WMH-CIDI 3.0) from 2016 to 2018. LCA solutions based on 29 candidate PTE items (e.g., loss of a loved one) for the full sample were compared to LCA solutions for the subsample exposed to at least one PTE.

Results: Individuals had experienced on average 2.0 (0-13) PTE in their lifetimes. A six-class solution was the best fit for PTE patterns in both the population-based ((n=10,714) sample and the trauma-exposed (n=9,219) sub-sample, however the specific make-up of the classes and profiles differed between the two. Across both samples there were classes reflecting exposure to natural disaster, accident, and illness. The remaining classes for the population-based sample included classes reflecting exposure to death, physical assault, or low trauma exposure. The remaining classes for the trauma-restricted subpopulation included those with predominant exposure to death (unexpected), death (witnessed), and violence.

Conclusions: Individuals experience distinct patterns of PTE and this differs if explored through a population-based sample or a PTE-restricted subsample. Future population-based studies seeking to identify and validate classes based on exposure to maltreatment or PTE should also conduct a sub-analysis restricting to only PTE-exposed individuals to ensure comparability across the literature. Further exploration of the predictive power of polytraumatization classes on subsequent mental health outcomes is warranted.

Predictors of any mental health disorder and major depressive disorder among adolescents and young adults in the Nepal Chitwan Valley Family Study, 2016-2018 Sabrina Herмосilla*
Sabrina Herмосilla Melanie Askari Taylor Marks

Background: Among youth in low-income countries, predictors of psychiatric disorders are understudied.

Methods: We used data from the individual World Mental Health version of the Composite International Diagnostic Interview (3.0) interview in the Nepal Chitwan Valley Family Study 2016-2018 to estimate individual (ethnicity, age, gender, marital status, self-rated health status) and community (violence, distance <15-minute walk to health services and schools) predictors of lifetime and past-year prevalence of any measured mental health disorder (MHD) (alcohol use disorder, abuse, dependence; anxiety; depression (MDD); or bipolar disorders) and MDD through generalized linear models (logit link), accounting for neighborhood clustering.

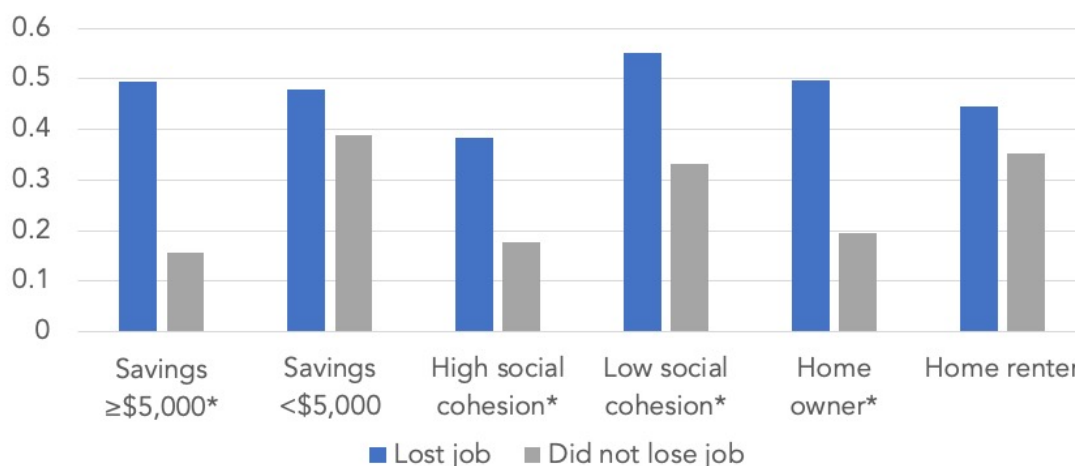
Results: Within the sample (n=3,221), past-year MHD and MDD (past-year and lifetime) was low (5.0%-2.1%, 8.9% lifetime), while 22.7% reported any lifetime MHD. Low caste ethnicity (adjusted odds ratio [aOR]=1.60, 95% CI: 1.04-2.48) increased odds of any past-year MHD, whereas access to schools decreased odds of any past-year MHD (aOR=0.44, 95% CI=0.25-0.78) and any past-year MDD (aOR= 0.36, 95% CI= 0.19-0.68). Separated/divorced/widowed marital status increased odds of past-year any MHD (aOR=10.95, 95% CI= 4.83-24.82) and MDD (aOR= 12.76, 95% CI= 5.65, 28.80). For each year increase in age, odds of any lifetime MHD and MDD increased (e.g., any MHD: aOR= 1.11, 95% CI= 1.06-1.17) but access to schools did not alter lifetime prevalence of any MHD (aOR=0.91, 95% CI= 0.57-1.45) or MDD (aOR=0.88, 95% CI= 0.54-1.43).

Conclusion: We documented low prevalence of past-year/lifetime MHD among youths in a low-income county, consistent with findings of higher MHD prevalence in high-income countries. Vulnerable individuals had higher odds of disorder. Access to community services, may buffer disorder onset in the short-term. Future research should examine familial-level predictors of adolescent mental health not included in this study.

Do pre-existing assets modify the relation between job loss and depression during COVID-19? Catherine Ettman* Catherine Ettman Salma Abdalla Gregory Cohen Laura Sampson Patrick Vivier Sandro Galea

The COVID-19 pandemic and its ensuing economic consequences have resulted in record job loss for Americans. Depression following unexpected job loss has been documented in other economic downturns and prior research suggests that assets protect against depression. We do not know whether specific pre-existing assets influence such relations. Using data from the COVID-19 and Life Stressors Impact on Mental Health and Well-being (CLIMB) study, a nationally representative sample of U.S. adults surveyed in March-April 2020 (N=1441), we measured the relation between job loss and depression and the modification of this relation by three kinds of assets: financial assets (household savings over \$5,000), social assets (social cohesion), and physical assets (home ownership). Depression was measured using the Patient Health Questionnaire-9 (PHQ-9; ≥10 cutoff). We found that persons who reported job loss due to COVID-19 had greater odds of depression than persons who did not, controlling for gender, race, age, and household size (OR: 2.3;95% CI 1.5, 3.7). Further, we found that assets modified the relation between depression and job loss. Among persons with low savings, 48.0% of persons who lost a job and 39.0% of persons who did not lose a job reported depression (p=0.22). However, among persons with high savings, 49.0% of persons who lost a job and 16.5% of persons who did not lose a job reported depression (p<0.001). Among persons with low social cohesion, 55.1% of persons who lost a job and 33.0% of persons who did not lose a job reported depression (p=0.002). Among persons with high social cohesion, 38.4% of persons who lost a job and 17.6% of persons who did not lose a job reported depression (p=0.003). Among home owners, 50.0% of persons who lost a job and 19.5% of persons who did not lose a job reported depression (p<0.001). Among home renters, 44.5% of persons who lost a job and 35.3% of persons who did not lose a job reported depression (p=0.25). These findings suggest that some financial, social, and physical assets may modify the relation between depression and job loss during COVID-19. Further work is needed to explicate mechanisms through which some assets, but not others, influence the job loss-depression relation in the context of economic downturns.

Weighted prevalence of depression by assets and job loss due to COVID-19



Note: High social cohesion defined as ≥15 (median) from a modified social cohesion and trust scale. Job loss defined by participant affirmation of "lost a job" in response to "Have any of the following affected your life as a result of the coronavirus or COVID-19 outbreak?" Data weighted to the U.S. population. * denotes p<0.05 in the difference between persons who lost jobs and persons who did not lose jobs within specific asset category.

Hospitalization after emergency department visit for deliberate self-harm and 12-month risk of suicide: A generalized random forest analysis Sidra Goldman-Mellor* Sidra Goldman-Mellor Harish S. Bhat

Suicide is the 10th leading cause of death in the U.S. Suicide rates are particularly elevated among emergency department (ED) patients seen for deliberate self-harm. Inpatient hospitalization is the standard treatment for self-harm patients deemed high-risk, but confounding by indication and ethical barriers to conducting randomized trials have precluded clear inference about whether hospitalization mitigates suicide risk. Observational designs that address confounding through statistical adjustment are a potentially useful alternative. Here, we used California statewide, individually-linked patient record and mortality data on $n=57,312$ deliberate self-harm ED patients. Applying generalized random forest (GRF) methods, we estimated 12-month suicide risk differences among self-harm patients who were vs. were not hospitalized, conditioned on patient- and hospital-level covariates. Conditional average treatment effects were calculated separately for gender- (male, female) and age-specific (10-29 years, 30-49 years, 50+ years) subgroups, to examine effect heterogeneity. Absolute suicide risk was significantly higher among admitted vs. discharged patients. GRF models indicated that hospitalization was associated with 5.4 excess suicides per 1,000 hospitalized patients among males (95% CI: 3.0, 7.8), and 2.4 (1.1, 3.6) and 7.3 (0.5, 11.2) excess suicides per 1,000 among patients aged 10-29 years and 50+ years, respectively. Hospitalization was not associated with suicide risk among female patients or those aged 30-49 years. We conclude that hospitalization after deliberate self-harm may not confer benefits in terms of suicide prevention. Improvements to post-discharge care, and alternatives to hospitalization, are needed. Study limitations include the observational design and lack of potentially important covariates, and additional research is warranted.

Objective and subjective neighbourhood characteristics and suicidality: a multilevel analysis Jen Dykxhoorn* Jennifer Dykxhoorn Joseph Hayes Kavya Ashok Alma Soberg Wallin Christina Dalman

Background

Characteristics of the neighbourhood environment, including population density, social fragmentation, and trust, have been linked to mental health outcomes. Using a longitudinal population-based cohort, we explored the relationship between objective and subjective neighbourhood characteristics and the odds of suicidal thoughts and attempts.

Methods

We conducted a longitudinal study of 20,764 participants living in Stockholm County who participated in the Stockholm Public Health Survey.

We used multilevel modelling to examine if suicidal thoughts attempts were associated with neighbourhood characteristics, independent of individual associations. We included objective and subjective measures to explore if there was a different relationship between these measures of the neighbourhood environment and suicidality.

Results

Associations between neighbourhood factors and suicidality were predominantly explained by individual characteristics, with the exception of neighbourhood deprivation and average residential trust. Each unit increase of deprivation was linked to increased odds of suicidal thoughts (OR1.04, 95%CI 1.00-1.07) and attempts (OR1.11, 95%CI 1.06-1.17). Decreasing residential trust was associated with increased odds of suicide attempts (OR1.09, 95%CI 1.02-1.17). There was no evidence that neighbourhood fragmentation or average trust in public and political institutions had an independent effect on suicidality once individual and sociodemographic factors were accounted for.

Conclusions

This study showed that much of the neighbourhood-level variation in suicidal thoughts and attempts could be explained by compositional factors, including sociodemographic clustering within neighbourhoods. The independent effect of neighbourhood deprivation and average residential trust provide evidence that the neighbourhood context may exert an independent effect on suicidality beyond the impact of individual characteristics.

Exploring social exclusion and the association with mental disorders Jen Dykxhoorn* Jen Dykxhoorn Michael McGrath Jude Stansfield Sarah Ledden James Kirkbride Kate Walters David Troy Laura Fischer Vanessa Pinfeld David Osborn

Abstract Social exclusion is a multidimensional concept which refers to the inability of certain groups or individuals to participate fully in society due to unequal power relationships. Social exclusion can be a powerful tool to patterns of disadvantage and their drivers, however it has evaded precise measurement due to its complexity. Further, the relationship between social exclusion and mental health have not been clearly elucidated. We used population-based data to measure social exclusion, to describe its distribution, and to explore its relationship with mental health.

Methods We used data from *Understanding Society*, population-based survey. We included adults who were living in England in (2009/10).

Exposure We identified 4 domains of social exclusion in the published literature and expert consultation: material, relational, political, and structural.

Outcome We measured mental disorders using the General Health Questionnaire (GHQ-12).

Analysis We identified measures relevant to each domain, conducted principle component analysis to generate domain scores, and summed the standardised scores to create a social exclusion score. We used logistic regression to estimate relationship between social exclusion and GHQ, accounting for missingness with multiple imputation.

Results Levels of social exclusion varied by ethnicity and showed a linear decrease by age. Regional variations revealed high levels of social exclusion in London and low levels in the South West. We found that these patterns varied across domains (e.g. the North East had high levels of political exclusion, but the lowest levels of relational exclusion).

Social exclusion increased the odds of mental disorders (aOR 1.16; 95%CI 1.15-1.18). This was largely driven by material exclusion (aOR 1.67; 95%CI 1.62-1.72) and increases in political exclusion decreased the odds of mental disorders (aOR 0.96; 95%CI 0.93-0.98).

Discussion We demonstrated that population surveys can create a multidimensional measure of social exclusion, but that attention should be paid to the separate domains as they had different population distributions. We found that overall rates of social exclusion increased the odds of mental health problems, suggesting that this may be a useful tool in understanding mental disorders.

Education for equity or inherited advantage? Depressive symptoms among first generation college graduates vs college graduates whose parents are also college graduates. Erika Meza* Erika Meza Sepehr Hashemi M. Maria Glymour Jacqueline M. Torres Anusha M. Vable

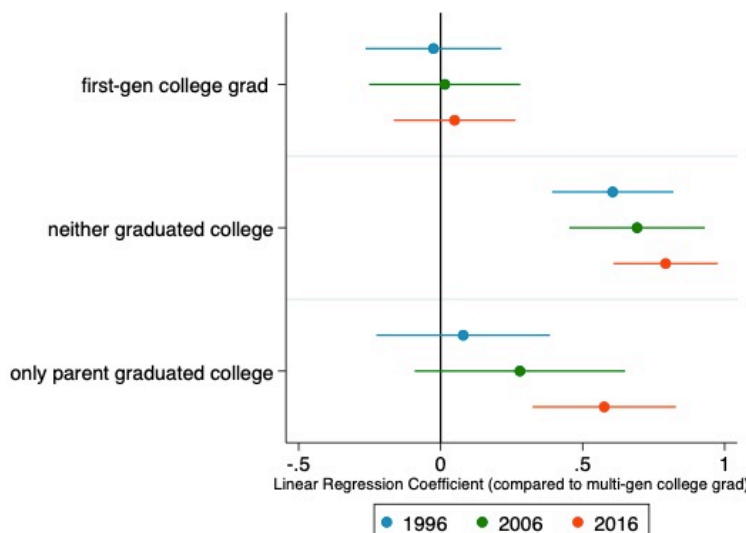
Introduction: Higher parents’ education and own education each predict less depression and lower depressive symptomatology; however, it is unclear if first-generation (or first-gen) college graduates (i.e., whose parents did not graduate from college) benefit equivalently as graduates with at least one parent that completed college (multi-generational college graduates). We evaluate if first-gen college graduates have equivalent depressive symptoms in midlife as multi-generational college graduates.

Methods: We used data from US Health and Retirement Study participants aged 55 to 63 in 1996 (N = 6,645), 2008 (N = 4,056), and 2016 (N=6,096). The exposure was a 4-category variable based on parents’ (highest of mother’s or father’s) and participant’s own completed years of education: first-generation college graduate (parents’ education <16; own >=16); multi-generational college graduate (both >=16: Reference); neither college graduate (both <16) and parents college graduate(s) but not respondent (parents >=16; own <16). Linear regression models evaluated the relationship between college completion and depressive symptoms measured by a modified, 8-item version of the Center for Epidemiologic Studies - Depression (CESD) scale. All models adjusted for age, sex, race/ethnicity, place of birth (Southern birth, immigrant) and childhood rurality.

Results: First- and multi-generation college graduates had equivalent depressive symptoms in all cohorts (e.g., Beta:-0.06; 95% CI: -0.30, 0.17 in 1996) (Figure 1). The relationship between not having a college degree and poorer mental health seemed to strengthen over time, especially for those whose parents graduated college (e.g.,Beta:0.08; 95% CI: -0.23, 0.39 in 1996 and Beta:0.58; 95% CI: 0.32, 0.83 in 2016).

Conclusion: Our findings suggest that a college degree is associated with lower depressive symptomatology in midlife, regardless of whether parents’ completed college.

Figure 1. Relationship between intergenerational education and depressive symptoms over time compared to the multi-generational reference group



The association of longitudinal monitoring of neuropsychiatric symptoms with progression to mild cognitive impairment among cognitively unimpaired subjects: A longitudinal cohort study Alok Kumar Dwivedi* Alok Dwivedi Bhaskar Thakur Ricardo Salazar Navkiran Shokar

Mild Cognitive Impairment (MCI) represents an intermediate stage of cognitive decline. Neuropsychiatric symptoms (NPS) are often noticed in the early stages of cognitive decline and greater changes in NPS over time may better predict progression to MCI. It is unclear how early changes in NPS may predict the incident MCI. To address this research question, we have utilized data from the Texas Alzheimer's Research and Care Consortium (TARCC) cohort study. Cohort studies including longitudinal exposures in medical studies often pose epidemiological modeling challenges. The time-varying covariate Cox model (TVCM) is generally used to analyze longitudinal data with survival events. The TVCM typically produces biased and inconsistent estimates. Some of the issues in TVCM may be avoided through two-stage models. However, two-stage models may yield biased inference due to the underestimation of standard errors of the parameter estimates. The various forms of joint models have been used to address issues involved in TVCM and two-stage models. We formulated a latent growth model for longitudinal NPS and a Cox model for time to MCI and compared it with TVCM, two-stage Cox model, and joint models with shared random effects. The proposed joint models showed an association between NPS and the risk of developing MCI according to Hispanic and non-Hispanic ethnic groups. Monitoring changes in NPS may early predict the development of MCI.

The Impact of Psychiatric Diagnosis on Patient-Reported Satisfaction and Quality of Life in Post-Mastectomy Breast Reconstruction: A Three-Year Analysis of 8,515 Patients

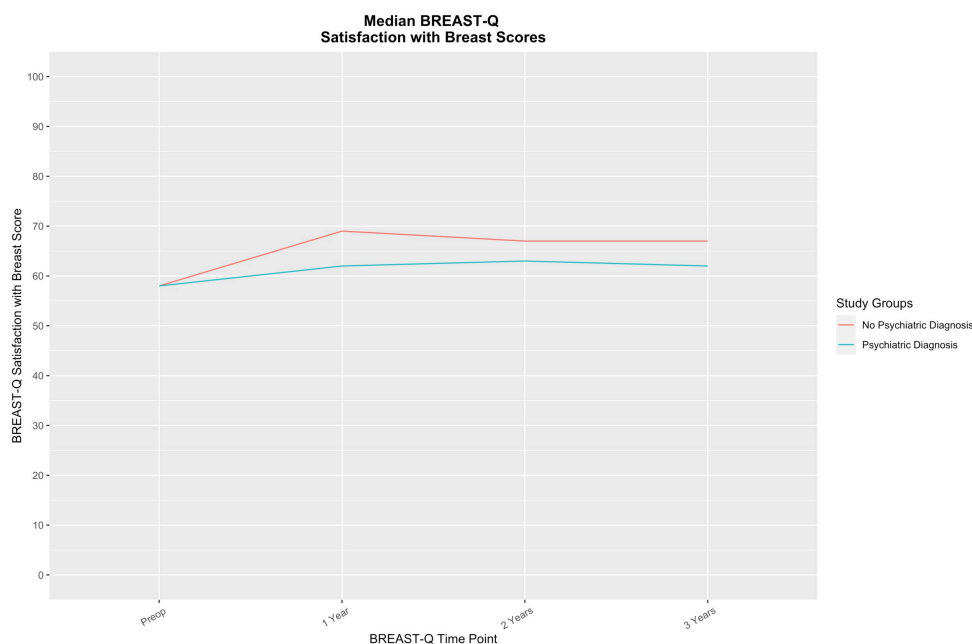
Meghana Shamsunder* Meghana Shamsunder Thais Polanco Shen Yin Babak Mehrara Colleen McCarthy Jonas Nelson

Background: Although it is clear that cancer diagnosis and breast reconstruction (BR) can have a negative impact on mental health, the effects of concurrent psychiatric diagnoses (PD) on postoperative quality of life (QoL) remain unknown. This study aims to assess the impact of PDs on QoL in this patient population.

Methods: Implant or autologous-based BR patients at a tertiary care center from 2007-17 were included. Demographics, cancer variables, PDs, and patient-reported outcomes (BREAST-Q Reconstruction Module) were extracted. PDs were grouped into eight categories (anxiety, depressive, substance-related, stress and adjustment, schizophrenia and psychotic, bipolar, personality, and other). Four-point differences in scores were clinically meaningful. Adjusted mixed-effects modeling assessed the impact of any PDs on BREAST-Q domain scores. Cross-sectional, multivariable linear regression models were used to analyze the impact of number and type of PD categories on scores.

Results: Of 8515 patients, 4812(56.5%) had a PD. Anxiety disorders were the most prevalent (77.1%), followed by depression (42.5%). After adjusting for clinical variables, having any PD was significantly associated with lower postoperative satisfaction(β : -3.6; 95% CI: -6.9, -0.4), physical well-being(β : -4.4; 95% CI: -7.2, -1.6), psychosocial well-being(β : -7.4; 95% CI: -11.1, -3.8) and sexual well-being(β : -9.4; 95% CI: -13.6, -5.3) scores as compared to patients with no PD. Anxiety and depressive disorders had significantly lower postoperative BREAST-Q scores (all domains; all $p < 0.01$). BREAST-Q scores progressively and significantly decreased as the number of PD categories per patient increased(all $p < 0.01$).

Conclusions: PDs, clinically and statistically, negatively impact quantitative measures of QoL in BR patients. Longitudinal, mental health treatment should be a key component of oncologic care.



Trajectories of housing affordability problems and mental health in the UK; a population-based cohort study Kate Dotsikas* Kate Dotsikas Jennifer Dykxhoorn David Osborn

Background: Rising housing costs and limited social housing stock have left UK residents with few options for consistent access to affordable housing. Evidence suggests the burden of housing costs negatively impacts mental health, however longitudinal evidence in the UK since the 2008 crisis is limited. This study assess the association between trajectories of housing affordability problems and mental health.

Methods: Data was taken from the UK Longitudinal Household Survey between 2009 and 2019. Group-based trajectory modelling was used to estimate trajectories of housing affordability problems in a cohort of 30,026 household heads. Participants spending 30% or more of equivalised household income on housing were categorised as facing affordability problems. The association between trajectory groups and mental health, measured by the 12-item General Health Questionnaire (GHQ), was assessed using linear regression.

Results: Six distinct trajectories of housing affordability problems were identified. Compared to the group with stable low probability of problems, the stable high group had a GHQ score on average 0.43 points higher (95% CI 0.11-0.75), while the high falling group had a GHQ score on average 0.63 points higher (95% CI 0.095-1.16), controlling for sex, age, and country.

Conclusions: This study provides evidence of a negative mental health impact of prolonged exposure to housing affordability problems. Results also suggest a long-term negative impact of past affordability problems, even in a group more recently facing decreasing problems.

Help-seeking behaviour among Adults who Died by Suicide or Attempted Suicide in Ontario, Canada Rebecca Barry* Rebecca Barry Paul Kurdyak Jürgen Rehm Claire de Oliveira Simon Chen Peter Gozdyra

Background: Many individuals do not seek help from a psychiatrist or general practitioner (GP) prior to death by suicide or a suicide attempt. The objective of this study was to determine the relationship between rurality and help-seeking behaviour prior to a suicide or suicide attempt by urban and rural status.

Methods: Data from 2007 to 2017 were obtained from administrative databases held at ICES, which capture all emergency department (ED), and physician visits across Ontario. Rurality was defined using the Rurality Index of Ontario (RIO) scores. Help-seeking was defined based on accessing health services one year prior to the event. Health services examined included psychiatrist, GP, and ED visits that were mental health and non-mental health related.

Results: We found that among those who completed suicide, those living in rural areas were significantly less likely to seek help from a psychiatrist (Rural male: OR=0.42, 95%CI=0.31-0.57; Rural female: OR=0.46, 95%CI=0.29-0.973). We also found the same association among those who attempted suicide (Rural male=0.49, 95%CI=0.43-0.56; Rural female=0.51, 95%CI=0.46-0.57). Rural males who attempted or completed suicide, and rural females who attempted suicide were less likely to seek help from a general practitioner for mental health reasons. Those living in rural areas were more likely to seek care from an ED for mental health reasons.

Interpretation: Findings suggest that those living in rural areas may have less access to care than their urban counterparts, and that this may lead to increased risk of suicide and suicide attempts. Potential solutions should address accessibility, availability and acceptability of mental health services in rural areas.

The joint effects of comorbid depression and other psychiatric disorders on suicide deaths and non-fatal suicide attempts in Denmark Tammy Jiang* Tammy Jiang David Nagy Anthony J. Rosellini Sandro Galea Erzsébet Horváth-Puhó Timothy L. Lash Henrik T. Sørensen Jaimie L. Gradus

Depression is highly comorbid with other mental disorders including PTSD, substance use disorder, and personality disorder. To date, research on the joint influence of comorbid depression with other mental disorders on suicide and non-fatal suicide attempts has yielded mixed results. Some studies have found evidence of additive risk whereas others found sub-additive risk between depression and other mental disorders. Conflicting findings may be due to differences in how comorbid mental disorders are handled analytically. These may be treated as confounders, mediators, or colliders. Longitudinal data can address this issue by establishing the temporal ordering of variables to avoid inappropriate adjustment. Our aim is to quantify the joint effects of depression and comorbid mental disorders on suicide and suicide attempts using longitudinal population based data from Danish registers. We conducted a case-cohort study with 14,103 suicide cases and 22,974 suicide attempts occurring between 1995 and 2015 in Denmark. The comparison general population subcohort was a 5% random sample of the source population in Denmark on January 1, 1995 (n = 265,183). The mean ages for depressed men and women were 42 (SD = 20) and 43 (SD = 23). We will examine pairwise combinations of depression with: organic disorders, substance use disorders, schizophrenia, manic episode, bipolar disorder, neurotic disorders, eating disorders, personality disorders, intellectual disabilities, developmental disorders, and behavioral disorders. We will use inverse probability weighted estimation of marginal structural Cox proportional hazards models to address time-varying confounding by age, marital status, income, physical health status, and psychiatric comorbidity and estimate the relative excess risk due to interdependence as a measure of interaction and corresponding 95% CIs. All analyses will be stratified by sex. Analyses are currently underway and findings will be presented during the meeting.

Mental Health Services and Complementary Alternative Medicine Use among US Midlife Adults with Mental Distress Pamela Jo Johnson* Pamela Jo Johnson Judy Jou Dawn M. Upchurch

Increasingly, adults self-treat with Complementary and Alternative Medicine (CAM). This is especially true for depression, anxiety, or other mental illness. We examined past year mental health (MH) services used by midlife adults with mental distress including use of CAM. **Methods:** We used nationally representative data for midlife adults from the National Survey of Drug Use & Health (NSDUH) 2006-2019. Past year mental distress severity, moderate (MMD) and severe (SMD): K6 screener identifies those with likelihood of diagnosable mental illness. MH services: inpatient alone/in combination, outpatient only, prescriptions only, outpatient & prescriptions. CAM use: any past year use for mental health. Analysis: Stata survey cross-tabs with design-based F-tests and logistic regression. **Results:** Overall, 8% of midlife adults had SMD and 19% had MMD in the past year. Those with SMD most often received outpatient with prescriptions (27%), while those with MMD most often had prescriptions only (16%). Over 40% with SMD and 70% with MMD did not receive any MH services. Of those who received care, 29% with SMD and 11% with MMD still reported unmet mental health care needs. Overall, 22% of those who received outpatient and 17% who received outpatient with prescriptions also used CAM for mental health. Compared to no MH services, those with outpatient only (OR=3.7; 95%CI 3.0-4.7), prescriptions only (OR=2.0; 95%CI 1.7-2.3), or both (OR=2.6; 95%CI 2.2-3.1) had higher odds of using CAM. Those with unmet mental health care needs had 1.7 times higher odds than those that did not (95%CI 1.5-2.1). **Conclusion:** Many midlife adults with mental distress may not be receiving the MH services they need. Some may seek CAM to support their medical care or to provide relief due to unmet care needs. Those with outpatient only were most likely to use CAM suggesting they may be seeking symptom relief unaddressed by psychotherapy alone. We discuss practical implications and future research needs.

Examining the Relationship between Behavioral Health and Musculoskeletal Injury-Related Limited Duty Time among Active Duty Soldiers in the U.S. Army Theresa N. Faller* Theresa Faller Kathryn M. Taylor Jamie T. Carreno Davidson Tanja C. Roy

Background: Musculoskeletal injury (MSKI) is the leading cause of limited duty time in the U.S. Army. A prior behavioral health (BH) disorder may prolong injury recovery, and longer MSKI recovery time may increase risk for a subsequent BH diagnosis. The aim of this study was to examine relationship between MSKI-related limited duty time and BH disorders. Clarifying this relationship may help healthcare providers better understand the needs of Soldiers with BH problems.

Methods: A cohort study was conducted among active duty Soldiers with a duty limiting incident temporary MSKI in calendar year 2017 using data from the Soldier Performance, Health, and Readiness (SPHERE) Database. MSKI-related duty limitations were identified from the eProfile database. ICD-10 codes from medical records were used to identify BH diagnoses. The relationship between limited duty time and preexisting BH diagnoses was assessed by negative binomial regression. The hazard of developing a BH problem following MSKI was evaluated by Cox proportional hazard models.

Results: Of the 86,428 Soldiers with a duty limiting MSKI, 9% had a prior BH diagnosis. The incidence rate of limited duty weeks among Soldiers with a preexisting BH condition was 1.051 times higher (95% CI 1.029-1.074) than the incidence rate among Soldiers without. Among Soldiers with no preexisting BH diagnoses, 24% developed a BH problem after injury. The hazards of developing a BH problem among these Soldiers increased by 1.6% per week (HR: 1.016, 95% CI: 1.015-1.018) following MSKI.

Conclusion: Our findings suggest that BH diagnoses influence the length of limited duty, and longer limited duty time for MSKI increases risk of BH diagnoses. Injured Soldiers with preexisting BH diagnoses may need additional support for full recovery. Soldiers with more severe MSKIs or on longer periods of limited duty may need preventative BH counselling. Further research should clarify the underlying mechanisms of these associations.

Physical activity as a mediator of the association between depressive symptoms and pain severity in knee osteoarthritis Alan Rathbun* Alan Rathbun Elizabeth Stuart Michelle Shardell Trang Nguyen Alice Ryan Joseph Gallo Michelle Yau Megan Schuler Marc Hochberg

Physical activity as a mediator of the association between depressive symptoms and pain severity in knee osteoarthritis Alan Rathbun* Alan Rathbun Elizabeth Stuart Michelle Shardell Trang Nguyen Alice Ryan Joseph Gallo Michelle Yau Megan Schuler Marc Hochberg

Background: Knee osteoarthritis (OA) is a common arthritic disorder in older adults. Psychiatric comorbidities are common, especially depressive symptoms, which are associated with greater pain severity. Behavior is a strong determinant of depression but whether it leads to increased joint pain remains unclear.

Objective: To assess physical activity as a mediator of the association between depressive symptoms and pain severity among persons with radiographic knee OA.

Methods: A two stage marginal structural with five years of repeated measures (Figure 1) was used to assess the natural direct effect (NDE) of depressive symptoms (Center for Epidemiologic Studies Depression [CES-D] scale) on pain severity (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC] pain scale) and natural indirect effect (NIE) mediated by physical activity (Physical Activity Scale for the Elderly) in persons ($n=2,318$) enrolled in the Osteoarthritis Initiative with radiographic knee OA. Depressive symptoms (CES-D score ≥ 16), pain severity (rescaled range=0-100), and physical activity were measured from baseline to third year, first to fourth year, and second to fifth year, respectively. Estimates were adjusted for time-invariant and -varying confounders.

Results: Depressive symptoms were associated with greater pain severity ($B=2.929$ WOMAC units; 95% CI: 1.582, 4.276). NDE and NIE were 2.923 WOMAC units (95% CI: 1.574, 4.271) and 0.006 WOMAC units (95% CI: 0.002, 0.010), respectively. Thus, $\leq 1\%$ of the association between depressive symptoms and pain severity was mediated by physical activity.

Conclusion: Physical activity does not clinically meaningfully mediate the association of depression with pain in knee OA.

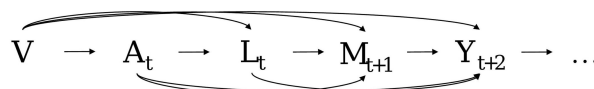


Figure 1. Directed acyclic graph showing hypothesized associations between depressive symptoms exposure (A), physical activity mediator (M), pain severity outcome (Y), and time-invariant (V) and -varying (L) confounders.

Neighbourhood income inequality and preschooler internalizing and externalizing problems: Cross-sectional evidence from Calgary Gregory Farmer* Gregory Farmer Roman Pabayo

Background

Several studies have linked neighbourhood social and economic characteristics to preschool aged children's emotional and behavioural problems. Although income inequality has been identified as a risk factor for mental health and behavioural outcomes among adolescents, few studies have been conducted among young children. The objective of the current study is to explore the association between area-level income inequality and internalizing and externalizing problems at among pre-school aged children.

Methods

We analyzed cross-sectional data from the All Our Families (AOF) longitudinal cohort located in Calgary, Alberta at 3-years postpartum. The analytical sample consisted of 1347 mother-preschooler dyads nested within 164 neighbourhoods. Mothers completed the National Longitudinal Survey of Children and Youth Child Behaviour Checklist (NLSCY- CBCL), which assessed internalizing and externalizing symptoms in their child. Analysis used multilevel logistic regression to assess a relationship between income inequality and preschooler internalizing and externalizing problems.

Results

Neighbourhood income inequality ranged from 0.23 to 0.55. Neighbourhood income inequality was not associated with either externalizing (OR= 0.84, 95%CI: 0.68, 1.05) or internalizing (OR=1.05, 95%CI: 0.85, 1.29) problems in preschoolers. However, after-tax household income was significant in both internalizing (OR = 1.49, 95%CI: 1.09, 2.05) and externalizing (OR= 1.38, 95%CI: 1.00, 1.91) problems.

Conclusion

Area-level inequality does not adversely affect preschool internalizing or externalizing problems at 3-years of age. In the case of income inequality, preschoolers may be too young to experience its effects, or are more sensitive to the household environment such as lower household incomes, as opposed to their neighbourhood environment.

LATEBREAKER

Mental Health

Using an Intersectional Approach to Examine the Relationship Between Adolescent Substance Use and Depressive Symptoms Tess Marusyk* Tess Marusyk Colleen Davison

Substance use has been associated with depression in adolescence and earlier initiation may be especially problematic. Social locations, such as those defined by gender, race, or socioeconomic status (SES), have been associated with early adolescent substance use and adolescent depression. However, their effects have primarily been examined independently, whereas Intersectionality Theory suggests they work synergistically. In a Canadian context, the objectives are to (1) provide a descriptive analysis of early substance users considering intersecting social locations (gender, race, and SES); (2) examine the overall association between early substance use and depressive symptoms later in adolescence; and (3) evaluate potential differences in the relationship at varying intersections of gender, race, and SES. This contemporary analysis uses a nationally representative sample of adolescents in grades 9 and 10 (n=7,933) from the 2018 Health Behaviour in School-aged Children Study. Reported alcohol, cigarette, or cannabis use prior to age 14 is considered early substance use. Depressive symptoms are measured by asking, "During the past 12 months, did you ever feel so sad or hopeless almost every day for two weeks or more in a row that you stopped doing some usual activities?". A descriptive and multilevel, multivariable analysis is being conducted, using two- and three-way stratification by gender, race, and SES. Preliminary results have shown that approximately one in four adolescents reported early substance use and over one-third reported experiencing recent depressive symptoms. Early substance use was associated with later depressive symptoms ($p < 0.0001$). The forthcoming regression model will estimate the relative risk for the overall sample and each stratified subgroup. This analysis using an intersectional lens may help better explain the relationship between early substance use and later adolescent depression and help identify particular subgroups at greater risk.

LATEBREAKER

Mental Health

Monitoring Self-Harm and Suicidal Ideation Hospitalization Risk Using Google Trends

Hilary Colbeth* Hilary Colbeth Krista Neumann Corinne Riddell Ellen Eisen Sidra Goldman-Mellor

Objective In 2017, approximately 1.5 million United States emergency department (ED) visits were related to self-harm or suicidal ideation, both of which are known to be associated with increased risk of suicide death. Since the early 2010's, research using Google Trends data has provided conflicting evidence on whether internet search volumes can act as indicators for suicide risk. Previous research has largely focused on the association between search volume and suicide mortality; however, little is known about the link between search volumes and ED visits for self-harm and suicidal ideation.

Methods Over a 9-year study period (2007-2015), search volume data related to suicidality were queried from the Google Health Application Programming Interface for California and Arizona. These states were chosen for their differing age distributions and rigorous ED injury coding policies. We assessed risk ratios (RR) of self-harm and suicidal ideation ED visits in association with Google search volumes, both overall and by age and sex using a Generalized Estimating Equations approach. Search volumes were lagged by 2 weeks and 1-3 months; separate models were fit for self-harm and suicidal ideation within each state.

Results Self-harm and suicidal ideation ED visit rates in Arizona were positively associated with monthly Google search volume, most strongly following a 2-month lag. Associations were strongest among those age 60+ years; in this group, for every one standard deviation increase in search volume, the RR was 1.20 for self-harm (95% CI: 1.04-1.37) and 1.33 for suicidal ideation (1.11-1.61)), a pattern that remained when stratified by sex. RRs from California were consistent with no association.

Conclusions Internet searches related to suicidality may provide a useful marker for population trends in healthcare utilization for self-harm and suicidal ideation, particularly among states with high proportions of older adults.

LATEBREAKER

Mental Health

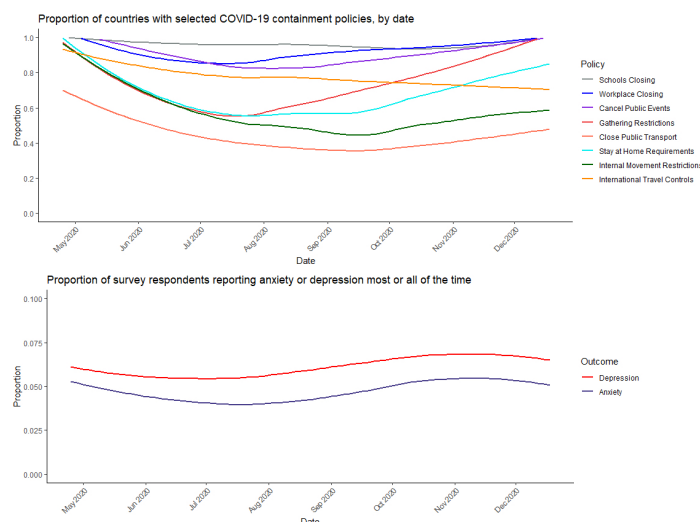
Association of COVID-19 Containment Policies with Anxiety and Depressive Symptoms: A Multi-National Study of 38 Countries Kira Riehm* Kira Riehm Elena Badillo-Goicoechea Esther Kim Luke Aldridge Rachel Presskreicher Carly Lupton-Smith Ting-Hsuan Chang Sarah LaRocca Frances Wang Frauke Kreuter Elizabeth Stuart

Introduction: Policies enacted to reduce transmission of COVID-19, such as stay-at-home orders, have been widely speculated to adversely affect mental health, but empirical evidence supporting these claims is scarce.

Methods: We analyzed survey data from 16,379,876 adults from 38 countries who participated in the daily COVID-19 Symptom Survey on Facebook in conjunction with time-varying policy data from the Oxford COVID-19 Government Response Tracker between April 24 2020 and December 20 2020. Using generalized linear models adjusted for country and individual-level covariates, we examined the association of eight containment policies (school closures, workplace closures, cancellation of public events, restrictions on the size of gatherings, public transportation closures, stay-at-home requirements, restrictions on internal movement, and international travel controls) with dichotomized anxiety and depressive symptoms measured with two items from the Kessler Psychological Distress Scale. Policy exposure variables were lagged to one week prior to individual survey dates to examine temporal associations.

Results: School closures, cancellation of public events, restrictions on the size of gatherings, and stay-at-home requirements were associated with 6.8-13.4% higher odds of anxiety symptoms and 5.8-12.5% higher odds of depressive symptoms. Workplace closures and public transportation closures were associated with 7.3% and 5.7% lower odds of anxiety symptoms and 10.9% and 3.5% lower odds of depressive symptoms, respectively. Restrictions on internal movement and international travel controls were not associated with either anxiety or depressive symptoms.

Conclusions: Containment policies implemented in response to COVID-19 appear to have heterogeneous associations with mental health. Our findings can be used to inform ongoing and future preventive approaches to population mental health worldwide, in contexts where health containment policies have been necessary.



LATEBREAKER

Mental Health

Feeling Safe: A Critical Look at the Effect of Neighborhood Features and Perceptions on Depressive Symptoms

Erika Infantino* Erika Infantino Tracie Barnett Carolyn Côté-Lussier Andraea Van Hulst Melanie Henderson Marie-Eve Mathieu Catherine Sabiston Lisa Kakinami

Background: Feeling unsafe in one's environment can have detrimental effects on health and is often due to a combination of physical characteristics and sociocultural influences. For children, their perception as well as their parents' perceptions of neighborhood safety and cohesion reportedly play a role on physical health, but their mental health effects are less clear.

Objective: The study's objective was to determine which neighborhood safety measure (self-perceived or objective indicators of physical neighbourhood disorder) predicts depressive symptoms in children.

Method: Baseline and two-year follow-up data of the Quebec Adipose and Lifestyle Investigation in Youth prospective cohort (n=424, mean age=9.6 years at baseline; 45.3% female) were used. Baseline measures included perception of neighborhood safety (child- and parent-reported), parental perception of neighbourhood cohesion, and objective auditor assessed measures of visible disorder. Multiple linear regressions were sex-stratified and examined whether safety features predicted youth's depressive symptoms (12-item Centre for Epidemiological Studies-Depression Scale, self-reported) at follow-up adjusting for age, weight status based on Z-BMI, parent education, annual household income, and population density (habitants/km²).

Results: Among girls, greater parent perceptions of neighborhood cohesion (B=-0.87, p=0.02) and greater visible disorder (B=-1.46, p<0.01) predicted lower depressive symptoms. Among boys, greater child perceived safety predicted lower depressive symptoms (B=-0.80, p<0.01).

Conclusion: Child perceived neighborhood safety predicted depressed-affect two years later among males; females' depressive symptoms were predicted by parent perceptions and visible disorder. When feeling safe, children are more likely to be physically active, helping their mental health. Thus, physical activity among other potential mechanisms should be further investigated.

LATEBREAKER

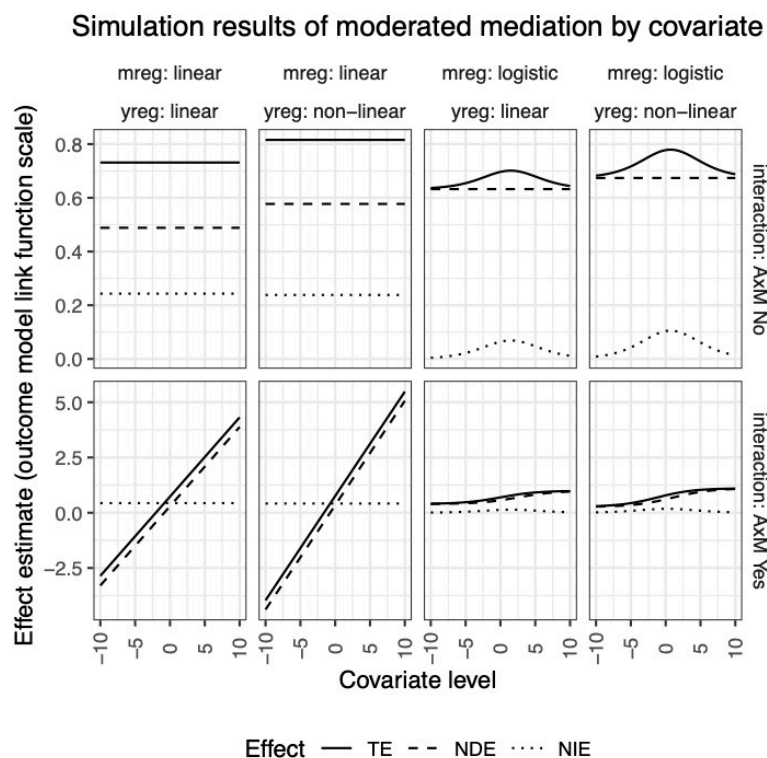
Mental Health

Concurrent and longitudinal analysis of teacher support, stressful life events, and depressive symptoms in early adolescence Miranda Delawalla* Miranda Delawalla Isaac Rhew Jessica Jenness Elizabeth McCauley Aaron Lyon Ann Vander Stoep

As students return to school during the pandemic, there is increased interest in the role of teachers in promoting child and adolescent mental health. This study evaluated concurrent and prospective associations between teacher support and depressive symptoms in young adolescents. Using sixth, seventh, and eighth grade measurements from the Developmental Pathways Project, a community-based, diverse cohort study of 521 middle school students, we estimated associations between adolescent-reported teacher support and adolescent/parent-reported depressive symptoms using generalized estimating equations, adjusting for relevant covariates including baseline depressive symptoms in prospective associations. We also assessed moderation of associations by exposure to stressful life events (SLEs) and sex. Youth with higher levels of perceived teacher support had lower levels of current (count ratio = 0.858; 95% CI: 0.822, 0.895; $p < 0.01$) and subsequent depressive symptoms (CR = 0.956; 95% CI: 0.927, 0.985; $p < 0.01$). There was evidence of an interaction between exposure to SLEs and teacher support, such that the negative association between teacher support and current (interaction- $p < 0.01$) and subsequent (interaction- $p = 0.03$) depressive symptom counts was weaker in adolescents with higher numbers of reported SLEs and stronger in those with fewer SLEs. Sex did not significantly modify the concurrent or prospective associations between teacher support and depressive symptoms, nor in models with three-way interactions between teacher support, SLEs, and sex. Generally, we found evidence that teacher support may contribute to prevention of depressive symptoms, but also that teacher support may be insufficient for students with exposure to multiple SLEs. These results may have implications for school districts as they plan programming for students who return to the classroom at increased risk for mental health problems and exposure to prolonged stressful circumstances.

Moderated Mediation in Causal Mediation Analysis: Treatment and Covariate Dependence in Regression-Based Approach Yi Li* Yi Li Maya B. Mathur Daniel H. Solomon Robert J. Glynn Kazuki Yoshida

Most applications of causal mediation analysis report only total effect, natural direct effect (NDE), natural indirect effect (NIE), and proportion mediated (PM) without mentioning conditional vs. marginal natures, covariate values, and mediator and outcome models. An underappreciated concept of *moderated mediation* can be at play without researchers realizing. Using the regression-based closed-form approach, we show how NDE and NIE are *moderated* by baseline treatment and covariate levels. NDE is covariate-dependent if treatment-mediator interaction is in the outcome model and is non-zero. NIE is covariate-dependent if the mediator model is logistic. When both mediator and outcome models are linear, NDE and NIE at mean covariate values have a marginal interpretation. We conduct simulations for 4 scenarios where mediator and outcome models are either binary or continuous (**Figure**). We give a drug epidemiology example where PM varies from 0 to 100%, depending on covariate values. We further include treatment-covariate and mediator-covariate interaction terms in mediator and outcome models. In such extended models, NDE is independent of covariates when the mediator model is linear and there is no treatment-mediator or treatment-covariate interactions in the outcome model, or when the mediator model is logistic and there is no covariate in the mediator model and no treatment-covariate and mediator-covariate interactions in the outcome model. NIE is independent of covariates when there is no covariate in the mediator model and no mediator-covariate interaction in the outcome model. Even with additional interaction terms, the marginal interpretation of effect estimates evaluated at the mean covariate values is retained if both mediator and outcome models are linear and there is no treatment-covariate interaction in the mediator model or no mediator-covariate interaction in the outcome model.



SARS-CoV-2 Seroprevalence Studies in the United States: Methodological Challenges and the Need for a Coordinated National Strategy Susanna Sabin* Megan Jehn Bonnie LaFleur Nir Menachemi Camila Tompkins J Mac McCullough

Policymakers need accurate estimates of the cumulative number of people previously infected with SARS-CoV-2 to plan and manage the pandemic. Seroprevalence studies using antibody tests help estimate progress towards herd immunity and guide public health response. Moreover, seroprevalence studies estimate the extent that cases underestimate infections and elucidate groups most at risk. Yet, in the absence of national coordination, states and jurisdictions have used different designs including random and non-random sampling approaches to determine seroprevalence. National coordination would enable better resource utilization, improve efficiency, foster data harmonization, and facilitate use of best practices. Standardized methodology would also allow cross-jurisdictional comparisons and pooled estimates to be calculated. We argue that more coordination and data sharing is needed to limit biases in seroprevalence approaches. Biases from nonrandom sampling approaches, such as laboratory surveillance of residual clinical samples, have limited generalizability because certain vulnerable groups do not routinely access healthcare services. In this study, we will compare the key methodological challenges, and discuss the broad feasibility and estimation performance of three different approaches that have been used to estimate SARS-CoV-2 seroprevalence in the US including: 1) CDC CASPER field methodology with door-to-door serology collection; 2) stratified random samples using public records data combined invitations for antibody testing at a given site; and 3) quantitative (non-fieldwork) estimation approaches. We will also discuss the impact of these varying methodological approaches to our shared understanding of cumulative SARS-CoV-2 infections in the US.

Should multiple imputation be stratified by exposure group when estimating causal effects via outcome regression? Jiaxin Zhang* Jiaxin Zhang S. Ghazaleh Dashti John B. Carlin Katherine J. Lee Margarita Moreno-Betancur

Despite recent advances in methods for causal inference in epidemiology, outcome regression remains the most widely used method for estimating causal effects in the time-fixed exposure and outcome setting. Missing data are common in epidemiologic studies and complete-case analysis (CCA) and multiple imputation (MI) are two commonly used methods for handling them. In randomized controlled trials (RCTs), it has been shown that MI should be conducted separately by treatment group, but the question of whether to impute by exposure group has not been addressed for observational studies, in which causal inference is understood as the task of emulating an RCT. We designed a simulation study to evaluate and compare the performance of five missingness methods: CCA, MI on the whole cohort, MI including an interaction between exposure and outcome in the imputation model, MI including interactions between exposure and all incomplete variables in imputation models, and MI conducted separately by exposure group. Bias, precision and confidence interval coverage were investigated. We generated data based on an example from the Victorian Adolescent Health Cohort Study, where interest was in the causal effect of adolescent cannabis use on young adulthood depression and anxiety in females. Three exposure prevalence scenarios and seven outcome generation models were considered, the latter ranging from no interaction to a strong positive or negative interaction between exposure and a strong confounder. Two missingness scenarios were examined: one with incomplete outcome, the other with incomplete outcome and confounders, each with three levels of complexity in terms of the variables or interaction on which missingness depended. The Figure shows the relative bias of analysis approaches across all scenarios considered. MI by exposure group usually led to the least bias. Considering the overall performance, MI by exposure group is recommended if MI is adopted in settings such as these.



Methods: CCA complete-case analysis; WC.MI MI on the whole cohort; EO.MI MI including an interaction between exposure and outcome in the imputation model; EI.MI MI including interactions between exposure and all incomplete variables in imputation models; and EG.MI MI conducted separately by exposure group. The complete case proportion is fixed to 70% for all scenarios.

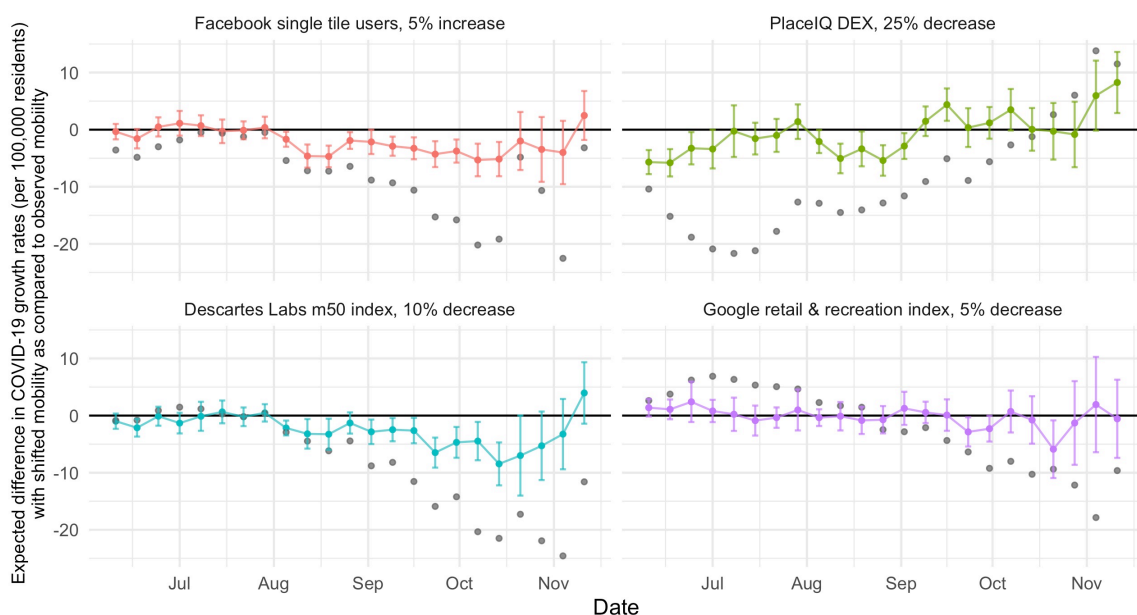
Examining shifts in mobility on COVID-19 case rates in U.S. counties Joshua Nugent* Joshua Nugent Laura Balzer

Background: Previous research has shown mixed evidence of associations between mobile phone-generated mobility data and COVID-19 case rates. Evaluating the causal impacts of mobility is complicated by confounding variables, varying epidemic arrival time, and changing government policies.

Methods: Using a modified treatment policy approach, we aimed to evaluate the county-level impact of stochastic interventions to shift mobility on the growth in COVID-19 case rates. We binned all data into weeks using a simple mean and defined the outcome as the number of new cases per 100,000 residents two weeks ahead. We selected 4 mobility indices covering a range of behaviors. As compared to each county's observed mobility each week, we examined a (i) 5% increase in Facebook's proportion of residents staying at home; (ii) 25% decrease in PlaceIQ's Device Exposure Index of the density of people at locations visited; (iii) 10% decrease in Descartes Lab's m50 Index of distances traveled; and (iv) 5% decrease in Google's retail/recreation index of non-essential business visits. Primary analyses used targeted minimum loss-based estimation (TMLE) with Super Learner and considered 30+ potential confounders, capturing social, economic, health, and demographic differences between counties. For comparison, we also implemented unadjusted analyses.

Results: Analyses included 1,177 U.S. counties, covering 90% of the population, from June 1 - November 14, 2020. For most weeks considered, unadjusted analyses suggested strong associations between the mobility indices and subsequent growth in case rates (Figure). However, after adjustment, none of the indices showed a consistent unidirectional association.

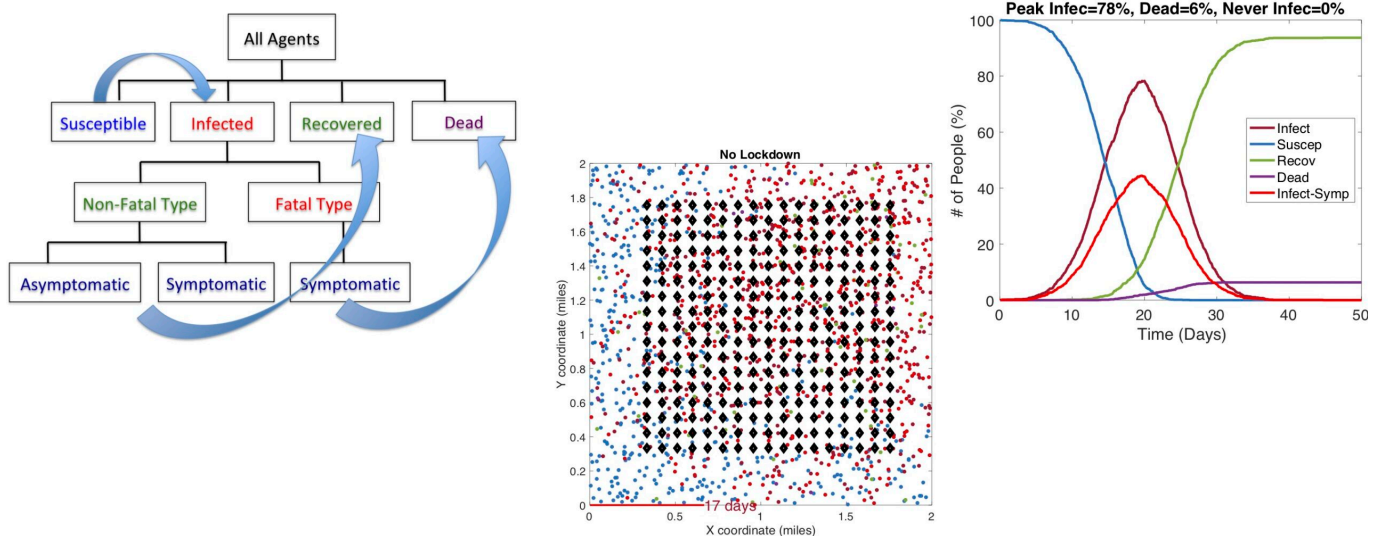
Conclusion: While mobility metrics may be correlated with COVID-19 case rates, adjusted analyses suggest that commonly studied indices are highly confounded. COVID-19 studies failing to adjust for measured confounders should be interpreted with caution.



Associations between mobility shifts and COVID-19 growth rates two weeks later for U.S. counties from June 1 - November 14, 2020. Gray points indicate unadjusted estimator. Indices measure percentage of people staying at home all day (Facebook), density of people at locations visited (DEX), distances traveled from home (m50), and utilization of nonessential businesses (Google).

Random-walk, agent-level pandemic simulation (RAW-ALPS) for analyzing effects of different lockdown measures Anuj Srivastava* Anuj Srivastava

There is a great interest in stochastic modeling and analysis of epidemiological data resulting from current the COVID-19 pandemic. Until a large amount of infection, containment, and recovery data from this pandemic becomes available, the community continues to rely on simulation models to help assess situations and to evaluate potential countermeasures. This paper develops an agent-level stochastic simulation model, termed RAW-ALPS, for simulating the spread of an epidemic in a confined community. The mechanism of transmission is agent-to-agent contact, using parameters reported for COVID-19 pandemic. The main goal of the RAW-ALPS simulation is to help quantify effects of preventive measures — imposition and lifting of lock downs — on infections, fatalities and recoveries. When unconstrained, the agents follow independent random walks and catch infections via physical proximity with infected agents. The lock down involves restricting appropriate agents to their domiciles. An infected agent under quarantine can only infect a co-inhabitant, thus causing a decline in infections during lock downs. Three types of lock down measures are considered: (1) the whole population (except essential workers), (2) only the infected agents, and (3) only the symptomatic agents. The simulation model requires a number of parameter choices — for population density, agent motion, infection, and recovery — that are typically taken from COVID-19 published literature. The model provides a quantification in changes in infection rates and casualties by imposition and maintenance of restrictive measures in place. It tracks both symptomatic and asymptomatic agents and allows for selective imposition of lock downs. We will explain the detailed simulation model, present some exemplary simulation results and provide summary statistics from a number of lock down scenarios. The results show that the most effective use of lock down measures is when all infected agents, including both symptomatic and asymptomatic, are quarantined, while allowing for free movements of all uninfected agents. This calls for regular and extensive testing of the population to isolate and restrict all infected agents, including the asymptomatic agents.



Outsourcing the construction of data generating functions in simulation studies Hayden Smith* Hayden Smith

Background: Data simulations are commonly used in the field of epidemiology. They can serve as a tool for teaching methods and concepts. Simulations are also used in the formal comparisons of analytic approaches. In this latter area there can exist generalizability threats related to implicit and explicit biases stemming from researcher degrees of freedom. Objective: to present a framework for conducting simulation studies based on the outsourcing of the development of the data generating functions (DGFs).

Framework: The researcher should write out a formal protocol for the simulation study. The document should state the purpose of the study (e.g., prediction based on best feature subset or variable de-confounding). Attention should be given towards hyperparameter tuning as well as the hypothesized robustness and planned criteria for evaluating the approach (i.e., loss function). The protocol should be published in a public space.

The researcher can then contract an impartial party to construct the DGFs. Functions should be based on study purpose and created using structural causal modeling, Markovian blankets, and causal graphs (e.g., daggity package in R), as applicable. Next, variable relationships can be explicitly defined (i.e., linear and non-linear terms, effect magnitudes and directionality). Based on the purpose of the study, multiple datasets may be necessary based on varying sample sizes and covariate relationships as well as omission and commission of relevant and non-relevant features. Lastly, the secondary party can provide the datasets or DGFs to the researcher based on the most appropriate approach for addressing the study question.

Conclusions: The use of blinding and third parties in research is not a new concept (e.g., data safety monitoring boards). The blinding of researchers to DGF construction in simulation studies may be a new step in attempting to formalize the process and move towards greater reproducibility and transparency.

Bayesian non-inferiority methods for dealing with non-normal outcomes in the observational setting

Hayden Smith* Hayden Smith

Background: The analysis of non-normally distributed outcomes can require data transformations or use of non-parametric approaches. Bayesian methods can be used in comparative effectiveness analytics in order to incorporate prior information and avoid focusing on null hypothesis testing. Objective: to present Bayesian non-inferiority approaches to deal with non-normally distributed outcomes in the observational setting.

Methods: An observational study was conducted to examine treatment protocol adherence (yes/no) for patients diagnosed with complicated parapneumonic infection and were admitted to three U.S. Midwestern hospitals. The outcome variable was patient length of stay (LOS), a typically right-skewed variable. Data were analyzed using a Bayesian generalized linear model with a natural log transformed outcome. Also fitted was a Bayesian quantile regression model using untransformed data. Both models adjusted for treatment variabilities (i.e., number of treatment doses and percentage drug coverage) using propensity score weighting and incorporated non-informative priors.

Results: Within study hospitals, there were 195 inpatients with a complicated parapneumonic infection. Of these patients, 121 (62%) were male and median age was 62 (interquartile range [IQR]: 52-73) years. One-hundred and fifty-five (79%) patients were protocol non-adherent. Estimated median length of stay for protocol adherent and non-adherent patients was 11.3 (95% credible interval [CrI]: 9.6, 13.3) and 12.4 (95% CrI: 10.9, 14.2) days, respectively. There was a 7.5% probability of protocol non-adherent patients having an estimated length of stay greater than 120% of adherent patients estimated stays. Differences in LOS across quantiles are presented in Figure.

Conclusions: A protocol non-adherent status tended to be associated with an increased LOS. Bayesian methods provided probabilistic interpretations of estimates and quantile regression allow for the examination of treatment heterogeneity.

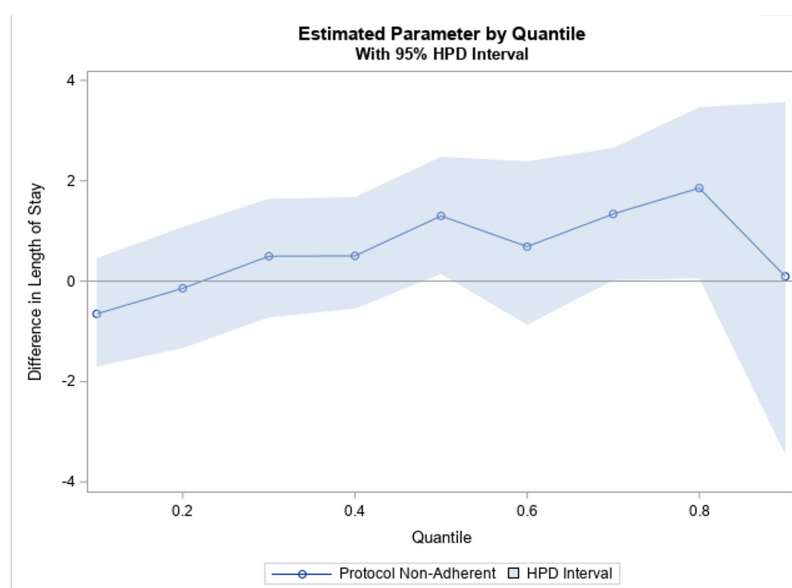


Figure. Difference in length of stay for treatment protocol non-adherent versus adherent patients with complicated parapneumonic infection from three Midwestern hospitals. Estimates presented per deciles and taken from a Bayesian quantile regression model with flat priors. HDP: highest density posterior.

Assessing Knowledge, Attitudes, and Practices towards Causal Directed Acyclic Graphs among Epidemiologists and Medical Researchers: a qualitative research project

Ruby Barnard-Mayers* Ruby Barnard-Mayers Ellen Childs Laura Corlin Ellen Caniglia Matthew P Fox John P. Donnelly Eleanor Murray

Background: Estimating the strength of causal effects is an important component of epidemiologic research, and causal graphs provide a key tool for optimizing the validity of these effect estimates. Although a large literature exists on the mathematical theory underlying the use of causal graphs to assess causal assumptions and develop analytic plans, less literature exists to aid applied researchers in understanding how best to develop and use causal graphs in their research projects.

Objective We sought to understand this gap by surveying practicing epidemiologists and medical researchers on their knowledge, attitudes, and practices towards the use of causal graphs in applied epidemiology and health research.

Methods We conducted an anonymous survey of self-identified epidemiology and health researchers via Twitter and via the Society of Epidemiologic Research membership listserv. The survey was conducted using Qualtrics and asked a series of multiple choice and open-ended questions about causal graphs.

Results In total, 439 responses were collected. Overall, a majority of participants reported being comfortable with using causal graphs and reported using them 'sometimes', 'often', or 'always' in their research. Having received training appeared to improve comprehension of the underlying assumptions of causal graphs. Many of the respondents who did not use causal graphs reported lack of knowledge as a barrier to using DAGs in their research. Of the participants who did not use DAGs, many expressed that trainings, either in-person or online, would be useful resources to help them use causal graphs more often in their research.

Conclusion Causal graphs are of interest to epidemiologists and medical researchers, but there are several barriers to their uptake. Additional training and clearer guidance are needed.

Childhood Externalizing Problems and Elevated Triglyceride Levels in Adolescence: Causal**Explanations** Paula Bordelois* Paula Bordelois Shakira F Suglia Mitchell S Elkind Karestan C Koenen Katherine M Keyes

Common childhood externalizing behaviors such as hyperactivity and conduct problems are risk factors for obesity throughout the life course. Whether these behavioral diagnoses increase cardiometabolic risk in early life independently of their effect on body adiposity is currently unknown. Using parents' ratings of their children's externalizing behaviors at ages 4 and 7 years (Strengths and Difficulties Questionnaire) we investigated the prospective association of childhood hyperactivity and conduct problems with clinically high levels of triglycerides (> 130 mg/dl) at age 17, in a large birth-cohort study, the Avon Longitudinal Study of Parents and Children (ALSPAC), N=7,730. Using causal mediation methods, we tested for natural indirect effects (NIE) mediated by diet, sleep, physical activity, smoking, alcohol use and body mass index, as well as natural direct or no mediated- effects (NDE). In fully adjusted logistic regression models, hyperactivity problems (OR= 1.74, 95% CI = 1.29-2.37) and conduct problems (OR= 1.60, 95% CI = 1.23-2.09) were associated with increased triglycerides. Mediation analysis showed that the association of hyperactivity (NDE OR= 1.48, 95% (CI=1.12 -1.89), NIE OR= 1.08, (95% CI=0.98-1.14) and conduct problems (NDE OR= 1.40, (95% CI=1.10 -1.72), NIE OR= 1.07, (95% CI=0.98-1.14)) with triglycerides were only partially mediated. Body mass index and lifestyle health behaviors jointly mediated (Proportion Mediated) 19.6 % and 19.3% of the total effects of hyperactivity and conduct problems on triglycerides, respectively. Childhood hyperactivity and conduct problems are associated with high levels of triglycerides in late adolescence. Hyperactivity and conduct problems appear to influence triglycerides mostly independently of body adiposity, and lifestyle health behaviors. Future research should confirm these findings and consider other novel mediators and common vulnerabilities of externalizing symptomatology and triglycerides.

Combining Weights and G-Computation to Examine Complex Treatment Regimes in External Targets with Limited Covariate Data

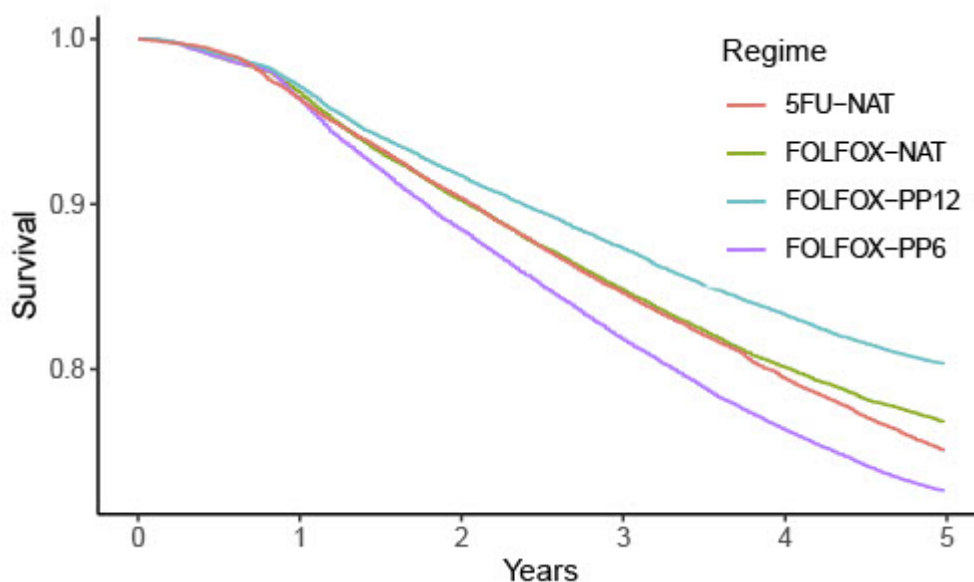
Michael Webster-Clark* Michael Webster-Clark
Jennifer L. Lund Hanna K. Sanoff Til Stürmer Daniel Westreich Alexander Keil

Recent methodologic advances leverage data from clinical trial populations to estimate treatment effects in patient groups that may differ from trial participants in key measured determinants of disease (e.g. age, sex). Most applications have estimated intent-to-treat or as-treated effects using straightforward weighting approaches. G-computation can estimate the effects of more complex treatment regimes; unfortunately, some variables required for the outcome and treatment models may not be observed in the target. If these variables are conditionally independent of trial participation, combining G-computation with weighting may yield unbiased estimates.

We used data from the pivotal randomized trial of 5-fluorouracil (5FU) vs oxaliplatin + 5FU (FOLFOX) for colon cancer to estimate mortality under four treatment regimes: up to 12 cycles of 5FU allowing deviations in dose consistent with the trial (5FU-NAT); up to 12 cycles of FOLFOX, allowing deviations (FOLFOX-NAT); up to 12 cycles of FOLFOX, following the trial protocol of dose reduction based upon side effects (FOLFOX-PP12); and up to 6 cycles of FOLFOX, similarly following protocol (FOLFOX-PP6). We estimated all-cause mortality and risk of experiencing a treatment-related paresthesia under each regime using G-computation and inverse-odds weighted sampling, targeting a population of stage III colon cancer patients in the US Oncology Network meeting trial eligibility criteria (N=4485). We used non-parametric bootstrapping to estimate confidence intervals (CIs).

Under FOLFOX-PP12, five-year mortality was lowest (risk difference vs 5FU-NAT: -5.3%, 95% CI: -14.4%, 3.8%; **Figure 1**) but paresthesia risk was highest (risk of 43%). Risk of paresthesia was much lower with FOLFOX-NAT (1%) or FOLFOX-PP6 (16%).

Combining G-computation with sampling weights allowed estimation of outcome risk under complex treatment regimens even when some parts of the treatment and outcome models were only observed in trial participants.



Causal inference with skewed outcome data: moving beyond the “ignore or transform” approach Daisy Shepherd* Daisy Shepherd Margarita Moreno-Betancur

With continuous outcomes, the average causal effect is typically defined using a contrast of mean potential outcomes. However, in the presence of skewed outcome data, the mean may no longer be a meaningful summary statistic and the definition of the causal effect should be considered more closely. When faced with this challenge in practice, the typical approach is to either “ignore or transform” - ignore the skewness in the data entirely, or transform the outcome to obtain a more symmetric distribution for which the mean is interpretable. In many practical settings, neither approach is entirely satisfactory. An appealing alternative is to define the causal effect using a contrast of median potential outcomes. Despite being a widely acknowledged concept, there is currently limited discussion or availability of confounder-adjustment methods to generate estimates of this parameter.

Within this study, we identified and evaluated potential confounding-adjustment methods for the difference in medians to address this gap. The methods identified are multivariable quantile regression, adaptations of the g-computation approach, weighted quantile regression and an IPW estimator. The performance of these methods was assessed within a simulation study, and applied in the context of an empirical study based on the Longitudinal Study of Australian Children. Results indicated that the performance of the proposed methods varied considerably depending on the simulation scenario, including the severity of skewness of the outcome variable. Nonetheless, the proposed methods provide appealing alternatives to the common “ignore or transform” approach, enhancing our capability to obtain meaningful causal effect estimates with skewed outcome data.

Are small-for-gestational-age preterm infants at increased risk of overweight? Statistical pitfalls in over-adjusting for body size measures Seham Elmrayed* Seham Elmrayed Krista Wollny Amy Metcalfe Darren Brenner Tanis R Fenton

Background

Numerous studies suggest that infants born small-for-gestational-age (SGA) have higher risks of later obesity. However, the observed associations between SGA and obesity may be due to over-adjusting for later body size measures. This study aimed to analyze the effect of controlling for later weight and height on the association between SGA and overweight in a cohort of very preterm infants.

Methods

Data were obtained from the Preterm Infant Multicenter Growth Study (n=1089). The association between SGA and overweight at 36 months CA was analyzed using multiple logistic regression models: 1) crude 2) adjusted for baseline covariates including maternal and paternal age and education, and maternal smoking 3) adjusted for baseline covariates with additional adjustments separately for weight and height z-scores at 21 months CA. Additionally, marginal structural models (MSMs) with stabilized inverse probability weights were used to estimate the direct effect of SGA on overweight.

Results

The crude model and the model that controlled for baseline covariates yielded a null association (OR 0.88, 95% CI 0.26, 2.96, OR 0.95, 95% CI 0.28, 3.29). Controlling for later height reversed the direction of the effect (OR 2.31, 95% CI 0.52, 10.26) and controlling for later weight reversed the effect and provided a strong and significant association (OR 6.60, 95% CI 1.10, 37.14). The marginal structural models with height and weight considered as intermediate variables indicated no direct effect of SGA on overweight (OR 0.83, 95% CI 0.14, 5.01, OR 0.71, 95% CI 0.18, 2.81).

Conclusions

Controlling for body size measures can falsely induce or reverse the association between small-for-gestational-age and overweight.

Methods for Modeling the Trajectory of Gestational Weight Gain: A Review of the**Literature** Anna Booman* Anna Booman Rachel Springer Jennifer Lucas Miguel Marino Jean O'Malley Amy Palma Teresa Schmidt Kristin Scott Kalera Stratton Jonathan Snowden Sarah Truclinh-Tran Kimberly Vesco Janne Boone-Heinonen

Gestational weight gain (GWG) has been investigated as a determinant of perinatal and maternal health outcomes, most typically using measures of the total amount of weight gained during pregnancy. However, women can follow different trajectories of gain and reach the same total weight gain, and prior evidence suggests that the timing of the weight gain may be important. There is no consensus on the appropriate way to assess weight gain trajectories. The objective of this study was to review methods used to model trajectories of GWG and discuss their advantages and disadvantages.

We performed a literature search in PubMed for studies that evaluated GWG as an exposure or an outcome. Articles were included in the review if they used methods that modeled weight gain patterns throughout pregnancy and included three or more weight datapoints per pregnancy.

Thirty-nine studies were included in the review. Several methods differentiate weight gain among trimesters, including trimester-specific models of linear GWG, rate of GWG, and the GWG adequacy ratio. Methods that model weight gain throughout pregnancy include the area under the GWG curve method, which estimates additional pound-days carried through pregnancy; calculation of z-scores, which is uncorrelated with the length of pregnancy; latent trajectory groups; and application of a super-imposition by translation and rotation model. Methods varied with regard to differentiation between body mass index classification, number of requisite time points, estimation of first trimester GWG, and flexibility of the GWG curve.

Numerous methods for modeling GWG trajectories have been used in prior studies, enabling investigation of the relationship between patterns of GWG and health outcomes. Further research will apply these techniques on an identical dataset to determine if they result in similar strengths of association between GWG and a health outcome. This research will help identify recommended techniques for modeling GWG.

The effect of missing data and multiple imputation on the detection of bias in cognitive testing due to low educational attainment Emma Nichols* Emma Nichols Jennifer Deal

Bonnielin Swenor Alison Abraham Michael Griswold Frank Lin Thomas Mosley Nicholas Reed A. Richey Sharrett Alden Gross

Item response theory (IRT) methods for the detection of differential item functioning (DIF) allow for the detection of bias in cognitive testing, and findings can inform the quantification of cognition. IRT and DIF-detection methods have been used increasingly often to identify bias in cognitive testing, but previous analyses have not considered the effect of missing cognitive data, and levels of missing data can be substantial in some studies. We used real-world data from the Atherosclerosis Risk in Communities Neurocognitive Study (ARIC-NCS) (N = 3580) to test the effect of missing data and Multiple Imputation with Chained Equations (MICE) on DIF detection. We imposed 10%, 30%, and 50% missingness that was either (1) random or (2) related to cognitive performance on cognitive test data among those with low educational attainment. The mean age in the ARIC-NCS sample was 79.9 years, and 60% were female, while 53% of the sample had low education (high school or lower). Missingness unrelated to cognitive performance only caused random error, but missingness related to cognitive performance led to systematic error. The magnitude of this systematic error increased with higher proportions of missing data. We found that the median error in DIF findings across the cognitive items considered was 0.03, 0.08, and 0.15 logits respectively, which resulted in incorrect inferences for 4%, 16%, and 30% of findings. However, with MICE the magnitude of error was reduced to 0.03, 0.04, and 0.09 logits for each missingness scenario, resulting in changes to inferences in 4%, 9%, and 16% of findings. In sum, missing data related to low education and cognitive status led to error in the detection of DIF due to low education, and this bias was reduced but not eliminated using MICE. Incorrect inferences in DIF testing have downstream consequences for the measurement of cognition, and it is therefore critical to consider the effect of missing data when evaluating bias in cognitive testing.

A machine learning method for reducing the complexity of high dimensional environmental data: an application to cognitive performance in children

Seth Frndak* Seth Frndak Guan Yu
Gabriel Barg Elena I. Queirolo Marie Vahter Fabiana Peregalli Nelly Mañay James R. Olson
Katarzyna Kordas

Background: Standard methods to analyze high-dimensional data in environmental epidemiology studies are lacking. Using data on child cognitive function, we provide a framework that incorporates machine learning to select highly predictive variables.

Methods: The dataset contained 338 children with Woodcock-Muñoz General Intellectual Ability (GIA) score, and 121 variables in domains: year of enrollment, child demographics, health history, anthropometry, pregnancy information, school characteristics, household enrichment, child's time use, diet, nutritional and toxicant exposure biomarkers, parental characteristics, neighborhood factors. We chose group LASSO because we included dummy coded categorical variables. Randomly divided 50/50 training and test datasets were created. 10-fold cross validation selected an optimal value of lambda. Final group LASSO-selected variables were recorded. This process was repeated 100 times resulting in 100 randomly sampled training and test datasets with 100 final variable sets. We recorded 10 most and least frequently selected variables.

Results: Top 10 selected variables included (descending order): mother's IQ, child serum ferritin, school preparation, HOME score, forgetting homework, parental discipline, season data collected, child sleep quality, serum zinc and frequency of spanking child. The least frequently selected variables included (ascending): urinary thiamine, number of books owned by child, caregiver communication with school, years since house last painted inside, child's dietary iron intake and processed food dietary pattern, blood lead, hours child plays outside, hours child watches TV, and parent smoking.

Conclusions: Variables consistent with causal thinking about IQ deficits in children (ex., maternal IQ) were selected. Others (ex., lead) were left out. Machine learning for variable selection requires expert knowledge, particularly if variables are intended for use in causal epidemiology.

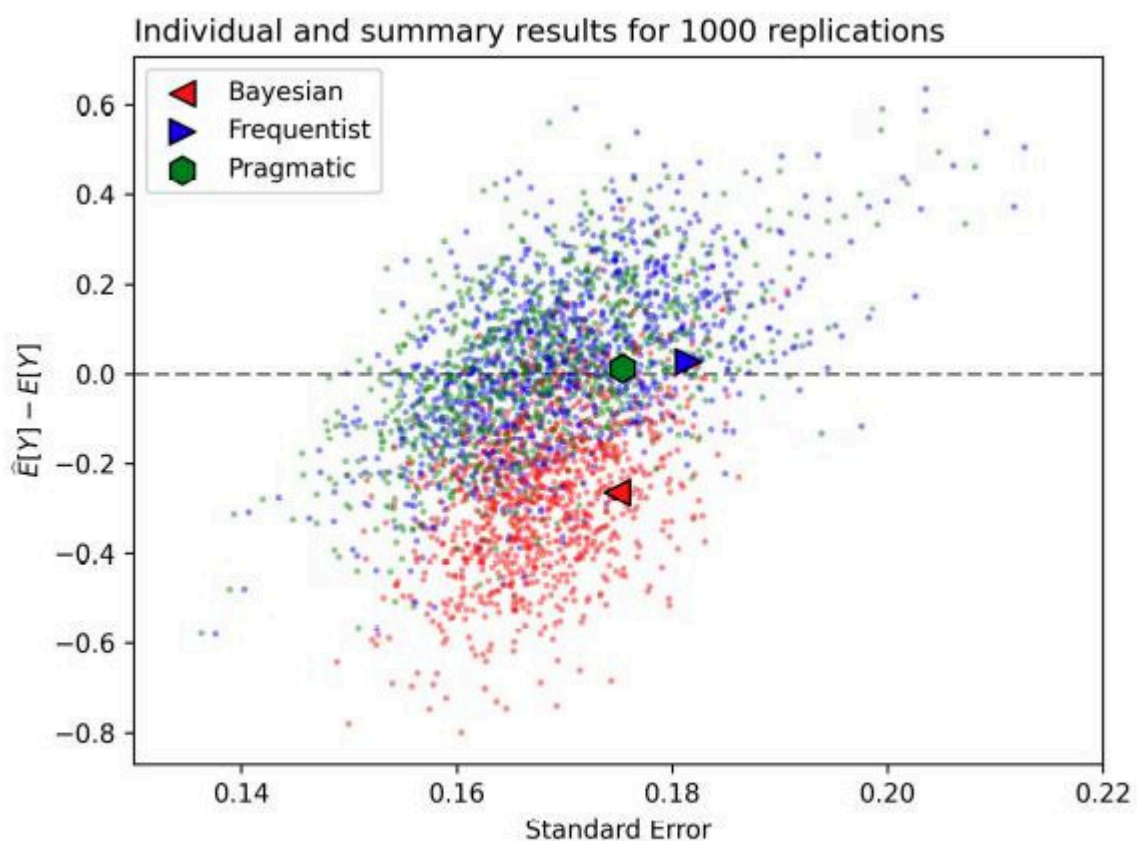
Handling missing data for causal effect estimation in longitudinal cohort studies using**Targeted Maximum Likelihood Estimation: a simulation study** S. Ghazaleh Dashti* S.

Ghazaleh Dashti Katherine J. Lee Julie A. Simpson Ian R. White John B. Carlin Margarita Moreno-Betancur

Causal inference from longitudinal cohort studies plays a pivotal role in epidemiologic research. One available method for estimating causal effects is Targeted Maximum Likelihood Estimation (TMLE), which is a doubly robust method, combining a model for the outcome and a model for the exposure and only one of the two has to be consistent to obtain unbiased estimates. It also offers asymptotically valid confidence intervals when these models are fitted using machine learning (ML) approaches, which allow the relaxation of parametric assumptions. However, it is unclear how missing data should be handled when using TMLE with ML, which is problematic given that missing data are ubiquitous in longitudinal cohort studies and can result in biased estimates and loss of precision if not handled appropriately. We sought to evaluate the performance of currently available approaches for dealing with missing data when using TMLE. These included complete case analysis, an extended TMLE method in which a model for the outcome missingness mechanism is incorporated in the procedure, the missing indicator method for missing covariate data, and multiple imputation (MI) using standard parametric approaches or ML algorithms to concurrently handle missing outcome, exposure and covariate data. Based on motivating data from the Victorian Adolescent Health Cohort Study, we conducted a simulation study to evaluate the performance (bias and precision) of these approaches for estimation of the average causal effect. We considered a simple setting, where the exposure and outcome were generated from main-effects regression models, and a complex setting, where the models also included two-way and higher order interactions. Our results aim to provide guidance for handling missing data in a range of missingness scenarios depicted using causal diagrams. We illustrate the practical value of these findings in an example examining the effect of adolescent cannabis use on young adulthood mental health.

A pragmatic stance on Bayesian and Frequentist methods with high-dimensional data Paul Zivich* Paul Zivich Stephen

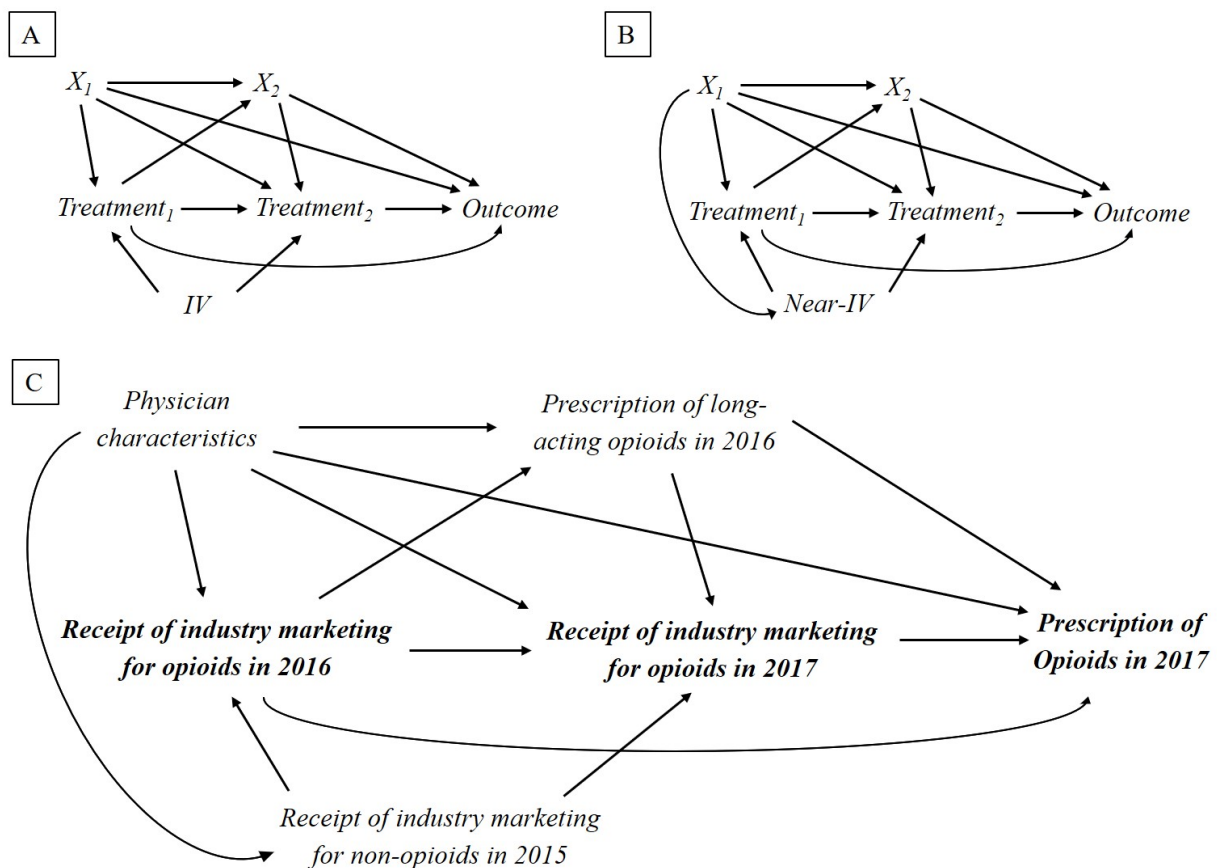
Neither Bayesian nor frequentist approaches fully address problems for models with high-dimensional covariates. Consider the simple case of estimating the population mean for a variable with non-trivial missing data, where missingness depends on a continuous covariate. Bayesians are unable to use propensity scores because the propensity score is not part of the likelihood. This inability to incorporate propensity scores becomes a problem for high-dimensional data, or when a non-parametric outcome model is infeasible. Conversely, frequentists are able to use both the outcome and propensity score models, but remain unable to incorporate outside information in a principled way. Practically speaking, this means a frequentist must be more uncertain than necessary when reliable prior information exists, or that frequentists must learn slower. In response to the above non-overlapping deficiencies, we; like Box, Good, and Greenland; propose the adoption of a pragmatic approach. We opt to combine features of Bayesian and frequentist approaches to reduce the squared error in a wide neighborhood where results are plausible. By simulation, we demonstrate that a pragmatic compromise can outperform either of the competing approaches. We discuss the tradeoffs epidemiologists face when choosing among such approaches.



Bayesian, frequentist, and pragmatic approaches to estimate the mean of continuous variable Y with data missing at random. The frequentist approach consisted of an augmented inverse probability weighting estimator with generalized additive models. The pragmatic approach updated the frequentist estimate with a slightly biased prior (bias=-0.5) via inverse variance weighting. Small dots indicate individual replications and large shapes indicate overall summarization of the results. Summary results indicate the mean bias and the Monte Carlo standard error.

Bias amplification in the g-computation algorithm for time-varying treatments Kosuke Inoue* Kosuke Inoue Atsushi Goto Tomohiro Shinozaki

The g-computation algorithm—a generalization of standardization—has been increasingly used in observational studies with time-varying treatments and confounders given its flexibility. It is often challenging to determine which variables need to be included in the algorithm, and unnecessary adjustment may introduce greater bias when there is unmeasured confounding between the time-varying treatments and the outcome, called ‘bias amplification’. Conditioning on instrumental variables (IVs; Figure A), which are associated with the outcome only through the treatment, or even near-IVs that are weakly associated with the outcome (Figure B), is known to induce such bias amplification in the point-treatment settings. However, it has been unknown whether and the extent to which the adjusting for IVs or near-IVs amplifies bias in the g-computation algorithm estimators for time-varying treatments compared to those ignoring such variables. In this article, after showing a case study of the association of industry marketing payments with physicians’ prescription of opioid products in the US (Figure C), we demonstrated Monte Carlo simulation results that compare the estimated effects of the time-varying treatments on the outcome across several g-computation models. We found that the estimated effect of the treatment showed greater bias due to an unmeasured confounder when the g-computation model included IVs for the treatments. This was also the case for near-IVs only when their association with the unmeasured confounder was very weak. These findings would help researchers to consider which variables should be included in the g-computation algorithm for time-varying treatments when they are aware of the presence of unmeasured confounding.



Comparing effect estimates in randomized trials and observational studies from the same population Anthony Matthews* Anthony Matthews Miguel Hernan Issa Dahabreh Anita Berglund Maria Fethting Karolina Szummer Tomas Jernberg Bertil Lindahl David Erlinge

Background

The ability for real world data to deliver similar results as a trial that asks the same question about the risks or benefits of a clinical intervention can be restricted not only by lack of randomization, but also limited information on eligibility criteria and outcomes. To understand when results from observational studies and randomized trials are comparable, we carried out an observational emulation of a target trial designed to ask similar questions as the VALIDATE randomized trial. VALIDATE compared the effect of bivalirudin and heparin during percutaneous coronary intervention on the risk of death, myocardial infarction, and bleeding across Sweden.

Methods

We specified the protocol of a target trial similar to the VALIDATE trial protocol, then emulated the target trial in the period before the trial took place using data from the SWEDEHEART registry; the same registry in which the trial was undertaken.

Results

The target trial emulation and the VALIDATE trial both estimated no difference in the effect of bivalirudin and heparin on the risk of death or myocardial infarction by 180 days: emulation risk ratio for death 1.21 (0.88, 1.54); VALIDATE hazard ratio for death 1.05 (0.78, 1.41). The observational data, however, could not capture less severe cases of bleeding, resulting in an inability to define a bleeding outcome like the trial, and could not account for intractable confounding early in follow-up.

Conclusion

Using real world data to emulate a target trial can deliver accurate long-term effect estimates. Yet, even with rich observational data, it is not always possible to estimate the short-term effect of interventions, or the effect on outcomes for which data are not routinely collected.

Toenail and serum measures as biomarkers of iron levels Ann Von Holle* Ann Von Holle
Clarice R. Weinberg Katie M. O'Brien Dale P. Sandler Margaret R. Karagas Brian P. Jackson Robert
Janicek Alexandra White

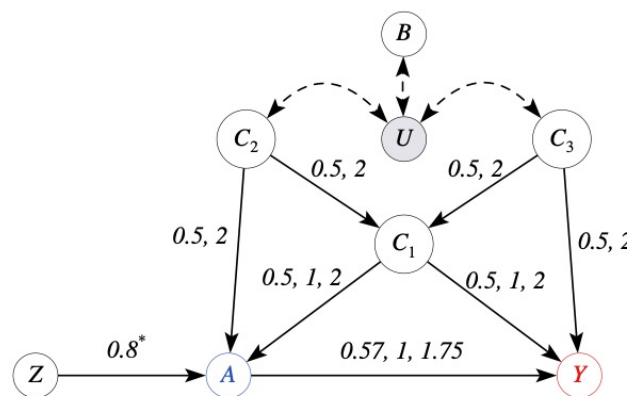
For epidemiologic studies, iron measurements are often based on serum. Toenails offer a convenient alternative to serum because of ease of collection, transport, and storage. No study has examined the correlation between the serum and toenail measures for iron. Our aim was to compare measures using serum and toenails iron measures on a cross-sectional and longitudinal basis. Using a sample from the US-wide prospective Sister Study cohort, we compared trace iron levels in toenails with three serum biomarkers: iron, ferritin and percent transferrin saturation. Participants (N=281) donated both blood and toenails at baseline (2003-2009) and a subsample (59%, n=165) provided specimens again about 8 (IQR: 7,9) years later. Cross-sectional analyses included Spearman's rank correlation to assess nail/serum association and coefficient of variation comparisons. We also considered maintenance of rank across time separately for nails and for serum, and compared Spearman's correlation coefficients of repeated measures for nail and serum values. Overall, nail and serum iron values did not correlate well with each other. Spearman correlations at baseline (follow-up) were 0.09 (0.04) for serum iron, 0.11 (0.02) for transferrin saturation, and -0.08 (0.01) for ferritin. Nail measures at baseline (follow-up) had a higher coefficient of variation 1.22 (0.94) than serum iron 0.36 (0.33), ferritin 1.01 (0.93), and transferrin saturation 0.38 (0.33). The Spearman correlation for nail iron between repeats across the two time points (0.47, 95% CI: 0.34, 0.60) was higher than for serum iron (0.25, 95% CI: 0.11, 0.39), transferrin saturation (0.33, 95% CI: 0.18, 0.47), and ferritin (0.45, 95% CI: 0.33, 0.58). Based on cross-sectional and repeated assessments, iron measures based on serum did not correlate with those based on toenails. Toenail iron measures appear to be repeatable, but cannot be taken as a proxy for serum iron values and may represent different mechanisms of iron storage.

Covariate selection using background knowledge and causal discovery methods Yongqi

Zhong* Yongqi Zhong Ashley Naimi

To estimate effects of interest, adjusting for pre-treatment covariates is accepted as a practical solution. However, given the uncertainty about underlying data generating mechanism, multiple sufficient covariate adjustment sets can often be considered based on domain-specific knowledge. Here, we explore the performance of different covariate adjustment sets using DAGs identified by background knowledge with and without causal discovery algorithms. We simulated 432 sets of data in M-related structured DAGs (Figure), and estimate the average treatment effect with g-computation, inverse probability weighting, augmented IPW and targeted maximum likelihood estimation, adjusting for causes of the exposure and/or the outcome with and without unnecessary covariates. We further evaluate the accuracy of causal discovery algorithms in selecting covariate adjustment sets. With the knowledge of true DAGs, while using different covariate adjustment sets yields similar absolute bias, adjusting for all covariates results in highest mean square errors (MSE). Without the knowledge of true DAGs, causal discovery algorithms provide 27% of accuracy in correctly selecting covariates that blocks the backdoor path from the exposure to the outcome. Regardless of the accuracy, adjusting for the causes of outcome or exposure identified by the causal discovery algorithms yields similar absolute bias and MSE to those identified by the knowledge of true DAGs. Our results suggest overall poor performance of causal discovery algorithms in identifying sufficient adjustment sets. Therefore, background knowledge is essential to identify DAGs for selecting covariate adjustment set (i.e., causes of the exposure and the outcome).

Figure. Data generating Mechanisms for M-related Causal Structures



1. Numbers on the edges are odds ratios (OR)
2. A total of 432 DAGs were simulated, each with a sample size of 1,228 and 2,000 Monte Carlos
3. Z, C₂, C₃ and B were the baseline covariates resampled from the The Effects of Aspirin in Gestation and Reproduction (EAGeR) trial
4. A, C₁ and Y were simulated with logistic regressions [$\beta = \log(OR)$]:

$$\begin{aligned} \text{logit} [P(C_1 = 1 | C_2, C_3)] &= \beta_{C_{10}} + \beta_{C_1 C_2} C_2 + \beta_{C_1 C_3} C_3 \\ \text{logit} [P(A = 1 | Z, C_1, C_2)] &= \beta_{A_0} + \beta_{AZ} I(Z = 1) + \beta_{AC_1} C_1 + \beta_{AC_2} C_2 \\ \text{logit} [P(Y = 1 | A, C_1, C_3)] &= \beta_{Y_0} + \beta_{YA} A + \beta_{YC_1} C_1 + \beta_{YC_3} C_3 \end{aligned}$$

Log-transformation of independent variables: must we? Giehae Choi* Giehae Choi Alexander P. Keil

Background: Researchers working with skewed exposure variables often log-transform data. This transformation can be motivated by distributional assumptions, toxicologic dose-response, outliers, or habit. However, such transformation may not always reduce bias.

Aim: To evaluate impacts of natural-log-transforming an exposure (X) on bias and variance of effect estimates for a continuous outcome (Y) in simulated cohort data.

Methods: We simulated data under three generating mechanisms (DGMs), $N=500$. For each DGM, we generated Gaussian outcomes under two dose-responses: $E(Y|X)=0.3 \cdot X$ or $E(Y|X)=0.3 \cdot \ln(X)$. We simulated X under the following scenarios: DGM 1) skewed exposure ($\ln(X) \sim N(-0.11, 0.47^2)$); DGM 2) DGM 1 plus 5% of values of X were drawn from a log-normal distribution with a high geometric mean ($\ln(X) \sim N(1.31, 0.47^2)$) or DGM 3) DGM 1 plus 5% of X had multiplicative, random measurement error. In each scenario, we fit 3 models: linear regression of Y on X, linear regression of Y on $\ln(X)$, and outlier-robust linear regression of Y on X. Using each model, we contrasted predicted values of $E(Y|X)$ at theoretical 25th and 75th percentiles of X to estimate the change in Y for an interquartile range increase in X, given by . Each scenario was repeated 1000 times.

Results: In DGMs 1-2, the correctly specified model resulted in the least biased estimate. For example, DGM 1 analyzed with untransformed X, [truth=0.172] was best estimated by standard [%bias (%B)=0.57; root mean squared error (RMSE)=0.052] or robust [%B=0.39; RMSE=0.054] linear regression using X; but biased using $\ln(X)$ [%B=9.63; RMSE=0.064]. Under misspecified models, the predicted values of Y at low and high values of X were further from the true regression lines (Figure). In DGM 3, using $\ln(X)$ resulted in the least biased estimate under both true models, but all approaches were biased >10%.

Conclusion: Skewed exposure variables do not always necessitate log-transformation of data and may increase bias.

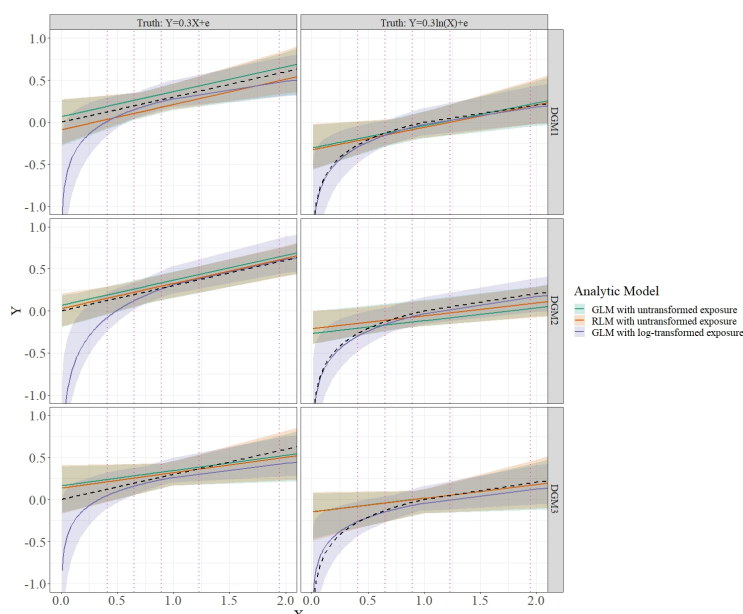


Figure. Truth (dashed) and predicted dose-responses from 1000 iterations (solid; median; band: range of 2.5th to 97.5th percentile) using 3 different analytic models. The 5th, 25th, 50th, 75th, and 95th percentiles of X are indicated with pink vertical lines.

LATEBREAKER

Methods/Statistics

Master protocol and parallel approach to analyze angioedema in patients with heart failure identified in an integrated care delivery system compared to administrative claims Carla Rodriguez-Watson* Carla Rodriguez-Watson John G. Connolly Aaron B. Mendelsohn Cheryl Walraven Mano Selvan Margaret A. Adgent Pamala A. Pawloski Sigrid Behr Jeffrey S. Brown Raymond G. Schlienger

Master protocols for parallel analyses across multiple sites has been used to study rare and novel events. Key to such analyses is an understanding of differences across data sources and transparent reporting. We describe the use of a master protocol for a non-distributed analysis across two networks in a real-world regulatory safety study.

The Innovation in Medical Evidence Development and Surveillance Network and Cardiovascular Research Network collaborated to expand a protocol originally developed for electronic health record (EHR) data linked to administrative claims to one using administrative claims (claims) only for the examination of angioedema risk in patients with heart failure receiving angiotensin receptor-neprilysin inhibitors vs. angiotensin-converting-enzyme inhibitors (ACEI).

Adapting an EHR+claims-based protocol to claims only required consideration for differences in data availability and granularity; differences in event ascertainment; and the potential impact of different approaches on data interpretation. Outcomes and exposures were identified through claims in both networks for the current analysis.

The IMEDS Network included 41,521 heart failure patients and leveraged tools developed by the FDA's Sentinel Initiative for distributed analyses in claims. The CVRN included 14,241 patients and used a common data model leveraging claims and EHR data. We observed similarities across data sources with respect to age, sex, and potential angioedema incidence rates in those on ACEIs.

Collaborating on a master protocol to accommodate different data sources and methodology yielded consistent results. This experience adds to the body of knowledge regarding the use of master protocols and parallel analyses across discrete data sources to efficiently increase sample size for rare outcomes/exposures, and to identify differences and similarities across datasets. Future work will enable comparisons when outcomes are defined using EHR compared to claims.

LATEBREAKER

Methods/Statistics

A review of the application of simulation to quantifying the influence of bias in reproductive and perinatal epidemiology Jennifer Dunne* Jennifer Dunne Gizachew Tessema Milica Ognjenovic Gavin Pereira

Aetiological epidemiology, the understanding of casual effects of exposures on outcomes, is central to reproductive and perinatal epidemiology. Establishing causal effects is particularly challenging due to the many selection and attrition processes from preconception to the postnatal period. Further challenging, is the potential for the misclassification of exposures, outcomes and confounders contributing to measurement error. The use of simulated data in epidemiological studies enables the illustration and quantification of the magnitude of various types of bias commonly found in reproductive and perinatal observational studies. This was a review of the application of simulation methods to the quantification of bias in reproductive and perinatal epidemiology and an assessment of value gained. A search of published studies available in English was conducted in August 2020 using the following databases: PubMed, Medline, Embase, CINAHL, and Scopus. A gray literature search of Google and Google Scholar, and a hand search using the reference lists of included studies was undertaken. In total 1,561 papers were identified of which 39 papers were included in this study. The included studies covered the three main areas of bias: information (n =14), selection (n = 15) and confounding (n = 8). One study quantified protection bias and one attenuation bias. Although the overall number of studies was relatively limited, there is increasing application of simulation to quantify bias, with 46% of the included studies published since 2015. The methods of simulating data and reporting of results varied, with more recent studies including causal diagrams. Few studies included code for replication. Further efforts are required to increase knowledge of how the application of simulation can quantify the influence of bias, including improved design, analysis and reporting. This will improve causal interpretation in reproductive and perinatal studies.

LATEBREAKER

Methods/Statistics

Analytic weighting scheme for recovering target sample and population characteristics in a SARS-CoV-2 sero-prevalence study Hayden Smith* Hayden Smith

Background: There is currently a global COVID-19 pandemic. Studies investigating the disease are based on samples and can have non-response threats, which can impact research accuracy and generalizability. Purpose: To present a multi-stage weighting scheme to recover target sample and population characteristics.

Methods: A sero-prevalence study was conducted in December 2020 – January 2021 within a Midwestern US health system. Approximately 6260 employees from four hospitals and associated clinics were invited to complete an electronic survey and blood draw for SARS-CoV IgG antibodies. Design weights were not relevant given participation was not restricted, however not all employees enrolled, and some did not complete both study components (i.e., survey and blood draw). Given these limitations, response status for the blood draw was modeled to create inverse probability weights. Next, population counts for auxiliary variables were used to generate calibration weights to match target population characteristics. Weights were applied to antibody (respondent) data to estimate prevalence and SARS-CoV IgG values.

Results: Of eligible employees, 2848(49%) completed the survey and 2140 (35%) had antibody testing. The unadjusted, adjusted, and calibrated SARS-CoV-2 prevalence values were 12.9% (95% CI: 11.5%, 14.4%), 13.3% (95% CI: 11.8%, 14.7%), and 13.3% (95% CI: 12.5%, 14.2%), respectively. The median unadjusted, adjusted, and calibrated antibody index values for subjects self-reporting history of infection were 2.69 (IQR: 1.01, 4.95), 2.66 (IQR: 0.98, 4.87), 2.66 (IQR: 0.98, 4.93), respectively. Additional job stratified estimates, antibody modeling, and sensitivity analyses will be presented at the conference with details on the weight building process (Figure).

Conclusions: Access to response status and auxiliary variables allows for weight construction, review of bias, and generalizations. The presented process could be adapted to transport estimates to new populations.

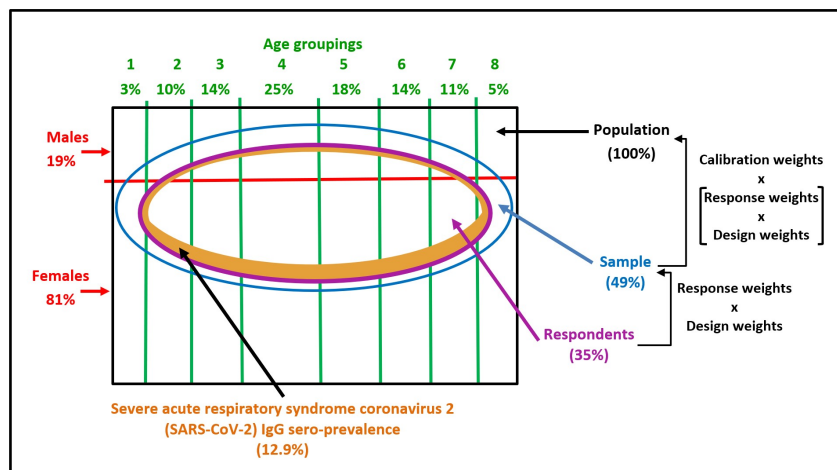


Figure. Weighting scheme: black rectangle represents the study population consisting of four hospitals and associated clinics; blue oval represents employees with a completed survey (design weights: 1/N); purple oval represents employees with a blood test (response weights: 1 / (pr(respondent | X)), X = survey information); cross hatchings represent population marginal counts used in the calibration process via iterative raking ratios based on exponential weights to ensure they are positive at the end of the optimization process.

LATEBREAKER

Methods/Statistics

Strategies of managing repeated measures: using Synthetic Random Forest to predict HIV viral suppression status among Initially Hospitalized HIV patients Jingxin Liu* Jingxin Liu Mindy Nelson Yue Pan Daniel Feaster

Background: The HIV/AIDS epidemic has had a substantial impact on the health and economy of many nations in the world. Although HIV treatment has dramatically improved the health, quality of life, and life expectancy of persons living with HIV (PLWH), few studies have predicted future viral suppression using repeated measures data.

Purpose: We compared four different strategies of using repeated assessments to predict future viral suppression among PLWH and reporting using substances.

Methods: The sample included 512 PLWHs who participated in both CTN-0049 and CTN-0064 studies (422 alive and 90 deceased between two CTN study periods). CTN-0064 was approximately 3 years after CTN-0049 completed. The HIV viral load suppression status (yes or no) at the baseline of CTN-0064 was the outcome. Predictors were taken from the 3 assessments in CTN-0049. The predictors for model 1 through model 4 were: 1) characteristics from the three time-point assessments of CTN-0049 (baseline, 6- and 12- months after randomization); 2) characteristics of only the baseline assessment of CTN-0049; 3) characteristics from only the 12-month assessment of CTN0049; and 4) the individual-specific growth model features of the time-varying predictors for CTN-0049 (intercept and slope) separately. The *Synthetic Random Forests* (SRF) procedure was utilized to build four predictive models. The Out-of-bag (OOB) error rate and the area under the Receiver Operating Characteristic (ROC) curve (AUC) were obtained to compare the predictive power.

Results: Based on the overall OOB error rate and the AUC curve, model 4 performed best, followed by model 3, then model 1, then model 2.

Conclusions: The person-specific trajectories had better predictive power than using raw features as predictors, and characteristics from closer time-point produced better model fit than using baseline aspects only. We also found that log-transformed copy of (historical) HIV viral load was the strongest predictor while controlling for others, the slower the virus was cleared in the body, the greater the chance of not being viral suppressed at the long-run follow-up.

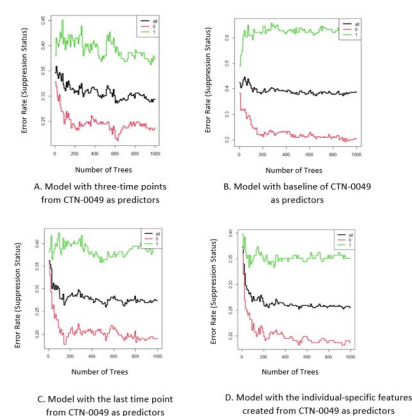


Fig 1. Out of bag prediction errors across number of trees used in random forest for all observations (black), non-suppressed group (red) and HIV suppressed group (green) (Color figure online)

LATEBREAKER

Methods/Statistics

Relative validity of alternative methods to assess self-reported physical activity in epidemiologic studies: Findings from the Men's Lifestyle Validation Study Claire Parnar*

Claire Parnar Andrea Chomistek Junaidah Barnett Kerry Ivey Laila Al-Shaar Susan Roberts Jennifer Rood Roger Fielding Jason Block Ruifeng Li Walter Willett Giovanni Parmigiani Edward Giovannucci Lorelei Mucci Eric Rimm

Objective: In the Men's Lifestyle Validation Study (2011-2013), we examined the relative validity of a physical activity questionnaire (PAQ) and web-based 24-hour recalls (ACT24) through comparison with multiple methods assessing activity and body composition.

Methods: Over one year, 609 men completed two PAQs, four ACT24 recalls, two 7-day accelerometer measures, one doubly-labeled water (DLW)-physical activity level (PAL) measure (repeated, n=100), and four resting pulse rate measurements. A subset (n=197) completed dual energy X-ray absorptiometry (DXA)(repeated, n=99). The method of triads was applied to estimate correlations with true activity using DLW-PAL and accelerometer as biomarker and reference measures.

Results: Estimated correlations (95% confidence intervals) of the PAQ with true activity were 0.60 (0.52, 0.68) for total activity, 0.69 (0.61, 0.71) for moderate to vigorous physical activity, and 0.76 (0.62, 0.93) for vigorous activity. Correlations (95% confidence intervals) of the average of four ACT24 measures with true activity were 0.53 (0.45, 0.63) for total activity, 0.58 (0.49, 0.69) for moderate to vigorous physical activity, and 0.42 (0.29, 0.62) for vigorous activity. For total activity, correlations (95% confidence intervals) of DLW-PAL and accelerometer measures with true activity were 0.70 (0.62, 0.78) and 0.68 (0.61, 0.78), respectively. Total activity and moderate to vigorous physical activity measured by PAQ, ACT24, and accelerometer were significantly correlated with DLW- and DXA-determined body fat and resting pulse rate.

Conclusion: Our study shows good validity of the PAQ using a combination of biomarker and device-based methods to estimate correlations with true activity. The estimated validity using four ACT24 assessments with true activity was lower. The PAQ provides useful information on physical activity, especially moderate to vigorous physical activity, for epidemiologic studies.

LATEBREAKER

Methods/Statistics

Teaching Causal Inference for High School Students: A Review of Instructional Methods for Early Exposure, Understanding, and Extended Scholarship Emily M. D'Agostino* Emily D'Agostino

Introduction: Causal inference is a fundamental component of epidemiology. Observing associations, intervening with manipulation, and addressing the counterfactual are central to teaching causal inference for graduate and undergraduate students. Although not previously explored, we can extend teaching causal inference to secondary students by reviewing current methods of instruction in the field, and applying robust student-centered progressive pedagogy to tailor these methods to high school youth. **Methods:** A systematic review of causal inference teaching and learning practices in epidemiology and statistics literature will be integrated with high school education strategies drawing from authentic instruction, active learning and student-centered techniques. The Target Trial framework will be emphasized to showcase new methods for promoting high school student understanding of causal studies and effects. Case studies will be offered on current topics of relevance to youth, including COVID-19 transmission, gun violence, and vaping.

Results: A review of instructional methods for teaching causal inference integrating high school student learning strategies will be presented. Case studies will draw from publicly available data on topics of immediate relevance to students' lives (COVID-19, gun violence, and vaping). Use of potential outcomes learning approaches, situated within the context of estimating causal effects will be discussed. Instructional strategies presented will meet Next Generation Science Standards for high school learning set by the National Academies of Sciences, Engineering and Medicine, and will be designed to equip a broad audience with early exposure to causal inference in support of continued scholarship in epidemiology and the use of evidence to support scientific claims.

Conclusion: The work presented will support early exposure to causal inference for high school students to promote greater diversity in, and advancement of the field.

LATEBREAKER

Methods/Statistics

Using case-control data to study secondary outcomes: Applying weights to overcome control to case sampling Michelle Huezo Garcia* Michelle Huezo Garcia Julie Peterson Samantha Parker Eric Rubenstein Martha Werler

Introduction: Case control designs allow for studying secondary outcomes not based on original case status, which is useful when studying rare exposures. However, when studying secondary outcomes, case control sampling causes outcomes to be overrepresented compared to the source population. Reweighting by the sampling fraction to represent the source population may correct for skewed distribution of outcomes that case control sampling produces. We apply this method to estimate associations between women with congenital physical disabilities (CPD) and common birth outcomes.

Methods: Mothers of cases and controls in the Slone Birth Defects Study were asked about personal and family history of birth defects and details of the study pregnancy. Women with CPD reported having one of the following: spina bifida, cerebral palsy, muscular dystrophy, contractures, or arthrogryposis and were matched to mothers without CPD by interview year and study site. Binomial regressions estimated risk ratios (RRs; 95% CIs) for CPD in relation to low birthweight (LBW), preterm birth (PTB) and small for gestational age (SGA) using unweighted and reweighted infant birth defect status to represent a 3% birth defect prevalence.

Results: In the unweighted analysis, infant birth defects were overrepresented in women with and without CPD, 85% and 70% respectively, while reweighted results to account for the prevalence of infant birth defects produced a distribution of 6% and 2% respectively. Unweighted analyses produced inflated proportions of LBW, PTB, and SGA overall and weak CPD-birth outcome associations. After reweighting, women with CPD were at higher risk for PTB (4.1; 2.6, 6.3) and SGA (1.7; 1.2, 2.5).

Conclusion: Reweighting infant case status produced observable associations between CPD, PTB and SGA. More research of pregnancy among women with CPD is needed, as we cannot exclude the possibility that bias, such as sampling methods, or random error could explain our findings.

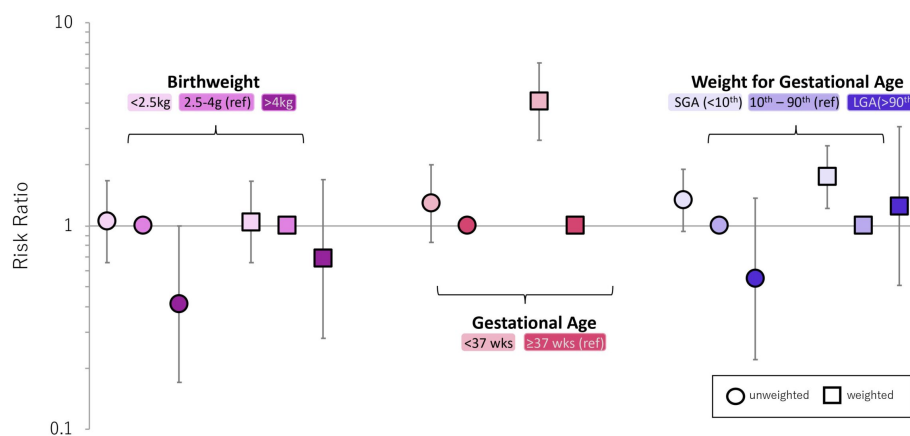


Figure. Unweighted and weighted risk ratios comparing birth outcomes of women with congenital physical disabilities to those without. Case-control data from the Slone Birth Defects Study reweighted to reflect 3% prevalence of deliveries affected by major congenital malformations.

The impact of antibiotic exposures in infancy on off-target microbes and antibiotic resistance genes Rebecca M. Lebeaux* Rebecca Lebeaux Juliette C. Madan Modupe O. Coker Erika F. Dade Thomas J. Palys Emily R. Baker Hilary G. Morrison Margaret R. Karagas Anne G. Hoen

Background: Important yet understudied consequences of antibiotics are their impacts on the abundance of off-target microbes and antibiotic resistance genes (ARGs) in the infant gut. Understanding these effects during the developmentally sensitive period of infancy is imperative as young children are exposed to more antibiotics than any other age group and antibiotic-induced disruptions are associated with multiple public health concerns including antibiotic resistance.

Methods: To profile bacterial species and ARGs, we utilized paired metagenomic stool samples collected at 6 weeks and 1 year from infants in the New Hampshire Birth Cohort. Medical records were used to deduce which infants were exposed to antibiotics within that time period. Our two main outcomes were the differential relative abundance of each species and ARG. Differential abundance between the time points was used to account for individual-level variation during the first year. We assessed antibiotic exposures' impacts on these outcomes separately for each ARG and species using linear regression. As ARGs exist within microbes, we assessed if ARGs were associated with antibiotic exposure after adjustment for each species' differential abundance.

Results: Among the 97 infants included, 29 were exposed to at least one antibiotic between 6 weeks and 1 year. We found 58 species and 68 ARGs present in at least 30% of samples and included them in regression analyses. Although we did not identify any species or ARG that was statistically significantly associated with antibiotic exposure after multiple testing correction, 5 ARGs (Figure 1) and 3 species produced meaningfully significant results with p-values < 0.05.

Conclusion: Despite not finding strong evidence that antibiotic exposures impact individual bacterial species or ARGs, follow-up with more samples and different classifications of the exposure and outcomes can be used to clarify how antibiotics affect off-target species or ARGs in the infant gut.

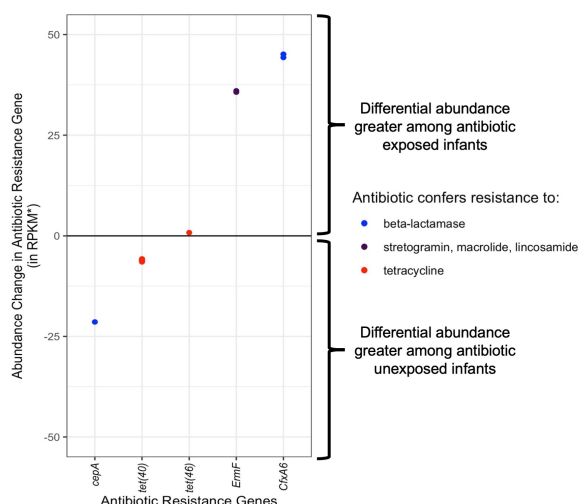


Figure 1: Antibiotic exposures between 6 weeks and 1 year of age impact the differential relative abundance of antibiotic resistance genes in infant guts. Each point represents an estimate from a linear regression model in which the exposure is history of at least one antibiotic prescription between 6 weeks and 1 year and the outcome is the differential abundance of an antibiotic resistance gene adjusted for the differential relative abundance of one species. 3944 linear regression models were run in total. Antibiotic resistance genes with multiple points represent multiple models in which the ARG was associated with antibiotic exposure controlling for a bacterial species. 62 regression models were statistically significant at $p < 0.05$, but were no longer statistically significant after multiple testing correction. *RPKM = reads per kilobase of reference sequence per million sample reads

LATEBREAKER

Molecular

Elevated urinary mutagenicity among those exposed to bituminous coal combustion**emissions or diesel engine exhaust** Jason Wong* Jason Wong Roel Vermeulen Yufei Dai Wei Hu Bu-Tian Ji W. Kyle Martin Sarah Warren Hannah Liberatore Dianshi Ren Huawei Duan Yong Niu Jun Xu Wei Fu Kees Meliefste Jufang Yang Meng Ye Xiaowei Jia Tao Meng Bryan Bassig H. Dean Hosgood Jiyeon Choi Mohammad Rahman Yuxin Zheng Judy Mumford Debra Silverman Nathaniel Rothman Qing Lan

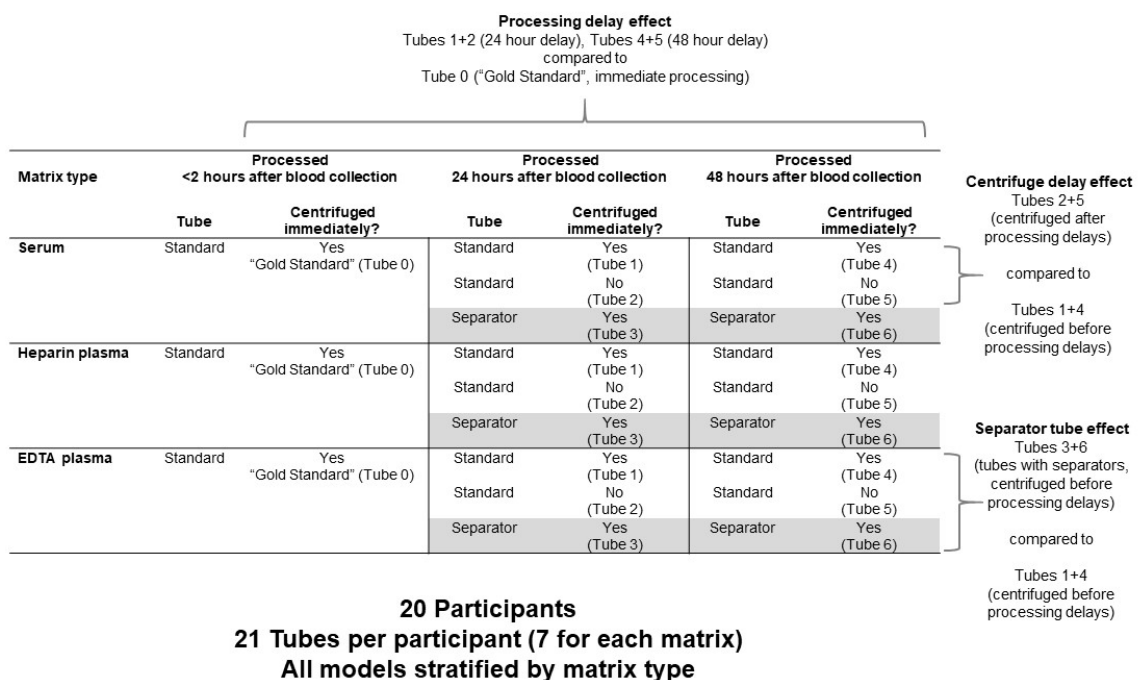
Urinary mutagenicity reflects systemic exposure to complex mixtures of DNA-damaging agents and has been linked to tumor development. Coal combustion emissions (CCE) and diesel engine exhaust (DEE) are prominent environmental risk factors for lung cancer, but their influence on urinary mutagenicity is unclear. We investigated associations between exposure to CCE or DEE and urinary mutagenicity. In two separate cross-sectional studies of non-smokers, organic extracts of urine were evaluated for mutagenicity levels using strain YG1041 in the *Salmonella* (Ames) mutagenicity assay. First, we compared levels among 10 bituminous (smoky) coal users from Laibin, Xuanwei, China, and 10 anthracite (smokeless) coal users. We estimated exposure-response relationships using concentrations of two lung carcinogens, 5-methylchrysene (5MC) and benzo[*a*]pyrene (B[*a*]P), from indoor air samples. Second, we compared levels among 20 highly exposed diesel factory workers and 15 unexposed controls, along with evaluating exposure-response relationships using elemental carbon (EC) as a DEE-surrogate. Age-adjusted linear regression was used to estimate associations. Laibin smoky coal users had significantly higher average urinary mutagenicity levels compared to smokeless coal users (28.4 ± 14.0 SD vs. 0.9 ± 2.8 SD rev/ml-eq, $p = 2 \times 10^{-5}$) and significant exposure-response relationships with 5MC ($p = 7 \times 10^{-4}$) and B[*a*]P ($p = 0.05$). DEE-exposed workers had significantly higher urinary mutagenicity levels compared to unexposed controls (13.0 ± 10.1 SD vs. 5.6 ± 4.4 SD rev/ml-eq, $p = 0.02$) and a significant exposure-response relationship with EC (p -trend = 2×10^{-4}). Exposure to CCE and DEE is associated with urinary mutagenicity, suggesting systemic exposure to mutagens.

LATEBREAKER

Molecular

The influence of pre-analytical processing conditions on B vitamers, amino acids, and diabetes-related biomarkers measured in blood Kara A. Michels* Kara A. Michels Stephanie J. Weinstein Paul S. Albert Amanda Black Michelle Brotzman Norma A. Diaz-Mayoral Mia M. Gaudet Nicole Gerlanc Wen-Yi Huang Alaina Shreves Nicolas Wentzensen Kathleen Wyatt Christian C. Abnet

Relatively few studies examine the effects of specimen handling on the measurement of biomarkers. To develop protocols for specimen collection within a new cohort study, we obtained serum, heparin plasma, and EDTA plasma from 20 adult volunteers (7 tubes per matrix type). The tubes were either immediately centrifuged, processed, and frozen (the “gold standard”) or were subjected to a range of processing conditions: stored with ice packs for 24- or 48- hours before processing and freezing, centrifuged before/after this delay, and collected in tubes with/without separators (Figure 1). We then directly quantified concentrations of 54 biomarkers. We used linear mixed models with random intercepts for subject to estimate geometric mean concentrations and relative percent differences across processing conditions, separately by matrix type. Relative to “gold standard” tubes, the measurement of many B vitamers, amino acids, and diabetes-related markers showed poor reproducibility that worsened with length of delayed processing. As examples, in serum, we noted changes in the concentrations of glutamic acid (38 and 76% increases with 24- and 48-hour delays, respectively), glycine (12 and 23% increases), serine (16 and 28% increases), and acetoacetate (-19.3 and -26.0% decreases). As expected, some B vitamers concentrations changed in opposite directions. After a 24-hour delay, serum riboflavin increased by 17% (95%CI 12 to 22%), while flavin mononucleotide decreased by -26% (95% CI -31 to -20%). Most markers were not greatly influenced by the timing of centrifuging or the use of separator tubes. Sample handling can influence the quantitative measurement of many biomarkers; our evidence supports the idea that processing delays should be minimized or at least consistent across samples used in an analysis.



Infection Incidence and Management in Multiple Sclerosis Patients After Initiating**Disease-Modifying Therapy**

Elizabeth C.S. Swart* Elizabeth Swart Douglas Mager, MA Natasha Parekh, MD, MS Lynn M. Neilson, PhD Rock A. Heyman, MD Rochelle Henderson, PhD Gail Bridges, PharmD Chester B. Good, MD, MPH

Background: Multiple sclerosis (MS) is a disease of the central nervous system, affecting roughly 2.5 million people worldwide. Disease-modifying therapy (DMT) has transformed MS care, but often costs patients over \$70,000/year. DMTs can be highly effective but can predispose MS patients to severe infections. Infections can unmask MS symptoms which may be confused for exacerbations.

Study Design: We performed a retrospective cohort analysis with pharmacy and medical claims from a national pharmacy benefit manager on a sample of MS patients initiating DMT from January 2016-June 2017. The analysis compared the rate of infections in the 6-month time period after therapy initiation by drug type: oral, infused or injectable. Rates of antibiotic/antimicrobial drug use were also assessed.

Results: 1,270 patients were included in the analysis. Patients receiving infusions accounted for 5.2% of the sample while those receiving injectable and oral drugs accounted for 52.4% and 42.4%, respectively. Infection rates were highest among patients receiving infusions at 25.8% over 6 months. Infection rates for patients receiving injectable and oral drugs were 18.5% and 19.3%, respectively. Infection rates were observed to be statistically nonsignificant between type of drug. Of those with infections, antibiotics and/or antimicrobials were prescribed to 94.1% (infused), 74.8% (injectable) and 77.9% (oral) of patients. Patients getting infusions had the highest incidence of herpes zoster (HZ) infection at 3.0%, followed by oral drugs at 0.9% and injectables at 0.8% (statistically nonsignificant differences).

Conclusions: We found differences in rates of bacterial and HZ infections (and antibiotic/antimicrobial use) among new DMT users by type of drug. As we could not account for baseline disability which may influence rates of infections, our findings document association, however continued pharmacovigilance for DMT in MS is warranted to inform the risk-benefit considerations of each DMT.

Evaluation of disparities in multiple sclerosis risk by age, sex, and nativity in Kuwait:1980-2019 Saeed Akhtar* Saeed Akhtar Raed Alroughani

Abstract

Objective: This cross-sectional cohort study quantified the disparities in MS risk by age, sex, nativity from 1980 to 2019.

Methods: Age-standardized MS incidence rate (ASIR) (per 100,000 person-years) overall and by subcohorts defined by cross-classification of the period (5-year groups) of diagnosis, age at onset, sex (female or male) and nativity (Kuwaiti or non-Kuwaiti) were computed and analyzed using multivariable negative binomial model.

Results: Overall MS ASIR (per 100,000 person-years) was 3.41 (95% CI: 1.61, 5.21), which increased exponentially from 1980 to 2014 before drifting downward in 2015-2019 period. Compared with adults (age \geq 40 years), men, non-Kuwaiti residents respectively, young adults (20-39 years), females and Kuwaiti nationals were significantly ($p < 0.05$) more likely to develop MS after adjusting for the period effect.

Conclusions: A high overall MS ASIR (per 100,000 person-years) was recorded with substantial temporal variation between 1980 and 2019. Young adults (20-39 years), females and Kuwaiti nationals constituted MS high-risk groups. The knowledge of underlying interface pathways between genetic and environmental factors may provide insights into MS pathogenesis and leads for future research.

Impact of inflammation on estimated iron deficiency prevalence in women ages 23-35 years with high body mass index Kristen Upson* Kristen Upson Parminder S. Suchdev Lisa M. Tussing-Humphreys Elizabeta Nemeth Quaker E. Harmon Gregory S. Travlos Ralph E. Wilson Donna D. Baird

Accurate diagnosis of iron deficiency (ID) is critical for clinical management and public health prevention. Yet, the widely used definition of iron deficiency in adults, plasma or serum ferritin $<15 \mu\text{g/L}$ may underestimate ID as ferritin is elevated with inflammation. Several approaches have been proposed to adjust ferritin for inflammation using C-reactive protein (CRP) and ferritin adjustment is now recommended by the World Health Organization in areas of widespread infection or inflammation. Since obesity induces low-grade inflammation and is common in the U.S., we investigated the impact of inflammation on ID prevalence estimation in the context of high body mass index (BMI). We used enrollment data from the Study of Environment, Lifestyle & Fibroids, a cohort of 1693 African-American women ages 23-35 years among whom 59% have a BMI of $\geq 30 \text{ kg/m}^2$. Among a subset of participants ($n=626$) with data on serum ferritin (SF) and high-sensitivity CRP, we estimated ID prevalence using three approaches compared to the unadjusted SF $<15 \mu\text{g/L}$: (1) correction factor if CRP $>5 \text{ mg/L}$ (0.81, geometric mean ratio of SF with CRP ≤ 5 and >5), (2) higher SF cut-off value ($<70 \mu\text{g/L}$) if CRP $>5 \text{ mg/L}$, and (3) the Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA) internal regression correction (IRC). Among participants, CRP $>5 \text{ mg/L}$ was common (33%). The unadjusted ID prevalence was 14%. After accounting for inflammation, ID prevalence ranged from 16% (correction factor) to 22% (BRINDA IRC) and 32% (higher cut-off value). Among women with BMI $\geq 40 \text{ kg/m}^2$ ($n=145$), ID prevalence varied from 14% (unadjusted) and 19% (correction factor) to 30% (BRINDA IRC) and 48% (higher cut-off value). Our results indicate higher ID prevalence after accounting for inflammation using CRP, particularly among women with a high BMI. Given the global obesity epidemic, further investigation of the impact of obesity-induced inflammation on the estimation of ID prevalence is warranted.

Positive effects of Japanese diet index score on annual change of transverse temporal gyrus in middle-aged and older Japanese community dwellers. Shu Zhang* Shu Zhang Rei Yukiko Akinori Takashi Yasue Kaori Fujiko Hiroshi Hidenori

Background Healthy diets are suggested to prevent age-related hearing loss, through plausible mechanisms such as vascular protective or neuroprotective effects. Though Japanese diet has been suggested to prevent age-related hearing loss, its effect on hearing-related brain areas has not been investigated yet.

Methods A prospective cohort study with two years of follow-up was conducted as part of the National Institute for Longevity Sciences-Longitudinal Study of Aging (NILS-LSA) project. A total of 1686 participants (860 males and 826 females, aged 40–89 years) were included. A 9-component weighted Japanese Diet Index (wJDI9) score (ranging from -1 to 12) was calculated with 9 food components, and wJDI9 score was categorized into three groups (T1 to T3) using age- (65 years) - sex-specified tertiles. Volumes of total gray matter (GM), transverse temporal (TT), and superior temporal (ST) were estimated by T1-weighted MPRAGE magnetic resonance imaging and longitudinal FreeSurfer. Annual change ratio (%) = [(volume at baseline - volume at follow-up)/volume at baseline/follow-up years × 100%]. General linear models were adjusted for age, sex, ApoE4, disease history, smoking status, alcohol drinking, physical activities, education, depressive symptom, energy and salt intakes, hearing threshold level, and noise at workplace.

Results The mean (SD) annual change ratio (%) was 0.60 (2.10) for TT, 0.47 (1.19) for ST, and 0.42 (1.11) for GM, respectively. In the multivariate-adjusted general linear model, a higher wJDI9 score was negatively associated only with annual change ratio of TT. Comparing to T1 (reference group), multivariate-adjusted β (95% CI) and *P*-value for T3 were -0.293 (-0.556, -0.031) and 0.029, respectively. For each 1-point increase of the wJDI9 score, multivariate-adjusted β (95% CI) and *P*-value were -0.148 (-0.279, -0.017) and 0.027. No associations were observed for annual change ratio of ST or GM.

Conclusions Adherence to a Japanese diet (defined by wJDI9) was associated with less annual TT atrophy. Further study in different settings is needed to confirm this association.

The effect of sleep duration on the association between food insecurity and childhood obesity Wendemi Sawadogo* Wendemi Sawadogo Tilahun Adera

Background: Childhood obesity has increased globally during the past four decades. Multiple studies have reported an association between food insecurity and obesity. However, little is known about the impact of sleep duration on this association specially among children. The purpose of this study was to examine the association between food insecurity and childhood obesity and to investigate whether sleep duration mediate such association.

Method: Data was obtained from the 2018 National Survey of Children's Health (NSCH). The study included children age 10 to 17 years. The exposure variable was food insecurity during the past year, the mediator variable was sleep duration during the past week, and Body Mass Index at the time of the survey was used to classify participants as with/without obesity. Covariates included age, sex, race/ethnicity, education, poverty ratio and physical activity. We employed logistic regression models to investigate the association between food insecurity and childhood obesity. Utilizing causal mediation analysis within a counterfactual framework, we decomposed the total effect of food insecurity into natural direct and indirect effect.

Result: The prevalence of obesity was estimated at 15.11% in our study population. The total effect of food insecurity on obesity was (OR=1.88; 95% CI: 1.68-2.07), the controlled direct effect of food insecurity on obesity was (OR=1.85; 95% CI: 1.65-2.04), and the natural indirect effect was (OR=1.02; 95% CI: 1.00-1.03). The proportion mediated by sleep duration was 3.65 (1.56-5.74).

Conclusion: Food insecurity increases the risk of obesity among children. Although the mediation effect of sleep duration is significant, the percentage mediated is relatively small. These results suggest that the association between food insecurity and obesity may develop mostly through pathways that do not involve sleep duration.

Dietary Correlates of SNAP and Other Assistance Programs Among Racially/Ethnically Diverse Children Junia Nogueira de Brito* Junia Nogueira de Brito Katie A. Loth Angela Fertig Amanda Trofholz Allan Tate Jerica M. Berge

Background: Low-income and racially/ethnically diverse families typically enroll in one or more cash and food assistance programs. However, little is known about children's dietary intake (DI) when their families are simultaneously enrolled in these programs. We aimed to investigate the association between participation in one or more assistance programs and children's DI.

Methods: Cross-sectional study among 1,033 low-income parents with children (aged 7 ± 1.5 years; 25% African American, 19% Hispanic/Latinx, 19% Hmong, 19% Native American, 13% Somali, 5% white). Parents indicated in an online survey which assistance programs they participated. We created three categories regarding family enrollment in assistance programs: (1) 'SNAP and other assistance programs' (i.e., WIC, free/reduced-cost school breakfast or lunch, Supplemental Security Income, Minnesota Family Investment Program, and Healthy Start or daycare assistance) ($n=457$), (2) 'assistance programs but not SNAP' ($n=305$), and (3) 'not enrolled in any assistance programs' ($n=271$). Parents reported child DI using a modified version of the Children's Eating Habits Questionnaire. Adjusted linear regressions evaluated the association between assistance categories and child DI.

Results: Enrollment in 'SNAP and other assistance programs' was associated with higher weekly consumption of food items high in sugar (e.g., cookies) and salt (e.g., salty snacks) relative to those enrolled in 'assistance programs but not SNAP' and 'not enrolled in any assistance programs.' Children whose families received any assistance had a slightly higher weekly intake of vegetables, fruits, and milk than those 'not enrolled in any assistance programs.'

Conclusions: Enrollment in assistance programs was associated with both healthy and unhealthy dietary factors in children. Future research needs to confirm these findings and consider household participation in various assistance programs when examining their impact on health behaviors.

Assessing the relationship between spatial availability of fast food and diet by community type Yasemin Algur* Yasemin Algur Pasquale E. Rummo Tara P. McAlexander Shanika De Silva Gina S. Lovasi Suzanne E. Judd Victoria Ryan Gargya Malla Alain Koyama David C. Lee Lorna Thorpe Leslie A. McClure

Background: Food access varies across communities and may differentially influence diet, working synergistically with other community factors.

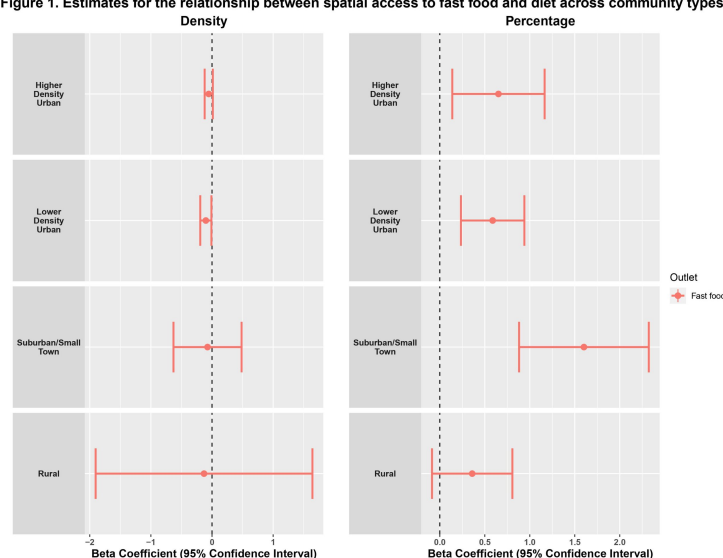
Objective: To examine the relationship between access to fast food (FF) and diet across community types.

Methods: Using baseline survey data from the REasons for Geographic and Racial Differences in Stroke study (2003-2007), we calculated participants' dietary inflammation score (DIS) (n=20,331). Higher DIS indicates greater pro-inflammatory exposure. We defined the spatial availability of FF restaurants using density (count/km²) and relative measures (count relative to all restaurants) using street-network buffers around the population-weighted centroid of each participant's census tract. We defined community type as higher density urban (HDU), lower density urban (LDU), suburban/small town, and rural, with a 1-, 2-, 6-, and 10-mile buffer size, respectively. Using generalized estimating equations, we estimated the association between each FF measure and DIS, stratified by community type, controlling for individual and neighborhood socio-demographics and supermarket access.

Results: Average DIS was -0.004 (SD=2.52; min=-14.23, max=9.86). A 10% increase in the percentage of FF restaurants was associated with a 6.5 (SE=2.62) point higher DIS (p=0.01) in HDU areas, a 5.87 (SE=1.80) point higher DIS (p=0.01) in LDU areas, and a 16.02 (SE=3.68) point higher DIS (p<0.001) in suburban/small towns; no significant associations were present in rural areas. A 1-unit increase in the density of FF restaurants was associated with a 0.10 (SE=0.05) decrease in DIS (p=0.03) in LDU areas.

Conclusions: Interventions could focus on restaurant diversity to mitigate dietary inflammation, especially in non-rural areas. The density of FF restaurants in LDU areas may be protective, potentially reflecting increased investment in commercial activity.

Figure 1. Estimates for the relationship between spatial access to fast food and diet across community types



Vitamin D and semen quality in an infertility treatment-seeking population Sunni Mumford*
Sunni Mumford Lindsey Sjaarda Douglas Carrell Jim Hotaling Brad Van Voorhis Abey Eapen James
Mills Zhen Chen Enrique Schisterman Erica Johnstone

Background: Vitamin D is hypothesized to play a key role in male reproduction as vitamin D receptors and metabolizing enzymes are expressed in the testis and prostate and have been shown to impact the male androgenic hormone axis. However, reported associations between vitamin D levels and semen quality are inconsistent.

Methods: In a longitudinal study of men (n=2369) seeking infertility care, serum 25(OH)D was measured at baseline and semen quality was assessed using standardized procedures by quantification of sperm concentration, volume, motility, morphology, count, and total motile count at baseline and 6-months post-enrollment and with DNA fragmentation at 6-months. The data were analyzed using weighted linear regression adjusted for age, body mass index, race, season at enrollment, abstinence time, income, and multivitamin use. Vitamin D status was categorized as deficient (<20 ng/mL, reference), insufficient (20-29.9 ng/mL), or sufficient (\geq 30 ng/mL).

Results: Overall, 29% of men had deficient levels of 25(OH)D at baseline, 41% were insufficient, and 30% were sufficient. 25(OH)D status was not associated with semen quality parameters assessed at baseline. 25(OH)D was also not associated with semen quality parameters at 6-months post-enrollment (percent change in total motile sperm count: 4%, 95% CI: -31%, 57% sufficient vs deficient; -13% (-39%, 25%, insufficient vs deficient). No associations were observed with sperm DNA fragmentation ($\beta=0.1$, 95% CI: -3.8, 3.9 sufficient vs deficient; $\beta=1.6$, 95% CI: -1.6, 4.7 insufficient vs deficient).

Conclusions: 25(OH)D levels were not associated with semen quality parameters in a cohort of men seeking infertility care who underwent multiple, standardized assessments of semen quality. Future research should investigate whether 25(OH)D in the male partner is related to pregnancy and its outcomes, irrespective of semen quality metrics.

Overall and Sex-Differences in Compliance Among Preschool-Age Children with the 2018 DHHS Physical Activity Guidelines Gaurav Dangol* Gaurav Dangol Sarah Burkart Lisa Chasan-Taber Sofiya Alhassan

Associations between low levels of physical activity (PA) and adverse health outcomes have been reported in preschool-age children (preschoolers). Utilizing previous PA guidelines, studies have shown that most children do not meet PA guidelines. Preschoolers (61%) spend a significant portion of their day at childcare centers. These centers play a role in getting preschoolers to meet PA guidelines. No study has currently examined preschoolers' PA prevalence during the preschool-day using the recently released Department of Health and Human Services (DHHS) PA guidelines. Therefore, the purpose of this cross-sectional study was to examine the prevalence of preschoolers meeting the 2018 DHHS PA guidelines during the preschool-day and the association between sex and meeting PA guidelines. Data utilized for this study was from the Preschoolers Actively Learning (PAL) Study (n=47). PA was assessed using Actigraph accelerometers. PA prevalence during the preschool-day was defined as at least 105 minutes of total [light, moderate, and vigorous] PA during the 7-hour waking period of the preschool-day. Sex was obtained from parent questionnaires. Multivariate logistic regression analysis modeled the odds of meeting guidelines on sex. In our sample, 26% of the preschoolers met the DHHS PA guidelines and participated in 85±10.7 minutes of total PA during the preschool-day. Being younger was significantly ($p<0.05$) associated with meeting PA guidelines as compared to older age. In age-adjusted analyses, we found that boys had an increased odds of meeting the PA guidelines (OR=4.67; 95% CI: 0.95-22.87, $p>0.05$) but this was not statistically significant. This study contributes to our understanding of PA prevalence in preschoolers during the preschool-day and sex differences associated with meeting PA guidelines. Findings highlight the need to target the preschool-day as a time frame to support preschoolers in meeting PA guidelines.

Association of sweetened soda, non-soda sweetened beverages and BMI with concentrations of 25-hydroxyvitamin D in US adults Wei-Ting Lin* Wei-Ting Lin Yu-Hsiang Kao Hui-Yi Lin David W. Seal Mirandy S. Li Chien-Hung Lee Tung-Sung Tseng

Vitamin D deficiency has been linked to lower bone mineral density, adiposity, metabolic dysfunction and hypertension risk. Sugar-sweetened beverages (SSB), particularly soda, has been recognized a high-fructose containing diet. A recent animal study showed that high-fructose diets could associate with lower 25-hydroxyvitamin D (25(OH)D) levels. This study aims to investigate the associations between sugar intake from soda and non-soda SSB, body mass index (BMI) and 25(OH)D levels. Total of 4,505 representative US adults aged above 20 years without liver conditions were selected from 2013-2014 National Health and Nutritional Examination Survey. Sugar intake from each type of SSB was identified and calculated using suggested USDA codes. SSB consumers were classified into soda consumers and non-soda consumers. Vitamin D deficiency is defined as a 25(OH)D level ≤ 20 ng/mL. Multinomial regression models were used to assess the effect of BMI on the association of sugar intake from soda and non-soda SSB with the 25(OH)D levels. All analyses were performed under survey modules with appropriate sampling weights. The prevalence of 25(OH)D insufficiency and deficiency was 37.8% and 24.1% in US adults, respectively. Both of sugar intake from SSB and BMI was significantly inversely associated with 25-hydroxyvitamin D levels ($p \leq 0.002$). No association was observed between total sugar intake in diet and 25(OH)D levels ($p = 0.094$). Among SSB consumers, a higher prevalence of 25(OH)D deficiency was observed in soda consumers than non-soda consumers (32% vs. 23%, $p = 0.002$). Compared to non-SSB consumers, a 1.70-fold higher risk of vitamin D deficiency were found in soda consumers who consumed ≥ 40 grams per day (95%CI=1.03-2.80) after adjusting for cofounders and BMI status. In conclusion, our study indicated that sugar intake from SSB was inversely associated with 25(OH)D levels, particularly in soda consumers. These associations were attenuated when accounting for BMI status.

Dietary Correlates of Periconceptional and First Trimester Ultra-Processed Food Intake

Samrawit F. Yisahak* Samrawit F. Yisahak Stefanie N. Hinkle Sunni L. Mumford Katherine L. Grantz Cuilin Zhang Jagteshwar Grewal

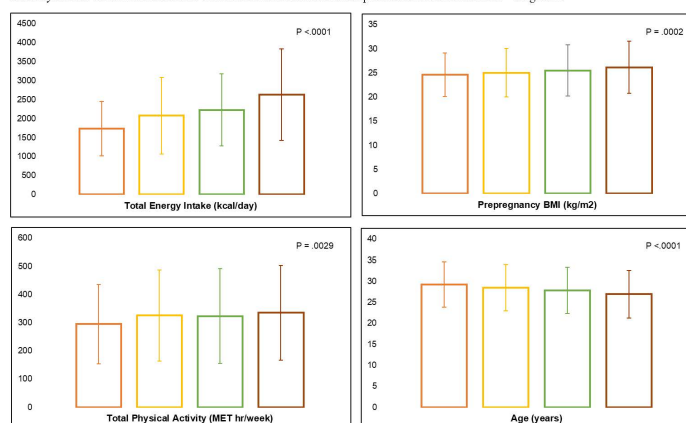
Objective: Characterizing diet by the extent of processing rather than nutrients/food groups has gained recent attention as a more translatable framework for nutritional counseling. Ultra-processed food (UPF) intake has been described in the general population, but is understudied among pregnant women. We described UPF intake in a diverse multisite US pregnancy cohort, and examined whether it is a marker of poor dietary quality by estimating the correlation with commonly used diet quality scores.

Methods: Women with singleton pregnancies (n=1605) completed a 145-item food frequency questionnaire (FFQ) at gestational weeks 8-13, reflecting diet in the past 3 months. Quantity of intake of 29 food and beverage items identified as UPFs was ranked into quartiles. Characteristics across quartiles of UPF were compared using chi-squared tests and ANOVA. Correlation and agreement between UPF and diet quality (continuous and quartiles) was examined using Pearson correlation coefficients (r) and weighted kappa statistics (κ), respectively.

Results: Median (IQR) UPF intake in the sample was 1139 (64, 2674) grams/day. Women with higher UPF intakes were more likely to identify as non-Hispanic black ($p < .0001$) and nonvegetarian ($p < .005$), and have lower income ($p < .05$). Other characteristics also varied significantly across UPF quartiles (**Figure**). UPF intake was inversely correlated with Healthy Eating Index-2010 ($r = -0.26$, $\kappa = -0.17$ (-0.20, -0.14)), Alternative Healthy Eating Index-2010 ($r = -0.22$, $\kappa = -0.15$ (-0.18, -0.12)), Dietary Approaches to Stop Hypertension ($r = -0.23$, $\kappa = -0.13$ (-0.16, -0.10)), but not alternate Mediterranean diet score ($r = -0.01$, $\kappa = -0.003$ (-0.04, 0.03)).

Conclusions: UPF intake among pregnant women had an inverse and minor correlation with some healthy diet quality scores. Future work should examine if this translates to associations of UPF with adverse pregnancy outcomes to ultimately inform dietary counseling during prenatal care.

Figure: Characteristics of women across increasing quartiles of periconceptional and first-trimester ultra-processed food intake in the Eunice Kennedy Shriver National Institutes of Child Health and Human Development Fetal Growth Studies – Singletons



Abbreviations: Kcal, kilocalories; BMI, body mass index; MET, metabolic equivalent of task
Values represent mean (standard deviation) across increasing quartiles (quartile 1 – quartile 4)

Adherence to healthy lifestyle recommendations and all-cause and cause-specific mortality risks among former cigarette smokers Maki Inoue-Choi* Maki Inoue-Choi Ami Fukunaga Yesenia Ramirez Charles E. Matthews Neal D. Freedman

Background: Many smokers quit smoking to improve their health. They may additionally benefit from adopting other aspects of a healthy lifestyle, although existing data is limited.

Methods: We assessed adherence to evidence-based lifestyle recommendations among 159,937 adults who self-identified as former smokers on the 1997 NIH-AARP Diet and Health study questionnaire. Adherence was scored for body weight (0-2), diet (0-3), physical activity (0-2), and alcohol intake (0-1) recommendations. Individual adherence scores were summed to make a total adherence score (0-8). HRs and 95% CIs for all-cause and cause-specific mortality through 2019 were calculated using Cox proportional hazards regression adjusted for age, sex, education, race/ethnicity, perceived general health, comorbid conditions, smoking intensity, and time since cessation. Analyses of individual lifestyle recommendations were mutually adjusted for each other.

Results: A higher total adherence score was associated with lower all-cause mortality in a dose-response manner (HR per unit increase =0.94, 95% CI=0.93-0.94, $p<0.0001$) regardless of how long before baseline participants had quit smoking or how many cigarettes per day they had smoked. Compared with the lowest total adherence score category (0-2), the HRs (95% CIs) for all-cause mortality were 0.87 (0.85-0.89) for score 3-4, 0.78 (0.76-0.80) for score 5-6, and 0.69 (0.67-0.71) for score 7-8. Participants with a higher total adherence score had lower risk of mortality from cancer, cardiovascular disease, and respiratory disease. When examined individually, the HRs (95% CIs) for highest versus lowest adherence score were 0.93 (0.92-0.93) for body weight, 0.96 (0.95-0.96) for diet, 0.91 (0.90-0.92) for physical activity, and 0.94 (0.92-0.96) for alcohol intake recommendations.

Conclusions: These results indicate that former smokers may additionally benefit from following lifestyle recommendations for body weight, diet, physical activity, and alcohol.

Urinary preconception phenolic compounds and fecundability among women attempting**pregnancy** Sunni L. Mumford* Keewan Kim Alexandra C. Purdue-Smithe Joshua R. Freeman Samrawit F. Yisahak Enrique F. Schisterman Sunni L. Mumford

Background/Aim: Diets rich in plant-derived phenolic compounds may be beneficial for reproduction through antioxidant and anti-inflammatory effects. However, it is unknown whether these compounds that are abundant in vegetables, fruits, seeds, teas, and herbs, may have a role in improving fecundability. Therefore, we evaluated associations between preconception dietary phenol biomarkers and fecundability among women attempting pregnancy.

Methods: In a prospective cohort study following 1,228 women for up to 6 menstrual cycles while trying to conceive, concentrations of 28 dietary phenols were measured in urine at baseline. Pregnancy was assessed using urine hCG. Discrete Cox regression models, accounting for left-truncation and right-censoring, were used to estimate fecundability odds ratios (FORs) and 95% confidence intervals (CIs) for associations between dietary phenols and fecundability. Models were adjusted for urinary creatinine concentrations and potential confounders.

Results: Levels of most of urinary phenols were well above the limit of quantification, except catechin and resveratrol where only trace amounts were measured. We observed increased fecundability with higher levels of preconception 3,4-dihydroxyhydrocinnamic acid (FOR 1.23, 95% CI 0.97, 1.57; Quartile 4 vs 1), enterolactone (FOR 1.36, 95% CI 1.06, 1.75; Quartile 4 vs 1), and p-coumaric acid (FOR 1.29, 95% CI 1.00, 1.65; Quartile 4 vs 1). In contrast, comparing the highest to the lowest quartile, 3,4-dihydroxyphenylacetic acid (FOR 0.72, 95% CI 0.51, 1.00) and gallic acid (FOR 0.71, 95% CI 0.52, 0.97) were associated with reduced fecundability. No other dietary phenols were associated with fecundability.

Conclusions: A few dietary phenolic compounds measured in urine were associated with fecundability, highlighting their potential role among women attempting pregnancy. Further study of foods rich in these compounds may be beneficial to provide more useful guidance to women trying to conceive.

LATEBREAKER

Nutrition/Obesity

Fried versus non-fried potatoes as a ratio to the dietary vegetable daily intake: is there an association with obesity? Results from the national 2019 BRFSS study Chia-lin Chang* Chia-Lin Chang S. Cristina Oancea

Obesity, which is a global epidemic that raises the risk of chronic diseases such as diabetes mellitus and hypertension, was affected by the complex interaction of one's biology, behavior, and environment. Out of the multitude of contributing factors to obesity, diet is one factor people can control. Unfortunately, the western-style diet often involves also starchy vegetables, like potatoes. Potatoes provide mostly carbohydrates and limited fiber and minerals to help maintain or achieve a healthy weight. The purpose of this study was to examine the relationship between the proportion of potatoes in adults' diet and obesity using the 2019 US representative BRFSS data (N=269,415) with a weighted prevalence of obesity of 32.8% (95%CI: 32.4, 33.1). In assessing potato intake proportion, the BRFSS section of fruit and vegetable consumption was used. Frequency of eating fried potato and non-fried potato was divided by total vegetable consumption frequency to reflect the dietary pattern. Weighted and adjusted logistic regression models were used to obtain weighted and adjusted odds ratios (WAOR) and 95% CIs. This study findings showed that adults who were eating a higher proportion of fried potatoes among all vegetables had significantly higher WAO of being obese (WAOR= 1.60; 95%CI: 1.44, 1.77) but consuming a greater proportion of non-fried potatoes significantly decreased the odds of obesity (WAOR= 0.69; 95% CI: 0.61, 0.79). Therefore in the US the method of preparing potatoes for consumption, among adults, makes a significant difference in the association with obesity. Future longitudinal studies should investigate the method of food preparation as a potential causal factor for obesity. Since the 2019 BRFSS study classifies all the other starchy vegetables as "Other", future studies should evaluate the individual consumption of specific starchy vegetables and their method of preparation in relation to obesity.

LATEBREAKER

Nutrition/Obesity

Cardiovascular Disease Risks and Health Behaviours Based on Body-Composition**Phenotype in NHANES (1999-2004)** Sabine Plummer* Sabine Plummer Tamara R. Cohen Lisa Kakinami

Background: Body mass index is poor at distinguishing between adiposity and muscle. Based on dual energy X-ray absorptiometry data, Prado et al. (2014) offered a diagnostic framework to analyze body composition by categorizing fat- and muscle-mass body composition into 4 phenotypes.

Objective: To assess the association between body-composition phenotypes with health behaviours and cardiovascular disease risks in a representative U.S. adult population.

Methods: Data were from NHANES (1999-2004; n=12,228). Four phenotypes based on being above/below the 50th percentile of age- and sex- adjusted reference curves of fat-mass and muscle-mass were identified. Multiple linear regressions were used to assess phenotypes (high [H] or low [L] adiposity [A] or muscle mass [M]) against health behaviours (minutes of moderate or vigorous physical activity, and screen time in the past week) and cardiovascular measures (total, and high-density lipoprotein [HDL] cholesterol; systolic [SBP] and diastolic blood pressure [DBP]). Low-adiposity/high-muscle (LA-HM) was the referent. Analyses incorporated the complex sampling design and survey weights, and were adjusted for age, sex, race, poverty income ratio, and education.

Results: HA-HM and HA-LM were associated with elevated total cholesterol (95% CI: 0.15,0.28, p<0.001; and 0.24,0.42, p<0.001; respectively). HDL was lower for HA-HM (CI: -0.11,-0.16, p<0.001), but higher for LA-LM (CI: 0.10,0.15, p<0.001). SBP (CI: 1.24,3.61, p<0.001) and DBP (CI: 1.63,3.21, p<0.001) were higher for HA-HM. LA-LM did not differ in total cholesterol or DBP. Physical activity was lower for LA-LM (CI: 23.78,41.08), HA-LM (CI: 44.04,69.62), and HA-HM (CI: 35.02,53.41), and screen time was higher for LA-LM (CI: 0.01,0.27); HA-LM (CI: 0.30,0.54), and HA-HM (CI: 0.33,0.52).

Conclusion: High adiposity phenotypes were associated with poorer health behaviours and cardiovascular risk factors, regardless of muscle-mass. Further longitudinal investigation is needed.

LATEBREAKER

Nutrition/Obesity

Long-term Association between Diet Quality and the Gut Microbiome: The Multiethnic Cohort Erica Ma* Erica Ma Gertraud Maskarinec Unhee Lim Carol J Boushey Lynne R Wilkens Loïc Le Marchand Timothy W Randolph Johanna W Lampe Meredith AJ Hullar

Background: As diet quality may affect the gut microbiome (GM) composition, we examined the association of the Healthy Eating Index (HEI)-2015 assessed 21 and 9 years before stool sample collection with measures of fecal microbial composition in a subset of the Multiethnic Cohort, which represents five ethnic groups.

Methods: Participants completed a validated quantitative food frequency questionnaire (QFFQ) at cohort entry (Q1, 1993-96), at follow-up (Q3, 2003-08), and at a clinic visit (OQ3, 2013-16) when they also provided a stool sample. Fecal microbial composition was obtained from 16S rRNA gene sequencing (V1-V3 region). HEI-2015 scores were computed based on the QFFQs. Using linear regression adjusted for relevant covariates, we estimated associations of diet quality with GM composition after Bonferroni adjustment and computed adjusted mean values of GM measures by tertiles of HEI-2015 scores.

Results: At Q1, Q3, and OQ3, the mean ages of the 5,936 participants were 54, 65, and 69 years, respectively. The HEI-2015 total scores increased from Q1 (67 ± 10) to Q3 (71 ± 11) and OQ3 (72 ± 10). Alpha diversity assessed by the Shannon Index was significantly higher with increasing tertiles of HEI-2015 as estimated from each questionnaire. Of the 152 bacterial genera tested, seven (*Anaerostipes*, *Coprococcus 2*, *Eubacterium eligens*, *Lachnospira*, *Lachnospiraceae ND3007*, *Ruminococcaceae UCG-013*, and *Ruminococcus 1*) were positively and five (*Collinsella*, *Parabacteroides*, *Ruminiclostridium 5*, *Ruminococcus gnavus*, and *Tyzzereella*) were inversely associated with diet quality assessed in Q1, Q3, and OQ3. The beta estimates per unit of the HEI-2015 score associated with the relative abundance of the 12 genera showed only small differences across the three questionnaires.

Conclusion: The quality of past diet, assessed as far as 21 years before stool collection, is equally predictive of GM composition as concurrently assessed diet, indicative of the long-term nature of this relation.



Psychosocial stressors at work and biomarkers of inflammation: The PROspective Quebec Study on Work and Health Caroline Duchaine* Caroline Duchaine Chantal Brisson Denis Talbot Mahée Gilbert-Ouimet Xavier Trudel Michel Vézina Alain Milot Caroline Diorio Ruth Ndjaboué Yves Giguère Danielle Laurin

Low-grade inflammation has been associated with the risks of cardiovascular diseases, diabetes, depression and dementia. Psychosocial stressors at work have also been associated with these chronic diseases in longitudinal studies. Few longitudinal studies have evaluated the association between these stressors and biomarkers of inflammation such as C-Reactive protein (CRP) and interleukin-6 (IL-6). This study aimed to evaluate the associations of exposure to psychosocial stressors at work with CRP, IL-6, and both combined into an inflammatory index. Data come from a cohort of 9188 white-collar workers recruited in 1991-1993 (T1) with two follow-ups after 8 (T2, 1999-2000) and 24 (T3, 2015-2018) years. Participants included in this study were randomly selected at T3 to give blood for further study on biomarkers (n=2557). Psychosocial stressors at work were assessed with validated questionnaires. CRP and IL-6 were measured using standardized protocols. Several covariates were included such as sociodemographic, anthropometric, lifestyles, and comorbidities. Prevalence ratios (PRs) for the highest quartile of CRP, IL-6 and inflammatory index at T3 according to psychosocial stressors at work measured at T2 were calculated using generalized estimating equations. Multiple imputation and inverse probability of censored weighting were done to correct for the differences between included and excluded participants because of death, lost to follow-up or refusal. In men, an association was observed between a combination of exposure to high psychological demand, low job control and low social support at work and the inflammatory index (PR of 1.42 (95% confidence interval: 1.06;1.90)). This result suggests that psychosocial stressors at work may increase low-grade inflammation in men. Further studies are needed to clarify the effect modification by sex. As these stressors are frequent and modifiable, they could be part of the primary prevention for chronic diseases.

Exposure to airborne crude oil chemicals and adult incident asthma Kaitlyn Lawrence*

Kaitlyn Lawrence Nicole Niehoff Alexander Keil W Braxton Jackson Matthew Curry Patricia Stewart
Mark Stenzel Lawrence Engel Dale Sandler

Background: Total hydrocarbons (THC), including the volatile organic compounds of benzene, toluene, ethyl-benzene, o-, m-, and p-xylenes and n-hexane (BTEX-H), are ubiquitous in the environment. BTEX-H have been linked to adverse respiratory health outcomes including, asthma-related symptoms, reduced lung function, and lung inflammation. Previous studies assessing these chemicals individually in relation to asthma have been inconclusive, but none have examined the joint impact of these chemicals as a mixture. **Objectives:** We assessed relationships between incident asthma and oil spill-related THC and BTEX-H exposure mixtures. **Methods:** We analyzed data from the 24,813 participants in the GuLF Study (enrolled 2011-2013) who were exposed to petroleum chemicals during the spill cleanup in 2010-2011 and who reported no asthma prior to exposure. We defined incident asthma as self-reported wheeze or self-reported physician diagnosis of asthma. Exposures to THC and BTEX-H were based on measurement data and work histories. We used modified Poisson regression to estimate 2-year risk ratios (RR) and 95% confidence intervals (CIs) for individual chemicals. We also used quantile-based g-computation to estimate a joint effect of the BTEX-H chemicals on asthma risk. **Results:** THC and BTEX-H exposure levels were associated with higher risk of asthma in an exposure-dependent manner (test for trend $p < 0.001$). A simultaneous, one quartile increase in all components of the BTEX-H mixture was also associated with higher odds of asthma: OR (95% CI) = 1.54 (1.43-1.66). **Conclusions:** Oil spill-related THC and BTEX-H exposures were associated with higher 2-year risk of asthma in a group of occupationally exposed adults. Findings illustrate the value of considering exposure to BTEX-H chemical mixtures in the assessment of occupational asthma risk.

A non-targeted approach to identify potential breast carcinogens in women firefighters after a fire event Jessica Trowbridge* Jessica Trowbridge Vincent Bessonneau MiaoMiao Wang June-Soo Park Ruthann Rudel Rachel Morello-Frosch

Background: Female firefighters remain understudied in both exposure and epidemiology studies. Furthermore, occupational studies generally focus on toxic chemicals that are well characterized. To identify potentially novel chemical exposures associated with a fire event among female firefighters, we applied non-targeted analysis methods to three longitudinal serum samples collected in the days and weeks after a fire.

Methods: To assess exposure to potential breast carcinogens among women workers after an urban structural fire event the Women Workers Biomonitoring Collaborative (WWBC), we recruited female firefighters in San Francisco and developed a biospecimen archive. Female firefighters (n=18) were recruited and provided 3 serum samples—within 48 hours, 1 week, and 1 month after fighting a fire. We applied a non-targeted analytical approach with liquid chromatography quadrupole time of flight mass spectrometry (LC-QTOF/MS) in both the positive and negative ionization modes.

Results: We detected over 20,000 features, representing potential chemical exposures in study participants. Exact mass of features was matched to a curated in-house library of 7,935 environmental chemicals and potential breast carcinogens, tentatively identifying 1,667 chemicals. MS/MS fragmentation analysis allowed us to further confirm 181 candidate chemicals. These chemicals included per- and poly-fluoroalkyl substances, endocrine disrupting chemicals and chemicals associated with mammary tumor development. In further analyses, we will select 5 novel chemicals that have different average levels or detection frequencies between the 3 post fire visits (visit 1 versus visit 2 or visit 3) for targeted confirmation and quantification.

Conclusions: Non-targeted analytical approaches coupled with targeted characterization of chemical exposures can contribute to the identification of novel chemicals of relevance to breast cancer risk for occupational epidemiology studies.

Organophosphate and organohalogen exposure and thyroid hormone disruption in a cohort of women firefighters and office workers from San Francisco

Jessica Trowbridge* Jessica Trowbridge Roy Gerona Michael McMaster Katherine Ona Cassidy Clarity Vincent Bessonneau Ruthann Rude Heather Buren Rachel Morello-Frosch

Flame retardants (FR) are suspected endocrine disrupting compounds and may be of particular concern for firefighters as they are commonly found in consumer products and have been detected in fire station dust and firefighter gear. Studies suggest that FR exposure can disrupt thyroid hormone (TH) function; however, this relationship has not been assessed among women firefighters. TH is important for thyroid mediated gene expression and infant neurodevelopment and TH may be relevant to downstream adverse health effects such as cardiovascular disease and cancer. In this study we measured 10 urinary FR metabolites in female firefighters (N=86) and office workers (N=84) from San Francisco: bis(1,3-dichloro-2-propyl) phosphate (BDCPP), bis(2-chloroethyl) phosphate (BCEP), dibutyl phosphate (DBuP), dibenzyl phosphate (DBzP), di-p-cresyl phosphate (DpCP), di-o-cresyl phosphate (DoCP), 2,3,4,5-tetrabromobenzoic acid (TBBA), tetrabromobisphenol a (TBBPA), 5-OH-BDE 47, and 5-OH-BDE 100. We assessed potential predictors of exposure levels and the association between FR exposures and thyroxine (T4) and thyroid stimulating hormone (TSH). BDCPP, BCEP and DBuP were the most commonly detected FR metabolites, among all study participants. Firefighters had higher median exposure levels of BDCPP, BCEP and DBuP compared to office workers. Among firefighters, a doubling of BDCPP was associated with a 2.88% decrease (95%CI -5.28,-0.42) in T4. We did not observe significant associations between FR and T4 among office workers nor between FR and TSH in either firefighters or office workers. Firefighters had significantly higher exposures to FR compared to office workers, and we observed a negative association between BDCPP and thyroxine in firefighters. Characterizing exposure to endocrine disrupting chemicals and assessing the association with biomarkers of early effect such as TH can inform prevention efforts without having to wait for adverse health outcomes to occur.

Incidence of Non-Hodgkin Lymphoma in the UAW-GM Autoworkers Cohort Kevin Chen*

Kevin Chen Sally Picciotto Sadie Costello Ellen Eisen

Objective: In prior studies, non-Hodgkin lymphoma (NHL) was associated with exposure to chlorinated compounds such as solvents and pesticides. The present study of 39,132 autoworkers in the United Auto Workers-General Motors Cohort examined the association between incident NHL and occupational exposure to soluble metalworking fluids (MWF), which typically contain chlorinated alkenes. Bias due to the healthy worker survivor effect (HWSE) can result in underestimation of the measure of association. We assessed the potential for this bias by examining pathway-specific associations.

Methods: Adjusted hazard ratios for incident NHL over a follow-up period of up to 42 years (1973 to 2015) were estimated using a Cox proportional hazards model with categorical levels of lagged cumulative exposure. Due to the ubiquity of soluble MWF exposure in this cohort, the reference group included those with exposure not exceeding 0.05 mg/m³-years. Pathway-specific adjusted hazard ratios were estimated for: (1) incident NHL and employment status; and (2) leaving work and cumulative exposure.

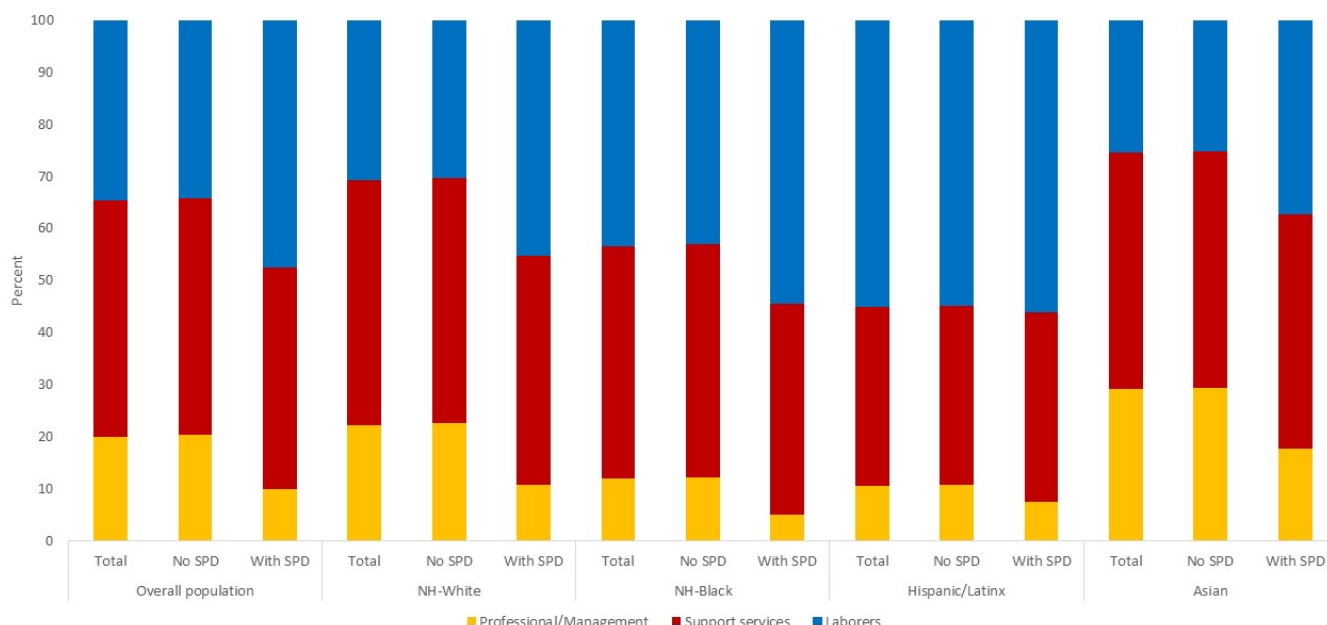
Results: Over the follow-up period, there were 393 incident cases of NHL. The hazard of incident NHL increased monotonically over the tertiles of cumulative exposure to soluble MWFs. Among those in the highest tertile of cumulative exposure, the adjusted hazard ratio was 1.64 (CI: 1.09 to 2.45). Pathway-specific analyses suggested that the hazard of incident NHL was higher among those who left work and that higher cumulative exposure was associated with a greater risk of leaving work.

Conclusions: Incidence of NHL was strongly associated with cumulative exposure to soluble MWFs, but the point estimates presented here may be underestimates of the true hazard ratios. The results of the pathway-specific analyses were consistent with a structural model encoding the HWSE; g-methods may be implemented to account for such bias.

Associations between Employment Industry along with Occupational Class and Serious Psychological Distress in the United States Julia Ward* Julia Ward W. Braxton Jackson II Ichiro Kawachi Chandra L. Jackson

Employment industry and occupational class have been shown to impact the mental health of employees, and racial/ethnic minority populations are more likely to work in high-risk, stressful occupations. However, prior studies investigating the relationship between occupation-related factors and psychological distress have lacked racial/ethnic diversity. We investigated associations between industry of employment along with occupational class and serious psychological distress (SPD) among a large, nationally representative, and racially/ethnically diverse sample of US adults. We pooled cross-sectional data from the 2004-2018 National Health Interview Surveys (N=388,811). Participants self-reported industry of employment and occupational class. SPD was defined as a Kessler Psychological Distress Scale score ≥ 13 . We assessed the age-standardized composition of employment industries and occupational classes, overall and by race/ethnicity. Adjusting for sociodemographic, health behavior, and clinical characteristics, we then used Poisson regression with robust variance to estimate PRs and 95% CIs of SPD for each employment industry and occupational class, overall and by race/ethnicity. Participants' mean age \pm SE was 46.7 ± 0.1 years, 51% were women, 65% were non-Hispanic (NH)-White, 14% were NH-Black, 16% were Hispanic/Latinx, and 5% were Asian. Across all employment industries, NH-Black and Hispanic/Latinx participants were more likely than NH-Whites and Asians to be laborers. Approximately 3% of participants reported SPD, who were generally more likely to be laborers across race/ethnicity. Compared to participants in professional/management positions, participants in support service and labor positions were more likely to have SPD ($PR_{\text{Support Services}} = 1.13$ [95% CI: 1.04-1.22]; $PR_{\text{Laborers}} = 1.21$ [95% CI: 1.11-1.32]). These findings warrant further investigation into occupation-related factors as an underlying mechanism perpetuating racial/ethnic disparities in mental health.

Figure 1. Age-standardized * Occupational Class among U.S. Adults Overall, by Race/Ethnicity, and stratified by Serious Psychological Distress (SPD), National Health Interview Survey, 2004-2018 (N=388,811)



Abbreviations: NH=non-Hispanic; SPD=serious psychological distress

* All estimates are weighted for the survey's complex sampling design. All estimates except for age are age-standardized to the U.S. 2010 population. Percentages may not sum to 100 due to missing values or rounding.

LATEBREAKER

Occupational

Access to Paid Sick Days Among U.S. Workers, 2007-2018 Candice Johnson* Candice Johnson
Kristen Said Ashley Price Dennis Darcey Truls Østbye

Background. In the United States, most workers rely on their employer to voluntarily provide paid sick days, with workers in high-paying white-collar jobs disproportionately likely to benefit. As a result, workers in low-wage jobs are less likely to be able to stay home when sick or to care for a family member's illness without loss of pay. Between 2007 and 2018, 11 states and D.C. enacted laws requiring most employers to offer paid sick days, potentially reducing these inequalities. Our objective was to examine national changes in access to paid sick days following introduction of these laws.

Methods. We used National Health Interview Survey data from the 50 U.S. states and D.C. from 2007 (before the first paid sick leave law was enacted, n = 8,957) through 2018 (the most recent year the survey collected comparable employment information, n = 9,014). We included full-time private sector adult workers. Participants reported if their main job offered paid sick leave or not. Survey-weighted descriptive statistics were used to examine changes in the percentage of workers with access to paid sick days over time by sociodemographic and workplace characteristics.

Results. Between 2007 and 2018, the percentage of full-time private sector workers with access to paid sick days increased by 5 percentage-points (pp), 63% to 68%. Workers with the greatest gains in access included Hispanic workers (+15 pp), Black workers (+10 pp), workers with less than a high school education (+10 pp), and workers aged 18-24 years (+9 pp). The difference in access to paid sick days between Hispanic and non-Hispanic white workers decreased from 19 pp (48% vs. 67%) in 2007 to 6 pp (63% vs. 69%) in 2018.

Conclusions. Full-time private sector workers saw increased access to paid sick days and decreased inequalities in access to paid sick days that coincided with enactment of paid sick leave laws.

LATEBREAKER

Occupational

Changes in Melatonin and Sex Steroid Hormone Production as a Result of Rotating Night Shift Work Barbara N Harding* Barbara N Harding Anna Palomar-Cros Oscar J Pozo Ana Espinosa Kyriaki Papantoniou Debra J Skene Gemma Castano-Vinyals Manolis Kogevinas

Introduction

Epidemiologic data on circadian disruption and subsequent hormone-related changes, which may explain the higher risk of disease such as prostate cancer among night shift workers, are limited.

Methods

This study included 51 male, rotating shift workers from a car industry in Barcelona, Spain, sampled twice at the end of a 3-week night-shift (21:30-05:00 hrs) and 3-week day-shift (05:30-13:30 hrs) rotation. Participants collected all urine voids over 24-hours during each shift. We determined the urinary concentrations of sex steroid hormones (estrogens, androgens and progestogens) and their main metabolites and 6-sulfatoxymelatonin (aMT6s, major melatonin metabolite). Individual cosinor analysis was used to evaluate hormone rhythms and to derive the acrophase (peak time) and the area under the curve (total production). Linear mixed models were used to examine intraindividual associations between night shift work and log-transformed 24-hour peak production time and total production adjusting for hours of daylight, compared to day shift work. We report geometric mean differences (GMDs) in peak production time and geometric mean ratios (GMRs) for total production.

Results

Participants had a mean age of 38 (± 9) years. The acrophase was delayed during the night shift for melatonin (GMD 8.52, 95% confidence interval [CI] 6.71, 10.32), androgens, e.g. testosterone (GMD 7.11, 95%CI 1.02, 13.20) and progestogens, e.g. 17-hydroxyprogesterone (GMD 4.74, 95%CI 3.01, 6.47). We found a higher production of 11-keto androgens (GMR 1.39, 95%CI 1.09, 1.77), and a lower production of adrenal progestogens, e.g. 16-cysteinyprogesterone (GMR 0.80, 95%CI 0.68, 0.94) when comparing the levels of hormones during the night shift to the referent day shift levels.

Conclusion

Night shift work was associated with melatonin and sex hormone-related changes in timing and total hormone production, providing insight into the mechanistic path for its association with hormone-dependent cancer.

Other

Risk factors for hyperthermia mortality among emergency department patients carlisha hall* carlisha hall

As temperatures increase in the U.S. due to climate change, heat-related mortality may become a significant public health challenge. Heat exposure can increase risk of death by exacerbating preexisting health conditions or through the onset of hyperthermia. The current study examines risk factors for heat-related deaths due to hyperthermia. We conducted a matched case-control study using statewide, longitudinally linked emergency department (ED) data and death records from California. Cases comprised California residents (≥ 18 years) who presented to a California-licensed ED and died of hyperthermia during the study period (2009-2012). For each case, up to five ED patients were randomly selected as live controls and matched on sex and age (± 2 years). Patients' demographic information and ED utilization history for alcohol use, drug use, psychiatric disorders, heart-related conditions, cerebrovascular conditions, chronic respiratory or lung disease, and neurodegenerative disorders were assessed in relationship to hyperthermia mortality. The final analysis included 78 cases and 385 matched controls. In bivariate conditional logistic regression models, hyperthermia mortality cases had higher odds of prior ED utilization for drug use (OR=2.56, 95% CI=1.47, 4.45) and psychiatric disorders (OR =1.75, 95% CI=1.05, 2.90) compared to controls. In multivariate models, cases were more likely than controls to have prior ED visits for drug use (OR=3.15, 95% CI=1.48, 6.67). Our findings suggest drug use may increase the likelihood of hyperthermia mortality. To help reduce heat-related mortality, EDs should consider interventions that target patients vulnerable to heat exposure. Meanwhile, more research is warranted to help develop effective strategies to minimize the impact of heat exposure.

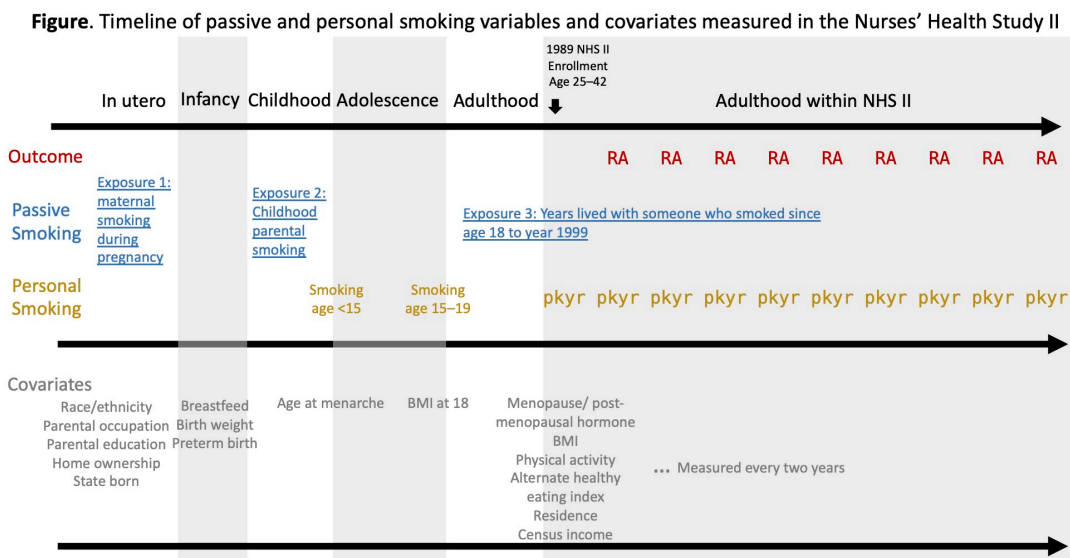
Passive Smoking Throughout the Life Course and the Risk of Incident Rheumatoid Arthritis in Adulthood Among Women. Kazuki Yoshida* Kazuki Yoshida Jiaqi Wang Susan Malspeis Nathalie Marchand Bing Lu Lauren C. Prisco Lily W. Martin Julia A. Ford Karen H. Costenbader Elizabeth W. Karlson Jeffrey A. Sparks

To investigate passive smoking throughout the life course and the risk of seropositive rheumatoid arthritis (RA), while controlling for personal smoking behavior.

We analyzed the female registered nurses in the prospective Nurses’ Health Study II using information collected via biennial questionnaires. We assessed the influence of (1) maternal smoking during pregnancy, (2) parental smoking during childhood, and (3) years lived with a smoker since age 18 (**Figure**). Incident RA and serologic phenotype (autoantibody status) was determined by medical record review meeting research criteria. Using the marginal structural model framework, we estimated the controlled direct effect (CDE) of each passive smoking exposure on adult incident RA risk by serologic phenotype, controlling for early life and time-updated adult factors including personal smoking.

Among 90,923 women, we identified 532 incident RA during mean 25 years of follow-up. Maternal smoking during pregnancy was associated with incident RA after confounding adjustment (HR 1.25 [95% CI 1.03, 1.52]). Childhood parental smoking was associated with incident seropositive RA after adjusting for confounders including maternal smoking during pregnancy but not later-life personal smoking (HR 1.41 [1.08, 1.83]). There was no association of adult passive smoking with RA (20+ years lived smoker: HR 1.02 [0.74, 1.40] vs. none). In the controlled direct effect analyses, childhood parental smoking was associated with seropositive RA (HR_{CDE} 1.93 [1.16, 3.22]) after additionally controlling for adult personal smoking, which was accentuated among ever adult smokers (HR_{CDE} 2.23 [1.25, 3.97]).

We found a potential direct influence of childhood parental smoking on later-life incident seropositive RA even after controlling for adult personal smoking. These findings suggest that parental smoking may be directly related to the risk of future incident seropositive RA beyond its influence on personal adult smoking.



Early neonatal mortality and its descriptive epidemiology among babies born with spina bifida in Finland, 2000-2014 Vijaya Kancherla* Vijaya Kancherla Sanjida Mowla Sari Sari
Räsänen Mika Gissler

Objective: We examined the prevalence of early neonatal mortality (death within first 7 days of birth) and selected infant and maternal factors associated with early neonatal mortality among babies born with spina bifida in Finland.

Methods: We linked multi-registry population-based data from the national registers in Finland for all liveborn infants with spina bifida born between 2000 and 2014. Prevalence and 95% confidence interval (CI) for early neonatal mortality was estimated using the Poisson approximation of binomial distribution. Selected infant and maternal characteristics of spina bifida cases were compared between those that experienced early neonatal mortality versus those that did not using Chi square or Fisher's Exact test. Crude odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression analysis. Multivariable analysis was not performed due to small sample sizes for selected covariables relevant for modeling.

Results: There were a total of 181 liveborn spina bifida cases (61% isolated) during the study period. Of these, 13 experienced early neonatal death. The prevalence of early neonatal mortality was 7.2% (95% CI=4.2%, 12.4%). Unadjusted analysis showed low gestational age (<37 weeks) (cOR=6.96; 95% CI=1.86; 29.01), and advanced maternal age at gestation (≥ 35 years) (cOR=5.33; 95% CI=1.21, 21.87) to be positively associated with early neonatal mortality among spina bifida-affected livebirths in Finland. Having multiple co-occurring birth defects, congenital hydrocephalus, and maternal anemia, also increased mortality odds; however, these associations were not statistically significant.

Conclusions: Our nationally representative study from Finland, with information of many infant and maternal variables that were not examined in previous studies, provided some new insights on factors associated with early neonatal mortality in spina bifida. These factors should be further examined.

Correlation between concentrations of six heavy metals in cord blood and postnatal blood of Jamaican children Mohammad H. Rahbar* Mohammad H. Rahbar Maureen Samms-Vaughan Manouchehr Hessabi Jan Bressler Shezeen Gillani Megan L. Grove Sydonnie Shakspeare-Pellington and Katherine A. Loveland

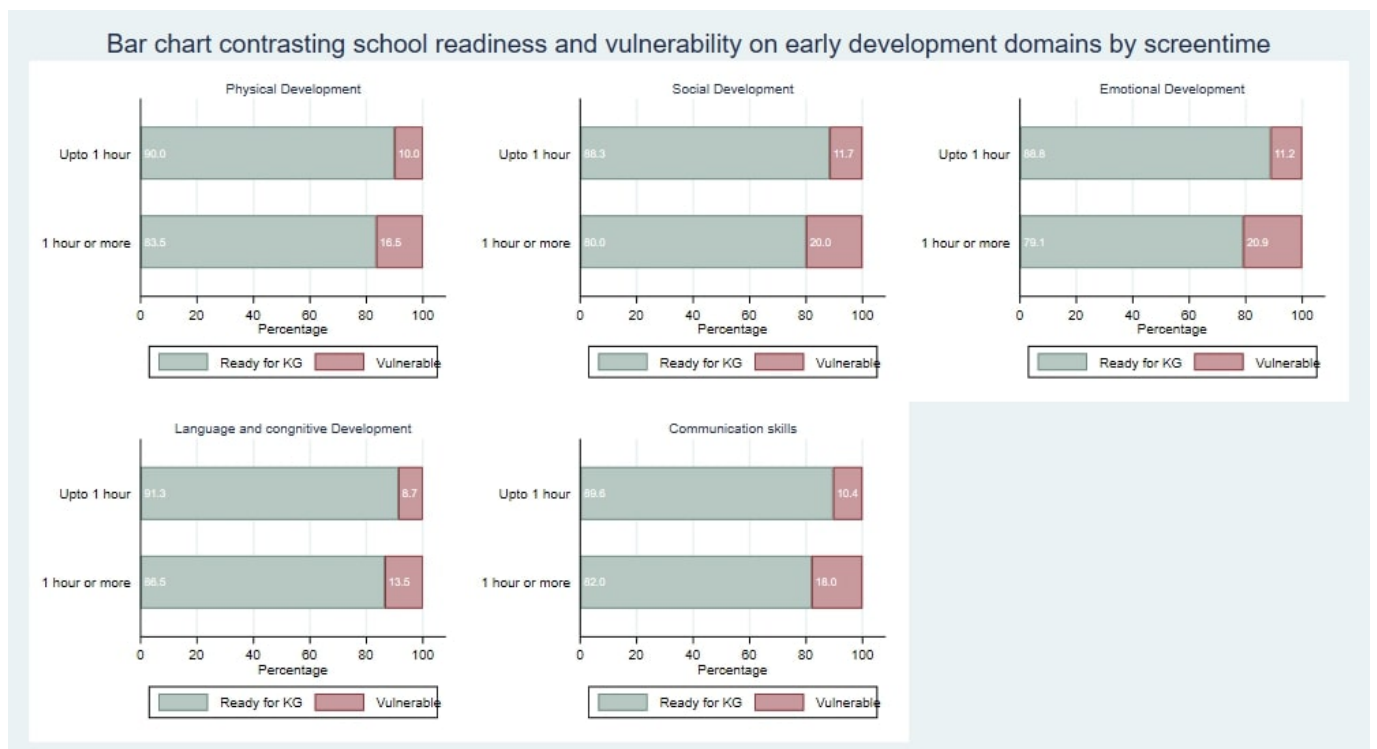
We investigated whether the concentrations of six metals [lead (Pb), mercury (Hg), arsenic (As), cadmium (Cd), manganese (Mn), and aluminum (Al)] are correlated in cord blood (prenatal samples) and postnatal blood samples from Jamaican children. We obtained cord blood samples from 21 pregnant women who participated in the second Jamaican birth cohort study from July 1, 2011 to September 30, 2011, and blood samples from their children who participated in a follow up study when the children were 4-8 years old. Since Mn concentrations were approximately normally distributed, we assessed the Pearson correlation coefficient between concentration of Mn in cord blood and postnatal blood. For metals with skewed distributions for concentrations, we assessed the Spearman's rank correlation coefficient. However, for Pb, Hg, and Al we log-transformed concentrations and then assessed these correlations. Since the majority of Cd and As concentrations in cord blood and postnatal blood were below their respective limits of detections, correlation analysis was not performed for these two metals. The mean ages of children at the postnatal visit and their mother at the child's birth were 5.5 and 29.8 years, respectively. About 47.6% of children were male. We found significant correlations between cord blood and postnatal blood concentrations of Pb ($r_{\text{Spearman}} = 0.45$; $P = 0.04$) and Mn ($r_{\text{Pearson}} = 0.48$; $P = 0.03$). For Al and Hg, $r_{\text{Spearman}} = 0.29$ and 0.08, respectively, but were not statistically significant (both $P \geq 0.20$). We also found that the median Mn concentration in cord blood was about four times that of postnatal blood, perhaps due to higher fish consumption of pregnant women in Jamaica compared to that of their children. Our findings of a significant correlation between prenatal and postnatal Pb blood concentrations for children 4-8 years old have not been reported previously. However, these findings may require replication in other populations.

The association between screen time and developmental health : Results from an early childhood study in British Columbia, Canada Salima Kerai* Salima Kerai Alisa Almas Eva Oberle

High levels of recreational screen time have been negatively associated with children’s healthy development in past research. However, most research has focused on older children and less is known about this effect in early childhood. Drawing from a large-scale linked database on preschool age children in British Columbia (BC), Canada, (n=2983) we examined whether time spent in screen-based activities (e.g., watching videos, virtual games) in 4-to 5-year old children predicted their social, emotional, cognitive, and physical developmental health six months later.

Screen time was measured with the Childhood Experiences Questionnaire (CHEQ; parent-reported survey). Developmental health outcomes were measured with the Early Years Development Instrument (EDI; teacher-reported survey). Each child was classified as “thriving” versus “vulnerable” on each of the five core EDI domains: 1) physical health/wellbeing, 2) social competence, 3) emotional maturity, 4) language/cognitive development, 4) communication skills/general knowledge. Generalized estimating equations logistic regression models were used to examine the association between screen time and each developmental health indicator.

Results showed that children with ≥ 1 hour of screen time per day had significantly higher odds of vulnerability across all developmental domains [physical (OR 1.58; 95% CI 1.23 – 2.04), social (OR 1.49; 95% CI 1.18 – 1.88), emotional (OR 1.39; 95% CI 1.12 – 1.73), language and cognition (OR, 1.56; 95% CI 1.18 – 2.08) and communication (OR 1.35; 95% CI 1.04 – 1.76)] after adjusting for sex, family income, ethnicity, urban versus rural population center, sleep, and physical activity. This study suggests that screen time exceeding 1 hour/day among preschool children before kindergarten entry is negatively associated with developmental health, an important indicator for school readiness, supporting the call to action to limit screen time for young children.



Phthalate-containing medications and secondary sex ratio Lauren A. Wise* Lauren Wise Anne Broe Thomas P. Ahern Per Damkier

Background: Phthalates are endocrine-disrupting chemicals found in selected consumer products and medications. Some studies have documented 50-fold higher urinary phthalate metabolite concentrations in humans exposed to phthalate-containing drugs. In a prior study, higher maternal urinary concentrations of mono-isobutyl phthalate, mono-benzyl phthalate, and mono-n-butyl phthalate were associated with an excess of male births.

Methods: Using data from Danish national health registries, we examined the association between maternal exposure to phthalate-containing drugs and secondary sex ratio (probability of male birth). During 2004 through 2017, we identified 73,155 singletons born to 66,641 mothers exposed to drugs available in both phthalate-containing and phthalate-free versions. We estimated odds ratios (OR) and 95% confidence intervals (CI) using generalized estimating equations to account for multiple births. Models were adjusted for demographic factors, reproductive history, and other drug use.

Results: The probability of male birth among unexposed women was 51.1%. Among women exposed to orthophthalate-containing drugs, that probability was 50.9% during preconception and 52.3% during the first trimester; among women exposed to polymer-containing drugs, those respective probabilities were 49.3% and 49.8%. For orthophthalate-containing drugs, the adjusted OR for male birth was 0.99 (CI: 0.92-1.07) for preconception exposure and 1.05 (CI: 0.96-1.14) for first-trimester exposure versus no exposure. For polymer-containing drugs, the adjusted OR was 0.93 (CI: 0.81-1.07) for preconception exposure and 0.95 (CI: 0.81-1.12) for first-trimester exposure versus no exposure. Results were similar when analyses were restricted to spontaneous conceptions or first-born children.

Conclusions: Exposure to phthalate-containing drugs during preconception or the first trimester of pregnancy was not appreciably associated with secondary sex ratio.

Center effect on short term mortality following pediatric surgery for congenital heart defects Rachel Zmora* Rachel Zmora Logan Spector Thomas Murray Kamakshi Lakshminarayan Lazaros Kochilas

Regionalization of complex surgeries, including pediatric repair of congenital heart defects (CHDs), has been proposed as a mechanism for improving outcomes. Research suggests that high volume centers as well as urban and teaching hospitals may have better short-term survival. We used data from the Pediatric Cardiac Care Consortium, a large, US-based registry of pediatric interventions for CHD linked with the National Death Index. We analyzed data from 47 centers that performed benchmark surgeries for the repair of CHDs between 1982 and 2003 using multi-level Cox regression models to examine center-level effects on mortality adjusting for known patient-level risk factors. We examined teaching hospital status, mean center-specific length of stay as well as total, procedure-specific, and complex annual surgery volume. We calculated hazard ratios by surgical procedure and complexity, based on the Risk Adjustment for Congenital Heart Surgery (RACHS) score, at 90 days and 1, 3, and 5 years. Models were adjusted for patient age and weight at surgery, sex, race, chromosomal defect, and surgical era. The centers were located in the Midwest, South, and West regions of the United States. 71% of centers were teaching hospitals and 87% were located in a metropolitan area. One year post-operation, every 10 additional procedure performed by a center was associated with 14% lower risk of mortality for simple repairs (HR = 0.864, 95% CI = 0.777, 0.961) and 24% lower risk of mortality for complex repairs (HR = 0.765, 95% CI = 0.684, 0.856) after adjusting for patient-level risk factors. Complex procedure was defined as a procedure with a RACHS score of 4 or higher. Teaching hospital status was not statistically significantly associated with improved mortality. Procedure-specific models are presented in Table 1. Our novel use of multi-level modeling suggests that regionalization of surgeries for the repair of CHDs may be warranted, particularly in the case of complex repairs.

Variables	Descriptive statistics	Model 1			Model 2		
		HR	95% CI	p-value	HR	95% CI	p-value
Simple*							
Procedure-specific volume	median (IQR) 21 (7-38)	0.74	(0.687, 0.797)	<.0001	0.864	(0.777, 0.961)	0.0072
Teaching hospital	N (%) 30 (67%)	1.203	(0.888, 1.631)	0.2326	0.782	(0.468, 1.307)	0.3486
Complex*							
Procedure-specific volume	median (IQR) 5 (2-11)	0.769	(0.715, 0.826)	<.0001	0.765	(0.684, 0.856)	<.0001
Teaching hospital	N (%) 30 (69%)	1.406	(0.934, 2.116)	0.1023	0.859	(0.591, 1.248)	0.426
Ventricular septal defect repair*							
Procedure-specific volume	median (IQR) 11 (4-20)	0.837	(0.769, 0.91)	<.0001	0.848	(0.769, 0.936)	0.001
Teaching hospital	N (%) 30 (67%)	1.316	(0.938, 1.846)	0.112	1.066	(0.737, 1.541)	0.7357
Tetralogy of Fallot repair							
Procedure-specific volume	median (IQR) 5 (3-9)	0.998	(0.952, 1.046)	0.9301	0.979	(0.927, 1.033)	0.4319
Teaching hospital	N (%) 30 (67%)	0.898	(0.434, 1.861)	0.7732	1.09	(0.471, 2.52)	0.8407
Fontan procedure							
Procedure-specific volume	median (IQR) 3 (2-6)	0.928	(0.897, 0.96)	<.0001	0.996	(0.962, 1.032)	0.8309
Teaching hospital	N (%) 29 (68%)	1.409	(0.814, 2.439)	0.2207	0.901	(0.596, 1.363)	0.6227
Glenn shunt							
Procedure-specific volume	median (IQR) 3 (1-7)	0.956	(0.928, 0.984)	0.0024	0.98	(0.954, 1.008)	0.1601
Teaching hospital	N (%) 30 (71%)	1.196	(0.717, 1.993)	0.4934	0.971	(0.663, 1.422)	0.8802
Coarctation of aorta repair							
Procedure-specific volume	median (IQR) 4 (2-6)	0.954	(0.884, 1.029)	0.2226	0.975	(0.897, 1.061)	0.5605
Teaching hospital	N (%) 29 (67%)	1.063	(0.511, 2.21)	0.8697	1.015	(0.458, 2.254)	0.9699
Norwood procedure							
Procedure-specific volume	median (IQR) 2 (1-4)	0.953	(0.933, 0.974)	<.0001	0.96	(0.939, 0.981)	0.0002
Teaching hospital	N (%) 28 (73%)	1.255	(0.879, 1.793)	0.2117	0.941	(0.678, 1.307)	0.7167
Arterial switch operation							
Procedure-specific volume	median (IQR) 3 (1-5)	0.919	(0.87, 0.971)	0.0025	0.974	(0.923, 1.028)	0.3351
Teaching hospital	N (%) 27 (70%)	0.997	(0.572, 1.738)	0.992	0.896	(0.541, 1.483)	0.6693
Truncus arteriosus repair							
Procedure-specific volume	median (IQR) 2 (1-3)	0.982	(0.9, 1.073)	0.6903	0.959	(0.875, 1.052)	0.3774
Teaching hospital	N (%) 27 (67%)	1.5	(0.909, 2.478)	0.1128	1.065	(0.572, 1.982)	0.8417

Model 1 adjusted for center-level variables only; model 2 also adjusted for age and weight at surgery, sex, race, presence of chromosomal defects, and surgical era; *scaled to 10 procedures

Is economic hardship associated with young children's cortisol levels? Jeanie Santaularia*
Jeanie Santaularia Alicia Kunin-Batson Megan Gunnar Nancy Sherwood Simone French Susan
Mason

Background

Economic hardship during childhood has been linked to poor physical and mental health. One pathway linking economic hardship to poor health is the hypothalamic-pituitary-adrenal axis, which releases cortisol in response to stress. This study aims to examine the association between five measures of economic hardship (poverty, food insecurity, financial hardship, economic hardship risk score, and a cumulative economic hardship risk score) and hair cortisol.

Methods

Baseline and 1-year data from the NET-Works obesity prevention trial (NET-Works, NCT0166891) were utilized. Five-hundred and thirty-four children ages 2-4 years ($M = 3.4$, $SD = 0.7$ years) from diverse racial/ethnic backgrounds (58% Hispanic) and predominantly lower income households (63% reporting annual household income $< \$25,000$ /year at their baseline visit) were enrolled. Hair cortisol was regressed on each economic hardship variable in a series of generalized linear regressions to estimate the average difference in hair cortisol associated with greater versus lesser hardship both cross-sectionally and longitudinally. All models were adjusted for child age, sex, race/ethnicity, and intervention (prevention vs control) arm.

Results

In the final adjusted models, all parameter estimates were modest and most non-significant, with two exceptions. For every one-unit increase in baseline economic hardship score, the average increase in hair cortisol at 1-year follow-up was 0.07 picograms per milligram (pg/mg) (95% CI: 0.01, 0.13). For every one-unit increase in the cumulative baseline and follow-up economic hardship score there was a 0.04 pg/mg (95% CI: 0.00, 0.07) average higher level of hair cortisol at 1-year follow-up.

Conclusions

Cortisol could be useful in providing meaningful assessment of the economic hardship—stress association. Future studies should continue to examine this association by investigating more specific pathways, longer longitudinal follow-up, and in larger population-based studies.

Maternal opioid use disorder and perinatal outcomes: a population-based study in British Columbia, Canada, from 2000 to 2019 Micah Piske* Micah Piske Fahmida Homayra Jeong Eun Min Haoxuan Zhou Annabel Mead Carolyn Marchand Megan Woolner Jennifer Ng Bohdan Nosyk

Background and Aims: While opioid agonist treatment (OAT) remains the evidence-based standard for treatment of opioid use disorder (OUD), evidence on its use in pregnancy and its associated perinatal outcomes is limited. We aimed to assess perinatal outcomes among mother-infant dyads following indication of OUD and determine the association between maternal OUD treatment factors and infant birth outcomes.

Methods: We conducted a population-based retrospective study among all women with indication of OUD prior to delivery and within the puerperium period (six weeks following birth) in British Columbia (BC), Canada, between 2000 and 2019 utilizing linked provincial health administrative data. We modelled the effects of maternal demographic and OUD treatment characteristics on birthweight, preterm birth, infant disorders related to gestational age and birthweight, and neonatal abstinence syndrome (NAS) via logistic regression.

Results: The population included 4,574 women, 6,693 deliveries, and 6,720 live births. The annual number of BC women with perinatal OUD increased from 166 in 2000 to 513 in 2019. As of 2019, 42% of women with OUD had engaged in OAT during pregnancy. Additionally, incidence of preterm birth, disorders related to gestational age or low birthweight, and NAS among mothers with OUD increased by 26%, 30%, and 3%, respectively since 2000. Continued OAT engagement to delivery was associated with lower odds of preterm birth [adjusted odds ratio AOR: 0.6; 95% confidence interval: 0.4, 0.6], and low birthweight [AOR: 0.4; (0.2, 0.8)]. Finally, treatment with buprenorphine-naloxone (compared to methadone) reduced odds of each outcome including NAS [AOR: 0.6; (0.4, 0.7)].

Conclusions: Perinatal OUD in BC tripled in incidence over a 20-year period. Sustained OAT during pregnancy reduces the risk of several adverse birth outcomes. The results highlight the need for expansion of integrated services that include OAT to support mothers with OUD and their infants.

Prescription opioid type and the risk of neonatal opioid withdrawal syndrome Daina Esposito* Daina Esposito Brian Bateman Martha Werler Loreen Straub Helen Mogun Sonia Hernandez-Diaz Samantha Parker Krista Huybrechts

Background: While often used during pregnancy, opioids carry the risk of neonatal opioid withdrawal syndrome (NOWS). Most studies of adverse outcomes of opioid use assess only a class-wide effect despite pharmacodynamic and pharmacokinetic heterogeneity across medications. As such, data on variation in the risk of NOWS based on opioid medication type are lacking.

Methods: This cohort study used the US nationwide Medicaid Analytic eXtract (MAX, 2000-2014) to compare women with 2+ opioid dispensings within 90 days prior to delivery based on active ingredient, half-life, and agonist strength of the opioid received. We identified NOWS in infants using a validated algorithm based on diagnostic codes in the 30 days after delivery. The relative risk (RR) of NOWS and corresponding 95% confidence interval (CI) were adjusted for an exposure propensity score including demographics, comorbidities, other medication use, and opioid use characteristics such as cumulative exposure using fine stratification.

Results: We compared 16,202 codeine, 1,244 tramadol, 4,540 oxycodone, 260 methadone, 90 hydromorphone, and 63 morphine users vs. 25,710 hydrocodone users. When compared to hydrocodone users, adjusted risk of NOWS was lower among codeine users (RR 0.57, 95% CI 0.46-0.70), similar for tramadol users (1.06, 0.73-1.56) and higher for oxycodone (1.87, 1.66-2.11), hydromorphone (2.03, 1.09-3.78), morphine (2.84, 1.30-6.22), and methadone users (3.02, 2.45-3.73). Strong agonists had a higher risk than weak agonists (1.97, 1.78-2.17), and long half-life opioids had a slightly increased risk compared to short half-life products (1.33, 1.12-1.56). Findings were consistent across multiple sensitivity and subgroup analyses.

Discussion: The risk of NOWS in infants with exposed to opioids during the 90 days before delivery was different based on the type of opioid used.

Evaluating sexually transmitted infections and hypertensive disorders of pregnancy in older women Brandie DePaoli Taylor* Brandie DePaoli Taylor Ashley Hill Akaninyene Noah Tyne Hernandez Maria J. Perez-Patron

Hypertensive disorders of pregnancy (HDP) are increasingly common, and the most severe forms can lead to serious maternal morbidity and mortality. Genital infections are not typically considered major risk factors for HDP and often these conditions are not examined in perinatal studies of common sexually transmitted infections including *Chlamydia trachomatis* (CT), syphilis, and *Neisseria gonorrhoeae* (GC). Our prior research suggested that CT may increase preeclampsia risk at term in young adults. Trends were observed in older women, but these women are not typically screened for CT and GC and thus excluded from studies. To expand on this work, we restricted this analysis to older women > 25 years. We used data from 27,442 single pregnancies without HIV enrolled in Peribank between July 2011 and September 2020. STIs were measured in 98.5% of women and 4% had CT, 0.7% had syphilis, and 0.4% had GC. Most women are Hispanic, on Medicaid, and are overweight/obese with a mean age of 32 years. Outcomes included gestational hypertension, mild preeclampsia, severe preeclampsia, superimposed preeclampsia, and preeclampsia with a preterm delivery. Logistic regression was used to calculate ORs and 95% CIs, the penalized likelihood approach was used when necessary. Analyses were adjusted for race, age, foreign born status, sociodemographic variables, substance use, other infections, and prior complications. E-values were calculated to examine robustness to unmeasured confounding. Syphilis was associated with gestational hypertension (OR 1.8, 95% CI 1.1-2.9). GC was associated with preterm preeclampsia (OR 5.6, 95% CO 1.7-18.4) and severe preeclampsia (OR 4.1, 95% CI 1.3-13.2). CT was associated with superimposed preeclampsia (OR 1.7, 95% CI 1.0-2.5). With the striking reemergence of STIs and lack of universal screening for GC and CT among older women, there is a need to revisit the burden of STIs in pregnant women.

Iron and folic acid and multiple micronutrient supplementation strategies during pregnancy and adverse birth outcomes in Botswana

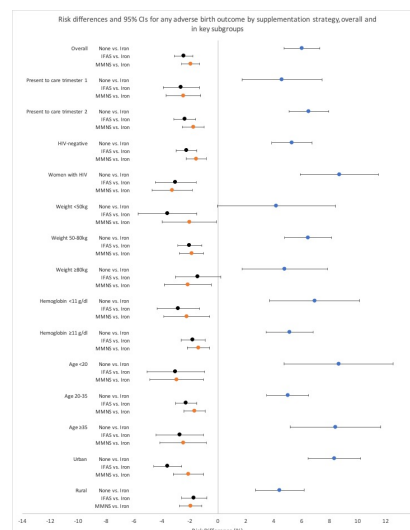
Ellen C. Caniglia* Ellen Caniglia Rebecca Zash Sonja A. Swanson Emily Smith Christopher Sudfeld Julia L. Finkelstein Modiegi Diseko Gloria Mayondi Mompati Mmalane Joseph Makhema Shahin Lockman Roger Shapiro

Background: Iron and folic acid supplementation (IFA) and multiple micronutrient supplementation (MMS) that includes IFA may reduce the high risk of adverse birth outcomes in Sub-Saharan Africa. However, there is limited evidence from clinical settings on the effectiveness of supplementation in women with HIV and in those at increased risk for malnutrition.

Methods: The Tsepamo Study captured data at up to 18 large delivery sites in Botswana from August 2014–November 2020. We compared 4 program-driven antenatal supplementation strategies among women who presented for care prior to 24 weeks gestation: no supplementation, iron alone, IFA, and MMS. We calculated risk differences (RDs) for any adverse birth outcome (stillbirth, preterm delivery [PTD], small-for-gestational-age [SGA] or neonatal death) and any severe birth outcome (stillbirth, very PTD, very SGA, or neonatal death). We adjusted for confounding by trimester of presentation to care, maternal HIV status, early pregnancy weight and hemoglobin (Hb), age, urban residence, year, and socioeconomic position via IP weighting. RDs were calculated separately by trimester of presentation to care, maternal HIV status, weight, Hb, age, and urban residence.

Results: 136207 women presented to care (23% with HIV) and received either no supplementation (6.1%), iron only (37.3%), IFA (23.2%), or MMS (33.4%). Compared to iron only, RDs (95% CIs) for any adverse birth outcome were 6.0% (4.7%, 7.3%) for no supplementation, -2.5% (-3.1%, -1.8%) for IFA, and -2.0% (-2.6%, -1.3%) for MMS (overall risk 28.9%). RDs were similar by trimester of presentation to care but larger in magnitude among women with HIV (-3.0% [-4.5%, -1.6%] for IFA and -3.3% [-4.7%, -1.8%] for MMS), women <50kg, women with anemia (Hb <11 g/dL), and women <20 or ≥35 years. Findings were similar for any severe birth outcome.

Conclusions: Antenatal IFA or MMS may improve birth outcomes compared with iron supplementation alone, particularly among women with HIV.



Gestational age trends in placental dysfunction among women with preeclampsia using a novel clustering approach Alexander J. Layden* Alexander J. Layden Marnie Bertolet James M. Roberts W. Tony Parks Janet M. Catov

Introduction: Preeclampsia is a life-threatening pregnancy syndrome hypothesized to have 2 subtypes with distinct placental pathogenesis: early (<34weeks) and late-onset (>34 weeks). Placental pathology evaluations are routinely conducted for preeclampsia, which may help elucidate subtypes. Few systematic methods exist to summarize the variables generated from pathology review.

Objective: Using the clustering method, latent class regression (LCR), we characterize placental features of preeclampsia across gestation.

Methods: We included 2863 women with preeclampsia determined by ICD-9 codes who delivered at Magee-Womens Hospital (Pittsburgh, PA) in 2008-2012 with a singleton pregnancy and an available pathology review (91% of preeclampsia cases). Gestational age was determined by best obstetric estimate and 15 abstracted placental features from pathology reviews were included. LCR simultaneously clustered placental features and estimated the likelihood of cluster membership with increasing gestational age. The optimal number of clusters was determined by comparing fit statistics.

Results: Placental findings in women with preeclampsia clustered into 4 groups: “maternal malperfusion” (22% of cases), “fetal malperfusion” (10%), “acute inflammation” (13%) and “low risk pathology” (55%). The most prevalent cluster before 34 weeks was maternal malperfusion (78%) while low risk pathology (66%) was most prevalent after 34 weeks. A 1-week increase in gestational age at delivery was associated with a lower odds of maternal malperfusion (OR: 0.55, 95% CI: 0.47,0.63) and fetal malperfusion (OR 0.79, 95% CI: 0.72,0.86), but a higher odds of acute inflammation (OR: 1.34, 95% CI: 1.26, 1.41) relative to the low risk pathology group.

Conclusions: In support of a 2-subtype hypothesis, we identified distinct placental clusters in women with early and late-onset preeclampsia. Our novel application of LCR offers a framework for studying preeclampsia and perhaps other placental conditions.

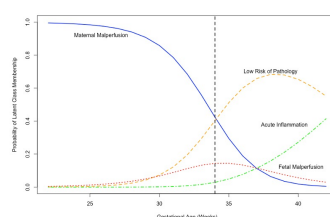


Figure: Predicted probability plot of placental pathology clusters across gestational age in women with preeclampsia using latent class regression. The dotted line at 34 weeks of gestation represents the conventional cut-off for early- and late-onset preeclampsia.

Pre-pregnancy BMI associated with placental dysfunction in early but not late preterm birth

Alexander J. Layden* Alexander J. Layden Marnie Bertolet W. Tony Parks James M. Roberts Janet M. Catov

Background: Maternal obesity is a risk factor for preterm birth (PTB), particularly before 32 weeks' gestation. Obesity may increase the risk of PTB through placental damage, but heterogeneity in PTB etiology hinders efforts to find key placental pathways.

Objective: We applied latent class analysis to identify placental pathology phenotypes in early (<32wks) and late PTBs (32 to <37wks) associated with pre-pregnancy BMI using placental pathology data.

Methods: Women with a singleton PTB at Magee-Womens Hospital (Pittsburgh, PA) in 2008-2012 and a placental evaluation (89% of PTBs) were stratified into early (n=900, 61% spontaneous) and late PTBs (n=3362, 57% spontaneous). Pre-pregnancy BMI was self-reported at first prenatal visit and 15 abstracted placental features were included. Placental features were clustered in early and late PTBs separately by latent class analysis. The optimal number of clusters was selected by comparing model fit statistics. The probability of cluster membership across BMIs was estimated in early PTBs and in late PTBs by latent class regression adjusting for race, smoking, education and parity.

Results: Early PTBs clustered into 4 groups: acute inflammation (38% of cases), maternal malperfusion with chorioamnionitis (29%), maternal malperfusion (25%), and fetal malperfusion (8%). As BMI increased from 20 to 50kg/m² the predicted probability of maternal malperfusion increased while the probability of maternal malperfusion with chorioamnionitis decreased. There was minimal change in the probability of acute inflammation or fetal malperfusion with increasing BMI (**Fig 1**). Late PTBs also clustered into 4 groups: maternal malperfusion (22%), acute inflammation (12%), fetal malperfusion (9%) and low risk pathology (58%). Unlike early PTBs, the predicted probabilities for all 4 clusters were relatively unchanged with increasing BMI in late PTBs.

Conclusions: Obesity may predispose women to PTB through placental dysfunction but mainly in early PTBs.

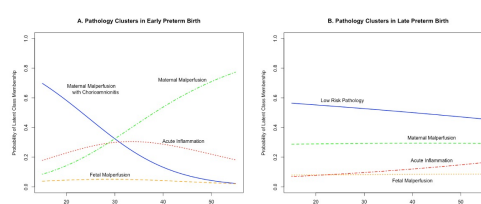


Fig 1. Predicted probability plots of placenta pathology clusters across pre-pregnancy BMI (kg/m²) using latent class regression in early (A) and late (B) preterm births. Models were adjusted for maternal race, education, smoking status, and parity.

Longitudinal changes in reproductive hormones, reproductive organs, and anogenital distance in infant boys: does soy formula affect minipuberty? Helen Chin* Helen Chin Andrea Kelly Donna Baird Walter Rogan David Umbach

Soy formula feeding is common in infancy and is a source of high exposure to phytoestrogens, documented to influence vaginal cytology in female infants. The influence of soy on the emergence and progression of minipuberty in males is unknown. We used data from the Infant Feeding and Early Development study to assess differences in reproductive hormones and hormone-responsive tissues in infant boys exclusively fed soy formula, cow-milk formula, or breastmilk. In this longitudinal cohort study, we followed 147 infant boys from birth to age 28 weeks with up to 9 data-collection visits. Infants participating in the study were normal birthweight (2500-4500 grams) and term gestational age (37-42 weeks). Over the study period we assessed serum testosterone concentrations, serum luteinizing hormone (LH) concentrations, stretched penile length, anogenital distance, and testis volume. We examined feeding-group differences in age trajectories for these outcomes using mixed-effects regression splines. We adjusted anatomical outcomes for weight-for-length z-score to account for age and body size changes. Our main comparison was between the two formula groups because women who breastfed differed from women who formula fed in multiple and likely unmeasured ways. Testosterone concentrations were in the mid-pubertal range at age 2 weeks (median: 176 ng/dL, quartiles:124, 232) and remained “pubertal” through age 12 weeks. Trajectories of testosterone, LH, and anatomical measures did not differ between boys fed soy formula (n=55) and boys fed cow-milk formula (n=54). Our findings suggest that these measures of early male reproductive development do not respond to infant phytoestrogen exposure, in contrast to the response observed in infant girls. More research is needed to understand infant hormone production and individual variability for these outcomes.

Association of maternal age and paternal age with congenital anomalies identified at birth.

Yuxiao Wu* Yuxiao Wu Wei Bao Buyun Liu Yang Du Mark Santillan Donna Santillan

Background: The trend of older parenthood is popular worldwide while there is no official guide at present for parents to have their babies. Previous studies suggested that maternal age over 35 years old might be a risk factor for congenital anomalies in the offspring. However, the association of maternal age for specific types of congenital anomalies remains unclear. Moreover, the association of paternal age with congenital anomalies remains inconclusive.

Objective: To examine the association of maternal age and paternal age with 12 types of congenital anomalies identified at birth in a large and multi-racial/multi-ethnic population.

Methods: In this nationwide population-based retrospective cohort study, we included 29,429,789 live singleton births documented in the National Vital Statistics System in the United States, 2011-2019. Information on maternal age, paternal age, congenital anomalies identified at birth, and maternal, paternal infant sociodemographic characteristics and medical history was retrieved from birth certificates. Maternal age and paternal age were categorized as <20 years old, 20-24 years old, 25-29 years old, 30-34 years old, 35-39 years old, 40-44 years old and >45 years old, 25-29 years old group was used as reference group for both maternal age and paternal age. Logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) for congenital anomalies overall and by subtypes.

Results: Of the 29,429,789 mother-infant and father-infant pairs, 1,389,542 (4.72%) mothers and 698,102 (2.37%) fathers were aged <20 years old, 5,715,673 (19.42%) mothers and 4,015,618 (13.64%) fathers were aged from 20 to 24 years old, 8,624,155 (29.30%) mothers and 7,279,676 (24.74%) fathers were aged from 25 to 29 years old, 8,552,097 (29.06%) mothers and 8,596,191 (29.21%) fathers were aged from 30 to 34 years old, 4,192,064 (14.24%) mothers and 5,487,185 (18.65%) fathers were aged from 35 to 39 years old, 888,536 (3.02%) mothers and 2,239,616 (7.61%) fathers were aged from 40 to 44 years old, and 67,722 (0.23%) mothers and 1,113,401 (3.78%) fathers were aged >45 years old. Compared with mothers aged from 25 to 29 years old, the adjusted ORs of congenital anomalies identified at birth were 1.22 (95% CI 1.17-1.27) for mothers aged <20 years old, 1.12 (95% CI 1.10-1.15) for mothers aged from 20 to 24 years old, 0.98 (95% CI 0.96-1.00) for mothers aged from 30 to 34 years old, 1.16 (95% CI 1.13-1.19) for mothers aged from 35 to 39 years old, 1.83 (95% CI 1.76-1.90) for mothers aged from 40 to 44 years old, and 2.42 (95% CI 2.19-2.67) for mothers aged >45 years old. For specific types of congenital anomalies such as Down syndrome, compared with mothers aged from 25 to 29 years old, the adjusted ORs were 0.78 (95% CI 0.61-1.00) for mothers aged <20 years old, 0.89 (95% CI 0.79-1.01) for mothers aged from 20 to 24 years old, 1.48 (95% CI 1.34-1.62) for mothers aged from 30 to 34 years old, 4.30 (95% CI 3.90-4.73) for mothers aged from 35 to 39 years old, 13.55 (95% CI 12.17-15.10) for mothers aged from 40 to 44 years old, and 22.79 (95% CI 18.96-27.39) for mothers aged >45 years old. No significant association was found for paternal age and congenital anomalies identified at birth.

Conclusions: Maternal age less than 25 years old and more than 35 years old were significantly associated with most subtypes of congenital anomalies identified at birth. And for most subtypes such as Down syndrome and suspected chromosomal disorder, there was a clear dose-response relationship between maternal age and congenital anomalies identified at birth, and the risk was sharply increased after 35 years old. No significant association of paternal age with congenital

anomalies was found in this study.

Keywords: maternal age, paternal age, pregnancy, offspring, congenital anomalies, birth defects, congenital malformations, cyanotic congenital heart disease, hypospadias, cleft lip, Down syndrome, gastroschisis, suspected chromosomal disorder, cleft palate.

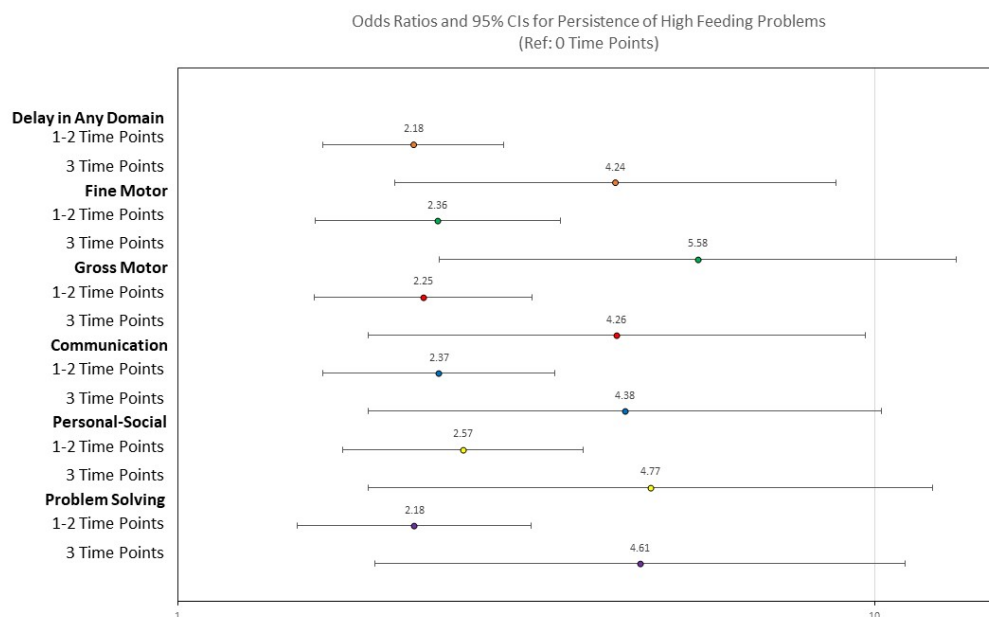
Feeding Problems as an Indicator of Developmental Delay in Early Childhood Diane L. Putnick* Diane Putnick Erin Bell Akhgar Ghassabian Sonia L. Robinson Rajeshwari Sundaram Edwina Yeung

Feeding problems are discussed the longest of all topics at well-child visits. High proportions of children with developmental disabilities have feeding problems, but it is unclear to what extent feeding problems indicate developmental delays in the general population.

In the Upstate KIDS cohort study (n=3,597), mothers reported the frequency of children’s behavioral feeding problems from 0 (*never*) to 3 (*often*) on 9-12 questions (e.g., crying during meals, pushing food away, gagging on food) and developmental delays in 6 domains (i.e., total, fine and gross motor, communication, personal-social, and problem-solving skills) using the Ages and Stages Questionnaire (ASQ) at 18, 24, and 30 months. A subset of children (n=516) were objectively assessed at 4 years using the Battelle Developmental Inventory (BDI-2).

Feeding problems (per point increase on a continuous scale) were increasingly associated with failure on the ASQ from 18 months (Odds Ratios (ORs) = 1.50 - 2.35) to 24 months (ORs = 2.44 - 3.04) to 30 months (ORs = 4.41 - 6.44). Children with persistently high feeding problems, ≥ 90th percentile at all time points (2% of the sample), were more than four times as likely to fail the ASQ (ORs = 4.24 - 5.58), and children with high feeding problems at one or two time points (20%) were more than twice as likely to fail the ASQ (ORs = 2.18 - 2.57), than children who never experienced high feeding problems (**Figure 1**). Children with one-point higher feeding problems at 30 months scored 3-4 points lower on all subscales of the BDI-2 at 4 years.

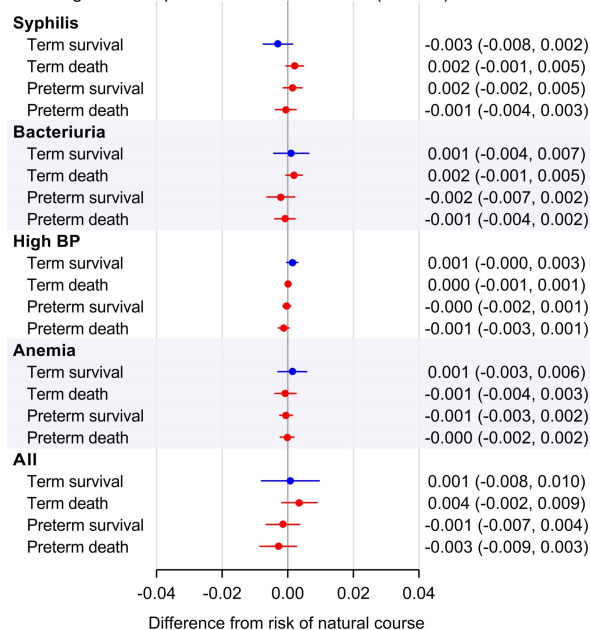
The American Academy of Pediatrics recommends developmental screening at 9, 18, and 30 months, but recent data suggests that over one-third of pediatricians did not screen all children under 3. Given that feeding problems are regularly discussed at well-child visits, frequent feeding problems that persist into the third year, could be used to identify children at risk for developmental delay for more targeted screening.



Impact of maternal anemia, syphilis, bacteriuria, and high blood pressure on preterm birth in Lusaka, Zambia Rachael K Ross* Rachael Ross Stephen R. Cole Joan T. Price Jeffrey S.A. Stringer

Many trials targeting known risk factors of preterm birth (PTB) have shown little effect. It may be the interplay of multiple factors that increases PTB risk, so targeting one factor may be inadequate, implying that joint interventions are needed. Typical risk factor analyses do not produce estimates of potential impact of interventions and cannot estimate joint intervention effects on multiple factors. We aimed to estimate the effect of eliminating PTB risk factors (syphilis, bacteriuria, high blood pressure (BP), and anemia) alone and together in a cohort of pregnant women in Lusaka, Zambia. Risk factors were assessed at prenatal care enrollment (<24 weeks gestation) and the outcome had four-categories: preterm death (stillbirth or neonatal), preterm survival, term death, term survival. We used g-formula to estimate population intervention effects. We fit a multinomial outcome model with indicators for syphilis and bacteriuria, restricted cubic splines for BP and hemoglobin (for anemia), and confounders. Outcome risks were estimated as the mean of predicted outcome probabilities under each simulated intervention: elimination of each risk factor alone and together. Risk differences (RD) were calculated against the natural course (no intervention). 1270 women were included and the risk factors were rare (<5%), except anemia (13%). 78% of pregnancies ended in term survival. The Figure shows the RDs under each simulated intervention. All RDs were ≤ 0.004 (4 tenths of 1 percent). Elimination of all risk factors together decreased the risk of preterm events (survival or death) by 0.004 (95% CI -0.012, 0.003), but term deaths increased (0.004, 95% CI -0.002, 0.009). Simulated intervention on the four risk factors alone and together did not have meaningful effects on PTB. Elimination of these factors may have limited impact because they were rare in this cohort, factors were adequately managed during prenatal care, or preconception intervention is needed.

Figure. Difference in risk under simulated elimination of preterm birth risk factors alone and together compared with natural course (n=1270)



Abbreviations: BP, blood pressure

Natural course was risk of outcomes under observed prevalence of risk factors. For intervention on high BP, systolic ≥ 140 mmHg was set to 139 and diastolic ≥ 90 mmHg was set to 89. For intervention on anemia, hemoglobin < 10.5 g/dL was set to 10.5. "All" means all the examined risk factors were eliminated. Proportion of women with a risk factor altered by simulated intervention: Syphilis 4.5%, Bacteriuria 4.9%, High BP 3.3%, Anemia 12.5%.

First Trimester Caffeine and Hypertensive Disorders of Pregnancy in a Prospective

Pregnancy Cohort Stefanie Hinkle* Stefanie Hinkle Samrawit F. Yisahak Jessica L. Gleason Sifang Kathy Zhao Jagteshwar Grewal Katherine L. Grantz Cuilin Zhang

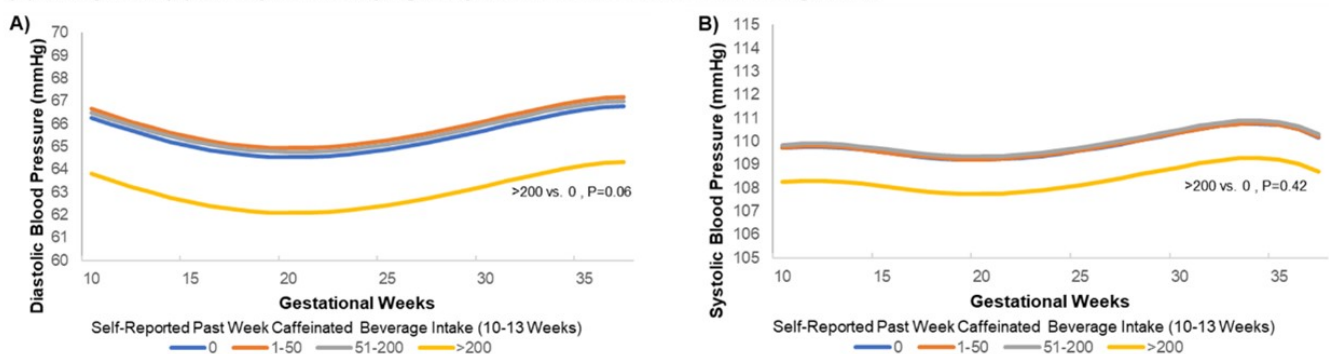
Objective: Pregnant women are advised to limit caffeine intake to <200 mg/day, yet the impacts of caffeine intake on obstetric health remain unclear. We examined associations of first trimester caffeine, from both caffeinated-beverage intake and in plasma with pregnancy blood pressure (BP), with risk of preeclampsia (PE) and gestational hypertension (GHTN).

Methods: For 2583 pregnant women in the NICHD Fetal Growth Studies-Singletons (2009-2013), daily total caffeine intake in the past week was estimated at 8-13 gestational weeks based on self-reported intake of caffeinated coffee, tea, soda, and energy drinks. Caffeine and paraxanthine were measured in plasma collected at 8-13 weeks. Systolic and diastolic BP (SBP, DBP) at each prenatal visit (median 10; max 28) and PE and GHTN diagnoses were extracted from medical records. Prospective associations of self-reported caffeine (0, 1-50, 51-200, >200 mg/d) and caffeine metabolites (quartiles) with longitudinal measures of BP over pregnancy were estimated using linear mixed effect models with cubic splines, and associations with PE and GHTN risk were estimated using multinomial logistic regression. Models were adjusted for age, parity, pre-pregnancy body mass index, hyperemesis, and demographic and lifestyle factors.

Results: In total, 99 PE (4%) and 83 GHTN (3%) cases were identified. Caffeinated beverage intake was not related to DBP ($P=0.09$) or SBP trajectory ($P=0.85$) (Figure). Caffeine or paraxanthine were also not related to BP trajectories. Odds ratios (95% confidence interval) by caffeinated beverage intake of 1-50, 50-200, and >200 mg/d vs 0 for PE were 1.3 (0.8, 2.1), 1.2 (0.7, 2.0), and 1.6 (0.2, 12.9) and for GHTN were 0.9 (0.5, 1.5), 0.9 (0.5, 1.7), and 1.4 (0.2, 11.0), respectively. Caffeine and paraxanthine were not related to PE or GHTN risk.

Conclusions: First trimester caffeine was not related to BP or risk of PE or GHTN. Further study of the association with specific caffeine sources are needed.

Figure. Prospective adjusted association between self-reported caffeinated beverage intake (mg/d) at 10-13 weeks gestation and diastolic (A) and systolic (B) blood pressure in pregnancy, NICHD Fetal Growth Studies-Singletons.



Models adjusted for age, race/ethnicity, pre-pregnancy BMI, nulliparity, education, employment, marital status, pre-pregnancy alcohol intake, pre-pregnancy total physical activity, plasma cotinine at 10-13 weeks, and hyperemesis.

Ambient temperature exposure during critical windows of pregnancy and risk of a hypertensive disorder of pregnancy Carrie Nobles* Carrie Nobles Katherine Grantz Marion Ouidir Danielle Stevens Jenna Kanner Matthew Rohn Jessica Gleason Pauline Mendola

Introduction: Exposure to high and low ambient temperatures increases blood pressure and risk of cardiovascular events, and may similarly impact development of a hypertensive disorder of pregnancy (HDP). Given the multiple susceptible windows and differing etiologies underlying development of HDP, we aimed to evaluate weekly exposure to ambient temperature with risk of preeclampsia (PE) and gestational hypertension (gHTN).

Methods: We utilized data from the NICHD Fetal Growth Study (n=2,334 low-risk singleton pregnancies, 11 U.S. sites) to evaluate the relationship between a weekly 2-degree Celsius difference in ambient temperature exposure with relative risk (RR) of developing PE and gHTN. Ambient temperature was abstracted from local weather monitoring stations and information on PE, gHTN and systolic (SBP) and diastolic (DBP) blood pressure from medical records. Mean uterine artery pulsatility index (UtAPI) was assessed at 16-23 and 24-30 weeks' gestation. Poisson regression with robust errors and generalized linear models included interaction terms to evaluate differences by warm (Apr.-Sept.) versus cold (Oct.-Mar.) season and adjusted for region, humidity, ozone, particulate matter <2.5 microns and participant characteristics.

Results: A total of 68 women (3.0%) developed PE and 41 (1.8%) gHTN. Between gestational weeks 8-17 in the warm season, a 2-degree Celsius increase in temperature was associated with greater risk of PE (e.g. Week 8 RR: 1.20, 95% CI 1.03-1.40; Week 12 RR: 1.18, 95% CI 1.00-1.39; Week 16 RR: 1.19, 95% CI 1.02-1.38 for week 16). Associations with gHTN were less clear. Higher temperatures between weeks 14-19 were associated with higher DBP, while lower temperatures in both the warm and cold seasons between weeks 15-23 were associated with higher UtAPI and SBP.

Conclusions: Findings suggest differential impacts of high and low ambient temperatures on HDP, including increased risk of PE with exposure to warm temperatures in early to mid-pregnancy.

Age of juice introduction and childhood weight status at 7-9 years old Sonia L. Robinson*
Sonia Robinson Rajeshwari Sundaram Diane L. Putnick Akhgar Ghassabian Jessica L. Gleason
Danielle Stevens Erin M. Bell Edwina H. Yeung

In 2017, the American Academy of Pediatrics (AAP) recommended delaying juice introduction until 12 months (mo.), revising a previous guideline to not introduce juice until 6 mo., due to concerns of weight gain. However, few studies have evaluated prospectively if juice introduction is related to childhood weight status.

We aimed to assess the relation of juice introduction with child weight status at 7-9 years (y) in the Upstate KIDS cohort. Women and their children were enrolled at 4 mo. postpartum ($n=4989$). Sociodemographics were obtained from questionnaires or birth certificates. At 4-18 mo., women reported if they had introduced juice and the age of introduction, which was categorized as <6, 6-12, and ≥ 12 mo. At 7-9 y, women reported their child's height and weight at their last doctor's visit ($n=1283$). Body mass index-for-age z-scores (BMIz) were calculated using the CDC reference for age and sex. Controlling for sociodemographics and maternal BMI, we assessed the association of juice introduction with childhood BMIz using generalized linear mixed models with inverse probability weights to account for non-response to follow-up, multiple imputations for missing exposure and covariates, and an autoregressive correlation matrix for correlations between repeated outcomes.

Prevalence of childhood obesity ($>95^{\text{th}}$ percentile) at 7, 8, and 9 y was 16.8, 18.2, and 21.3%, respectively; mean (SD) BMIz was 0.4-0.5 (1.4-1.5). After adjustment, the risk of childhood obesity was 2.43 (95% CI 1.28, 4.59) times higher in children with juice introduction at <6 versus ≥ 12 mo. Further, juice introduction at <6 versus ≥ 12 mo. was related to a 0.35 higher BMIz (95% CI 0.09, 0.61) at 7-9 y. Juice introduction at 6-12 versus ≥ 12 mo. was not significantly related to childhood obesity or BMIz.

While the AAP recently updated their guidelines for juice introduction, childhood obesity was most starkly associated with introduction at <6 mo. with less observed benefit of delaying until 12 mo.

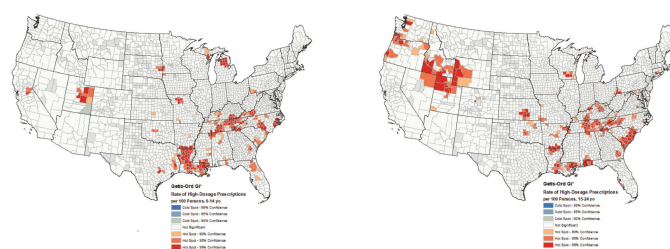
Geographic Patterns of High-dosage Opioid Prescribing Practices in Children, Adolescents, and Young Adults in the United States, 2018 Victoria Jent* Victoria Jent Madeline Renny H. Shonna Yin Magdalena Cerdá

Aims: To examine geographic variations in high-dosage opioid prescribing practices in children, adolescents, and young adults in the contiguous U.S. and determine county-level characteristics associated with increased rates of high-dosage opioid prescribing in 2018.

Methods: Opioid prescription data from January 1, 2018 to December 31, 2018 for patients <25y were extracted from the IQIVIA XPoint database. This database accounts for >90% of retail prescription dispensing in the U.S. Counties with <3 pharmacies are excluded from the study. Rate of high-dosage prescriptions per 100 persons were calculated for two age cohorts (90 MME/day for $\geq 15y$; > 2 MME/kg/day for <15y). Global Moran's I statistic was used to assess spatial autocorrelation; local spatial clustering was assessed using Getis-Ord G_i^* to identify county-level clusters of high/low rates (first-order queen contingency). Multivariable Quasipoisson regression was utilized to assess county-level rates of high-dosage opioid dispensing for the two age cohorts adjusting for socioeconomic, demographic, Census divisions, and rurality.

Results: Global Moran's Index for the rate of high-dosage opioid dispensing presented positive spatial autocorrelation: <15y ($I=0.18$, $Z\text{-Score}=14.79$, pseudo p-value = 0.001), $\geq 15y$ ($I=0.20$, $Z\text{-Score} = 17.81$, pseudo p-value = 0.001). Getis-Ord G_i^* identified hot spots for both age groups (<15 = 292 counties, $\geq 15 = 346$ counties) and cold spots for < 15y (3 counties), <0.05 p-value. In both age groups, hot spots were primarily located in the South and the West. Regression analyses reported differences in high-dosage prescribing rate by U.S. Census Divisions (reference group: New England). High-dosage prescriptions for <15y were 2.42 more times likely to occur in West South Central (CI: 1.91, 3.08) and 2.40 more times in East South Central divisions (CI: 1.91, 3.08). For $\geq 15y$, high dosage prescriptions were 1.73 more times likely to occur in the Mountain (CI: 1.51, 1.98) and 1.47 times more likely in East South Central

Conclusion: County-level high-dosage opioid prescribing hot spots for children, adolescents, and young adults were mainly located in the South and West regions of the U.S. Targeted interventions in these regions may be necessary to ensure safe and appropriate opioid prescribing.



A systematic review of the epidemiologic evidence supporting the association between prenatal exposure to toxic and essential metals and preterm birth Lauren A Eaves* Lauren Eaves Alexander P. Keil Radhika Dhingra Julia E. Rager Tracy A. Manuck Rebecca C. Fry

Aim: In order to provide an updated and comprehensive summary, we systematically reviewed the epidemiologic evidence of the associations between prenatal exposure to arsenic, cadmium, chromium, copper, mercury, manganese, lead, zinc and preterm birth (PTB) or gestational age at delivery.

Methods: The Medline/PubMed database was searched in April 2020 for epidemiologic studies published in peer-reviewed journals after January 1, 1995. A total of 1029 studies were identified and screened utilizing the title and abstract. Of these, 104 were assessed for further eligibility by reading the full-text and 60 studies were ultimately included. A Risk of Bias (ROB) assessment will be conducted using the preliminary Risk Of Bias In Non-randomized Studies of Exposures tool.

Results: The included studies were primarily United States-based cohort studies using biomarker-based exposure assessment and the number of studies varied by metal: arsenic (24), cadmium (16), chromium (6), copper (9), mercury (14), manganese (7), lead (25) and zinc (8). There is strong evidence that prenatal exposure to either cadmium or lead is associated with higher risk of PTB and weaker evidence that exposure to arsenic or mercury may also be associated with higher risk. Evidence regarding exposure to remaining metals and PTB and/or delivery gestational age remains limited. Despite likely co-exposure, joint effects of multiple metals have been assessed in only two studies to date. We expect that the ROB assessment will highlight a lack of appropriate control for confounding by co-occurring metals and potential bias from biomarker-based exposure measurement at delivery. Further, we note a need to disaggregate by preterm birth phenotype, given different biological pathways.

Conclusions: Future research would benefit from disaggregation of phenotypes and thorough consideration of co-occurring metals, including investigations of metal-mixtures.

Study	Exposure assessment	Timing	Exposure corresponding to OR	Notes
Environmental exposure assessment				
Huang 2018 (California USA)	drinking water, water-system average		IQR difference	
Landgren 1996 (Sweden)	groundwater, town average		above mean (151 ug/m3) vs below	
Berkowitz 2006 (Iaaho, USA)	county level air emissions		positive, exposed vs non-exposed counties	
Biomarker exposure assessment				
Taylor 2015 (UK)	maternal blood	1st trimester	>5 ug/dl vs <5 ug/dl	
Vigen 2011 (Iran)	maternal blood	1st trimester	1 ug/dl increase	
Yu 2019 (China)	maternal blood	1st-2nd trimester	not detailed	
Li 2017 (China)	maternal blood	2nd trimester	3rd tertile (±1.71 ug/dl) vs 1st tertile (<1.18 ug/dl)	
Ashrap 2020 (Puerto Rico)	maternal blood	2nd-3rd trimester; average of up to two samples	2nd tertile (1.18-1.70 ug/dl) vs 1st tertile (<1.18 ug/dl)	
Jelliffe-Pawowski 2006 (California, USA)	maternal blood	1st-3rd trimester	IQR difference	
Zhu 2010 (New York, USA)	maternal blood	1st-3rd trimester	-10 ug/dl vs <10 ug/dl	
Perkins 2014 (Massachusetts, USA)	maternal blood	1st-3rd trimester	4th quartile (3.18-9.9 ug/dl) vs 1st quartile (<1 ug/dl)	
Kim 2018 (Boston, USA)	maternal urine	3rd trimester	4th vs 1st quartile	
Wai 2017 (Singapore)	maternal urine	3rd trimester	IQR difference: (0.62 ppb) vs (0.17 ppb)	
Cheng 2017 (China)	maternal urine	3rd trimester	delivery	
Torres-Sanchez 1999 (Mexico)	cord blood	delivery	3rd tertile (>4.06 ug/g creatinine) vs 1st tertile (<2.29 ug/g creatinine)	
Freire 2019 (Spain)	placenta	delivery	2nd tertile (2.29-4.06 ug/g creatinine) vs 1st tertile (<2.29 ug/g creatinine)	
PTB subtype specific effects				
Ashrap 2020 (Puerto Rico)	maternal blood	2nd-3rd trimester; average of up to two samples	4th quartile (>16.9 ug/dl) vs 1st quartile (<5.1 ug/dl)	spontaneous PTB
Kim 2018 (Boston, USA)	maternal urine	3rd trimester	3rd quartile (8.14-9.9 ug/dl) vs 1st quartile (<5.1 ug/dl)	placental PTB
Tajiri 2016 (Japan)	maternal blood	2nd-3rd trimester	2nd quartile (5.1-14.9 ug/dl) vs 1st quartile (<5.1 ug/dl)	early PTB (<34 wks)
Zhang 2015 (China)	maternal urine	delivery	2nd quartile (5.1-14.9 ug/dl) vs 1st quartile (<5.1 ug/dl)	late PTB (34 < <37 wks)
Exposure window specific effects				
Yu 2019 (China)	maternal blood	1st trimester	3rd tertile (p-11.67 ug/g creatinine) vs 1st tertile (<5.41 ug/g creatinine)	PTB LBW
Ashrap 2020 (Puerto Rico)	maternal blood	2nd trimester	not detailed	
Jelliffe-Pawowski 2006 (California, USA)	maternal blood	late 2nd-3rd trimester	not detailed	
Fetal sex specific effects				
Perkins 2014 (Massachusetts, USA)	maternal blood	1st-3rd trimester	IQR difference	male
Zhang 2015 (China)	maternal urine	1st-3rd trimester	4th vs 1st quartile	female
		delivery	3rd tertile (± 13.13 ug/g creatinine) vs 1st tertile (< 5.86 ug/g creatinine)	male
		delivery	3rd tertile (± 10.12 ug/g creatinine) vs 1st tertile (< 4.96 ug/g creatinine)	female

A comparative analysis of the InterVA model versus physician review in determining causes of neonatal deaths using verbal autopsy data from Nepal Dinesh Dharel* Dinesh Dharel Penny Dawson Daniel Adeyinka Nazeem Muhajarine Dinesh Neupane

Background: Verbal autopsy is a common method of ascertaining the cause of neonatal death in low resource settings where majority of causes of deaths remain unregistered. We aimed to compare the causes of neonatal deaths assigned by computer algorithm-based model, InterVA (Interpreting Verbal Autopsy) with the usual standard of Physician Review of Verbal Autopsy (PRVA) using the verbal autopsy data collected by Morang Innovative Neonatal Intervention (MINI) study in Nepal.

Methods: MINI was a prospective community intervention study aimed at managing newborn illnesses at household level. Trained field staff conducted a verbal autopsy of all neonatal deaths during the study period. The cause of death was assigned by two pediatricians, and by using InterVA version 5. Cohen's kappa coefficient was calculated to compare the agreement between InterVA and PRVA assigned proximate cause of death, using STATA™ software version 16.1.

Results: Among 381 verbal autopsies for neonatal deaths, only 311 (81.6%) were assigned one of birth asphyxia, neonatal infection, congenital anomalies or preterm-related complications as the proximate cause of death by both InterVA and PRVA, while the remaining 70 (18.4%) were assigned other or non-specific causes. The overall agreement between InterVA and PRVA-assigned cause of death categories was moderate (66.5% agreement, kappa=0.47). Moderate agreement was observed for neonatal infection (kappa=0.48) and congenital malformations (kappa=0.49), while it was fair for birth asphyxia (kappa=0.39), and preterm-related complications (kappa=0.31); but there was only slight agreement for neonatal sepsis (kappa=0.19) and neonatal pneumonia (kappa=0.16) as specific causes of death within neonatal infections.

Conclusions: We observed moderate overall agreement for major categories of causes of neonatal death assigned by InterVA and PRVA. The moderate agreement was sustained for the classification of neonatal infection but poor for neonatal sepsis and neonatal pneumonia as distinct categories of neonatal infection. Further studies should investigate the comparative effectiveness of an updated version of InterVA with the current standard of assigning the cause of neonatal death through longitudinal and experimental designs.

Prenatal antidepressant medication usage patterns and delivery outcomes among preconception users Nerissa Nance* Nerissa Nance Sylvia Badon Kathryn K. Ridout De-Kun Li Lyndsay Avalos

Introduction

Antidepressant medication use is common and effective in reproductive-aged women. Little is known about antidepressant use patterns in pregnancy and their effects on delivery outcomes among women with preconception use. This study described patterns of antidepressant use among these women and examined associations between usage patterns and delivery outcomes.

Methods

We conducted a retrospective cohort study of women with live births at Kaiser Permanente Northern California (2014-2017) and an antidepressant fill in the 6 months prior to pregnancy that overlapped with the 8th week of pregnancy. Using electronic health records, we identified whether women continued use (refilled throughout pregnancy), stopped and reinitiated (refill after 30+ day gap in supply), or discontinued (no refills). We used Poisson regression to examine the association between these patterns and preterm birth and Neonatal ICU (NICU) admission, adjusting for demographic characteristics and depression severity.

Results

Among 3,246 women with preconception antidepressant use, 33% continued use throughout pregnancy, 20% stopped and reinitiated, and 47% discontinued after early pregnancy. A greater proportion of women who continued use were college graduates and non-Hispanic white. Women who stopped and reinitiated or discontinued use had 38-46% lower risk of preterm birth and NICU admission than women who continued use (Table).

Conclusions

Nearly half of women with preconception antidepressant medication use discontinued use during early pregnancy. Early pregnancy antidepressant users who continue use may be at higher risk of adverse delivery outcomes, which may reflect underlying depression severity and should be considered alongside risk of depression relapse in pregnant women.

Table. Adjusted Relative Risk for the association of antidepressant use patterns during pregnancy with delivery outcomes in 3,246 women.

	Preterm birth		Neonatal ICU admission	
	N (%)		N (%)	
N with outcome (%)	384 (12)		344 (11)	
Continued use	169 (16)	Referent	156 (15)	Referent
Reinitiation	61 (9)	0.57 (0.43, 0.75)	53 (8)	0.54 (0.40, 0.72)
Discontinuation	154 (10)	0.62 (0.50, 0.76)	135 (9)	0.61 (0.49, 0.76)

*Model is adjusted for maternal age (years), race/ethnicity (non-Hispanic white, Hispanic, Asian, non-Hispanic Black, other), education (high school graduate or less, some college, college graduate or more), Medicaid during pregnancy (Y/N), nulliparity (Y/N), alcohol use during pregnancy (Y/N), tobacco use during pregnancy (Y/N), other drug use during pregnancy (Y/N), and depression severity (maximum PHQ-9 score during pregnancy).

Findings did not change with additional adjustment for psychotherapy during pregnancy.

Caesarean sections among immigrant women compared to Canadian born women Erin Hetherington* Erin Hetherington Kamala Adhikari Natalie Scime Amy Metcalfe

Background: The global rise in caesarean sections (CS) has led to concerns about overuse of this medical intervention. In higher income countries, CS are generally more frequent among immigrant women, but a crude examination of rates does not account for medical history and women's expectations, which may differ by country of origin. This study examines differences in CS rates between immigrants to Canada compared to Canadian born women according to duration in Canada and rates of CS in country of origin.

Methods: This study uses linked data from hospitalization records and the Canadian Community Health Survey for women who delivered a baby in a hospital between 2002-2017 in Canada (excluding Quebec). Odds of CS in immigrants (recent and non-recent) compared to Canadian born women were calculated using logistic regression controlling for demographic and medical factors and stratified by parity. Immigrants were further categorized by the CS rate in their country of origin as low (<10%), medium (≥ 10 to <35%) or high ($\geq 35\%$).

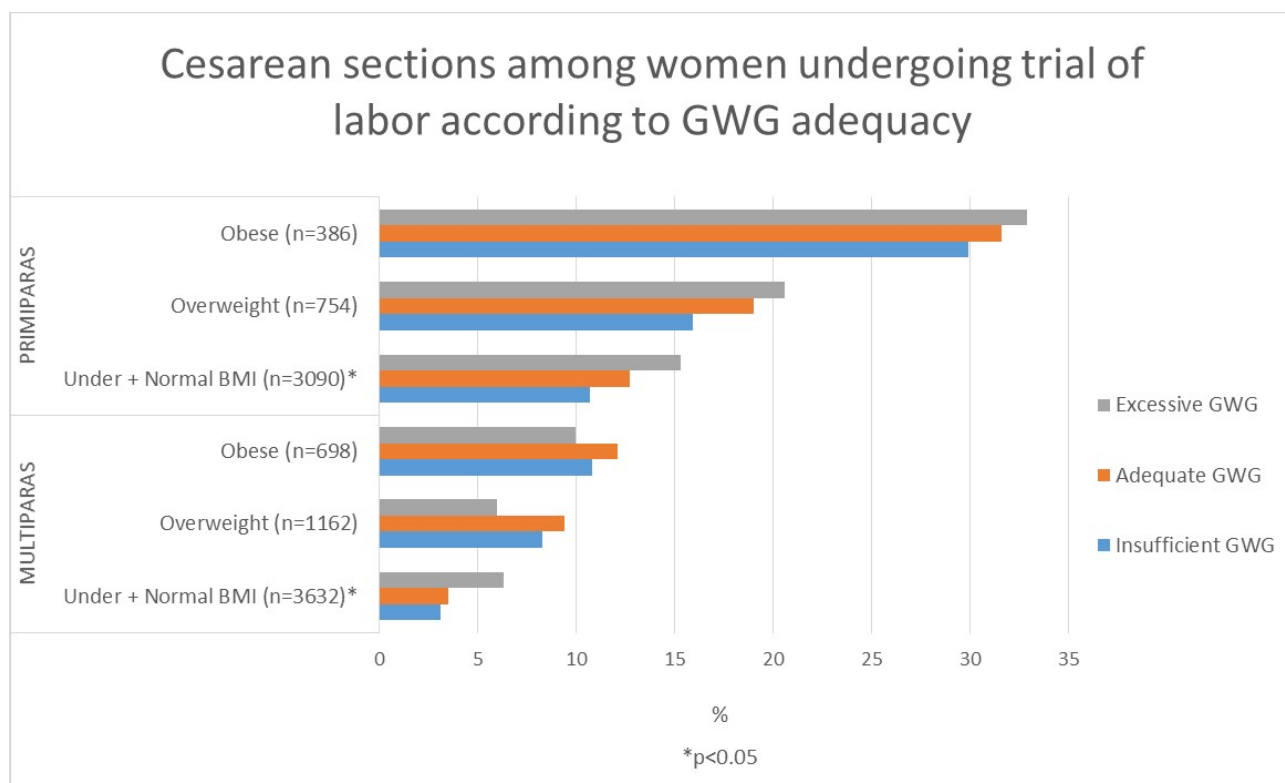
Results: Of the 53,505 women included, 89% were Canadian born, 4% were recent immigrants (<5 years) and 7% were non-recent immigrants. Overall, 27.9% of Canadian born women had a CS, 30.0% of recent immigrants and 31.4% of non-recent immigrants (31%). The adjusted odds of caesarean section among recent immigrants (aOR 1.12 95%CI 0.95, 1.34) and non-recent immigrants (aOR 1.11 95%CI 0.98, 1.25) did not statistically differ from Canadian born women. Recent immigrants from countries with lower CS rates had higher odds of CS (1.34, 95%CI 1.05, 1.70), whereas recent immigrants from medium and high CS rate countries did not differ from Canadian born women.

Discussion: After accounting for demographic and medical factors, few differences remained in CS rate between immigrants and Canadian born women. Country of origin practices are unlikely to reflect preferences for CS in immigrant women to Canada.

Associations between gestational weight gain adequacy and obstetric intrapartum

interventions: observational population-based study in France Melissa Amyx* Melissa Amyx
Jennifer Zeitlin Béatrice Blondel Camille Le Ray

Gestational weight gain (GWG) recommendations were published by the Institute of Medicine (IOM), as excessive (GWG) is associated with gestational complications (e.g., diabetes, hypertension). However, GWG as a risk factor for intrapartum interventions is understudied. Our objective was to evaluate associations between GWG adequacy and obstetric interventions (cesarean section [CS]; oxytocin administration; episiotomy use). Using nationally-representative French National Perinatal Survey 2016 data, we included term cephalic singleton pregnancies with trial of labor (N=9724). GWG was calculated as end of pregnancy minus prepregnancy weight and categorized as inadequate, adequate, or excessive by prepregnancy BMI (under-<[<18.5], normal [18.5-24.9], over-[25-29.9] weight; obese $\geq 30\text{kg/m}^2$) using 2009 IOM thresholds. Intervention rates by GWG adequacy were determined. Multilevel GEE logistic regression models, adjusted for *a priori* confounders, evaluated intervention-GWG adequacy associations. Analyses were stratified by BMI (under+normal weight; overweight; obese) and parity (primiparas; multiparas). Regardless of parity, among under+normal weight women, excessive GWG was associated with increased CS (Figure); following adjustment, the association persisted only among under+normal weight multiparas (aOR 1.8, 95%CI 1.2, 2.7). Similarly, excessive GWG was associated with increased oxytocin use among under+normal weight women (primiparas: 65.0% vs 60.8% for adequate GWG; multiparas: 36.2% vs 29.1% for adequate GWG; $p<.05$), an association which persisted among under+normal weight multiparas (aOR 1.3, 95%CI 1.1, 1.6). Further, oxytocin use was increased among overweight primiparas with excessive GWG (72.5% vs 58.7% for adequate GWG; $p<.05$; aOR 1.8, 95%CI 1.1, 2.9). No consistent associations were found for episiotomy. Excessive GWG may be a more important risk factor for specific intrapartum obstetric interventions among under+normal weight women than among obese women.



The Association Between Neighborhood Crime and Adverse Birth Outcomes in Latina**Women** Brittany Griffin* Brittany Griffin Penelope Pekow Brian Whitcomb Qian Yu Lisa Chasan-Taber

Women of Puerto Rican descent have disproportionately high rates of low birthweight (LBW), preterm birth, and small-for-gestational age (SGA) infants compared to non-Latina Whites. Established individual-level risk factors only account for a portion of these birth disparities. Previous studies on neighborhood-level risk factors are inconsistent. Therefore, we evaluated the association between neighborhood crime and adverse birth outcomes in Proyecto Buena Salud, a prospective cohort study of 1,195 predominantly Puerto Rican women conducted from 2006-10 in Western Massachusetts. Residential address data was used to place participants in neighborhoods based on census block group at enrollment. Overall and violent neighborhood crime within census blocks were defined using FBI Uniform Crime data. Adverse birth outcomes were abstracted from medical records. Ten percent of women experienced preterm birth, 8.2% had LBW, and 12.3% had SGA infants. Women in the highest quartile of violent neighborhood crime reported lower education and income, higher levels of depression, and Spanish preference (all $p < 0.05$).

Women in the highest quartile of violent neighborhood crime had higher odds of SGA (odds ratio [OR] 2.1, 95% confidence interval [CI] 1.2-3.4) compared to women in the lowest quartile after adjusting for parity, age, BMI, gestational weight gain, education level, and smoking. We did not observe statistically significant associations between violent neighborhood crime and preterm birth (OR 0.9, 95% CI 0.5-1.5) or LBW (0.9, 95% CI 0.5-1.6) in adjusted analyses. We did not observe statistically significant associations between women in the highest quartile of overall neighborhood crime and adverse birth outcomes.

This study was the first, to our knowledge, to study neighborhood crime and adverse birth outcomes among Latinas. Future studies with larger samples are warranted to address the impact of neighborhood disadvantage in high-risk groups.

Origins of Cerebral White Matter Damage: Exploring the Placental Transcriptome Brain**Axis** Carmen A Marable* Carmen Marable TM O'Shea RC Fry Kyle Roell

Cerebral white matter damage is the most common form of neonatal brain injury in preterm newborns. However, the etiologic factors that predispose to white matter damage for preterm newborns has not been well characterized. The placenta, while a temporary organ, plays a critical role in neonatal brain development. Through the Extremely Low Gestational Age Newborn (ELGAN) cohort, we aimed to investigate the relationship between the placental transcriptome and white matter damage by leveraging paired placental mRNA, and neonatal cranial ultrasound data. From the original cohort of 1198 children born extremely preterm (23 to 27 weeks gestation), we examined a sub-cohort of 381 children with paired placental mRNA and ultrasound data. Cerebral white matter damage was defined as ventriculomegaly or echolucency. Differential gene expression testing was performed on RNA sequencing data, representing 11,981 transcripts using differential gene expression testing and false discovery rate correction through the Benjamini-Hochberg procedure. In relation to echolucency obtained from the ultrasound, a total of 623 placental transcripts displayed associated expression levels. In relation to ventriculomegaly, a total of 266 placental transcripts displayed associated expression levels. Interestingly, a common set of 231 genes was identified to be dysregulated in the placenta in relation to both echolucency and ventriculomegaly. This common gene set was enriched for genes that encode proteins that play roles in inflammation, cell cycle, rRNA processing, translation, and signaling of the transforming growth factor beta (TGF-beta) pathway. There was a strong trend for decreased expression of these placental genes in relation to white matter damage assessed via ultrasound. The research described in this study will help characterize molecular events in the placenta as it relates to white matter damage among preterm newborns. Since ultrasound identifies only macroscopic white matter damage, in future studies we will conduct additional analyses using MRI data.

Predictors of injuries suggestive of child maltreatment during first year of life in California: A prospective cohort study using statewide birth cohort and hospital records

Kriszta Farkas* Kriszta Farkas Jennifer Ahern Susan M. Mason

Most research on risk factors for child maltreatment has relied on official child protection data, which may suffer from various reporting biases. Medical record diagnostic codes that have been validated as reliable measures of maltreatment are a potential complementary data source. Using a large population-based dataset of all births in California, 2005-2012, linked to maternal hospital and emergency department (ED) admissions during pregnancy and maternal and infant readmissions in the year following delivery/birth, we aimed to estimate sociodemographic, pregnancy, infant, and medical correlates of injuries suggestive of child maltreatment. Maltreatment was captured in infant ED and hospital readmission records using ICD-9-CM codes indicative of probable maltreatment. Modified Poisson and binomial linear regression models, with robust standard errors to account for multiple births to the same woman, were used to estimate risk ratios and risk differences (per 10,000), respectively, and 95% confidence intervals. Of the 3,765,370 births included in the analysis over the 8-year study period, 14,464 infants were admitted to the hospital or ED for an injury indicative of probable maltreatment in the first year of life (38.4 per 10,000). In adjusted analyses, neonatal abstinence syndrome (RR: 1.8 (1.3, 2.5), RD: 40.4 (11.0, 69.8)), public insurance (RR: 1.3 (1.2, 1.3), RD: 9.3 (7.7, 10.9)), and maternal mental illness (RR: 1.3 (1.2, 1.4), RD: 9.8 (5.6, 14.0)) and violence exposure (RR: 1.2 (1.0, 1.5), RD: 11.5 (-0.9, 23.9)) were the strongest risk factors for maltreatment. Maltreatment risk was lower among women with higher education, Hispanic/Latino ethnicity, and foreign nativity, and for multiple gestation. Future work should examine the potential etiologic role of these sociodemographic, infant, and maternal risk and protective factors in child maltreatment and their implications for prevention strategies.

Serum per- and polyfluoroalkyl substance concentrations and common cold among children and adolescents in NHANES 2013-2014 Yu Zhang* Carmen Messerlian Yu Zhang Vicente Mustieles Yang Sun Stelios Vagios Angela Slitt Yixin Wang Carmen Messerlian

Background

Per- and polyfluoroalkyl substances (PFAS) exert immunosuppressive effects in experimental animals. Few epidemiologic studies investigated PFAS in relation to the common cold as a marker of immune function during development.

Methods

This study included 517 children aged 3-11 years and 394 adolescents aged 12-19 years in the National Health and Nutrition Examination Study (NHANES) 2013 - 2014 cycle. Serum concentrations of perfluorooctanoic acid (PFOA), perfluorooctane sulfonic acid (PFOS), perfluorononanoic acid (PFNA) and perfluorohexane sulfonic acid (PFHxS) were quantified. Common cold was self-reported by the participant or parent as having a head cold or chest cold in the last month. Multivariable logistic regression was utilized to examine the adjusted association between individual PFAS and common cold. The joint effect of PFAS mixture was evaluated using Probit Bayesian Kernel Machine Regression (BKMR).

Results

Per doubling of serum PFHxS concentration was associated with a 31% (OR=1.31, 95%CI: 1.06, 1.62) and a 23% (OR=1.23, 95%CI: 0.96, 1.59) increased odds of common cold for children and adolescents, respectively. Serum PFNA concentration was positively associated with common cold in children (OR=1.36, 95%CI: 1.04, 1.79) while an inverse association was observed for adolescents (OR=0.42, 95%CI: 0.22, 0.80). A suggestive positive association for PFOA and common cold was found in both age groups. No association was observed for PFOS in either group. BKMR confirmed the individual associations and showed a clear increasing trend of common cold estimates across quantiles of the total PFAS mixture concentration among children, with no obvious pattern in the adolescents.

Conclusion

Serum PFHxS and PFNA concentrations were associated with increased odds of common cold in young children. Using common cold as a general measure of immunosuppression, this study may have important implications for the immunotoxicity of selected PFAS in childhood.

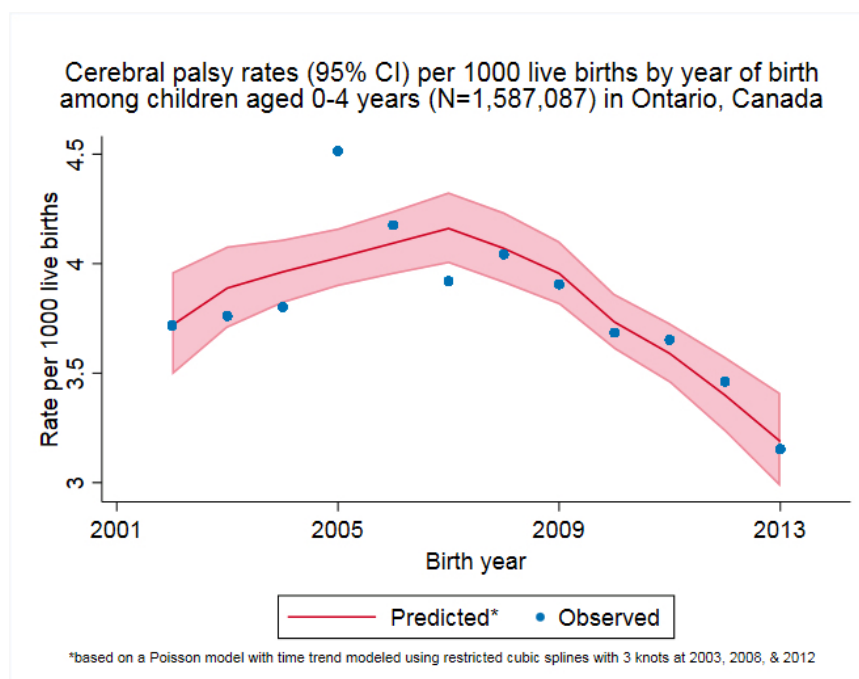
Temporal trends in cerebral palsy rates in children born in the province of Ontario, Canada, 2002-2013: A population-based retrospective cohort study Asma Ahmed* Asma Ahmed Laura C. Rosella Seungmi Yang

Background: Studies in Europe and Australia have examined temporal trends in cerebral palsy (CP) rates with inconsistent findings, and corresponding figures from North America are still scarce. Little is known about changes in CP rates by important sociodemographic characteristics over time.

Methods: We identified 1,587,087 live births born in the province of Ontario, Canada between 2002 - 2013 and ascertained CP diagnosis made before age 5 in health administrative databases. We examined differences in CP rates overall and by child, maternal, and area-based socioeconomic characteristics over time.

Results: CP rates increased from 3.72 (95% confidence interval: (3.49, 3.96)) per 1000 live births in 2002 to 4.16 (4.00, 4.33) in 2007 before starting a steady decline afterward, reaching a low of 3.19 (2.98, 3.41) in 2013. As expected, CP rates were considerably higher in children with low gestational age (GA) and birth weight (BW), although rates in the low BW/GA categories were steadily decreasing over the study period. CP rates were higher in boys, multiples, children with congenital malformations, and in those delivered by caesarean section; these gaps have narrowed over time. Children of young (<20 years), old (>35 years), primiparous, and grand multiparous (4+) mothers had higher rates of CP over time. We also observed socioeconomic disparities in CP rates that mostly remained stable over the study period.

Conclusion: This is the first population-based study to examine not only overall CP rates over time but stratified by important birth and sociodemographic characteristics. It is encouraging that CP rates were decreasing in recent years both overall and across GA and BW categories, which may suggest a potential positive impact of advances in obstetric and neonatal care together with neuroprotective strategies. The persistence of socioeconomic disparity over time warrants further investigation.



Maternal cigarette smoking cessation and the risk of preterm birth Kexin Zhu* Kexin Zhu
James Shelton Vanessa Barnabei Zhongzheng Niu Lina Mu

Background

Smoking during pregnancy was found to increase preterm birth (PTB) risk, although the underlying mechanism remained unclear. We aimed to examine the association of trimester-specific smoking cessation behaviors with PTB.

Methods

We included 206,867 singleton non-anomalous live births of 20-42 weeks gestation in Western New York between 2004-2017. Based on the self-reported average number of cigarettes smoked per day during 3 months prior to pregnancy and in each trimester, we categorized pregnant women into six groups: non-smokers, those who quit during the 1st, 2nd, 3rd trimester, or smoked throughout pregnancy, and intermittent smokers. We used logistic regression to examine the association between smoking cessation behaviors and PTB <37 weeks, adjusting for potential confounders. We explored potential effect modification by illegal drug use during pregnancy using interaction terms and joint effect analysis.

Results

Overall, 7.2% of women had a preterm birth; 14.8% smoked throughout pregnancy and 3.2%, 1.8%, and 0.8% reported quitting smoking during the 1st, 2nd, and 3rd trimester, respectively. Compared to non-smokers, smoking cessation only during the 3rd trimester and smoking throughout pregnancy was associated with 39% (OR=1.39, 95% CI: 1.15-1.68) and 26% (OR=1.26, 95% CI: 1.20-1.33) higher odds of PTB, respectively, while quitting smoking during the 1st or 2nd trimester, or intermittent smoking was not associated with PTB. Cigarette smoking per day was positively associated with PTB in a dose-response manner ($P < .0001$), regardless of the stage of pregnancy. Those who smoked throughout pregnancy with illegal drug use had 1.67 (95% CI: 1.52-1.84) times the odds of PTB compared to non-smokers without illegal drug use, although we did not observe significant interaction term ($P=0.10$).

Conclusion

Smoking throughout pregnancy is associated with an increased risk of PTB. However, quitting before the third trimester might offer a reduction in this risk.

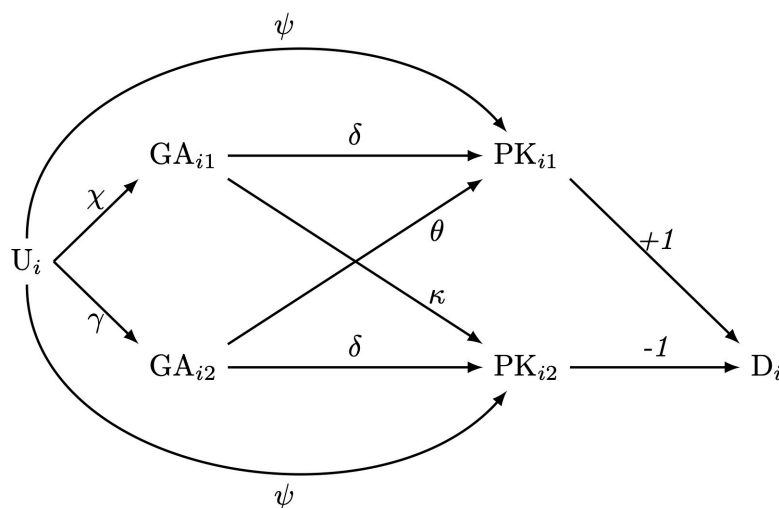
Preconception sleep hygiene and risk of pregnancy loss Joshua Freeman* Joshua Freeman
Brian Whitcomb Elizabeth Bertone-Johnson Laura Balzer Lindsey Sjaarda Keewan Kim Robert Silver
Alexandra Purdue-Smithe Enrique Schisterman Sunni Mumford

Sleep prior to conception may be important for pregnancy. Clock genes, which partly regulate sleep, play a role in embryo implantation and placentation, and thus may be related to pregnancy loss. However, epidemiological evidence on sleep and pregnancy loss is limited to studies of women recruited during pregnancy after which many pregnancy losses have occurred. We addressed this gap by evaluating sleep behaviors prior to conception among 1,228 reproductive aged women with 1-2 prior pregnancy losses who were prospectively followed for ≤ 6 cycles while attempting to conceive and throughout pregnancy if they conceived. Pregnancies were identified via urinary hCG and confirmed by clinical ultrasound; losses were identified as subsequent absence of pregnancy. We calculated sleep duration, sleep midpoint (median time between going to bed and waking up corrected for sleep debt), and social jet lag (difference in weekend-weekday sleep midpoints) from baseline self-report. We used Log-Poisson models to estimate RRs of sleep characteristics with pregnancy loss, controlling for demographics, caffeine, exercise, parity, and weighting to account for conditioning on pregnancy. Overall, 23.6% (188/797) of pregnancies ended in a loss. Sleep duration was not associated with pregnancy loss (< 7 hrs vs 7-9 hrs: RR 0.99, 95% CI: 0.65-1.49; ≥ 9 hrs vs 7-9 hrs: RR 1.25, 95% CI: 0.8-1.97). Preconception sleep midpoint and social jet lag were also not associated with pregnancy loss. Results did not differ when considering hCG-detected and clinical losses separately. In our prospective cohort of pregnancy planning women, we observed no associations between preconception sleep and pregnancy loss. These findings expand on prior studies by following women from preconception to capture early pregnancy losses and suggest that preconception sleep may not be related to pregnancy loss.

Support: NICHD, NIH.

Gestational age and siblings' literacy: spillover effects in the family David Mallinson* David Mallinson Felix Elwert Deborah Ehrenthal

Contemporary research findings on early-life health and development suggest that a child's health shock may harm their siblings' academic performance. These insights are guided by resource reallocation theory: parental investments shift from healthier children to affected siblings to compensate for the health shock's deleterious effects, which may impair unaffected siblings' development. Using a longitudinal birth cohort from Wisconsin, we investigate whether a child's gestational age affects their older sibling's literacy at kindergarten. We sampled 20,014 sibling pairs that were born during 2007-2010 and took Phonological Awareness Literacy Screening-Kindergarten (PALS-K) tests during 2012-2016. Exposures were gestational age (completed weeks), preterm birth (<37 weeks), and very preterm birth (<32 weeks). To estimate spillover, we use gain-scores, a fixed effects estimator that differences siblings' school year-standardized PALS-K scores to offset family-level, sibling-invariant confounding. We first regress the gain-score on siblings' exposures, and we then sum the exposures' partial regression coefficients to generate a "spillover coefficient." The resulting spillover coefficient yields a lower-bound spillover effect estimate of the younger siblings' gestational age on their older siblings' PALS-K score. Our directed acyclic graph in **Abstract Figure** illustrates the model that guides our gain-score regression. Multivariate regressions indicate that a one-week increase in younger siblings' gestational age improves the older siblings' PALS-K score by 0.011 standard deviations (SD) (95% CI: 0.001, 0.021 SD). This lower-bound spillover estimate was greatest among siblings whose mothers reported having a high school diploma/equivalent only (0.024 SD; 95% CI: 0.004, 0.044 SD). With evidence that children's shorter gestation harms older siblings' literacy, our findings underscore the relevance of early-life health shocks and their spillover effects on family members.



Abstract Figure. A causal directed acyclic graph of the relationship between gestational age and Phonological Awareness Literacy Kindergarten-Screening (PALS-K) test performance. Subscripts i and j denote cluster and sibling, respectively. GA_{ij} indicates gestational age, PK_{ij} indicates the PALS-K score, D_i is the difference between siblings' test scores (i.e., the gain-score), and U_i is an unobserved family-level confounder. Greek letters denote linear effects.

History of pandemic H1N1-containing influenza vaccination and risk for spontaneous abortion and birth defects Celeste Romano* Celeste Romano Clinton Hall Zeina G. Khodr Anna T. Bukowinski Gia R. Gumbs Ava Marie S. Conlin

Background: One recent study suggested a possible association between receipt of pandemic H1N1 (pH1N1)-containing vaccines in consecutive influenza seasons and spontaneous abortion, but corroborating scientific evidence is limited. We leveraged a population of vaccine-compliant, pregnant military women to examine history of pH1N1-containing influenza vaccination and adverse pregnancy outcomes.

Methods: Pregnancies and live births from Department of Defense Birth and Infant Health Research program data were linked with military personnel immunization records to identify women vaccinated with a pH1N1-containing vaccine in pregnancy prior to 21 6/7 weeks' gestation, October 2009–April 2015. Cox and modified Poisson regression models estimated associations between vaccination with pH1N1- vs non-pH1N1-containing influenza vaccine in the season prior to the index pregnancy, and spontaneous abortion and birth defects, respectively. Cox models were calculated for two periods of follow-up: vaccination through 1) 21 6/7 weeks' gestation and 2) 28 days postvaccination.

Results: Of 26,264 pregnancies, 21,736 (82.8%) were among women who received a pH1N1-containing vaccine in the prior influenza season and 4,528 (17.2%) were among women who received the non-pH1N1-containing vaccine in the prior influenza season; among 23,121 infants, 19,365 (83.8%) and 3,756 (16.2%) had mothers exposed and unexposed to pH1N1-containing vaccine in the prior influenza season, respectively. The adjusted hazard ratio (aHR) for spontaneous abortion approximated 1.0 across the complete follow-up period [95% confidence interval (CI): 0.89-1.13] and was slightly elevated when censored at 28 days postvaccination, though the CI was imprecise (aHR: 1.19, 95% CI: 0.97-1.46). No associations with birth defects were observed.

Conclusion: This work lends additional support for the safety of vaccination against pH1N1 in pregnancy, regardless of the vaccine received in the prior influenza season.

Prenatal opioid analgesic exposure and risk of birth defects: a population-based study Alexa C. Bowie* Alexa Bowie Martha M. Werler Maria P. Velez Wenbin Li Andi Camden Astrid Guttman Susan B. Brogly

Background: The teratogenic effect of opioid analgesics is unclear. We sought to quantify the risk of birth defects after prenatal opioid analgesic exposure.

Methods: Using universal coverage administrative health data for Ontario, we assembled a cohort of mother-infant pairs without opioid use disorder with an estimated date of confinement April 2013-March 2018 ($N = 623,182$). The Ontario Narcotics Monitoring System database, which records all prescribed opioid analgesics from July 2012 on, was used to ascertain exposure. Birth defects were identified with the Metropolitan Atlanta Congenital Defects Program classification. Risk ratios (RR) for any and 1st trimester exposure (any opioid analgesic, codeine, morphine, oxycodone) in relation to any defect, organ system defects (cardiovascular, gastrointestinal, genitourinary, CNS), and specific defects were estimated. High dimensional propensity scores (HDPS) including *a priori* confounders with inverse probability treatment weighting was used for confounding adjustment.

Results: Defect prevalence was 2.2%. Overall, 4.1% of pairs were exposed to opioid analgesics during pregnancy (2.0% 1st trimester), mainly to codeine (2.3%), morphine (1.1%), and oxycodone (0.9%). Compared with unexposed, the risk of any birth defect was higher with any opioid analgesic exposure ($RR_{adj} 1.16$, 95% CI: 1.07-1.25) but not with 1st trimester exposure ($RR_{adj} 1.05$, 95% CI: 0.92-1.19). An elevated risk of any defect was observed for 1st trimester morphine ($RR_{adj} 1.32$, 95% CI: 1.05-1.67) but not other agents. Only a higher risk of gastrointestinal intestinal defects was observed with any opioid analgesic exposure ($RR_{adj} 1.35$, 95% CI: 1.12-1.62) or 1st trimester exposure ($RR_{adj} 1.46$, 95% CI: 1.11-1.93).

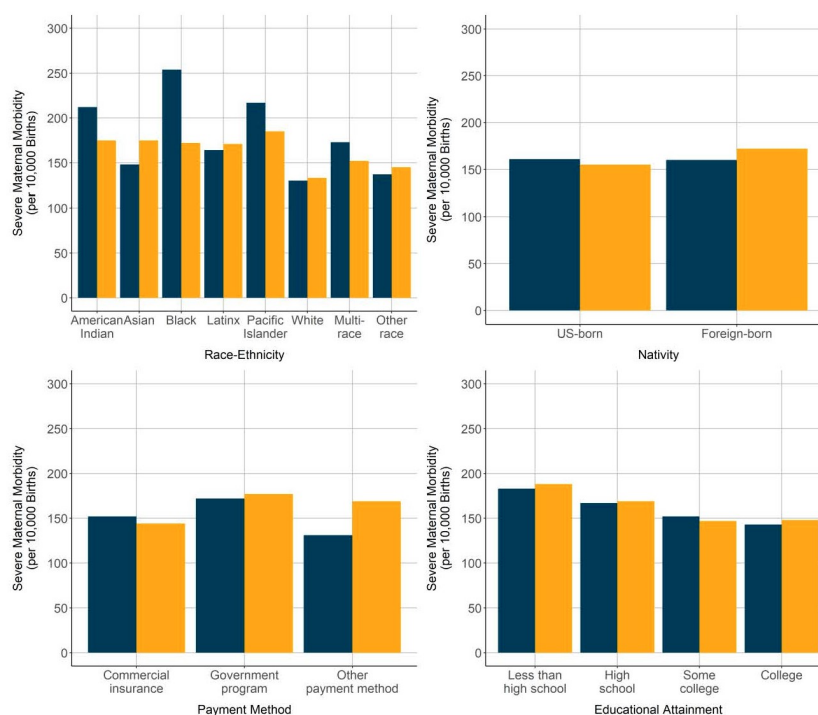
Conclusions: Prenatal exposure to opioid analgesics and morphine in the 1st trimester was associated with an elevated risk of birth defects after accounting for confounding.

Obstetric comorbidity scores and evaluating disparities in severe maternal morbidity

Stephanie Leonard* Stephanie Leonard Elliott Main Deirdre Lyell Suzan Carmichael Chris Kennedy
Christina Johnson Mahasin Mujahid

Background. We previously developed and validated a comorbidity scoring system in unselected state and national birth data to predict severe maternal morbidity (SMM) – a well-established indicator of serious complications at birth. Our objectives were to evaluate the validity of the scoring system across racial-ethnic and socioeconomic groups and to determine the effect of standardizing for the comorbidity score on disparities in SMM. **Methods.** We analyzed live births in California during 2011-2017 with linked birth certificate and birth hospitalization discharge data (n = 3,308,554). We assessed the performance of the comorbidity scoring system in subpopulations (groups) defined by race-ethnicity, nativity, payment method, and education. We then calculated the risk-standardized incidence of SMM in each group, and estimated SMM disparities before and after adjustment for the comorbidity score using logistic regression models. **Results.** The comorbidity scoring system performed well across groups (area under the ROC curve ranged from 0.79-0.87 and minimal variation in precision-recall curves; calibration curves demonstrated goodness of fit). All nonwhite groups had elevated SMM incidence, compared with white, before and after comorbidity score standardization; however, standardization increased the disparity for the Asian and Latinx groups and decreased the disparities for the other racial-ethnic groups (**Figure**). Standardization for comorbidities also increased disparities for the foreign-born group and the non-commercial insurance groups. Increasing education was associated with decreasing SMM incidence, which was largely unaffected by comorbidity score standardization. **Conclusion.** These results support the use and validity of a newly developed comorbidity scoring system to evaluate disparities in SMM. Differences in comorbidities partially explained disparities in SMM for some racial/ethnic and socioeconomic groups and masked the magnitude of disparities for others.

Figure. Severe maternal morbidity incidence before (blue) and after (yellow) standardization for the obstetric comorbidity score, California live births, 2011-2017.



Determining the clinical course of asthma in pregnancy Danielle Stevens* Danielle Stevens
Neil Perkins Zhen Chen Rajesh Kumar William Grobman Akila Subramaniam Joseph Biggio
Katherine Grantz Seth Sherman Matthew Rohn Pauline Mendola

Asthma is the most common chronic disease affecting pregnancy and poor asthma control has been associated with adverse pregnancy outcomes. However, the trajectory of asthma control during pregnancy is not well understood or characterized. We sought to identify and characterize trajectories of gestational asthma control in a US-based prospective pregnancy cohort. Daily diary entries on activity limitation, nighttime wakening, inhaler use, and respiratory symptoms were clustered into gestational asthma control trajectories using a k-means algorithm for joint longitudinal data. Among 308 women with asthma, two trajectories of gestational asthma control were identified and labeled “same” (n=184; 59.5%) or “worse” (n=124; 40.5%). Contrary to prior studies, we did not observe women with better asthma control in pregnancy. Women belonging to the “worse” trajectory experienced frequent and stable activity limitation and inhaler use, as well as frequent and increasing nighttime wakening and respiratory symptoms. Women belonging to the “same” trajectory experienced infrequent and stable activity limitation, inhaler use, and respiratory symptoms, as well as infrequent and slightly increasing (~ 1 day/gestational week) nighttime wakening. Several sociodemographics and clinical characteristics (e.g., multiparity, exercise-induced asthma) were associated with belonging to the “worse” gestational asthma control trajectory. Results from pregnant women without asthma (n=107) suggest pregnancy alone was not responsible for changes in symptoms over time. In this contemporary obstetric population receiving care according to standard clinical practice, gestational asthma control worsened for about 40% of women. Several predictors of later decline in asthma control were identified, which may help clinicians to recognize women in need of more active asthma management.

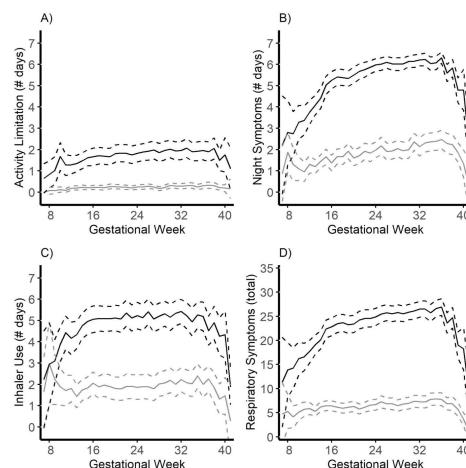


Figure. Mean multivariate trajectories of algorithm-assigned asthma control during pregnancy restricted to women with asthma in the Breathe-Wellbeing, Environment, Lifestyle, and Lung Function Study, USA (2015-2019). Panel A) Activity limitation (days/gestational week). Panel B) Night wakening (days/gestational week). Panel C) Inhaler use (days/gestational week). Panel D) Respiratory symptoms (total instances of wheeze, cough, chest tightness, chest pain, and shortness of breath/gestational week). Black lines indicate mean trajectory (95% confidence intervals (CI)) for women assigned to the “worse” gestational asthma control category. Grey lines indicate mean trajectory (95% CI) for women assigned to the “same” gestational asthma control category.

LATEBREAKER

Perinatal & Pediatric

Associations between neighborhood COVID-19 pandemic stress, SARS-CoV-2 infection, and preterm birth in New York City Teresa Janevic* Teresa Janevic Erona Ibroci Jezelle Lynch Stephanie Sestito Nina Molenaar Anna Rommel Lotje De-Witte Joann Stone Veerle Bergink Elizabeth Howell

Concern exists that the COVID-19 pandemic will increase risk of preterm birth (PTB), potentially due to inflammatory processes related to SARS-CoV-2 infection or “pandemic stress” due to the social and economic crisis. We analyzed data from an ongoing prospective pregnancy cohort of SARS-CoV-2 infection during pregnancy in New York City to examine the association between neighborhood pandemic stress (defined as increased in unemployment rates from January-December 2020 and COVID-19 mortality rates) and PTB, taking into account SARS-CoV-2 IgG status. The current analyses include 762 women who delivered at two hospitals between April-November 2020. We used publicly available zip code estimates of unemployment rate increases, COVID-19 mortality, and baseline neighborhood vulnerability. SARS-CoV-2 serologic enzyme-linked immunosorbent assay was performed on a blood sample obtained during pregnancy. We ascertained preterm birth (<37 weeks) and covariates from the electronic medical record. We used log-binomial regression with robust standard error by zip code to estimate associations between neighborhood pandemic stress and PTB, adjusting for baseline neighborhood vulnerability, SARS-Cov-2 IgG+ status, race-ethnicity, insurance status, age, and parity. 132 (17%) women were SARS-CoV-2 IgG positive. SARS-CoV-2 infection during pregnancy was not associated with PTB (adjusted relative risk (aRR)=1.1, 95% Confidence Interval (CI)=0.6, 2.1). Women in neighborhoods with high unemployment rate increase had 60% higher risk of PTB than those in other neighborhoods (aRR=1.6, 95%CI=1.0, 2.7). Neighborhood COVID-19 mortality was not associated with PTB (aRR=1.1, 95%CI=0.6, 1.9). Multiplicative or additive interaction between SARS-CoV-2 IgG+ and pandemic stress was not present. We found modest evidence of associations between neighborhood pandemic stress and PTB, even after adjusting for baseline disadvantage and neighborhood demographic composition.

LATEBREAKER

Perinatal & Pediatric

Prospective Associations of Mode of Delivery with Offspring Pubertal Development Izzuddin Aris* Izzuddin Aris Sheryl L. Rifas-Shiman Lidia Minguez Alarcon Joanne E. Sordillo Marie-France Hivert Emily Oken Jorge E. Chavarro

Objectives

Cesarean delivery is posited to influence the infant microbiome, which may have long term effects on health outcomes. However, few studies have examined whether mode of delivery is related to the onset of puberty. We investigated this relationship in Project Viva, a pre-birth cohort from eastern Massachusetts.

Methods

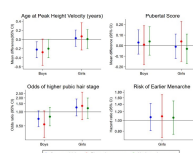
We abstracted information on delivery mode from electronic medical records from 1,345 children followed since birth (1999-2002), and examined the following markers of pubertal development: age at peak height velocity (PHV); age at menarche (girls only); early adolescent (median 12.9 years) parent-reported pubertal development score and child-reported pictograph Tanner pubic hair staging. We used multivariable regression models to examine associations of delivery mode with these 4 pubertal indices, adjusting for the following confounders: demographic and socioeconomic factors; maternal pre-pregnancy body mass index, pregnancy conditions and maternal age at menarche; gestational age at delivery and birth weight-for-gestational-age z-score.

Results

In this study, 23% of participants were born by cesarean delivery. Girls had an earlier age at PHV (11.2 vs 13.1 years) and higher pubertal score (2.9 vs. 2.2 units) than boys. Mean (SD) age at menarche in girls was 12.1 (1.0) years. In boys, those born by cesarean delivery had significantly earlier age at PHV (β -0.23 years; 95% CI -0.41, -0.06) than those born by vaginal delivery, after adjusting for confounders. These associations were similar for planned (no labor) and unplanned (labor) cesarean delivery. No significant associations were observed for early adolescent pubertal score and Tanner pubic hair staging in boys. In girls, delivery mode was not associated with pubertal timing or staging in early adolescence.

Conclusion

Our findings suggest that cesarean delivery predicts earlier pubertal development only among boys.

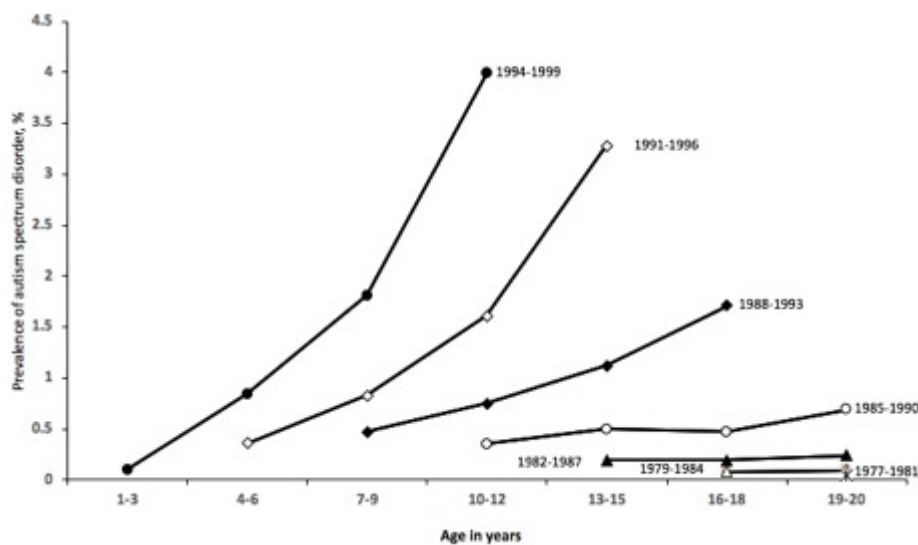


LATEBREAKER

Perinatal & Pediatric

Epidemiologic patterns of Autism Spectrum Disorder in pediatric inpatients in the United States, 1997-2016 Stanford Chihuri* Stanford Chihuri Guohua Li Ashley Blanchard Carolyn DiGuseppi

Autism Spectrum Disorder (ASD) is a neurodevelopmental condition characterized by persistent deficits in social communication and interaction and by restricted, repetitive behaviors. The reported prevalence of ASD has increased markedly in the United States, due in part to improved screening and diagnostic techniques. The impact of improved detection on the epidemiologic patterns of ASD, however, is not well understood. We examined the birth cohort patterns in ASD diagnoses among inpatients aged 1-20 years, using data from the triennial Kids' Inpatient Database (KID) from 1997 through 2012, and 2016. ASD cases were identified according to the ICD-9-CM and ICD-10-CM codes. During the study period, KID recorded a total of 10,736,847 hospital discharges; of these, 71,327 (0.66%) had a diagnosis of ASD. The prevalence of ASD was higher among males compared to females (1.28% vs. 0.26%) and was highest among non-Hispanic Whites (0.86% vs. 0.57% in non-Hispanic Blacks, 0.52% in Hispanics, and 0.75% in Other races). Prevalence rate of ASD increased from 0.16% in 1997 to 1.97% in 2016 ($Z = -205.67$, $p < 0.001$). The absolute increase was higher among males compared to females (0.26% to 3.60% vs. 0.06% to 0.81%), in the youngest birth cohort compared to the oldest birth cohort (0.11% to 3.90% vs. 0.01% to 0.08%), and among non-Hispanic Whites (0.16% to 2.41%) compared to non-Hispanic Blacks (0.19% to 1.51%), Hispanics (0.09% to 1.49%), and Other races (0.16% to 1.90%). Results from weighted analysis were consistent with those from unweighted analysis. These findings show a marked increase in ASD prevalence over the years with more rapid increase among younger birth cohorts, males and non-Hispanic Whites. Our findings demonstrate the utility of hospital discharge record data for ASD surveillance.



LATEBREAKER

Perinatal & Pediatric

The Association Between Diet Quality Indices and Gestational Age and Birth Weight among Latinas Megan Harvey* Megan Harvey Sofija Zagarins Bess Marcus Milagros Rosal Penelope Pekow JoAnn Manson Katherine Tucker Tiffany Moore Simas Glenn Markenson Lisa Chasan-Taber

Prior studies of the impact of maternal diet on birth outcomes have not typically assessed compliance with recommended dietary guidelines and have not focused on Latinas, a group with poorer diet quality and more adverse maternal outcomes, relative to non-Latina White women. Therefore, we evaluated the association between four established diet indices and gestational age (GA) and birth weight among 168 predominantly Puerto Rican participants enrolled in Estudio PARTO, a randomized trial of a lifestyle intervention in Western Massachusetts from 2013-2017. Diet was measured at a mean of 28.1 (SD=6.6) weeks GA by trained bicultural/bilingual personnel via three 24-hour recalls. The Healthy Eating Index 2015 (HEI 2015), Alternate Healthy Eating Index 2010 (AHEI 2010), alternate Mediterranean Diet Score (aMED), and Healthy Plant-Based Diet Index (HPDI) were calculated, with higher scores indicating better quality. Mean GA at delivery was 39.2 wks (SD=1.5) and mean birth weight was 3446.1g (SD=523.3). Participants reported mean intakes of 1856 kcal (SD=555) per day. Mean diet quality scores were 54.9 (SD=14.6, HEI 2015), 36.6 (SD=11.6, AHEI 2010), 24.4 (SD=5.5, aMED), and 51.8 (SD=7.7, HPDI). Women who were married, older than 35, non-smokers, with lower total energy intake and who preferred speaking Spanish had significantly higher diet quality (all $p < 0.05$). After adjusting for age, history of preterm birth, energy intake, activity level, and intervention arm, higher diet quality scores were not associated with gestational age (HEI 2015 $\beta = 0.10$ $p = 0.20$; AHEI 2010 $\beta = 0.11$ $p = 0.17$; aMED $\beta = 0.07$ $p = 0.38$; HPDI $\beta = -0.03$ $p = 0.74$), nor birth weight (HEI 2015 $\beta = 0.03$ $p = 0.73$; AHEI 2010 $\beta = 0.06$ $p = 0.50$; aMED $\beta = -0.01$ $p = 0.98$; HPDI $\beta = 0.04$ $p = 0.64$). Future research should seek to elucidate relevant diet patterns for Latinas and the association between dietary quality and birth outcomes among this ethnic group.

LATEBREAKER

Perinatal & Pediatric

Long-term neuropsychiatric risk across gestational age subgroups: a Danish population-based cohort study Jingyuan Xiao* Jingyuan Xiao Yuntian Xia Yongfu Yu Wan-Ling Tseng Eli Lebowitz Lars Henning Pedersen Jørn Olsen Jiong Li Zeyan Liew Andrew Thomas DeWan

Abstract

Importance: Previous studies have indicated children born at non-optimal gestational durations are at risk for neurodevelopmental disabilities, yet evidence regarding finer classification of gestational age groups and the risk for multiple major neuropsychiatric disorders beyond childhood is limited.

Objective: To comprehensively evaluate the associations between six gestational age groups and the risk of nine major types and eight subtypes of childhood and adult-onset neuropsychiatric disorders.

Design: Nationwide register-based cohort study.

Setting: Denmark.

Participants: Danish individuals born between January 1, 1978 and December 31, 2016 (N=2,327,639).

Exposure: Gestational age subgroups classified based on data obtained from the Danish Medical Birth Register. (in completed weeks): very preterm (20-31), moderately preterm (32-33), late preterm (34-36), early term (37-38), term (39-40, reference), and late/post-term (41-45).

Main Outcomes and Measures: Neuropsychiatric diagnostic records up to August 10, 2017, ascertained from the Danish Psychiatric Central Register using ICD-10 codes F00-F99. We used Poisson regression to estimate the incidence rate ratio (IRR) and 95% confidence interval (CI) for neuropsychiatric disorders in childhood and adulthood, adjusting for selected sociodemographic factors.

Results: For the three preterm groups, a gradient of decreasing IRRs was found from very preterm to late preterm groups for having any or each of the nine neuropsychiatric disorders (e.g., very preterm: IRR=1.49, 95% CI=1.43-1.55; moderately preterm: IRR=1.23, 95% CI=1.18-1.28; late preterm: IRR=1.17, 95% CI=1.14-1.19 for any disorders) compared with term birth. Individuals born early term had 7% higher rates (IRR=1.07, 95% CI=1.06-1.08) for any neuropsychiatric diagnoses and 31% for mental retardation (IRR=1.31, 95% CI=1.25-1.37) when compared to those born at term. The late/post-term group had lower IRRs for most disorders, except childhood autism in which the rate was higher for individuals born post-term compared with the term.

Conclusions and Relevance: Higher incidences of all major neuropsychiatric disorders were observed not only in the spectrum of preterm but also beyond the traditional threshold of fetal maturity. Early term and late/post-term births might not share a homogeneous low risk for neuropsychiatric disorders with individuals born at term. Intervention strategies aimed at perinatal risk factors contributing to nonoptimal gestation might reduce long-term risks for neuropsychiatric disorders in the population.

LATEBREAKER

Perinatal & Pediatric

Maternal diabetes and childhood cancer risk in offspring: population-based case control study Xiwen Huang* Xiwen Huang Johnni Hansen Beate Ritz Chai Saechao Julia E. Heck

Background: Maternal diabetes may be linked to childhood cancer in the offspring. We aimed to determine the effect of maternal diabetes and diabetes medications on the risk of childhood cancer.

Methods: This study included all Danish cancer cases (n= 6420) born between 1977 and 2013, aged 0–19 at diagnosis (diagnoses occurring between 1977 and 2016). The controls were frequency matched by birth year and sex (ratio 1:25) and randomly selected from the Danish Central Population Registry. Data on maternal diabetes and its type (i.e., type I/II, gestational), insulin/metformin prescriptions during pregnancy, childhood cancer, and covariates were obtained from nationwide registers. Conditional logistic regression adjusted for potential confounders was used to estimate the effects. Additionally, we performed an exploratory analysis examining the effect of diabetes medications on the risk of childhood cancer.

Results: Maternal type I diabetes was associated with a higher risk of central nervous system tumors (CNS) (adjusted OR 2.42, 95% CI 1.40-4.21) for all birth years and a higher risk of acute lymphoblastic leukemia (ALL) (adjusted OR 2.58, 95% CI 1.55-4.28) in births after the year 1995. A similar increase in ALL but not in CNS tumors was observed with gestational diabetes. In offspring of a mother with diabetes of any type, our data suggest that the risk of all cancer combined was higher with the use of any diabetes medications (adjusted OR 1.34, 95% CI 0.79-2.25) compared to the risk without diabetes medications (adjusted OR 1.06, 95% CI: 0.76-1.49).

Conclusions: Type I and gestational diabetes appear to be associated with an increased risk of selected childhood cancer in the offspring. Our results suggest an etiologic role of maternal diabetes in childhood cancer. Future investigation into the potential risk-increasing effect of diabetes medications on cancer risk in offspring is warranted.

LATEBREAKER

Perinatal & Pediatric

Live Birth Bias in Estimating Effects of Time-Varying Prenatal Exposures: A Simulation**Study** Yuyuan Lin* Yuyuan Lin Ngoc Tram Nguyen Onyebuchi A. Arah Zeyan Liew

Background: In perinatal and pediatric epidemiology, prenatal exposure effect studies are subject to live-birth-bias (LBB) when the analyzed sample is restricted to live births. This bias structure was previously proposed as a form of collider bias in which conditioning on live birth status induces a non-causal association between exposure and outcome. In this study, we explored the impact of LBB on the estimation of the effects of time-varying prenatal exposures on offspring health outcome.

Method: We use directed acyclic graphs to illustrate the structural relationships between trimester-specific exposures, covariates, pregnancy losses, and child health outcome. We then used Monte Carlo simulations to investigate multiple hypothetical scenarios that assumed trimester-specific prenatal exposures affect pregnancy losses but do not cause the child health outcome. We estimated the impact of LBB in these scenarios when estimating the effects of trimester-specific exposures on child health.

Results: When the trimester-specific exposure variables are positively correlated because of a common exposure source and pregnancy losses can be induced by the exposures throughout gestation, the magnitude of LBB tends to increase. However, the bias direction and magnitude change when the trimester-specific exposures are negatively correlated e.g. a seasonal exposure if it occurs in early gestation the likelihood for an exposure in late pregnancy is lower. The overall direction and magnitude of bias also vary when exposures affect subsequent exposures later in pregnancy.

Conclusion: The magnitude and direction of LBB can be uncertain when the bias structure is complex and time-varying, making heuristics misleading here. There is need for the development of analytic methods that can estimate causally interpretable quantities in the presence LBB following pregnancy losses in complex time-varying exposure effects, mediation and confounding settings.

LATEBREAKER

Perinatal & Pediatric

Characterizing Self-reported Systemic Infection and Inflammatory Markers in Pregnancy

Allison Avrich Ciesla* Allison Ciesla Kristin Scheible Hannah Murphy Ana Vallejo Sefair Richard Miller Jessica Brunner Emily Barrett Thomas O'Connor

Prenatal maternal infection has been linked with multiple child health disturbances, particularly neurodevelopmental disorders. However, there remains considerable variation in how infection is measured in pregnancy cohorts. Many studies rely on self-reported infections, but that is often based on a single time point or retrospective recall, sometimes long after birth. We are not aware of any studies linking reports of infection to biological measures of inflammation, the presumed mechanism. For this study, we describe infection data from self-report and measures of immune activation from analyses of blood samples taken throughout pregnancy.

The Understanding Pregnancy Signals and Infant Development (UPSIDE) cohort study in Rochester, NY has enrolled 326 pregnant women in their first trimester and followed 294 subsequent term-birth children, with continued follow-up through age 4. Women were asked in the third trimester of pregnancy to recall several systemic infections (i.e. flu, urinary tract, respiratory) they may have had, along with the months in the current pregnancy in which the infection occurred. Blood samples at each trimester were assayed for immune markers using a multiplex platform.

Forty-six percent reported at least one infection in pregnancy (and the 3 months leading up to conception), with 15% and 21% reported infections in the first and second trimesters, respectively. The highest reported infections were respiratory (17%), urinary tract (15%), yeast (7%) and flu (7%). Initial analyses found higher levels of IL-7 (in the 7th month), IL-23 (in the 7th month), and TNF α (in the 8th month) for participants reporting an infection in that month of pregnancy, compared to those without an infection in the same corresponding month of pregnancy. The utilization of both self-reported infection and repeated measures of inflammatory markers in pregnancy will help to determine infections in pregnancy for use in associations with peri- and post-natal outcomes.

LATEBREAKER

Perinatal & Pediatric

Prevalence and Treatment of Balance and Dizziness Problems among U.S. Children Aged 3-17 Years - A Healthy People 2020 Update Chuan-Ming Li* Chuan-Ming Li Howard J. Hoffman Christa L. Themann Devin L. McCaslin Anne E. Hogan Bryan K. Ward

Purpose To examine trends in prevalence and treatment of balance and dizziness problems (BDPs) among U.S. children aged 3-17 years in accordance with Healthy People 2020 objectives.

Methods Data from the 2012 and 2016 National Health Interview Surveys were analyzed to evaluate Healthy People 2020 objective 13.1, which sought to increase the proportion of children who have tried recommended methods for treating BDPs. Parents/caregivers reported whether their child had experienced BDPs (including vertigo, poor balance, coordination problems, frequent falls, light-headedness/fainting, or blurred vision) in the preceding 12 months, and whether they had tried treatments recommended by a doctor, physical or occupational therapist, or other health care professional. Estimates were weighted to represent the U.S. childhood population.

Results BDP prevalence increased slightly but not significantly from 5.3% (3.3 million; 5.6% females, 5.0% males) in 2012 to 5.6% (3.5 million; 5.8% females, 5.5% males) in 2016. The increase in reported prevalence was significant among Hispanic children (4.5% to 6.2%; $p=0.05$). The proportion of children who received treatment for BDPs during the preceding 12 months also increased slightly but not significantly between 2012 and 2016 (30.6% to 33.3%). Significant or marginally significant changes in BDP treatment were observed among females (29.0% to 36.0%; $p=0.09$), non-Hispanic (NH) black (26.8% to 46.1%; $p=0.005$), and Hispanic (20.4% to 29.0%; $p=0.05$). Among children with "moderate/big/very big" BDPs, significant changes in treatment rates were observed among NH black (43.6% to 64.3%; $p=0.05$) and Hispanic (33.2% to 58.1%; $p=0.007$).

Conclusions BDPs in childhood may have lifelong adverse sequelae. Although increases in treatment prevalence were observed in Hispanic and NH black children, overall access to treatment for children with BDP remains low. Increased efforts to address this childhood public health issue are warranted.

Use of Drugs with Anticholinergic and Sedative Properties and Fall-related Fractures

Among Older Adults Shahar Shmuel* Shahar Shmuel Virginia Pate Marc J. Pepin Janine C. Bailey Yvonne M. Golightly Laura C. Hanson Til Stürmer Rebecca B. Naumann Danijela Gnjidic Jennifer L. Lund

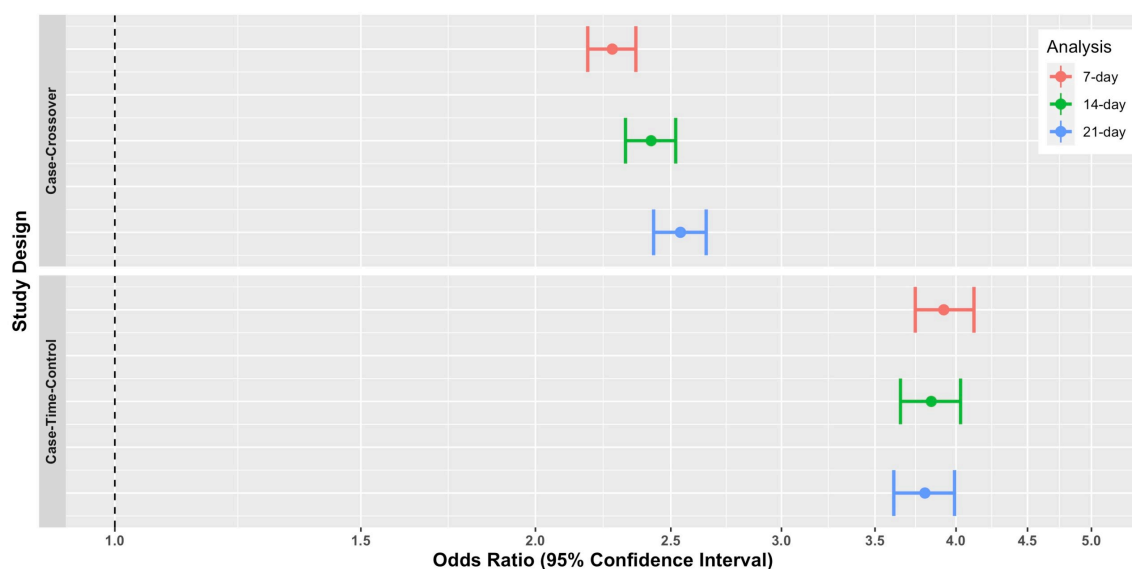
Background: Unintentional falls are a leading cause of injury for older adults, and evidence is needed to understand modifiable risk factors.

Objectives: To evaluate if dispensing prescription drugs with anticholinergic/sedating properties is temporally associated with an increased odds of fall-related fractures.

Methods: We conducted a cohort study of a 20% nationwide, random sample of US Medicare beneficiaries with nested self-controlled analyses during 2014-2016. New users of drugs with anticholinergic/sedating properties who were 66+ years old, had Medicare Parts A, B, and D coverage but no claims for drugs with anticholinergic/sedating properties in the year prior were included. We followed new users until first non-vertebral fall-related fracture (primary outcome), Medicare disenrollment, death, or end of study. We estimated the 1-year risk and 95% CIs of first fracture. In our nested case-crossover analysis, we restricted to patients experiencing a fall-related fracture, and estimated ORs and 95% CIs comparing anticholinergic/sedating drug exposure (any vs. none) during a 14-day hazard period preceding the fracture to exposure during an earlier 14-day control period. We also used a control group (no fracture) to adjust for potential exposure-trend bias in a case-time-control analysis.

Results: A total of 1,097,989 new users were included. The 1-year risk of fall-related fracture, accounting for death as a competing risk, was 5.0% (95% CI: 5.0%-5.0%). Among beneficiaries with a fall-related fracture who met the case-crossover eligibility criteria (n=41,889), the adjusted OR for the association between anticholinergic/sedating drug dispensing and fractures was 2.42 (95% CI: 2.32-2.52); ORs were larger in case-time-control analyses (Figure).

Conclusions: New use of anticholinergic/sedating drugs was temporally associated with an increased odds of fall-related fractures. Healthcare providers should consider fall risk when prescribing these drugs to older adults.



Fracture risk associated with long-term risedronate versus alendronate therapy during osteoporosis treatment gaps: a propensity-matched cohort analysis Kaleen N. Hayes* Kaleen Hayes Kevin A. Brown Angela M. Cheung David Juurlink Suzanne M. Cadarette

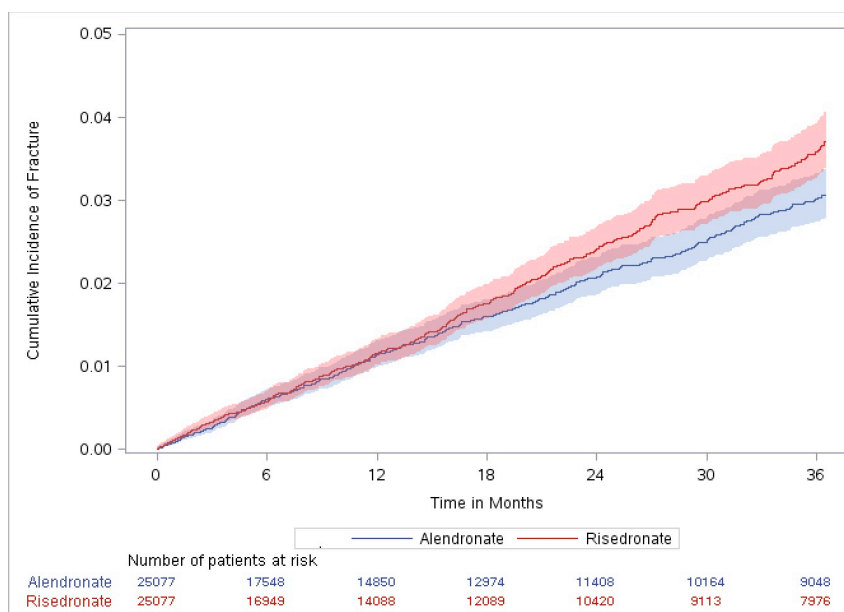
Background: An osteoporosis drug holiday up to 3 years is recommended for most patients following 3-5 years of risedronate [RSD] or alendronate [ALD]) therapy. RSD has a shorter half-life than ALD and may be associated with a higher fracture risk during drug holidays.

Objective: To estimate relative 3-year fracture risk after discontinuation of long-term (≥ 3 years) RSD versus ALD therapy.

Methods: We followed patients aged ≥ 66 years with ≥ 3 years of continuous ALD or RSD therapy (80% proportion of days covered) and a subsequent ≥ 120 -day gap in therapy. Patients receiving long-term RSD were matched to patients receiving long-term ALD on sex and the logit of the propensity score (caliper 0.1) that included risk factors for fracture, using a greedy matching algorithm without replacement. Patients were followed from day 121 of gap for a maximum of 3 years until hip fracture (primary outcome), censoring on death, re-start of osteoporosis therapy, and end of data availability. Cox proportional hazards models with robust variances were used to estimate the association between long-term RSD vs. ALD therapy on hip fracture during therapy gaps.

Results: Of 60,636 eligible patients, 50,154 were matched (mean age 74 years; 82% women). During follow-up, 3.6% of RSD patients and 3.0% of ALD patients experienced a hip fracture. Hip fracture risk was higher during therapy gaps among patients treated with RSD vs. ALD (HR 1.18 [95% CI 1.04-1.34]). In secondary analyses, the effect estimate was larger in men (HR 1.37 [95% CI 0.95-1.97]) than women (HR 1.16 [95% CI 1.01-1.33]) and smaller during shorter follow-up periods (1-year follow up: HR 1.03 [95% CI 0.85-1.24]; 2-year follow-up: HR 1.14 [95% CI 0.98-1.32]).

Conclusion: Long-term RSD therapy was associated with higher fracture risk during gaps longer than 2 years. Additional research is needed to confirm this association and consider whether other fracture risk factors modify the association to inform drug holiday recommendations.



Potential direct effect of tumor-necrosis factor inhibitors on cardiovascular risk controlling for disease activity measure Kazuki Yoshida* Kazuki Yoshida Hongshu Guan Leslie Harrold Daniel H. Solomon

Interest exists in the inflammatory hypothesis of cardiovascular disease (CVD). Tumor necrosis factor inhibitors (TNFi), used in rheumatoid arthritis (RA), blocks a CVD-related inflammatory pathway. TNFis may have a CVD benefit compared methotrexate (MTX). We aimed to examine the controlled direct effect (CDE), representing the direct influence of TNFi on CVD beyond its influence on RA activity, a known CV risk factor.

We examined the clinically diagnosed RA in a US registry. We followed patients starting at drug initiation and followed until the end of follow-up or first CVD. Follow-up RA activity was a nuisance exposure to be controlled for. Baseline adjustments were conducted for age, gender, race, and RA and CVD relevant variables. We constructed IPW for RA activity (remission, low, moderate, high) in each 6-month interval with time-varying covariates. Outcome analyses were conducted with pooled logistic regression. CDEs were defined based on the RA activity trajectories to which both treatment groups were hypothetically fixed.

We found 5,027 initiators of TNFi (with or without MTX) and 3,203 initiators of MTX. In the unadjusted analysis, HR comparing TNFi vs. MTX was 0.77 [0.58, 1.04]. Adjusting for the baseline confounders gave a HR estimate of 0.96 [0.70, 1.33]. Allowing for RA activity trajectories to be fixed across groups in any trajectories, the CDE estimate was HR 1.20 [0.75, 1.91]. When restricting analysis to observations with constant RA activity beyond baseline, the corresponding CDE estimate was HR 1.19 [0.57, 2.47]. CDE estimates under specific constant RA activity trajectory varied from 0.96 to 1.21, but remained statistically non-significant.

We did not demonstrate a drug-specific benefit beyond RA activity suppression in our analysis. This may indicate RA activity suppression is more important regardless of drug choices. However, we cannot rule out residual confounding of post-treatment disease activity, which could favor less potent MTX.

Table Controlled direct effect (CDE) of the initial assignment to the initiation of TNFi with or without MTX compared to the initiation of MTX monotherapy

CDAI*	Group	N†	PY‡	MACE	MACE/1000PY	CDE
Any	MTX	3,181	10,221.5	76	7.4	Ref
	TNFi	5,017	17,508.3	101	5.8	1.20 [0.75, 1.91]
Always Fixed	MTX	3,181	3,138.5	22	7.0	Ref
	TNFi	5,017	5,057.9	30	6.0	1.19 [0.57, 2.47]
Fixed at:						
Always Remission	MTX	562	513.0	2	4.1	Ref
	TNFi	754	774.2	4	5.4	NA**
Always Low	MTX	1,232	1,345.8	8	5.9	Ref
	TNFi	1,787	1,864.5	11	5.8	1.21 [0.29, 5.04]
Always Moderate	MTX	897	771.1	7	9.6	Ref
	TNFi	1,481	1,313.9	8	6.5	0.96 [0.26, 3.50]
Always High	MTX	491	508.6	5	9.0	Ref
	TNFi	995	1,105.2	7	6.2	1.12 [0.13, 9.97]

* Controlled direct effects can be different depending on the mediator trajectory to which both treatment groups were hypothetically fixed.

- **"Any"**: Any post-baseline CDAI trajectories are allowed, but they were adjusted (statistically fixed via modeling) for comparison of MACE across treatment groups.
- **"Always Fixed"**: Observations were censored as soon as the post-baseline CDAI category deviated from the category observed in the first 6 months of treatment. Thus, the CDAI trajectory is always fixed in one of the four levels. These "Always Fixed" trajectories were adjusted (statistically fixed via modeling) for comparison of MACE across treatment groups.
- **"Always Remission"**: A subset analysis of the "Always Fixed" analysis using only the observations that stayed in remission including and after the first 6 months of treatment.
- **"Always Low"**: A subset analysis of the "Always Fixed" analysis using only the observations that stayed in low disease activity including and after the first 6 months of treatment.
- **"Always Moderate"**: A subset analysis of the "Always Fixed" analysis using only the observations that stayed in moderate disease activity including and after the first 6 months of treatment.
- **"Always High"**: A subset analysis of the "Always Fixed" analysis using only the observations that stayed in high disease activity including and after the first 6 months of treatment.

† Some baseline-only observations were removed after accounting for the censoring via inverse probability of censoring weights.

‡ Follow-up were terminated when the CDAI category deviated from the first post-baseline CDAI category (thus, the wider confidence interval).

** Estimates were not available due to non-convergence issues.

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Risk of major bleeding associated with concomitant use of selective serotonin reuptake inhibitors and oral anticoagulants: systematic review and meta-analysis Alvi Rahman* Alvi Rahman Na He Soham Rej Robert W. Platt Christel Renoux

Background: Selective serotonin reuptake inhibitors (SSRIs) are the most prescribed class of antidepressants and are associated with a modest increase in the risk of major bleeding. However, in patients treated with oral anticoagulants (OACs), the additional risk of major bleeding conferred by using SSRIs may be substantial.

Objective: To estimate the risk of major bleeding associated with the concomitant use of SSRIs and OACs, compared with OAC use only, in patients aged 18 years and above.

Methods: We searched MEDLINE, Embase, PsycINFO and the Cochrane Central Register of Controlled Trials for clinical trials and observational studies. Two independent reviewers conducted title/abstract and full-text screening, data extraction, and risk of bias assessment. Given sufficient homogeneity of studies, we conducted a random-effects meta-analysis using the Hartung-Knapp-Sidik-Jonkman method to estimate a pooled HR.

Results: We included 13 studies in the review, of which seven were cohort studies and six were nested case-control studies. We identified substantial bias in some studies, such as immortal time bias, exposure misclassification, prevalent user bias, potential mediator adjustment, and residual time-fixed and time-varying confounding. Following assessment for clinical and methodological heterogeneity, seven studies with a total of 85,398 patients were eligible for the meta-analysis. The pooled HR for risk of major bleeding associated with the concomitant use of SSRIs and OACs was 1.40 (95% CI: 1.13-1.75), compared with OAC use only. Furthermore, concomitant use of these drugs was associated with an increased risk of gastrointestinal bleeding (HR: 1.30; 95% CI: 0.70-2.61), however uncertainty was high.

Conclusions: In patients treated with OACs, the concomitant use of SSRIs significantly increased the risk of major bleeding, compared to OAC use only. These findings suggest that physicians may need to tailor treatment when prescribing SSRIs to patients using OACs.

How COVID-19 Randomized Controlled Trials Reported on Demographic and Clinical

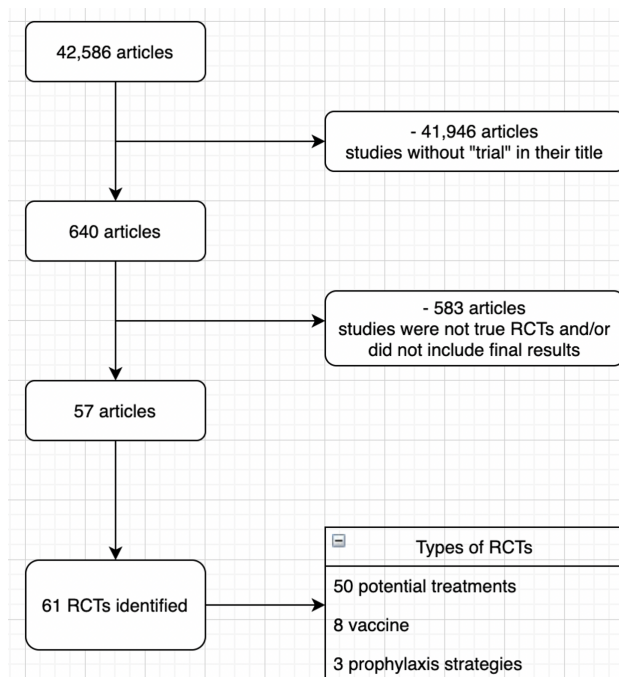
Characteristics Joyce Pak* Joyce Pak Jennifer L. Lund Alexander Keil Daniel Westreich Til Stürmer David Wohl Claire Farel M. Bradley Drummond Michael Webster-Clark

Mortality in COVID-19 patients varies by sex, age, race, and comorbid conditions. Because of this variation, treatments to prevent or treat COVID-19 are likely to have heterogeneous effects, making the external validity randomized controlled trials (RCTs) especially important. To assess this validity, understanding the patterns of participation and the extent to which they report key demographic and clinical characteristics is critical.

We queried English-language articles from PubMed, Web of Science, clinicaltrials.gov, and the CDC library of gray literature databases using keywords of 'coronavirus', 'covid', 'clinical trial' and 'randomized controlled trial' from January to October 2020. We restricted to studies with "trial" in their title and reviewed abstracts to confirm they were RCTs with final results. Finally, we abstracted the demographic and clinical characteristics reported in Table 1.

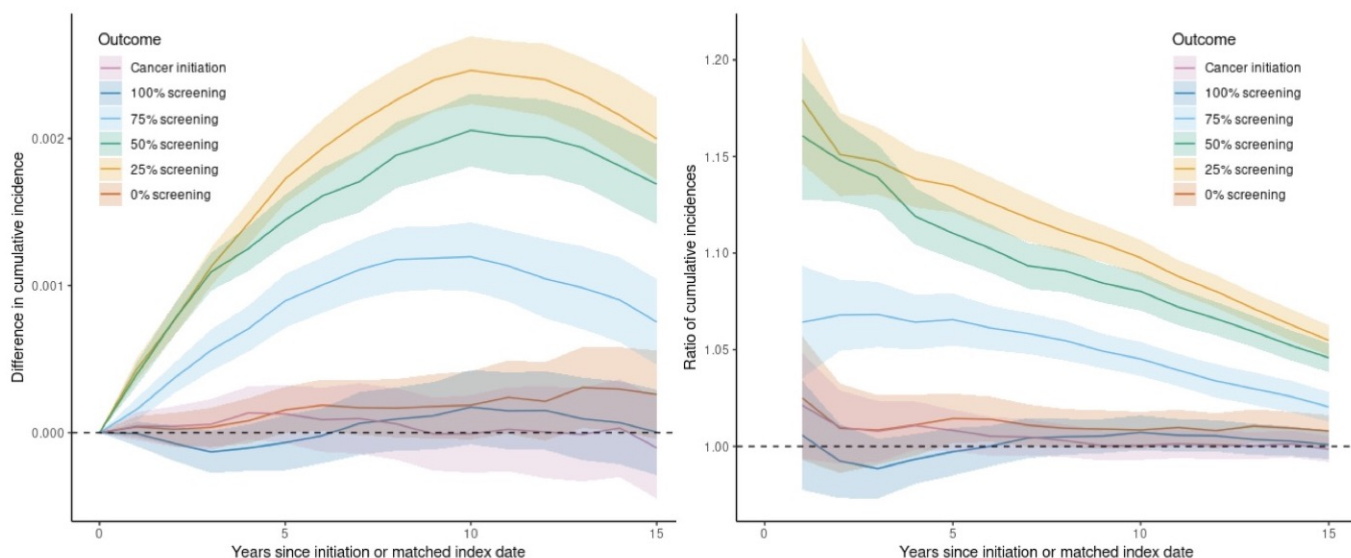
From an initial 42,586 manuscripts, we identified 61 RCTs described in 57 articles (Figure 1). The trials were largely conducted in China (20), Iran (9), and the U.S. (8). Most (50) studied potential treatments, while fewer studied vaccines (8) and prophylaxis strategies (3). Study populations ranged from 10 to 5040 participants with a median of 89. All 61 reported on age, 59 on sex, 48 on the prevalence of at least one comorbidity, 22 on use of oxygen therapy, and 14 on race. Pregnant women were explicitly excluded from 46 of the trials. No trials reported on income, urban vs rural residence, or other indicators of socioeconomic status (SES).

Reporting on age, sex, and comorbid conditions may assist in characterizing the RCT populations; however, limited reporting on race and other markers of SES makes it difficult to draw conclusions in the most impacted populations without assuming homogeneous treatment effects. These findings highlight the need for more robust reporting of clinical and demographic factors in COVID-19-related RCTs.



Modeling cancer risk following drug initiation under various screening regimens: a discrete event simulation Sophie E Mayer* Sophie Mayer Jessie K Edwards Jesper Hallas Jennifer Lund Til Sturmer

Screening's ability to advance cancer detection may result in the appearance of non-causal relationships between medication initiation and cancer risk when screening and treatment have shared predictors. We used discrete event simulation to model the lifetime risk of breast cancer initiation, growth and detection, and competing mortality in 100 cohorts of 100,000 women between the ages of 20-84. "High healthcare access" was positively associated with cancer screening between the ages of 50-75 and with treatment. Treatment initiation was modeled as a binary variable, with age at initiation distributed normally; true disease risk was independent of both treatment and healthcare access, leading to a true null treatment effect. Two-year screening coverage in the population varied between 0 and 100%. We used Aalen-Johansen risk estimation to calculate cumulative incidence (incidence) of breast cancer initiation and detection under each screening regimen and within treatment arms in the presence of competing mortality. The 10-year incidence of breast cancer increased from 2.48% (95% CI: 2.47, 2.49) to 2.83% (95% CI: 2.82, 2.84) with increasing screening coverage in the population; all observed risks of cancer incidence underestimated the incidence of cancer initiation (3.60%, 95% CI: 3.58, 3.61). In settings in which screening-eligible individuals were either always or never screened, minimal bias was observed in the estimated RD and RR throughout the 15-year follow-up period. However, when a proportion of the population received screening, screening occurred differentially across treatment groups, leading to bias in both the RD and RR across the 15 years of follow-up. These findings illustrate the sensitivity of both marginal and stratified risk estimates and their contrasts to the level of screening coverage in a population. Furthermore, they highlight the need for methods to account for differential outcome assessment in real-world analyses of longitudinal data.



LATEBREAKER

Pharmacoepidemiology

Genital tract infections associated with sodium-glucose co-transporter 2 inhibitors use in type-2 diabetes: A population-based cohort study. Wajd Alkabbani* Wajd Alkabbani
Arsene Zongo Dean Eurich Baiju R Shah Jasjeet K Minhas-Sandhu Wasem Alsabbagh John-Michael Gamble

Background: Sodium-glucose cotransporter-2 inhibitors (SGLT2-i) are novel class of anti-diabetics that work by reducing renal reabsorption of glucose. Due to their unique mechanism of action, the induced glucosuria can increase susceptibility to genital tract infections (GTIs).

Objective: To assess the association between SGLT2-i use and GTI among type-2 diabetes patients.

Methods: This was a population-based cohort study using primary care data from the UK's Clinical Practice Research Datalink (CPRD), and administrative healthcare data from Alberta (AB), Canada. We defined exposure as new use of SGLT2-i or dipeptidyl peptidase-4 inhibitor (DPP4-i) between 2013-2018, among new metformin users, who did not experience GTI in the year prior to exposure. We defined the outcome as either hospitalization or physician visit due to a GTI, including balanitis, vulvovaginal candidiasis, genital candidiasis, vulvovaginitis, vaginal thrush, bacterial vaginitis, vulvitis, and vulval abscess. We adjusted for confounding by high-dimensional propensity score matching and estimated hazard ratios (HR) using cox proportional hazards regression. Aggregate data from each database were combined by random-effects meta-analysis. We repeated the analysis using different antidiabetic comparators.

Results: The two cohorts included 49,888 patients (29,169 CPRD, 20,719 AB), of which 27.4% were exposed to SGLT2-i in CPRD and 37.5% in AB. There were a total of 482 events among SGLT-i users and 680 among DPP4 users. Matching resulted in 7,472 pairs in CPRD (mean age [SD]= 57.6 [11.1]; 42.4% females) and 7,539 pairs (56.7 [11.1]; 39.4%) in AB. The risk of GTI was higher for SGLT2-i compared to DPP4-i users (pooled HR 1.89, 95% CI 1.10 - 3.21). Similarly, the risk was higher for SGLT2-i compared to other antidiabetic agents, although not statistically significant; sulfonylureas (pooled HR 1.74, 95% CI 0.77 - 3.92), glucagon-like peptide-1 receptor agonists (pooled HR 1.64, 95% CI 0.65 - 4.09), thiazolidinediones (pooled HR 1.49, 95% CI 0.79 - 2.81), and insulin (pooled HR 1.15, 95% CI 0.71 - 1.87).

Conclusion: SGLT2-i use is associated with a higher risk of GTIs compared to DPP4-i use. These findings from real-world data are consistent with those from placebo controlled randomized controlled trials.

LATEBREAKER

Pharmacoepidemiology

Metformin and Risk of Adverse Pregnancy Outcomes Among Pregnant Women with Gestation Diabetes in The United Kingdom: A Population-Based Cohort Study Ya-Hui Yu* Ya-Hui Yu Robert W. Platt Oriana Hoi Yun Yu Kristian B. Filion

Objectives

To compare the rate of adverse pregnancy outcomes with metformin versus insulin among women with GDM in the United Kingdom.

Methods

We conducted a retrospective cohort study using linked data from the Clinical Practice Research Datalink, its pregnancy register, and Hospital Episode Statistics. We included pregnancies of women without diabetes history and initiated metformin or insulin between a gestational age of 20 weeks and the end of pregnancy from 1998 to 2018. We defined exposure using an intention-to-treat approach, with person-time classified into either the metformin or insulin group based on the treatment prescribed at cohort entry. The primary outcome was a composite outcome of large for gestational age (birthweight > 90th percentile) and macrosomia (birthweight > 4000 grams). The secondary endpoints were preterm birth, Cesarean delivery, and hypertensive disorders during pregnancy. We used inverse probability weighted-Cox proportional hazards models with a time scale of time since treatment initiation to estimate the adjusted hazard ratios (HRs) and 95% confidence intervals (CI) for the association between the risk of adverse pregnancy outcomes and the use of metformin versus insulin, accounting for baseline covariates.

Results

Our cohort included 2,330 pregnancies from 2,231 women with GDM. A total of 42% of women were prescribed insulin and 58% were prescribed metformin at cohort entry. The mean gestational age at treatment initiation was 31.8 weeks (standard deviation: 4.4). Compared to insulin use, metformin use was associated with a decreased risk of a composite endpoint of large for gestational age and macrosomia (HR: 0.61, 95% CI: 0.50, 0.75). Metformin use was also associated with decreased risks of Cesarean delivery (HR: 0.82, 95% CI: 0.72, 0.92), and preterm birth (HR: 0.82, 95% CI: 0.61, 1.09). The HR for hypertensive disorders during pregnancy was 0.90 (95% CI: 0.64, 1.27). In sensitivity analyses that used gestational age as the underlying time axis, we observed similar trends.

Conclusions

Our study suggests that, compared to the use of insulin, the use of metformin is associated with decreased risks of large for gestational age and macrosomia and of Cesarean delivery among women with GDM.

Preconception migraines and spontaneous abortion: a prospective cohort study Holly Crowe* Holly Crowe Amelia Wesselink Lauren Wise Elizabeth Hatch

Migraines affect nearly a quarter of reproductive-aged women. Previous research has shown a modest increase in risk of spontaneous abortion (SAB) among migraineurs. We used data from a preconception cohort study in the U.S and Canada to examine the association between physician-diagnosed migraines and SAB risk. From 2013-2020 we enrolled 13,043 women; 6,325 conceived during 12 cycles of follow up and 1,208 (19%) reported SAB. At baseline, we collected data on migraine history, frequency, and medication use. Pregnancy losses <20 weeks of gestation were reported on bimonthly follow-up and early (~8 weeks) and late pregnancy (~32 weeks) questionnaires. We used Cox proportional hazards models, with gestational weeks as the time scale, to estimate hazard ratios (HR) and 95% CIs, adjusting for demographics, lifestyle, and reproductive history. Overall, 1332 (21%) of women reported a history of migraines, 45% of whom took migraine medication in the past 4 weeks. Of the 605 women taking medication, 91% took medication only when experiencing symptoms, most commonly over-the-counter pain relievers (75%). While 42% of migraineurs reported no migraines in the past 4 weeks, 29% reported 1 migraine, 14% reported 2 migraines, and 16% reported ≥ 3 migraines. Overall, a history of migraines was not appreciably associated with risk of SAB (HR=1.04, CI: 0.91-1.20). Among migraineurs, recent use of migraine medication showed little association with SAB (HR=1.08, CI: 0.84-1.38). There was also little association between migraine frequency and SAB: HRs for 1, 2, or ≥ 3 vs. 0 migraines in the past 4 weeks were 0.88 (CI: 0.65-1.19), 0.98 (CI: 0.65-1.40), and 0.94 (CI: 0.65-1.36), respectively. Our findings provide little support for the hypothesis that a history of migraine or use of migraine medications are associated with SAB risk.

Employment Status in the United States and Use of Long-Acting Reversible Contraception or Moderately Effective Contraception before and after the Affordable Care Act: An Analysis of the National Survey of Family Growth 2006-2010 and 2015-2017 Vijaya

Kancherla* Vijaya Kancherla Mark Lachiewicz Tiffany Hailstorks

Objective: The Affordable Care Act (ACA) was introduced in the United States (US) in 2010. We assessed the association between employment status and long-acting reversible or moderately effective contraception use among women aged 15-44 years before and after the passage of the ACA, and if this association differed by race/ethnicity.

Methods: We used data from the 2006-2010 and 2015-2017 cycles of the National Survey of Family Growth (NSFG) indicating pre- and post-ACA periods, respectively. Employment at the time of the survey was measured as a dichotomous variable. Multivariable logistic regression was used to estimate adjusted prevalence odds ratios (aPOR) and 95% confidence intervals (CI) of use of long-acting reversible or moderately effective contraception as compared to least effective or no methods of contraception. Effect modification was assessed by race/ethnicity.

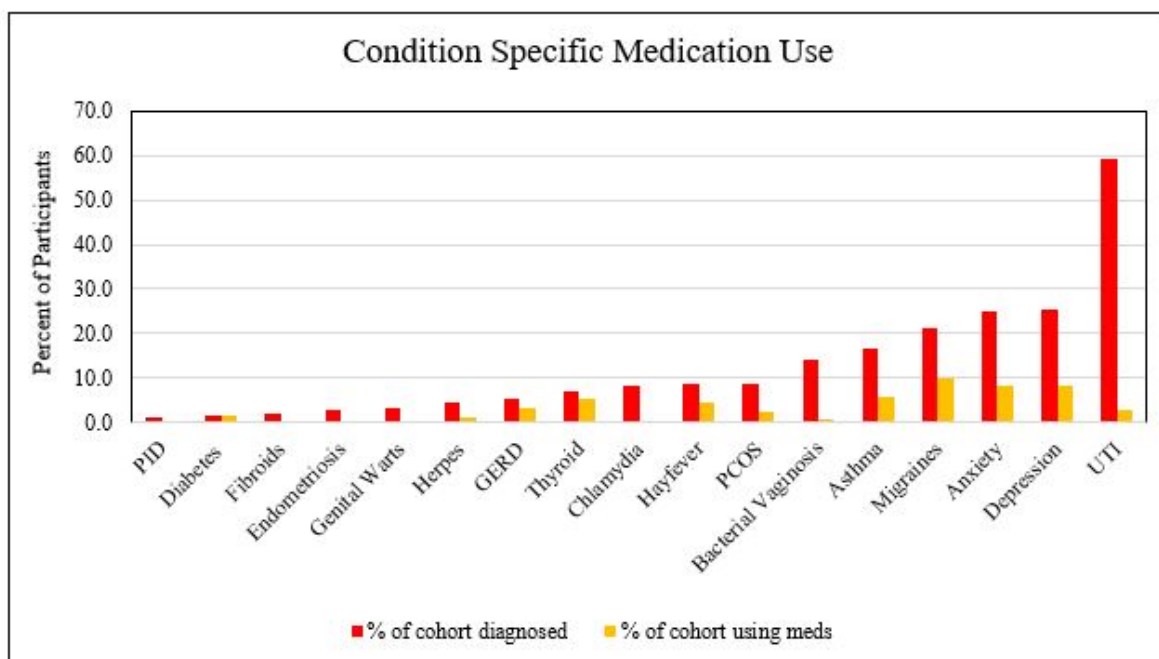
Results: Overall, 5,572 women were examined pre-ACA, and among them 53.2% were using long-acting or moderately effective contraception; post-ACA (n=2,340), this proportion increased to 54.7%. Pre-ACA, non-Hispanic White women who were employed were significantly more likely to use long-acting reversible or moderately effective contraception (aPOR=1.66; 95% CI=1.28, 2.14). Post-ACA, there was no significant relationship between employment status and long-acting reversible or moderately effective contraceptive use in non-Hispanic white women (aPOR=0.94; 95% CI=0.67, 1.33). For other race/ethnic groups, we found no statistically significant association for the main effect during pre-ACA or post-ACA study periods.

Conclusions: Contrary to our expectation, we found no significant association between employment and use of long-acting reversible or moderately effective contraceptives by race/ethnicity during post-ACA period in a nationally representative study. Future studies should examine how short-term loss or interruption of employment impacts contraception use in the target population of US women.

A descriptive study of prescription and over-the-counter medication use among pregnancy planners in the United States and Canada Holly Crowe* Holly Crowe Amelia Wesselink Lauren Wise Elizabeth Hatch

Pregnancy planners may seek to decrease their medication use to minimize potentially harmful exposures before pregnancy detection. However, most research focuses on medication use during pregnancy or use of known teratogens. We used data from an online preconception cohort study to describe medication use among women trying to conceive, a hard-to-reach population. From 2013 through 2020, we enrolled 12,467 eligible female pregnancy planners. At baseline, women reported ever-diagnoses of several common conditions: urinary tract infection, depression, anxiety, migraine, asthma, bacterial vaginosis, polycystic ovarian syndrome, hayfever, chlamydia, thyroid disorder, gastroesophageal reflux disease, herpes, genital warts, endometriosis, fibroids, diabetes and pelvic inflammatory disease. Urinary tract infections (59%), depression (25%), and anxiety (25%) were the most frequently reported conditions. Although medication for these conditions are generally safe to use during pregnancy, some antibiotics and psychiatric medications are of unknown risk or contraindicated. Women reported prescription or over-the-counter medication use for these conditions or other indications during the past 4 weeks. Overall, 81% of women reported any recent medication use; 29% used pain medication, 36% used medication for a common condition and 18% used medication for other indications. Of the women using medication for a common condition, 18% used medication for migraines (9% of the overall cohort), 15% used medication for depression (8% of the overall cohort) and 15% used medication for anxiety (8% of the overall cohort). Of the women using medication for other indications, 17% used antihistamines, 6% used decongestants, 6% used antidepressants, 5% used steroids, and 5% used stimulants. Additional research into potential reproductive effects of migraine medications, depression and anxiety medications, antihistamines, and other commonly used medications among pregnancy planners is warranted.

Figure 1: Condition Specific Medication Use in Pregnancy Study Online



Preconception caffeine metabolites and fecundability among women attempting to**conceive** Alexandra Purdue-Smithe* Alexandra Purdue-Smithe Keewan Kim Stefanie Hinkle Karen Schliep Neil Perkins Lindsey Sjaarda Robert Silver Enrique Schisterman Sunni Mumford

Caffeine is the most frequently used psychoactive substance in the United States and more than 90% of reproductive-age women report some level of intake daily. Women are often counseled to limit caffeine intake while attempting pregnancy despite conflicting evidence on associations between caffeine and fecundability. Importantly, prior studies examining caffeine intake and fecundability measured exposure via self-report only, which is subject to measurement error and does not account for factors that influence caffeine metabolism. We therefore evaluated associations of preconception serum caffeine metabolites (i.e., caffeine, paraxanthine, and theobromine) and self-reported intake of caffeinated beverages, with fecundability among 1,228 women aged 18-40 years who were attempting to conceive in the EAGeR trial. Using Cox proportional hazards models, we estimated fecundability odds ratios (FOR) and 95% confidence intervals (CI) according to each metabolite. At baseline, 84%, 73%, and 90% of women had detectable levels of serum caffeine, paraxanthine, and theobromine, respectively. 797 women became pregnant during 6 months of preconception follow-up. After adjusting for age, BMI, smoking, and other potential confounders, neither serum caffeine (Tertile 3 vs 1 FOR=0.87; 95% CI=0.71-1.08), paraxanthine (Tertile 3 vs 1 FOR=0.92; 95% CI=0.75-1.14), nor theobromine (Tertile 3 vs 1 FOR=1.15; 95% CI=0.95-1.40) were associated with fecundability. Intakes of total caffeinated beverages (>2 vs 0 servings/d FOR=0.94; 95% CI=0.73-1.21), coffee (>2 vs 0 servings/d FOR=0.87; 95% CI=0.58-1.30), soda (>2 vs 0 servings/d FOR=0.93; 95% CI=0.71-1.21), and tea (>1 vs 0 servings/d FOR=1.03; 95% CI=0.49-2.20), were also not associated with fecundability. Our findings suggest that preconception caffeine exposure, as measured by both serum metabolites and self-report, do not appear to play an important role in conception.

Case-control study of adiposity measures and adenomyosis risk: The impact of control selection on results Kristen Upson* Kristen Upson Sawsan As-Sanie Holly R. Harris Victoria L. Holt

Adenomyosis, characterized by the presence of endometrial glands and stroma within the myometrium, is associated with substantial morbidity. Given the historic reliance on hysterectomy for diagnosis, epidemiologic understanding of adenomyosis has been hampered by bias from control selection, resulting in inconsistent results across studies. This includes mixed results for body mass index (BMI), the only adiposity measure examined in prior studies, and adenomyosis risk. We investigated overall adiposity (BMI, weight) and central adiposity (waist circumference (WC), waist-to-hip ratio (WHR)) using a novel case-control design in a study of female enrollees ages 18-59 of a large, integrated healthcare system in Washington State. We identified incident, pathology-confirmed adenomyosis cases diagnosed 2001-2006 (n=386) and employed two control groups: 1) randomly selected age-matched enrollees with intact uteri ("population controls", n=323) and 2) hysterectomy controls (n=233). Self-reported weight and BMI at the reference date (first visit for symptoms leading to adenomyosis diagnosis) and measurements of WC and WHR were collected during in-person interviews. We used logistic regression to estimate ORs and 95% CIs, adjusting for age, reference year, menarche age, education, and gravidity. In analyses using population controls, weight and BMI were associated with increased adenomyosis risk (weight ≥ 190 vs. < 135 lbs: OR 2.2, 95% CI: 1.3, 3.6; BMI ≥ 30.0 vs. < 25.0 : OR 1.8, 95% CI: 1.2, 2.7). We also observed increased adenomyosis risk with increased WC and WHR (WC > 35 vs. ≤ 35 inches: OR 1.6, 95% CI: 1.1, 2.2; WHR > 0.88 vs. ≤ 0.88 : OR 1.3, 95% CI: 0.9, 2.1). In contrast, we observed attenuated associations for weight and BMI and null associations for WC and WHR in analyses using hysterectomy controls. Our results highlight the impact of control selection in the epidemiologic study of adenomyosis and contributes new data on this understudied condition.

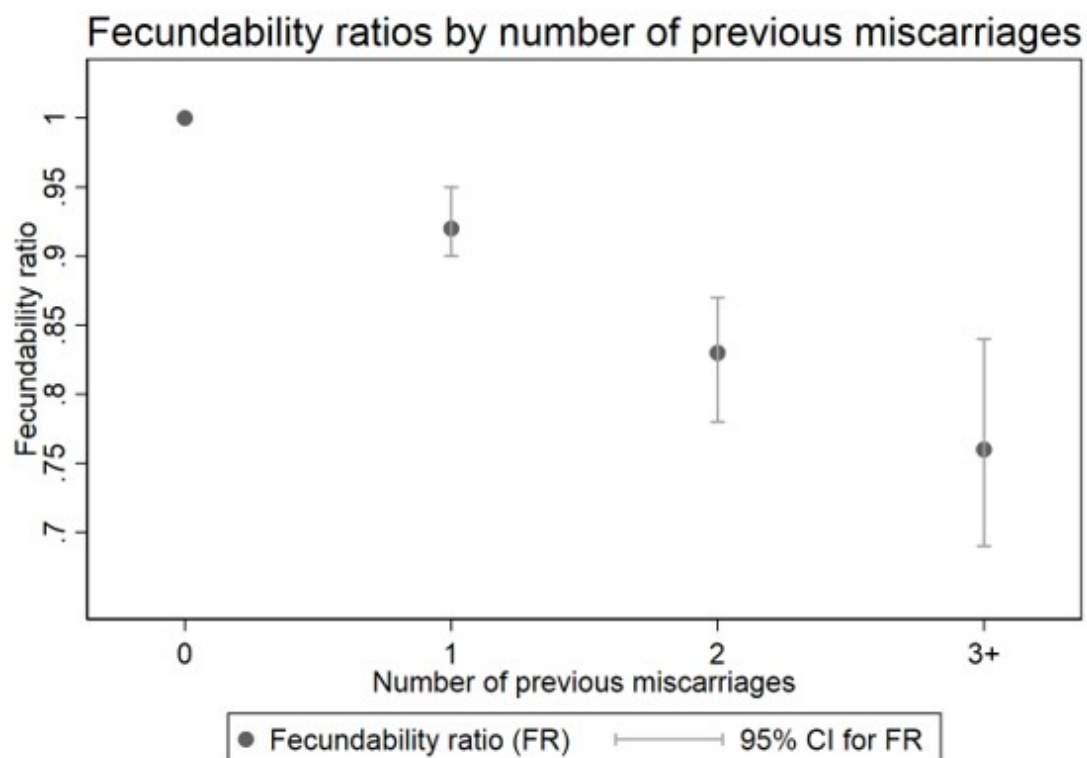
Miscarriage history and subsequent fecundability: Results from the Norwegian Mother, Father and Child Cohort Study Lise A. Arge* Lise Andrea Arge Siri E. Håberg Allen J. Wilcox Øyvind Næss Olga Basso Maria C. Magnus

Background: A link between miscarriage and later fecundability is debated, with studies reporting both lower and higher fecundability after miscarriage. We examined the association between number of prior miscarriages and subsequent fecundability within the Norwegian Mother, Father and Child Cohort Study (MoBa).

Method: We used information on time to pregnancy (TTP) and previous pregnancy outcomes from 48 152 planned MoBa pregnancies conceived without treatment among women with at least one prior pregnancy. TTP was calculated using trying time in months adjusted for cycle length. We estimated fecundability ratios (FRs) and 95% confidence intervals using proportional probability regression, with cycles as the unit of analysis and the cycle number included as an indicator variable. We compared women with 1, 2 and 3 or more prior miscarriages to women with no prior miscarriages. The analysis was adjusted for maternal age, education, income, body mass index and smoking during pregnancy.

Preliminary results: Compared to the reference group with no prior miscarriages, FRs and confidence intervals were 0.92 (0.90-0.95), 0.83 (0.78-0.87) and 0.76 (0.69-0.84) for 1, 2 and 3 or more miscarriages respectively. A sensitivity analysis including women with unplanned pregnancies showed similar results.

Conclusion: The results suggest that women with a higher number of prior miscarriages have reduced fecundability. This may reflect a contribution of occult pregnancy losses to TTP, or the presence of shared underlying causes for fecundability and miscarriage.



Longitudinal semen quality and live birth among an infertility treatment-seeking population

Elizabeth A DeVilbiss* Elizabeth A DeVilbiss Lindsey A Sjaarda

Background: While a semen analysis remains the cornerstone of the evaluation of male fertility potential, relations between semen quality across the spectrum of male fertility and live birth are not well understood. Prior studies report mixed findings, and no prior work has examined relations between longitudinal semen quality and live birth.

Methods: Couples seeking fertility consultations in a large clinical trial (n=2369) received *in vitro* fertilization (IVF), intrauterine insemination (IUI), or ovulation induction (OI) medications only or no fertility treatment over follow-up. Semen quality was assessed at baseline and 2-, 4- and 6-months post-enrollment by quantification of sperm concentration, volume, motility, morphology, count, and total motile count. Adjusted identity-binomial models estimated risk differences between quartiles of semen parameters across all study visits and live birth, stratified by fertility treatment received. Stabilized inverse probability weights accounted for men who missed study visits and multiple imputation addressed additional missingness. Live birth was ascertained for all participants from pregnancies occurring within 9 months of enrollment.

Results: Among couples utilizing OI only or no treatment (n=1377), the lowest quartile of each semen parameter was associated with 13 to 22 fewer live births per 100 couples, relative to the highest quartile. Among couples utilizing IUI (n=613), the lowest quartile of concentration, count, and total motile count, were associated with 6 to 9 fewer live births per 100 couples. Associations were largely null among participants utilizing IVF (n=380). Thirty-five percent of couples attained a live birth.

Conclusions: In this large study of couples intending fertility treatment, low semen quality was associated with reduced probabilities of live birth among couples utilizing non-IVF treatments or no fertility treatment. IVF appeared to overcome the impact of reduced semen quality.

Table. Weighted* and adjusted† absolute risk differences ‡ for live birth by quartile of semen parameter across all study visits in the FAZST trial, overall and stratified by fertility treatment received.

Adjusted	IVF	IUI	OI only or none
Volume (mL)			
≤ 2.40	-5.62 (-13.7, 2.46)	-5.37 (-10.8, 0.04)	-1.24 (-5.18, 2.70)
>2.40 – 3.41	-3.02 (-10.4, 4.38)	-4.80 (-10.3, 0.72)	-2.10 (-5.98, 1.75)
3.41 – 4.64	0.57 (-7.03, 8.18)	-3.33 (-9.07, 2.41)	-0.42 (-4.30, 3.45)
>4.64	Referent	Referent	Referent
Motility (%)			
≤ 42.75	-0.86 (-8.96, 7.24)	-0.25 (-5.76, 5.27)	-13.0 (-16.8, -9.14)
>42.75 – 58.5	-2.84 (-10.8, 5.09)	2.45 (-2.94, 7.84)	-0.54 (-4.54, 3.46)
>58.5 – 68.25	-6.61 (-14.8, 1.59)	2.86 (-2.56, 8.26)	1.92 (-2.24, 5.99)
>68.25	Referent	Referent	Referent
Concentration (million/mL)			
≤ 24.0	0.71 (-6.89, 8.31)	-5.63 (-11.2, -0.09)	-21.7 (-25.2, -18.2)
>24.0 – 67.14	-1.88 (-10.0, 6.25)	-3.94 (-9.12, 1.23)	-7.88 (-11.9, -3.87)
>67.14 – 122.5	-3.19 (-11.6, 5.26)	2.88 (-2.69, 8.45)	-4.10 (-8.07, -0.14)
>122.5	Referent	Referent	Referent
Morphology (% normal)			
≤ 2.5	-5.87 (-13.5, 1.75)	-4.44 (-10.1, 1.21)	-18.0 (-21.6, -14.5)
>2.5 – 5.0	-8.88 (-16.7, -1.06)	-1.95 (-7.35, 3.45)	-7.09 (-11.5, -2.65)
>5.0 – 8.0	-1.86 (-10.4, 6.70)	-7.23 (-12.7, -1.75)	-0.45 (-4.51, 3.60)
>8.0	Referent	Referent	Referent
Count (million)			
≤ 68.26	0.87 (-6.84, 8.58)	-9.26 (-14.9, -3.61)	-20.8 (-24.5, -17.2)
>68.26 – 207.96	-4.38 (-12.4, 3.60)	-7.15 (-12.6, -1.67)	-6.13 (-10.2, -2.04)
>207.95 – 443.86	-4.09 (-12.4, 4.23)	-2.35 (-7.93, 3.23)	-3.04 (-7.02, 0.94)
>443.86	Referent	Referent	Referent
Total motile count (million)			
≤ 29.62	4.35 (-4.01, 12.7)	-6.33 (-12.4, -0.25)	-16.9 (-20.9, -12.8)
>29.62 – 118	-0.84 (-9.03, 7.35)	-6.29 (-11.9, -0.63)	-5.48 (-9.57, -1.40)
>118 – 282.8	-3.86 (-12.2, 4.51)	0.70 (-4.90, 6.30)	-0.98 (-4.82, 3.32)
>282.8	Referent	Referent	Referent
DNA fragmentation (%) ‡			
≤ 15.522	Referent	Referent	Referent
>15.522 – 24.646	2.58 (-14.1, 19.2)	4.53 (-7.06, 16.1)	-6.35 (-15.4, 2.72)
>24.646 – 37.803	5.48 (-11.6, 22.0)	10.4 (-2.09, 23.0)	2.33 (-6.99, 11.7)
>37.803	6.03 (-11.2, 23.2)	-5.04 (-16.6, 6.49)	-10.1 (-19.6, -1.15)

* Weighted for stabilized inverse probability of missing study visit at each time point

† Adjusted for log age (continuous), log BMI (continuous) and absence time at visit (≤ 2 days, >2-4 days, >4 days), motility and total motile count additionally adjusted for morphology (continuous)

‡ Estimated using generalized linear models (binomial model with identity link)

§ Measured via the Comet assay, assessed at 6-month study visit only

Longitudinal semen quality in an infertility treatment-seeking population Elizabeth A DeVilbiss* Elizabeth A DeVilbiss Lindsey A Sjaarda C. Matthew Peterson Jim Hotaling James L Mills Pauline Mendola Douglas T. Carrell Erica Johnstone Zhen Chen Neil J. Perkins Ginny Ryan Amy Sparks Rachel Whynott Traci Clemons Sunni L Mumford Enrique F Schisterman

Background: Semen analyses are the cornerstone of male infertility treatment. While guidelines recommend two semen analyses due to inter-test variability, there is a lack of robust data on how semen parameters change over time.

Methods: In a longitudinal study of men (n=2369) seeking infertility care, semen quality was assessed using standardized procedures by quantification of sperm concentration, volume, motility, morphology, count, and total motile count at baseline and 2-, 4- and 6-months post-randomization. The data were analyzed using weighted generalized linear models accounting for repeated study visits per participant; adjusted models accounted for study site, randomized treatment, infertility treatment stratum, male fertility diagnosis at baseline, physical activity, age, BMI, abstinence duration, smoking status, and fever since last visit.

Results: Sperm concentration, morphology, count, and total motile count did not change significantly over 6 months of follow-up. Motility was reduced by 0.9-1.0% at 2- and 4- months follow-up, but did not differ at 6 months relative to baseline. Only semen volume was reduced 0.1 to 0.2 mL from baseline at each of the three follow-up visits. Semen quality parameters were missing for 14%, 27%, and 31% of men at the 2-, 4-, and 6-month study visits, respectively.

Conclusions: Semen parameters did not seem to meaningfully vary over 6 months of follow-up. In similar populations, a single assessment may be sufficient to guide fertility care. While a small decrement in semen volume was observed, the clinical importance of this requires further evaluation.

Table. Weighted longitudinal semen parameters assessed over 6 months among participants in the FAZST trial*

Visit	Unadjusted		Adjusted ^{b,c}	
	Volume	Difference	Volume	Difference
Baseline	3.63 (3.56, 3.70)		3.47 (3.2, 3.74)	
2-month	3.54 (3.47, 3.61)	-0.10 (-0.15, -0.04)	3.40 (3.14, 3.67)	-0.07 (-0.12, -0.01)
4-month	3.50 (3.43, 3.59)	-0.13 (-0.21, -0.05)	3.34 (3.07, 3.61)	-0.12 (-0.20, -0.05)
6-month	3.46 (3.38, 3.54)	-0.18 (-0.27, -0.09)	3.30 (3.03, 3.57)	-0.17 (-0.26, -0.08)
Visit	Motility		Motility	
	Difference	Difference	Difference	Difference
Baseline	53.6 (52.8, 54.4)		45.2 (41.8, 48.6)	
2-month	52.6 (51.7, 53.5)	-1.00 (-1.71, -0.30)	44.3 (41.0, 47.7)	-0.86 (-1.56, -0.15)
4-month	52.5 (51.5, 53.4)	-1.15 (-2.11, -0.18)	44.2 (40.8, 47.6)	-0.97 (-1.92, -0.02)
6-month	53.0 (52.0, 54.0)	-0.57 (-1.67, 0.53)	44.8 (41.4, 48.3)	-0.36 (-1.44, 0.71)
Visit	Concentration		Concentration	
	Difference	Difference	Difference	Difference
Baseline	88.1 (84.3, 91.8)		60.2 (45.7, 74.7)	
2-month	87.8 (83.9, 91.7)	-0.31 (-3.48, 2.88)	61.2 (46.9, 75.6)	1.04 (-2.19, 4.27)
4-month	88.3 (83.8, 92.7)	0.15 (-4.31, 4.61)	61.3 (46.5, 76.0)	1.06 (-3.30, 5.42)
6-month	88.0 (83.2, 92.8)	-0.09 (-5.37, 5.19)	61.3 (46.6, 76.0)	1.11 (-3.89, 6.11)
Visit	Morphology		Morphology	
	Difference	Difference	Difference	Difference
Baseline	5.77 (5.58, 5.96)		4.03 (3.20, 4.85)	
2-month	5.67 (5.48, 5.85)	-0.11 (-0.31, 0.10)	3.95 (3.14, 4.76)	-0.08 (-0.29, 0.13)
4-month	5.79 (5.58, 6.00)	0.02 (-0.24, 0.27)	4.08 (3.25, 4.92)	0.06 (-0.20, 0.31)
6-month	5.86 (5.63, 6.08)	0.08 (-0.20, 0.36)	4.15 (3.31, 4.98)	0.12 (-0.15, 0.40)
Visit	Count		Count	
	Difference	Difference	Difference	Difference
Baseline	308 (291, 326)		195 (125, 296)	
2-month	294 (274, 314)	-14.2 (-22.5, -6.00)	188 (117, 258)	-7.08 (-16.9, 2.76)
4-month	302 (271, 334)	-3.71 (-8.08, 19.4)	193 (119, 267)	-1.88 (-24.8, 21.1)
6-month	292 (261, 330)	-12.8 (-44.8, 19.1)	197 (111, 292)	-8.09 (-36.8, 20.7)
Visit	Total motile count		Total motile count	
	Difference	Difference	Difference	Difference
Baseline	184 (184, 205)		113 (70.2, 156)	
2-month	183 (172, 195)	-11.0 (-18.6, -3.41)	107 (64.2, 149)	-6.48 (-14.5, 1.50)
4-month	188 (171, 205)	-6.03 (-20.7, 8.66)	110 (65.6, 154)	-3.43 (-17.3, 10.5)
6-month	184 (166, 201)	-10.5 (-28.0, 7.03)	106 (61.2, 151)	-7.25 (-23.5, 8.94)

* Parameters weighted for stabilized inverse probability of missing study visit at each time point; motility includes % progressive motile and % non-progressive motile, morphology is quantified as % normal forms, count is calculated as concentration*volume, and total motile count is calculated as volume*concentration*motility.
^b Time-invariant covariates: Site, treatment, stratum, male fertility diagnosis at baseline, exercise tertile at baseline, log age (continuous) and log BMI (continuous) at baseline.
^c Time-dependent covariates include parameters assessed at study visit: abstinence time (≤ 2 days, >2 days, >4 days), smoking status (non-smoker, yes - last cigarette >24 hours, yes - last cigarette ≤24 hours), fever since last visit (none, 99.0-100.4°F, 100.4-102.2°F, temp >102.2-105.0°F)

Impact of COVID-19 on Physical Activity in Pregnant Women using Objective Measures

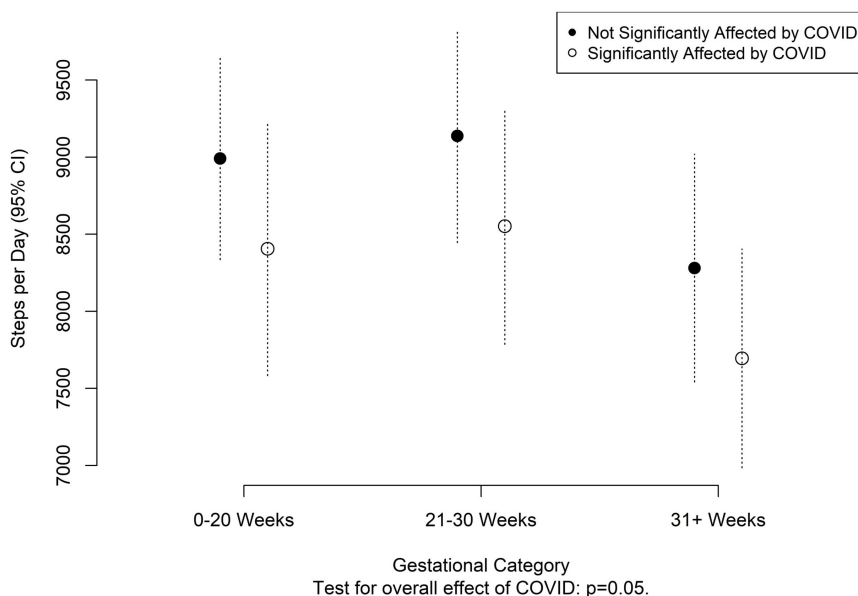
Susan Park* Susan Park John W. Staudenmayer Robert T. Marcotte Scott J. Strath Patty S. Freedson
Lisa Chasan-Taber

Purpose: Physical activity has been shown to decline throughout pregnancy. In March of 2020, restrictions due to the COVID-19 pandemic led to drastic changes in the work-life balance for many U.S. women. We examined the impact of the COVID-19 pandemic on patterns of physical activity in women at various stages of pregnancy.

Methods: We used data from the prospective Physical Activity in Pregnancy Study conducted from April 2019 to January 2021. Pregnant women (N= 46) wore an ActiGraph GT3X on the non-dominant wrist for three weeks: once during early, middle, and late pregnancy. After March 2020, participants were asked in each measurement session to self-report whether and how their lifestyle was significantly affected by the COVID-19 pandemic. Steps per day were downloaded from the ActiGraph at the end of each week. ActiGraph wear time was based upon self-report or, if missing, using the Choi wear time algorithm. Only participants with 10 hours of wear time for at least 4 days were included. Linear mixed effects regression models adjusted for gestational age, pre-pregnancy BMI, parity, and age were used to estimate the effects of COVID-19 on steps per week.

Results: Women had a mean age of 32.7 years (SD 4.14), 52% were overweight/obese, and 1.17 (1.40) children. In early, middle, and late pregnancy, 17%, 35%, and 61% of the women reported being significantly affected by COVID-19, respectively. Compared to those not significantly affected by the pandemic, women who were affected accumulated 600 fewer steps/day (95% CI: -1,214, 5) in adjusted analyses ($p=0.05$).

Conclusions: Findings suggest the negative impact of the pandemic on steps during pregnancy. Given the benefits of maintaining adequate physical activity during pregnancy, findings may have important implications for intervening to prevent subsequent adverse maternal and fetal health outcomes among women who were pregnant during COVID-19.



Patterns of anti-hypertensive medication use in pregnancy and risk of SMM in individuals with pre-pregnancy hypertension Shalmali Bane* Shalmali Bane Suzan Carmichael Elizabeth Wall-Wieler Maurice Druzin

Chronic hypertension is a known driver of severe maternal morbidity (SMM). Anti-hypertensive medications (Anti-HT meds) like ACE-inhibitors and ARBs are not recommended during pregnancy due to risk of adverse fetal outcomes; medications like Labetalol or Methyldopa are recommended instead. The impact of specific classes of anti-HT meds during pregnancy on the fetus is documented; there is limited research on the impact on maternal health.

Our objective was to assess the impact of patterns of anti-HT med use in pregnancy (not recommended, safe, stopped) on risk of SMM in those with chronic hypertension. Our cohort consisted of pregnancies (resulting in live birth or stillbirth) in the Optum database from July 2007-Oct 2017 with adequate coverage, a chronic hypertension diagnosis and a prescription for anti-HT meds 6 months prior to pregnancy (n = 11,759). SMM from birth to 42 days postpartum was defined per the CDC definition of 21 indicators. RRs were computed using modified Poisson regression with robust standard errors and adjusted for maternal age, education and birth year. Overall, 83% of births were associated with filling an anti-HT prescription during pregnancy, and 6.3% with SMM. When medication was stopped during pregnancy, the 95% CI crossed 1 for pre-pregnancy safe- (adjusted RR: 0.91, 95% CI 0.67, 1.23) and not recommended med use (1.20, 95% CI 0.91, 1.58). Compared to those using safe anti-HT meds pre- and in pregnancy (42% of births), risk of SMM was higher when switching from safe to not recommended (2.7, 95% CI 1.8, 4.1, 1% of births), not recommended to safe (1.4, 95% CI 1.2, 1.8, 14%), and using not recommended meds pre- and in pregnancy (1.5 95% CI 1.2, 1.7, 26%).

This study provides evidence that choice of anti-HT medications before and during pregnancy is associated with SMM, in addition to the known impact on fetal outcomes. Further work is needed to establish if this is due to hypertension severity, pregnancy planning, or quality of care.

Subsequent risk of stillbirth, preterm birth, and small for gestational age: A cross-outcomes analysis of adverse birth outcomes in California women from 1997-2011 Shalmali Bane* Shalmali Bane Suzan Carmichael Julia Simard

Individuals who experience an adverse birth outcome like stillbirth, preterm birth, or small for gestational age (SGA) have an increased risk of outcome recurrence in a subsequent pregnancy. There is limited research on these cross-outcome risks, i.e., given an adverse outcome in index pregnancy, the risk of a different adverse outcome in subsequent pregnancy. Therefore, we assessed the cross-outcome risk in subsequent pregnancy given stillbirth, preterm birth, or SGA in the index birth.

We used birth certificate and fetal death data from 1997-2011 for all California births. Stillbirth was defined as delivery at ≥ 20 weeks of gestation of a fetus that died in utero; preterm birth as live birth at 20-36 weeks; and SGA as birthweight < 10 th percentile for infants of the same sex and gestational age. RRs were computed using modified Poisson regression, accounting for correlation between individuals with multiple birth pairs; models were adjusted for variables known to be associated with adverse birth outcomes (e.g., maternal age).

Of 1,973,807 births, 0.6%, 6.4%, and 10.7% of index births were stillborn, preterm, and SGA, respectively. Individuals experiencing a stillbirth at index birth had an adjusted RR 1.97 (95% CI 1.88, 2.08) for the next birth being preterm and 1.39 (95% CI 1.31, 1.47) for subsequent SGA. Among those with preterm birth at index birth, the adjusted RRs were 2.16 (95% CI 2.00, 2.32) and 1.47 (95% CI 1.45, 1.49) for stillbirth and SGA. Among those with SGA at index birth, the adjusted RRs were 1.57 (95% CI 1.46, 1.68) and 1.52 (95% CI 1.50, 1.55) for stillbirth and preterm birth.

Individuals experiencing an adverse outcome in one pregnancy had an increased risk of a different adverse outcome in a subsequent pregnancy. These findings support the relatedness of the outcomes (due to behavioral or biological etiologies) and could inform reproductive planning discussions for individuals experiencing an adverse birth outcome, if subsequent pregnancy is desired.

Baseline Characteristics of Hispanic women with Pregnancy Hyperglycemia: Estudio Parto

Madhuri Palnati* Madhuri Palnati Lisa Chasan-Taber Bess Marcus Katherine Tucker Penelope Pekow Maegan Harvey Milagros Rosal

Women who develop glucose intolerance during pregnancy are at high risk for the subsequent development of type 2 diabetes. Thus, pregnancy and postpartum are critical time-periods for interventions designed to prevent subsequent onset of diabetes in vulnerable populations. We investigated the prevalence of diabetes risk factors using baseline data from Estudio Parto, a randomized controlled trial of 204 Hispanic women with pregnancy hyperglycemia conducted from 2013-17 in Western Massachusetts. The Pregnancy Physical Activity Questionnaire was used to assess meeting ACOG guidelines for physical activity. Depression was measured using the Edinburgh Postpartum Depression Scale (EPDS) and diet was assessed by three 24-hour dietary recalls. Acculturation was assessed via the Psychological Acculturation Scale and sleep quality via the Pittsburgh Sleep Quality Index (PSQI). Participants were young (mean age = 27.7 years), 77% were overweight or obese, 44% were born outside the US, 76% had low acculturation; mean PSQI score was 6.9 (SD 4.3) indicating poor sleep quality and 15% had at least probable minor depression (EPDS>13). Almost half of participants (45%) had isolated hyperglycemia, 20% had impaired glucose tolerance and 35% had gestational diabetes mellitus. One-third (34%) met ACOG guidelines for physical activity and 8% planned to exclusively breastfeed. Diet quality was low, with only one quarter of participants meeting the American Diabetes Association recommendations for total fat (26%); fewer met guidelines for saturated fat (22%), fiber (4%), and sodium (19%). Of the 25% participants who smoked before pregnancy, 6% continued smoking. Of the 50% who consumed alcohol before pregnancy, 26% continued consumption. Findings demonstrate the need to support this at-risk population in making healthy lifestyle changes during pregnancy, thereby ultimately decreasing diabetes risk.

A prospective study of time to pregnancy and incidence of spontaneous abortion Amelia K Wesselink* Jennifer Yland Amelia K Wesselink Elizabeth E Hatch Tanran R Wang Kenneth J Rothman Lauren A Wise

Background: Time to pregnancy (TTP) may be an important confounder in studies of preconception exposures and spontaneous abortion (SAB). Several studies have indicated that subfertility may increase risk of SAB but results are inconclusive.

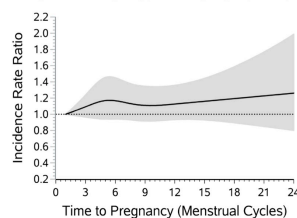
Objective: To prospectively evaluate the association between TTP and SAB.

Methods: Pregnancy Online Study (PRESTO) is a web-based preconception cohort of couples in the U.S. and Canada aged 21-45 years. At baseline, participants reported the typical length of their menstrual cycle and the number of menses they had since they began trying to conceive. Data on menstrual cycle dates, pregnancy status, SABs (including gestational week of SAB), and covariates were collected from baseline and follow-up questionnaires. TTP was calculated as the total attempt time in menstrual cycles. Among female participants who conceived during follow-up, we estimated incidence rate ratios (IRRs) and their 95% confidence intervals. We fit Cox models, using gestational weeks as the time scale. We also fit a restricted cubic spline model to allow for a non-linear relation between TTP and SAB.

Results: Among 6,325 participants, 19% reported a SAB. 7% of couples conceived using fertility treatments. Overall, 63% of couples conceived within 6 cycles, and 90% of couples conceived within 12 cycles. Compared with participants who conceived within 2 menstrual cycles, the IRRs for those who conceived in 3-5, 6-11, or ≥ 12 menstrual cycles were 1.06 (95% CI: 0.90, 1.26), 1.06 (95% CI: 0.89, 1.25), and 1.07 (95% CI: 0.86, 1.33), respectively. Results were similar when we stratified by body mass index (<25 vs. ≥ 25 kg/m²) and gestational age (<8 vs. ≥ 8 weeks). Among women ≥ 30 years of age, the IRR comparing those with TTP ≥ 12 cycles to those with TTP <3 cycles was 1.23 (95% CI: 0.91, 1.65). The spline indicated a weak positive association between TTP and SAB.

Conclusion: In this prospective preconception cohort study, TTP was not appreciably associated with SAB.

Figure 1. Restricted cubic spline for the association between time to pregnancy (menstrual cycles) and incidence of spontaneous abortion, among 6,325 PRESTO participants (2013-2020)



Spline modeled with knots at the 25%, 50%, 75%, and 90% percentiles of time to pregnancy (3, 5, 9, and 12 cycles). Adjusted for maternal age at conception, body mass index, marital status, race/ethnicity, current smoking, education, income, region, type of health insurance, physical activity, alcohol intake, caffeine intake, sugar sweetened beverage intake, use of multivitamins or folic acid supplements, major depression inventory score, perceived stress scale score, night's sleep duration, most recent method of contraception, parity, endometriosis, fibroids, and polycystic ovarian syndrome, history of spontaneous abortion.

A prospective study of pregravid contraceptive use and incidence of spontaneous abortion

Amelia K Wesselink* Jennifer Yland Elizabeth E Hatch Amelia K Wesselink Ellen M Mikkelsen
Kenneth J Rothman Lauren A Wise

Background: The effects of contraceptives on the endometrium and endogenous hormone levels may persist after discontinuing use. The relationship between pregravid contraceptive use and spontaneous abortion (SAB, pregnancy loss < 20 weeks' gestation) is poorly understood.

Methods: We evaluated the association between pregravid contraceptive use and SAB in Pregnancy Online Study (PRESTO), a North American preconception cohort study of couples aged 21-45 years. At baseline, we collected data on contraceptive history and select covariates. On follow-up questionnaires, participants reported the date of their last menstrual period, their current pregnancy status, pregnancy loss since the previous follow-up, and the gestational weeks and date of SAB (if applicable). Among women who conceived in fewer than 6 menstrual cycles, we used Cox models to estimate incidence rate ratios (IRRs) and 95% CIs using gestational weeks as the time scale.

Results: Overall, 19% of 3,388 participants reported SAB. 18% of women had used natural contraceptive methods (*e.g.*, withdrawal) most recently, 32% combined oral contraceptives (COCs), 15% progestin intrauterine devices (IUD), 4% copper IUDs, 4% vaginal rings, 2% implants, and 1% injectable contraceptives. There was little association between contraceptive method and SAB for COCs (IRR = 1.09; 95% CI: 0.86, 1.38), progestin IUDs (IRR = 1.07; 95% CI: 0.81, 1.41), vaginal rings (IRR = 1.07; 95% CI: 0.70, 1.63), and implants (IRR = 0.97; 95% CI: 0.51, 1.81), compared with natural methods. IRRs were 1.15 for copper IUDs (95% CI: 0.76, 1.74) and 3.21 for injectables (95% CI: 1.74, 5.93). Selected associations were stronger among women aged ≥ 30 years (copper IUDs: IRR=1.33; 95% CI: 0.77, 2.29) and among women with BMI <25 (injectables: IRR=7.26, 95% CI: 3.22, 16.37).

Conclusion: Pregravid use of some hormonal contraceptives may be associated with SAB risk.

Nitrate in drinking water during pregnancy and spontaneous preterm birth: A retrospective within-mother analysis Allison Sherris* Allison Sherris Mike Baiocchi Scott Fendorf Stephen P. Luby Wei Yang Gary M. Shaw

Background: Nitrate is a widespread groundwater contaminant and leading cause of drinking water quality violations in California. Associations between nitrate exposure and select adverse birth outcomes have been suggested, but few studies have examined gestational exposures to nitrate and risk of preterm birth (before 37 weeks gestation).

Objective: We investigated the association between elevated nitrate in drinking water and spontaneous preterm birth through a within-mother retrospective cohort study of births in California.

Methods: We acquired over six million birth certificate records linked with hospital discharge data for California births from 2000-2011. We used public water system monitoring records to estimate nitrate concentrations in drinking water for each woman's residence during gestation. After exclusions, we constructed a sample of 1,443,318 consecutive sibling births in order to conduct a within-mother analysis. We used separate conditional logistic regression models to estimate the odds of preterm birth at 20-31 and 32-36 weeks, respectively, among women whose nitrate exposure changed between consecutive pregnancies.

Results: Spontaneous preterm birth at 20-31 weeks was increased in association with tap water nitrate concentrations during pregnancy of 5-10 mg/L (OR=1.47, 95% CI=1.29-1.67) and ≥ 10 mg/L (OR=2.52, 95% CI=1.49-4.26) compared with < 5 mg/L (as nitrogen). Smaller associations were observed for spontaneous preterm birth at 32-36 weeks. Our findings were similar in several secondary and sensitivity analyses including in a conventional case-control design.

Discussion: The results suggest that nitrate in drinking water is associated with increased odds of spontaneous preterm birth. Notably, we estimated modest increased odds at concentrations below the federal drinking water standard of 10 mg/L.

Mothers' reproductive history and spontaneous abortion in daughters Anne Sofie D. Laursen*
 Anne Sofie D. Laursen Elizabeth E. Hatch Lauren A. Wise Kenneth J. Rothman Henrik T. Sørensen
 Olga Basso Ellen M. Mikkelsen

Little is known about the relationship between mothers' reproductive history and daughters' spontaneous abortion (SAB). We investigated the association between mothers' history of subfertility and SAB and risk of SAB among daughters in a Danish cohort of couples trying to conceive spontaneously. We ascertained pregnancies from bimonthly questionnaires and restricted the sample to 7,122 women who became pregnant within one year of study entry. Mothers' subfertility and history of SAB were self-reported by daughters at study entry using the questions; "Did your mother have trouble conceiving?" and "Did your mother experience SABs?" (*yes, no, do not know*). Daughters' SABs were identified in the Danish National Patient Registry and by self-reported follow-up data. We used Cox proportional hazards regression models with gestational weeks as the time scale to compute hazard ratios (HRs) with 95% CIs for SAB, adjusting for parental education and mothers' smoking during pregnancy. We identified 1,111 SABs. Fourteen percent of pregnant women reported that their mother had trouble conceiving and 21% that their mother had at least one SAB. Women whose mothers had trouble conceiving had slightly longer time-to-pregnancy, more frequently reported that their mothers had SABs and reported lower educational attainment of their mothers compared with women whose mothers did not have trouble conceiving. Women who reported that their mother had trouble conceiving had a higher rate of SAB (HR: 1.19, 95% CI: 1.00-1.41) compared with women who reported "no", while "not knowing" was not associated with SAB (HR: 0.94, 95% CI: 0.80-1.12). We did not observe meaningful associations between mothers' history of SAB and SAB in daughters. These results indicate that mothers' subfertility is associated with a higher risk of SAB in daughters. In further analyses, we will investigate the influence of mothers' age, number of children and sisters' SABs as well as impute "not knowing".

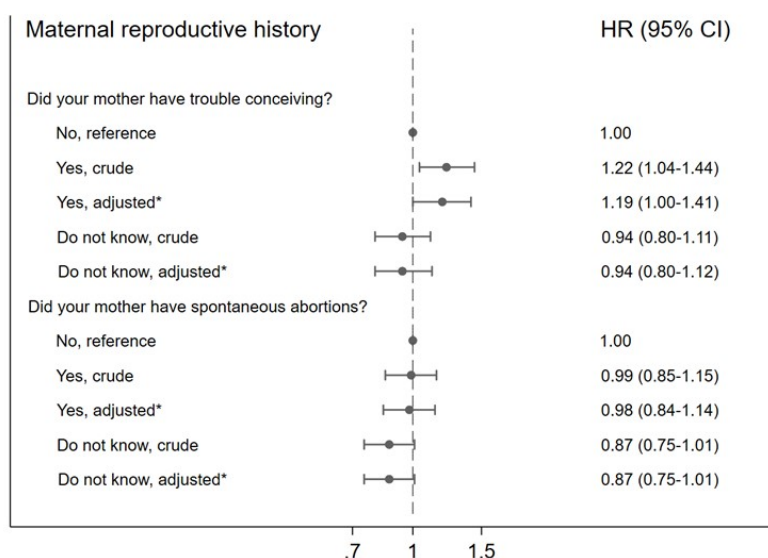
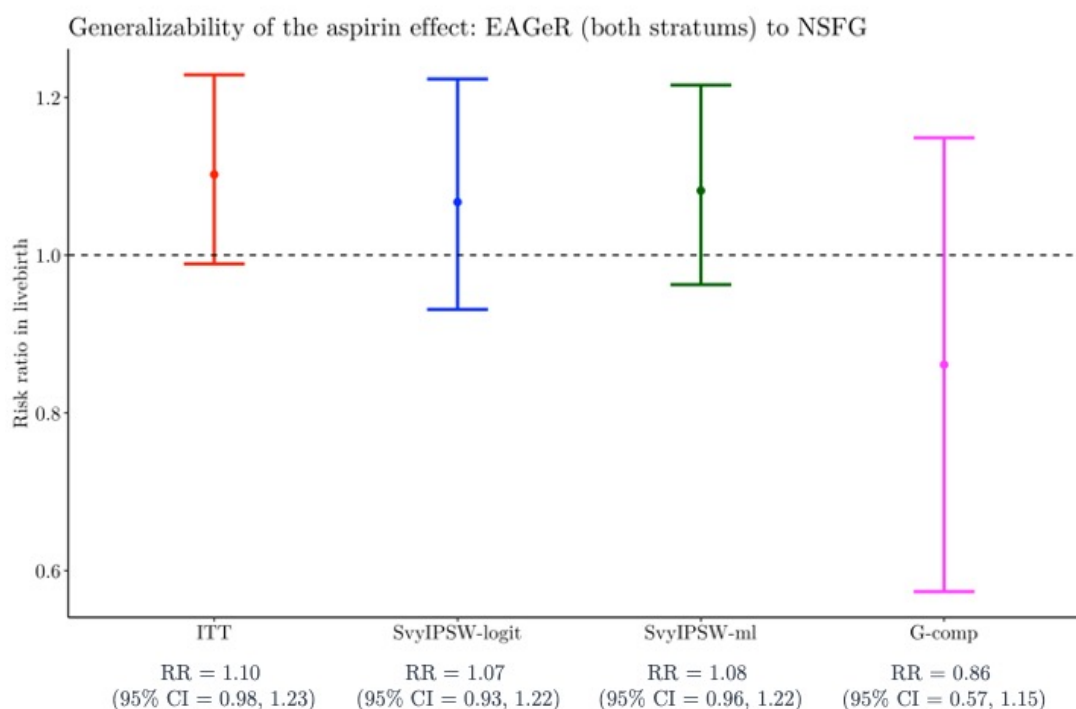


Figure 1. Maternal reproductive history and spontaneous abortion in daughters. *Adjusted for maternal and paternal educational attainment and maternal smoking during pregnancy.

Generalizing evidence from the effects of aspirin in gestation and reproduction (EAGeR) trial to the general U.S. population. Gabriel Conzuelo-Rodriguez* Gabriel Conzuelo-Rodriguez Ashely I. Naimi

Pregnancy loss is the most common complication of human reproduction. Aspirin is hypothesized to reduce the risk of subsequent losses when administered early in gestation. Under this premise, the Effects of Aspirin in Gestation and Reproduction (EAGeR) trial was devised to evaluate the benefits of preconception daily low-dose aspirin in women with a previous pregnancy loss. However, as is common, EAGeR participants were not sampled randomly from its target population, jeopardizing the generalizability of its findings. Here, we use the parametric g-formula and inverse probability of sampling weights (IPSW), to generalize EAGeR results to a more representative sample of US women. EAGeR enrolled 1,228 women 18 to 40 years with a previous pregnancy loss. Effect modifiers for our study consisted of age at conception, body mass index, race, income, education and marital status. Data from the National Survey of Family Growth (NSFG) were used to construct a sample of women with similar eligibility criteria that better reflected the diversity in the US population. Compared to EAGeR, the NSFG sample had a lower proportion of women classified as non-Hispanic White (5.4% and 22.8%), high-school education (86.2% and 68.7%), and married (91.5% and 60.5%). Treatment effects are presented in Figure 1. In the original EAGeR trial, women who were assigned to aspirin were 1.10 times as likely to have a livebirth compared to those in placebo (95%CI = 0.98, 1.23). Generalizing results using IPSW yielded similar findings, regardless of whether logistic regression or machine learning was used for the sample membership model. However, the g-formula yielded a risk ratio of 0.86; with 95% CI = 0.57, 1.15. Important limitations should be considered, including absence of adherence data in the target population and need for unverifiable modeling assumptions. Currently, our generalizability estimates are consistent with the original EAGeR trial findings.



LATEBREAKER

Reproductive

The association between established diet quality indices and gestational weight gain in Hispanic women Sofija Zagarins* Sofija Zagarins Megan Harvey Katherine Tucker Bess Marcus Milagros Rosal Tiffany Moore Simas JoAnne Manson Glenn Markenson

Maternal diet is a contributing factor to gestational weight gain (GWG). However, it remains unclear whether adherence to recommended dietary guidelines or healthful dietary patterns is associated with adequate GWG, as defined by the Institute of Medicine (IOM). Hispanic women in the US have higher rates of excess GWG than the general population, and dietary quality tends to be lower in certain US Hispanic groups, including Puerto Ricans. We evaluated these associations using data from 168 Hispanic (predominantly Puerto Rican) participants enrolled in Estudio PARTO, a randomized controlled trial conducted in Western Massachusetts (2013-17). Trained bicultural/bilingual personnel assessed diet at a mean \pm SD of 28.6 \pm 6.3 weeks gestation via 3 24-hour recalls. We calculated the Healthy Eating Index 2015 (HEI-2015), Alternate Healthy Eating Index 2010 (AHEI-2010), alternate Mediterranean Diet Score (aMED), and Healthy Plant-Based Diet Index (HPDI). Mean GWG was 27.9 \pm 16.0 pounds, with 22.8% of participants meeting the IOM guidelines for adequate GWG, and 56.9% exceeding guidelines. Mean diet scores were 54.9 \pm 14.6 (HEI-2015), 36.5 \pm 11.6 (AHEI-2010), 24.4 \pm 5.5 (aMED), and 51.8 \pm 7.7 (HPDI). Diet scores were all higher (indicating better dietary quality) in women who were less acculturated; among those reporting Spanish, vs. English as their primary language, scores ranged from 2.14 (HPDI; $P=0.03$) to 7.7 (HEI-2015; $P=0.003$) points higher. Diet scores were not significantly associated with GWG in linear regression models adjusted for age, pregnancy activity level, energy intake, and intervention arm. Each one-SD increase in diet score was associated with a 0.55 to 1.02-pound decrease in GWG (all $P>0.05$). Findings suggest that existing diet indices may have limited utility in predicting GWG in Hispanic women. Future research should explore the association between acculturation and dietary quality, as well as the development of diet indices specific to a Hispanic population.

LATEBREAKER

Reproductive

Outcomes after controlled ovarian stimulation and embryo transfer in women with cancer: a systematic review and meta-analysis Clare Meernik* Clare Meernik Charles Poole Stephanie Engel Mary Peavey Barbara Luke Hazel Nichols

Cancer and its treatment can increase infertility risk and may necessitate assisted reproductive technology (ART) to achieve pregnancy. However, current evidence gaps may contribute to lack of knowledge and utilization of ART. We conducted a systematic review and meta-analysis of studies comparing ART outcomes between women with and without cancer after controlled ovarian stimulation and embryo transfer. PubMed, Embase, and Scopus were searched for studies that evaluated any of the following: length of ovarian stimulation; gonadotropin dose; peak estradiol; total or mature oocytes retrieved; fertilization; embryos obtained; oocyte/embryo survival after thaw; implantation; cycle cancellation; pregnancy; or live birth. Of 5,241 unique records identified, 40 studies met inclusion criteria, representing a median per study of 52 women with cancer and 114 women without cancer. Random-effects models were used to calculate mean differences (MD) (continuous outcomes) and risk ratios (RR) (binary outcomes) with 95% prediction intervals (PI). Preliminary analyses of stimulation length, gonadotropin dose, peak estradiol, total and mature oocytes, and cycle cancellation indicate substantial among-study heterogeneity. No differences were observed in the number of embryos obtained among women with vs. without cancer ($k=8$; MD = -0.18, 95% PI: -1.15, 0.79), nor in the clinical pregnancy rate ($k=7$; RR=0.75, 95% PI: 0.36, 1.57) or live birth rate ($k=8$; RR=0.77, 95% PI: 0.30, 1.98). Further analyses are ongoing, including subgroup analysis and meta-regression to examine the influence of study characteristics, such as cancer type, indication for ART among controls, age at ART, and timing of ART initiation relative to cancer treatment. This review will provide an updated and comprehensive synthesis of ART outcomes among women with cancer, which can aid clinicians and cancer patients in more informed discussion of the expected success of ART relative to a non-cancer population.

LATEBREAKER

Reproductive

The Variations in the Effect of Foreign-Born Status (FBS) on Sexually Transmitted Infections among Expecting Mothers by Race/Ethnicity Akaninyene Noah* Akaninyene Noah Ashley Hill Maria Perez-Patron Camilla Comeaux Brandie Taylor

Prior research on the Hispanic paradox and healthy migrant effect show foreign-born status (FBS) offers some protective effect against adverse birth outcomes—although its magnitude can differ by race/ethnicity. Sexually transmitted infections (STI) are associated with adverse birth outcomes such as preterm birth and growth restriction. However, studies have yet to examine (1) the link between FBS and common STIs among pregnant women and (2) if these associations vary by race/ethnicity. Our study population included 38,786 singleton pregnancies, mean age of 29.3 years, enrolled in Peribank between July 2011 and September 2020. The population was 21% non-Hispanic (NH) White, 15% NH Black, 58% Hispanic, and 6% other race. Fifty-two percent were born outside the US. We examined the association between FBS and *Neisseria gonorrhoeae* (GC), syphilis, and *Chlamydia trachomatis* (CT), prevalent in 0.5%, 4% and 0.7% of the cohort. We conducted a stratified analysis using logistic regression to calculate odds ratios (OR) and 95% confidence intervals (CI) for the entire population and subgroups by race/ethnicity, the penalized likelihood approach was used when needed. Our model was adjusted for age, socioeconomic variables, substance use, chronic health conditions, co-infections, and prior maternal complications. We examined all three STIs, combined and individually, and noticed similar results. Before stratification, FBS was associated with lower odds of combined infection (OR 0.8, 95%CI 0.7 - 0.9) compared to US born women. After stratification, FBS was only associated with lower odds of infection among NH Blacks (OR 0.6, 95%CI 0.4 - 0.8). NH Whites (OR 0.5, 95%CI 0.2 - 1.2) and Hispanics (OR 0.9, 95%CI 0.7 - 1.0) did not show significant association with infection. Future studies should examine factors that may reduce STI odds, especially among FB NH Black women to shape prevention strategies.

LATEBREAKER

Reproductive

A prospective cohort study of cervical dysplasia and time-to-pregnancy. Mette L. Kristensen*
Mette L. Kristensen Marianne Waldstrøm Anne Sofie D. Laursen Katrine Eriksen Sinna P. Ulrichsen
Elizabeth E. Hatch Lauren A. Wise Kenneth J. Rothman Ellen M. Mikkelsen

Genital infections with human papillomavirus (HPV) can lead to cervical dysplasia. The prevalence of HPV infection is 25% in Danish women <30 years. We investigated the association between cervical dysplasia and fecundability, defined as the probability of conceiving per menstrual cycle, in two Danish preconception cohorts. Participants completed a baseline questionnaire on sociodemographic, anthropometric and lifestyle factors, and reproductive and medical history. Bimonthly follow-up questionnaires obtained data on pregnancy status and date of last menstrual period. Data on cervical cytologies and biopsies were retrieved from The National Pathology Registry, which holds records of all cervical specimens examined in Denmark. Women were categorized based on their most severe diagnosis of cervical dysplasia within ten years before study entry. We included 9,523 women: 68.9% with normal cells, 10.8% with mild dysplasia, 2.1% with moderate dysplasia, 5.4% with severe dysplasia, and 12.7% with other non-malignant cervical diagnoses. We computed fecundability ratios (FR) and 95% confidence intervals (CI) using a proportional probabilities regression model. Women contributed cycles from study entry until pregnancy, initiation of fertility treatment, loss to follow-up or end of follow-up (12 cycles) whichever came first. We adjusted for potential confounders in the analyses. Compared with normal cells, FRs for dysplasia were mild, 1.05 (95% CI 0.97-1.14); moderate, 0.97 (95% CI 0.81-1.17); and severe, 0.96 (95% CI 0.86-1.08). When stratifying by time since diagnosis the FRs for diagnosis <2 years before study entry were 0.72 (95% CI 0.51-1.01) for moderate dysplasia and 0.87 (95% CI 0.72-1.05) for severe dysplasia compared with normal cells. Preliminary results indicate little overall association between severity of cervical dysplasia and fecundability, whereas there may be a slight reduction in fecundability for recent diagnosis of moderate dysplasia.

Assessing Physical and Mental Health Functioning Among Those with Comorbid COPD and Depression: Findings from the World Trade Center Health Registry Cristina D. Pollari*

Cristina Pollari Jennifer Brite Howard E. Alper James E. Cone

Chronic obstructive pulmonary disease (COPD) continues to be one of the leading causes of death in the United States and impacts quality of life. Prior research has demonstrated an association between COPD and depression in the general population, but no study has investigated this relationship among 9/11 survivors. We examined the prevalence of post-9/11 onset comorbid COPD and depression and its association with physical and mental health functioning.

We examined 3,925 enrollees from the World Trade Center Health Registry's Health & Quality of Life 15 Years After 9/11 Survey. Physician diagnosed COPD was self-reported. Depression was assessed using the Patient Health Questionnaire 8-item and total scores were categorized as probable depression (≥ 10) versus no probable depression (< 10). We created a four-level variable that included comorbid COPD and depression, COPD only, depression only, and no COPD or depression. Physical and mental health functioning was determined by the SF-12, a 12-item measure with 8 health domains, which create composite physical and mental health scores, with higher scores indicating greater functioning. Multivariable linear regression was used to examine the association between comorbid COPD and depression with physical and mental health functioning, controlling for covariates.

Among those with post-9/11 onset COPD, 38% had comorbid post-9/11 depression. Those with comorbid COPD and depression had an 8.82 (95% CI: -11.18, -6.45) point decrease in physical health composite score and a 17.58 (95% CI: -20.41, -14.75) point decrease in the mental health composite score, compared to those without either COPD or depression. Those with COPD only or depression alone also showed a reduction in physical and mental health functioning, but not at the extent of the comorbid group.

Our findings suggest physical and mental health functioning is significantly impaired among those with comorbid COPD and depression.

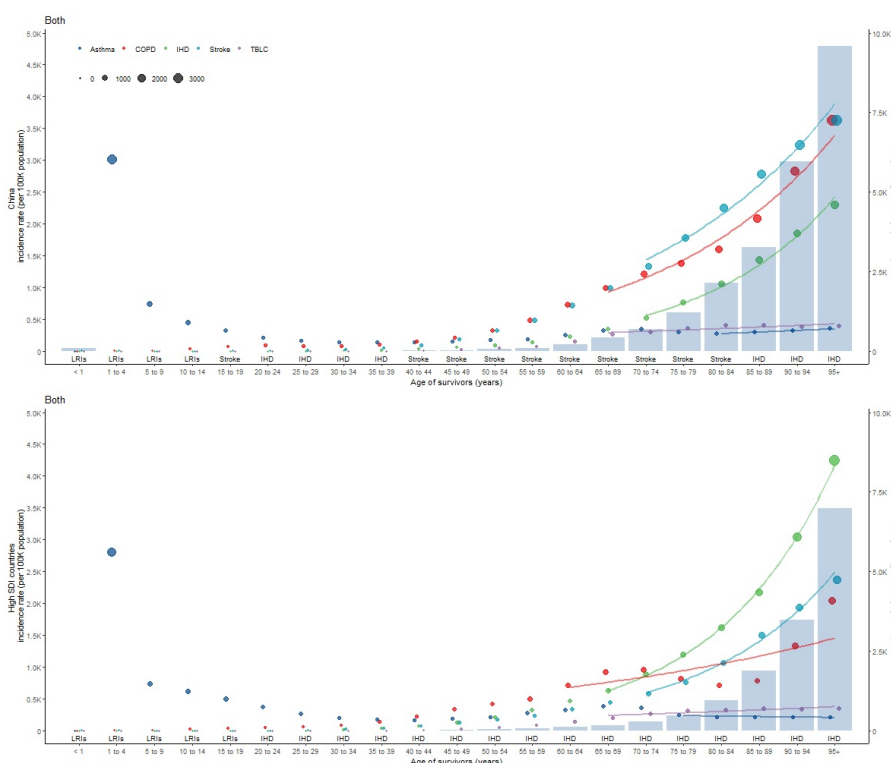
Comparison of COPD patterns between China and high socio-demographic index countries using summary statistics from the Global Burden of Disease Study 2017 Zhao Yang* Zhao Yang CM Schooling Man Ki Kwok

Background: China has developed rapidly recently with increasing concern about air pollution, and triple the chronic obstructive pulmonary disease (COPD) mortality rate compared to high socio-demographic index (SDI) countries. Few studies have explored possible reasons. Established risk factors (e.g., smoking and air pollution) are key, but cannot fully explain the difference. This study explored explanations for these differences.

Methods: We described age-standardized COPD patterns in China and high SDI countries, compared rankings for six well-established COPD risk factors, and estimated change points in age-specific incidence and mortality for COPD and its co-morbidities based on the Global Burden of Disease Study 2017.

Results: Trends in age-standardized incidence and mortality rates of COPD in China and high SDI countries declined and converged during 1990-2017, but differences remained, especially in age-standardized mortality. Smoking was the leading attributable risk factor followed by ambient air pollution, with higher ranking for occupational risks in China than in high SDI countries. The change point was ~80 years for age-specific COPD mortality in both China and high SDI countries. However, the change point for incidence was 5-year later in China (~65 years) than in high SDI countries (~60 years), as shown in **Figure 1**. The change points for mortality due to COPD co-morbidities (e.g. ischemic heart disease and stroke) also varied between settings (**Figure 1**).

Conclusions: Differences in risk factors largely shaped the differences in COPD patterns between China and high SDI countries. Varying patterns of mortality due to co-morbidities might also contribute to the discrepancy in mortality rates, by affecting competing risks of death.



Recruitment strategies and response rates in a national prospective colorectal cancer screening cohort: results from year 1 of the Voyage study Kathleen J. Yost* Kathleen Yost Amy L. Weaver Rachel E. Carlson Christine R. Kirt Emily J. Kirsch David K. Edwards V. Bonny Kneeder Jennifer J. Lafflin Jennifer L. St. Sauver Lila J. Finney Rutten Janet E. Olson

Background

Long term outcomes of individuals screened for colorectal cancer (CRC) with the multi-target stool DNA (mt-sDNA) assay (Cologuard®) have not been studied. Mayo Clinic and Exact Sciences Laboratories (ESL) are collaborating on a prospective cohort study (Voyage) of individuals with a Cologuard screening test order. With an enrollment target of 150,000, participant recruitment is critical to achieve study objectives.

Objectives

To assess representativeness of the study sample at different stages of recruitment, and to conduct an embedded incentive trial to maximize participation.

Methods

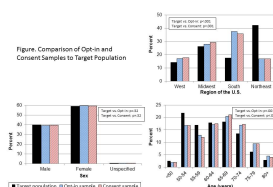
Randomly selected individuals with Cologuard orders received at ESL (target population) are invited to participate in the Voyage study through an initial welcome letter that includes instructions to return an opt-in form to Mayo Clinic. Those who opt-in receive a recruitment packet with a consent form, baseline questionnaire, and return envelope. Distributions by age, sex, and geographic region of participants at both opt-in and consent were compared to those of the target population. A subset of opt-in participants was randomized to receive a book of 20 postage stamps (~\$11 value) with the recruitment packet (pre-incentive) or after the completed questionnaire and consent form were returned (post-incentive).

Results

In the study's first year (10/17/2019 - 9/30/2020), 600,258 individuals were randomly selected and 15,224 (2.5%) opted in. The consent rate among opt-ins prior to the embedded trial was 52.1%; the pre- vs. post-incentive consent rate was 60.8% vs. 52.0% ($p < 0.001$), respectively. The opt-in and consent samples were similar to the target population with respect to sex (both $p = 0.32$) but differed by geographic region and age (all $p < 0.001$; **Figure**).

Conclusion

Pre-incentives were superior to post-incentives and are planned for the remaining recruitment. Future analyses will adjust for possible biases due to differential non-response by age and/or geographic region.



LATEBREAKER

Screening

Missing Permanent Teeth and Regular Cancer Screening among American Indian/Alaska Native Adults: Findings from the 2018 Behavioral Risk Factor Surveillance System Lindsey Manshack* Lindsey Manshack Cristina Oancea

Background: Detailed epidemiologic analyses provide better understanding of and characteristics associated with risks, barriers, and protective factors leading to cancer screenings. American Indian/Alaska Natives (AI/AN) remain severely underrepresented within cancer epidemiologic cohorts, precluding accurate understandings of risks and demographic characteristics that may influence cancer disparities. This study investigated within the AI/AN racial group the association between missing permanent teeth (MPT) and regular cancer screenings among AI/AN adults. Methods: A 2018 Behavioral Risk Factor Surveillance System sample of 6,258 AI/AN respondents with six or more MPT (≥ 6 MPT) were compared to those with less than six MPT (< 6 MPT) using weighted multivariable logistic regression models. Cancer survivors were excluded from the analyses. Models controlled for age, education, employment, income, insurance, marital status, obesity, heavy drinking, and smoking. Results: AI/AN females with ≥ 6 MPT had 54% significantly lower (weighted and adjusted odds ratio (WAOR) 0.46[95%CI:0.26-0.82]) odds of ever receiving breast cancer screening and 81% significantly lower (WAOR 0.19[95%CI:0.11-0.34]) odds of ever receiving cervical cancer screening when compared to their counterparts with < 6 MPT, respectively. Conversely, AI/AN males had 91% significantly higher odds for both, ever having prostate (WAOR 1.91 [95%CI:1.18-3.08]) and colorectal (WAOR 1.91 [95%CI:1.20-3.04]) cancer screenings when compared to their counterparts with < 6 MPT, respectively. Conclusion: Our findings suggest that AI/AN females with ≥ 6 MPT may have increased risk of cancer mortality due to not receiving regular cancer screenings. Investigating within populations often aggregated as monolithic “other” will allow for more targeted cancer prevention techniques which may help reduce the burden of AI/AN cancer mortality.

LATEBREAKER

Screening

A social risk screening tool for identifying patients starting HIV treatment who may benefit from “cash plus” interventions combining financial incentives with other services to support retention in care Carolyn Fahey* Carolyn Fahey Werner Maokola Emmanuel Katararo Rashid Mfaume Prosper Njau Sandra McCoy

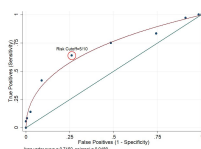
Financial incentives have demonstrated success at improving retention in HIV care, however modest incentives alone may not always sufficiently overcome barriers. To inform future targeting of additional support to those most vulnerable, we developed and evaluated a screening tool to predict risk of loss to follow-up (LTFU) among patients starting antiretroviral therapy (ART) given financial incentives.

We analyzed data from a 2018-2019 randomized controlled trial at 4 clinics in Shinyanga, Tanzania. Intervention participants included 346 adult (≥ 18 years) ART initiates (≤ 30 days) allocated a monthly financial incentive conditional on clinic attendance (\approx US \$4.50 or \$10.00) for ≤ 6 months; 36 (10.4%) were LTFU (≥ 28 days) at 6 months [vs. usual care: 30/184 (16.3%), χ^2 p=0.05]. This analysis identified the optimal set of baseline survey predictors of 6-month LTFU among intervention participants using cross-validated LASSO regression, developed a screening tool from these predictors, and evaluated its classification performance with a ROC curve.

Model-selected ordinal predictors of 6-month LTFU included self-rated health, mental health, education, and employment; summing response levels of these indicators created a risk score (0-10) for each individual (Table). A ‘high risk’ cutoff at 5/10 (Figure) optimized the tradeoff of true positives (63.9%) versus false positives (26.1%) and yielded a sub-group size feasible to target for more intensive support (30%).

A simple 4-item screener administered to individuals starting HIV treatment can help identify future LTFU risk using limited resources. Building on the effectiveness of financial incentives, social risk screening and predictive analytics could enable timely and efficient allocation of complimentary ‘cash plus’ strategies to prevent LTFU, such as combining incentives with social support.

Predictors	Retained in Care (n=310), mean (SD)	Lost to Follow-Up (n=36), mean (SD)	T-test p-value
Self-rated health (0:“excellent” to 4:“poor”)	1.6 (1.0)	2.2 (1.2)	0.001
Feeling no interest in things (0:“not at all” to 3=“extremely”)	0.27 (0.58)	0.64 (0.87)	0.001
Educational attainment (0:>primary, 1:primary, 2:<primary)	1.2 (0.70)	1.4 (0.65)	0.050
Worked in the past week (0:yes, 1:no)	0.39 (0.49)	0.61 (0.49)	0.012
Risk Score (0:lowest to 10:highest)	3.5 (1.5)	4.9 (2.0)	<0.001



Life-course socioeconomic mobility and biological aging in older adults Gloria Huei-Jong Graf* Gloria Huei-Jong Graf Daniel Belsky Yalu Zhang

BACKGROUND. Lower socioeconomic status is associated with faster biological aging, the gradual and progressive decline in system integrity that accumulates with advancing age. Efforts to promote upward social mobility may therefore extend healthy lifespan. However, recent studies suggest upward socioeconomic mobility may have biological costs related to the stresses of crossing social boundaries.

METHODS. We analyzed data from 2016 Health and Retirement Study (HRS), including blood chemistry and DNA methylation data from the Venous Blood Study (n=9286). We quantified biological aging using measures associated with socioeconomic status in prior studies: PhenoAge and GrimAge DNA methylation “clocks”, the DunedinPoAm DNA methylation measure of Pace of Aging, and three blood-chemistry algorithms. We quantified social mobility as rank change from childhood to later life based on participant reports about their family’s economic circumstances in childhood and about household wealth in later life.

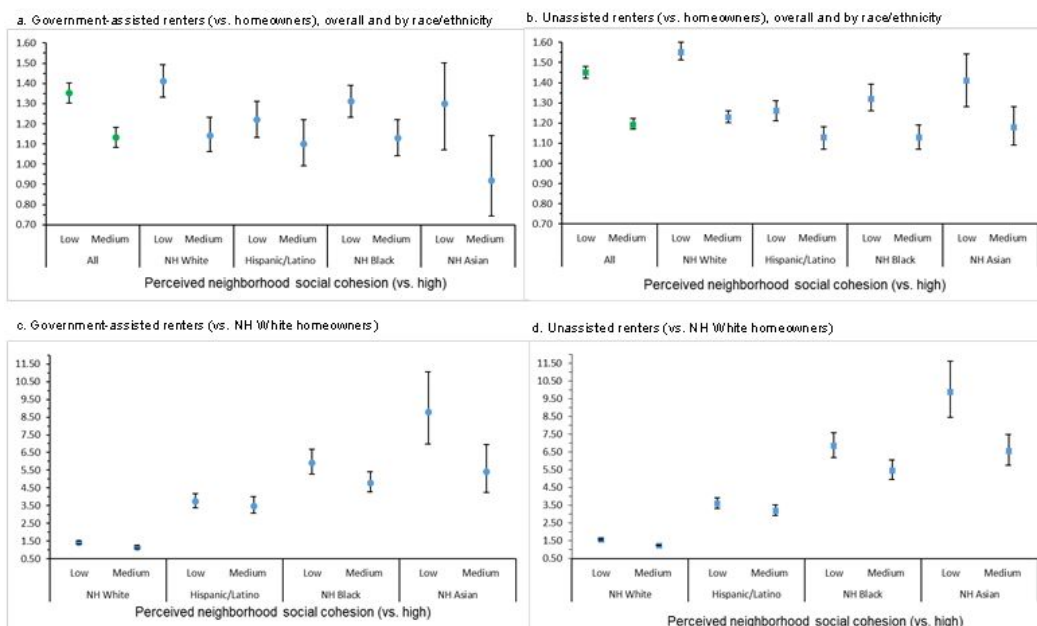
RESULTS. Participants’ childhood and later-life socioeconomic circumstances were moderately correlated ($r=0.2$); we observed substantial rank mobility (percentile-rank mobility $SD=25$). HRS participants who grew up in more socioeconomically advantaged households and who accumulated more wealth across their lives exhibited less-advanced/ slower biological aging in later life. Those who achieved upward social mobility also showed less-advanced/slower biological aging. Effect-sizes for a 1 SD difference in mobility ranged from about 0.1 to 0.2 SDs of biological aging depending on whether mobility was measured using the delta method or residualized change. Associations of upward mobility with slower aging were similar for men and women and for Black and White participants, and were consistent for DNA methylation and blood-chemistry measures of biological aging.

CONCLUSIONS. Upward socioeconomic mobility is associated with less-advanced/slower biological aging in later life.

Racial/ethnic differences in perceived neighborhood social cohesion by type of housing tenure in the United States Erlene E. Martinez-Miller* Erlene Martinez-Miller W. Braxton Jackson II Dana M. Alhasan Symielle A. Gaston Dayna A. Johnson Ichiro Kawachi Chandra L. Jackson

Neighborhood social cohesion (nSC) has been associated with better health and may vary by housing tenure as, for instance, homeowners likely have more neighborhood attachment than renters. Yet, it is unclear if nSC varies by housing tenure and further by race/ethnicity despite racial/ethnic differences in sociopolitical/economic circumstances that shape housing and health. Using National Health Interview Survey data (2013-2018), we assessed cross-sectional associations between housing tenure (homeowners, unassisted renters, government-assisted renters) and perceived nSC (4-item scale; low, medium, high) overall, within race/ethnicity (non-Hispanic White [NHW], Hispanic/Latinx [Lx], NH-Black [NHB], NH-Asian [NHA]), and between renters and NHW homeowners. Adjusting for sociodemographic and health characteristics, we estimated PRs (95% CI) using Poisson regression with robust variance. Among 165,511 participants, mean age was 47 years; 65% were homeowners, renters were 30% unassisted and 5% government-assisted; and 67% were NHW, 15% Lx, 12% NHB, and 5% NHA. Housing tenure varied by race/ethnicity: of NHWs, 76% were homeowners and 40% government-assisted renters. Overall, the prevalence of low nSC among government renters was 35% higher (1.35 [1.30, 1.40]) than homeowners. For all races/ethnicities, government-assisted and unassisted renters had a higher prevalence of low and medium vs. high nSC compared to homeowners, except for NHA government-assisted renters reporting medium nSC (Figure a,b).The magnitude of low and medium nSC was higher for minorities than NHW homeowners, particularly NHBs and NHAs (Figure c,d). Prevalence of low nSC among NHA unassisted renters was 6.55 (5.73, 7.49) times that of NHW homeowners with high nSC. In conclusion, nSC was lower for both renter types than homeowners; disparities were widest between NHW homeowners and minority renters. Future research should understand and enhance nSC, especially among renters and racial/ethnic minorities.

Figure. Selected adjusted* cross-sectional associations between individual housing tenure and perceived neighborhood social cohesion: National Health Interview Survey, 2013-2018 (N=165,511)



Abbreviations: NH, non-Hispanic.
 *Models adjusted for race/ethnicity, gender, age, marital status, educational attainment, annual household income, employment status, occupational class, region of residence, alcohol consumption, serious mental illness, "ideal" cardiovascular health, body mass index, and self-rated health.

The Association between Loneliness and Cardiovascular Disease in the US and South Korea: Longitudinal Study of National Representative Samples Harold H. Lee* Harold Lee Sakurako S. Okuzono Ruijia Chen Laura D. Kubzansky

Background: A wealth of research indicates that loneliness is associated with increased risk of developing cardiovascular disease (CVD). However, most studies are conducted in populations among Western developed countries, in which the culture is more independent than in East Asia. We compared the loneliness-CVD associations in Americans and South Koreans. Considering the more interdependent culture in South Korea, we hypothesized that the link would be stronger among South Koreans than Americans.

Methods: We used nationally representative data from the Health and Retirement Study (n=15,954, mean age at baseline=64±10 yr, 2004-2015) and the Korean Longitudinal Study of Aging (n=8,109, mean age at baseline=58±10 yr, 2006-2016). In both cohorts, baseline loneliness was assessed using an item in the CES-D questionnaire (Lonely? Yes/No). CVD incidence is defined as reporting new-onset CVD on the biennial questionnaire or CVD death by proxies. Separately among South Korean and Americans, we estimated adjusted hazard ratios (HR) of incidence CVD according to loneliness (Yes/no), adjusting for potential confounders assessed at baseline, including sociodemographic factors, health conditions, and health behaviors.

Results: Over ~10 years, 3,173 Americans (20%) and 752 Koreans (9%) developed CVD. In the unadjusted models, loneliness was associated with an increased likelihood of developing CVD in Americans (HR:1.55, 95%CI: 1.41,1.70) and Koreans (HR: 1.25, 95%CI: 1.04, 1.51). In the adjusted models, loneliness was associated with an increased likelihood of developing CVD in Americans (HR:1.23, 95%CI: 1.12,1.34), but the effect was attenuated in Koreans (HR: 1.10, 95%CI: 0.90, 1.35).

Conclusions: Loneliness was more strongly associated with an increased likelihood of developing CVD among Americans than South Koreans. We do not find support for the hypothesis that the loneliness-CVD relation is more potent in an interdependent culture.

Discrimination, Psychosocial Factors, and Antihypertensive Treatment: A Four-Way Decomposition Analysis in The Health and Retirement Study Kendra D. Sims, MPH* Kendra Sims David Batty PhD, DSc Jessina C. McGregor, PhD FSHEA Ellen Smit, PhD Michelle C. Odden

Introduction Experiences of discrimination have been associated with suboptimal antihypertensive therapy use among persons with hypertension. Whether adverse psychosocial health mediates this relationship is unknown.

Methods This study included two concatenated waves of Health and Retirement Study participants with self-reported hypertension (N=8557, 73% Non-Hispanic White, 17% Non-Hispanic Black, and 10% Hispanic/Latinx) over four years (2008-2014). Our dichotomized main exposures, as assessed via two validated psychometric scales at baseline, were ever experiencing discrimination in everyday life within the past months of assessment or in at least one of seven discriminatory circumstances over the life course; reported depressive symptomology and subjective social standing were the psychosocial mediators of interest. We used causal mediation methods to decompose the following effects of each psychosocial factor on overall associations between each discrimination measure and self-reported antihypertensive use at the subsequent wave: neither interactive nor mediating, only interactive, both interactive and mediating, and only mediating.

Results Each dichotomized discrimination measure was associated with a lower likelihood of subsequent antihypertensive use (unmediated everyday OR: 0.83 (95% (0.70, 0.98)); unmediated lifetime OR: 0.81 (95% (0.69, 0.96)). Ever experiencing everyday discrimination or any lifetime discrimination was modestly associated with increased depressive symptomology and decreased subjective social standing. The estimates for the controlled direct effect, due to neither interaction nor mediation, resembled the unmediated associations for each discrimination measure and depressive symptoms, as well as lifetime discrimination and social standing. The association between everyday discrimination and antihypertensive use was stronger in the presence of higher subjective social standing, interactive OR: 0.80 (95% (0.55-1.17)), although the confidence intervals were wide. Lifetime discrimination was modestly indirectly associated with reduced antihypertensive use via depressive symptomology (mediating OR: 0.98 (95% CI: 0.96, 1.00)).

Conclusions Discrimination over the lifetime may reduce antihypertensive use, partially via depressive symptoms. Moreover, the effect of everyday discrimination on antihypertensive use appears to be stronger among those with high subjective social standing; however, the estimates were imprecise.

Industrial harmony or class discord? Class differences in exposure to workplace domination and exploitation Jerzy Eisenberg-Guyot* Jerzy Eisenberg-Guyot Seth J. Prins

Introduction: Applying a relational social class theory to nationally representative data, we estimated class differences in exposure to workplace domination and exploitation (lacking control over the processes, conditions, and fruits of one’s labor), structural features of the employee-employer relationship that cause health inequities. **Methods:** We used data on respondents ages 16+ to the 2002-2018 US General Social Survey Quality of Working Life Module (n=6,806). First, after multiple imputation to address missingness, we assigned respondents to the worker, manager, petite bourgeois, or capitalist classes based on their supervisory authority and self-employment status. Next, using age- and year-adjusted log-linear Poisson models, we estimated class differences in exposure to workplace domination and exploitation, proxied by measures of automation, autonomy, conflict, and hazards. In secondary analyses, we examined class-by-race and class-by-gender interaction. Finally, within the working class, we used the Poisson models to examine race-by-gender differences in such factors. **Results:** We identified substantial class differences in exposure to workplace domination and exploitation, particularly regarding measures of autonomy and conflict (Fig 1). For example, capitalists were 89% less likely than workers to report not having the freedom to decide how to do their jobs (prevalence ratio [PR]: 0.11, 95% CI: 0.05-0.24) and 77% less likely than workers to report poor worker-management relations (PR: 0.23, 95% CI: 0.10-0.50). We did not identify class-by-race or class-by-gender interaction. Finally, within the working class, prevalence of the measures was similar, although Black workers, particularly Black women, tended to report greater domination and exploitation than other workers. **Discussion:** Focusing on structural factors like domination and exploitation rather than their psychosocial consequences (e.g., job strain) can help elucidate health inequities’ root causes.

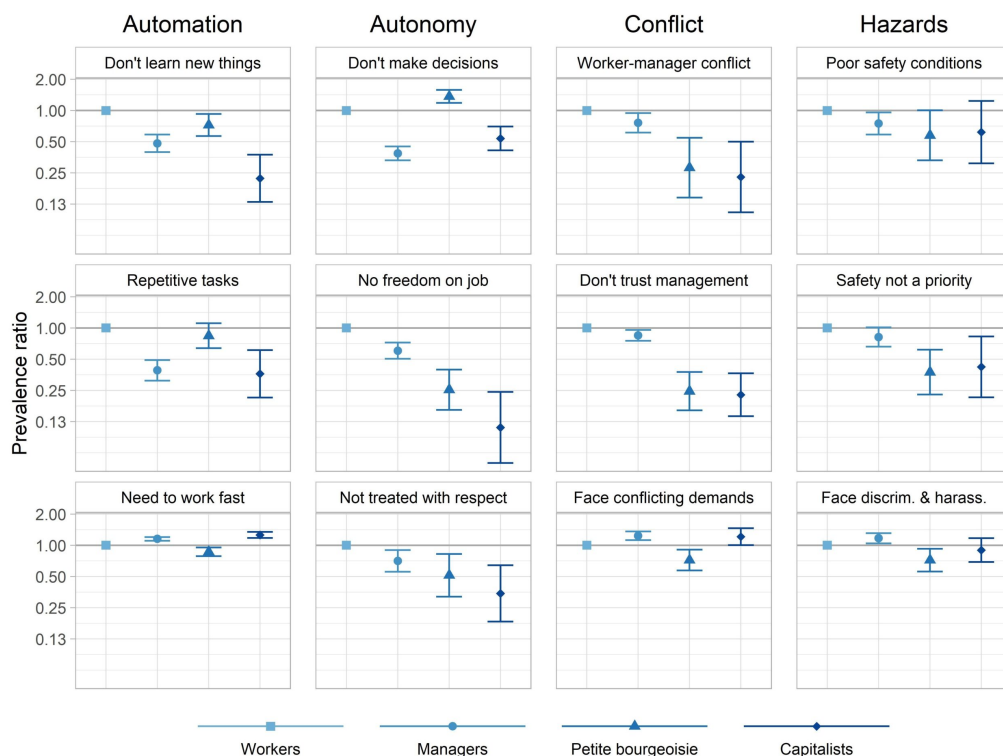


Figure 1. Prevalence of adverse condition among each class relative to the prevalence among workers estimated from age- and year-adjusted log-linear Poisson models. Confidence intervals calculated using Taylor series linearization.

Structural sexism in the United States and women's alcohol consumption and binge drinking Sarah McKetta* Sarah McKetta Katherine Keyes

Background: Alcohol consumption and binge drinking have been increasing among women in the mid-life, concurrent with social and economic gains. Variation in state-level structural sexism (i.e., gender inequality in social, legal, and economic institutions) may be related to women's alcohol consumption patterns.

Methods: We examine the relationship between structural sexism—measured using a factor-analytically derived measure reflecting state-level gender inequality in political representation and economic status—and alcohol consumption frequency and binge drinking among women born 1970-1987 in Monitoring the Future (N=20,859 unique respondents, N=102,516 observations between 1988-2016). We control for state alcohol climate, religiosity, poverty, and population density as well as individual sociodemographic characteristics and religiosity. We test two mediators: depressive symptoms and college completion.

Results: In fully-adjusted models, increases in structural sexism were associated with decreases in alcohol consumption frequency (RR: 0.978, 95% CI: 0.976, 0.981) and the probability of any binge drinking (OR: 0.923, 95% CI: 0.914, 0.932). For alcohol consumption frequency, college completion partially mediated the relationship (estimated indirect effect 0.980, corresponding to 14% reduction of total effect). Depressive symptoms did not mediate the relationship for either outcome.

Conclusion: Lower levels of structural sexism – either historically or across geographies—are related to increases in both alcohol consumption and binge drinking among women. Increases in women's equality are positive and important social forces, but have conferred new and sometimes problematic exposures that have implications for women's alcohol use; alcohol use in the US population, including among women, should be prioritized for public health and treatment efforts to improve population health.

Association of Delaying School Start Time with Sleep-Wake Behaviors Among Adolescents

Kaitlyn M Berry* Kaitlyn Berry Darin J Erickson Aaron Berger Kyla Wahlstrom Conrad Iber Kelsie M Full Susan Redline Rachel Widome

Introduction: Few adolescents spend enough time asleep on school nights. This problem could be addressed by delaying high school start times, but does this translate to reduced prevalence of sleep-wake problems like awakening too early or feeling sleepy during the day?

Methods: The START study (n=2414) followed a cohort of students from five Minnesota high schools to evaluate impacts of school start time delays. Participants were enrolled in 9th grade (Baseline) when all schools started early (7:30 or 7:45am). At Follow-Up 1 (10th grade) and Follow-Up 2 (11th grade), two schools had delayed their start times by 50 and 65 minutes while three comparison schools started at 7:30am. Six sleep-wake behaviors were assessed at all three time points via survey. Generalized estimating equation models were used to investigate changes in sleep-wake problems between policy change and comparison schools.

Results: The prevalence of sleep-wake problems at Baseline ranged from 11% for being late to class due to oversleeping to 48% for needing to be told to wake multiple times in the morning. Compared to students from comparison schools, students at policy change schools reported smaller increases in the prevalence of feeling sleepy daily and oversleeping and being late to class between 9th and 11th grade. After implementation of the delayed start, awakening too early was more common among students at policy change schools compared to the comparison schools.

Conclusions: This longitudinal study provides evidence that delaying high school start times reduces daytime sleepiness and school tardiness.

Figure 1

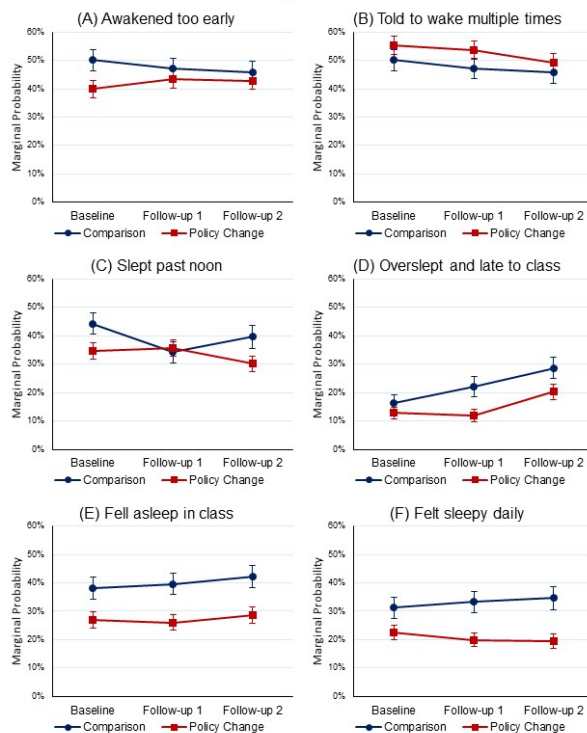


Figure 1 displays the predicted probabilities of each sleep-wake problem by condition (policy change vs comparison). Predicted probabilities are derived from GEE models that include a fixed effect for school and are adjusted for school, sex, race, parental education, and free lunch eligibility.

Racial/ethnic differences in the association between social support and sleep in the United States Dayna A. Johnson* Dayna Johnson Radhika Asrani Billye D. Lewis Tené Lewis

Social support (SS) is associated with better health, and may enhance resilience to stress - a determinant of sleep disparities. However, the specific types of SS that benefit sleep are unclear, and whether these associations vary by race/ethnicity are unknown. Using National Health Interview Survey data (2007-2008), we assessed cross-sectional associations between types of SS (number of friends, financial, marital, and emotional support) and self-reported short sleep duration (<7 hours) overall and within race/ethnicity groups (Black, Hispanic and White men and women). After adjustment of covariates, we estimated PRs (95% CI) using logistic regression (marginal standardization) and sleep in minutes (95% CI) using linear regression accounting for survey design and weights. Among 3,711 participants, mean age was 57 years; 37% slept <7 hours; 21% Black, 26% Hispanic and 53% White. Black adults had the highest prevalence of short sleep (55%). Overall, participants with financial support and married individuals had a lower prevalence of short sleep, 23% (0.68, 0.88) and 17% (0.72, 0.95), than those without financial support and unmarried, respectively. Participants with all four types of SS had a 49% lower prevalence of short sleep compared to those without SS. Among Hispanic adults, >5 friends and financial support were associated with sleeping 18.5 (7.7, 29.2) and 14.2 (5.3, 23.1) minutes longer, respectively. Among White adults, marital support was associated with sleeping 16.2 (7.1, 25.3) minutes longer, and the association was most pronounced among women. Emotional support was associated with longer sleep duration (38 minutes) among Black men only, not women. Overall, friends, financial, marital support and multiple types of SS were associated with healthy sleep duration. The association of SS and sleep varied by the type of support and race-sex. Targeting specific types of SS may help to improve sleep duration among those most-at-risk.

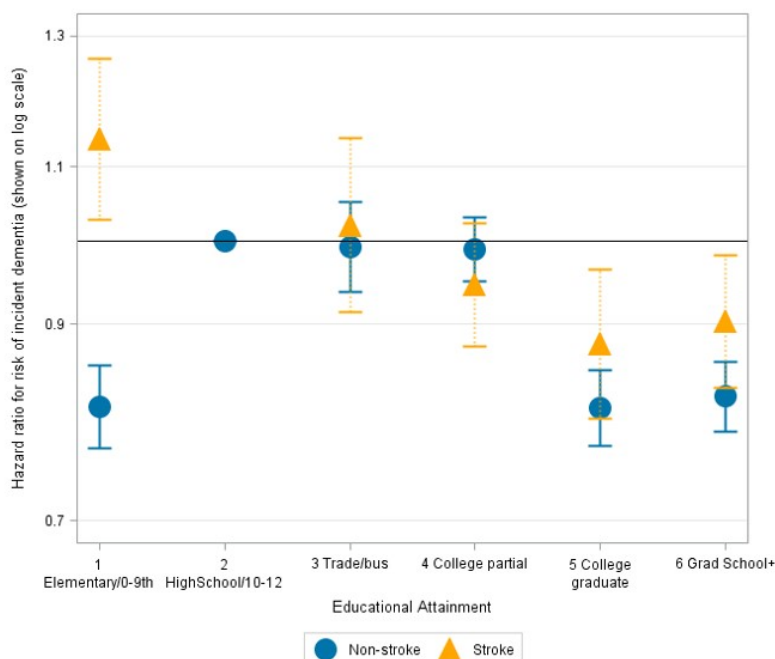
Education and cognitive resilience: the influence of education for post-stroke dementia incidence Chloe Eng* Chloe Eng Maria Glymour Rachel Whitmer John Kornak Elizabeth Rose Mayeda Paola Gilsanz

Background: Higher education is associated with lower dementia risk in the general population, possibly attributable to resilience towards neurodegenerative pathology. Whether education is also protective against dementia after the neurologically debilitating event of a stroke is unclear.

Methods: We analyzed Kaiser Permanente Northern California members born 1946 or earlier who participated in the Multiphasic Health Checkups (MHC) in 1964-1996, remained members and were stroke-free as of January 1, 1996 (n=216,430). Stroke and dementia diagnoses were obtained from medical records from January 1, 1996-September 30, 2017. MHC education was recorded as 0-9 years, 10-12 years (reference category), trade/business school, some college, college degree, or graduate degree. Cox proportional hazards models were used to estimate whether education predicted dementia after stroke onset. Stroke was treated as a time-varying exposure with age as the time scale, adjusted for race/ethnicity and gender.

Results: Across 3,496,488 person-years, 20,825 people suffered a stroke and 19,384 people were diagnosed with dementia (26.8% of people with stroke and 7% of stroke-free people). Overall, those experiencing stroke had a 5.25 times higher dementia risk (95% CI: 5.08, 5.43) than those who did not; effect of stroke on dementia risk varied by education (p<0.01). Among those experiencing a stroke, dementia risk was higher with 0-9 years of education (HR=1.26, 95% CI: 1.14, 1.40) compared to those with 10-12 years and lower for people with some college (HR=0.91, 95% CI: 0.84, 0.98), college degree (HR: 0.81, 95% CI: 0.74, 0.89) or graduate education (HR=0.85, 95% CI: 0.78, 0.92).

Conclusion: Increased education may allow individuals to maintain some cognitive function after the onset of stroke. Further research is needed to consider the potential for selective survival by education among those with lower education.



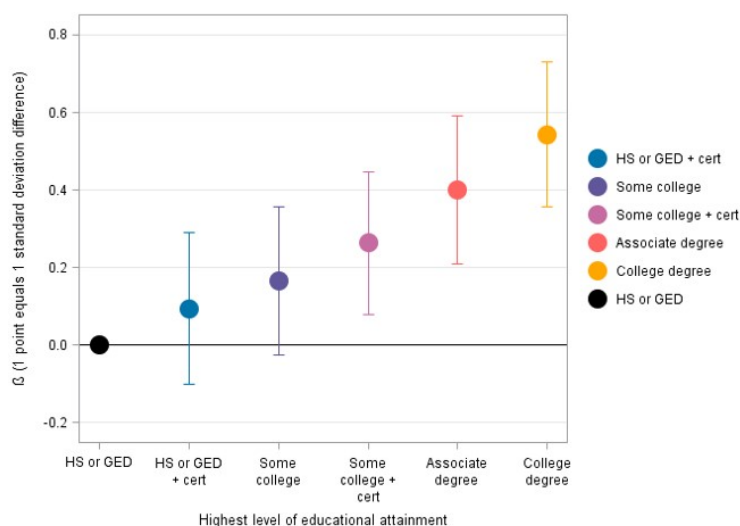
Schooling and late-life cognition among African American older adults: the role of alternative postsecondary education Chloe Eng* Chloe Eng Paola Gilsanz Lisa Barnes Maria Glymour Kristen George Dan Mungas Rachel Whitmer

Background: College degree attainment is associated with better late-life cognition, but historically has not been uniformly accessible across racial groups in the US. Whether alternative accreditations to traditional four-year college degrees confer benefits for late-life cognition are unknown.

Methods: The Study of Healthy Aging in African Americans (STAR) recruited long-term African American members of Kaiser Permanente,; we examined participants with education of a HS degree/GED without and with additional formal certificate attainment, some college without and with additional certificate, associate degree, or 4-year college degree (n=602), excluding those who did not complete high school or with postgraduate education (n=157) or missing covariates (n=5). Baseline cognitive function was measured with the Spanish and English Neuropsychological Assessment Scales (SENAS). SENAS domains (episodic memory, semantic memory, executive functioning) were analyzed in mixed models as a composite z-score, and in domain-stratified linear regression models adjusted for sex, age, geographic birth region, and maternal education.

Results: Any formal postsecondary education was associated with higher late-life cognition compared to HS degree or GED in an upward trend for SENAS composite z-scores with increasing education: certificate attainment only after HS/GED ($\beta=0.09$, 95% CI: -0.10, 0.29), some college ($\beta=0.16$, 95% CI: -0.03, 0.36), some college with additional certificate ($\beta=0.26$, 95% CI: 0.08, 0.45), associate degree ($\beta=0.40$, 95% CI: 0.21, 0.59), and college degree ($\beta=0.54$, 95% CI: 0.36, 0.73). Results were similar in models stratified by SENAS cognitive domain.

Conclusion: Postsecondary formal education of any amount may contribute towards better late-life cognition in older African Americans. Future research is needed to disentangle whether effects may be attributable to increased exposure to the formal learning environment or increased resulting socioeconomic opportunities.



The protective relationship between education and smoking strengthened between 1992 and 2004, then stabilized. Sepehr Hashemi, DMD* Sepehr Hashemi Shelley DeVost M. Maria Glymour Justin S. White Anusha M. Vable

BACKGROUND:

Education is associated with reduced smoking behaviors, however, recent potential changes in the education-smoking gradient over time are unclear.

METHODS:

Health and Retirement Study respondents aged 50-56 at enrollment in 1992 (N = 5851), 1998 (N = 2013), 2004 (N = 2708), 2010 (N = 4075), or 2016 (N = 3507) reported years of education and current smoking behaviors (ever smoker, current smoker). Due to the different relationships between education and smoking among those with more or less than 11 years of schooling, education was operationalized as a linear spline with a knot at 11 years. Analyses were adjusted for gender, mother's education, race / ethnicity (Black, White, Latino, Other), birthplace (Southern born, immigrant), and birth year.

RESULTS:

Up to 11 years of schooling, additional years of education were not associated with smoking behaviors. Among those with more than 11 years of education, each additional year of education predicted lower odds of ever smoking (OR in 1992 = 0.93, 95%CI: 0.89, 0.97), current smoking (OR in 1992 = 0.86, 95%CI: 0.83, 0.89), and increased odds of smoking cessation among those who ever smoked (OR in 1992 = 1.16, 95%CI: 1.11, 1.22). The protective relationship between education and ever smoking increased over time (Figure 1; OR = 0.93 (95% CI: 0.89-0.97) in 1992; 0.88 (0.84-0.93) in 1998; 0.79 (0.74-0.84) in 2004). There was a weaker change over time in the strength of the relationship between 11 or more years of education and current smoking or smoking-cessation.

CONCLUSION:

Among those with 11 or more years of education, each additional year of education predicted lower odds of ever smoking or current smoking, and higher odds of smoking cessation. The relationship between education and ever smoking became stronger from 1992 to 2004 and subsequently stabilized.

Perceived day-to-day discrimination and eating behaviors: Findings from EAT 2018 Cynthia Yoon* Cynthia Yoon Vivienne M. Hazzard Rebecca L. Emery Susan M. Mason Dianne Neumark-Sztainer

Background

Race-, gender-, and weight-related discrimination are associated with maladaptive eating behaviors. However, the relationships between day-to-day types of discrimination and eating behaviors remain unclear.

Purpose

We examined associations among perceived day-to-day discriminatory experiences and a variety of eating behaviors by gender.

Methods

Data were collected from a population-based study, EAT 2018: Eating and Activity Over Time (N=1400, ages 18-30 in 2017-2018). Exposures included perceived discrimination related to respect, customer service, and perceived intelligence. Outcomes included adaptive eating (i.e., intuitive eating and mindful eating scores) and maladaptive eating (i.e., overeating and binge eating). Linear regressions were used to examine the associations of discriminatory experiences with intuitive eating and mindful eating scores. Modified Poisson regressions were used to estimate prevalence ratios (PRs) for associations of discriminatory experiences with overeating and binge eating.

Results

Among men, discrimination related to perceived intelligence was associated with significantly lower scores of intuitive eating ($\beta=-0.30$, [95% CI=-0.58, -0.02]) and mindful eating ($\beta= -0.39$, [95% CI=-0.74, -0.04]); All types of discriminatory experiences (i.e., discrimination related to respect, customer service, and perceived intelligence) were associated with greater prevalence of overeating (PR range= 1.79-2.05) and binge eating (PR range= 3.49-4.65).

Among women, all perceived discriminatory experiences were associated with significantly lower scores of intuitive eating (β range=-0.55 to -0.63) and mindful eating (β range= -0.27 to -0.45) and greater prevalence of overeating (PR range= 1.44-1.69) and binge eating (PR range= 1.58-1.79).

Conclusion

Public health efforts to encourage adaptive eating and prevent engagement in maladaptive eating should take into account the potential contribution of subtle forms of discrimination.

The impact of the minimum wage on suicide rates in Hong Kong Abigail Rath* Abigail Rath C
Mary Schooling HY Eric Lau

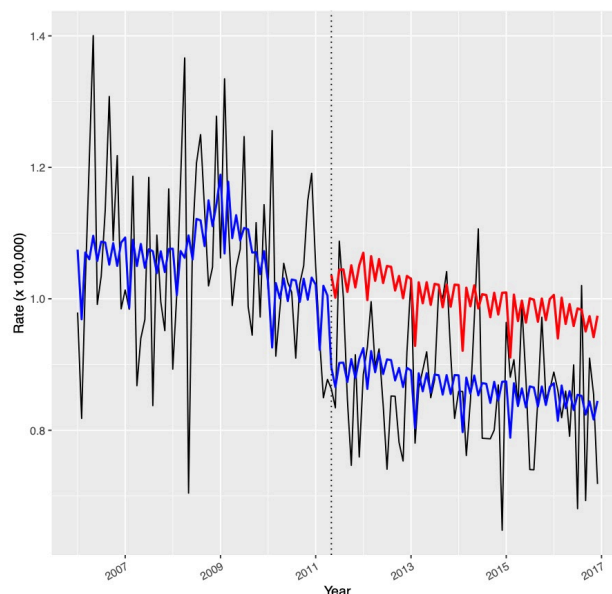
Background/Objective: Increases in minimum wages have been associated with reductions in suicide rates in the United States, but little evidence is available for Asia where social and contextual factors, as well as drivers of suicide, may be different. We investigated the impact of the introduction of the minimum wage in May 2011 on suicide rates in Hong Kong for the period January 2006 to December 2015.

Methods: Using an interrupted time series design, we investigated immediate and gradual changes in monthly suicide rates after the introduction of the minimum wage taking into account secular trends. We conducted stratified analyses by age (working and retired) and gender.

Results: There were 9396 recorded suicides in Hong Kong during the 11 year study period. The introduction of the minimum wage was associated with an immediate decrease of 13.6% in the suicide rate (95% confidence interval (CI): 5.5% to 21.0%, $P=0.001$). The largest effect was among working aged men, with an immediate decrease of 16.9% (95% CI: 5.2% to 27.2%, $P = 0.006$). No gradual effects were found. We estimate 661 suicides were prevented during the study period, 68% of them in working aged men (451 out of 661), 28% of them in working age women (188 out of 661) and the remaining in the retired population.

Conclusions: Our results provide new evidence that, similar to findings in Western settings, minimum wages may help to reduce suicide in Asia, particularly for working age men. Our study highlights the importance of examining the health impacts of government economic policy and suggests minimum wages may provide policy makers with an upstream population-based strategy to reduce suicide rates.

Figure: Monthly suicide rates (cases/100,000) in Hong Kong during the period 2006 to 2016*



*Age and sex standardised and deseasonalised observed (solid black line) suicide rates. The vertical line indicates the date the minimum wage was introduced. The solid blue line indicates the predicted standardised and deseasonalised suicide rates under the Poisson regression model adjusted for the unemployment rate, GDP, the introduction of the minimum wage and the temporal trends before and after the introduction of the minimum wage. The red line indicates the predicted rates under the counterfactual scenario had the minimum wage not been introduced and the pre-minimum wage temporal trend had continued.

LATEBREAKER

Social

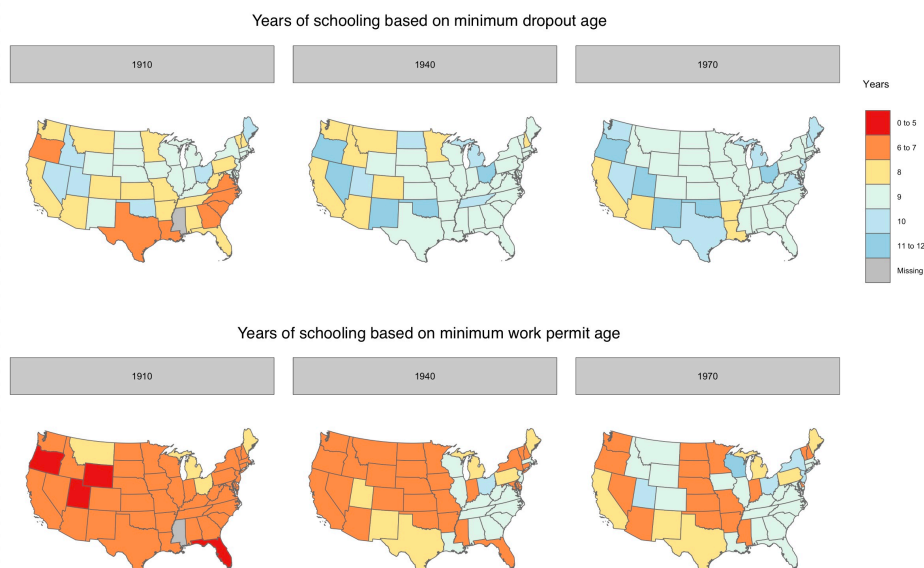
State-mandated increased years of K-12 education decreased blood pressure, particularly for those in the upper tail of the systolic blood pressure distribution: An instrumental variable analysis of a natural experiment Amanda Irish* Amanda Irish Erika Meza Kirsten Bibbins-Domingo Justin White Anusha Vable

Introduction. More schooling predicts better cardiovascular disease (CVD) outcomes, but most work is correlational and gives little insight into causality. We leveraged a natural experiment, variation in compulsory schooling laws (CSLs), which affected K-12 education, from 1908 to 1964 across states in the US, to evaluate how increased education impacted later-life CVD.

Methods. We performed a two-sample instrumental variables (IV) analysis. The first stage was conducted using the US census 5% sample from 1980 (N = 5,318,338) using changes in CSLs as the instrument for educational attainment, while the second stage used data from the Health and Retirement Study (HRS) to estimate effects of education on CVD outcomes: measured systolic (SBP), and diastolic blood pressure (DBP; N = 9,007), and self-reported stroke (14,504). Quantile (continuous blood pressure) and logistic (stroke) models were adjusted for individual- and state-level covariates to account for potential confounding of the relationship between exposure to CSL policies and CVD outcomes. Analyses were restricted to those with 12 or fewer years of education because this is the population affected by CSLs.

Results. The first stage demonstrated CSLs were a strong predictor of education (F = 207.4). Using quantile regression, we found that each additional year of education resulted in a 1.87 mmHg (95% CI: -3.48, -0.25) decrease in median SBP, and a 2.47 mmHg (95% CI: -4.41, -0.52) decrease at the 75th percentile. Additional years of education did not affect SBP at the 25th percentile, DBP, or stroke (OR 1.18, 95% CI: 0.88, 1.59).

Conclusion. Increased years of K-12 education resulted in decreased systolic blood pressure, with greater decreases at the high-risk tail of the distribution. Results suggest interventions to increase K-12 education could disproportionately benefit those at the highest risk for cardiovascular disease.



LATEBREAKER

Social

Gender norms and mental health among older adults in Japan: A JAGES cross-sectional study

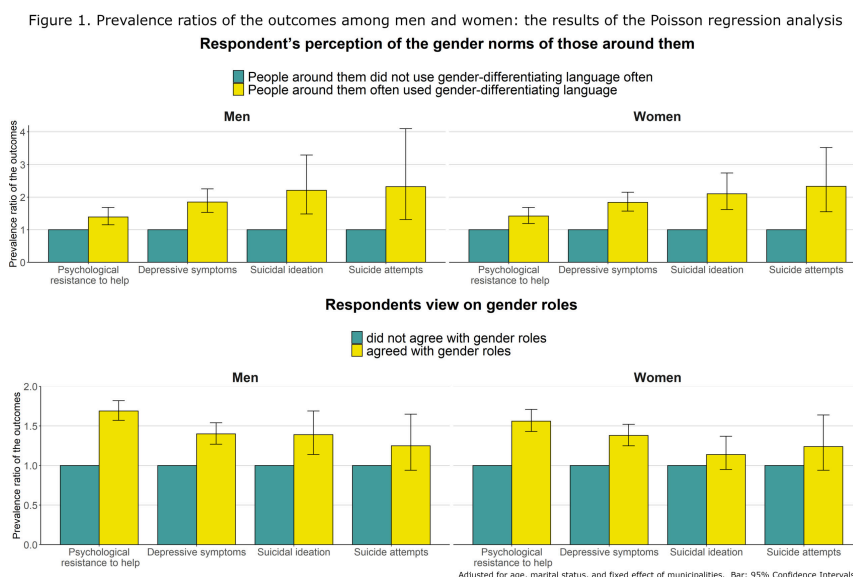
Mariko Kanamori* Mariko Kanamori Mayumi Oka Kosuke Takemura Yumiko Kobayashi Katsunori Kondo Naoki Kondo

Aims Gender norms are important in community and society structure and can potentially affect older people's mental health. This study aimed to examine whether such norms are associated with older people's mental health-related outcomes. We also tested whether the association between individuals' subjective norms about gender roles and outcomes differed based on the perception of gender norms of those around them.

Methods As part of the 2019 wave of the Japan Gerontological Evaluation Study, cross-sectional data were collected from 24,624 respondents aged 65 years or older across 63 municipalities. Gender norms were measured through two dimensions: respondents' perception of gender-differentiating language of those around them and whether individuals agreed with gender roles (e.g., "It is primarily a woman's role to raise children and look after the home."). A gender-stratified Poisson regression model was used to calculate prevalence ratios of mental health outcomes, including depressive symptoms, suicidal ideation, suicide attempts, and psychological resistance to help.

Results Compared to people with relatively ungendered norms, the prevalence of all outcomes was higher among both men and women with gendered norms. Regression analyses adjusted for age, marital status, fixed effect of each municipality, and individual subjective norms about gender roles showed that those who perceived that people around them often used gender-differentiating language had a 1.3–2.3 times higher risk for all outcomes. When individual subjective norms about gender roles were weak, differences in the prevalence of depressive symptoms or suicidal ideation based on the perception of gender-differentiating language around them were more pronounced. This effect modification was clear among men in rural municipalities.

Conclusions In both men and women, gender norms were positively associated with mental health outcomes and psychological resistance to help.



LATEBREAKER

Social

Effects of 2019's social protests on emergency health services utilization and case severity in Santiago, Chile Alvaro Castillo-Carniglia* Alvaro Castillo-Carniglia Abraham I.J. Gajardo Thomas D. Wagner Kristina Devi Howell Andrés González-Santa Cruz Jay S. Kaufman

Background: On October 18th, 2019, protestors gathered across Chile on massive protests calling for social equality. The government responded by declaring a state of emergency and deploying the Chilean army and police, who utilized anti-riot shotguns and tear gas as a means of crowd control. In this study we estimated the effects of the October 2019 Chilean protests on emergency health services utilization and inpatient admission rates in public hospitals near the protest focal point in Santiago, Chile.

Methods: We used a time series analysis of aggregated weekly emergency department (ED) admissions (2015-2019). Data included three large public hospitals located within 3 km of the focal point of the main protest in Santiago, Chile. The exposure period was defined as the onset of social protests on October 18 to December 31, 2019. We considered six outcomes, namely the number of weekly consultations and hospitalizations by trauma and respiratory causes, as well as the proportion of hospitalizations among consultants per 1,000. We implemented Bayesian structural time series models to calculate the absolute and relative effects and their 95% credible intervals (CrI).

Results: Health services utilization, assessed through ED consultations, declined by 11% (trauma; 95% CrI: -39.4, 17.8) and 41% (respiratory; 95% CrI: -93.65, 12.66) during the social protests. In contrast, trauma hospitalizations increased by 16% (95% CrI: 2.8, 29.9), and the proportion of hospitalizations among consultations increased by 38% for trauma (95% CrI: 9.6, 65.2) and 63% for respiratory causes (95% CrI: 31.0, 96.0).

Conclusion: The October 2019 Chilean protests appear to have affected the use of emergency health system services by lowering the number of consultations due to trauma and respiratory causes, while increasing the proportion of hospitalizations among consulting patients. Crowd-control protocols must be reviewed to prevent adverse effects of civil unrest on population health.

LATEBREAKER

Social

Intensity of Social Support Matters: A Latent Class Analysis to Identify Levels of Social Support Associated with Optimal ART Adherence among Women Living with HIV Aruna Chandran* Aruna Chandran Fiona Bhondoekhan Tracey Wilson Joel Milam Mardge Cohen Adaora A Adimora Adebola Adedimeji Jennifer Cocohoba Carrigan Parish Marcia McDonnell Holstad Seble Kassaye Mirjam-Colette Kempf

Introduction: Social support is associated with improved HIV care and quality of life. While patient preference is important in designing social support interventions, it is crucial to understand how different levels of perceived social support influence particular health outcomes.

Methods: The study sample comprised of 1,707 women living with HIV (WLHIV) from one of 10 sites in the Women's Interagency HIV Study and responded to 12+ social support questions at baseline. We utilized latent class analysis to identify three classes of baseline emotional and tangible perceived social support, termed "Strong", "Wavering" and "Weak". In generalized estimating equation robust modified poisson models with independent correlation structures, the relative risks of optimal antiretroviral therapy (ART) adherence ($\geq 95\%$) and undetectable viral load by social support levels were explored controlling for sociodemographic covariates.

Results: "Weak" vs. "Strong" perceived social support was associated over time with an 8% lower risk of optimal ART adherence for emotional (adjusted Relative Risk (aRR) 0.92, 95% Confidence Interval (CI): 0.88, 0.95) and 6% lower risk for tangible (aRR 0.94, 95% CI: 0.89, 0.98) support. Importantly, "Wavering" vs "Strong" support also showed a lower risk of 5% (aRR 0.95, 95% CI: 0.92, 0.98) for emotional and 4% (aRR 0.96, 95% CI: 0.93, 0.99) for tangible support. "Strong" vs. "Weak" support had a similar association with undetectable viral load (aRR: 0.94, 95% CI: 0.89, 0.98), but "Strong" vs. "Wavering" support was not statistically significant.

Conclusion: Our study suggests differential associations across types and levels of perceived social support on ART adherence and undetectable viral load among WLHIV. Intensity of social support may influence HIV care outcomes, and stronger social support may be needed for some individuals. It is important to quantify the level as well as type of social support that is needed to optimize HIV outcomes.

LATEBREAKER

Social

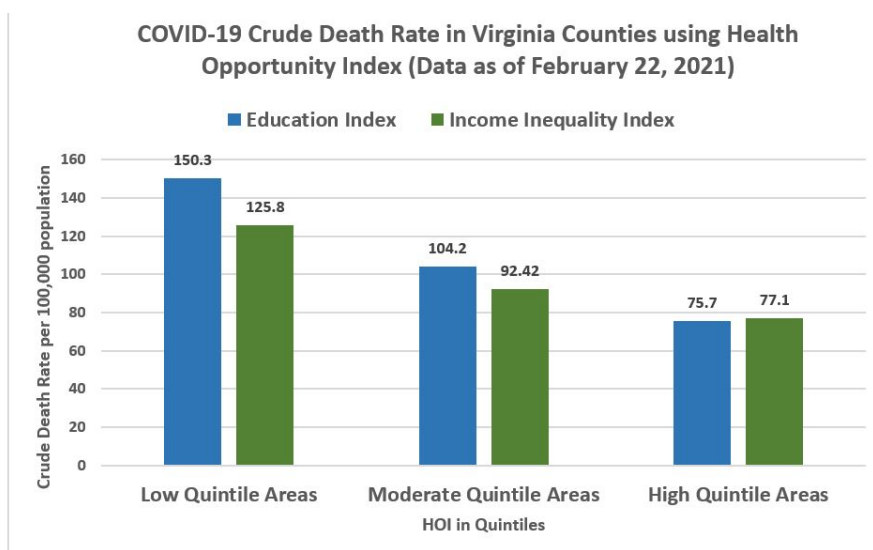
Association of COVID-19 mortality and social determinants of health Priyadarshini Pattath*
Priyadarshini Pattath Rexford Anson-Dwamena

Background: Recent research demonstrates that social determinants of health (SDH) contribute to COVID-19 mortality along with individual factors, as the burden is not equal across populations and areas, signifying the impact of the neighborhood. This analysis used publicly available database on COVID-19 through February 22, 2021, to determine the association between social determinants of health and COVID-19 mortality in Virginia.

Methods: The Health Opportunity Index (HOI) was developed by the Virginia Department of Health to identify vulnerable populations. The HOI is a multivariate tool that uses complex SDH indicators of a community and is comprised of 13 indices - affordability, income inequality, Townsend deprivation, job participation, employment access, education, air quality, segregation, food accessibility, population density, population churning, walkability, and access to care. Principal component analysis was used to develop the composite HOI. The HOI was further aggregated into five quintiles at the county level. Crude COVID -19 death rate was calculated for each county and multiple regression analysis was performed.

Results: There were 7,486 deaths due to COVID-19 in Virginia as of February 22, 2021. Education index ($r = -.35$), health inequality ($r = -.48$) and access to care ($r = -.28$) were significantly associated with COVID-19 crude death rates in Virginia counties ($R^2 = 0.39, p < .001$).

Conclusion: Findings indicate that COVID-19 mortality was highest in the counties in the lowest quintiles of education index and access to healthcare (Figure). Mortality rate was also highest in the counties in the lowest quintile of income inequality and is a critical variable highlighting the disparity between high-income and low-income population. COVID-19 mitigation strategies may involve disaggregated mortality data to target people from low-income, low-education communities and the healthcare systems that serve them.



Note: "Very low" and "Low" quintiles were combined to form "Low Quintile." "High" and "Very High" quintiles were combined to form "High quintile."

LATEBREAKER

Social

Complicating narratives of sexual minority mental health: An intersectional analysis of frequent mental distress at the intersection of sexual orientation, gender identity, and race/ethnicity Tubanji Walubita* Tubanji Walubita Ariel Beccia Esther Boama-Nyarko Eric Ding Katarina Ferrucci Bill Jesdale

Studies indicate that sexual minorities experience poor mental health. However, few studies have examined mental health outcomes in sexual minorities while including other intersecting dimensions of social identity. Therefore, this study had two objectives: 1) to quantify the prevalence of frequent mental distress among adults living in the U.S. across intersecting social identity categories and 2) to evaluate the contribution of intersectional interactions to any observed inequities. We used data from the Behavioral Risk Factor Surveillance System 2014-2019 (N=1,024,261) to perform an intersectional Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (I-MAIHDA). Participants were nested in 45 intersectional strata defined by combining 3 sexual orientation (gay/lesbian, bisexual, heterosexual), 5 gender identity (transgender women, transgender men, gender nonconforming, cisgender women, cisgender men), and 3 racial/ethnic (non-Hispanic Black, Hispanic/Latinx, non-Hispanic white) categories. We estimated the predicted probability of frequent mental distress for each stratum, which we interpreted as the prevalence. We then calculated the Variance Partition Coefficient (VPC) and the Proportional Change in Variance (PCV). We found that multiply marginalized strata, particularly those including sexual and gender minorities, tended to have the highest prevalence of frequent mental distress. Groups with racial/ethnic minorities were equally represented among low and high prevalence strata. The VPC indicated that slightly over 10% of observed variance in prevalence was attributable to group-level rather than individual-level differences, while the PCV revealed that a small but notable amount of the observed heterogeneity in prevalence was due to intersectional interactions between the dimensions of social identity. I-MAIHDA is a promising method for examining the patterning of sexual orientation-based mental health inequities at the population-level.

LATEBREAKER

Social

Interrogating structural inequalities in COVID-19 Mortality in England and Wales Gareth Griffith* Gareth Griffith Gwilym Owen George Davey Smith David Manley Laura Howe

Background

Numerous observational studies have highlighted structural inequalities in COVID-19 mortality in the UK. Such studies often fail to consider the complex spatial nature of such inequalities in their analysis, leading to the potential for bias and an inability to reach conclusions about the most appropriate structural levels for policy intervention.

Methods

We use publicly available population data on COVID-19 related- and all-cause mortality between March and July 2020 in England and Wales to investigate the spatial scale of such inequalities. We propose a multiscale approach to simultaneously consider four spatial scales at which processes driving inequality may act and apportion inequality between these.

Results

Adjusting for population age structure, number of care homes and residing in the North we find highest regional inequality in March and June/July. We find finer-grained within-region increased steadily from March until July. The importance of spatial context increases over the study period. No analogous pattern is visible for non-COVID mortality. Higher relative deprivation is associated with increased COVID-19 mortality at all stages of the pandemic but does not explain structural inequalities.

Conclusions

Results support initial stochastic viral introduction in the South, with initially high inequality decreasing before the establishment of regional trends by June and July, prior to reported regionality of the “second-wave”. We outline how this framework can help identify structural factors driving such processes, and offer suggestions for a long-term, locally-targeted model of pandemic relief in tandem with regional support to buffer the social context of the area.

COVID-19 and parental substance use in the perinatal period: A cross-sectional survey of substance use among post-partum women and their partners in the early stages of the COVID-19 pandemic Olivia Frank* Olivia Frank Kathryn M. Denize Robert Talarico Carlie Boisvert Alysha LJ Harvey Ruth Rennicks White Deshayne B. Fell Meagan Ann O'Hare Gordon Yanfang Guo Malia SQ Murphy Daniel Corsi Kari Sampsel Shi Wu Wen Mark Walker Darine El-Chaâr Katherine A. Muldoon

Background: There is concern about the rise in substance use caused by the stress of the COVID-19 pandemic, however, little is known about patterns among the perinatal population and their households. Our objective was to assess patterns and risk factors of substance use among women who gave birth during the COVID-19 pandemic, and their partners.

Methods: We conducted a cross-sectional survey of obstetrical patients from The Ottawa Hospital (TOH) that delivered since the COVID-19 pandemic (March 17th-June 16th, 2020) and were >20 days post-partum. Participants reported on changes in their own substance use (i.e., alcohol, tobacco, cannabis) and that of their partners since the pandemic began. Modified Poisson multivariable models were used to estimate aRRs and 95% CIs for associations with potential risk factors including: parity, post-partum depression, immigration status, household income, and job loss.

Results: Complete survey data were available for 216 women. The median maternal age was 33 years (IQR:30-36) and infant age was 76 days (IQR:66-90). Any substance use was reported by 113 (50%) women; 15 (6.9%) reported increases in use since the pandemic began. A total of 162 (75%) women reported partner substance use; 45 (20.8%) reported increases in their partner's substance since COVID-19 began. Adjusting for all risk factors, the risk factor most strongly associated with increased maternal substance use was post-partum depression (aRR:5.78, 95%CI:2.22-15.05) and the factor most strongly associated with increased partner substance use was changes in childcare (aRR:2.46, 95%CI:1.38-4.39).

Conclusion: In our sample, 7% of mothers and 21% of partners had a reported increase in substance use. Increased substance use was five times higher among mothers with post-partum depression and twice as high among partners with changes in childcare. Our findings highlight the importance of childcare support and perinatal mental health screening during the pandemic.

Does smoking increase the risk of getting COVID-19? Luis E Segura* Luis Segura Natalie S Levy Josefina A Morales-del-Angel Silvia S Martins

Background: A number of comorbidities (e.g., diabetes, hypertension, lung disease and asthma) and older age appear to increase the risk of COVID-19 infection and severe outcomes. Most of these comorbidities are also associated with smoking. Smoking is hypothesized to increase the risk of COVID-19 infection but retrospective studies using hospital data have found both harmful and protective effects of smoking on COVID-19 disease severity. We use a US nationally representative cohort to estimate the effect of smoking on COVID-19 infection risk.

Methods: Data came from three biennial waves (2012, 2014, and 2016) of the Health and Retirement Study (HRS) and the 2020 HRS COVID-19 subsample (N=3,266). We estimated the association between smoking cigarettes (100 cigarettes per year) during all four waves and diagnosis of COVID-19 among adults aged 50 and older on both the relative scale (Risk Ratios, RR) and additive scale (Risk Difference, RD) using the parametric g-formula and adjusting for comorbid chronic disease (lung disease, hypertension, and diabetes).

Results: Our sample comprised individuals who had a median age of 59 (IQR = 12) and 53.1% reported female gender. The proportion of individuals aged 50 and older that had a COVID-19 diagnosis in 2020 was 2.0%, 11.4% were current smokers in 2012, 9.4% in 2014, 13.9% in 2016, and 11.9% in 2020. After marginalizing over age and gender at baseline, and comorbid chronic diseases at each wave, we found no association between smoking cigarettes on the multiplicative (RR = 0.55; 95%CI = 0.09 - 3.56) or additive (RD = -0.0063; 95%CI = (-0.0221, 0.0096) scale.

Conclusion: Our results do not suggest an effect of smoking on COVID-19 infection. Previous mixed results, specifically protective effects of smoking on COVID-19 outcomes using hospital data, may have resulted from time-varying confounding and collider bias.

Evaluating the Role of Recovery Capital on Willingness to Enter Treatment for Emergency Department Patients with Opioid Use Disorders Daniel K. Cho* Daniel Cho Brendan Jacka
Brandon D.L. Marshall Francesca L. Beaudoin

Background

The opioid epidemic in the United States remains a pressing public health concern. For many individuals with opioid use disorder (OUD), the emergency department (ED) may be their only contact point with the healthcare system. Opioid-related ED visits may be a critical time for interventions to prevent negative health consequences (e.g., overdose) and also to increase engagement with OUD treatment services. We aimed to assess the relationship between greater resources and support—"recovery capital"—and willingness to enter OUD treatment among ED patients.

Methods

The Navigator Trial is a multisite RCT comparing peer navigation with licensed clinical social workers on treatment engagement, recurrent overdose, and recovery for patients at risk of opioid overdose attending two EDs in Rhode Island. Participants completed the Brief Assessment of Recovery Capital-10 (BARC-10) before the behavioral intervention, and reported willingness to enter treatment after. The relationship between recovery capital (BARC-10 ≥ 47) and willingness to enter treatment was assessed using logistic regression, adjusting for sociodemographic characteristics and current engagement in some form of SUD treatment.

Results

Among 354 participants—64% male, 31% non-White, 30% currently in treatment, median age 35 years—the median BARC-10 score was 42, with 31% having high recover capital. Following the intervention, willingness to enter treatment during the ED visit was endorsed by 40% of participants. In adjusted analysis, participants with lower recovery capital were more likely to report treatment willingness (adjusted OR: 1.35; 95% CI: 1.05, 1.72) compared to those with high recovery capital.

Conclusion

Counterintuitively, higher recovery capital was not associated with willingness to enter OUD treatment. Screening, brief intervention, and referral efforts should seek to engage all patients who may benefit from OUD treatment, not just those who have high recovery capital.

Temporal trends in simultaneous use of alcohol and cannabis among US adolescent boys and girls

Navdep Kaur* Navdep Kaur Deborah Hasin Pia M Mauro Qixuan Chen Mark Olfson Silvia S Martins Katherine M Keyes

Aim

Simultaneous use of alcohol and cannabis to enhance each other's effect is common and damaging to adolescents. There are recent diverging time trends in overall use of alcohol and cannabis that also differ by gender, but little is known about trends in simultaneous use of these substances.

Methods

Data were drawn from the 2000-2019 Monitoring the Future surveys of N~179,000 US 12th graders. We created a 5-level measure including past-year simultaneous use, defined as use of alcohol and cannabis at the same time to enhance each other's effect. Other categories included no use, alcohol-use-only, cannabis-use-only, and past-year alcohol and cannabis use (not simultaneously). Multinomial logistic regression models estimated the association between alcohol/cannabis use and survey year (2000-2004, 2005-2009, 2010-2014, 2015-2019). Models adjusted for survey mode (paper vs. tablet), and included time interactions with sex, parental education, race/ethnicity, and lifetime cigarette use.

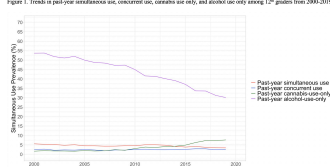
Results

Between 2000-2019, simultaneous use decreased from 5.6% to 3.4%. Alcohol-use-only decreased (53.7% to 30.1%), while cannabis-use-only remained stable before 2006 and increased thereafter (1.7% to 7.6%). Compared to no use in 2000-2004, risk of simultaneous (RRR=0.55, 95% CI: [0.48, 0.62]) and alcohol-use-only (RRR=0.48, 95% CI: [0.45, 0.52]) decreased in 2015-2019, while cannabis-use-only risk increased (RRR=2.58, 95% CI: [2.26, 2.95]). Risk of past-year simultaneous use and alcohol-use-only declined more rapidly for boys than girls, whereas risk for cannabis-use-only increased faster for girls than boys (interaction $F=41.80$, $p<0.001$).

Conclusion

There were slower reductions in simultaneous alcohol/cannabis use risk for girls than boys. Declines in simultaneous alcohol/cannabis use are largely concomitant with historical declines in alcohol use, portending further harm reduction associated with decreased adolescent alcohol use.

Figure 1. Trends in past-year simultaneous use, concurrent use, cannabis use only, and alcohol use only among 12th graders from 2000-2019



Note: Concurrent use is defined as past-year cannabis and alcohol use, but not use of both cannabis and alcohol simultaneously. Alcohol use only is defined as past-year alcohol use and no report of past-year cannabis or simultaneous use. Cannabis use only is defined as past-year cannabis use and no report of past-year alcohol or simultaneous use.

Investigation of the Association between Marijuana Use and E-Cigarette Use among U.S.**Adults** S. Cristina Oancea* S. Cristina Oancea Mary Ochs**Introduction**

Previous literature has found that long-term use of e-cigarettes and marijuana, causes, independently, adverse health outcomes. Limited research exists on the association between marijuana and e-cigarette use among U.S. adults. The current study investigates this association.

Methods

The study sample is based on the BRFSS 2018 (N= 28,858). Weighted unadjusted and adjusted logistic regression models were conducted to investigate the association between marijuana and e-cigarette use among U.S. adults. The study's outcomes of interest are: ever having used an e-cigarette, daily use of e-cigarettes, and using e-cigarettes only some days. Confounders included in the analyses (where applicable, based on the model) were: age, race, gender, marital status, education level, employment status, income level, healthcare coverage, current smoking, and heavy drinking.

Results

Results showed a significant weighted and adjusted association between marijuana use and ever having smoked an e-cigarette (weighted and adjusted odds ratio (WAOR)=2.48; 95% CI: 2.07, 2.98), and marijuana use and smoking e-cigarettes some days (WAOR=1.88; 95% CI: 1.42, 2.48), but no significant association between marijuana use and daily use of e-cigarettes (WAOR=0.84; 95% CI: 0.60, 1.17). Most importantly, never married non-current traditional cigarette smokers who use marijuana had almost 5 times significantly greater odds (WAOR=4.97; 95% CI: 3.16, 7.82) of ever having used an e-cigarette than their counterpart who never used marijuana.

Conclusions

The current study's findings demonstrate that marijuana use is linked to e-cigarette use among U.S. adults. The association offers insight into legal considerations, such as the laws surrounding e-cigarettes/tobacco products and marijuana use in the U.S., as well as healthcare and public health considerations regarding preventative measures and impacts of adverse health effects of e-cigarettes and marijuana use among the most susceptible populations.

Longitudinal trajectories of prenatal alcohol use- results from a community-based prevalence study

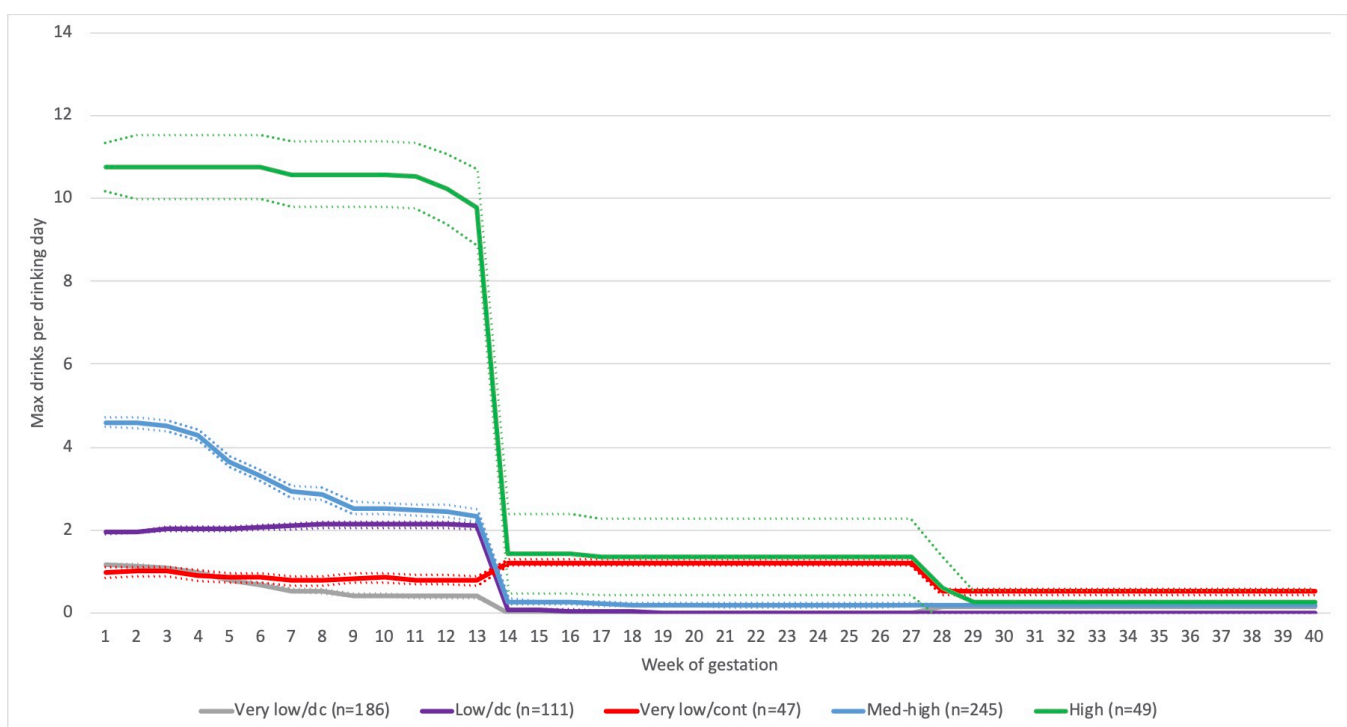
Gretchen Bandoli* Gretchen Bandoli Julie Kable Claire Coles Christina Chambers

Purpose. Timing, quantity and frequency of prenatal alcohol exposure all contribute to the effects of alcohol on the developing fetus; many exposure methods do not account for all three. Our objective was to use longitudinal cluster analysis to characterize prenatal alcohol use.

Methods. Using data collected as part of the Collaboration of Fetal Alcohol Spectrum Disorders Prevalence (CoFASP) study in the US, we performed k-means longitudinal cluster analysis on prenatal alcohol use across gestation. Average daily and maximum number of drinks per drinking day (max DDD) were calculated from maternal or collateral interviews (n=1704); 638 reported any consumption in pregnancy and were included in trajectory creation.

Results. Five trajectories were selected to describe max DDD patterns (figure 1): very low/discontinuing (n=186), low/discontinuing (n=111), very low/continuing (n=47), med/high (n=245), and high (n=49). Women who continued alcohol longer in pregnancy had characteristics more like women in the highest two trajectories (smoking, drug use, later pregnancy recognition). Six trajectories best described average daily alcohol use: very low/discontinuing (n=378), very low/continuing (n=98), low/continuing (n=56), low/discontinuing (n=37), medium/high (n=35), and high (n=31). Contrasting the low continuing and discontinuing groups, those who continued drinking later in gestation were younger, had lower education, were single or divorced while pregnant, smoked, and had later pregnancy recognition; very similar to characteristics of women in the highest trajectory. When comparing between max DDD and average daily drinking, there was concordance between trajectory membership in both the highest and lowest trajectories. There was less concordance between the other trajectories, highlighting that average daily consumption and episodic consumption can differ within individuals.

Conclusion. Patterns of alcohol may better identify women best served by intervention efforts.



Patterns of care among people with hepatitis C virus infection and risky alcohol use in a safety-net health system Mirsada Serdarevic* Brooke MacDonald Matthew Cvitanovich Dustin DeMoss Rohit Ojha

Background: Excessive alcohol use is common among people with hepatitis C virus (HCV) infection and increases the rates of adverse hepatic outcomes and mortality. The Centers for Disease Control and Prevention (CDC) recommends alcohol use screening and intervention for risky alcohol use at the time of HCV diagnosis. The extent to which these guidelines are adopted in practice is not well understood. Therefore, we aimed to describe patterns of care among people with HCV infection and risky alcohol use.

Methods: We used data from the Hepatitis C Outcomes Registry (HepCOR), which is a longitudinal registry of people diagnosed with HCV infection in a safety-net health system in Texas. Eligible individuals were aged ≥ 18 years with a positive HCV-RNA test between January 1, 2013 and December 31, 2018 with follow-up through December 31, 2019, no history of cirrhosis or hepatocellular carcinoma, and an Alcohol Use Disorder Identification Test (AUDIT) score indicating risky alcohol use (AUDIT score ≥ 8). We estimated the proportion of individuals with risky alcohol use receiving a brief intervention, referral to a specialist, or pharmacotherapy within 30 days.

Results: We identified 537 people with HCV infection who received an AUDIT screen, of whom 96 met the criteria for risky alcohol use (median age was 50 years, 68% were male, and 64% were non-Hispanic White). Brief intervention with no referral (36%) was the most common intervention followed by referral to a specialist (30%), no intervention (28%), and pharmacotherapy (6%).

Conclusions: A substantial proportion of people with HCV infection and risky alcohol use do not receive an intervention, which suggests suboptimal implementation of guideline-based care. Future studies are needed to identify and address barriers to implementing interventions for risky alcohol use among people with HCV infection, and improve guideline-based care.

Opioid use, motivation to quit, and treatment status related to COVID-19: a cross-sectional study Maria Parker* Maria Parker Jon Agley Zachary Adams Andrea Villanti

Objectives: Persons with opioid use have been identified as a vulnerable population with the emergence of COVID-19. We examined the relationship between treatment for opioid use, changes in opioid use, and changes in motivation to stop opioid use since learning about COVID-19.

Methods: Participants who had misused opioids or used heroin were recruited using Amazon Mechanical Turk (mTurk; n=562). Participants were surveyed regarding demographics and substance use related topics, including questions on their perceptions of health risks, opioid use, and motivation to quit use amid the COVID-19 pandemic.

Results: On average, participants indicated modest agreement with the notion that opioid use increased their risk of COVID-19 (score: 4.1 of 7.0). Since learning about COVID-19, 31.2% decreased their opioid use, and 26.0% reported increased motivation to quit. For the relationship between opioid use and motivation to quit, 37.5% of participants reported both their use and motivation to quit stayed the same; 16.6% reported decreased use and increased motivation to quit. Participants whose opioid use increased (AOR=3.8; 95% CI: 2.0, 7.5) or motivation to quit opioids increased (AOR=1.9; 95% CI: 1.0, 3.7) were significantly more likely to be in treatment than those whose use or motivation stayed the same.

Conclusions: Respondents were ambivalent about how opioid use related to their risk of COVID-19. Although many participants reported no change in use or motivation to quit, roughly twice as many participants decreased (vs. increased) opioid use and increased (vs. decreased) motivation to quit, suggesting an opportune time for clinical outreach and intervention.

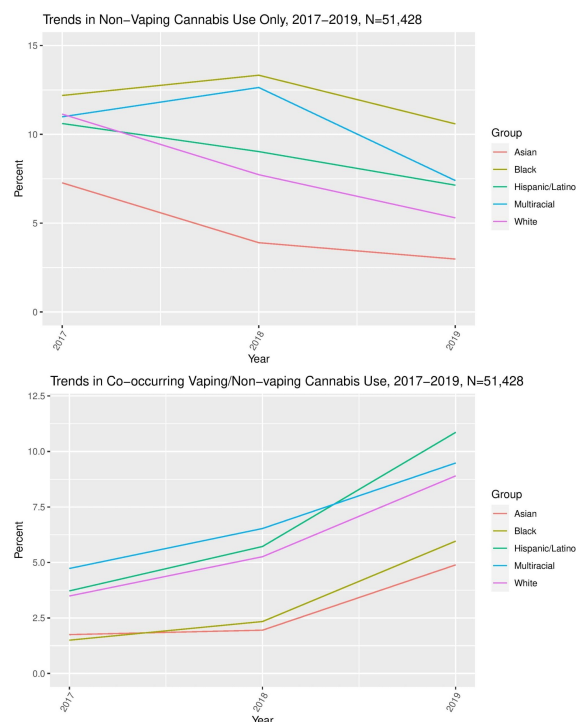
Adolescent vaping of cannabis, 2017-2019: trends by co-use in other methods of administration, and emergent disparities Noah Kreski* Noah Kreski Kerry Keyes

Background: Vaping devices have shaped how adolescents use cannabis. While there are recent increases in the prevalence of cannabis vaping, less is understood about how these trends intersect with other forms of cannabis use (e.g., combustible), as well as sociodemographic differences in the way that vaping trends have changed over time.

Methods: We used annual cross-sectional survey data from Monitoring the Future, 2017-2019, to examine trends in sociodemographic differences in past month cannabis use (N=51,428 US adolescents, grades 8, 10, and 12) by sex (male, female) and race/ethnicity (Asian/Pacific Islander, Black, Hispanic/Latino, Multiracial, white). Cannabis was examined as three levels: no use, past month use without vaping, and past month use with vaping.

Results: From 2017-2019, past month cannabis use with vaping increased from 3.3% to 8.9% of adolescents, while past month cannabis use without vaping declined from 10.8% to 6.5%. While boys had a higher prevalence of vaping cannabis (2017 boys: 4.2%, girls: 2.4%) this gap has narrowed (2019 boys: 9.3%, girls: 8.5%). Differences in cannabis use behaviors emerged by race/ethnicity. Past month use without vaping was highest among Black students (Figure 1, 10.6% in 2019, 95% CI: 8.6, 12.5), and lowest among Asian and Pacific Islander (API) students (3.0% in 2019, 95% CI: 1.5, 4.4). For use with vaping, however, API students had the lowest prevalence (4.9% in 2019, 95% CI: 2.9, 6.8), followed by Black students (6.0% in 2019, 95% CI: 4.8, 7.1); Hispanic/Latino students had the highest prevalence (10.9% in 2019, 95% CI: 9.2, 12.5).

Conclusion: Vaping is an increasingly prevalent cannabis delivery system among adolescents that is offsetting declines in other forms of cannabis use, and this requires immediate prevention and intervention efforts. Programmatic efforts should recognize differences by sex and race/ethnicity, and continue to monitor trends.



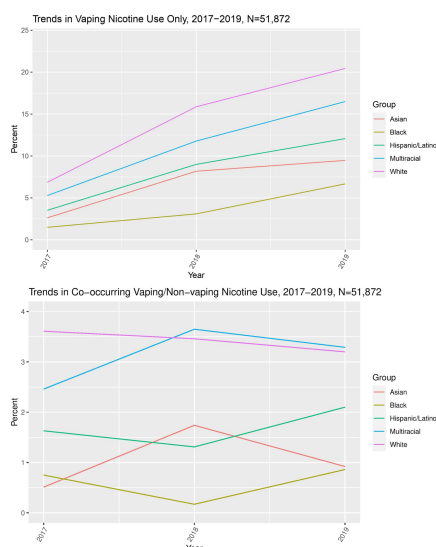
Adolescent vaping of nicotine, 2017-2019: trends by co-use with other methods of administration, and emergent disparities Noah Kreski* Noah Kreski Kerry Keyes

Background: The introduction of vaping devices has impacted how adolescents engage with nicotine. The prevalence of vaping has increased in recent years, but less is known about how these trends intersect with traditional combustible delivery systems (e.g. cigarettes), as well as sociodemographic differences in the way that vaping trends have changed over time.

Methods: We used annual cross-sectional survey data from Monitoring the Future, 2017-2019, to examine trends in sociodemographic differences in past month nicotine use (N=51,872 US adolescents, grades 8, 10, and 12) along factors of sex (male, female) and race/ethnicity (Asian and Pacific Islander, Black, Hispanic/Latino, Multiracial, white). Nicotine was examined across four levels: no use, combustible use only, vaping use only, and co-occurring vaping and combustible use.

Results: From 2017 to 2019, combustible-only nicotine use declined (2.8% to 1.0%), vaping-only use increased from 4.9% to 15.7%, and co-occurring vaping and combustible use remained static (from 2.5% to 2.6%). Few sex differences are apparent in vaping nicotine (e.g., 2019 nicotine vaping-only among boys: 15.9%; girls: 15.5%). However, clear differences in vaping behaviors emerged by race/ethnicity. Use of nicotine by vaping only was highest among white students (20.4% in 2019, 95% CI: 18.9, 21.9), and lowest among Black students (6.7% in 2019, 95% CI: 5.4, 8.0). Racial/ethnic differences are widening over time, with the largest increases in nicotine vaping-only among whites (Figure 1).

Conclusion: Vaping is an increasingly prevalent substance delivery system among adolescents, and prevention and intervention efforts should recognize not only the large proportion of young people only using nicotine through vaping, but also demographic differences. Vaping nicotine is equally prevalent among girls and boys, yet differently patterned across racial and ethnic categories.



Associations Between Adverse Childhood Experiences and Hepatitis C Virus Infection and Risk Behaviors Among Opioid Using Young Adults in New York City Ejakuwa Abubakar*
Ejakuwa Abubakar Honoria Guarino Pedro Matheu-Gelabert Hongbin Zhang

Background: Adverse childhood experiences (ACE) have long been recognized as risk factors for negative health behaviors and health outcomes. There is, however, little data on the relationship between adverse childhood experiences (ACE) and hepatitis C virus (HCV) risk behavior and HCV infection. This study aims to assess the association between adverse childhood experiences (ACE) and HCV infection and HCV related risk behaviors among opioid-injecting young adults in New York City.

Methods: Using data obtained from a sample of 348 opioid-using New York City-resident young adults aged 18-29 years recruited in 2014-2016 using respondent driven sampling and who reported lifetime injection drug use, multivariate regression analyses were performed to assess the association between adverse childhood experiences (measured with the ACE scale) and HCV antibody status, as well as the association between adverse childhood experiences and HCV risk behavior (i.e., early initiation of injection drug use, sharing of needles/syringes and other drug injection equipment and daily drug injection).

Results: The mean age of respondents was 24.9 years (± 3.05 years), 65% were male, the mean ACE score was 3.7 (± 2.7), and 31.2% tested antibody-positive for HCV infection. After adjustment for age, gender, race, and education, ACE score showed significant associations with HCV sero positivity (OR=1.08, CI= 1.01 - 1.14), early initiation of injection drug use (OR=1.60, CI=1.28 - 2.01) and sharing of secondary drug injection equipment (OR=1.15, CI=1.04 - 1.27).

Conclusion: Adverse childhood experiences are significantly correlated with HCV sero positivity, sharing of secondary drug injection equipment and early initiation of injection drug use.

Scientific significance: Assessment for and management of adverse childhood experiences in opioid injecting young people may be indicated for interventions aimed at reducing HCV transmission among these individuals.

Fentanyl Overdose Concerns Among People Who Inject Drugs in Baltimore, MD: The Role of Race, Sex, and Medications for Opioid Use Disorder Abenaa Jones* ABENAA JONES Kristin Schneider Jennifer Maggs Lauren Dayton Karin Tobin Carl Latkin

Background: People who inject drugs (PWID) have an elevated risk of fentanyl-related overdoses, warranting exploration into their concern for this adverse outcome.

Objective: This study examines the prevalence of fentanyl overdose concerns among PWID and the role of race, sex, and medications for opioid use disorder (MOUD) in these concerns.

Methods: Data were derived from 369 PWID, recruited using street-based outreach between 2016-2019. Participants reported concerns about themselves or their peers overdosing from fentanyl, perceived fentanyl presence in heroin, MOUD, and socio-demographic characteristics.

Results: Among the participants, 68% were male, 50% self-identified as Black, and 33% overdosed in the past six months. After controlling for socio-demographic characteristics, female sex was associated with being very concerned about fentanyl overdoses for themselves (RR:2.14; 95%CI:1.22, 3.71) or peers (RR:2.27; 95%CI:1.16, 4.42). Compared to Black participants, White participants were less likely to be very concerned about fentanyl overdoses for themselves (RR:0.35; 95%CI:0.19, 0.65) and participants from other races were less likely to be very concerned for their peers (RR:0.27; 95%CI:0.09, 0.88). Participants on MOUD were more likely to be “quite a bit” concerned (RR:2.29; 95%CI:1.24, 4.25) and very concerned for their peers (RR:2.03; 95%CI:1.11, 3.70), but not themselves. Perceiving fentanyl to be in most or all heroin was associated with being very concerned for peers (RR:3.52; 95%CI:1.41, 8.82).

Conclusion: While most participants (70%) perceived fentanyl to be in all or most of heroin, the level of concern for fentanyl-related overdose varied. Understanding the mechanisms behind different levels of concern may aid harm reduction initiatives.

Disparities in Breastfeeding Initiation and Continuation among Women with Substance Use during Pregnancy Nichole Nidey* Nichole Nidey Kathleen Groh Alicia Agnoli Tanya Froehlich Christine Wilder Stephanie Weber

Background: Breastfeeding is critically important for maternal and infant health. Prenatal tobacco and illicit substance exposure increase offspring risk for sudden infant death syndrome (SIDS), while breastfeeding decreases SIDS risk. The extent of breastfeeding uptake for this vulnerable group is currently unknown. Therefore, the objective of this study was to determine the extent to which women who report tobacco and/or illicit substance use during pregnancy initiate breastfeeding and continue at least 6 weeks compared to women without these exposures.

Methods: This study used data from the 2016-2018 CDC Pregnancy Risk Assessment Monitoring System from 8 states which collected information about perinatal substance use, breastfeeding initiation, and breastfeeding continuation (N=15,945). The PRAMS dataset obtained smoking status from infant birth certificates and other substance use from self-report questions. Weighted Rao-Scott chi-square tests were used to examine the association of substance use with breastfeeding initiation and continuation. Next, weighted, multivariable logistic regression models were utilized to estimate the odds of breastfeeding initiation and continuation for women with and without prenatal substance use, adjusting for relevant demographic (Model 1) and demographic + clinical (Model 2) characteristics.

Results: After adjusting for maternal characteristics, women who smoked and used illicit substances during pregnancy had a decrease in the odds of initiating breastfeeding by 40% (OR 0.60 (95% CI 0.40, 0.90)) when compared to their peers who did not smoke or use substances. Similarly, among women who initiated breastfeeding (n = 13,121), those who smoked and used illicit substances during pregnancy were less likely to continue breastfeeding at least 6 weeks (OR 0.60 (95% CI 0.40, 0.91)) when compared to their peers who did not smoke or use substances.

Conclusion: Women with prenatal smoking and substance use are less likely to initiate breastfeeding and continue breastfeeding, underscoring the need for interventions to boost breastfeeding in this vulnerable group. Future studies are needed to examine maternal health conditions, and infant outcomes (e.g., preterm birth) as potential mediators, thereby furthering understanding of mechanisms by which prenatal substance use leads to reductions in breastfeeding and indicating targets for intervention development. Breastfeeding support coupled with substance and smoking cessation interventions have the potential to improve maternal and infant health for this population.

Prescription opioid supply and socioeconomic determinants of drug overdose deaths: A systematic review of spatial relationships David S. Fink* David Fink Julia Schleimer Katherine M. Keyes Charles Branas Magdalena Cerda Paul Gruenwald Deborah Hasin

Drug overdoses are among the leading causes of loss of years in life expectancy in the United States (U.S.) in the 21

st

Century. Political and scientific attention concerning the rising rates of drug overdose deaths have been focused on changes in supply-side factors related to the availability of prescription opioids and changes in the economic conditions that shape drug demand. However, a systematic review on association between both prescription opioid supply and socioeconomic conditions has not yet been performed but is needed to examine their potential role in the ongoing drug overdose crisis. This systematic review explores the extent to which area-level prescription opioid supply and socioeconomic conditions is associated with drug overdose mortality in the US. We performed a systematic review (in MEDLINE, EMBASE, PsychINFO, Web of Science, and EconLit) for observational studies, published in English, and indexed through July 2020 and additional studies from references lists. Observational studies from U.S. states that examined an ecological association between area prescription opioid supply or economic conditions and fatal drug poisonings were included. In total, 26 published studies met the inclusion criteria, of which 7 studies examined prescription opioid supply only, 17 studies examined economic conditions only, and 2 studies examined both prescription opioid supply and socioeconomic conditions. Low-strength evidence suggested that both greater prescription opioid supply and worse socioeconomic conditions were associated with higher rates of drug overdose deaths in areas. The results were invariant with respect to study design, study population, data sources, and different definitions of fatal drug poisonings. There is a high risk of bias from inadequate adjustment for potential confounding variables and inadequate modelling of spatial and temporal autocorrelation. Future research should work towards rigorous theory and evidence on how social and structural factors, including prescription opioid supply and socioeconomic conditions, interact to shape the drug use environment and risk of drug overdose deaths.

The effect modifying role of marital and cigarette smoking status on the relationship between marijuana use and tooth loss: results from the 2018 BRFSS study Rachel Guyer*

Rachel Guyer S. Cristina Oancea

Oral health is a vital component of overall health in the individual. Periodontal disease and dental caries can contribute to tooth loss and are implicated in several multi-system diseases, which present health-related and economic costs to the individual. Cigarette smoking and alcohol consumption are known risk factors for tooth loss, but limited research exists on the relationship between marijuana use and tooth loss resulting from periodontal disease. The sample group for this study (N=44,327) was based on the 2018 Behavioral Risk Factor Surveillance System (BRFSS) questionnaire administered in the United States. Multivariable weighted and adjusted logistic regression models were used to investigate the association between marijuana use and tooth loss. The potential effect modifying role of confounders was also evaluated. The analysis was controlled for age, sex, race, education, employment, income, current smoking, and heavy drinking. The weighted and adjusted odds (WAO) of having at least 6 teeth removed due to tooth decay were significantly greater among individuals who used marijuana when compared to their counterparts who did not, in the following groups: never married adults who were not currently smoking cigarettes (WAOR=2.01; 95%CI: (1.10-3.67)); separated, divorced, or widowed adults who were not currently smoking cigarettes (WAOR=1.80; 95%CI: (1.80-3.00)). This study furthers research on the potential negative effects of marijuana use on health. Severe periodontal disease may be caused by marijuana leading to tooth loss, which can have a profound impact on an individual's overall quality of life and lead to various illnesses. This cross-sectional study will need to be followed by a longitudinal study to examine the potential causal effect of chronic and frequent marijuana use on periodontal health.

Associations between Individuals' Exposure to Alcohol Outlet Density and Trips to Alcohol Outlets Christina A. Mehranbod* Christina A. Mehranbod Ariana N. Gobaud Christopher N. Morrison

Background: Individuals who live in areas with greater concentrations of alcohol outlets consume more alcohol. Two complementary theoretical mechanisms could explain these associations. The proximity hypothesis states that individuals who live near more outlets have greater direct access to alcohol; the amenity hypothesis states that exposure to alcohol outlets normalizes alcohol consumption and thereby contributes indirectly to increased consumption.

Aims: The aim of this study is to test the proximity hypothesis, and to examine the spatial scales over which these direct associations may operate.

Methods: We conducted a cross-sectional study of participants in Victoria, Australia using survey data from the Victoria State Government Department of Transport Victoria Integrated Survey of Travel and Activity for 2014 - 2018. This survey randomly selects households in Victoria, Australia to complete a travel survey for one day. Logistic regression models estimated the odds of travelling to an alcohol outlet—separated into bars, restaurants, and off-premise outlets—at two geographic areas, local government areas (LGA) and postcodes.

Results: Of the 23,512 individuals included in this analysis, 355 (1.5%) travelled to a bar, 3,232 (13.7%) travelled to a restaurant, and 79 (0.3%) travelled to an off-premise outlet on the day of the survey. Individuals who lived in postcodes with greater bar density had increased odds of visiting a bar (OR=1.015, 95% CI 1.007 to 1.023), and individuals who lived in postcodes with greater restaurant density had increased odds of visiting a restaurant (OR=1.006, 95% CI 1.004 to 1.008). On the LGA-level, higher restaurant density and off-premise outlet density were associated with increased odds of visiting a restaurant and off-premise outlet, respectively (Restaurant: OR=1.006, 95% CI 1.005 to 1.008; Off-premise outlet: OR=1.119; 95% CI 1.049 to 1.194).

Conclusions: Alcohol outlet density is associated with visits to bars, restaurants, and off-premise alcohol outlets, supporting the proximity hypothesis relating alcohol outlet density to consumption. Associations differ between alcohol outlet types at different geographic scales. These mechanisms may operate complementarily to indirect amenity effects.

LATEBREAKER

Substance Use

Factors associated with transdermal alcohol concentration from the SCRAM biosensor among persons living with and without HIV Veronica L Richards* Veronica Richards Yiyang Liu Jessica Orr Robert F. Leeman Nancy Barnett Kendall Bryant Robert L. Cook Yan Wang

Background: Alcohol biosensors can objectively monitor alcohol use by measuring alcohol concentration (TAC). However, it is unclear how sociodemographic, biological, and other personal factors that influence alcohol metabolism are associated with TAC. The main aim of this study was to examine how sociodemographic factors (sex, age, race/ethnicity), biological factors (body mass index, liver enzymes: alanine aminotransferase [ALT] and aspartate transaminase [AST]), and other personal factors (HIV status, alcohol use disorder) were associated with TAC while controlling for level of alcohol use.

Methods: Data from a prospective study involving contingency management for alcohol cessation among persons living with HIV (PLWH) and without HIV that used the SCRAM biosensor were analyzed. Forty-three participants ($M_{age}=56.6$ years; 63% male; 58% PLWH) yielded 183 SCRAM-detected drinking days. Two indices derived from SCRAM: peak TAC (reflects level of intoxication) and TAC area under the curve (TAC-AUC; reflects alcohol volume)— were the main outcomes. Self-reported alcohol use (drinks/day) measured by Timeline Followback was the main predictor. To examine whether factors of interest were associated with TAC, individual Generalized Estimating Equations (GEE) were conducted. A multivariate GEE model was followed to include all significant predictors to examine their associations with TAC beyond the effect of self-reported alcohol use.

Results: Self-reported alcohol use ($B=.29$, $p<.01$) and elevated AST ($B=.67$, $p=.01$) were significant predictors of peak TAC. With TAC-AUC as the outcome, positive HIV status, female sex, elevated AST, and self-reported alcohol use were positively associated with TAC-AUC at the bivariate level. Self-reported alcohol use ($B=.85$, $p<.0001$) and female sex ($B=.67$, $p<.05$) remained significant in a multivariate GEE.

Conclusions: Future studies should consider the sex and liver function of the participant when using alcohol biosensors to measure alcohol use.

LATEBREAKER

Substance Use

Associations Between Race/Ethnicity and Increased Substance Use Frequency During the Early COVID-19 Pandemic

Emily Goldmann* Daniel Hagen Kyle Snyder Danielle Ompad Johannes Truhl

Background:

Studies have noted an increase in substance use in the U.S. since the COVID-19 pandemic began, particularly for those with mental health problems. Despite substantial racial/ethnic disparities in COVID-related socioeconomic and health-related outcomes, studies that examine changes in substance use by race/ethnicity are lacking.

Methods:

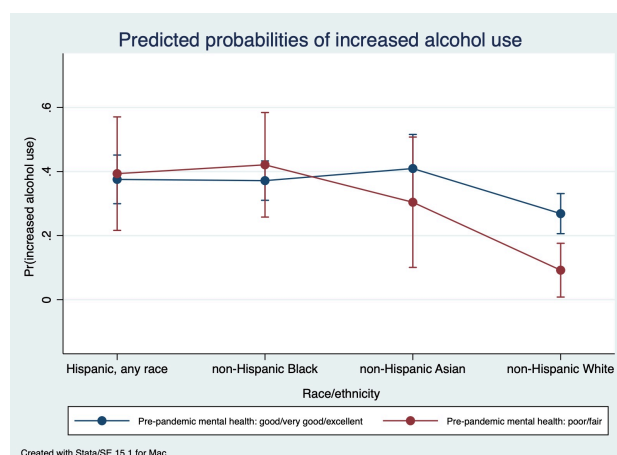
Data were collected in 5 Southern U.S. metropolitan areas (Atlanta, Austin, Dallas, Houston, New Orleans) in May/June 2020 using random-digit-dial telephone and web-based surveys (n=1,727); racial/ethnic minorities were oversampled and survey weights were applied. Past-week alcohol and cannabis use frequency, past-week consumption compared to a “normal week” (increased vs. decreased/unchanged), and self-rated pre-pandemic mental health (fair/poor vs. good/very good/excellent) were ascertained. Associations of race/ethnicity with changes in alcohol and cannabis use were evaluated in separate binary logistic regression models adjusting for gender, age, education, marital status, and use frequency; models allowing for interaction between race/ethnicity and pre-pandemic mental health were also estimated.

Results:

Approximately 33% rated their alcohol use and 36% rated their cannabis use as higher compared to a “normal week”. In adjusted models, odds of increased use of alcohol and cannabis were significantly higher for minority respondents compared to non-Hispanic Whites, with odds ratios ranging from 1.96 to 3.05 (all $p < 0.01$). Poor pre-pandemic mental health was significantly associated with lower odds of increased alcohol use only among non-Hispanic Whites, not among racial/ethnic minority respondents (Figure 1); no such interaction was observed for cannabis.

Conclusion:

Increased substance use during the current pandemic was common, particularly among racial/ethnic minority groups. Substance use treatment programs should respond to this increased need, for example by expanding telehealth services targeted to minority populations.



LATEBREAKER

Substance Use

Effect of Exposure to the FDA Health Warning Label on Electronic Cigarettes Among Adolescents: National Youth Tobacco Survey (2017-2019) Valery Mardini Cespedes* Valery Mardini Cespedes Amanda Perez Kristopher Arheart Laura McClure Olusanya Joshua Oluwole Tarek Mohamad Ghaddar Taghrid Asfar Alejandra Casas

Introduction: The use of electronic nicotine delivery systems (ENDS or e-cigarettes) is epidemic among youth in the US. ENDS emit toxic substances that damage youths' developing brains and lead to dependence, yet misperceptions about their safety are widespread. Health warning labels (HWLs) effectively communicate the risks of tobacco use. Since 2018, the FDA has required ENDS packages to display a textual HWL: "WARNING: This product contains nicotine. Nicotine is an addictive chemical." This study examines the prevalence and correlates of youth exposure to the HWL, and its effect on harm and addiction perception.

Methods: Data were pooled from the 2017-2019 National Youth Tobacco Survey. Adolescents 10-18yrs (n=19,966) were divided into 3 groups: current ENDS users (CU, used ENDS in last month; 27.3%), ENDS nonusers (NU, never used ENDS or have not in last month; 65.1%), or susceptible users (SU, think they will use ENDS in the next year; 18.4%). Prevalence rates and multivariable logistic regression analyses for HWL exposure vs. non-exposure were performed.

Analysis: Overall, 78.5% of CU, 59.2% of NU, and 73.7% of SU were exposed to the FDA HWL. Exposed CU, NU, and SU were more likely to think that ENDS are harmful vs the unexposed (OR=1.45, 95%CI=1.11-1.90; 1.86, 1.55-2.23; 1.26, 1.04-1.37, respectively). Exposed NU were less likely to be Black or Hispanic (0.71, 0.59-0.85; 0.87, 0.77-0.98, respectively) and more likely to have a household member who uses tobacco (1.60; 1.35-1.91), yet more likely to think of using ENDS in the next year (1.98, 1.33-2.93) compared to the unexposed.

Conclusion: Exposure to the FDA HWL among youth increased perception of ENDS harm but did not change perception of addiction. Exposure to the HWL among NU and SU did not prevent them from considering using ENDS in the next year. Improvement and adaptation of ENDS HWLs are needed to enhance their effect on CU and prevent NU and SU from ENDS initiation.

Rapid Planning and Deployment of a COVID-19 Surveillance System for Local Data-Informed Decision-Making: An Academic, School District, and Public Health Collaboration

Ayaz Hyder* Ayaz Hyder Anne Trinh Pranav Padmanabhan John Marschhausen Alexander Wu
Alexander Evans Radhika Iyer Alexandria Jones

Objectives: To describe the rapid planning and deployment of a school-based COVID-19 surveillance system in a metropolitan US county.

Materials and methods: We used several data sources to construct disease- and school-based indicators for COVID-19 surveillance in Franklin County, which is an urban county in Central Ohio, US. These data were collected, processed, analyzed, and visualized in the COVID-19 Analytics and Targeted Surveillance System for Schools (CATS). The CATS system included web-based applications (public and secure versions), automated alerts and weekly reports for diverse sets of stakeholders, such as public, school administrators and boards, and local health departments.

Results: We deployed a pilot version of CATS in under two months and onboarded 14 school districts in Central Ohio into CATS. Public-facing web-based applications are providing parents and students with local information for data-informed decision-making. We created an algorithm to enable local health departments to precisely identify school districts and school buildings at high risk of an outbreak and active SARS-CoV-2 transmission in school settings.

Practice implications: Data-informed decision-making is highly valued among school districts, but challenges remain for public health departments to provide local data, especially during pandemics. Piloting a surveillance system in two diverse school districts helped us to scale the surveillance system. Building on preexisting relationships and alignment of values was critical to the establishment and sustainability of the collaboration. Planning and deploying proactive and innovative public health practices during a global pandemic is no easy task but possible under the right conditions with the right collaborators.

Community Based Systems Dynamics for Reproductive Health: A Case Study from Urban Ohio, USA Ayaz Hyder* Ayaz Hyder Mikaela Smith Shawnita Sealy-Jefferson Robert Hood Shibani Chettri Ashley Dundon Abigail Underwood Danielle Bessett Alison Norris

Background: Reproductive health outcomes, risk factors, and policies are complexly interrelated.

Objectives: To describe the application of community-based system dynamics (CBSD) for reducing racial inequalities in Black-White infant mortality rates through a reproductive justice lens.

Methods: The CBSD approach involves: 1) group model building workshops; 2) modeling; and 3) implementation and dissemination. Primary workshop outcomes were: 1) a comprehensive diagram of factors for the reproductive health system in urban Ohio settings and 2) a set of co-developed materials for disseminating workshop findings and models.

Lessons Learned: Many opportunities exist for the cross-fertilization of best practices between CBSD and community based participatory research, shared learning environments offer benefits for modelers and domain experts and identifying local champions from the community helps to better manage group dynamics.

Conclusions: The CBSD approach is practical, scalable, and well-suited for addressing complex issues in reproductive health.

Smoking behavior changes after diagnosis of inflammatory disease and risk of mortality

Xinwei Hua* Xinwei Hua Emily Lopes Kristin Burke Ashwin Ananthakrishnan James Richter Chun-Han Lo Andy Chan Hamed Khalili

Background: Cigarette smoking has been shown to increase the risk of Crohn's disease (CD) while having protective and therapeutic effects against ulcerative colitis (UC). We examined changes in smoking behavior after CD and UC diagnosis and their impact on all-cause mortality.

Methods: We included participants diagnosed with incident CD or UC from three prospective cohorts: Nurses' Health Study (1978-2014), Nurses' Health Study II (1991-2013), and Health Professionals Follow-up Study (1988-2014). We assessed smoking and other risk factors biennially and confirmed diagnoses of CD or UC by medical record review. We used biennial questionnaire data within 4 years prior to diagnosis and 4 years after diagnosis to define smoking behavior changes around the time of CD and UC diagnosis. Follow-up for date and cause of death was completed through linkage to the National Death Index. Cox proportional hazard regression was used to estimate HR and 95% CI for associations between smoking behavior changes and all-cause mortality.

Results: After a median of 14 years of follow-up, we documented 104 deaths among 421 CD patients and 97 deaths among 522 UC patients. Among prediagnostic current smokers, 32% diagnosed with CD quit, and 60% diagnosed with UC quit after diagnosis. Compared to continued smokers, the multivariable-adjusted HRs (95% CI) were 0.28 (0.15-0.54) for those who quit smoking after diagnosis and 0.15 (0.07-0.32) for nonsmokers among patients with CD. Similarly, among patients with UC, smoking cessation after diagnosis was associated with a lower risk of all-cause mortality (HR=0.51, 95% CI=0.18-1.41) although it was not statistically significant.

Conclusions: In three large cohorts of health professionals, we demonstrated that smoking cessation around the time of CD and UC diagnoses is associated with a decreased risk of all-cause mortality.

Implementing an automate data collection system with web, mobile and Short-message-service (SMS) texting in gestational diabetes mellitus (GDM) management in Vietnam

Trang Pham* Trang Pham Hieu Huynh Ha Ngo Trang Huynh

Intro

Self blood glucose monitoring (SBGM) is crucial in GDM management. In Vietnam, patients and care providers (CP) record blood glucose measurements (BGM) on paper and bring them to health checkups. Utilizing SMS is affordable and feasible especially in remote area. We developed and implement a user-friendly software that utilizes web, mobile app and SMS in data capturing and visualization to facilitate and improve the process of clinical GBM management and SBGM.

Methods:

A cloud-based, open-source software (IOH-GDM) supporting Vietnamese language, utilizing SMS, web and mobile app for data collection was developed and integrated with the hospital's health information system (HIS). Patients and CP at the Gestational DM Unit of the High-Risk Pregnancy Department of Hung Vuong Hospital (HRPD) used the software to monitor BGM in GDM inpatients. Evaluation was done by survey after the first 100 patients were entered into the software. The Hung Vuong hospital internal review board approved the softwrae design, implementation, and intergration process into clinical practice.

Results:

All patients admitted to the HRPD were included in the IOH-GDM system. After 40 days of implementation, 122/141 (86.5%) inpatients with GDM had BGM data entered in the systems. The IOH-GDM was used for daily monitoring BGM, patient education and training for SBGM after discharge. CP either verified the value patient recorded or entered patients' BGM on web or mobile app in addition to recording them on paper-based medical records.

CP did not set frequency for daily BGM in 32.8% (40/122) cases, all were not on insulin; but, these patients did entered data into the system (100%). Among 101 patients with preset BGM schedule, 18.8% (19/101) did not entered data. Mean percent of data input based on expected datapoints for the preset schedule was 55.1 ± 24.8 . Of 102 patients participated in satisfaction and system usability survey, 97.1% complete all questions. Usability was around 90% in every item of ease-of-use, usable for daily SBGM. CP valued the intergration with HIS and the ability to collect longitudinal data for research purposes.

Conclusion:

In low-middle income and non-English speaking countries, having a native language software that supports multiple data collection modes, utilizing SMS and visualizing data showed potential impacts in patient empowerment, enhance care quality through real-time data monitoring and strengthen the patient-provider partnership.

Treatments for primary dysmenorrhea: an umbrella review of systematic reviews and meta-analyses of randomized controlled trials

Stefania Papatheodorou* Stefania Papatheodorou
Evangelos Evangelou Ines Belaroussi

Background: Dysmenorrhea has a significant negative impact on the quality of life, productivity, and workdays lost of affected females. Numerous meta-analyses and systematic reviews have claimed that several types of pharmacological and non-pharmacological interventions are effective in treating primary dysmenorrhea.

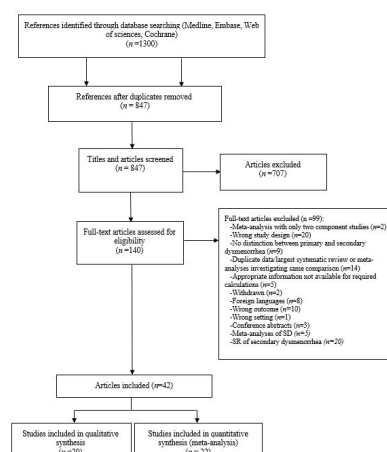
Objective: The aim of this umbrella review was to identify systematic reviews and meta-analyses on the effectiveness of pharmacologic and nonpharmacologic interventions for primary dysmenorrhea, to summarize available evidence for these treatments and to evaluate if there is evidence for biases in this literature and assess the robustness of epidemiologic evidence.

Study design: A systematic literature search was carried out in PubMed, EMBASE, Web of Science, and the Cochrane Database of Systematic Reviews from inception to 6 March 2020 to identify systematic reviews and meta-analyses of studies examining the effectiveness of pharmacologic and non-pharmacologic therapies for primary dysmenorrhea.

Results: From the 847 eligible articles, forty-two articles were included. Twenty-two out of the 42 eligible papers (52%) provided quantitative synthesis corresponding to 50 unique comparisons investigating pharmacological (70%) and nonpharmacological (30%) interventions for primary dysmenorrhea covering six domains (medication, acupuncture, physical activity, herbal therapy dietary supplementation, and other non-pharmacological treatments, e.g heat, manual therapy). Only two out of 22 articles were rated as high quality using the AMSTAR 2 tool.

Forty-four out of 50 (88%) comparisons reported a nominally statistically significant summary result ($P < 0.05$) as per random-effects, suggesting the superiority of the investigated intervention compared to an active or inactive control group, or a mix of both. GRADE approach demonstrated a low level of evidence in 90% of the comparisons while no association was supported by high-level evidence. Comparisons with a moderate level of evidence were NSAIDs versus placebo, acupoint therapy vs no treatment, and manual acupuncture vs NSAIDs.

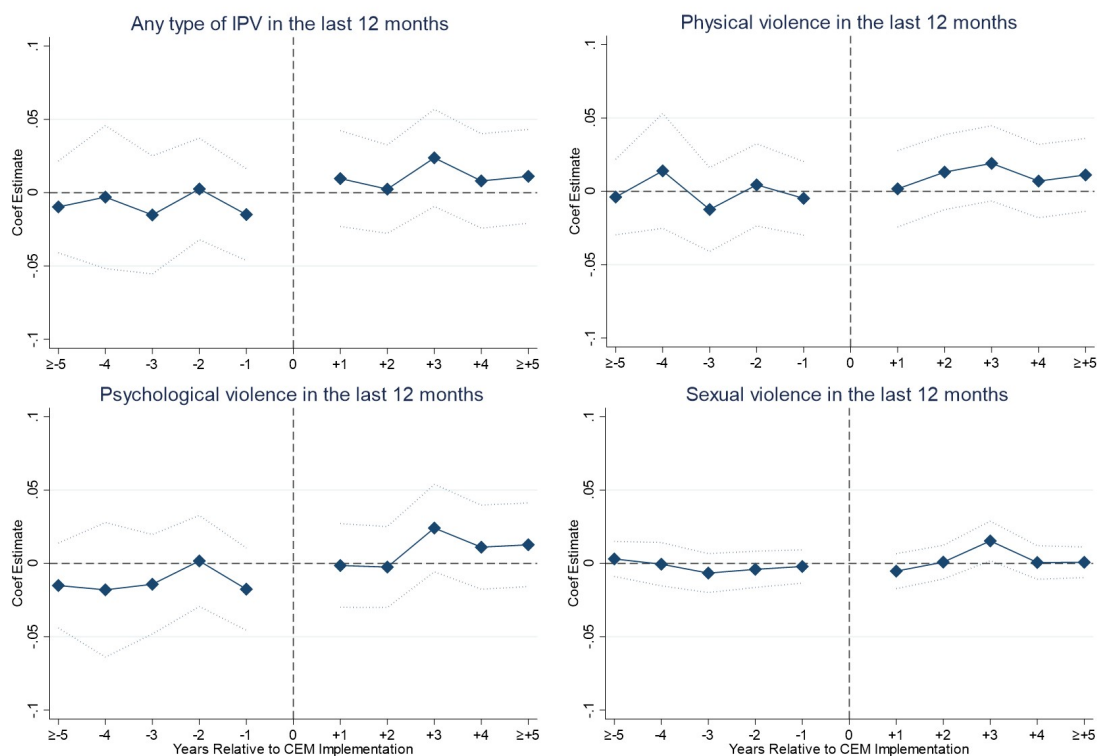
Conclusion: This umbrella review demonstrates that there is a wide range of treatment comparisons showing the benefit of some interventions, but high-quality evidence is lacking.



Are We Doing Enough To Combat Violence Against Women? Examining The Policy Effectiveness of “Women’s Emergency Centres” In Peru Renzo Calderon-Anyosa* Renzo Calderon-Anyosa Jay Kaufman

A strategy to combat intimate partner violence (IPV) in Peru includes the creation of “Women Emergency Centers” (CEM: Centro de Emergencia Mujer). These centers provide free comprehensive assistance and preventive services. Our aim is to conduct a policy analysis to evaluate the impact of the CEMs on reported IPV from 2004 to 2016. We link the outcome assessment at the individual level (any type of violence, physical, psychological or sexual violence experienced in the last 12 months) from the Demographic Health Survey to the creation year of each CEM. This accounts for cross-sectional variation to the exposure of the CEMs at any given year in each district and variation across time because CEMs were implemented in different years. This spatial and temporal variation allows us to conduct a difference-in-differences linear probability model with year and district fixed effects. In order to assess lags effects as well as the pre-treatment parallel trend assumption, an event study was conducted. Figure 1 shows the event study for the effect of the CEM implementation on the different types of IPV. No pre-treatment differences were observed (identifying assumption). CEMs did not show an effect in any type of IPV in the last 12 months. Although the CEMs appeared to have a null effect, this type of intervention has two effects that could potentially go in opposite directions: 1) it could reduce “true” cases of IPV, and 2) it could increase IPV reporting due to an increase in awareness. It is still to be determined whether the null effects correspond to the cancellation of the effect between the decrease in true cases and the increase in reporting. Our next steps are aimed at separating these 2 effects since assessing the effectiveness of nationwide interventions like the implementation of CEMs gave us a better understanding of the capacity to prevent IPV with interventions as such. In the same way, this could contribute to improve and redirect current policies.

Figure 1. Event study: CEM implementation effect on different types of IPV



Postpartum Loss of Medicaid Coverage in Wisconsin Marina C. Jenkins* Marina Jenkins
Daphne Kuo Deborah Ehrental

In most U.S. states, Medicaid eligibility for pregnancy ends two calendar months after delivery. Depending on income, this policy may lead to coverage loss after childbirth which may affect continuity and quality of postpartum care. This study aimed to understand the extent of the problem and identify mothers most affected by coverage loss during the first postpartum year.

We used 2014-2016 Wisconsin birth records linked to Medicaid enrollment to determine mother's coverage by calendar month up to 12 months following a covered delivery. We defined Medicaid loss as not being enrolled 3+ months; a gap in coverage was defined as being uncovered 3+ months but regaining coverage. The primary outcome was time in months of postpartum Medicaid loss. Covariates were race/ethnicity, parity, age, and a diagnosis of hypertension or diabetes. Analysis included descriptive statistics and hazard ratios adjusted for all co-variates and was performed in SAS v9.4.

Of 67,456 Medicaid-covered births in the sample 53.0% of mothers were white non-Hispanic (NH), 30.7% primiparous, average age 26.6 (SD=5.5). Overall, 14.5% (n=9,799) lost Medicaid during the postpartum year: 6.9% (n=678) immediately after delivery, 27.6% (n=2,708) by 6 months and 32.3% (n=3,162) by 12 months. Another 33.2% (n=3,251) experienced a gap in coverage. Race, lower parity, and younger age were associated with Medicaid loss. Asian/Pacific Islander, Laotian/Hmong and white (NH) mothers were more likely to lose Medicaid than other groups (p<.001). Mothers with <3 prior live births, and those <19 years, were more likely to lose Medicaid (p<.001). There were no differences for those with diabetes or hypertension.

Most mothers with a Medicaid-covered births were continuously enrolled in Medicaid during the first postpartum year. Those not continuously enrolled may or may not have gained private insurance. Expanding Medicaid pregnancy coverage to one year postpartum may benefit certain groups.

Concordance of Gestational Diabetes Mellitus at First Live Birth between Electronic Health Records and Vital Statistics Birth Records Data in Florida, 2012-2017 Yi Zheng* Yi Zheng Hui Hu

Background: Birth records data are widely used to study gestational diabetes mellitus (GDM), a major pregnancy complication with adverse impacts on both women and their offspring. Although birth records data contain a wide range of information, previous studies showed that potential misclassifications exist in GDM. Electronic health record (EHR) data provide more accurate diagnosis information and usually can serve as the gold standard. In this study, we aim to examine the concordance of GDM between EHR and birth records data in Florida.

Methods: We linked EHR data from the OneFlorida Data Trust in 2012-2017 with Florida statewide birth records data from the Bureau of Vital Statistics, Florida Department of Health. In total, 286,245 records of pregnant women were successfully linked. We further excluded women who did not receive a glucose challenge test as indicated by the procedure and lab records in the EHR, those with unknown GDM status from the birth records data, and those who did not give live birth for the first time. Using GDM status from the EHR as the gold standard, we calculated the sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), percent agreement, and Kappa value. Both unstratified analyses and stratified analyses by sociodemographic status (i.e., maternal age, race/ethnicity, education, marital status, prepregnancy body mass index, and the trimester when prenatal care began) were conducted.

Results: Among a total of 154,543 pregnant women included in this study, 7,244 and 19,545 GDM cases were identified in birth records and EHR data, respectively. Overall, the percent agreement was 90.8% and Kappa was 0.43 (95% confidence interval [CI]: 0.42, 0.44), indicating a moderate agreement. Sensitivity (0.32, 95% CI: 0.32, 0.33), specificity (0.99, 95% CI: 0.99, 0.99), PPV (0.87, 95% CI: 0.86, 0.88) and NPV (0.91, 95% CI: 0.91, 0.91) were also calculated. Stratified analyses by sociodemographic status showed Kappa ranged from 0.35 (among those with maternal age <20 years) to 0.47 (among those with maternal age >35 years).

Conclusions: We found a moderate concordance of GDM between the birth records and EHR data in Florida in 2012-2017, which also vary by sociodemographic status. More efforts are needed for future studies assessing GDM using birth records data to address the misclassifications.

Correlates of poor sleep quality among reproductive-aged Black women Chad M. Coleman*

Chad M. Coleman Traci N. Bethea Amelia K. Wesselink Lauren A. Wise Ganesa Wegienka

Suboptimal sleep quality has been associated with adverse health outcomes. Sleep disturbances are increasing in prevalence in the United States (U.S.), and are more common among U.S. Black women and women of low socioeconomic status. We sought to characterize sleep quality among a cohort of Black women of reproductive age and identify correlates associated with poor sleep quality. The Study of Environment, Lifestyle and Fibroids is a prospective cohort study of Black women recruited from 2010-2012 from Detroit, MI. At the 80-month follow-up visit, participants completed the validated Pittsburgh Sleep Quality Index (PSQI) to assess self-reported sleep quality and characteristics, with global scores ranging from 0-21. Participants also reported their demographic, lifestyle, health, and menstrual cycle characteristics. We used age, income, and education-adjusted logistic regression models to calculate odds ratios and 95% confidence intervals for each potential correlate with poor sleep quality (global PSQI score >5). The average global score among the 976 participants who completed the PSQI was 7.05 ± 3.74 (range of 0-20) and 589 (60.4%) women had a PSQI >5. Broadly, variables associated with poor sleep quality included night shift work, being married or partnered, body mass index $\geq 35 \text{ kg/m}^2$, self-reported lower quality of life and perceived health status, and menstrual cycle characteristics. Some of the strongest correlates of poor sleep were current cigarette smoking (<10/day, aOR 1.29, 95% CI 0.81-2.06; ≥ 10 /day, 1.62, 95% CI 0.75-3.47), education less than bachelor's degree (\leq high school or GED, 1.19, 0.75-1.88), annual household income <\$50,000 (\leq \$20,000, 1.68, 1.11-2.54), physician diagnosed depression (3.48, 95% CI 2.24-5.39), and anxiety (3.24, 95% CI 2.10-4.98). Data collection is ongoing. Latent classes will be created using all examined variables to identify similar groups of women and compare global and domain-specific PSQI scores across classes.

Vulvar pain and mental health outcomes among college-aged students: Findings from the Healthy Minds Study Chad M. Coleman* Chad M. Coleman Julia C. Bond Caroline Pukall Sarah Lipson Bernard L. Harlow

Vulvar burning or pain on contact is a highly prevalent condition. Women with chronic vulvar pain report reduced quality of life and mental health. However, there is limited research on the impact of vulvar pain and mental health outcomes among college-aged students. We assessed associations of depression and anxiety symptoms, history of trauma or stress disorders, and suicidal ideation, among Boston University students participating in the Healthy Minds Study who did and did not endorse vulvar pain using the Vulvar Pain Assessment Questionnaire (VPAQ). There were 993 (46.3%) of 2145 eligible respondents that completed the VPAQ, of which 832 (83.8%) did not endorse a history of vulvar pain, 131 (13.2%) endorsed vulvar pain for <3 months, and 30 (3.0%) for ≥3 months. We assessed symptom scores of depression (PHQ-9) and anxiety (GAD-7), categorized as tertiles, and whether women had self-reported experiences of trauma or suicidal ideation. Age-adjusted logistic regression models were used to generate odds ratios and 95% confidence intervals. Compared to women with no history of vulvar pain, women with vulvar pain lasting <3 months and ≥3 months had increased odds of depressive symptoms in the highest tertile (OR=1.73, 95%CI 1.08-2.78; OR=2.25, 95%CI 0.86-5.88; respectively), and increased odds of anxiety symptoms in the highest tertile (OR=1.80, 95%CI 1.12-2.88; OR=2.61, 95%CI 1.07-6.35; respectively). In addition, comorbid anxiety and depressive symptoms in the highest tertile of scores was strongly associated with vulvar pain (<3 months: OR=2.07, 95%CI 1.15-3.71; ≥3 months: OR=4.08, 95%CI 1.26-13.25). Finally, compared to women with no history of vulvar pain, women with vulvar pain lasting <3 months and ≥3 months were more likely to report trauma and stress related disorders (OR=1.72, 95%CI 0.91-3.28; OR=2.36, 95%CI 0.76-7.06; respectively), and suicidal ideation (OR=1.52, 95%CI 0.90-2.57; OR=1.36, 0.46-4.01; respectively). Data analysis is ongoing.

Association of WASH-related violence and depressive symptoms in adolescent girls and young women in HIV prevention trials network 068 Ruvani Jayaweera* Ruvani Jayaweera Dana Goin Rhian Twine Torsten B. Neilands Catherine MacPhail Ryan G. Wagner Sheri A. Lippman Kathleen Kahn Audrey Pettifor Jennifer Ahern

Background

Over 2.5 billion people around the world lack access to improved water, sanitation, and hygiene (WASH); the vulnerability to violence that women and girls face during WASH activities is often overlooked. There is a lack of research on experiences of WASH-related violence, though qualitative evidence has highlighted how water and sanitation facilities in some settings are a source of anxiety or fear. This study aims to quantify the association between experience or fear of violence when using the toilet or collecting water and depressive symptoms among a cohort of young women in South Africa.

Methods

Data for this study are from the HPTN 068 cohort of adolescent girls in rural Mpumalanga Province, South Africa. Participants were aged 13 - 21 at baseline and followed annually for up to 4 years. Lifetime experience of violence or fear of violence when using the toilet and collecting water was collected by self-report; depressive symptoms in the past week were measured using the Center for Epidemiological Studies Depression Scale (CES-D). We used g-computation to calculate the risk difference of depression (CES-D score > 15) associated with each domain of violence, controlling for baseline covariates.

Results

One-fifth (20.4%) of respondents reported ever experiencing violence when using the toilet; 22.8% reported ever experiencing violence when collecting water, and 31.8% reported depression. In preliminary results, the absolute marginal risk of depression was substantially higher for experience of violence when using the toilet (RD 12.4%, 95% CI: 1.9%-22.9%), or when collecting water (RD 9.2%, 95% CI: 0.4%-17.9%), as well as for worry about violence when using the toilet (RD 14.6%, 95% CI: 5.1% - 24.1%), or when collecting water (RD 14.4%, 95% CI: 4.7%-24.1%).

Conclusion

Experience of WASH-related violence is common among young women in rural South Africa, and experience or worry of experiencing violence is associated with higher risk of depressive symptoms.

The Smoking-Hypertension Paradox in Pregnancy: Confounding and Competing Risks in a Multiethnic US Cohort from 1998 to 2019

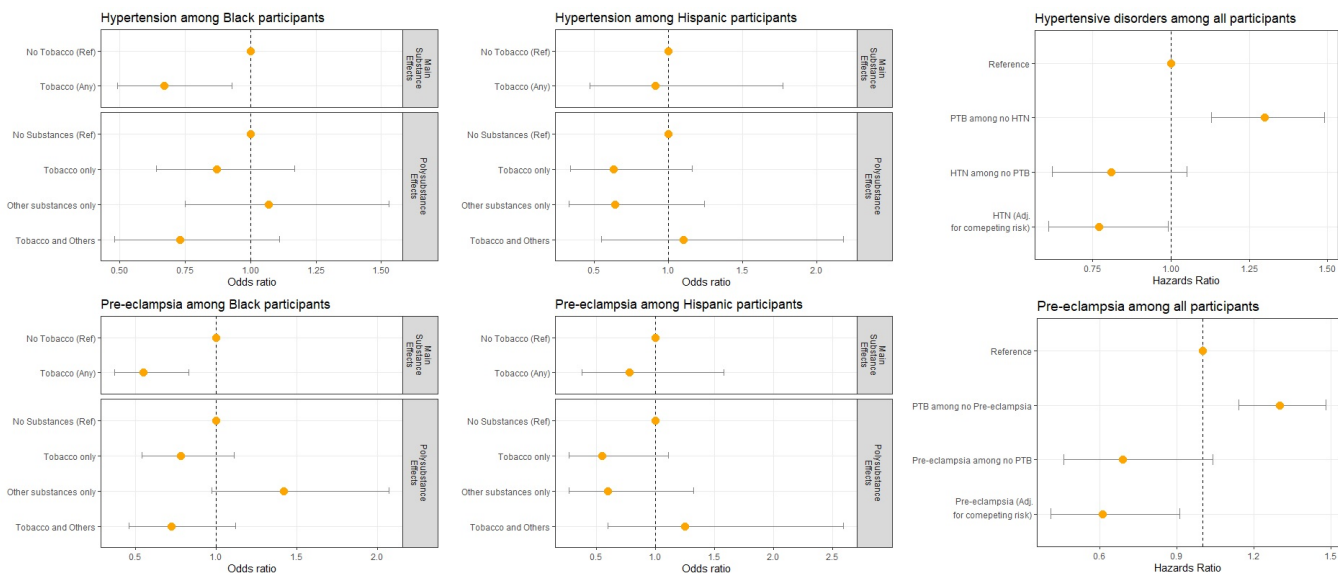
Henri M. Garrison-Desany* Henri Garrison-Desany
 Christine Ladd-Acosta Xiumei Hong Guoying Wang Irina Burd Zila van der Meer Sanchez Xiaobin Wang Pamela J. Surkan

Background: Smoking during pregnancy is related to reduced risk of a spectrum of hypertensive (HTN) disorders known as the “smoking paradox.” We sought to identify the impact of potential confounding and competing risks that may explain this association.

Methods: We used baseline data from women enrolled in the Boston Birth Cohort from 1998 to 2019. The sample of 8,510 participants included 4,027 non-Hispanic Black participants and 2,428 Hispanic participants. Women self-reported using any tobacco, alcohol, cannabis, opioids, or cocaine during pregnancy. We used logistic regression to assess effect modification of race/ethnicity, confounding by indication due to concurrent substances or prior pregnancy on (1) any hypertensive disorder and (2) pre-eclampsia. We also used cause-specific Cox models and Fine-Gray models to assess the effect of early gestational age as a collider or competing risk to pre-eclampsia, respectively.

Results: We first replicated the paradox showing tobacco smoking to be protective for hypertensive disorders among Black participants (aOR: 0.72, 95% CI: 0.54–0.97), but observed a null effect for Hispanic participants (aOR: 0.82, 95% CI: 0.43–1.59). Black participants who used opioids during pregnancy had a 2.58 increase in adjusted odds (95% CI: 1.22–5.45) of HTN disorders. Among Hispanic participants, using cannabis during pregnancy increased the odds of HTN disorders (aOR: 2.41, 95% CI: 1.00–5.84). In our cause-specific Cox regression, tobacco use during pregnancy was no longer significantly associated with pre-eclampsia or hypertensive disorders after stratifying for preterm birth (PTB).

Conclusions: In this multi-ethnic cohort, the smoking paradox was either not observed, reversed, or became null after accounting for race/ethnicity, other substance use, and competing risk of preterm birth. These findings highlight that colliders and competing risk have likely biased findings of smoking-hypertension association in pregnancy.



An Examination of the Relationship between Gender, Empowerment and IPV Beliefs among Young Adults in Mysore, India Yandra Mariano* Yandra Mariano Makella Coudray Purnima Madhivanan Dionne Stephens

Background:

Intimate partner violence (IPV) has been defined in existing literature as an ongoing problem around the world; in India, an estimated 40% of women experience some form of IPV victimization. This study aims to identify the beliefs young Indian adults have about relationships, dating, IPV, and the cultural factors that can influence these beliefs.

Methods:

This study was conducted in collaboration with Florida International University (FIU), the Samrudhhi Foundation (SF), and the Public Health Research Institute of India (PHRII). A total of 266 English speaking participants, between 18 to 25 years, residing in Mysore, India participated; 142 were women (53.4%) and 123 were men (46.2%) participants. Participants completed a survey and focus group discussion, which assessed sociodemographic data, views on IPV, acceptable dating behaviors, and cultural beliefs. Chi-squared tests were used to assess the relationship between sociodemographic variables and various cultural beliefs. This study was approved by the PHRII and FIU institutional review boards.

Findings:

There was a significant association found between sex and adversarial gender beliefs [encouragement of men pursuing higher education ($p=0.000$), and gender autonomy and independence ($p=0.000$)]. The following significant values were found between sex and the attitudes towards women measure: the encouragement of women romantically pursuing men ($p=0.035$), male leadership ability in contrast to women ($p=0.000$), and women pursuing and making sexual advances on male romantic interest ($p=0.000$). Finally, there was a significant difference found between sex and the following beliefs about wife-beating measures: taking action after witnessing wife-beating ($p=0.000$), a woman leaving husband or fiancé after being beaten ($p=0.004$), and female autonomy after being beaten by husband or fiancé ($p=0.044$).

Interpretation:

The results of this study have concluded that women are more likely to be empowered than men. However, both genders in this sample still adhered to some oppressive gender norms, especially when discussing empowerment and autonomy of IPV victims. These findings may have been subjected to social desirability and recall biases.

Word Count: 344

Risk Factors of Alcohol use during pregnancy: findings from a national survey data of Mongolia Erdenetuya Bolormaa* Erdenetuya Bolormaa Seung-Ah Choe**Background**

Antenatal substance use is associated with significant risks to the unborn child. Alcohol is teratogenic and consumption during pregnancy can result in abortions, fetal alcohol syndrome (FAS), and congenital anomalies as well as low birth weight (LBW), preterm birth and perinatal death. In addition, children exposed to alcohol in the fetal period are more likely to develop mental disorders and behavioral problems including antisocial personality or hyperactivity in adolescence and adulthood. Alcohol abuse has been recognized as one of the primary public health challenges in Mongolia. We aimed to assess associated factors with alcohol and tobacco use during pregnancy.

Materials and methods: We analyzed the data of National Study on Gender-based Violence conducted in 2017 (<http://web.nso.mn/nada/index.php/catalog/central/about>). The sampling frame includes units from all 21 provinces and nine districts of the capital city.

Participants underwent face-to-face interviews providing their information on demographic characteristics, reproductive history, partner and health-related behavior during pregnancy. We explored association between pre-pregnancy factors selected from prior studies with alcohol drinking during pregnancy among women who had the latest childbirth within 5 years. We calculated odds ratios (OR) for alcohol drinking during pregnancy using R (ver.4.0.2).

Result: Among a total of 1,718 mothers, 5.1% (n=88) reported they used alcohol during their latest pregnancy. When the husband had a problem of excessive alcohol drinking (1.98, 95%CI: 1.24, 3.16) and did not want the pregnancy (2.49, 95% CI: 1.11, 5.58), the ORs of alcohol use were higher than reference groups. Smoking during pregnancy (OR, 12.51, 95%confidence interval (CI): 5.84, 26.81) was strongly associated with alcohol use during pregnancy. Associations with younger age, lower education, and higher parity were not evident regardless of model specification.

Conclusion: In a cohort of young Mongolian mothers, partner's excessive alcohol drinking and pregnancy intention were predictive for maternal alcohol use during pregnancy. This finding highlights the role of partner in preventing alcohol use in pregnant mothers.

Pesticide residue intake from fruit and vegetable consumption and risk of uterine fibroids

Colette Davis* Colette Davis Nichole Garzia Kara Cushing-Haugen Kathryn Terry Yu-Han Chiu Jorge E. Chavarro Stacey A. Missmer Holly Harris

Objective: Dietary factors may play a role in uterine fibroids etiology due to their potential to modify endogenous hormones and their inflammatory effects - these processes may be influenced by food contaminants including pesticides. We sought to examine the association between pesticide residue intake from consumption of fruits and vegetables and risk of ultrasound or hysterectomy-confirmed fibroids.

Design: Prospective cohort study using data collected from 52,982 premenopausal women from 1999-2009 in the Nurses' Health Study II.

Methods: Every four years, diet was assessed with a validated food frequency questionnaire. We classified fruits and vegetables into high- or low-pesticide-residues using a validated method based on surveillance data from the U.S. Department of Agriculture. Multivariable Cox proportional hazards models were used to calculate RR and 95% CIs for the association between high and low PRBS and fibroids.

Results: During 10 years of follow-up (median age at baseline 42 years), 4,285 incident cases of ultrasound or hysterectomy-confirmed fibroids were reported. No association was observed between intake of high-pesticide residue (RR for 5th vs 1st quintile=0.91; 95% CI=0.80-1.03; $p_{\text{trend}}=0.12$) nor the low-pesticide residue (RR for 5th vs 1st quintile=1.01; 95% CI=0.88-1.14; $p_{\text{trend}}=0.84$) fruits and vegetables and fibroids.

Conclusions: No clear associations were observed between intake of high or low pesticide residue fruits and vegetables and risk of uterine fibroids. These results suggest that pesticide residues on fruits and vegetables are not strong contributors to fibroid risk among women in their 30s, 40s, and 50s. Additional studies examining an exposure window more proximal to fibroid initiation among younger women and assessing class specific pesticides are needed.

Predictive models for iron status in postmenopausal women Ann Von Holle* Ann Von Holle
 Katie M. O'Brien Dale P. Sandler Clarice R. Weinberg

Serum iron levels may be important contributors to health outcomes, but it is not often feasible to measure levels in the large scale or long-term studies needed to study health risks. Predictive exposure models that use factors such as supplement use, lifestyle, and blood donation that have been associated with iron status, may provide a more feasible alternative for studying health effects associated with iron status.

Methods

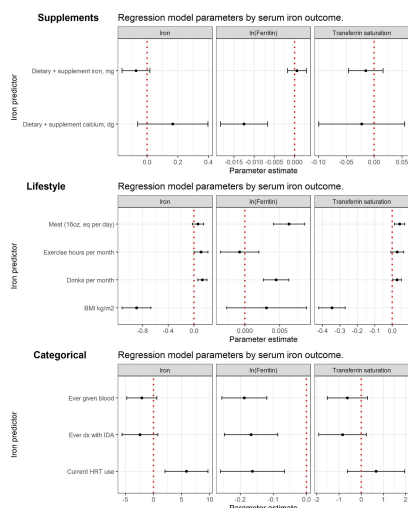
Using three serum iron measures (iron (mg/dL), ferritin (mg/dL), and transferrin saturation (%)) collected at study entry in the US-wide Sister Study, we estimated associations with common iron predictors at baseline with simple age-adjusted multivariable linear regression models or splines depending on fit for women who were postmenopausal at study entry (n=2,088).

Results

Positive linear associations with log transformed serum ferritin (coefficient; 95% CI) included alcoholic drinks per month (0.004; 0.003, 0.006), meat consumption (per 16 ounces per day) (0.006; 0.004, 0.009), and body mass index (BMI, kg/m²) (0.003; -0.003, 0.009). Inverse associations included history of blood donation (-0.19; -0.26, -0.12), ever-diagnosed with iron deficiency anemia (-0.17; -0.25, -0.09), current hormone replacement therapy (HRT) use (-0.17; -0.26, -0.07), dietary and supplemental calcium (dg) (-0.012; -0.018, -0.007), and exercise (hours per month) (-0.001; -0.003, 0.002). Serum ferritin increased until around 20 months since the last menstrual period then declined. Directions of association for these predictors were similar for iron and transferrin saturation outcomes except for BMI, HRT, and exercise. The R² indicating proportion of variance in outcome explained by the predictors was 0.08 for iron, 0.10 for ferritin and 0.08 for transferrin saturation.

Summary

Common predictors of iron status largely match expected directions of association, but they do not explain a large proportion of variance of serum iron indicators commonly used in clinical practice.



Is prenatal diet associated with the composition of the vaginal microbiome? Emma Rosen*
Emma Rosen Anna Maria Siega-Riz Chantel Martin Kim Ludwig Patricia Basta Gregory Buck Myrna Serrano Jennifer Fetweiss Michael Wu Shan Sun Anthony Fodor Stephanie Engel

Background: The vaginal microbiome is a constellation of bacterial species whose balance helps maintain a woman's health. Shifts away from a *Lactobacillus*-dominated microbiome have been associated with adverse pregnancy outcomes such as preterm birth and miscarriage, though high levels of *Lactobacillus iners* may indicate a transition to an unhealthy microbiome. The effects of diet on vaginal microbiota and differences by race remain largely unexamined, though it represents an important and modifiable influence on vaginal health.

Methods: For this study, we leveraged a racially diverse prenatal cohort of North Carolina women enrolled between 1995-2001. Women completed food frequency questionnaires about diet over the previous 3 months and foods were categorized into subgroups: fruits, vegetables, nuts/seeds, whole grains, low-fat dairy, sweetened beverages, and red meat. Vaginal swabs collected in mid-pregnancy were sequenced using 16S metagenomics. We divided women into 3 groups based on species predominance: *Lactobacillus iners*, *Lactobacillus* miscellaneous, and Bacterial Vaginosis (BV)-associated bacteria. Adjusted Poisson models with robust variance estimators were run to assess the risk of being in a specific vagitype compared to the referent. Models were stratified on maternal race (black/white).

Results: In this study of 634 women, higher consumption of dairy was associated with increased likelihood of membership in the *L. crispatus* group compared to the *L. iners* group in a dose-dependent manner (RR for quartile 4 vs. 1: 2.01 [95% CI: 1.36, 2.95]). Results were stronger among black women compared to white women (3.04 [1.42, 6.53] vs. 1.62 [1.06, 2.49]). There were no detected associations between any other food groups or risk of membership in the BV-group.

Conclusions: Higher consumption of low-fat dairy was associated with increased likelihood of vagitype dominated by *L. crispatus*. These results should be cautiously interpreted given the cross-sectional design.

Exposure to endocrine disrupting chemicals (EDCs) and cardiometabolic health during pregnancy: the HOME Study Ann Vuong* Ann Vuong Joseph M Braun Andreas Sjodin Antonia M Calafat Kimberly Yolton Bruce P Lanphear Aimin Chen

Toxicology studies have identified pregnancy as a window of susceptibility for endocrine disrupting chemicals (EDCs) and women's cardiometabolic health. No study in humans, however, has examined EDC mixtures and cardiometabolic health during pregnancy. We used the Health Outcomes and Measures of the Environment (HOME) Study to examine whether bisphenol A (BPA), polybrominated diphenyl ethers (PBDEs), per- and polyfluoroalkyl substances (PFAS), and phthalates are associated with blood pressure, fasting plasma glucose, and lipids in 388 pregnant women. We measured PBDEs and PFAS in serum at 16 weeks gestation, while BPA and phthalates were quantified in urine at 16 and 26 weeks. We used linear regression and Bayesian Kernel Machine Regression (BKMR) to estimate associations of individual EDCs and their mixtures with cardiometabolic health during pregnancy. A 10-fold increase in BDE-28 was associated with a 13.1 mg/dL increase in glucose (95% CI 2.9, 23.2) in linear regression. The BKMR model also identified BDE-28 as having a positive association with glucose. BDE-28, BDE-47, and BDE-99 were positively associated with cholesterol in both single- and multi-pollutant models, whereas a suggestive negative association was noted with BDE-153. Mono-n-butyl phthalate ($\beta=-7.9$ mg/dL, 95% CI -12.9, -3.0) and monobenzyl phthalate (MBzP) ($\beta=-6.3$ mg/dL, 95% CI -10.6, -2.0) decreased cholesterol in linear regression, but only MBzP was an important contributor with BKMR. Overall, we observed positive associations of PBDEs with glucose and cholesterol levels during pregnancy, while negative associations were found between some phthalates and cholesterol. No relationship was noted for BPA or PFAS with cardiometabolic health during pregnancy.

LATEBREAKER

Women's Health

Concordance of self-reported sexual intercourse frequency between members of heterosexual couples attempting conception Julia Bond* Julia Bond Lauren Wise

Background

Many research questions require accurate information on sexual behaviors. However, there is no “gold standard” for assessing sexual behavior. Concordance of inter-partner reports of sexual behavior has been proposed as one method of estimating the reliability and, indirectly, validity of self-report data.

Methods

We analyzed data from Pregnancy Study Online (PRESTO) among heterosexual dyads attempting conception. Self-reported sexual frequency at baseline was assessed using the same question in both partners: “In the past month, about how often did you have sexual intercourse with your partner?” Response options were: <1 time/month, 1 time/month, 2-3 times/month, 1 time/week, 2-3 times/week, 4-6 times/week, or daily. We used weighted and unweighted Kappas to assess the intra-partner concordance of reported frequency and log-binomial regression to estimate probability ratios (PRs) and 95% CIs) for predictors of discordance.

Results

Our sample included 2,127 couples. 1,374 reported concordant sexual frequency (64.6%), while men reported less frequent sex in 497 (23.4%) couples and more frequent sex in 256 (12.0%) couples. Unweighted and weighted Kappas were 0.51 (95% CI 0.48-0.54) and 0.63 (95% CI 0.61-0.66), respectively. Longer relationship length was associated with men underreporting relative to their partners (PR=1.19, 95% CI 0.96-1.49). Being unmarried and more educated than one's female partner were associated with men overreporting relative to their partners (PR=1.44, 95% CI 1.00-2.08; PR=1.45, 95%CI 1.07-1.96, respectively).

Discussion

Our study highlights challenges of accurate measurement of a construct with no gold standard. We found that sexual frequency had only moderate concordance among couples planning to conceive, and that selected social factors affected concordance.

LATEBREAKER

Women's Health

Neighborhood Disadvantage and SARS-CoV-2 Infection during Pregnancy in New York City

Erona Ibroci* Erona Ibroci Teresa Janevic Jezelle Lynch Stephanie Sestito Nina Molenaar Anna-Sophie Rommel Lotje De Witte Joanne Stone Elizabeth Howell Veerle Bergink

COVID-19 disproportionately impacts New York City (NYC) minority and low-income communities. Few studies explored risk of SARS-CoV-2 infection among pregnant women from those communities, since previous research relied on SARS-CoV-2 PCR test surveillance data and did not focus on pregnant women. Our objective is to investigate the relationship between neighborhood disadvantages and SARS-CoV-2 infection during pregnancy. The current analysis includes 763 women from an ongoing pregnancy cohort who delivered at two hospitals in New York City between April-November 2020. Neighborhood disadvantage was measured by a previously published index on COVID-19 infection risk based on NYC ZIP code data. It accounted for factors affecting viral spread, such as ability to social isolate, commuting, essential work, income, population density, and food access. We categorized the index into quartiles (Q1: highest disadvantage, Q4: lowest disadvantage). Blood samples collected during pregnancy were tested for SARS-CoV-2 IgG titers through serologic enzyme-linked immunosorbent assays. The covariates race/ethnicity, insurance, age, and parity were collected from electronic medical records. Log-binomial regression models measured adjusted risk ratio (aRR) estimates and 95% confidence intervals between women living in Q1, Q2, or Q3 vs Q4 and SARS-CoV-2 infection. 132 (17%) women had detectable SARS-CoV-2 IgG titers before delivery. Women in high disadvantaged neighborhoods had increased risk of SARS-CoV-2 infection during pregnancy (Q1 vs. Q4 aRR: 1.9 (1.1, 3.3); Q2 vs. Q4 aRR: 2.4 (1.6, 3.8); Q3 vs. Q4 aRR: 1.8 (1.2, 2.9)) compared to those in the lowest disadvantaged neighborhoods. Our findings show that neighborhood disadvantage is independently associated with risk of COVID-19 infection during pregnancy.

LATEBREAKER

Women's Health

The impact of intimate partner violence in the postpartum period on postpartum care utilization: Evidence from the Pregnancy Risk Assessment Monitoring System, 2012 - 2015

Timothy Ihongbe* Timothy Ihongbe

Introduction

Intimate partner violence (IPV) is a major public health concern in the US and adversely impacts women's reproductive health as early as the preconception period through the period of pregnancy up to the postpartum period. IPV in the prenatal period has been associated with inadequate utilization of prenatal care services. However, the impact of IPV in the postpartum period on postpartum care utilization has not been fully explored. This study aims to examine the impact of postpartum IPV victimization on postpartum care visit (PPCV) attendance.

Methods

Data from the 2012-2015 Pregnancy Risk Assessment Monitoring System (PRAMS) for the states of Pennsylvania and Wyoming were utilized (N=6397). Multivariable logistic regression was used to examine the association between postpartum IPV victimization and PPCV attendance, adjusting for confounding factors and accounting for the complex nature of the survey.

Results

About 1.8% of women reported IPV victimization during the postpartum period and approximately 10% did not attend their PPCV. Results from multivariable logistics regression showed that IPV victimization during the postpartum period was significantly associated with lower odds of PPCV attendance (adjusted OR=0.41, 95% CI= 0.19-0.88).

Conclusions

This study showed that IPV victimization during the postpartum period significantly reduces the likelihood of women attending their PPCV. This highlights the importance of screening for IPV victimization right from the preconception period up till the postpartum period as the PPCV provides an important opportunity to assess the physical and psychosocial well-being of mothers, as well as counsel them on family planning and behaviors that may impact their health and that of their infant.

LATEBREAKER

Women's Health

Reproducibility and Relative Validity of Alternative Methods for Assessing Physical Activity in Epidemiologic Studies Laila Al-Shaar* Laila Al-Shaar Claire H. Pernar Andrea K. Chomistek Eric B. Rimm Jennifer Rood Meir J. Stampfer A. Heather Eliassen Junaidah B. Barnett Walter C. Willett

Purpose: We evaluated the reproducibility and validity of a self-administered physical activity questionnaire (PAQ) and web-based 24-hour recall (ACT24) among 683 participants of the Women's Lifestyle Validation Study conducted among subgroups of the Nurses' Health Studies (2010-2012).

Methods: Two PAQs, four ACT24s, two 7-day accelerometer measurements, four resting pulse rate (RPR) measurements, and one doubly-labeled water (DLW) measurement (repeated in 90 participants), were collected over 15 months. Intraclass correlation coefficients (ICCs) were computed to assess reproducibility. Spearman rank correlation coefficients were calculated and deattenuated to account for within-person variation in the comparison method. Method of triads was used to estimate the correlation between true physical activity (PA) and activities estimated by the PAQ and ACT24.

Results: High reproducibility was observed among all activity types assessed by the PAQ (median ICC=0.64), but not ACT24. The deattenuated Spearman correlation (95% confidence interval) between PAQ and accelerometer was 0.43 (0.37, 0.50) for total PA and 0.42 (0.35, 0.48) for moderate to vigorous intensity PA (MVPA). These correlations were similar when DLW-physical activity level (PAL) was used as a comparison method. For all active behaviors, ACT24 had lower validity even when the average of four days was used. Using RPR or DLW-body fat percent as comparison methods to evaluate the relative validity of different assessment methods, the strongest inverse correlation was with MVPA assessed by the PAQ. Using the method of triads, the correlation of PAQ with true total PA was 0.54 (0.47, 0.62), and 0.60 (0.52, 0.69) with true MVPA. These correlations were lower for ACT24.

Conclusion: The PAQ provided reasonably valid estimates for total PA and MVPA when evaluated by multiple comparison methods. ACT24 may be used in validation studies if multiple assessments are collected to account for within-person variations.

LATEBREAKER

Women's Health

The Association of Demographic Concordance between Recruiter and Potential Participant and Recruitment Success Kyra Jones* Kyra Jones Alexandra Sitarik Ganesa Wegienka Christine Cole Johnson Christine Joseph

Rationale:

Race concordance between recruiter and potential participant in terms of recruitment success is often studied in urban populations but is understudied in diverse populations comprising urban and suburban potential participants, as are recruiter age and sex.

Methods:

Using the Wayne County Health, Environment, Allergy, and Asthma Longitudinal Study (WHEALS) birth cohort, characteristics of recruiters and participants by recruitment success were tested using ANOVA for continuous covariates and chi-square tests. Risk ratios (RR) for the probability of recruitment success were obtained using Zou's modified Poisson approach. Interactions for recruiter characteristics were examined by participant age and race.

Results:

WHEALS had a total of 15 different recruiters (mean age 35 years), of which 4 were nurses, 9 were White, 6 Black, and 12 were female. Of the 1,984 potential participants included in the analysis, 1069 (53.9%) were successfully recruited. Mean age of participants = 29 years; 55% were Black, 32% were White and 13% were Other races. Overall, recruiter race was not associated with recruitment success ($p=0.44$), however a recruiter by participant race interaction was observed ($p=0.74$). Black recruiters were less successful at recruiting persons of "Other" races compared to White recruiters, RR (95% CI)=0.60 (0.37, 0.98); $p=0.041$. In terms of age, older recruiter age was associated with lower probability of recruitment success among Black participants, RR=0.93 (0.89, 0.97); $p<0.001$. Interactions were also observed for recruiter sex and age (interaction $p=0.012$), where female recruiters were less successful than males, among participants 30 or older, RR=0.87 (0.76, 1.00); $p=0.051$. Nurses had more success recruiting than non-nurses, RR= 1.11 (1.03, 1.21); $p=0.009$. This effect was modified by participant race, RR=1.18 (1.01,1.38), $p=0.045$; and 1.51 (1.11, 2.06), respectively, for Whites and Other.

Conclusions:

We did not find evidence of a "race concordance effect", however, recruiter characteristics had a significant impact on recruitment success that often depended upon participant demographics. While other factors may influence success (e.g., recruitment scripts, tone, etc.), further exploration of these patterns is warranted.