Society for Epidemiologic Research

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Abstract Book

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Breakthrough COVID-19 Cases in a Pre-Delta Setting, California State Prison Solano Helena
Archer* Helena Archer

Background:

The COVID-19 pandemic has a devastating effect in US prisons, with both direct and indirect
consequences for those living and working in prisons and their families. However, limited
information is known about SARS-CoV-2 transmission in the carceral setting, especially as it relates
to vaccine effectiveness and high-density living.

Methods:

We conducted on-site interviews and abstracted patient data from records on the first outbreak in
the California state prison system following widespread vaccination of residents (May 2021). In this
outbreak, which occurred in closed door, double-celled buildings, we identified a cohort of 720
residents who were presumed to be exposed to SARS-CoV-2 during this time period. To provide
supporting context, on-site interviews were conducted with residents, staff, and leadership.

Results:

Over a 3-week period, 92 confirmed positive cases were identified, with 14 (14.5%) "breakthrough"
cases among residents who had received 2 doses of an mRNA vaccine. Using log binomial
regression, vaccine effectiveness against testing positive was 79% (95% CI: 65%, 88%), and against
reported symptomatic infection was 92% (95% CI: 73%, 99%). Genetic sequencing of 9 isolates by
CDCR identified all as Epsilon variant cases. No severe infections were reported, and results did not
differ significantly when prior infection, age, or comorbidities were considered. Among those who
lived in shared cells, unvaccinated residents had a 26% lower rate of infection when their cellmate
was vaccinated than when they were also unvaccinated; the infection rate among vaccinated
residents did not differ on cellmate vaccination status.

Conclusion:

This study provides critical information on vaccine effectiveness in a high-density setting, and is
further supported by detailed testing and movement data on residents. Further research considering
other variants and in larger population samples will support policy guidance for both the carceral
and broader settings.

COVID-19 Pandemic

Burnout and Depressive Symptoms among Health Care Workers during the COVID-19 Pandemic: Insights from the HERO Registry Michelle Kelsey* Michelle Kelsey Vishal Rao Pratik Manandhar Laine Thomas Henry Michtalik Kathryn Adair Kisha Turner Sanjay Desai Christopher Forrest Jay Lusk Laura Webb Lauren Cohen John Russ Syed Hasan Naqvi Adrian Hernandez Emily O'Brien

Background: Burnout is common among health care workers (HCWs), but specific risk factors are unknown. We evaluated factors associated with burnout and depressive symptoms among HCWs during the COVID-19 pandemic.

Methods: The Healthcare Worker Exposure Response and Outcomes (HERO) program recruited HCWs to an online registry. We used data collected from April 2020 to May 2021. HCWs completed a single-item burnout questionnaire and Patient Reported Outcomes Measurement Information Systems (PROMIS-4) depression survey monthly. We used multivariable regression to evaluate associations between regional COVID-19 burden, workplace characteristics, and outcomes of burnout and depressive symptoms (PROMIS-4 T-score ≥60).

Results: There were 20,536 complete burnout questionnaires submitted by 7,492 HCWs and 20,634 complete depression instruments submitted by 7,491 HCWs. Over half (54%) reported burnout at least once during follow-up. Working fewer weekly hours was associated with lower odds of burnout (OR [95%CI] for 1-19 hrs/week 0.77 [0.66–0.91]; 20-39 hrs/week 0.86 [0.78–0.94]) compared with 40-59 hrs/week, as was older age (OR per 5-years 0.87 [0.86–0.89]) and male sex (0.58 [0.53–0.62]). Burnout was more likely among nurses (1.26 [1.09–1.47]), physical therapists (1.47 [1.16–1.86]), respiratory therapists (1.52 [1.16–2.01]), and medical assistants (1.56 [1.11–2.19]) compared to administrative staff. One-third of HCWs (31%) reported depressive symptoms, with higher odds among nurses (1.34 [1.11–1.61]), laboratory/pharmacy staff (1.34 [1.07–1.68]), and respiratory therapists (1.97 [1.45–2.68]) (**Figure**).

Conclusion: Burnout and depressive symptoms among HCWs working during the first year of the COVID-19 pandemic exceeded 50% and 30%, respectively. Younger HCWs, women, and individuals working in nursing, respiratory therapy, and medical assistant roles were at highest risk for both burnout and depressive symptoms.
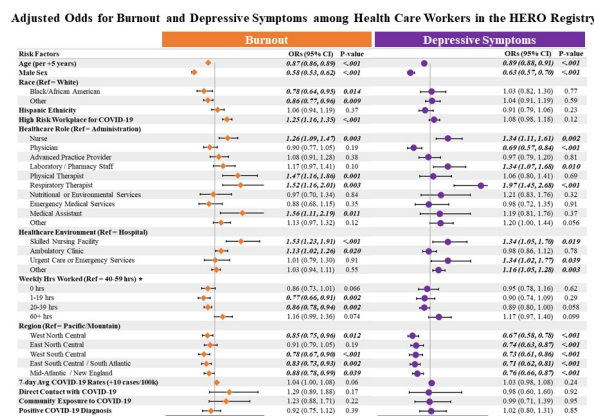

Adjusted Odds for Burnout and Depressive Symptoms among Health Care Workers in the HERO Registry

Risk Factors	Burnout		Depressive Symptoms	
	ORs (95% CI)	P-value	ORs (95% CI)	P-value
Age (per +5 years)	0.87 (0.86, 0.89)	<.001	0.89 (0.88, 0.91)	<.001
Male Sex	0.58 (0.53, 0.62)	<.001	0.63 (0.57, 0.70)	<.001
Race (Ref = White)				
Black/African American	0.78 (0.64, 0.95)	0.014	1.03 (0.82, 1.30)	0.77
Other	0.86 (0.77, 0.96)	0.009	1.04 (0.91, 1.19)	0.59
Hispanic Ethnicity	1.06 (0.94, 1.19)	0.37	0.91 (0.79, 1.06)	0.23
High Risk Workplace for COVID-19	1.25 (1.16, 1.35)	<.001	1.08 (0.98, 1.18)	0.12
Healthcare Role (Ref = Administration)				
Nurse	1.26 (1.09, 1.47)	0.003	1.34 (1.11, 1.61)	0.002
Physician	0.90 (0.77, 1.05)	0.19	0.69 (0.57, 0.84)	<.001
Advanced Practice Provider	1.08 (0.91, 1.28)	0.38	0.97 (0.79, 1.20)	0.81
Laboratory / Pharmacy Staff	1.17 (0.97, 1.41)	0.10	1.34 (1.07, 1.68)	0.010
Physical Therapist	1.47 (1.16, 1.86)	0.001	1.06 (0.80, 1.41)	0.69
Respiratory Therapist	1.52 (1.16, 2.01)	0.003	1.97 (1.45, 2.68)	<.001
Nutritional or Environmental Services	0.97 (0.70, 1.34)	0.84	1.21 (0.83, 1.76)	0.32
Emergency Medical Services	0.88 (0.68, 1.15)	0.35	0.98 (0.72, 1.35)	0.91
Medical Assistant	1.56 (1.11, 2.19)	0.011	1.19 (0.81, 1.76)	0.37
Other	1.13 (0.97, 1.32)	0.12	1.20 (1.00, 1.44)	0.056
Healthcare Environment (Ref = Hospital)				
Skilled Nursing Facility	1.53 (1.23, 1.91)	<.001	1.34 (1.05, 1.70)	0.019
Ambulatory Clinic	1.13 (1.02, 1.26)	0.020	0.98 (0.86, 1.12)	0.78
Urgent Care or Emergency Services	1.01 (0.79, 1.30)	0.91	1.34 (1.02, 1.77)	0.039
Other	1.03 (0.94, 1.11)	0.55	1.16 (1.05, 1.28)	0.003
Weekly Hrs Worked (Ref = 40-59 hrs) ∗				
0 hrs	0.86 (0.73, 1.01)	0.066	0.95 (0.78, 1.16)	0.62
1-19 hrs	0.77 (0.66, 0.91)	0.002	0.90 (0.74, 1.09)	0.29
20-39 hrs	0.86 (0.78, 0.94)	0.002	0.89 (0.80, 1.00)	0.058
60+ hrs	1.16 (0.99, 1.36)	0.074	1.17 (0.97, 1.40)	0.099
Region (Ref = Pacific/Mountain)				
West North Central	0.85 (0.75, 0.96)	0.012	0.67 (0.58, 0.78)	<.001
East North Central	0.91 (0.79, 1.05)	0.19	0.74 (0.63, 0.87)	<.001
West South Central	0.78 (0.67, 0.90)	<.001	0.73 (0.61, 0.86)	<.001
East South Central / South Atlantic	0.83 (0.73, 0.93)	0.002	0.71 (0.62, 0.81)	<.001
Mid-Atlantic / New England	0.88 (0.78, 0.99)	0.039	0.76 (0.66, 0.87)	<.001
7-day Avg COVID-19 Rates (≥10 cases/100k)	1.04 (1.00, 1.08)	0.06	1.03 (0.98, 1.08)	0.24
Direct Contact with COVID-19	1.29 (0.89, 1.88)	0.17	0.98 (0.60, 1.60)	0.92
Community Exposure to COVID-19	1.23 (0.88, 1.71)	0.22	0.99 (0.71, 1.39)	0.95
Positive COVID-19 Diagnosis	0.92 (0.75, 1.12)	0.39	1.02 (0.80, 1.31)	0.85

Figure Legend: This figure displays the adjusted odds for burnout and depressive symptoms (PROMIS-4 T-score ≥60) after adjustment for age, sex, race/ethnicity, region, health care environment, estimated work exposure risk, role in health care setting, weekly hours worked prior to enrollment, weekly hours worked prior to COVID-19, weekly hours worked prior to survey, direct exposure to COVID-19, community exposure to COVID-19, positive Nasal/Oral/Antibody test for COVID-19, no known exposure to COVID-19, 7-day average regional COVID-19 case load, and pandemic period. *Refers to weekly hours worked prior to survey.*

Association between COVID-Related Discrimination, Mental Health, and Sleep among a Nationally Representative Diverse Sample of U.S. Adults: COVID-19's Unequal Racial Burden Survey, 2020-2021 Paula Strassle* Paula Strassle Miciah Wilkerson Ana I. Maldonado Amalia Londono Tobon Allana T. Forde Chandra L. Jackson Anita L. Stewart Anna M. Napoles

COVID-related discrimination against minorities has been well documented; however, its impact on mental health is unknown. We conducted an online survey of Asian, Black/African American, Latino (English and Spanish-speaking), and White adults (1000 each), and American Indian/Alaska Native, Hawaiian/Pacific Islander, and multiracial adults (500 each) from 12/2020-2/2021, N=5500. Eligible participants were proximity matched and weighted to a target sample from the 2018 American Community Survey, allowing us to generate nationally representative cohorts within each racial/ethnic group. Participants were asked how often they experienced discriminatory behaviors "because they think you might have COVID-19" (modified Everyday Discrimination Scale). Mental health outcomes included depression/anxiety (Patient Health Questionnaire-4), stress (modified Perceived Stress Scale), and sleep disturbances (PROMIS Short Form Sleep Disturbance scale). Multinomial logistic (depression/anxiety) and linear (stress, sleep disturbances) regression, adjusting for sociodemographics, were used to estimate association between COVID-related discrimination and mental health. 1214 adults (22.1%) reported experiencing COVID-related discrimination (sometimes/always: 12.4%; rarely: 9.7%), and was associated with increased odds of depression/anxiety (mild: OR 3.17, 95% CI 2.37-4.24; moderate/severe: OR 6.97, 95% CI 5.29-9.18), more stress (mean difference 0.73, 95% CI 0.62-0.83), and more disturbed sleep (mean difference 0.43, 95% CI 0.32-0.54); these strong associations were only observed among racial/ethnic minorities (all p≤0.001), Fig. COVID-related discrimination was associated with poorer mental health, more stress, and poorer sleep among most racial/ethnic minorities but was only weakly associated in White and multiracial adults. Mental health assistance during the COVID-19 pandemic should be culturally tailored and address COVID-related discrimination and its effects among minority groups.
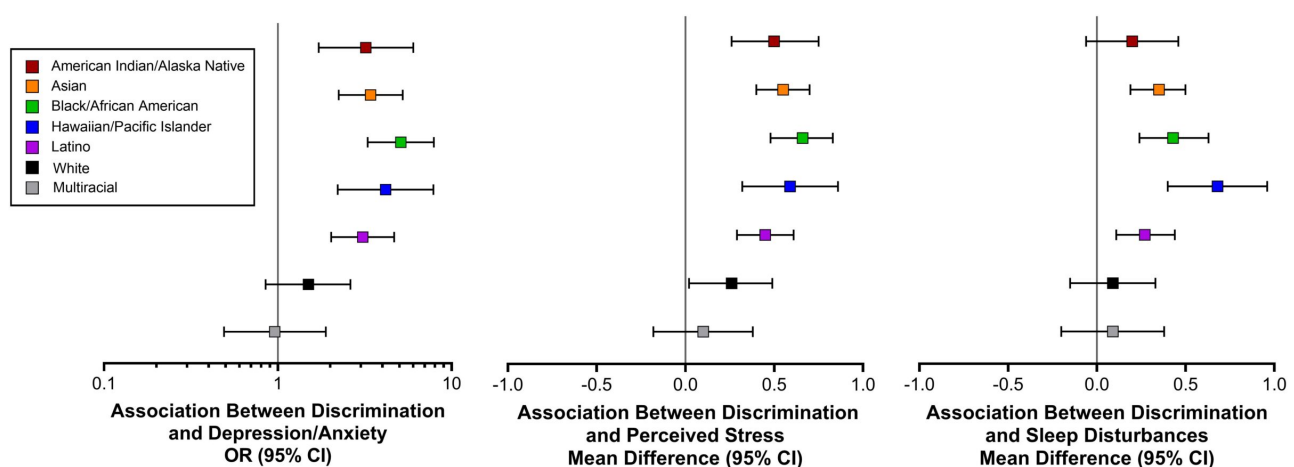
Figure. Adjusted odds and mean differences between those who sometimes/always experienced COVID-related discrimination, compared to none, stratified by race/ethnicity, COVID-19's Unequal Racial Burden (CURB) survey, 12/8/2020-2/17/2021, n=5500. Models were adjusted for age, gender, English proficiency, annual household income, and education.

**Racial/ethnic differences in the association between mistrust in the U.S. healthcare system and unwillingness to test for and vaccinate against COVID-19** Judy Nanaw* Judy Nanaw Allana Forde Jessica Fernandez Paula Strassle

Background: Racial/ethnic differences persist in COVID-19 testing and vaccine unwillingness, but less is known about whether the differences are associated with perceptions of the U.S. healthcare system. We examined whether mistrust in the healthcare system was associated with unwillingness to get COVID-19 tested or vaccinated, and if the associations varied across race/ethnicity.

Methods: We conducted an online survey (1/2021-3/2021) of 5500 adults (1000 Asian, 1000 Black/African American, 1000 Hispanic/Latino, 1000 White, 500 American Indian/Alaska Native, 500 Native Hawaiian/Pacific Islander, 500 multi-racial). Participants were proximity matched and weighted to a target sample in the 2018 American Community Survey to create nationally representative cohorts within each racial/ethnic group. Participants were asked how often they trusted the U.S. healthcare system, if they received or would receive a COVID-19 test, and if they planned to receive a COVID-19 vaccine. Logistic regression using complete cases (n=5424) examined the associations between mistrust and unwillingness to get tested or vaccinated, adjusting for age, gender, household income, education, and health insurance status.

Results: Overall, 18.6% of participants reported never/almost never trusting the healthcare system, 15.5% were unwilling to get tested, and 30.0% were unwilling to be vaccinated. Greater mistrust was associated with unwillingness to get tested (never/almost never vs always: OR 3.19, 95%CI 2.65-3.84) and vaccinated (never/almost never vs always: OR 1.73, 95%CI 1.47-2.02). Mistrust had a larger effect on testing in Black/African American adults and a smaller impact on vaccination among Asian, Hispanic/Latino, and Native Hawaiian/Pacific Islander adults (Figure).

Discussion: Our results reinforce the importance of trust in the healthcare system when encouraging COVID-19 testing and vaccination; moreover, mistrust may differentially influence these practices across racial/ethnic groups.
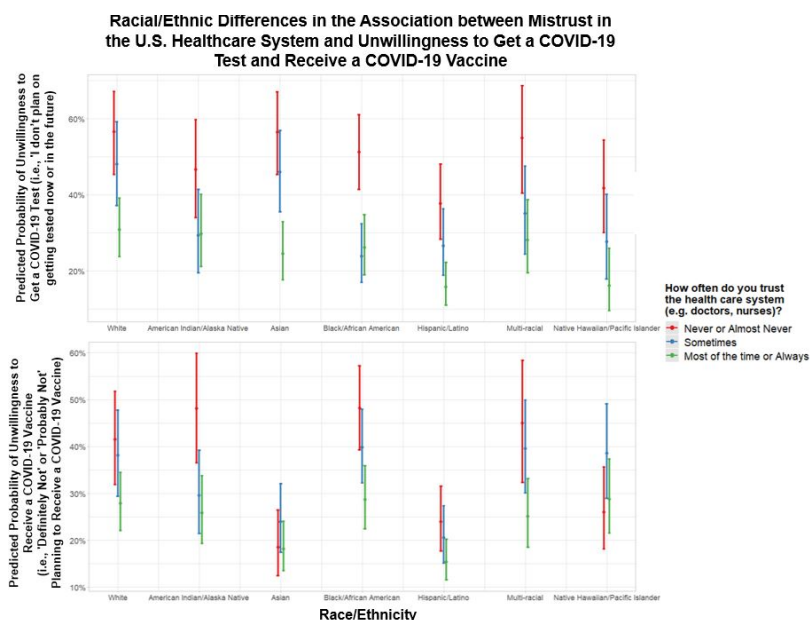
COVID-19 cases are associated with food insufficiency in the United States during the COVID-19 pandemic Leah Chapman* Leah Chapman Jean Hu Sarah Seidel

Food insufficiency, a more severe form of food insecurity defined as "households that sometimes or often do not have enough to eat," is expected to increase due to the COVID-19 pandemic. Using 30 weeks of cross-sectional data from the Household Pulse Survey (April 23, 2020-May 24, 2021, n=2,618,027) and CDC surveillance data, this presentation: 1) describes the association between the COVID-19 pandemic (as measured by daily new confirmed cases) and food insufficiency in the U.S. during a 13-month period of the pandemic and 2) examines which households in the U.S. had the highest odds of reporting food insufficiency during the pandemic. To measure food insufficiency, Pulse asks: "In the last 7 days, which of these statements best describes the food eaten in your household? 1) Enough of the kinds of food (I/we) wanted to eat; 2) Enough, but not always the kinds of food (I/we) wanted to eat; 3) Sometimes not enough to eat; 4) Often not enough to eat." Participants who select option 1 or 2 are classified as food sufficient, and 3 or 4 as food insufficient. New daily cases averaged 65,160.93 throughout the study period. Multivariate logistic regression models indicated a 70,000-unit increase in COVID-19 cases was associated with a 13% higher odds of food insufficiency (OR=1.13, 95% CI: 1.12-1.15). Participants with mild (OR= 2.72, 95% CI: 2.61-2.84), moderate (OR= 4.58, 95% CI: 4.36-4.81), or severe (OR= 8.75, 95% CI: 8.42-9.09) anxiety/depression and Black participants (OR= 2.36, 95% CI: 2.29-2.44) had the highest odds of reporting food insufficiency during the pandemic. During pandemics, special attention should be given to communities of color and those with poorer mental health for preventing food insufficiency. Furthermore, evaluation of the impact of meal distribution and meal delivery programs (such as Meals on Wheels or federally assisted meal programs) on the nutritional status of vulnerable populations during the pandemic is needed.
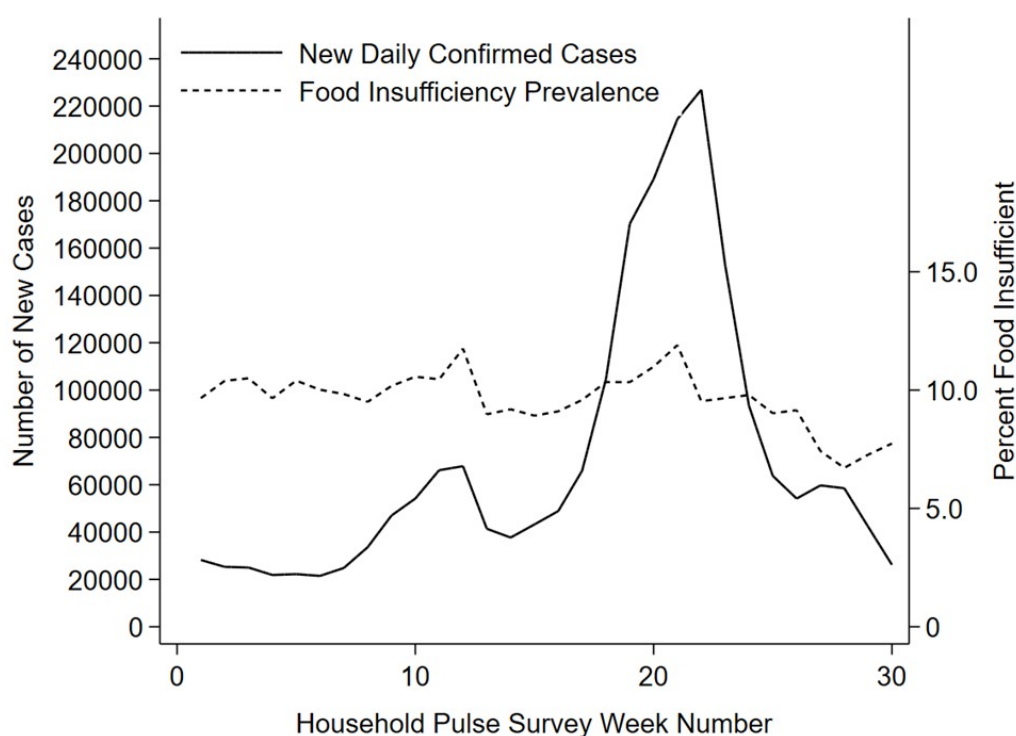
COVID-19 Pandemic

Social Impacts of the COVID-19 Pandemic: A Qualitative Analysis of Discussions Between Persons with Early-Stage Dementia and their Adult-Child Caregivers Talha Ali* Talha Ali Sarah Valeika Emily L. Mroz Erika Mendez Andrew B. Cohen Joan K. Monin

Physical distancing measures during the pandemic have had unintended social, psychological, and economic consequences for older adults living with dementia. However, some evidence indicates that persons with dementia are relatively unburdened by the pandemic. As such, it remains unclear how much and in what ways, the pandemic has impacted persons with dementia and their caregivers. In the present study, qualitative interviews were conducted with 43 dyads of parents with early-stage dementia and their adult-child caregivers to determine: (1) how they describe the social and emotional impacts of the COVID-19 pandemic to one another, and (2) whether they use specific communication patterns during these discussions. Interviews were conducted between Dec 2020 and Nov 2021. Dyads were prompted to discuss together how the COVID-19 pandemic had affected them and their daily life for 7 minutes over Zoom. Interview transcripts were qualitatively analyzed using constant comparative methods by a four-member team. The following four major themes emerged: impacts to social engagement, social support, relationship quality, and communication patterns. Adult children reported feeling distressed over changes in their social activities, limited in-person interaction, and having to work from home. Parents with dementia, despite becoming isolated, reported that they were not bothered by a reduction in social interaction. Participants reported feeling anxious about exposing others to the virus and because of uncertainty about the future, and a fear of losing social skills to communicate with others after the pandemic. In discussing their concerns about the pandemic, parents and adult children often made meaning of their situation by expressing hope for the future, finding benefit in difficult circumstances, and by reframing their situation by comparing it to others' more difficult circumstances. Findings indicate that older adults with dementia are more resilient than expected.

A Clinical Prediction Rule to Guide Diagnostic Testing in Children Under-5 Presenting with Diarrhea in LMICs Sharia M Ahmed* Sharia Ahmed Benjamin Brintz Patricia Pavlinac James A Platts-Mills Karen L Kotloff Daniel T Leung

Diarrheal diseases are a leading cause of death for children under-5, mostly in low and middle income countries (LMICs). Identification of etiology helps guide pathogen-specific therapy, but diagnostic testing availability is often limited in LMICs, and symptomology guides treatment. We developed a clinical prediction tool to guide clinicians in identifying when to use a hypothetical point-of-care diagnostic for making diarrhea treatment decisions.

We used clinical and demographic data from the Global Enteric Multicenter Study (GEMS) study to build predictive models to identify pediatric diarrhea patients that could potentially benefit from antibacterial therapy (Shigella or Vibrio cholerae attributable fraction ≥0.5) in children ≤59 months presenting with moderate-to-severe diarrhea (MSD) in Africa and Asia. We screened variables using random forests, and assessed predictive performance with random forest regression and logistic regression using 5-fold cross-validation.

Of the 5287 cases with etiology, 1520 (29%) had an etiology that would benefit from antibiotic therapy. Our ability to predict which diarrhea patients would potentially benefit from antibiotic therapy was high, with an AUC=0.81 (95% CI: 0.80, 0.82) for a model including only the top two predictive variables, age and presence of bloody diarrhea. We show that by using our CPR to triage who receives diagnostic testing and with only 36% of children targeted for point-of-care testing, 26% more children would receive necessary antibiotics and 41% fewer children would receive unnecessary antibiotics compared to using bloody diarrhea (dysentery) as the only criteria for antibiotic use. The influence of point-of-care diagnostic test accuracy was also explored.

Accuracy of Clinical Prediction Rule (CPR)-Guided Testing
point-of-care Se=0.90; point-of-care Sp=0.90
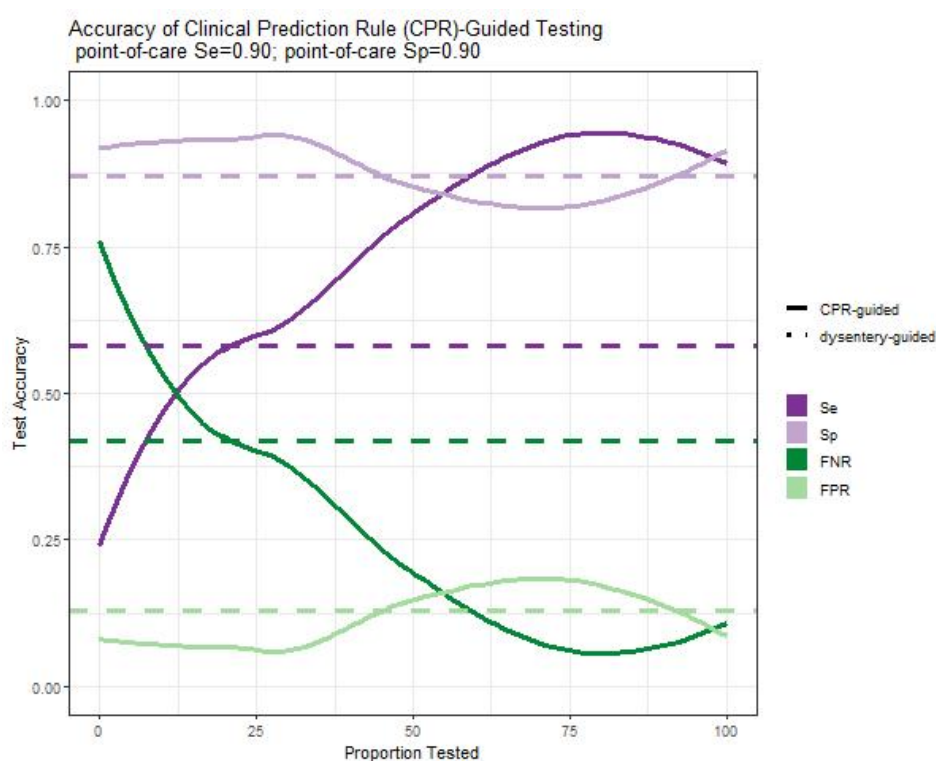
Distinct drivers of unsuccessful TB treatment outcomes in Brazil: a multinomial logistic regression analysis Lauren Peetluk* Lauren Peetluk Felipe Ridolfi Gustavo Amorim Megan Turner Marina Figueiredo Marcelo Cordeiro-Santos Solange Calvacante Afranio Kritski Betina Durovni Timothy Sterling Valeria Rolla

Background: Successful tuberculosis (TB) treatment is necessary for disease control. The World Health Organization (WHO) has a target TB treatment success rate of ≥90%, but many countries fall short of this goal.

Methods: Using data from Regional Prospective Observational Research in Tuberculosis (RePORT)-Brazil cohort, we evaluated baseline clinical and demographic factors associated with the different components of unsuccessful TB outcomes, defined by the WHO as death, treatment failure, and loss to follow-up (LTFU). Cure or treatment completion was the referent outcome. The study included culture-confirmed, drug-susceptible, pulmonary TB patients initiated on standard TB therapy who were enrolled 2015-2019 and followed for up to two years. Multinomial logistic regression with inverse probability weighting based on pre-specified confounders were used to evaluate determinants of each unsuccessful outcome.

Results: Of 915 participants included, 727 (79%) were successfully treated, 26 (3%) died during treatment, 44 (5%) had treatment failure, and 118 (13%) were LTFU. Death was associated with anemia (OR=5.3, 95%CI: 1.4-19.7), diabetes (OR=3.1, 95%CI: 1.4,-6.7), and being a person living with HIV (PLWH) (OR=3.9, 95%CI: 1.3-11.4). Treatment failure was associated with PLWH (OR=2.7, 95%CI: 1.2-6.2) and diabetes (OR=2.2, 95%CI: 1.1-4.4). Prescription of DOT was protective for treatment failure (OR=0.5, 95%CI: 0.3-0.9) and death (OR=0.5, 95%CI: 0.2-1.0). LTFU was associated with current drug use (OR=5.3, 95%CI: 3.0, 9.4), current tobacco use (OR=2.9, 95%CI: 1.7-4.9), and PLWH (OR=2.0, 95%CI: 1.1-3.5).

Conclusions: The treatment success rate in this cohort was below WHO target. Whereas clinical comorbidities were most strongly associated with treatment failure and death. behavioral factors were most associated with LTFU. Since the determinants of unsuccessful outcomes are distinct, intervention strategies will need to be specifically tailored to each component to improve TB treatment success rates and future studies should limit use of composite outcomes.

Figure. Coefficient plot of inverse probability weighted multinomial logistic regression model of baseline factors associated with the the components of unsuccessful TB treatment outcomes in the study population (N=915). Successful outcome (cure and treatment completion, N=727) was the reference outcome.
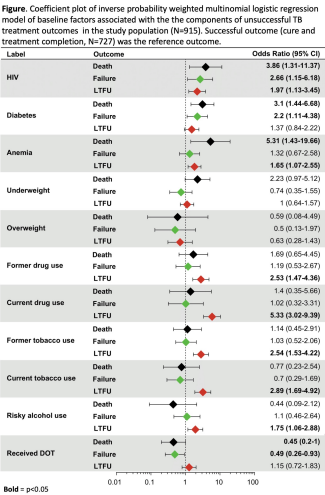
A new recommendation for enhanced seasonal influenza vaccines in adults age 65 and older could have wide-ranging impacts on influenza burden in the United States Sinead Morris* Sinead Morris Lisa Grohskopf Carrie Reed Matthew Biggerstaff

In the United States (US), vaccination against seasonal influenza is recommended for everyone over the age of 6 months. Although there are many licensed seasonal influenza vaccines in the US, their effectiveness varies according to several factors, including age of the recipient. High-dose, adjuvanted, and recombinant vaccines may be more effective in adults age 65 and older than standard-dose unadjuvanted inactivated vaccines. However, the Advisory Committee on Immunization Practices (ACIP) does not preferentially recommend use of these enhanced vaccines (EVs) over standard vaccines (SVs), at least in part due to concerns that individuals may delay or forego vaccination if an EV is unavailable. Here we use mathematical modeling to explore how a recommendation for the preferential use of EVs in adults 65 and older may impact influenza burden in the US during exemplar 'high' and 'low' severity seasons. We assume such a recommendation would increase uptake of EVs but could cause delays in the timing of EV vaccination relative to SV and/or reductions in overall coverage if individuals offered SVs do not take them. We find that in a best-case scenario, with no assumed delay or reduction in coverage, a new recommendation could decrease the number of symptomatic cases, hospitalizations and deaths in adults 65 and older by 0-3% compared to current EV/SV uptake. However, in intermediate and worst-case scenarios, with assumed delays of 3 or 6 weeks and 10 or 20% reductions in coverage, numbers could increase by 1-7%. Sensitivity analyses show that this impact is primarily mediated by the reduction in coverage, although the delay in coverage and the effectiveness of EVs relative to SVs are also important. Overall, our results stress the importance of ensuring timely and adequate access to EVs and promoting the use of SVs when these are unavailable to ensure that potential preferential recommendations for EVs do not inadvertently increase seasonal influenza burden in the US.
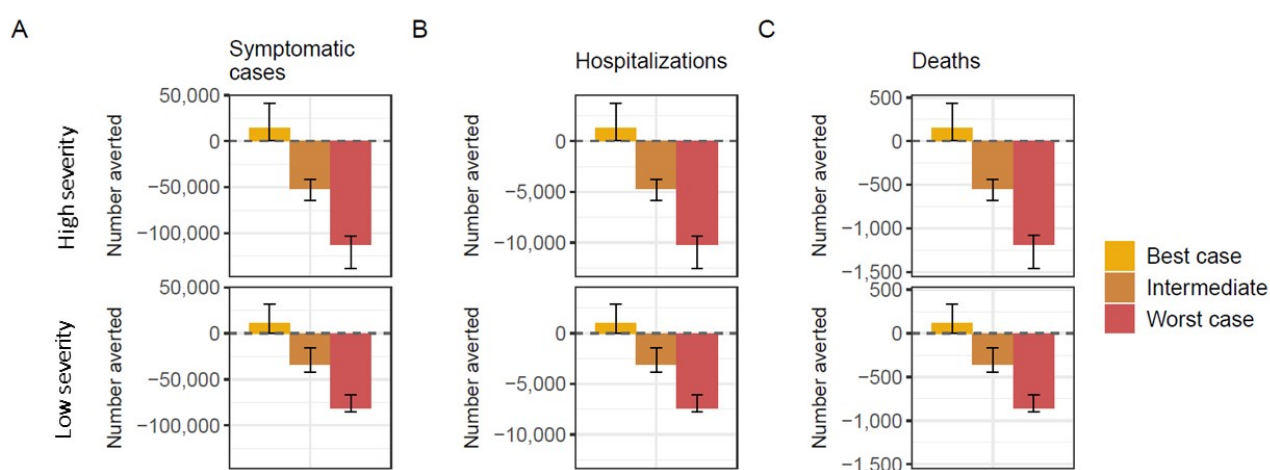
Figure 1. Averted influenza burden following a new recommendation for enhanced vaccines in persons 65 and older under different trade-off scenarios. Bars indicate the mean number of averted symptomatic cases (A), hospitalizations (B) and deaths (C) from 1000 different vaccine parameter combinations; error bars are the 95th percentiles. Each panel shows results for a typical high severity season (top) and low severity season (bottom). Positive values indicate a decrease in burden relative to the corresponding simulation with no recommendation in place, and therefore a positive impact.

Inequity in performance of a prediction model to identify people who may benefit from HIV preexposure prophylaxis in community health centers Jun Hwang* Jun Hwang Miguel Marino David Ezekiel-Herrera Jonathan Todd Kenneth Mayer Douglas Krakower Julia Marcus

Background: Prediction models could prompt clinicians to discuss HIV preexposure prophylaxis (PrEP) with the patients most likely to benefit. We developed an electronic health record (EHR)-based model for integration into clinical decision support for PrEP in community health centers (CHCs) and evaluated equity in its performance.

Methods: We extracted EHR data from adults with ≥1 outpatient visit and no prior HIV diagnosis during 2012-2019 in a national network of CHCs (OCHIN). Using 80 demographic and clinical variables, we applied least absolute shrinkage and selection operator (LASSO) regression with 10-fold cross-validation to predict incident HIV diagnosis within 3y. We assessed model performance using area under the receiver operating characteristic curve (AUC) in a withheld 20% subset, overall and by sex and race/ethnicity. We assessed how the addition of census-level data on social determinants of health (e.g., poverty, education) impacted equity in performance.

Results: Of 1,712,910 patients, 42% were male, 43% non-Hispanic White, and 16% non-Hispanic Black. Most had public or no insurance (89%) and 57% were below the federal poverty line. Overall, 7,749 (0.5%) had an incident HIV diagnosis within 3y. LASSO retained 51 variables, with an AUC of 0.84 (95% CI=0.83-0.85). Model performance was lower for females (AUC 0.75, 0.72-0.73) compared with males (AUC 0.80, 0.79-0.81), and for non-Hispanic Black patients (AUC 0.76, 0.74-0.78) compared with non-Hispanic White patients (AUC 0.85, 0.83-0.87). Data on social determinants of health did not improve equity in model performance.

Conclusion: Although EHR-based models could prompt PrEP discussions in CHCs with patients likely to benefit, models underperform in subgroups at increased risk of HIV (non-Hispanic Black people) and/or underrepresented among PrEP users (females), even with social determinants of health data. Further research is needed to improve equity in identification of people who may benefit from PrEP.

Figure: Receiver operating characteristic curves of an electronic health record-based prediction model to identify people who may benefit from HIV preexposure prophylaxis in community health centers, overall and by sex and race/ethnicity. TPR = true positive rate; FPR = false positive rate.
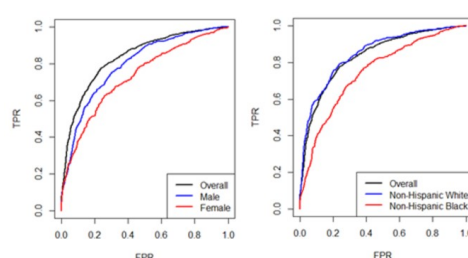
Social-spatial network structures among young urban and suburban persons who inject drugs: Implications for hepatitis C and HIV transmission Qinyun Lin* Qinyun Lin Javier Andres Rojas Aguilera Marynia Kolak Mary Mackesy-Amiti Leslie Williams Juliet Pineros Basmattee Boodram

Background: Fueled by the opioid epidemic, hepatitis C (HCV) incidence has increased four-fold between 2008-2019, primarily driven by young people who inject drugs (PWID) from non-urban areas. Social and risk (i.e., injection) networks are recognized as drivers of HCV transmission; however, the role of social and geographic spaces in fostering risk behavior and network formation is understudied.

Method: Egocentric injection network and geographic data for young (aged 18-30) PWID and their injection, sexual and social support network members (i.e, where reside, inject drugs, purchase drugs, and meet sex partners) were examined using baseline data from an ongoing longitudinal study (n=277). Participants were stratified based on place(s) of residence in the past year, i.e., urban, suburban, and transient (both urban and suburban) to i) elucidate geospatial concentration of HCV risk risky activities within multi-dimensional risk environment based on kernel density estimation; and ii) examine spatialized social networks for each group.

Result: Participants were mostly non-Hispanic white (59%) and urban (50%), suburban (26%), and transient (24%). We identified a spatial area with concentrated risky behaviors for each residence group on the West side of Chicago where a large outdoor drug market area is located (Figure 1). The urban group (79%) reported a smaller concentrated area (11 census tracts) compared to the transient (92%) and suburban (90%) with 20 and 41 tracts, respectively. Significant (p<0.01 for all) differences were observed in social network structures: urban had the residence homophily, transient had more non-redundant connections, and suburban had the smallest but most connected networks (density).

Conclusion: We identified a convergence of HCV risk spaces among PWID from urban, suburban and transient groups in a large outdoor urban drug market areas, which highlights the need for considering the role of risk spaces and social networks in the development of HCV transmission.
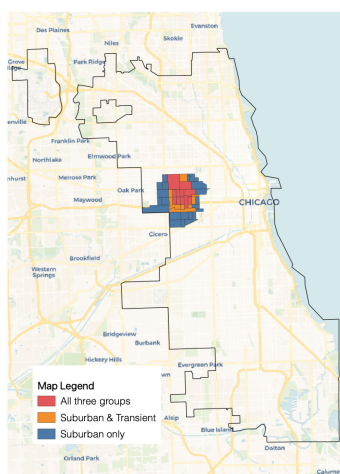

Figure 1. Risky spatial avenues for urban, suburban, and transient groups.

Autism Spectrum Disorder, Prenatal Greenspace Exposure, and Mediation by Reduced Air Pollution: A Population-Based Birth Cohort Study in Vancouver, Canada Lief Pagalan* Lief Pagalan Tim F. Oberlander Gillian E. Hanley Laura C. Rosella Celeste Bickford Whitney Weikum Nancy Lanphear Bruce Lanphear Michael Brauer Matilda van den Bosch

Autism spectrum disorder (ASD) incidence has increased in past decades. Few studies have examined modifiable environmental risk factors, and fewer have examined protective exposures. Greenspace has been associated with a lower prevalence of ASD and may reduce air pollution exposure, a suspected ASD risk factor.

We measured the association between prenatal greenspace exposure and ASD risk and examined if reduced levels of air pollution in areas of higher greenspace mediated this association.

The population-based birth cohort consisted of all pregnant mothers in Vancouver, Canada, from 2004–2009, with follow-up to 2014. Diagnoses were based on Autism Diagnostic Observation Schedule and Autism Diagnostic Interview-Revised instruments. Greenspace was quantified as the average of the annual mean Normalized Difference Vegetation Index (NDVI) within a 250 m buffer of a postal code. Air pollutant exposures (particulate matter with a diameter less than 2.5 µm [PM2.5], nitric oxide [NO], and nitrogen dioxide [NO2]) were derived from validated land use regression models and calculated as the mean concentration per month during pregnancy. We calculated odds ratios (ORs) using logistic regression per NDVI interquartile range (IQR) increase, adjusting for child sex, birth month and year, maternal age and birthplace, and neighbourhood-level urbanicity and income. We used marginal structural models and a potential outcomes framework to calculate marginal risk differences (RDs) and decompose the total effect of greenspace on ASD into natural direct and indirect effects.

Of 129,222 births, 1,921 (1.5%) children were diagnosed with ASD. The adjusted OR for ASD per NDVI IQR increase was 0.96 (95% CI: 0.90, 1.02). Natural direct, natural indirect, and total effect RDs were null for PM2.5, NO, and NO2 mediation models.

Prenatal green space exposure was associated with a small reduction in the odds of ASD. No mediating effects were observed through reduced air pollution.

Traffic-related air pollution and pregnancy loss in Eastern Massachusetts, USA Michael Leung* Michael Leung Sebastian Rowland Anna M Modest Michele R Hacker Stefania Papatheodorou Joel Schwartz Brent A Coull Ander Wilson Marianthi-Anna Kioumourtzoglou Marc G Weisskopf

Background: Prior studies that have examined associations with pregnancy loss have mostly relied on losses identified by medical records (i.e., a subset of all losses). We apply a novel time-series approach that leverages data on live births to infer effects on pregnancy loss. Analyzing live birth-identified conceptions (LBICs) —the difference between the total number of conceptions and those that end in loss for a given time window— can tell us about associations with pregnancy loss (even those undetected). Using this approach, we estimate the association between prenatal nitrogen dioxide (NO_2) —a traffic emissions tracer— and pregnancy loss in a Massachusetts-based cohort.
Methods: We used data on 21,204 live births from pregnancies conceived in 2003-2015 and had their prenatal care at Beth Israel Deaconess Medical Center in Boston, USA. We used a linear distributed lag model to estimate the association between weekly NO_2 during pregnancy and LBICs adjusted for temperature and time trends. Confidence intervals were obtained through bootstrap.
Results: The mean number of LBICs per conception week was 30 (standard deviation [SD]: 6.5). Weekly NO_2 concentrations (mean: 23.3 parts per billion [ppb], SD: 6.5 ppb) were below the current USEPA annual standards. Higher prenatal NO_2 in gestational weeks 6-21 was associated with fewer LBICs, and the strongest association was in week 14. A 10-ppb higher NO_2 exposure sustained throughout pregnancy was associated with 11.0 (95% CI: 8.0, 14.1) fewer LBICs. That is, out of 30 LBICs per conception week, 11 would be lost if average NO_2 was 10-ppb higher in every week of pregnancy. **Conclusion:** We show through the analysis of LBICs that higher prenatal NO_2 was associated with pregnancy loss, and that the critical exposure window was in weeks 6-21. The described approach can quantify the change in the number of pregnancy losses per conception week as it is simply the complement of the change in live births from that week's conceptions.
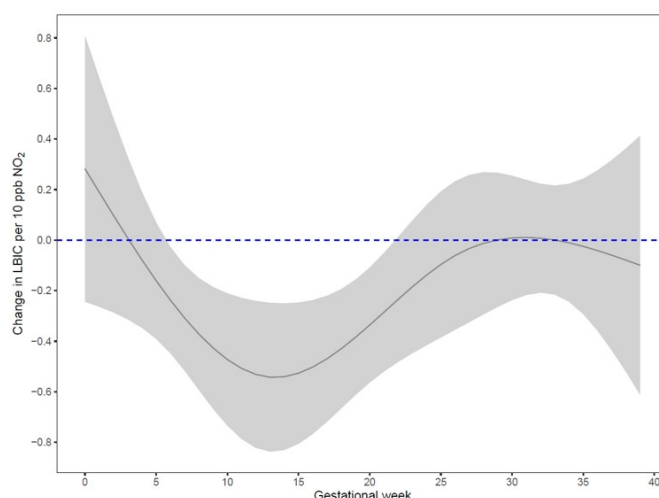

Figure 1. The time-varying association between weekly nitrogen dioxide (NO_2) and the number of live birth-identified conceptions (LBICs) from deliveries at Beth Israel Deaconess Medical Center, Massachusetts in 2003-2015 (n=21,204) estimated using a linear distributed lag model adjusted for temperature and time trends. The black line shows the lag-response estimates, grey shaded area shows the 95% confidence intervals obtained through bootstrap with 1000 replications, and the blue dashed line indicates the null hypothesis of no effect across all gestational weeks. The cumulative association is the sum of the lag-specific estimates throughout pregnancy; that is, based on the above lag-response curve, a 10-ppb higher NO_2 in each week of pregnancy would result in 11.0 (95% CI: 8.0, 14.1) fewer LBICs.

A population-based cohort study of traffic congestion and term birth weight using vehicle telematics data Mary D. Willis* Mary Willis David Schrank Chunxue Xu Helen Harris Beate Ritz Elaine Hill Perry Hystad

Background: Over 11 million Americans reside within 150 m of a major highway, an area of high air pollution exposure. Traffic congestion further contributes to this problem but has not been evaluated in epidemiological studies to-date. We hypothesize that the degraded air quality due to traffic congestion specifically will have an adverse impact on infant birth weight.

Methods: Using a population-based birth cohort in 2015-2016 for the State of Texas, we calculated traffic congestion around each geocoded maternal address at delivery for 100 m, 300 m, and 500 m buffer distances. We leveraged novel congestion and vehicle volume measurement data from the Texas Most Congested Roads database, which contains measurements of traffic volume, delay, and emissions from connected vehicle and device data. Our study population was limited to addresses within 1,000 m of a road in this database to reduced unmeasured confounding. We used linear regressions to evaluate the association between traffic congestion and term birth weight, adjusting for sociodemographic characteristics and vehicle volume.

Results: Among 580,992 births, we find consistent negative associations between congestion and term birth weight. We observed a 15.8 g reduction in term birth weight (95% CI: -20.5, -11.1) among the highest quintile of congestion exposure at 500 m compared to births with no congestion exposure in this buffer distance. Results are similar, if somewhat attenuated, for truck-specific congestion. For congestion-specific vehicle emissions, we observe a -17.6 g reduction in term birth weight (95% CI: -21.4, -13.9) when comparing the highest and lowest quintiles.

Conclusion: Our study provides important new evidence that traffic congestion is associated with adverse infant health outcomes, in addition to total traffic volumes on nearby roads. Therefore, programs and policies to reduce traffic congestion may have positive co-benefits for infant health with respect to birth weight.
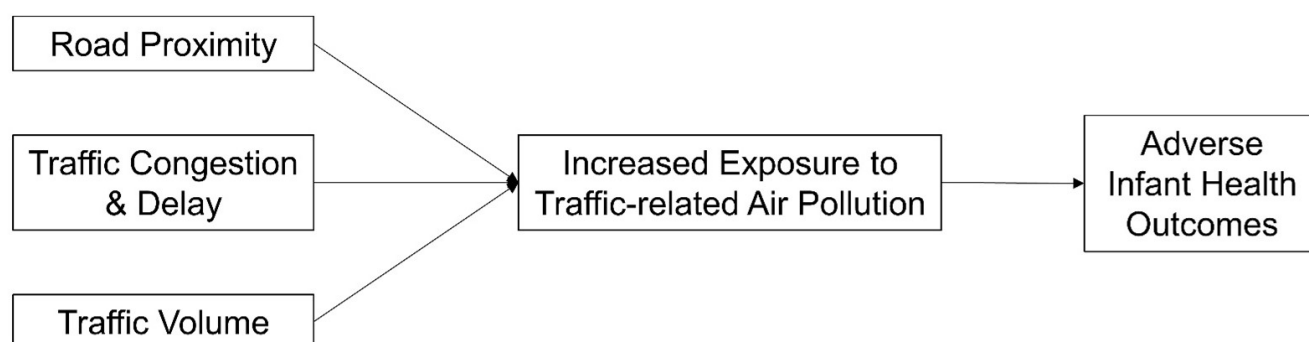
Figure 1: Conceptual diagram of hypothesized pathways by which traffic congestion and delay may uniquely influence infant health outcomes. No studies to date have focused on the traffic congestion and delay.

Hypothetical interventions on fruit and vegetable intake to mitigate lead and cadmium induced mortality in US adults Nasser Laouali* Nasser Laouali Youssef Oulhote Tarik Benmarhnia

Context: In the recent decades, lead and cadmium exposure have declined sharply, although they are ranked second and seventh most significant potential threat to human health through increasing oxidative stress and inflammation. Thus, a human-focused approach for health protection against these metals toxicity are needed. In parallel, fruit and vegetable (FV) intake may prevent from chronic inflammation. Therefore, we sought to estimate the effects of an hypothetical intervention on FV intake on the expected mortality distributions in participants with different concentrations of blood lead (BLLs) and urinary cadmium (UCd).

Methods: We used data on 14,311 adults aged ≥20 years enrolled in the NHANES-III between 1988 and 1994 and followed up through Dec 31, 2015. At baseline, daily FV servings were assessed using 24-hour dietary recalls and plasma biomarkers of FV intake were measured. Mortality was determined from the National Death Index records. We used the parametric g-formula with pooled logistic regression models to estimate the absolute risk of all-cause, cardiovascular, and cancer mortality under different potential threshold interventions on the daily FV servings and FV intake in low and high groups of BLLs and UCd concentrations.

Results: Median follow-up was 22.5 years, 5,167 (36%) participants died; 1,550 were attributable to cardiovascular disease and 1,135 to cancer. In participants with low BLLs, intervention to set everyone in the top quartile of FV intake compared to the natural course was associated with a decreased risks of all-cause by -0.54% (95% CI, -2.34 to 1.06), cardiovascular by -0.56% (95% CI, -1.92 to 32.30) and cancer by +0.16% (95% CI, -0.92 to 2.30). In participants with high BLLs, the corresponding decreased risks were -1.57% (95% CI, -5.47 to 3.45), -1.29% (95% CI, -3.43 to 22.50) and -0.32% (95% CI, -1.90 to 4.20), respectively. The same pattern of associations was observed for Ucd and where biomarkers of FV intake were considered.

Conclusion: Our findings suggest that a higher intakes of FV may help prevent metals adverse effect in adult. The lower the existing level as for any pollutant, the harder it is to further reduce through regulation. Thus, a paradigm shift is required from a pollutant focused to a combination with human-focused approach for health protection against these metals.
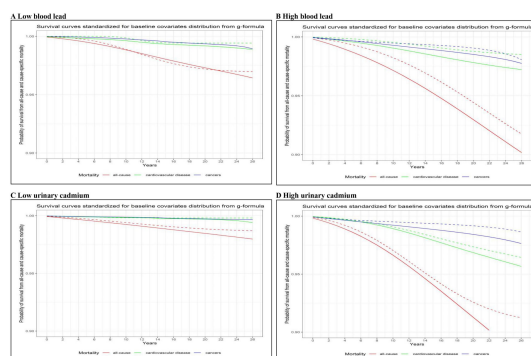

Figure: Adjusted all-cause and specific-cause of mortality under intervention on daily fruits and vegetables intake in participants with low and high metals concentrations using parametric g-formula with pooled logistic regression models. The solid line represents the natural course (no intervention) and the dashed lines the intervention (all participants in the top quartile of daily fruits and vegetables servings).

Relationships between Urinary Metals and Diabetes Traits among Mexican Americans in Starr County, Texas Margaret Weiss* Margaret Weiss Yu-Hsuan Shih Molly Scannell Bryan Brian P. Jackson David Aguilar Craig L. Hanis Maria Argos Robert M. Sargis

Background: Hispanics/Latinos have higher rates of type 2 diabetes (T2D); however, the origins of these disparities are poorly understood. Environmental endocrine-disrupting chemicals (EDCs), including metals and metalloids, are implicated as diabetes risk factors. Data indicate that Hispanics/Latinos may be disproportionately exposed to EDCs, yet remain understudied with respect to exposure-associated diabetes risk. Starr County, Texas, is a Mexican American community with markedly elevated rates of T2D and diabetes-associated mortality; it is also a region with high levels of groundwater arsenic.

Objective: This study aims to evaluate the associations between urinary metal concentrations and glycemic status in 414 non-diabetic adults living in Starr County, Texas.

Methods: We used multivariable linear regression to quantify the differences in homeostatic model assessment for pancreatic beta-cell function, insulin resistance, and insulin sensitivity (HOMA-β, HOMA-IR, HOMA-S, respectively), plasma insulin, plasma glucose, and hemoglobin A1c (HbA1c) associated with urinary metal concentrations adjusted for *a priori* confounders. Metal mixture effects were evaluated using quantile-based g computation.

Results: After multivariable adjustment, urinary molybdenum was associated with lower HOMA-β, HOMA-IR, and plasma insulin levels and higher HOMA-S with a significant dose-response. Total urinary arsenic was associated with reduced postprandial glucose, and a higher proportion of monomethylated arsenic (MMA) was associated with reduced HOMA-IR, fasting glucose, and HbA1c.

Conclusion: Our data indicate that molybdenum and arsenic exposures are associated with shifts in glucose homeostasis among Hispanics/Latinos without diabetes. Furthermore, a higher proportion of MMA was found to drive the effect of arsenic. This study is one of the first to comprehensively evaluate associations of urinary metals and arsenic with continuous glycemic measures in a Mexican American population.

The relationship between outdoor light at night and prostate cancer risk in the Health Professionals Follow-Up Study Ilkania M. Chowdhury-Paulino* Ilkania Chowdhury-Paulino Hari S. Iyer Grete Wilt Rachel C. Nethery Francine Laden Jaime E. Hart Lorelei A. Mucci Sarah C. Markt

Purpose

Circadian disruption is considered a likely carcinogen by the World Health Organization and is a potential risk factor for advanced prostate cancer (PCa). Studies have found that exposure to light may disrupt circadian systems and that outdoor light at night (oLAN), specifically, is associated with an increased risk of breast cancer. We evaluated whether exposure to oLAN increases the risk of PCa, particularly more aggressive forms of the disease.

Methods

We prospectively followed 49,451 participants in the Health Professionals Follow-up Study beginning in 1986 through 2016. We estimated cumulative oLAN with 1 km^2 resolution using data from the US Defense Meteorological Satellite Program's Operational Linescan System, which was available for 1996, 1999, 2000, 2002, 2004, 2005 and 2010. Exposure was assigned 1996 values for addresses before 1996 and the most recent past LAN measure for addresses after 1996. Fatal PCa is defined as death from PCa as the underlying cause and lethal PCa as diagnosis of distant metastases or death due to PCa. We used Cox models to estimate hazard ratios and 95% confidence intervals adjusting for PCa risk factors, neighborhood SES (nSES), and urbanicity.

Results

Over 30 years of follow-up we observed 7,176 PCa cases, including 1,097 lethal and 915 fatal cases. The distribution of PCa risk factors was similar, but population density and nSES differed across levels of oLAN. The mean level of oLAN in this study was 37.3 $nW/cm^2/sr$. An interquartile increase in cumulative oLAN was weakly associated with lethal (HR: 1.03, 95% CI=0.96, 1.11) and fatal (HR: 1.05, 95% CI=0.97, 1.14) PCa in adjusted models. We found no relationship between oLAN and total PCa (HR: 1.00, 95% CI: 0.97, 1.03).

Conclusion

We found a weak association between oLAN and more aggressive PCa. In future analyses, we will explore whether this association varies by nSES and population density and the association between oLAN and sleep quality.

Association of sugar-sweetened beverage taxes in U.S. cities and perinatal health outcomes
Kaitlyn Jackson* Kaitlyn Jackson Justin White Rita Hamad Deborah Karasek

One in five pregnant women report consuming sugar-sweetened beverages (SSBs) at least once per day, and sugar consumption during pregnancy is associated with high-risk perinatal conditions. SSB taxes have proliferated as a public health measure, yet evidence of the impacts of SSBs taxes to reduce consumption and downstream effects on perinatal outcomes is limited. We aimed to examine if SSB taxes enacted in five US cities were associated with decreased prevalence of perinatal complications. We conducted a longitudinal retrospective study using 2013-2018 US national birth certificate data, applying a difference-in-differences approach to compare changes in prevalence of perinatal outcomes between pregnant women and infants living in US cities with SSB taxes with those residing in untaxed US comparator cities before vs up to 15 quarters post tax implementation. Subgroup analyses assessed heterogeneity. Measures of maternal and neonatal health outcomes were gestational diabetes mellitus (GDM), hypertensive disorders of pregnancy, gestational weight gain, infant birthweight, gestational age, preterm birth, low birth weight, large-for gestational-age, small-for-gestational-age, and appropriate-for-gestational-age. The sample included 5,552,995 mothers. SSB taxes were associated with a 14% decreased prevalence of GDM (-0.77 percentage points [pp]; 95% CI, -1.04 to -0.51) in taxed cities compared to large cities without a tax, after tax implementation, with differences by population subgroup. There were small changes in infants born small-for-gestational-age (-0.30 pp; 95% CI, -0.43 to -0.16), large-for gestational-age (0.28 pp; 95% CI, 0.16 to 0.41), and in birthweight (4.6 g; 95% CI, 2.3 to 6.9). SSB taxes levied in US cities were associated with a decline in GDM prevalence. SSB taxes may be an effective policy instrument to improve health during pregnancy, a critical window during which short-term exposures can have lifelong consequences for mother and child.

Preconception pain medication use and spontaneous abortion: a prospective cohort study

Holly Crowe* Holly Crowe Lauren Wise Elizabeth Hatch Kenneth Ellen Mikkelsen Henrik Sørensen Amelia Wesselink

Pain medications are used by >50% of women in the preconception period. Previous research focused on prescription medication recorded in administrative databases. We examined the association between self-reported use of prescription or over-the-counter pain medications and incidence of spontaneous abortion (SAB, loss of pregnancy <20 weeks' gestation) using data from a North American preconception cohort study. Participants reported medication use in the 4 weeks before baseline and during follow-up on self-administered bimonthly questionnaires and SABs on questionnaires during preconception (every 8 weeks) and pregnancy (~8 and ~32 weeks of gestation). We used Cox proportional hazards models with gestational weeks as the time scale to compute hazard ratios (HRs) and 95% confidence intervals (CIs), adjusting for demographics, lifestyle, and reproductive/medical history. We analyzed data from 8,128 participants enrolled during 2013-2021 who conceived over 12 months of follow-up. Twenty percent reported SAB. Overall, 5533 (68%) participants reported recent pain medication use on their last preconception follow-up, commonly for headache and muscle pain. Ibuprofen was the most reported medication (44% of participants), followed by acetaminophen (34%), naproxen (7%), aspirin (6%), and opioids (3%). Preconception use of any pain medication, compared with non-use, was not appreciably associated with SAB incidence (HR=0.94, CI: 0.85-1.06) nor was use of specific medications: 0.89 (CI: 0.80-0.99) for ibuprofen use, 0.90 (CI: 0.73-1.10) for naproxen use, 1.00 (CI: 0.81-1.25) for aspirin use, 1.05 (CI: 0.94-1.17) for acetaminophen use, and 0.95 (CI: 0.70-1.29) for opioid use. Results were similar after stratifying by medication use timing relative to conception. Our results indicate that preconception pain medication use of any type is not appreciably associated with increased risk of SAB. However, we were not able to consider dose, indication, or use after pregnancy detection.

Neonatal and Maternal Adverse Outcomes Following Use of Buprenorphine and Methadone for Treatment of Opioid Use Disorder in Pregnancy Elizabeth A Suarez* Elizabeth Suarez Krista F Huybrechts Loreen Straub Sonia Hernández-Díaz Hilary Connery Jonathan Davis Kathryn Gray Hendrée Jones Barry Lester Mishka Terplan Helen Mogun Brian T Batemen
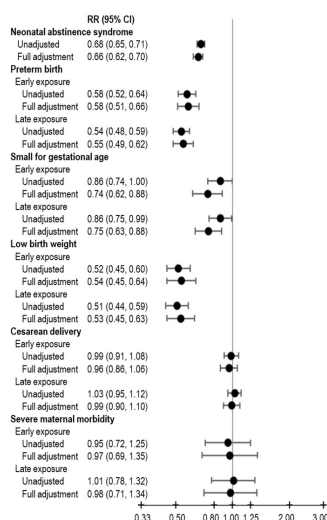
Opioid agonist therapy is strongly recommended for pregnant patients with opioid use disorder to prevent adverse effects of overdose and withdrawal. Buprenorphine may be associated with more favorable neonatal and maternal outcomes compared to methadone, but existing data are limited.

We conducted a cohort study in publicly insured pregnant patients in the Medicaid Analytic eXtract from 2000-2014 comparing buprenorphine and methadone exposure. Exposure during early pregnancy (day 0 through 133), late pregnancy (day 134 through delivery), and in the 30 days prior to delivery was assessed using dispensing and administration codes. Outcomes included neonatal abstinence syndrome, preterm birth, low birth weight, small for gestational age, cesarean delivery, and severe maternal morbidity. We estimated risk ratios and adjusted for a wide range of confounders using overlap weights.

We identified 4,349 and 4,331 pregnancies with early and late pregnancy buprenorphine exposure, respectively, and 1,927 and 2,287 pregnancies with early and late pregnancy methadone exposure. After adjustment, buprenorphine compared to methadone exposure in the 30 days prior to delivery was associated with a lower risk of neonatal abstinence syndrome (RR 0.66, 95% CI 0.62-0.70). Similarly, risk was lower for preterm birth (0.58, 0.51-0.66), small for gestational age (0.74, 0.62-0.88), and low birth weight (0.54, 0.45-0.64) among buprenorphine exposed compared to methadone exposed in early pregnancy. No association was observed for cesarean delivery or severe maternal morbidity. Results were consistent for late exposure and in sensitivity analyses that targeted unmeasured confounding and exposure misclassification.

Buprenorphine treatment in pregnancy is associated with more favorable neonatal outcomes than methadone. While both therapies are recommended for treating opioid use disorder during pregnancy, these results may support improving access to buprenorphine for pregnant patients.

Figure. Relative Risk Estimates for Adverse Neonatal and Maternal Outcomes Comparing Buprenorphine Treatment to Methadone Treatment

	RR (95% CI)
Neonatal abstinence syndrome	
Unadjusted	0.68 (0.65, 0.71)
Full adjustment	0.66 (0.62, 0.70)
Preterm birth	
Early exposure	
Unadjusted	0.58 (0.52, 0.64)
Full adjustment	0.58 (0.51, 0.66)
Late exposure	
Unadjusted	0.54 (0.48, 0.59)
Full adjustment	0.55 (0.49, 0.62)
Small for gestational age	
Early exposure	
Unadjusted	0.86 (0.74, 1.00)
Full adjustment	0.74 (0.62, 0.88)
Late exposure	
Unadjusted	0.86 (0.75, 0.99)
Full adjustment	0.75 (0.63, 0.88)
Low birth weight	
Early exposure	
Unadjusted	0.52 (0.45, 0.60)
Full adjustment	0.54 (0.45, 0.64)
Late exposure	
Unadjusted	0.51 (0.44, 0.59)
Full adjustment	0.53 (0.45, 0.63)
Cesarean delivery	
Early exposure	
Unadjusted	0.99 (0.91, 1.08)
Full adjustment	0.96 (0.86, 1.06)
Late exposure	
Unadjusted	1.03 (0.95, 1.12)
Full adjustment	0.99 (0.90, 1.10)
Severe maternal morbidity	
Early exposure	
Unadjusted	0.95 (0.72, 1.25)
Full adjustment	0.97 (0.69, 1.35)
Late exposure	
Unadjusted	1.01 (0.78, 1.32)
Full adjustment	0.98 (0.71, 1.34)

0.33   0.50   0.80 1.00 1.25   2.00   3.00

HIV, Cardiometabolic Health, and Birth Outcomes among HIV-infected and HIV-uninfected South African Women Angela Bengtson* Angela Bengtson Yezhi Pan Hlengiwe Madlala Mushi Matjila Gregory Petro Zandile Maqwatini Azetta Fisher Landon Myer

HIV and antiretroviral therapy (ART) increase the risk of cardiometabolic complications in non-pregnant persons, but little is known about their cardiometabolic impact in pregnancy. In Cape Town, we enrolled HIV+ and HIV- women in routine antenatal care at 24-28 weeks' gestation. At enrollment, women underwent a fasted 2-hour oral glucose tolerance test for gestational diabetes (GDM), diagnosed by WHO guidelines; blood pressure and anthropometry were assessed by trained research staff. Hypertension was defined as ≥130/80 mmHg. All HIV+ women were on combination ART. Among 315 women (166 HIV+, 149 HIV-) the median gestational age at first antenatal care was 17 weeks (IQR 12, 21), 53% were obese (BMI≥ 30.0 kg/m^2, 49% HIV+ vs 56% HIV-), and 18% were primigravida (11% HIV+ vs 26% HIV-). Overall, 5% of women had GDM and 13% had hypertension. HIV was marginally associated with GDM (RR 3.3 95% CI 0.7,15.5), but not hypertension (RR 0.8 95% CI 0.4,1.5), adjusted for pre-pregnancy BMI and age. Among 228 deliveries, emergency cesareans were more likely among women with GDM (RR 3.9; 95%CI 2.0,7.8) and hypertension (RR 2.2 95%CI 1.2,3.8), adjusted for age, pre-pregnancy BMI and HIV status. Hypertension increased the risk of small for gestational age (birthweight <10th percentile; RR 4.3 95%CI 1.5,8.2) and low birthweight (<2500 grams; RR 2.6 95% CI 1.2,5.8), while GDM increased the risk of large-for-gestational age (birthweight >90th percentile; RR 3.7 95%CI 1.4, 9.9). The risk of preterm birth was somewhat higher among women with GDM (RR 2.0 95% CI 0.8, 4.9) and hypertension (RR 1.9 95% CI 0.9,3.9), perhaps reflecting the high level of emergency cesareans. Our finding suggest HIV+ women may be at increased risk of GDM and that hypertension and GDM were associated with a range adverse birth outcomes for HIV+ and HIV- women Addressing cardiometabolic complications in pregnancy may improve birth outcomes among HIV+ and HIV- women.

Table. Associations between gestational diabetes and hypertension in pregnancy and birth outcomes among 228 HIV+ and HIV- women in South Africa

	Overall	Gestational Diabetes (GDM)			Hypertension		
	N=228	No GDM n=215 (95%)	GDM n=11 (5%)	RR 95% CI	No Hypertension n=198 (87%)	Hypertension n=30 (13%)	RR 95% CI
Preterm Birth	40 (17.4)	35 (16.1)	4 (36.4)	2.0 (0.8, 4.9)	32 (16.0)	8 (26.7)	1.9 (0.9, 3.9)
Low birthweight	29 (12.7)	26 (12.0)	3 (27.3)	2.0 (0.7, 5.6)	22 (11.1)	7 (23.3)	2.6 (1.2, 5.8)
High birthweight	16 (7.0)	15 (6.9)	0 (0.0)	--*	13 (6.5)	3 (10.0)	1.7 (0.5, 5.9)
Small for gestational age	20 (8.7)	19 (8.8)	1 (9.1)	1.0 (0.1, 6.7)	14 (7.0)	6 (20.0)	4.3 (1.5, 8.2)
Large for gestational age	41 (17.9)	36 (16.7)	4 (36.4)	3.7 (1.4, 9.9)	34 (17.1)	7 (23.3)	1.3 (0.6, 2.6)
Emergency Cesarean	51 (22.7)	43 (20.8)	6 (54.6)	3.9 (2.0, 7.8)	39 (19.9)	12 (41.4)	2.2 (1.2, 3.8)

Preterm birth: birth <37 weeks' gestation. Low birthweight: <2500 grams. Small for gestational age: birthweight <10th percentile for gestational age. Large for gestational age: birthweight> 90th percentile for gestational age. RRs estimated using Poisson models with robust variance estimators and adjusted for HIV status, continous age and continous pre-pregnancy BMI. * could not be estimated due to empty cell among women with GDM.

Emulating a sequence of target trials to avoid immortal time bias in pregnancy studies – an application to antibiotic initiation and preterm delivery Ellen C. Caniglia* Ellen Caniglia Rebecca Zash Christina Fennell Modiegi Diseko Gloria Mayondi Jonathan Heintz Mompati Mmalane Joseph Makhema Shahin Lockman Sunni L. Mumford Eleanor J. Murray Sonia Hernandez-Diaz Roger Shapiro

Background: Immortal time bias is introduced when treatment initiation occurs after time zero of follow-up and is common in observational studies of medication use during pregnancy. We describe how emulating a series of hypothetical randomized trials (target trials) avoids immortal time bias and apply the approach to antibiotic initiation and preterm delivery.

Methods: The Tsepamo Study captured birth outcomes at up to 18 delivery sites in Botswana from 2014-2021. To investigate the relationship between antibiotic initiation after 24 weeks gestation and preterm delivery (24-37 weeks gestation) among women presenting for antenatal care <24 weeks gestation we: 1) started follow-up at 24 weeks and defined exposure as antibiotic initiation between 24-37 weeks gestation (susceptible to immortal time bias) and 2) conducted 13 sequential target trials of antibiotic initiation versus no initiation during each week from 24-37 weeks gestation. For each trial, eligible women had not previously initiated antibiotics and remained pregnant at the start of that week. We used log-binomial models to calculate risk ratios (RR) and 95% confidence intervals (CI).

Results: Of 111,403 eligible women, 17,009 (15%) initiated antibiotics between 24-37 weeks gestation. The RR (95% CI) for preterm delivery comparing antibiotic initiation to no initiation between 24-37 weeks was 0.92 (0.89, 0.96). In the series of target trials which address immortal time bias, the RRs (95% CIs) ranged from 1.06 (0.93, 1.22) to 1.28 (1.14, 1.43) (Figure).

Conclusions: Because the time period between time zero and treatment initiation is "immortal" to the outcome, defining exposure based on treatment initiation after time zero biased the RR for the association between antibiotic initiation and preterm delivery downwards. Conducting a series of target trials can avoid this immortal time bias in pregnancy studies by aligning exposure initiation and start of follow-up.

Figure. Risk ratios and 95% confidence intervals for preterm delivery comparing antibiotic initiation to no initiation between 24-37 weeks gestation (red) and by week of antibiotic initiation (black), The Tsepamo Study.
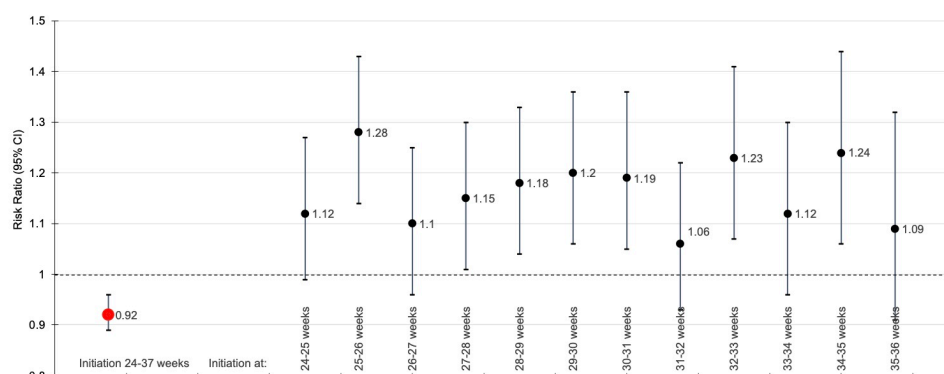
The problems with two-way fixed effects: Identifying target parameters and estimating bias
Dana Goin* Dana Goin Corinne Riddell

Background: Difference-in-difference (DiD) designs have been used to estimate the average treatment effect on the treated (ATT) when studying the impacts of policy changes or natural experiments on health outcomes. When there are multiple time points and staggered policy adoption or exposure timing variation, two-way fixed effects (TWFE) have been used as a DiD extension, in which indicators for place and time are included in a regression model. However, recent work in the econometrics literature shows TWFE is biased when estimating the ATT. Our goal is to demonstrate for an epidemiologic audience why and under what scenarios TWFE is biased.

Methods: We used birth files from the National Center for Health Statistics to compare estimates of the effect of the Affordable Care Act on the risk of preterm birth from TWFE and a group-time average treatment effect (GTATE) estimator. We also conducted a simulation study to investigate how TWFE and GTATE perform when estimating constant, heterogeneous, and dynamic treatment effects. We explored whether limiting to ever-treated units for the comparison group affects the estimators' bias under these scenarios.

Results: When there are constant treatment effects, both the TWFE and the GTATE estimators had low bias and confidence interval coverage approximately 95%. When treatment effects are heterogeneous across places, the GTATE was still unbiased while the TWFE was slightly biased, with confidence interval coverage approximately 90%. The ever-treated TWFE had the worst performance in this scenario, with confidence interval coverage below 75%. The dynamic treatment effects showed a similar pattern, although the coverage was worse for the ever-treated GTATE (70%), the TWFE (80%), and the ever-treated TWFE (0%).

Conclusions: Using TWFE to estimate the ATT for exposures staggered over multiple time periods is recommended only when there are constant treatment effects; otherwise, the GTATE estimator has better performance.

Integrating g-methods with difference-in-differences: Identifying and estimating population-wide effects of sustained interventions under alternative causal assumptions

Audrey Renson* Audrey Renson Paul N. Zivich Alexander P. Keil Michael G. Hudgens Whitney R. Robinson Allison E. Aiello

Background: Many epidemiologic questions concern sustained interventions in populations defined by public health priorities. Existing methods to answer such questions require a measured covariate set sufficient to control confounding, which can be questionable in observational studies. Difference-in-differences relies instead on the parallel trends assumption, allowing for some types of time-invariant unmeasured confounding. However, existing difference-in-differences implementations are limited to point treatments in restricted subpopulations.

Methods: We derived nonparametric identification results, along with parametric and semi-parametric estimators for the effects of sustained interventions in an unrestricted target population, under causal consistency, positivity, and parallel trends conditional on time-varying covariates. We assessed performance of estimators via a simulation study, and present an example based on COVID-19 stay-at-home orders. Estimators and data are available in an R package.

Results: Under our assumptions, average potential outcomes under a sustained intervention are identified in settings where exposure status is consistent with the intervention at baseline, but may deviate at different times. Simulations over a range of sample sizes suggest our inverse-probability-weighted (IPW) and iterated conditional g-computation estimators are approximately unbiased, consistent and asymptotically normal for the effects of interest. Using the iterated conditional estimator, if our assumptions hold, a U.S. stay-at-home order during Apr-Jul 2020 would have saved $\approx$7,900 (95% CI, 3,600-12,000) lives up to Jul 2020. The IPW estimator allows for a check on model specification but is less precise (Figure).

Conclusion: Our integration of difference-in-differences with g-methods provides a new causal inference approach that targets sustained interventions for whole populations, and may prove useful when unmeasured time-invariant confounding is suspected.
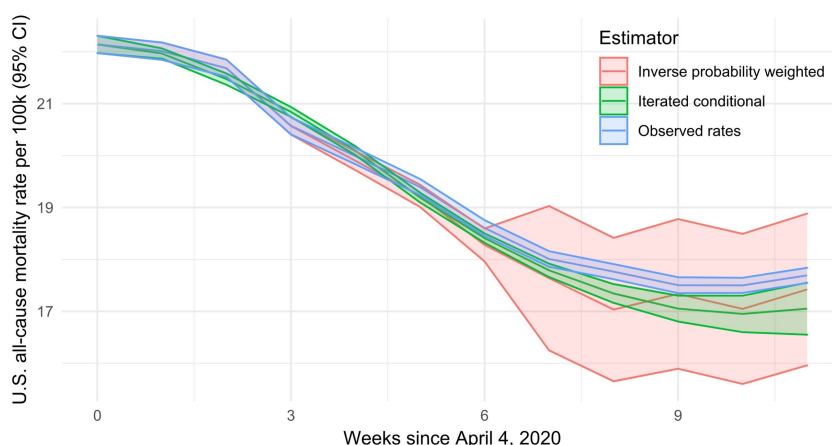
Figure: Example analysis implementing novel difference-in-differences-based estimators of sustained treatment effects. Lines are estimated all-cause mortality rates under a hypothetical interventions setting most (43/50) U.S. states to continue stay-at-home orders to July 1, 2020 (red and green), compared to observed mortality rates (blue). Bands are 95% pointwise confidence intervals based on 500 bootstraps.

**Measuring the effect of sobriety checkpoints on road traffic deaths in Mexico: a difference-in-difference approach with variation in treatment timing.** Pricila Mullachery* Pricila Mullachery D. Alex Quistberg Mariana Lazo Katy Indvik Carolina Perez-Ferrer Nancy Lopez-Olmedo Arantxa Colchero Usama Bilal

Up to a third of global road traffic deaths and 20% in Mexico are attributable to alcohol. Drunk driving is illegal in Mexico, but enforcement varies locally. In 2013, Mexico launched a sobriety checkpoints program in cities with high rates of alcohol-related motor vehicle collisions. This study measures the causal effect of the program on the rate of road traffic deaths (2005-2019) per 10,000 registered passenger vehicles.

Treatment is defined as the existence of at least one sobriety checkpoint. Among the 105 cities (i.e., municipalities) participating in the program, 54 were treated in 2013, 16 in 2014, 16 in 2015, 10 in 2016, 7 in 2017, and 2 in 2019. We used difference-in-difference with multiple time periods and variation in treatment timing (Callaway and Sant'Anna, 2020). This approach uses cities treated after 2013 to create comparison groups; as cities receive the treatment in subsequent years, they are reassigned to the treated group. We estimated the average treatment effect on the treated (ATT) using linear regression models adjusted for confounders combined with inverse probability weighting. We also estimated dynamic treatment effects (DTE) and conducted sensitivity analyses that (1) excluded Mexico City (due to unique population size and prior policies) and (2) used larger geographic units covering urban extents to account for potential spillover effects.

The ATT showed a 11.4% reduction in traffic fatalities among treated cities in the post-treatment period compared to the pre-treatment period (95% Confidence Interval, -15.9; -6,6). These results were robust in sensitivity analyses. DTE showed that trends were mostly parallel in the pre-treatment period. There was a clear trend indicating that rates were increasingly lower in treated vs. comparison group in the post-treatment period, particularly after year 2 of implementation (Figure).

These findings provide support for efforts to implement sobriety checkpoint programs in Latin America.

Figure: Dynamic treatment effect of sobriety checkpoints on traffic fatalities
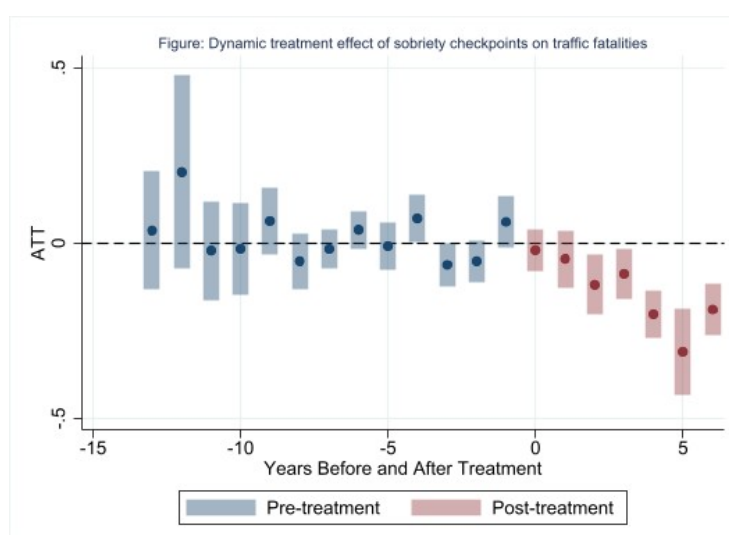
The Functional Synthetic Control Method: Setting the PACE for the Synthetic Control Aaron Shev* Aaron Shev Andrew Farris Chris McCort Rose Kagawa Hannah Laqueur Veronica Pear

We propose a new approach to the Synthetic Control Method (SCM) using the Principal Analysis by Conditional Expectation (PACE) algorithm for functional data analysis. The SCM is traditionally used to estimate the effect of a treatment on a single unit in the panel data setting and has become an increasingly important method for observational studies over the past decade. Improving the SCM has been an active area of research resulting in several proposed modifications aimed at addressing major shortcomings of the original SCM. Our method further improves upon the SCM by taking a functional data analysis approach that not only bolsters the performance of the classic SCM, but also can be used in conjunction with other commonly used synthetic control extensions.

The functional data analysis approach considers observed data on any given unit to comprise samples from an underlying random trajectory. The proposed method first estimates continuous functions for the treated unit and those units in the donor pool. It then then conducts a synthetic control analysis on these estimates. This provides several benefits. Fitting continuous curves allows the method to inherently handle missing or irregularly sampled data. Noise reduction from using smooth curves, as opposed to the observed values, allows for good pre-treatment fit in cases where poor fit may have made using SCM inadvisable. The proposed method eliminates the step of choosing arbitrary summaries of pre-treatment data for optimizing weights by using the loadings of the functional principal components instead. Finally, PACE uses information from the mean trajectory of units to estimate unit trajectories even when units are sparsely sampled. In a preliminary Monte Carlo simulation of 1,000 data sets, our proposed method yielded a 13% reduction in RMSE estimating the true treatment effect. With little additional computation time required, our proposed method offers substantial improvements to the standard SCM framework.

Have paved trails and protected bike lanes led to more bicycling in Atlanta? A generalized synthetic-control analysis with smartphone data Michael Garber* Michael Garber Dana Flanders Kari Watkins Felipe Lobelo Michael Kramer Lauren McCullough

Bicycling is an important form of physical activity in populations. Research assessing the effect of infrastructure on bicycling with high-resolution smartphone data remains limited in low-bicycling U.S. settings, including the Southeastern U.S. Atlanta has been expanding its bicycle infrastructure, including off-street paved trails such as the Atlanta BeltLine and some protected bike lanes. We estimated the effect of five groups of off-street paved trails and protected bike lanes on bicycle ridership in their corresponding areas (Figure). To classify areas as treated or not over time, we first subdivided the study area into half-square-mile hexagons. We then classified hexagons as treated in that month using two definitions: 1) one ("wide-net") if the hexagon overlapped a half-mile-buffer radius around the trail or lane, and 2) a second ("narrower") if the hexagon overlapped the trail or lane itself. To measure bicycling, we used two years (2016-10-01 to 2018-09-30) of monthly Strava data along with data from 15 on-the-ground counters to adjust for spatiotemporal variation in app use.

Using the generalized synthetic control method, we estimated monthly ratio and difference effects for each treatment area, along with corresponding cumulative effects (i.e., summarized over month). In addition, we estimated joint effects of all treatment infrastructure when viewed as one intervention. The generalized synthetic control method is well-suited for this situation, as multiple units were treated at different times.

Considering all infrastructure as a joint intervention, an estimated 1.10 (95% CI: 1.03, 1.17) times more bicycle-distance was ridden than would have been expected in the same areas had the infrastructure not been built, using the narrower treatment-area definition. The Atlanta BeltLine Westside Trail and Proctor Creek Greenway had especially robust effect estimates (e.g., ratios of 1.45 [95% CI: 1.16, 1.87] and 1.55 (1.18; 2.17) under each treatment-area definition, respectively). Other infrastructure was estimated to have had weaker positive or no effects on bicycle-distance ridden.

This study advances research on the topic because of its setting in the U.S. Southeast, its simultaneous assessment of several infrastructure groups, and its data-driven approach to estimating effects.

Causal Inference
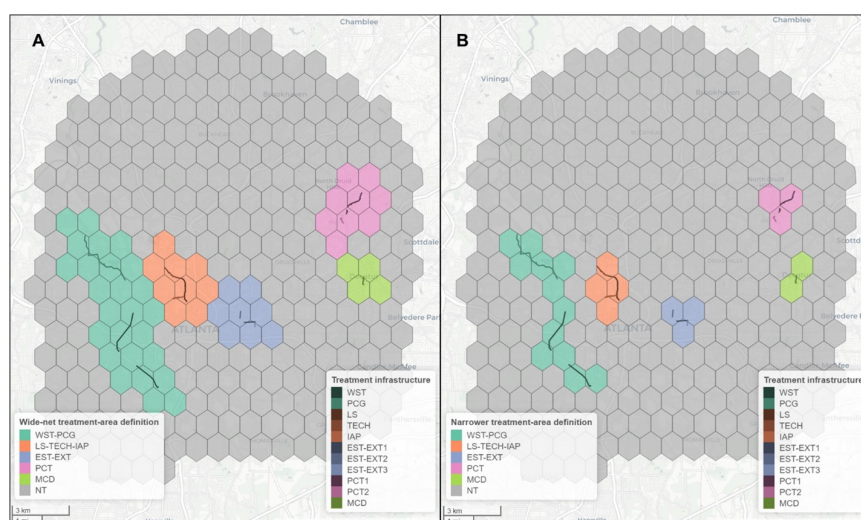
Regression discontinuity in electronic health record data to determine the causal effects of clinical interventions: an application to intensive lifestyle intervention for prediabetes Julia M. Lemp* Julia M. Lemp Christian Bommer Min Xie Sebastian Vollmer Till Bärnighausen Pascal Geldsetzer

Aim: While clinical trials have demonstrated efficacy of lifestyle interventions in preventing Type 2 Diabetes (T2DM), their effectiveness in routine care has yet to be established. Using a novel quasi-experimental approach, this study aimed to determine the causal effects of the English Diabetes Prevention Programme (DPP), a lifestyle intervention consisting of at least 13 sessions that was first introduced in 2016, on glycemic control.

Methods: We used a regression discontinuity (RD) design in the Clinical Practice Research Datalink, a large primary care database of electronic health records in the UK. We considered January 2017 to December 2018 as the enrolment period, with follow-up ending in July 2020. Our RD exploits the fact that only patients with an HbA1c of 42 mmol/mol or higher were eligible for the DPP. We used local linear regression, with separate regression lines fitted above and below the cutoff and data-driven bandwidth selection. The primary outcome was the last HbA1c measurement taken during follow-up. Secondary outcomes were T2DM incidence, initiation of diabetes medication, BMI, weight, blood pressure, HDL, LDL, mortality, and emergency hospitalization.

Results: 1 294 325 adult patients had an HbA1c record in 2017-2018 and were included in the analysis. There was a jump of 11 percentage points in the probability of receiving the DPP at the HbA1c-based eligibility cutoff. The DPP reduced HbA1c (-1.23 mmol/mol, 95% CI -2.14, -0.33) and BMI (-0.74, 95% CI -1.47, -0.01), and increased the probability of being diagnosed with T2DM during follow-up (3.9%, 95% CI 2.0%, 5.9%). The remaining outcomes largely suggested protective health effects but were not statistically significant.

Conclusion: Our analysis demonstrates the feasibility of an RD approach in large-scale electronic health record data to determine the causal effects of clinical and health services interventions. Our estimated effect sizes were comparable to those observed in clinical trials.
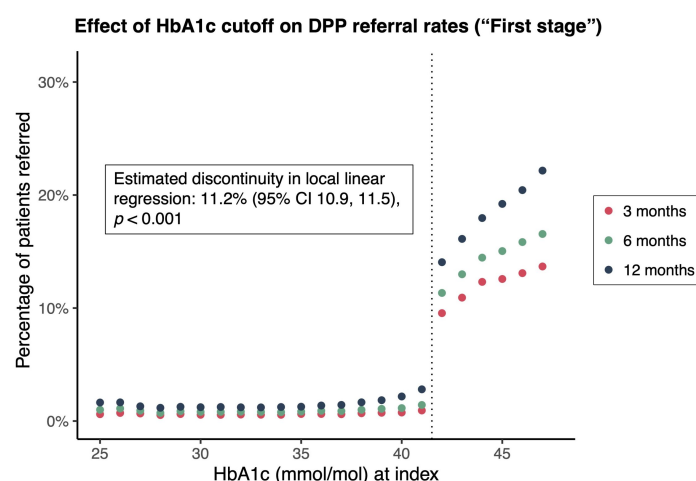

Effect of HbA1c cutoff on DPP referral rates ("First stage")

Estimated discontinuity in local linear regression: 11.2% (95% CI 10.9, 11.5), $p < 0.001$

Figure. DPP = Diabetes Prevention Programme. Percentage of patients referred to intensive lifestyle intervention (DPP) by initial HbA1c measurement within 3, 6, and 12 months after said HbA1c measurement. The vertical, dotted line marks the discontinuity in referral rates (11.2%, 95% CI 10.9, 11.5) at the HbA1c-based eligibility cutoff of 42 mmol/mol.

Plasma proteomic signature of decline in gait speed and grip strength Xiaojuan Liu* Xiaojuan Liu Stephanie Pan Vanessa Xanthakis Ramachandran S. Vasan Anne B. Newman Bruce M. Psaty Jason Sanders Chenkai Wu Thomas R. Austin Russell P. Tracy Robert E. Gerszten Michelle C. Odden

Introduction: Gait speed and grip strength are well-established physical function measures predictive of adverse health outcomes in the elderly. The biological mechanisms underlying functional decline with aging remain unclear. This investigation examined the plasma proteomic profile associated with longitudinal changes of gait speed and grip strength in community-dwelling adults.

Methods: We applied SOMAscan assay to measure 1,161 plasma proteins on 2,871 participants (60% women, aged 76 years) in Cardiovascular Health Study (CHS) in 1992/1993 and 1,550 participants (55% women, aged 54 years) in Framingham Offspring Study (FOS) in 1991-1995. Gait speed and grip strength were measured annually for 6 years in CHS and at cycles seven (1998-2001) and eight (2005-2008) in FOS. The associations of individual protein levels (log-transformed and standardized) with longitudinal gait speed and grip strength declines in two populations were examined separately by linear mixed effect models with adjustment for age, sex and key confounders. Meta-analyses were implemented using random effect models and Bonferroni adjustment was applied to correct for multiple testing.

Results and Conclusions: Plasma levels of 18 and 12 proteins were associated with changes in gait speed and grip strength, respectively (Bonferroni-corrected $p < .05$). The proteins most strongly associated with gait speed decline were growth/differentiation factor 15 (GDF-15) (uncorrected Meta-analytic $p = 1.60 \times 10^{-15}$), pleiotrophin (PTN) (1.29×10^{-8}), and metalloproteinase inhibitor 1 (TIMP-1) (2.02×10^{-8}). The proteins most strongly associated with grip strength decline were GDF-15 (1.39×10^{-7}), carbonic anhydrase III (6.60×10^{-7}), and TIMP-1 (3.21×10^{-6}). Several statistically significant proteins are involved in the alternative complement pathway, extracellular matrix remodeling or immune function. These novel proteomic biomarkers may inform our understanding of the pathophysiology of functional decline.
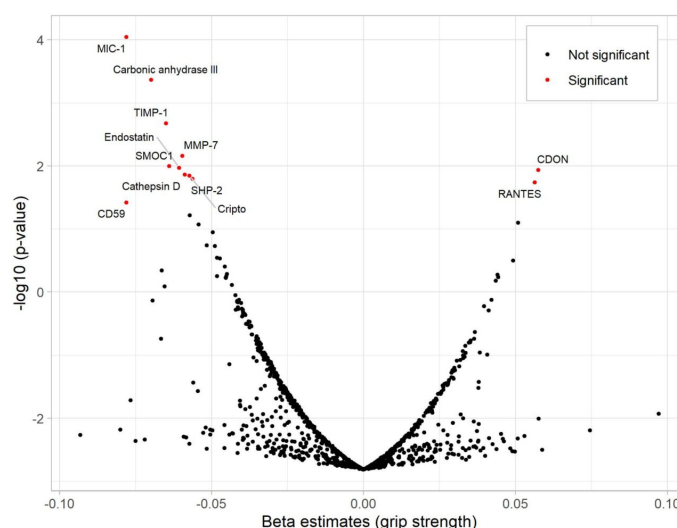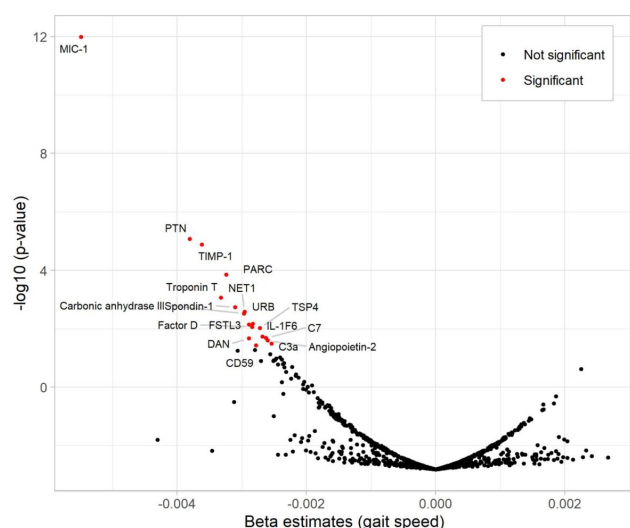
Approaches to ascertaining hearing impairment and their impact on the studies of the association between hearing loss and dementia Therese Chan* Therese Chan Stacey Fisher Douglas Manuel Amy Hsu

Background: It has been estimated that approximately 40% of dementia cases are attributed to modifiable risk factors. One emerging modifiable risk factor for dementia that has not been well-studied is hearing impairment, which has a high population attributable fraction of 23%. However, it is unclear what methods of ascertaining hearing impairment (e.g., self-report versus a hearing test) will be most predictive of future dementia status. The study objective is to explore approaches for measuring hearing impairment and its relationship to 3-year incident dementia status.

Methods: We used baseline (2011 to 2015) and 3-year follow-up data from the Canadian Longitudinal Study on Aging. We excluded individuals who were under 55 years of age, reported physician-diagnosed dementia at baseline, and/or did not have follow-up data on dementia status. Hearing ability was measured using self-rated hearing, self-reported hearing aid use, and audiometric testing. Hearing impairment was defined as having fair or poor self-rated hearing (versus excellent, very good, or good), using hearing aids, or having a pure tone average of 1000, 2000, 3000, and 4000 Hz above 60 dB.

Results: Of the 19,830 older Canadians included in the study, the baseline mean age was 66 years (SD=8), 53% were female, 5% were non-white, and 0.2% had dementia at follow-up. Among individuals with physician-diagnosed dementia at follow-up, 16% rated their hearing as fair or poor, 16% were using hearing aids, and 19% had audiometrically defined hearing loss at baseline. Those without dementia at follow-up had 13%, 6%, and 4.5% on these measures, respectively. Results from age- and sex-adjusted models showed that individuals with fair/poor hearing, individuals using hearing aids, and individuals with audiometry-derived hearing loss had 2.0 (95% CI 1.1-3.7), 1.8 (95% CI 0.9-3.6), and 2.9 (95% CI 1.4-6.1) times the odds of incident dementia, respectively, compared to individuals without the respective definitions of hearing impairment.

Conclusion: The results of this analysis suggest varying degrees of association between hearing impairment and dementia status depending on the method of hearing impairment ascertainment.

Aging

Falls and trajectories of activities of daily living in older adults Claire Adam* Claire Adam Erin Semmens Annette Fitzpatrick Anjum Hajat Cindy Leary Sindana Ilango Christina Park

Background: Falls have the potential to impact activities of daily living (ADLs). Understanding this association informs how falls can affect older adults' ability to live independently, and for the development of appropriate post-fall interventions. **Objective:** To model trajectories of difficulty with instrumental activities of daily living (IADLs) and ADLs before and after the first fall observed during the study period and to identify the characteristics of those in each trajectory. **Methods:** This study included 1513 participants from the Ginkgo Evaluation of Memory Study (GEMS) who reported their history of falls and measures of ADLs and IADLs both before and after the first fall. Falls and I/ADL scores were ascertained every 6 months for up to 7 years. Latent class trajectory modeling was used to classify I/ADL trajectories pre- and post- initial fall and determine the characteristics of participants more likely to have increased difficulty with I/ADLs. **Results:** 18% of participants had increasing difficulty with ADLs post-fall, while 82% had minimal to no change in difficulty. 13% of participants had increasing difficulty with IADLs, 7% had steeply increasing difficulty, and 80% of participants had minimal to no difficulty with IADLs post-fall. Significant differences in participant demographics, health status, and neighborhood characteristics were observed for the various trajectories. **Conclusions:** Having difficulty with I/ADLs negatively impacts older adults' ability to live independently and safely. Understanding the characteristics of older adults most likely to have difficulty with I/ADLs post-fall, is essential for the development of interventions targeting populations at greatest risk.

The effects of volunteering in cognitive function of older adults in the Health and Retirement Study, data from 2008 to 2016. Ester Villalonga Olives* Ester Villalonga Olives Josué Almansa Tasneem Khambaty

The increase in the aging population is associated with higher rates of cognitive decline and dementia. The literature indicates that volunteering may be advantageous in mitigating cognitive decline in older age, but the underlying mechanisms are unclear. Based on previous theoretical frameworks we examined cognitive activity, social activity, and physical activity as potential mediators of the association between volunteering and cognitive function.

We used three waves of Health and Retirement Study panel data from 2008, 2012, and 2016 (N=10,546). Self-reported questionnaires were used to assess volunteering frequency (no volunteering, <100 hours and ≥100 hours), and an index of cognitive functioning was used to assess memory, mental processing, knowledge, language, and orientation. A multigroup (3 waves) structural equation model was estimated to assess differences over time, adjusted for age, sex and education considering sampling weights and complex sample design.

Volunteering had a positive effect on cognitive function, with volunteering ≥100 hours having a stronger effect compared to <100 hours. The direct effect of volunteering on overall cognitive function was statistically significant across waves, except for volunteering <100 hours for wave 2. All indirect effects of volunteering on cognitive function through cognitive activity (<100 hours: 0.04, ≥100 hours: 0.06) and moderate physical activity (<100 hours: 0.0; ≥100 hours: 0.03) were statistically significant compared to no-volunteering ($p<0.01$) for wave 1, and remained similar across waves. Approximately half of the effect of volunteering on cognitive functioning was mediated, mostly via cognitive activity.

Volunteering is a healthy lifestyle choice that plays a strong protective role on cognitive function primarily by increasing cognitive activity. Interventions that help older adults to be part of volunteering activities may have promise for preserving cognitive function into later life.

Health Disparities

Joint effects of air pollution mixtures and neighborhood socioeconomic deprivation on cognitive decline in Metro Atlanta, USA Grace Christensen* Grace Christensen Zhenjiang Li John Pearce Michele Marcus James Lah Lance Waller Stefanie Ebelt Anke Huels

Urban settings include multiple, correlated air pollutants and socioeconomic status (SES) factors but their combined impact on cognitive health is unknown. Here, we compare traditional adjusted single exposure models and the unsupervised clustering algorithm Self-Organizing Maps (SOM) to estimate the individual and joint effects of air pollution and SES on cognitive decline. The Emory Healthy Aging Study in Atlanta (age 50+ years, N=11,897, 2015-2020) measures subjective cognitive decline via the Cognitive Function Instrument (CFI). We obtained air pollution estimates from the CMAQ chemical transport model and neighborhood SES (nSES) indicators at census-tract level from the US Census Bureau. SOM created exposure clusters based on the joint distribution of air pollution and nSES in each census tract. Adjusted linear regression models were used to estimate associations between SOM clusters and CFI score. Single exposure linear regression models suggest an interquartile range (IQR) increase in air pollutants had a protective effect on CFI (e.g., CO β: -0.04; 95% CI: -0.06, -0.01). These protective effects can be explained by the high CO concentrations in high-nSES neighborhoods identified by SOM, indicating protective effects of high-nSES against adverse effects of air pollution. Additionally, participants living in the lowest nSES and highest air pollution cluster had CFI scores 0.15 (95% CI: 0.06, 0.24) points higher on average compared to those from the highest nSES and low air pollution cluster, indicating synergistic effects of air pollution and nSES. In diverse cities like Atlanta, where gentrification and traffic load can yield high nSES neighborhoods with high air pollution, the relationship between air pollution and nSES can be complicated. Using environmental mixtures methods to examine joint effects of air pollution and nSES and their spatial distribution is necessary to get unbiased estimates of the effect of air pollution and cognitive decline.
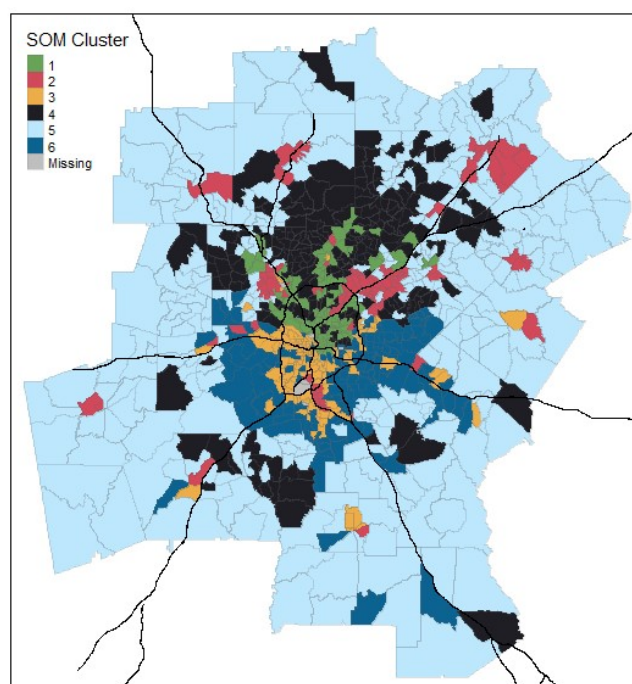
The Associations of SNAP Use and Memory Function among US Older Adults: Findings from the Health and Retirement Study Peiyi Lu* Peiyi Lu Katrina Kezios Jongseong Lee Christopher T. Wimer Adina Zeki Al Hazzouri

Studies on the health effect of Supplemental Nutrition Assistance Program (SNAP) on the cognitive health of older adults are scarce. In this study, we examined the associations of SNAP use and memory function trajectories among US older adults. Our sample included 3,555 SNAP-eligible participants (aged 50+) from the 1996 Health and Retirement Study survey, among whom 559 were SNAP users and 2,996 were non-users. SNAP eligibility was constructed based on household income and assets compared to the federal criterion. Memory function was assessed biennially from 1996 through 2016. To account for pre-existing differences in characteristics and variations in survey attrition between SNAP users and non-users, we modeled the probability of SNAP use and of attrition using pre-SNAP exposure (i.e., 1994) demographic and health covariates. We then modeled trajectories of memory function across SNAP use using linear mixed effect models weighted by the inverse probability of treatment (i.e. SNAP use) and of attrition. We also cross-examined the results in a propensity score (PS) matched sample (N=1,050). SNAP users in 1996 had lower socioeconomic status and worse health at baseline than SNAP non-users, and were more likely to be lost to follow-up. Results using IP-weights suggested SNAP users had worse memory scores at baseline but slower memory decline compared with non-users (annual decline rate is -0.038 standard units [95%CI=-0.044, -0.033] for non-users and -0.043 [95%CI=-0.046, -0.040] for users). Results from the PS-matched sample also showed SNAP users had slower memory declines compared with non-users (annual decline rate was -0.052 units [95%CI=-0.055, -0.050] for non-users and -0.048 units [95%CI=-0.051, -0.046] for users). After accounting for pre-existing differences between *eligible* SNAP users and non-users as well as differential loss to follow-up, our findings suggested that SNAP participation is associated with slower memory decline among eligible older adults.

The Impact of Air Conditioning on Heat Index Related-mortality in Texas Prisons during Warm Months Julianne Skarha* Julianne Skarha Keith Spangler David Dosa Josiah Rich David Savitz Antonella Zanobetti

Background: There is a large body of epidemiologic evidence that heat is association with mortality. One of the most effective strategies to mitigate the effects of heat is through air conditioning (AC). Texas regulates the internal temperature of jails to stay between 65° to 85° degrees but these same standards do not apply to state and private prisons. Qualitative research indicates that the lack of air conditioning has detrimental health effects on person held in prisons in Texas but there is limited quantitative research on this topic.

Research Goal: To determine the effect of air conditioning on heat index-related mortality during warm months in Texas state and private prisons from 2001 – 2017

Methods: We used data from the United States Department of Justice from 2001 – 2017 on mortality while in the custody of a prison in Texas. Using the case-crossover approach with a distributed-lag nonlinear model, we estimated the association of maximum daily heat index in the warm season with mortality in prisons with AC and prisons without AC. We centered the models at 80° F heat index. We also estimated the association of extreme heat (days above the 90th percentile heat index for the prison location) with mortality in prisons with AC and prisons without AC.

Results: There were 2,341 and 893 deaths in prisons without AC and prisons with AC in Texas, respectively. The majority of deaths were among people who were male (95%). There were similar age and race mortality distributions between the two prison groups but mortality in prisons with AC was more likely to occur in a low security setting and an urban county. A one-degree increase above 80°F in warm months was associated with a 0.58% (95% CI: -0.01%, 1.17%) in mortality in prisons without AC and a -0.51% (95% CI: -2.09%, 1.10%) decrease in mortality in prisons with AC. An extreme heat day was associated with a 12.96% (95% CI: -3.47%, 32.19%) increase in mortality in prisons without AC while it was associated with a -15.97% (95% CI: -36.37%, 10.96%) decrease in mortality in prisons with AC.

Conclusion:Mortality was not associated with heat index in prisons with AC but was in prisons without AC.

Association between heat index and all-cause mortality in Texas prisons from 2001 - 2017
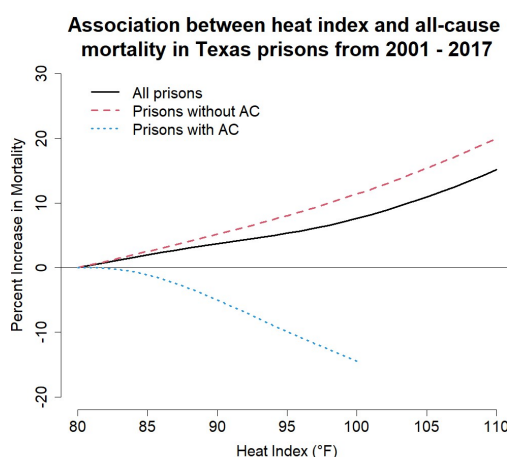
Associations between drug-specific arrests and criminal legal system referrals to drug treatment, 1992-2017 Pia M. Mauro* Pia Mauro Erin Annunziato Ruth T. Shefner Seth J. Prins

Background: People referred to substance use treatment via the criminal legal system are less likely to receive evidence-based treatment than if they are referred through other sources, including self-referrals. We examined associations between state-level drug arrests and criminal legal referrals to substance use treatment.

Methods: We used data from specialty substance use treatment admissions in the Treatment Episode Data Set (1992-2017) and drug arrests from the Uniform Crime Reporting Program Arrests series (1991-2016). We described trends in yearly state-level admission rates and drug arrests per 100,000 people both overall and by drug, to correspond with drug-specific arrest offense categories (i.e., cannabis, opioid/cocaine, synthetic opioids). We fit multi-level negative binomial models with state and year random intercepts to test the association between criminal legal system referrals and drug arrests, with arrests and state census covariates lagged by one year.

Results: Average state-level criminal legal system referrals to treatment decreased from 294.02 (in 1992) to 239.41 (in 2017) per 100,000 people, while drug arrests increased from 274.96 (in 1991) to 430.28 (in 2016) per 100,000 people. Overall, increasing state-level drug arrest was associated with increasing criminal legal referrals to treatment (aIRR=1.000439, 95% CI=1.000241, 1.000637), adjusting for state-level covariates. Associations were also observed for cannabis (aIRR=1.001893, 95% CI=1.001527, 1.002260), opioid/cocaine (aIRR=1.001296, 95% CI=1.000886, 1.001706), and synthetic opioids (aIRR=1.025303, 95% CI=1.021350, 1.029271).

Conclusion: Increases in drug arrests were positively associated with court-mandated treatment referrals, which often do not include evidence-based practices. The magnitude of the referral-arrest associations was strongest for synthetic opioids. Studies should assess whether policies that change drug-related arrests could lead to changes in court-mandated treatment.
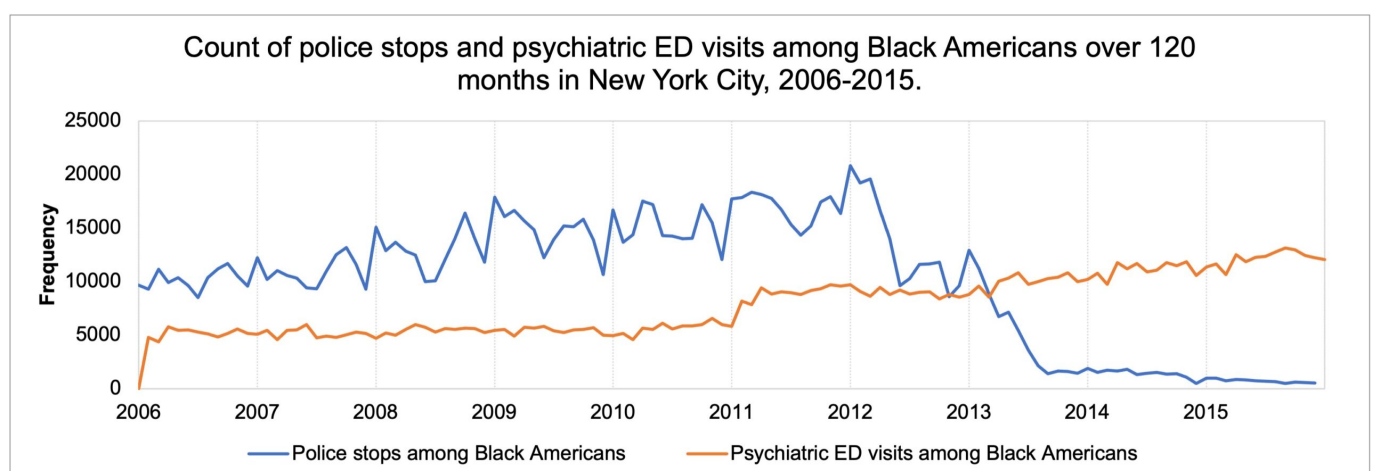
New York City's Stop, Question, and Frisk Policy and Psychiatric Emergency Department Visits among Black Americans, 2006-2015 Abhery Das* Abhery Das Tim Bruckner

Background: Under the Stop, Question, and Frisk (SQF) policy, New York City (NYC) police stopped Black Americans at more than twice the rate of non-Hispanic whites, after controlling for crime and precinct differences. The racial bias in police stops incites greater distrust of police and has been hypothesized to hold broader health implications in these communities. Previous studies, however, do not address whether police stops during SQF correspond with greater psychiatric emergencies among Black Americans more broadly (i.e., at the population-level).

Methods: We examine whether monthly police stops during SQF correspond positively with monthly psychiatric Emergency Department (ED) visits among Black Americans. We utilized as the exposure variables all police stops, stops including frisking, and stops including use-of-force among Black Americans. We examined as the outcome monthly psychiatric ED visits among Black Americans in NYC between 2006-2015. We applied Box-Jenkins time-series methods to identify and control for temporal patterns over the 120 months analyzed.

Results: Black Americans in NYC had 938,356 psychiatric emergencies over the test period. We find that all police stops, stops including frisking, and stops including use-of-force correspond with monthly increases in psychiatric ED visits among Black Americans (all stops – coef=0.02, 95%CI= 0.006,0.043; stops including frisking – coef=0.05, 95%CI= 0.015,0.083; stops including use-of-force – coef=0.12, 95%CI= 0.031,0.201). A one standard deviation increase in police stops equates to a 2.72% increase in psychiatric ED visits among Black Americans in that same month.

Conclusion: Racially biased and unconstitutional police encounters may have acute mental health implications for the broader Black community not directly involved in the encounter itself. In particular, use of force under racially-biased police stops in NYC may have substantial mental health consequences.

Count of police stops and psychiatric ED visits among Black Americans over 120 months in New York City, 2006-2015.

Policing/Incarceration

Impact of jail-based methadone or buprenorphine treatment for opioid use disorder on overdose mortality immediately after release from New York City jail, 2011-2017 Sungwoo Lim* Sungwoo Lim Teena Cherian Monica Katyal Ross MacDonald Keith Goldfeld Ryan McDonald Ellen Wiewel Maria Khan Noa Krawczyk Sean M. Murphy Ali Jalali Philip J. Jeng Joshua Lee

Opioid overdose is a leading cause of death during the immediate time after release from jail or prison. Although methadone or buprenorphine treatment for opioid use disorder (MOUD) can reduce overdose risk, most jails in the United States do not provide MOUD, and research in estimating its impact in jail settings is limited. To address this gap, we tested the hypothesis that in-jail MOUD is associated with lower overdose mortality risk post-release. We used matched administrative records from New York City and New York State for analysis. The cohort consisted of 15,803 adults with opioid use disorder who were released from New York City jails to the community between 2011 and 2017. They experienced 31,388 incarcerations, which included 17,119 treatment (in-jail MOUD) and 14,269 comparison events (out-of-treatment). We conducted multivariable time-to-event data analysis. Specifically, to account for confounding on association between time-varying, non-random in-jail MOUD receipt and overdose mortality, we performed the Cox regression model adjusting for time-invariant (gender), time-varying covariates (age, mental illness, prior incarceration count, felony charge, short jail stay, emergency department visits for 3 months prior to MOUD), and a frailty factor. Overall incarceration- and person-level characteristics were similar between the two groups, except for a higher percentage of felony charges in the comparison group. For 1 year after release, 111 overdose deaths occurred, and crude death rates were 0.49 and 0.83 per 100 person-years for in-jail MOUD and comparison groups, respectively. In-jail MOUD was associated with lower overdose mortality risk for 1-year post-release (adjusted HR = 0.59, 95% CI = 0.39, 0.91). Restricting data to the first month after jail release, the impact of in-jail MOUD became stronger (adjusted HR = 0.23, 95% CI = 0.09, 0.57). These findings call for urgent life-saving action to implement MOUD in the United States jail system.

Social

Neighborhood Proactive Policing and Racial Inequities in Preterm Birth Jaquelyn Jahn*
Jaquelyn Jahn Maeve Wallace Katherine Theall Rachel Hardeman

Background: Proactive policing is widely implemented in urban contexts to deter violence by stopping, searching and surveilling communities, but increasingly research suggests this practice disproportionately targets Black communities and can have negative health consequences. This study measures neighborhood exposure to proactive policing as a manifestation of structural racism and its association with preterm birth.

Methods: We linked geocoded birth records for all residents of Orleans Parish (n=9,102) with and New Orleans Police Department stop data (2018-2019). We defined preterm birth as <37 weeks gestation. Proactive policing was operationalized as the annual census tract rate of stops due to a "suspicious person" or "suspicious vehicle. We fit race-stratified multilevel Poisson models with tract-level random intercepts to estimate prevalence ratios for preterm birth across quintiles of stop rates, controlling for several individual- and tract-level covariates. We then assessed the degree to which neighborhood police stops might contribute to the Black-White racial inequity in preterm birth._

Results: Black birthing people were exposed to an average of 43.7 proactive stops per 100,000 and 15.8% of these births were preterm, compared to 30.7 stops and an 8.0% preterm birth prevalence among White birthing people. Whereas 19.2% of Black birthing people lived in neighborhoods with the highest rates of proactive police stops, only 8.4% of White birthing people lived in these areas. Fully adjusted models among Black birthing people show a monotonic increasing pattern across quintiles of proactive stops (Q5 vs. Q1 RR: 1.41 95% CI: 1.04, 1.93), but models among White birthing people show a non-significant monotonic decreasing pattern (Figure 1).

Conclusions: High levels of proactive policing are associated with increased risk of preterm birth for Black people, and this exposure likely contributes to racial inequities in reproductive health.

Social
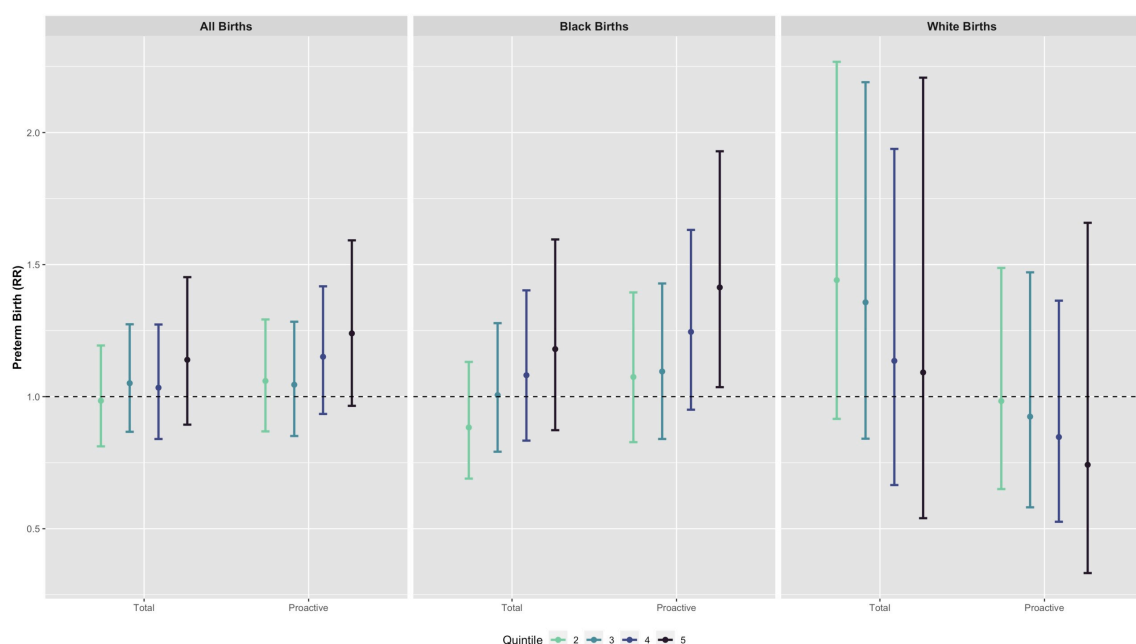
Estimating the relationship between lifetime maternal exposure to the criminal legal system and adolescent externalizing behaviors Shadiya L. Moss* Shadiya L. Moss Katherine M. Keyes

In 2020, there were more than 2.3 million Americans locked behind bars in prisons and jails. More than half of these individuals are estimated to be parents of children under the age of 18 years. Children of parents exposed to the criminal legal system experience various negative health consequences throughout the lifecourse, such as externalizing behaviors. However, evidence on the effect of maternal exposure to the criminal legal system on child and adolescent externalizing behaviors has been mixed. This study aimed to empirically estimate the association between lifetime maternal exposure to the criminal legal system and adolescent externalizing behavior.

Respondents included 14-19 years-olds (N=1,808) from the longitudinal cohort study Fragile Families and Child Wellbeing Study (2014-2017). Survey constructed, direct and indirect measures of maternal exposure to the criminal legal system were used to construct a binary lifetime maternal exposure to the criminal legal system variable. Youth reported past-year externalizing behaviors (e.g., steal something worth less than $50) using a 13-item delinquent behavior scale (range 0-13). Regression models were adjusted for maternal education, employment, income, poverty status, maternal and paternal depression and alcohol use, and youth physical abuse.

Lifetime maternal exposure to the criminal legal system was associated with adolescent cumulative number of externalizing behaviors (β=0.53, 95% CI: -0.04, 1.11), and the following items: gotten into a serious physical fight (OR: 2.83, 95% CI: 0.93-8.64), taken part in a group fight (OR: 2.58, 95% CI: 0.91, 7.27), and deliberately damaging property that didn't belong to them (OR=3.80, 95% CI: 1.37-10.51).

Findings provide support that forcibly removing mothers from the care of their children increases their children's engagement in externalizing behaviors, which may be associated with exposure to the criminal legal system in the future.

Environment/Climate Change

Childhood neurocognitive effects of outdoor ambient temperature fluctuations Scott
Delaney* Scott Delaney Keith Spangler Rachel Nethery Henning Tiemeier Marc Weisskopf

Background

As climate change accelerates, the frequency of extreme weather events, including rapid
fluctuations in outdoor temperatures (e.g., heat and cold waves), will increase and affect every
domain of human health, including neurodevelopment. However, the potential effects of heat and
cold waves—and, relatedly, deviations from expected temperatures—on childhood cognition are
poorly understood. This study investigates the acute impact of temperature fluctuations on child
cognitive performance.

Methods

We linked cognition data from 11,446 children aged 9-10 in the Adolescent Brain Cognitive
Development Study to meteorologic data from the PRISM Climate Group. Children completed NIH
Toolbox neurocognitive assessments of executive functioning, attention, memory, and language
abilities at one of 21 sites in the United States, resulting in age-normed total cognition scores
(mean=101, sd=18). We calculated daily deviations from the prior 14 days' mean maximum heat
index ("Expected HI") for 20 days prior to and including each child's assessment. We modeled the
lagged relationships of continuous exposures and outcomes using penalized splines in distributed lag
nonlinear models adjusted for age, sex, race / ethnicity, parental income and education, site, day of
week, month, and year.

Results

701 children completed cognitive tests on days with heat indexes at least 10ºC above or below the
Expected HI. Results suggest a -1.8 (95% CI: -3.5, -0.1) unit decrease in total cognition score for a
10ºC increase (upward fluctuation) in heat index over the Expected HI throughout the lag period.
Equivalent effects for downward fluctuations appeared somewhat smaller (-0.6; 95% CI: -4.2, 0.7).

Conclusion

Acute exposure to large upward or downward fluctuations in outdoor temperatures may be
associated with decreased cognitive performance in children. These results suggest a novel
mechanism by which climate change may impact childhood cognitive development.

Association Between Heat Index Fluctuations and Cognitive Performance

Environment/Climate Change
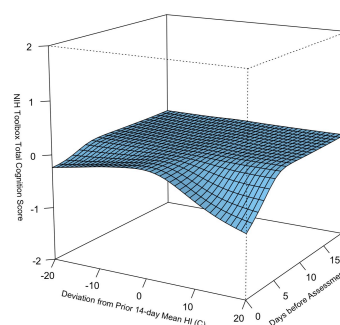
Associations between neighborhood greenery and birth outcomes: An ecosystem services approach Wei-Lun Tsai* Wei-Lun Tsai Thomas Luben Kristen Rappazzo

Urban greenery is associated with improved health outcomes. Greenery metrics across studies are designed using various methodologies. This study introduces greenery metrics with designs to identify ecosystem services that may be most relevant to birth outcomes. Metrics that characterize shade and aesthetics in pedestrian environment, large scale ecosystem services, and tree buffering effects for hazard mitigation from busy roadways were generated for a 250m buffer from home using 1m landcover from the US EPA EnviroAtlas project. Greenway density was also used as a measure for local infrastructure. Low birth weight (LBW, birth weight < 2500 grams) and preterm birth (PTB, gestational age < 37 weeks) for singleton births (N=119535) for years 2003 – 2015 were identified from the North Carolina (NC) Department of Health and Human Services for Durham, Orange, and Wake Counties, NC. Logistic regression was performed to evaluate the effect of greenery on the odds of LBW and PTB with adjustment for confounders. Analysis was stratified by race/ethnicity, as many studies reported differences in accessibility to greenery across these groups. Results showed tree cover along street or surrounding homes was associated with decreased odds of LBW and PTB. The association was strongest (i.e., largest decrease in odds for an adverse birth outcome) for the metric that characterized tree buffering busy roadways for hazard mitigation (aOR: 0.979, 95% CIs: 0.964 – 0.995 for LBW and 0.986, 95% CIs: 0.972 – 1.000 for PTB given a 10% increase in tree cover). Stratified analysis by race/ethnicity showed that most of the protective effects of greenery were observed only for non-Hispanic white individuals. Findings from this study suggest that neighborhood greenery may help reduce the odds of LBW and PTB the most through mitigating potential hazardous pollutants from busy roadways. This abstract does not necessarily reflect the views and policies of the U.S. Environmental Protection Agency.

Residential Proximity to Oil and Gas Development and Markers of Psychosocial Stress and Depression in a North American Preconception Cohort Study Mary D. Willis* Mary Willis Amelia K. Wesselink Jaimie L. Gradus Yael I. Nillni Joan A. Casey Elizabeth E. Hatch Lauren A. Wise

Background: The oil and gas industry is rapidly expanding across the United States, and now more than 17.6 million Americans reside within 1.6 km of an active oil or gas extraction site. The confluence of swiftly changing community conditions and consequences of this industry may create stress and anxiety among residents who live near these sites, particularly women who are trying to conceive (Figure 1).

Methods: In a large North American preconception cohort study (Pregnancy Study Online [PRESTO]), we examined associations between residential proximity to active oil or gas development and markers of psychosocial stress and depression in the preconception period. From 2013 to 2021, women aged 21-45 years who were trying to conceive without fertility treatment completed an online baseline questionnaire that included validated instruments to evaluate stress, depression, and sleep quality: Perceived Stress Scale (high stress: ≥ 20), Major Depression Inventory (high depressive symptoms: ≥ 20), and Pittsburgh Sleep Quality Index (short sleep duration: <7 hours). Using geocoded residential addresses at baseline, we calculated the distance to the nearest active oil or gas development site. We restricted our sample to 3,878 participants who resided within 50 km of a site. We used log-binomial regression models to estimate prevalence ratios (PR) and 95% CIs, adjusting for sociodemographic, behavioral, and medical history characteristics.

Results: Residence within 2 km of active oil or gas development in the preconception period was associated with high stress levels (PR=1.18, 95% CI: 1.03, 1.37) and short sleep duration (PR=1.16, 95% CI: 0.99, 1.37) compared with residence 20-50 km away. These associations attenuated beyond 2 km. Results were similar for high depressive symptoms, but associations persisted to 10 km.

Conclusion: We found evidence that residential proximity to oil and gas development is associated with adverse preconception mental health symptomatology.
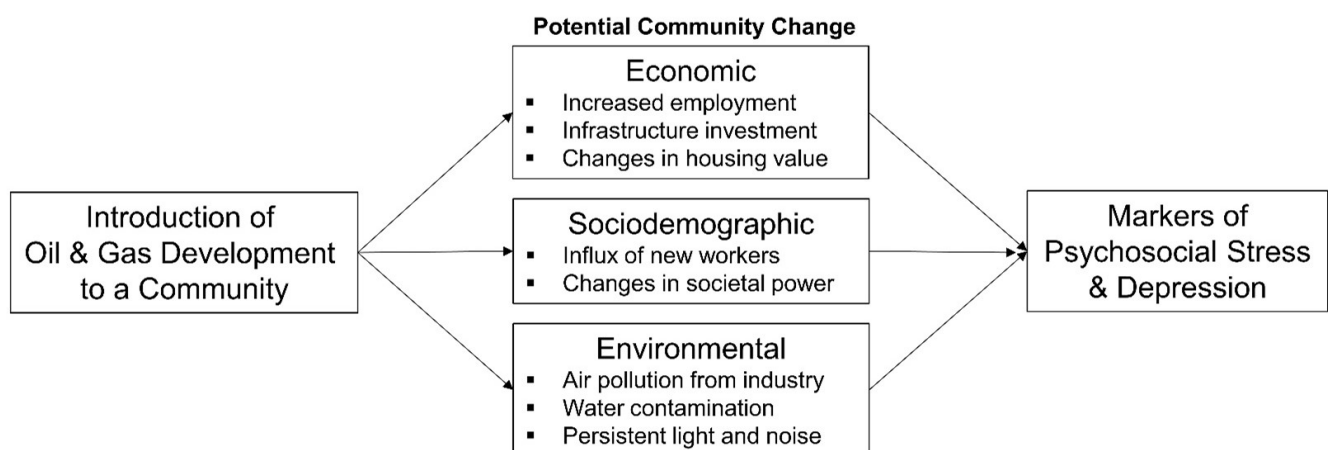
Figure 1: Conceptual diagram of hypothesized pathways by which oil and gas development may influence mental health outcomes

Heat, season, and reproductive success Anne Marie Z. Jukic* Anne Marie Jukic Hannah R. Jahnke D. Robert McConnaughey Clarice R. Weinberg Donna D. Baird Allen J. Wilcox

Climate change brings extreme heat patterns and heat may affect conception and pregnancy loss. We analyzed data from the North Carolina Early Pregnancy Study (EPS), a prospective study of women attempting pregnancy combined with data from the National Weather Service's report of hourly average heat index from surface monitors at the Raleigh-Durham Airport from 1982–86. We estimated average, 1-day peak, and 3-day peak heat index levels during the following critical reproductive windows: spermatogenesis, the menstrual cycle before the index cycle (lag cycle), the follicular and luteal phases of the index cycle, and time near implantation. We used logistic regression to model both the per cycle probability of conception (fecundability) and the risk of early pregnancy loss. We adjusted for age, education, previous window heat index, hours of daylight, income, partner age, and season using the sine and cosine of the menstrual cycle start date and stratified by cool months (October-April), and warm months, (May-September). A 10°F increase in heat index in peak heat index during the lag cycle was associated with higher conception (OR(CI): 2.0 (1.0, 4.0)) in cool months but not in warm months (OR(CI): 1.1 (0.47, 2.42)). A 10°F increase in 3-day peak of heat index during the follicular phase was associated with higher fecundability in warm months (OR(CI): 2.0 (1.0, 3.9)); but not in cool months (OR(CI): 0.94 (0.63, 1.4)). Increasing peak or 3-day peak heat index during the follicular phase were associated with increased early pregnancy loss (OR(CI): 2.3 (1.0, 6.0), 3.3 (1.4, 9.2), respectively) in cool months, not in warm months, OR(CI): 0.26 (0.04, 1.4) and 0.27 (0.03, 1.5). Increasing heat index may be associated with increased conception rates and increased early pregnancy loss.
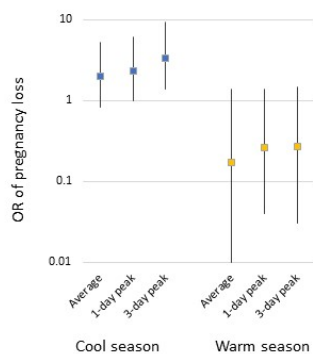
Follicular phase heat index exposures and early pregnancy loss. Associations shown for a 10-degree increase in the heat index metric.

The impact of exposure measurement error on the estimated dose-response relationship between long-term exposure to PM2.5 and mortality Yaguang Wei* Yaguang Wei Xinye Qiu Mahdieh Danesh Yazdi Alexandra Shtein Liuhua Shi Adjani A. Peralta Brent A. Coull Joel D. Schwartz

Background: Exposure measurement error is a central concern in air pollution epidemiology. As studies have been using ambient air pollution predictions as proxy exposure measures, the potential impact of exposure error on health effect estimates needs to be comprehensively assessed.

Objectives: We generate wide-ranging scenarios to assess direction and magnitude of bias caused by exposure errors under plausible dose-response relationships between annual exposure to fine particulate matter ($PM_{2.5}$) and all-cause mortality.

Methods: In this simulation study, we use daily $PM_{2.5}$ predictions at 1-km spatial resolution to estimate annual $PM_{2.5}$ exposures for ZIP Codes of residence across the contiguous US between 2000–2016. We consider scenarios in which we vary the error type (classical or Berkson) and the true dose-response relationship between $PM_{2.5}$ exposure and mortality (linear, linear-quadratic, or soft-threshold–i.e., smooth approximation to "hard-threshold" model). In each scenario, we generate numbers of deaths using error-free exposures and confounders of concurrent air pollutants and neighborhood-level covariates, and perform epidemiological analyses using error-prone exposures under correct specification or misspecification of the dose-response relationship between $PM_{2.5}$ exposure and mortality, adjusting for the confounders.

Results: We simulate 1000 replicates of each of 162 scenarios investigated. In general, both classical and Berkson errors can bias the dose-response curve towards the null. The magnitude of all the biases is small even when using three times the predicted uncertainty to generate exposure error.

Discussion: Simulation results suggest that the causal determination for long-term $PM_{2.5}$ exposure and mortality is unlikely to be undermined since the estimated effect is generally smaller than the truth. The small magnitude of biases suggest that the epidemiological findings are relatively robust against exposure error from ambient predictions.
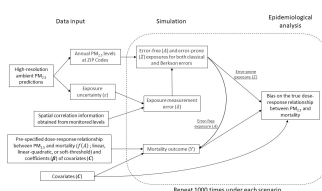
Neighborhood conditions and pregnancy outcomes: understanding the role of perceived and extrinsic measures of neighborhood quality Stephanie Eick* Stephanie Eick Lara Cushing Dana Goin Amy Padula Tracey Woodruff Rachel Morello-Frosch

Background: Living in a disadvantaged neighborhood has been associated with adverse birth outcomes. Most prior studies have conceptualized neighborhoods using census tract boundaries and few have examined the role of neighborhood perceptions. We examined associations between extrinsic and perceived neighborhood quality measures and adverse birth outcomes.

Methods: Participants resided in the San Francisco Bay Area of California and were enrolled in the Chemicals in Our Bodies cohort. The Index of Concentration at the Extremes (ICE) for income, Area Deprivation Index (ADI), and the Urban Displacement Project's measure of gentrification were included as extrinsic neighborhood quality measures. Poor perceived neighborhood quality was assessed using an interview questionnaire that asked about living in a disorderly neighborhood, neighborhood safety, and neighborhood dissatisfaction. Linear regression models were utilized to examine associations between neighborhood quality, and gestational age and birthweight for gestational age z-scores.

Results: Those who perceived their neighborhood as poor quality largely resided in extrinsically disadvantaged neighborhoods. Relative to the most advantaged tertile, the most disadvantaged tertile of ICE (β= -0.57, 95% confidence interval [CI]= -1.04, -0.1) and the ADI (β= -0.38, 95% CI= -0.72, -0.05) was associated with shorter gestational age in unadjusted models. Those who perceived their neighborhood as being of poor quality (β= -0.31, 95% CI= -0.67, 0.06) and unsafe (β= -0.41, 95% CI= -0.82, -0.01) had shorter gestational age relative to those reporting better neighborhood perceptions. Associations were attenuated after adjustment for confounders.

Conclusions: Living in an extrinsically disadvantaged neighborhood is associated with adverse birth outcomes, independent of how the neighborhood is perceived. Our findings support prior work highlighting the residential neighborhood as an important contributor to adverse birth outcomes.
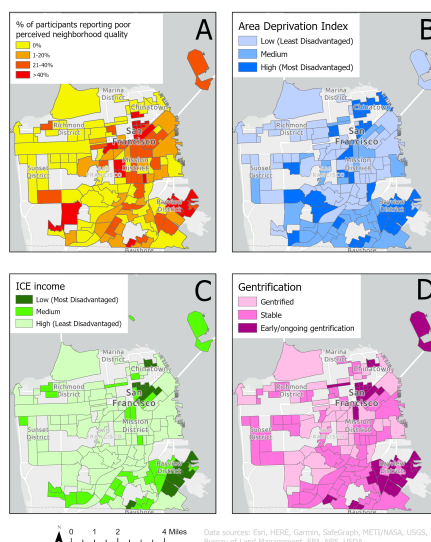
Residential segregation and prenatal depression in non-Hispanic Black and Hispanic mothers in North Carolina, 2005-2009 Sarah Haight* Sarah Haight Lea Ghastine Catherine Hoyo Chantel Martin

Research on residential segregation and mental health is inconsistent and rarely assessed during pregnancy, a high-risk time for depression. We investigate this relationship in a sample of non-Hispanic (NH) Black and Hispanic mothers. Demographics, residence, and self-reported depressive symptoms (Center for Epidemiological Studies Depression [CESD] screener), were obtained from the Newborn Epigenetic Study (NEST), a North Carolina pregnancy cohort (2005-2009). Using U.S. Census data (2006-2010), census tract residential segregation (NH Black vs NH white and Hispanic vs NH white) was measured with the Index of Concentration at the Extremes (ICE). ICE scores range from -1 (highest concentration of low privilege) to 1 (highest concentration of high privilege). Generalized linear mixed models estimated average change in CESD score associated with ICE score, accounting for neighborhood clustering and adjusting for individual's age, education, parity, marital status, smoking, and neighborhood deprivation. Among 773 participants, average CESD scores (ranging 0-60) were 14.1 (SD=9.7) and 12.1 (SD=10.2) for NH Black and Hispanic mothers, respectively. Average ICE scores were 0.21 (SD=0.45) and 0.11 (SD=0.29) for NH Black and Hispanic, respectively. For NH Black mothers, a 1-unit increase in ICE score (towards an extreme concentration of NH white) was associated with a reduction of 1.5 in CESD score (95% CI=-5.3, 2.3). After adjustment, estimates crossed over the null indicating increased depressive symptoms for NH Black mothers living in areas with increased concentrations of NH white populations (β=8.0; 95% CI=-3.7, 19.7). Among Hispanic mothers, a 1-unit increase in ICE score was associated with an average reduction of 2.7 in CESD score (95% CI=-6.8, 1.5). The impact of residential segregation on prenatal mental health may differ by race/ethnicity and effects may attenuate after accounting for individual- and neighborhood-level factors.

The predictive interplay of county-level jail incarceration and community economic distress on preterm birth among Black women in the US South Brooke EE Montgomery* Brooke EE Montgomery George C Pro Nickolas D Zaller

Introduction: The disparity in preterm births between non-Hispanic US-born Black and White women has not been fully explained. Biological mechanisms connected to structural racism by downstream factors like mass incarceration and economic disadvantage are hypothesized. Understanding the cause of this disparity is essential to developing interventions to address it. Examining with-in group differences among Black women in the South – a group with poor birth outcomes – may explain across-race disparities.

Methods: We used 2018 county-level jail admission data from the Vera Institute and 2019 county-level preterm birth data among Black women from CDC Vital Statistics, resulting in a one-year lag between jail exposure and subsequent birth. We used a negative binomial model to predict preterm birth rate from jail rate, with state defined as a random effect. We included an interaction between jail rate and a composite score of community economic distress to determine whether the effect of jail rate was conditional on economic distress. We had complete data for 73% of counties in ten states in the US South (N=1,006).

Results: In 2018, the mean jail admission rate in the South was 6,634 (per 100,000). In 2019, the mean percentage of preterm births was 11.1%. The effect of jail admission on preterm birth varied by levels of economic distress (interaction F-value = 5.4, p<0.0001). The predicted percentage of preterm births was positively affected by jail rate only in counties with very high levels of economic distress (Fig 1).

Conclusion: We identified that incarceration does not affect preterm births equally, such that Black women in Southern US counties with high economic distress and high jail rates being more likely to have preterm births. Further investigation of the compounding moderating effects of incarceration and economic stress on preterm birth disparities may elucidate the complex causal mechanisms that underlie these correlated multi-level factors.

Figure 1: Predicted percentage of county-level premature births from Black mothers in the US South by county-level jail admission rates
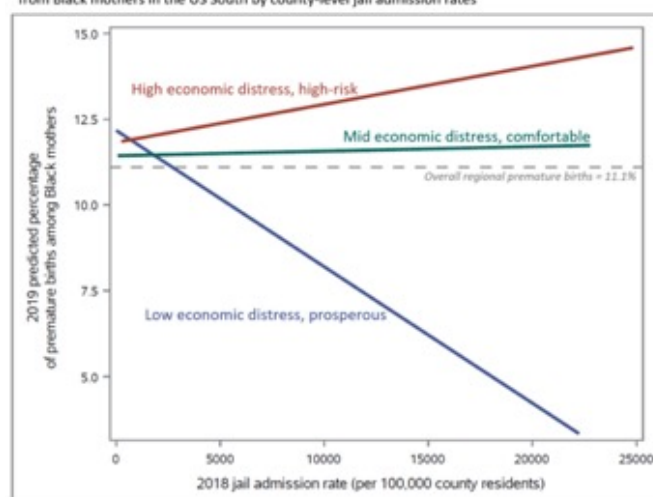
Notes: Interaction estimate derived from a generalized linear mixed model with negative binomial distribution
N=1,006 counties (AL, AR, FL, GA, LA, MS, NC, SC, TN, TX)

School suspension and expulsion predict higher dementia risk in late life with implications for racial health inequities: Findings from the National Longitudinal Survey of Youth 1979 Cohort Catherine Duarte* Catherine Duarte Jennifer Ahern Irene Yen Alison Cohen Anusha Vable

Exclusionary school discipline – which removes students from their classrooms via suspension or expulsion – is a mechanism of structural racism that disproportionately shapes the experiences of minoritized children in US schools and may have implications for their health. Though studies find inequitable exposure to adverse childhood experiences (ACEs) or educational conditions contribute to racial inequity in dementia burden, few have examined effects of early-life school-based adversity. In National Longitudinal Survey of Youth 1979 (NLSY79) data (N=7125), we used linear regression to evaluate if early-life exclusionary discipline (3-levels: no discipline, ever suspended, ever expelled by mean age 14.8 yrs) predicted 20-year cumulative dementia risk. Dementia risk was estimated with a risk score calculator previously developed and validated using cognitive and social factors measured up to mid-life in the *Health and Retirement Study*. Applying this calculator in NLSY79, we estimated participants' cumulative 20-year dementia risk from age 50 to 70. We used interaction terms to test for effect modification by indicators of structural marginalization (race/gender). We adjusted for childhood sociodemographics with sensitivity analyses accounting for school performance/behavior, substance use, and parental death. Compared to no punitive discipline, both suspension (RD:0.021;95%CI: 0.013-0.028) and expulsion (RD:0.064;95%CI:0.045-0.084) – which Black men and women disproportionately experienced – were associated with increased dementia risk. We also found evidence of effect modification: compared to White women, expulsion predicted higher dementia risk for White men (interaction term:0.056;95%CI:0.011-0.102) and Black women (interaction term:0.044;95%CI:-0.020-0.108), with even greater risk for Black men (interaction term:0.077;95%CI:0.025-0.128). These results suggest punitive discipline increases later-life dementia risk and contributes to racial health inequities.

Heterogeneous effects of neighborhood gentrification on the burden of late-stage breast cancer across race and ethnicity: An exploratory analysis from Miami-Dade County, Florida

Jordan Baeker Bispo* Jordan Baeker Bispo Zinzi Bailey Kilan Ashad-Bishop Neha Goel Ray Balise Erin Kobetz

Gentrification-related financial and social stress disproportionately impact minoritized groups and may thwart the accessibility of breast cancer (BC) screening. In this study we explored associations between neighborhood gentrification and late-stage BC diagnosis in Miami-Dade County (MDC), FL using data from the US Census and FL cancer registry. Census tracts with a median household income below that of MDC in 2000 were considered eligible to gentrify. Eligible tracts were defined as having 1) not gentrified, 2) gentrified, or 3) gentrified intensely from 2000-2010 according to relative changes in median home value and gross rent, educational attainment, and racial/ethnic composition. We then identified non-Hispanic White (NHW), non-Hispanic Black (NHB) and Hispanic patients from eligible tracts who were diagnosed with BC before (1997-2000) or after (2010-2013) the gentrification interval. To evaluate associations between gentrification and late-stage BC, we used chi-square tests and multivariable logistic regression, stratified by race/ethnicity. Data from 7,876 women in 368 eligible tracts were analyzed. For each racial/ethnic group, the distribution of late-stage BC in 1997-2000 was independent of gentrification. In 2010-2013, the association between gentrification and late-stage BC was marginally statistically significant for NHB, but not NHW or Hispanics; among NHB, 45% of BC diagnoses were late-stage in tracts that did not gentrify, 51% in tracts that gentrified, and 60% in tracts that gentrified intensely (p=.05). Adjusting for age, the odds of late-stage BC in 2010-2013 were 76% higher for NHB in tracts that gentrified intensely relative to NHB in tracts that did not (OR=1.76, 95% CI=1.05–2.95). Sensitivity analyses on BC cases from tracts matched on their propensity to gentrify afforded similar inferences. These data suggest that intense gentrification had an adverse effect on late-stage BC diagnosis among NHB in Miami, but not other racial/ethnic groups.

Adaptive validation substudy design to detect and account for time trends in classification parameters

Julie Barberio* Julie Barberio Richard F. MacLehose Thomas P. Ahern Michael Goodman Darios Getahun Michael J. Silverberg Timothy L. Lash Lindsay J. Collin

Background: Conventional approaches to sampling participants for validation substudies (i.e., balanced design, simple random sample) require completed follow-up. If the degree of variable misclassification changes over time, a single summary value will misrepresent classification accuracy. The adaptive validation approach allows for prospective monitoring of validation data, enabling time trend detection and subsequent bias adjustment.

Objective: To develop a method for evaluating whether a time trend exists in classification parameters, and provide guidance for sampling validation data to account for time trends.

Methods: Using the Study of Transition, Outcomes and Gender (STRONG) transgender youth cohort, where transmasculine/transfeminine status is misclassified, we compared two adaptive validation approaches. First, blocks of ten participants by observed exposure status were sampled in order of enrollment. Second, we repeated sampling without regard to enrollment timing as a control analysis. A beta-binomial Bayesian model was used to iteratively update estimated positive and negative predictive values. We also applied our approach to simulated datasets in which cohort members were enrolled over ten years and the magnitude of exposure misclassification changed over time.

Results: In the STRONG cohort, we noted a positive trend in the classification of transmasculine/transfeminine status over time when using the order-of-enrollment sampling scheme with adaptive validation. This is likely due to changes in the social environment and improved medical reporting. We saw no trend when adaptive validation participants were sampled randomly, as expected. Simulation results support the need for analyzing changes in validation parameters over the follow-up period.

Conclusions: When a time trend in classification parameters exists, conventional validation approaches using a single summary classification parameter value may compromise validity of bias-adjusted measures.

Figure. Positive and negative predictive values of transmasculine/transfeminine status[1] classification in the Study of Transition, Outcomes and Gender (STRONG) transgender youth cohort
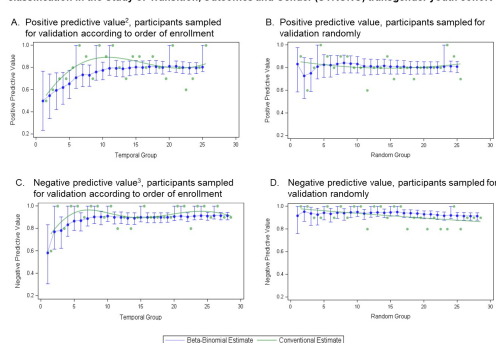
[1]Transmasculine/transfeminine status can be determined from knowledge of sex assigned at birth in the gold standard medical record given that all members of this cohort are transgender. Sex recorded in the concurrent electronic medical record is known to be misclassified because it could either represent sex recorded at birth or concurrent gender identity.

[2]Positive predictive value is defined as the probability that sex assigned at birth in the gold standard medical record was male among those whose concurrent electronic medical record gender code was male (n=252).

[3]Negative predictive value is defined as the probability that sex assigned at birth in the gold standard medical record was female among those whose concurrent electronic medical record gender code was female (n=283).

For (A) and (C), participants were grouped based on time of cohort enrollment and therefore group number corresponds to temporal ordering.

For (B) and (D), participants were grouped randomly to serve as a control analysis and therefore group number does not correspond to a dimension of time.

Evaluating Analytic Methods for Trial Designs that Utilize Historical Controls in the Context of Cystic Fibrosis Mark Warden* Mark Warden Amalia Magaret Steve Mooney Noah Simon Nicole Mayer-Hamblett

Background The treatment of cystic fibrosis (CF) has substantially improved over the past decade with the emergence of highly effective disease-modifying therapeutics called CF transmembrane conductance regulator protein (CFTR) modulators. However, their widespread use creates logistic difficulties for clinical trials of new CF therapeutics sometimes requiring unfeasibly large sample sizes to detect small effect sizes in a population experiencing drastic clinical improvement under CFTR modulators. Novel study designs that address the need for more efficient and ethically feasible trials need to be developed, particularly designs that use historical controls.

Methods We will conduct a simulation study to quantify how well each of three analytic methods ameliorates possible incongruencies between historical and active data in a simulated clinical design trial that utilizes historical controls. The three analytic methods include inverse probability weighting (IPW), propensity score-based power priors, and commensurate priors. We will assess a simulated time to event outcome with Poisson regression, comparable to pulmonary exacerbations in CF, and explore the conditions under which each method performs best.

Results Early analyses show that IPW achieved unbiased results when most covariates measuring active trial and historical population differences were available. A hazard ratio (HR) of 0.63 (0.50, 0.80) was obtained when historical participants were used exclusively as the control arm. The expected HR was 0.55 (0.34, 0.86). Early results also show that failure to adjust for differences between current and historical study populations results in biased estimates of efficacy and poor coverage. The three above methods will be compared in terms of coverage, power, and bias.

Conclusions A comprehensive comparison of analytic approaches to utilize historical controls will be critical to streamline drug development plans and continue development of CF therapeutics.

Comparing cluster-randomized and ring trial designs for ring interventions in emerging infection and disease elimination settings: a simulation study Anna Nguyen* Anna Nguyen Yoshika Crider Davis Mumbengegwi Michelle S. Hsiang Jade Benjamin-Chung

Background: In emerging infection and disease elimination settings, interventions are often targeted to people who live in "rings" around index cases. Cluster-randomized trials (CRTs) of ring interventions may have low statistical power due to strong spatiotemporal clustering and low incidence in these settings. Ring trials, which randomize each ring as index cases are detected, may overcome these challenges. We compared statistical power of cluster-randomized and ring trials in a simulation study.

Methods: We fit cluster-level malaria hazard functions using data from a trial conducted in a setting with low malaria incidence and strong spatiotemporal clustering in Namibia (NCT02610400). We simulated a ring intervention delivered within 500m of index cases in the intervention arm. In CRTs we randomized 56 administrative areas as clusters at baseline. In ring trials, using the same underlying data, we randomized rings as index cases occurred. Both designs included 100m buffers around rings. For each design, we estimated intention-to-treat effects with robust standard errors and statistical power in 1,000 simulated trials. We examined different levels of intervention effectiveness, spillover effects, baseline incidence, spatial clustering, and treatment coverage.

Results: For all baseline incidence levels, ring trials had a greater or equal statistical power compared to CRTs. In transmission settings with incidence <20 per 1,000, power was below 80% in both designs unless effect sizes were very large. In settings with incidence = 5 per 1,000, power was < 80% for all effect sizes. CRTs had lower false positive rates than ring trials with larger differences at high baseline incidence. Variation in results by other factors will be discussed.

Conclusion: Our findings suggest that ring trials have higher statistical power compared to CRTs for evaluating ring interventions in low transmission settings.

Statistical Power by Baseline Incidence

Causal Inference
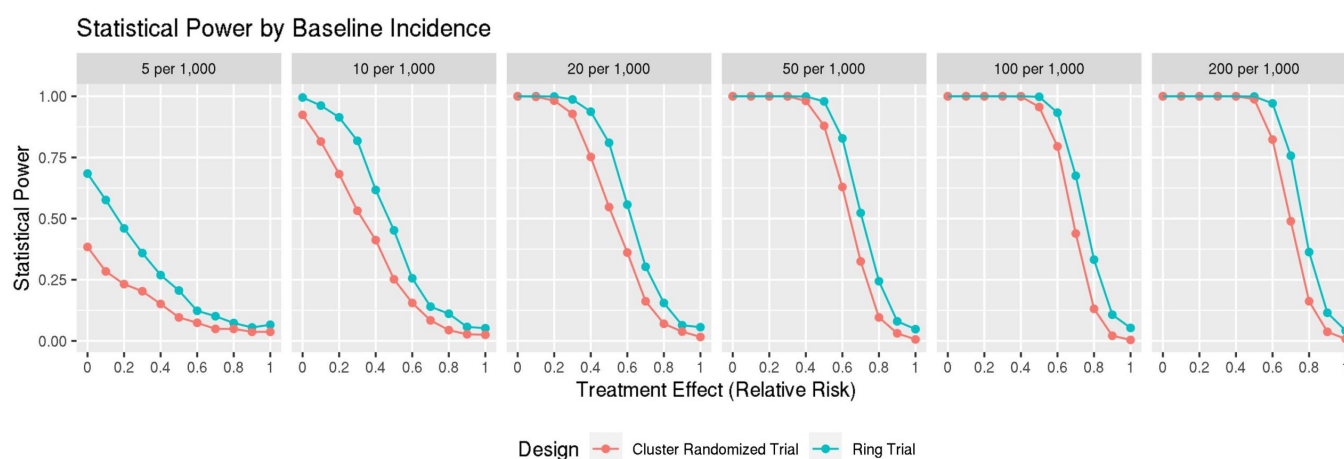
Mendelian randomization with pharmaceutically modifiable biomarkers Joy Shi* Joy Shi

Sonja Swanson Elizabeth Diemer Miguel A. Hernán

Biomarker levels are often affected by medications, e.g., LDL cholesterol is affected by statin therapy. Therefore, when a biomarker is the exposure of interest, an analysis which ignores medication use may be estimating the combined contributions of the biomarker and the medications that affect it. When time-varying information on medication use is incorporated into an analysis—say, of LDL cholesterol and coronary heart disease—two possible approaches are: (1) to restrict the analysis to non-users of statins (Figure 1A); and (2) to conduct the analysis under a hypothetical intervention of no statin use in the entire population (Figure 1B). The latter approach requires adjustment for confounders of the effect of statins on coronary heart disease via g-methods.

The implications of these approaches to handle medication use have not been studied for Mendelian Randomization (MR) studies. An important concern is that, because MR studies use a genetic variant as if it were an instrumental variable (IV), restriction to non-users may induce selection bias. We used simulated and real data to evaluate different analytical approaches that could be applied in a MR study designed to estimate the effect of a time-varying exposure affected by medication use.

We considered two IV estimators—(1) two-stage least squares; and (2) g-estimation of structural nested cumulative failure time models (SNCFTMs). Our simulations demonstrated that restricting on medication use resulted in biased estimates, regardless of the IV estimator. Unbiased estimates were obtained when the g-formula was used in combination IV estimation, but only if the IV estimator appropriately handled repeated measures of a time-varying exposure and outcome (e.g., g-estimation of SNFTMs). In the presentation, we will further discuss results from applying these analytic approaches to national biobank data to estimate the effect of LDL cholesterol on cardiovascular disease in the presence of widespread statin use.
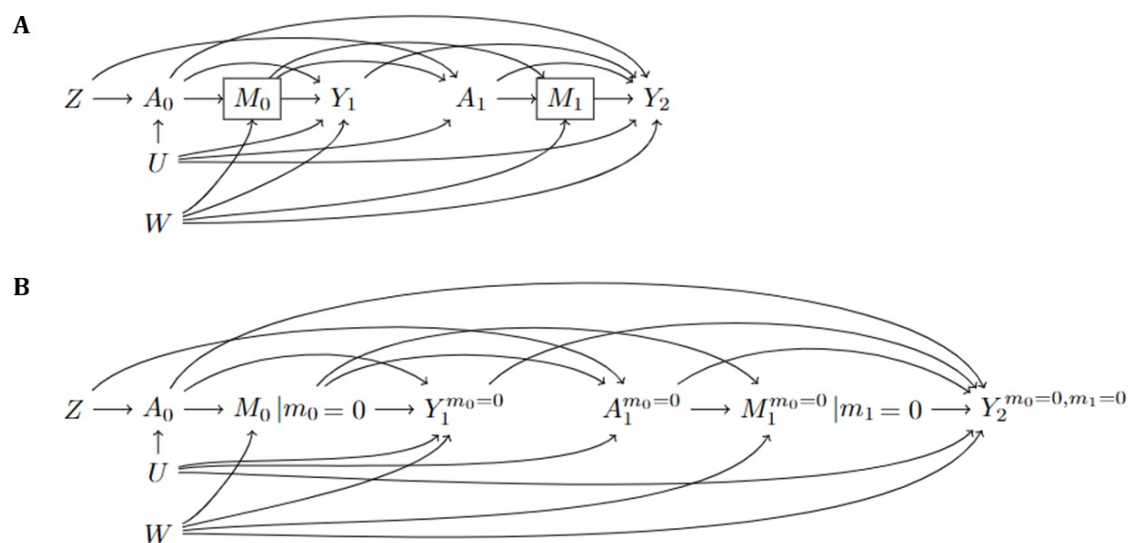

Figure 1. Causal diagrams for time-fixed instrument Z (instrument), U (unmeasured confounder) and W (measured confounder) at baseline; and time-varying variables A_k (exposure), M_k (medication use), and Y_{k+1} (outcome). For simplicity, only two time points are presented in (A) the causal directed acyclic graph which depicts conditioning on medication use and (B) the single world intervention graph which depicts the counterfactual world in which there is no medication use.

Across-Cohort Heterogeneity in Collaborative, Pooled and Harmonized Study Designs

Yongqi Zhong* Yongqi Zhong Elizabeth Stuart Bryan Lau

Cohort consortia are collaborative study designs that aim to achieve a similar research goal by combining individual cohorts. Pooled analysis using cohort consortium data holds several major benefits, including increased sample size, and possibly increased generalizability. However, across-cohort heterogeneity can be a major challenge when using data sourced from different studies, with a key question being when it is appropriate to combine cohorts for a specific research question, and when they are too different for reliable combining. We formalize the concept of cohort heterogeneity in the context of cohort consortia, define three types of cohort heterogeneity, and discuss the implications of cohort heterogeneity as applied to the diverse goals of epidemiologic research. Three types of cohort heterogeneity in terms of the distributions of pertinent variables are discussed: heterogeneity in the joint distribution, heterogeneity in the conditional distribution, and heterogeneity in the exposure-outcome effects. We examine scenarios where different hierarchies of cohort heterogeneity influence the output (estimand) of descriptive, prediction, and association/causation epidemiologic studies. Understanding cohort heterogeneity facilitates investigators to identify and minimize biases that may occur in pooled analysis.

Cancer

Use of Straightening and Other Hair Products and Risk of Uterine Cancer Che-Jung (Rong) Chang* Che-Jung (Rong) Chang Katie M. O'Brien Alexander P. Keil Symielle A. Gaston Chandra L. Jackson Dale P. Sandler Alexandra J. White

Background: Hair products may contain hazardous chemicals with endocrine-disrupting and carcinogenic properties. Previous studies have found hair product use to be associated with a higher risk of hormone-sensitive cancers including breast and ovarian cancer; however, no previous study has investigated the relationship with uterine cancer.

Methods: We examined associations between hair product use and uterine cancer among 33,947 eligible participants in the Sister Study, a large racially/ethnically diverse prospective cohort. Participants were aged 35-74 years at enrollment (2003-2009) and women with a prior hysterectomy were excluded. In baseline questionnaires, participants self-reported their use of hair products in the prior 12 months, including hair dyes, straightening products, and permanents/body waves. We estimated the hazard ratio (HR) and 95% confidence intervals (CIs) of the associations between hair product use and uterine cancer using Cox proportional hazard models.

Results: With an average of 10.9 years of follow-up, 378 uterine cancer cases were identified. Compared to never users, ever use of straightening products in the previous 12 months was positively associated with uterine cancer (HR = 1.80, 95%CI 1.12-2.89). The association was stronger in frequent users (>4 times/year) versus never users (HR = 2.57, 95%CI 1.46-4.50; p-for-trend < 0.01). Use of other hair products, including dyes and permanents/body waves, was not consistently associated with uterine cancer risk.

Conclusion: These findings are the first epidemiologic evidence of an association between use of straightening products and uterine cancer. More research is warranted to confirm our findings and identify the specific chemicals driving this observed risk.

Pesticide exposure, genetic susceptibility, and prostate cancer risk in the Agricultural Health Study Lauren Hurwitz* Lauren Hurwitz Laura Beane Freeman Gabriella Andreotti Jonathan Hofmann Christine Parks Dale Sandler Jay Lubin Sonja Berndt Stella Koutros

Background: Specific pesticides have been associated with risk of prostate cancer, but interactions with genetic susceptibility loci have rarely been studied. We examined the joint associations of pesticides and genetic variants with prostate cancer risk.

Methods: We studied 1,162 cases (588 aggressive) and 2,206 frequency-matched controls nested in the Agricultural Health Study cohort. History of pesticide use was self-reported at enrollment. Genotyping was conducted using the OncoArray-500K BeadChip (Illumina Inc). Logistic regression models estimated the joint associations of pesticides previously linked to prostate cancer (fonofos, terbufos, malathion, aldrin, linuron, and dimethoate) and 256 individual genetic variants and an aggregated polygenic risk score (PRS) with risk of total and aggressive prostate cancer. Likelihood ratio tests assessed multiplicative interaction.

Results: We observed multiplicative interaction between fonofos and the PRS in relation to risk of total and aggressive prostate cancer. Compared to the reference group (non-exposed, PRS scores <median), those with fonofos exposure and PRS scores >median had elevated risks of total (OR 1.35, 95% CI 1.06-1.73, p-int=0.03) and aggressive (OR 1.49, 95% CI 1.09-2.04, p-int=0.19) prostate cancer. There was also evidence of interaction between the six pesticides and individual genetic variants occurring in genomic regions associated with 1) cancer signaling pathways, 2) hormonal perturbations relevant for prostate cancer, 3) DNA damage response and 4) neurological traits; many of the examined pesticides have known neurologic mechanisms.

Conclusion: Joint exposure to the organophosphate insecticide fonofos and genetic susceptibility may further elevate the risk for total and aggressive prostate cancer, above the independent effects of each. These results, as well as those observed for individual genetic markers, suggest potential mechanisms by which these pesticides may increase prostate cancer risk.

Comparisons between area- and individual-level measures of socioeconomic status: a report from the Children's Oncology Group (COG) Jinhee Cha* Jinhee Cha Logan G Jenny N Erin

Background: Area-level socioeconomic status (SES) is often used as a proxy for individual-level data when data is not available. Correlations between area-level SES and individual-level SES differ based on sociodemographic variables. We examined correlations between area-level SES and individual-level SES, among childhood cancer patients enrolled in Childhood Cancer Research Network (CCRN) Children's Oncology Group (COG) protocols, overall and after stratifying by sociodemographic variables. **Methods:** We included childhood cancer cases in three epidemiologic studies (germ cell tumor, n=788; hepatoblastoma, n=38; and osteosarcoma, n=225) who were also enrolled on the CCRN COG protocol. Address at diagnosis was collected upon enrollment on CCRN. We geocoded addresses and created a census tract-level SES variable using American Community Survey data. Census tract-level SES was determined through factor analysis of seven attributes of SES, divided into quintiles. Individual-level data, including parental education, family income, and number of people supported by income (GCT and OS studies only), were collected through questionnaires completed by the patient's parents. A relative income score for each household was calculated by dividing household income by national-level poverty thresholds, adjusted for the number of household members. Spearman's rank correlations were calculated between the area-level SES variable, relative income and parental education. **Results:** Preliminary results overall suggest that correlations between area-level SES and individual-level SES variables (relative income and education) are fair (both 0.39; p-value < .001). Blacks or African Americans had the highest correlation between the area-level SES and relative income ($\rho = 0.66$; p-value < .001) as well as area-level SES and education ($\rho = 0.55$; p-value < .001). **Conclusions:** Preliminary results suggest that an area-level SES variable is a sufficient proxy for individual-level SES variables.
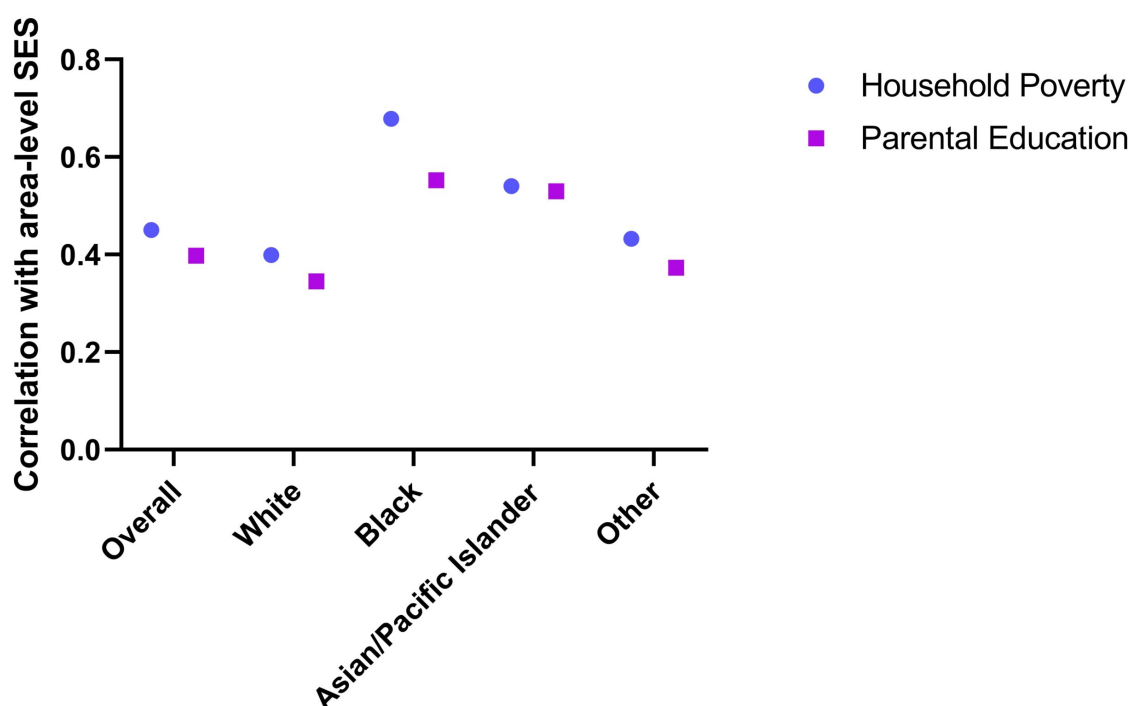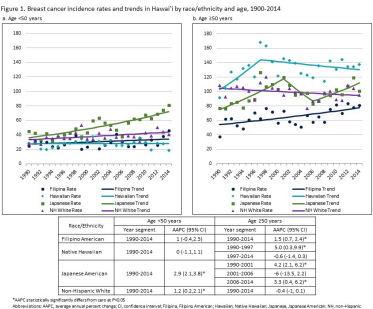
Cancer

Breast cancer incidence and trends among Asian American, Native Hawaiian, and non-Hispanic White women in Hawai'i: evaluating racial/ethnic differences by age and breast cancer subtype Ugonna Ihenacho* Ugonna Ihenacho Meg A. McKinley Anna H. Wu Annie Vu Brenda Y. Hernandez Lenora W.M. Loo Iona Cheng

Native Hawaiian (NaH) and Japanese American (JA) women in Hawai'i have a higher breast cancer (BC) incidence than their non-Hispanic White (NHW) counterparts, but BC incidence patterns by age and BC subtype across disaggregated racial/ethnic groups are unknown. We used 1990-2014 data from 18,500 women diagnosed with incident invasive BC in the SEER Hawai'i Tumor Registry to evaluate BC incidence and trends by race/ethnicity (NaHJA, Filipino American [FA], and NHW), by age (<50 and ≥50 years) and by BC subtype (hormone receptor [HR]+/human epidermal growth factor receptor 2 [HER2]+, HR+/HER2-, HR-/HER2+, triple negative [TN]BC).

BC incidence among women ages <50 years was highest in JA (age-adjusted incidence rate per 100,000: 70.6) followed by NHW (43.5), FA (34.1), and NaH women (24.6). BC incidence among women ages ≥50 years was highest among NaH (136.5), followed by JA (105.0), NHW (97.1), and FA women (78.8). When we investigated BC subtype by age, the high incidence among JA women <50 years was due largely to high rates of HR+/HER2- and TNBC. In contrast, the high incidence among NaH women ≥50 years was due to high rates of the HR+/HER2+ and HR+/HER2- subtypes.

In 1990-2014, the average annual percent change (AAPC) increased 2.9% and 1.2% among JA and NHW women <50 years, respectively, with smaller increases among FA and NaH women <50 years. Increasing trends were observed among FA (1990-2014 AAPC 1.5%) and JA women ≥50 years in recent years (2006-2014 AAPC 3.3%). An increase was observed among NaH ≥50 years from 1990-1997 (5.0%) but remained stable through 2014.

These differences in BC incidence demonstrate the importance of disaggregated analyses among Asian American, Native Hawaiian, and Pacific Islander (AANHPI) populations in Hawai'i and assessments of differences by age and subtype. Research exploring factors contributing to disparities in BC incidence among disaggregated racial/ethnic groups, by age and BC subtype among AANHPI in Hawai'i are warranted.

Figure 1. Breast cancer incidence rates and trends in Hawai'i by race/ethnicity and age, 1900-2014

a. Age <50 years   b. Age ≥50 years

Race/Ethnicity	Age <50 years		Age ≥50 years	
	Year segment	AAPC (95% CI)	Year segment	AAPC (95% CI)
Filipino American	1990-2014	1 (-0.4,2.5)	1990-1997	1.5 (0.7, 2.4)*
Native Hawaiian	1990-2014	0 (-1.1,1.1)	1990-1997	5.0 (0.3,9.9)*
			1997-2014	-0.6 (-1.4, 0.3)
Japanese American	1990-2014	2.9 (2.1,3.8)*	1990-2001	4.2 (2.1, 6.2)*
			2001-2006	-6 (-13.5, 2.2)
			2006-2014	3.3 (0.4, 6.2)*
Non-Hispanic White	1990-2014	1.2 (0.2,2.1)*	1990-2014	-0.4 (-1, 0.1)

*AAPC statistically significantly different from zero at P<0.05
Abbreviations: AAPC, average annual percent change; CI, confidence interval; Filipino, Filipino American; Hawaiian, Native Hawaiian; Japanese, Japanese American; NH, non-Hispanic.

Comparative effectiveness of treatment approaches for early invasive breast cancer among socioeconomically marginalized women Rachel J. Meadows* Rachel J. Meadows Yan Lu Aaron Gehr Kalyani Narra Anuradha Lingam Bassam Ghabach Rohit P. Ojha

Background: Randomized controlled trials suggest breast conserving therapy (BCT) and mastectomy have similar overall survival (OS) and disease-free survival (DFS) for early-stage breast cancer patients. Nevertheless, this evidence was based on inadequate representation of socioeconomically marginalized women with barriers to care. We aimed to compare the effect of BCT and mastectomy on survival among socioeconomically marginalized women with breast cancer. **Methods:** We emulated a target trial using institutional registry data from the JPS Oncology and Infusion Center, an urban safety-net Comprehensive Community Cancer Program. We included women aged 18 – 64 years diagnosed with stage I or II first primary breast tumors ≤5 cm between July 2011 and December 2017. We used clone and censor with a 12-month grace period to mimic assignment to BCT or mastectomy, where observations were censored upon deviation of treatment assignment during the grace period. We used inverse probability of censoring weights and pseudovalues with bootstrapped 95% confidence limits (CL) to estimate marginal 5-year differences in restricted mean survival time (RMST) between BCT and mastectomy (reference category). **Results:** Our study population comprised 205 women with breast cancer. Median age was 53 years, 61% were racial/ethnic minorities, and 65% were uninsured. The RMST difference in 5-year OS between BCT and mastectomy was -0.39 months (95% CL: -6.8, 7.1), and the RMST difference in 5-year DFS was 1.0 month (95% CL: -6.8, 7.1). **Conclusions:** Assuming exchangeability, positivity, consistency, no measurement error, and no model misspecification, our point estimates suggest similar early survival for BCT and mastectomy among socioeconomically marginalized women with breast cancer, but our results are compatible with differences up to 7 months favoring mastectomy or BCT. Our findings are useful for extending the evidence about BCT and mastectomy to socioeconomically marginalized women.

Figure 1. Comparison of overall and disease-free survival after breast conserving therapy or mastectomy among socioeconomically marginalized women with early-stage breast cancer.
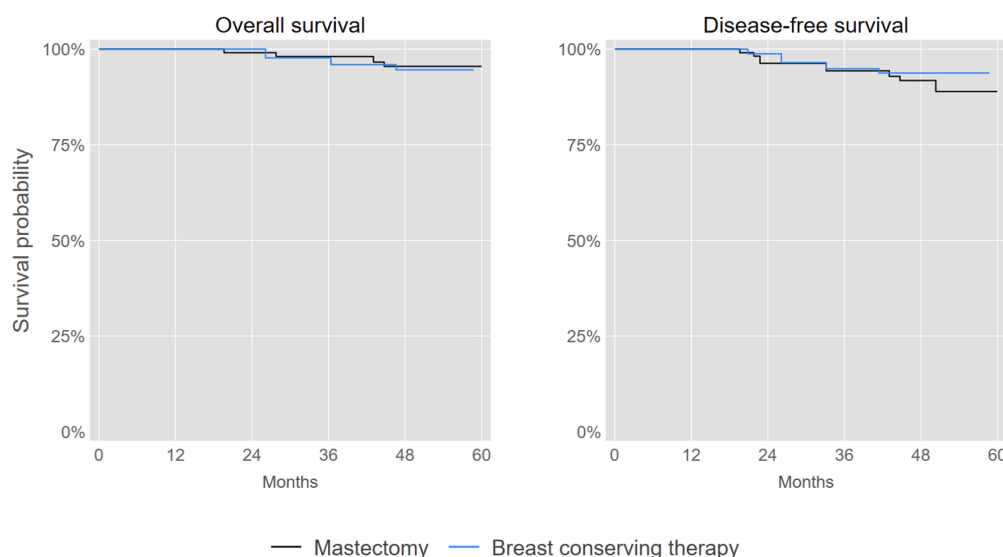
Cancer

Trends in lung cancer mortality rates among never smokers in the United States, 1991-2018 Meredith Shiels* Meredith Shiels Barry Graubard Timothy McNeel Lisa Kahle Neal Freedman

Background: In the U.S., lung cancer death rates have been declining for decades, due to pronounced declines in cigarette smoking and also improved treatments. However, about 12% of lung cancers occur among never smokers, and it is unclear whether lung cancer death rates among never smokers have changed over time. We estimated lung cancer death trends separately among ever and never smokers aged 30-79 years during 1991-2018.

Methods: HRs for smoking and lung cancer death and smoking prevalence were estimated from the National Health Interview Survey (NHIS) linked to National Death Index. HRs were adjusted for age, sex, race/ethnicity and education. Population attributable fractions (PAFs) for ever smoking and lung cancer deaths were then estimated in 3 age groups: 30-49, 50-69 and 70-79-year-olds accounting for the NHIS complex survey design. Annual PAFs were multiplied by yearly US lung cancer mortality rates from National Center for Health Statistics death certificate data to partition rates into those among ever and never smokers.

Results: During 1991-2018 the prevalence of being a never smoker increased among both men (35.1% to 54.6%) and women (54.0% to 65.4%). Compared to ever smokers, never smokers had 86% lower risk (HR=0.14; 95%CI: 0.12-0.16) of lung cancer death. The proportion of lung cancer deaths attributable to smoking declined from 55.2% to 40.5% among 30-49-year-olds, 79.6% to 72.7% among 50-69-year-olds and 82.5% to 78.4% among 70-79-year-olds. During 1991-2018, age-standardized lung cancer death rates declined 41.2% among ever smokers (123.0 to 72.3/100,000) and 49.3% among never smokers (42.4 to 21.5/100,000; Figure).

Conclusions: The decline in smoking prevalence in the U.S. over the past three decades has resulted in an increasing proportion of lung cancer deaths among never smokers. However, lung cancer death rates have declined among never smokers, perhaps due to a decline in secondhand smoke exposure and improvements in lung cancer treatment.

Lung Cancer Death Rates by Smoking Status
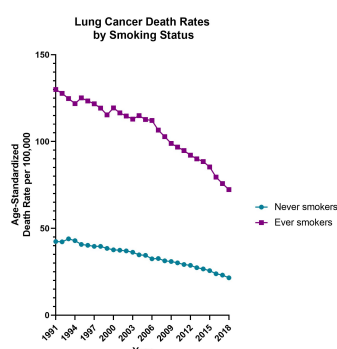
An Assessment of Selection Bias in Multigenerational Cohort Studies Jingyuan Xiao* Jingyuan Xiao Yongfu Yu Gunnar Toft Jiong Li Zeyan Liew

Background There is an increasing epidemiological interest in estimating effects of grandmaternal (F0) pregnancy experiences (i.e., prenatal exposure of parents (F1)) on grandchildren (F2)'s health risks. Such analysis requires data from three generations, yet whether selection bias would arise from excluding F1 exposure groups that have not reproduced during the study period has not been investigated. We conducted a case study to investigate this using our three-generational linkage study from Denmark.

Methods We analyzed whole-population data on singleton F1 women and men (1978-2001) registered in the Danish Medical Birth Registry. F1 individuals were followed up to 2017 to obtain birth and medical records of F2. The main exposure of interest was preterm status of F1. We evaluated whether preterm-born F1 would have a child by the end of follow-up, thus eligible for selection into a multigenerational cohort analysis. We conducted an Inverse Probability Selection Weighting analysis to examine whether our previously reported association between F1 preterm birth and F2 autism spectrum disorder (ASD) risk would change after accounting for probability of selection across F1 exposure groups.

Results Both F1 women (N=654,571) and men (N=197,389) born preterm had approximately 40% lower odds of having a child (women, OR=0.62, 95% CI=0.59, 0.64; men, OR=0.61, 95% CI=0.46, 0.81) compared with non-preterm F1 counterparts. After adjusting for selection, the association between F1 women preterm status and F2 ASD was strengthened (OR increased from 1.31 (95%CI = 1.11,1.54) to 1.98 (95% CI = 1.62, 2.44)), but the association for men did not change.

Conclusions Preterm-born individuals may have altered reproductive patterns and were less likely to be included in a population-based multigenerational cohort study. This selection may influence the results when estimating health risks in the F2 generation associated with F0 pregnancy exposures or F1 early life factors.

Social

Neighborhood racial and economic polarization and timing of pubertal onset in girls Julia Acker* Julia Acker Brandon Chu Sara Aghaee Pushkar Inamdar Salma Shariff-Marco Scarlett Gomez Charles Quesenberry Louise Greenspan Larry Kushi Mahasin Mujahid Julianna Deardorff Ai Kubo

Early puberty among women is a risk factor for breast cancer and cardiovascular disease, and Black and Hispanic girls experience puberty earlier than girls of other racial/ethnic backgrounds. Neighborhood racial and economic polarization may contribute to these disparities by conferring differential exposure to mechanisms underlying early puberty (e.g., stress, obesity, endocrine disruptors). However, studies of neighborhood-level determinants of puberty timing are lacking. We used multilevel Weibull regression models accommodating left, right, and interval censoring to examine associations between the *Index of Concentration at the Extremes* (ICE) and age at pubic hair (pubarche) and breast development onset (thelarche) among 46,299 girls born from 2005–11 in Kaiser Permanente Northern California. ICE is a measure of spatial social polarization that quantifies the extent to which residents are concentrated at the extremes of racial and economic privilege. American Community Survey 2010 5-year estimates were used to compute Census-tract level ICE quintiles for racial and economic polarization separately (ICE–race/ethnicity, ICE–income) and in combination (ICE–income+race/ethnicity). Significant dose–response relationships emerged wherein each quintile of declining privilege corresponded to earlier pubertal onset, with the strongest effects observed for ICE–race/ethnicity. For example, estimated time ratios for girls living in the least privileged (Q1) versus most privileged (Q5) neighborhoods as measured by ICE–race/ethnicity correspond to approximately 3- and 5-months' difference in age at pubarche (TR=0.97, 95% CI=0.97–0.98) and thelarche (TR=0.96, 95% CI=0.96–0.97), respectively, after adjusting for maternal education, age at delivery, and parity. Effects were attenuated but remained significant after adjusting for race/ethnicity and prepubertal BMI. Findings provide preliminary evidence that neighborhood social dynamics contribute to girls' puberty timing.

Reproductive

Childhood adversity and fecundability in a North American preconception cohort Sharonda
M. Lovett* Sharonda Lovett Olivia R. Orta Renée Boynton-Jarrett Yael I. Nillni Amelia K. Wesselink
Collette N. Ncube Elizabeth E. Hatch Lauren A. Wise

Childhood adversity is an established health determinant, and two prospective studies report an
association between childhood adversity and reduced fecundability (probability of conception per
menstrual cycle). Evidence also suggests social support may mitigate the adverse effects of
childhood adversity through several pathways. We evaluated the association between childhood
adversity and fecundability and whether childhood social support modifies this association.
Pregnancy Study Online (PRESTO) is a preconception cohort study of North American women aged
21-45 years. Participants completed bimonthly questionnaires until pregnancy or a censoring event
(stopped trying, fertility treatment initiation, loss to follow-up, or 12 months of follow-up), whichever
came first. In June 2019, we sent a supplemental questionnaire on life course adversity (SQ) to
former and current PRESTO participants; thereafter, women completed the SQ 30 days post-
enrollment (n=5,489). The SQ included an adapted Adverse Childhood Experiences (ACE) scale from
the Behavioral Risk Factor Surveillance System. Childhood social support was assessed using an
adapted Berkman-Syme Social Network Index where we defined a score ≥4 as high vs. low social
support. We used proportional probabilities regression to estimate fecundability ratios (FR) and 95%
confidence intervals (CIs), adjusted for age, multivitamin use, contraception, and parental education.
Overall, 78% experienced ≥1 ACE and 88% reported high social support in childhood. Relative to
ACE scores of zero, FRs for ACE scores 1-3 and 4-8 were 0.87 (CI: 0.79-0.95) and 0.82 (CI:
0.74-0.91), respectively. FRs for ACE scores 4-8 relative to ACE scores of zero were 0.84 (CI:
0.75-0.95) among women reporting high social support and 0.67 (CI: 0.45-0.99) among women
reporting low social support. Greater childhood adversity was associated with reduced fecundity in
adulthood. Associations were stronger among those with low social support in childhood.

COVID-19 Vaccine Surveillance Safety in Early Pregnancy: Design Factors Affecting Association Between Vaccine and Spontaneous Abortion Gabriela Vazquez Benitez* Gabriela Vazquez Benitez Jacob L Haapala Malini B DeSilva Jingyi Zhu Heather Lipkind Mathhew F Daley Darios T Getahun Nicola P Klein Kimberly K Vesco Stephanie A Irving Jennifer C Nelson Joshua TB Williams Simon J Hambidge James Donahue Candace Fuller Elyse O Kharbanda

While COVID-19 vaccination during pregnancy is recommended, continued safety monitoring in near-real-time is needed. Using data from eight integrated health systems within the Vaccine Safety Datalink (VSD) , we previously reported no association of receiving a COVID-19 vaccine in the 4-weekss prior to a spontaneous abortion (SAB) as compared to ongoing pregnancies over seven 4-week surveillance periods. We evaluated the association using a case-control design and estimated the Odds Ratio (OR) adjusted by site, 4-week surveillance periods, maternal age, race-ethnicity, and supervision of care. Early in the surveillance a protective effect was observed. To address this finding, we extended the scope of this work to describe how surveillance findings vary across cumulative surveillance periods. Additionally, using data from a single VSD, we evaluated several design choices: expanding the exposure window to 6 weeks, modifying the index date for ongoing pregnancies from last day of the surveillance period to the midpoint, and evaluating the association using a time dependent exposure model. A protective effect initially observed with data through March 3, 2021 (OR 0.78; 95%CI: 0.69–0.89, n= 62255) when low vaccine uptake was observed, attenuated with the inclusion of data through May 31,2021 (OR: 0.99; 95%CI: 0.93–1.06, n= 94490). Analysis for the single site showed a lower OR for a 4-week as compared to a 6-week window, and an OR closer to the null when using a midpoint index date. Hazard ratio (HR) for SAB following a COVID-19 vaccine exposure showed no association (HR 0.97; 95%CI: 0.76–1.23, n=4070). Timing of the surveillance affected the size of the vaccine-SAB association. However, results were robust to design choices.

Breastfeeding history and adenomyosis risk using data from a population-based case-control study employing two control groups Mandy S. Hall* Mandy S. Hall Claudia Holzman Ana I. Vazquez Sawsan As-Sanie Holly R. Harris Kristen Upson

Adenomyosis is characterized by the presence of endometrial tissue within the muscular wall of the uterus and is associated with substantial morbidity. While the etiology of adenomyosis remains unknown, an estrogenic milieu is recognized to contribute to disease pathogenesis. We hypothesize that lactation, in which infant suckling inhibits ovulatory cycles and induces a hypoestrogenic state, is associated with decreased adenomyosis risk. We investigated this hypothesis using data from a case-control study of adenomyosis conducted among female enrollees ages 18-59 years of a large, integrated healthcare system in Washington State. In that study, incident, pathology-confirmed adenomyosis cases diagnosed 2001-2006 were identified (n=386) and two control groups were employed: 1) randomly selected age-matched enrollees with intact uteri ("population controls", n=323) and 2) hysterectomy controls (n=233). Data on breastfeeding history were collected by in-person interview; for each live birth reported, each participant was asked if she breastfed the infant and for how long. We restricted the analytic sample to those with at least one live birth (331 cases, 246 population controls, and 198 hysterectomy controls) and used logistic regression to estimate ORs and 95% CIs for the associations between adenomyosis and 1) ever breastfeeding and 2) lifetime total breastfeeding duration, adjusting for age, reference year, smoking, education, and parity. In analyses using population controls, history of ever breastfeeding was associated with a 40% decreased risk of adenomyosis (OR 0.6, 95% CI: 0.3-1.0). The magnitude of association was stronger with longer total breastfeeding duration (≥12 months vs. 0-<3 months: OR 0.4, 95% CI: 0.3-0.6). In our analyses using hysterectomy controls, we observed similar patterns of associations that were attenuated in magnitude. Our results indicate that a potentially modifiable factor, breastfeeding, may decrease adenomyosis risk among parous women.

Associations of Neighborhood Disinvestment and Gentrification with Hypertensive Risk: the Health and Retirement Study Kendra D. Sims* Kendra Sims Perry W. Hystad G. David Batty Kirsten Bibbins-Domingo Ellen Smit Michelle C. Odden

Motivation: Disinvestment, signified by the systematic withdrawal of needed socioeconomic resources, and reinvestment via gentrification may seem opposing neighborhood-level exposures. However, both may cause marginalized older adults to have fewer financial and social assets to manage comorbidities. It has not been tested whether disinvestment and gentrification have distinct associations with hypertension risk.

Methods: We used data on 15579 participants in the Health and Retirement Study with blood pressure measurements. Using 2000 Census data, we denoted census tracts with disproportionately high minority residents, low socioeconomic status, and high renters for their corresponding county as disinvested. We operationalized gentrification among disinvested census tracts between 2000 Census and 2008-2012 American Community Survey data, based on greater than county-average increases in housing costs and Non-Hispanic White residents of high socioeconomic status. We used generalized estimating equations to evaluate the relative risk of measured hypertension averaged over two time points (2010-2012 and 2014-2016) among participants in census tracts that either gentrified or remained disinvested.

Key results: 32% of participants were classified as hypertensive. 44% of participants lived in disinvested tracts in 2000; 26% of disinvested tracts appeared to gentrify by the 2008-2012 American Community Survey. After multivariable adjustment, among Non-Hispanic Black participants, relative to socioeconomically invested census tracts, the time-averaged risk of measured hypertension was higher among those residing in census tracts that remained disinvested (RR; 95% CI: 1.22, 1.08; 1.37) or gentrified (RR; 95% CI: 1.29, 1.12; 1.49). Neighborhood disinvestment or gentrification was not, however, associated with hypertensive risk among Non-Hispanic White or Hispanic participants.

Conclusion: Among Black older adults, neighborhood disinvestment and gentrification appeared to be associated with elevated hypertension risk.

Health Disparities
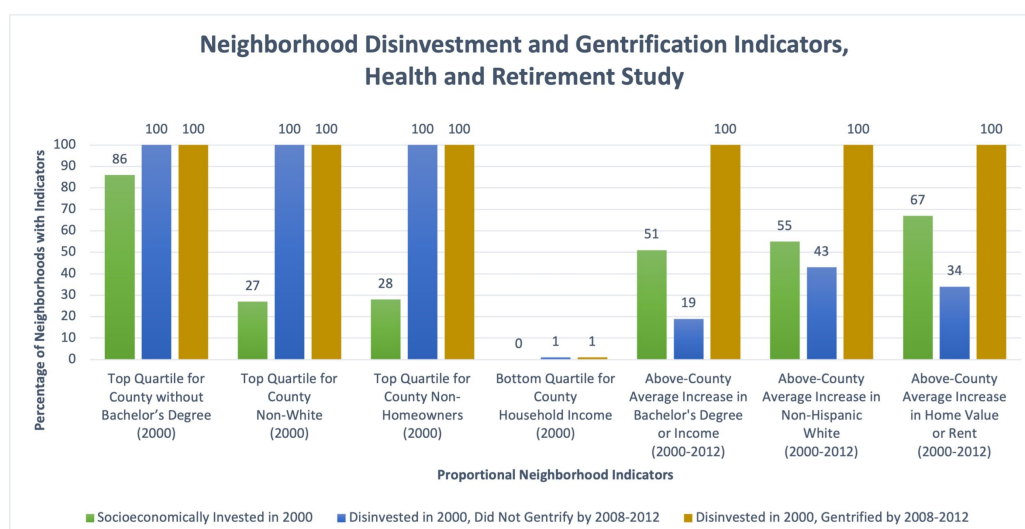
The effects of historical redlining on present-day neighborhood social vulnerability in the United States Oluwatosin Ogunmayowa* Oluwatosin Ogunmayowa Charlotte Baker

Historical neighborhood segregation (e.g., redlining) and higher neighborhood social vulnerability both increase the prevalence of poor health outcomes and behaviors; however, our understanding of how historical redlining influences present-day neighborhood social vulnerability is limited. In this study, we assessed whether: 1) historical redlining is associated with present-day neighborhood social vulnerability in the U.S., 2) the influence of historical redlining on present-day neighborhood vulnerability varied across U.S. cities, and 3) variation in the relationships across cities is due to historical change in education access. We obtained Home Owners' Loan Corporation (HOLC) residential security map and Centers for Disease Control and Prevention Social Vulnerability Index data to analyze these relationships. We identified significant association between HOLC security grades of neighborhood and all present-day social vulnerability index (SVI) after adjusting for 1940s sociodemographic variables. Using multilevel models, we found significant differences in neighborhood SVI by HOLC grade with neighborhoods formerly assigned less favorable grades by HOLC in the 1930s showing significantly greater vulnerability presently than those that were graded more favorably [i.e., "D (Hazardous)" > "C (Definitely Declining)" > "B (Still Desirable)" > "A (Best)"]. For example, neighborhoods that were formerly graded B, C, and D were 0.068-, 0.107-, and 0.114-unit greater in present-day overall SVI score, respectively, than neighborhoods previously graded A (mean score of 0.477). Also, we found that the relationship between historical redlining and present-day neighborhood vulnerability varied by city and that the variation in the relationship was explained by change in educational access in cities between 1940 and 2018. SVI scores in all HOLC delineated neighborhoods (including those formerly redlined) decreased as access to education increased in cities across the U.S.

Association between historical redlining and current environmental quality in the Los-Angeles-Long Beach-Anaheim Metropolitan Statistical Area Monica P Jimenez* Monica Jimenez Danelle T Lobdell Alison K Krajewski Kristen M Rappazzo Christine L Gray Lynne C Messer Jyotsna S Jagai Thomas J Luben

Environmental quality (EQ) varies between neighborhoods, with poorer EQ observed in neighborhoods with lower income levels and/or lower proportion of White residents. In the 1940's, the Home Owners Loan Corporation created maps showing neighborhoods rated as high risk for mortgage lending, which denied residents, usually racial, ethnic, and religious minorities, the opportunity to become homeowners and accumulate wealth. We explored if designation as a high risk/ redlined neighborhood in 1940 predicted more contemporary (2006-2010) census tract-level air and built EQ within one California Metropolitan Statistical Area (Los-Angeles-Long Beach-Anaheim, LALBA). To create the exposure, a census tract shapefile layer was with overlayed high-resolution digital maps of historical redlining. These maps include the 1940 neighborhood assignment of redlining ratings, which include Best, Still Desirable, Declining, and Hazardous, which were combined to create a two-category exposure as follows: Best or Still Desirable (desirable) and Declining or Hazardous (redlined). Linear models estimated the associations between historical redlined ratings and air, built, and the combined air/built index EQ. Higher air, built, and combined index scores (outcome) indicate poorer EQ. We observed poorer combined EQ (0.25 change in index score [95% CI: 0.19, 0.31]) and built EQ index score (0.36 [0.28, 0.45]), and no difference in air EQ index score when comparing redlined areas to desirable areas. This suggests, on average, historically redlined areas have a current combined EQ index score which is 0.25 points higher (worse in EQ) than areas which were historically considered desirable in the LALBA metropolitan area. These results suggest that the United States' historic racist policies, including redlining neighborhoods, are associated with poorer EQ up to 70 years later and may contribute to disparities in exposure to detrimental environments. This abstract does not reflect EPA policy.

Remapping Racial/Ethnic Inequities in Severe Maternal Morbidities: The Legacies of Redlining in the State of California Xing Gao* Xing Gao Jonathan M. Snowden Curisa Tucker Amani M. Allen Rachel Morello-Frosch Barbara Abrams Suzan L. Carmichael Mahasin S. Mujahid

Historical mortgage redlining, a racially discriminatory policy, may contribute to the persistently elevated rate of severe maternal morbidity (SMM) among racialized birthing people. We examined associations between Home-Owner Loan Corporation (HOLC) redlining grades and SMM in a racially and ethnically diverse cohort of all live hospital births at ≥20 weeks gestation between 1997-2017 in California. SMM was defined as having one of 21 procedures and diagnoses, per an SMM index developed by the CDC. We characterized census tract-level redlining using HOLC's security maps, created between 1935-1940, for eight California cities. Race and ethnicity-stratified mixed effects logistic regression models assessed the odds of SMM associated with HOLC grades within non-Hispanic Black, Asian/Pacific Islander, American Indian/Alaskan Native, and Hispanic groups, adjusting for maternal sociodemographic information, pregnancy-related factors, and neighborhood deprivation index. The study sample included 2,014,580 births, with 24,423 cases of SMM (1.2%). Living in a census tract that was previously graded as "hazardous", compared to census tracts graded "Best" and "Still Desirable", was associated with 1.15 (1.02-1.29) and 1.11 (1.04-1.19) times the odds of SMM among Black and Hispanic birthing people, independent of individual sociodemographic factors. These associations persisted after adjusting for pregnancy-related factors and neighborhood deprivation index. Historical redlining, a tool of structural racism that directly influenced the trajectories of neighborhoods' social and material conditions over the last century, remains associated with higher risk of experiencing SMM among Black and Hispanic birthing people today. These findings demonstrate that understanding and addressing the enduring impact of macro-level historical and contemporary mechanisms that uphold structural racism is a vital step in achieving racial and ethnic equity in maternal health.

Social

Longitudinal associations between racial residential segregation, air pollution, and mortality

Carolyn Fahey* Carolyn Fahey Hiwot Zewdie Mary Jewell Claire Leiser Elizabeth Spalt Joel Kaufman Anjum Hajat

Background

Air pollution (AP), which is unequally distributed across communities, is detrimentally associated with myriad health outcomes. However, few studies have prospectively evaluated the modifying role of racial residential segregation (RRS) on AP and health outcomes, including mortality.

Methods

We used harmonized data from two cohort studies, Multi-Ethnic Study of Atherosclerosis (MESA) and Reasons for Racial Differences in Stroke (REGARDS) (N=30,446). For the years 2000-2015, annual average $PM_{2.5}$ and NO_2 predictions were estimated from spatio-temporal models and RRS was measured by metropolitan area and Census tract-level multi-race divergence, Black-white dissimilarity, and single-race isolation indices. We modeled cross-sectional and longitudinal associations between RRS and AP using linear regression. Next, we modeled associations between baseline AP and all-cause and cardiovascular (CVD) mortality using Cox proportional hazards models stratified by race, including interaction terms between AP and RRS to evaluate effect measure modification. All models were adjusted for sex, age, education, income, cohort, and clustering by metro area or tract.

Results

Participants were 59% White and 41% Black, 54% female and mean baseline age of 64 years. Those living in more segregated metro areas had higher levels of baseline and longitudinal AP exposure, as measured by all RRS indices except White isolation. A total of 7144 deaths occurred over 281,930 person-years. AP was associated with higher risk of CVD mortality among Black participants, especially those with above median RRS (White-Black dissimilarity interaction-p=0.026, HR_{NO2}=1.06, 95% CI: 1.02-1.10; Black isolation interaction-p=0.015: HR_{NO2}=1.05, 95% CI: 1.01-1.08).

Conclusions

Segregated communities of color are at higher risk of air pollution exposure and associated mortality. Future interventions and policy-making efforts to reduce health disparities should address both social and environmental inequities.

Substance Use

Rapid detection of suspected opioid overdose deaths: a pilot project Shawn Thomas* Shawn Thomas Brandon Delise

Background: In 2020, there was a 55% increase in accidental drug overdose deaths in Nevada driven by fentanyl, a highly addictive synthetic opioid. Death certificate data is typically delayed 3+ months, and is insufficient to inform quick response efforts. As a result, there was a need to identify overdose deaths in near-real time to respond quickly to prevent further loss of life.

Methods: A case definition to detect suspected opioid overdose <1 month after death was developed in collaboration with the local health department and Medical Examiner/Coroner (ME/C) office. An initial search in the ME/C database was conducted to pull a preliminary list of cases using date of death, manner of death, circumstances of death, and manner type. A manual review of these cases was then performed to detect cases based on decedents opioid use history, witness report of opioid use, physical scene evidence, clinical evidence of overdose, and preliminary toxicology. Analyses were conducted to validate the case definition, with a focus on sensitivity and positive predictive value (PPV).

Results: From October 1-December 31, 2020, 103 drug overdose deaths were opioid-related. Using the case definition, 90 of the opioid-related overdose deaths were identified <1 month after death, Sensitivity=87.4%, PPV=90.9%. The cases: 56.7% based on decedent's opioid use history, 24.4% based on witness report of opioid use, 73.3% based on physical scene evidence, 25.6% based on clinical signs of overdose on scene, and 71.1% based on preliminary toxicology results.

Discussion: The utilized case definition had a high positive predictive value in detecting opioid overdose deaths <1 month after death. Jurisdictions may find this rapid detection of overdose framework helpful when identifying opioid overdose deaths in near real-time. To combat the rise in polysubstance overdose deaths, future directions include widening the scope of the case definition to encompass all suspected drug overdose deaths.

Geographic and temporal trends in fentanyl-involved overdose deaths in Connecticut, 2009-2019 Haidong Lu* Haidong Lu Thomas Thornhill Forrest Crawford Julia Dennett Gregg Gonsalves Lauretta Grau

Background: Since 2012 fentanyl-related overdoses have risen from 4% of all overdoses in the state of CT to 82% of these deaths in 2019. In this paper, we investigate the geographic and temporal trends in fentanyl-involved overdose deaths in Connecticut during 2009-2019, and examine the relationship of fentanyl-involved overdose deaths and overall trends of opioid overdose deaths.

Methods: Data on the dates and locations of opioid overdose deaths that occurred during 2009-2019 were obtained from Connecticut Office of the Chief Medical Examiner. Using a Bayesian space-time regression model adjusted for demographic covariates, we estimated the spatial and temporal trends of fentanyl-involved overdose death as well as overall opioid-involved overdose death at the town level.

Results: During 2009-2019, 6,632 opioid-involved overdose deaths were identified. Among these, 3,234 (49%) were fentanyl-involved, and 3,398 (51%) were non-fentanyl fatal overdoses. Significant spatial and temporal variation in the probability of fentanyl involvement given an opioid overdose death was identified from Bayesian space-time model. The spatial patterns suggest opioid-involved deaths in the north-eastern region of Connecticut had higher probability being fentanyl-involved, while the New Haven and its neighborhoods and the south-western region of Connecticut, primarily Greenwich, had a lower risk. The estimated temporal trend shows the probability of fentanyl involvement given an overdose death increased monotonically since 2014.

Conclusion: Results suggests that geographic variation exists in the probability being fentanyl-involved given an opioid overdose death. Further studies are warranted to explore the factors contributing to the geographic heterogeneity and continuing dispersion of fentanyl fatal overdoses in Connecticut as well as in other neighboring states. Such efforts could inform overdose prevention and intervention strategies.

Figure: Marginal posterior means of the autoregressive spatial and temporal random effects from the Bayesian space-time binomial model for fentanyl-involved overdose deaths. The random effects were exponentiated. Larger values of exponentiated coefficients indicate the higher probability being fentanyl involved given an opioid overdose death at town level in Connecticut.

Substance Use
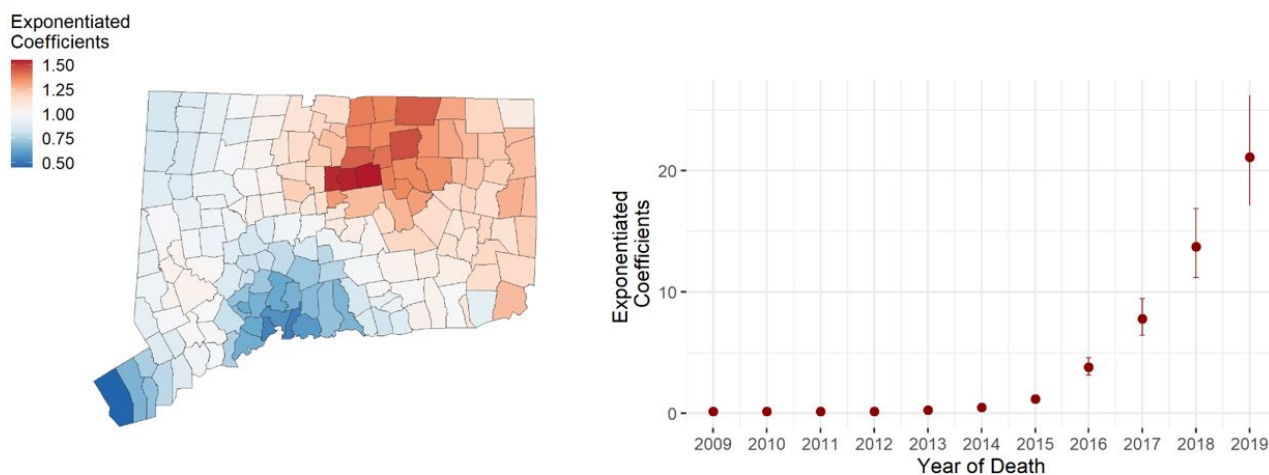
Racial/ethnic inequities in opioid overdose deaths in New York City residents from 2000 to 2020: Recent increases among Black New Yorkers Melanie Askari* Melanie S. Askari Michelle L. Nolan Ashly E. Jordan

Background: Opioid overdose deaths (OODs) have increased both nationally and in New York City (NYC) over the past two decades. We assessed differences in trends of OODs by race/ethnicity in NYC from 2000-2020.

Methods: OODs were derived by linking NYC Office of the Chief Medical Examiner and NYC Department of Health and Mental Hygiene Bureau of Vital Statistics data and defined as deaths where the medical examiner certified the manner was accidental and the death was assigned an underlying or multiple cause ICD-10 code of X40–X44, F11–F16, or F18–F19 (excluding F-codes with 0.2 or 0.6 third digit). Joinpoint regression models estimated the annual percent change (APC), assuming constant variance, in age-adjusted rates (AAR) of OODs by race/ethnicity (White, Black, Latino). The permutation test was used to select the best fitting model. Results from the most recent joinpoint segment are presented.

Results: Of the 15,096 OODs in 2000-2020, 21.8% were among Black, 44.3% among White, and 30.2% among Latino New Yorkers (NYers). For all racial/ethnic groups, the best fitting model had one joinpoint (White = 2010, Latino = 2011, and Black = 2013). Among White NYers, the AAR of OOD increased by 9.9% annually (95% CI = 7.3%, 12.6%) from 2010 to 2020. Among Latino NYers, the AAR of OOD increased by 17.4% annually (95% CI = 13.0%, 21.8%) from 2011 to 2020. Among Black NYers, the AAR of OOD increased by 25.0% annually (95% CI = 14.6%, 36.3%) from 2013 to 2020. By 2020, rates of OOD were similar among Black (30.8 per 100,000 residents), Latino (29.1 per 100,000 residents), and White NYers (28.7 per 100,000 residents).

Conclusions: Compared to White New Yorkers, increases in OODs among Latino and Black NYers began later, and occurred at a faster rate. Given the pace at which OODs are increasing among Black and Latino NYers, expansion of place-based interventions to prevent OODs, such as overdose prevention centers or naloxone distribution, could mitigate emerging inequities in OODs.

Figure 1: Trends in overdose deaths involving any opioid among New York City residents by race/ethnicity, 2000 to 2020
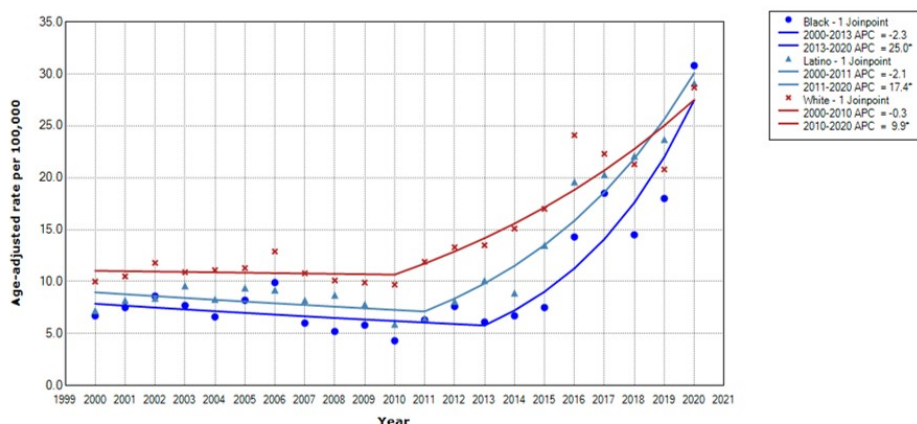
Notes: APC= annual percent change. *Indicates that the APC is significantly different from zero at the alpha= 0.05 level. Solid lines illustrate joinpoint regression model results. One joinpoint was selected as the best fit number of joinpoints for each racial/ethnic group. Source: New York City Office of the Chief Medical Examiner & New York City Department of Health and Mental Hygiene, 2000 - 2020.

Substance Use

Sociodemographic and geographic disparities in excess fatal drug overdoses during the COVID-19 pandemic Mathew Kiang* Mathew Kiang Ellicott C. Matthay Yea-Hung Chen Maria Glymour Kirsten Bibbins-Domingo Keith Humphreys

The COVID-19 pandemic is co-occurring with a drug addiction and overdose crisis. Quantifying the impact of the overdose crisis across sociodemographic groups and geography is critical for targeting equitable interventions. Here, we estimate the number of excess fatal drug overdoses in California in 2020, by race/ethnicity, educational attainment, and geographic region.

Between January 5, 2020 and December 26, 2020, there were 8,588 fatal drug overdoses—a 44% increase over the same period one year prior. Using overdispersed Poisson models, we estimated that 2,067 (95% CI: 1,908 to 2,226) of these fatal drug overdoses were excess deaths, representing 5.24 (4.83 to 5.64) excess fatal drug overdoses per 100,000 population. Excess fatal drug overdoses were driven by opioids (4.45 [95% CI: 4.16 to 4.74]) per 100,000), especially synthetic opioids (2.83 [95% CI: 2.55 to 3.12] per 100,000). The non-Hispanic Black population was disproportionately affected with 9.96 (95% CI: 7.52 to 12.40) excess fatal drug overdoses per 100,000 population compared to 5.94 (95% CI: 5.14 to 6.73) per 100,000 population in the non-Hispanic white population. There was a steep, nonlinear educational gradient with 14.54 (95% CI: 12.77 to 16.31) excess fatal drug overdoses per 100,000 population among those with only a high school degree compared to 1.91 (95% CI: 1.24 to 2.58) per 100,000 among those with a 4-year college degree. There was a strong spatial patterning with the highest levels of excess mortality in the southernmost region and consistent decreases at more northern latitudes (7.66 vs 2.00 per 100,000).

Fatal drug overdoses increased in 2020 beyond prior secular trends, disproportionately among non-Hispanic Black and less educated populations. There was a strong geographic gradient with southernmost regions disproportionately affected relative to northern regions. Local, tailored public health interventions are urgently needed to reduce growing inequities in overdose deaths.

Substance Use
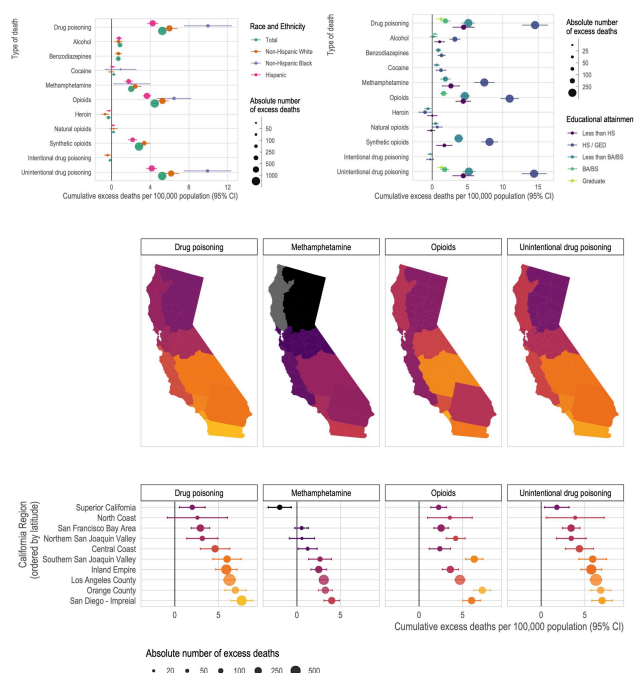
An interrupted time-series analysis of the impact of COVID-19 on the variability in fentanyl concentrations in the unregulated drug supply of Vancouver, Canada Samuel Tobias* Samuel Tobias Cameron J. Grant Richard Laing Mark Lysyshyn Jane Buxton Kenneth W. Tupper Lianping Ti

Fentanyl adulteration of the unregulated drug supply has driven the increase in overdose deaths in Vancouver, Canada for several years. Variability in the potency of drug samples has led to significant unpredictability that is likely contributing to health harms, including overdose mortality. Using data from a community drug checking service, our study sought to evaluate how COVID-19 and related measures affected the variability in fentanyl concentrations within the unregulated opioid supply.

Using a quantification model for fentanyl, historical Fourier-transform infrared spectra from fentanyl-positive drug checking samples in Vancouver were analyzed to determine fentanyl concentration. An interrupted time-series analysis using an autoregressive model was conducted to measure how the variance in monthly fentanyl concentrations was affected following the declaration of the COVID-19 public health emergency in March 2020, using a lagged intervention date of April 1, 2020 to account a delayed impact of pandemic measures.

Among the 4,713 fentanyl-positive samples available for analysis, monthly variance of fentanyl concentrations ranged from $7.9\%^2$ in December 2017 to $159.2\%^2$ in September 2020. An interrupted time-series analysis showed that the variance in monthly fentanyl concentrations increased significantly following the declaration of the COVID-19 public health emergency, with a level change of 26.1 (95% CI: 7.2 – 45.0, p=0.011) and a slope change of 15.8 (95%CI: 10.2 – 21.4, p<0.001) post-interruption.

Variance in monthly fentanyl concentrations increased significantly following the declaration of the COVID-19 public health emergency. While it remains unclear whether the observed increase in the variability of fentanyl concentration in illicit opioids was a direct result of COVID-19 and related measures, the volatility of fentanyl concentrations in the unregulated drug market is likely to have posed significant health harms to people who use drugs in Vancouver.

Substance Use
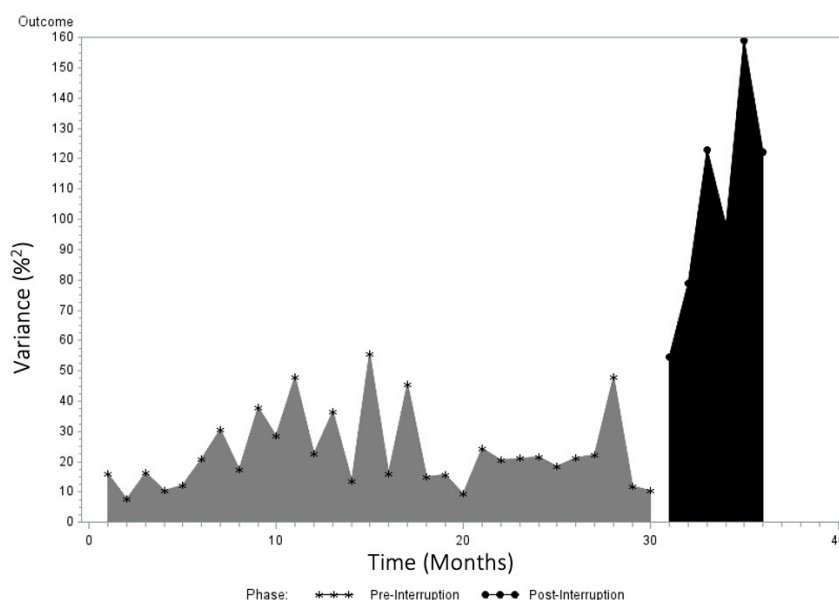
Simulating the simultaneous impact on opioid overdose death of medication for opioid use disorder and naloxone in four New York counties Ava D Hamilton* Ava D Hamilton Magdalena Cerdá Katherine M Keyes

Background: The United States is in the midst of an opioid overdose epidemic; 21.6 per 100,000 people died of opioid-related death in 2019. Simulation models offer a tool to help us understand and address this complex, dynamic, nonlinear, social phenomenon. As part of the HEALing Community Study, we examined how much we would have to increase buprenorphine initiation and retention and naloxone availability to reduce opioid overdose death by 40% in four New York counties, given existing local barriers and facilitators.

Methods: Using an agent-based model called SiCLOPS (Simulation of Community-Level Overdose Prevention Strategies), we modeled the opioid epidemic at the individual level over time in Erie, Ulster, Cayuga, and Suffolk Counties from 2012-2024. Agents exist along the pathway from opioid use to OUD to MOUD (Figure 1). Interventions were implemented in SiCLOPS to demonstrate the combined effects of increased buprenorphine initiation (1.5 to 4 times increase), buprenorphine retention (1.5 x increase), and naloxone availability (3 to 7 times increase) on opioid overdose death in NY counties.

Results: Counties need various combinations of increases in services. The same relative increase is very different at the absolute level when we compare counties. While Erie and Ulster could achieve a 40% reduction with 3 times the increase in naloxone, at 2.5 times the increase in buprenorphine initiation (at base buprenorphine retention), Suffolk required 3 times the increase, and Cayuga 3.5 times the increase in buprenorphine.

Conclusion: Our current results demonstrate the need for tailored county-level interventions as interventions depend both on the absolute and relative baseline levels of naloxone and buprenorphine in each county.
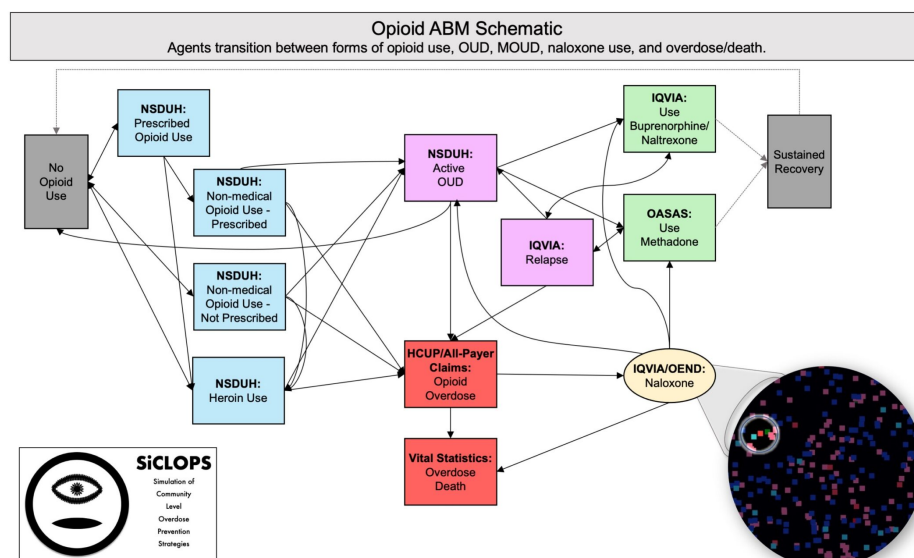
Using Iterative Causal Forest to Identify Heterogeneous Treatment Effects: Sodium-glucose Cotransporter-2 inhibitors (SGLT2i) versus Glucagon-like Peptide-1 Receptor Agonists (GLP1RA) on Hospitalization for Heart Failure in US Older Adults Tiansheng Wang*
Tiansheng Wang Alexander P. Keil Siyeon Kim Richard Wyss Phyo Than Htoo Michele Jonsson Funk John B. Buse Michael R. Kosorok Til Stürmer

Large trials have shown antidiabetic SGLT2i reduces the risk of hospitalization for Heart Failure (HHF), while GLP1RA's effect on HHF is still not clear. We aim to implement the machine learning (ML) algorithm we developed, iterative casual forest (iCF) (**Fig 1A**), to identify the additive interactions between SGLT2i and covariates, and subgroups with heterogeneous treatment effect (HTE) for HHF.

We implemented a new user design identifying initiators of SGLT2i and GLP1RA using 20% random sample of fee-for-service Medicare beneficiaries aged 65+ with parts A (inpatient), B (outpatient physician services), and D (dispensed prescription drugs) coverage for ≥ 1 year from 1/1/2012 to 12/31/2017 and without prior end stage renal disease. We quantified treatment effect by the risk difference (RD) for HHF between SGLT2i and GLP1RA in initial treatment analysis over a maximum 2-year follow-up requiring patients to enter the cohort no later than 12/31/2015. Our cohort includes 10,358 SGLT2i initiators and 9,985 GLP1RA initiators and 380 (7.82%) were censored as they lost part A or B of Medicare coverage during follow-up, which was adjusted by inverse probability censoring weight (IPCW) conditioning on baseline covariates. Death was treated as a competing risk by setting the risk for HHF after death to 0. We grew iCF with 200 trees and increased the iteration number incrementally from 1000 to 10000. In each identified heterogeneous group by iCF (if any), we first calculated the propensity score by logistic regression to adjust for confounding, then assessed conditional average treatment effects (CATEs) applying IPTW and IPCW.

The causal forest produced a P-value of 0.0003 for heterogeneity test. When the iteration number is ≥ 7000, the subgroup decisions from iCF shared the same pattern that split patients by edema, endocrine disorder, age, and sex **(Fig 1B)**. Edema is one of the fundamental signs of heart failure (HF), the largest CATE (adjusted RD of -3.18, -5.26 to -1.11) in subpopulation with edema (a proxy for HF) could be explained by SGLT2i's beneficial effect on HF.

Our finding is consistent with previous studies and shows our iCF method can successfully identify heterogeneous subgroups and additive interactions. The iCF is a promising method to identify subgroups with HTE in large cohorts with known, sufficient confounders.
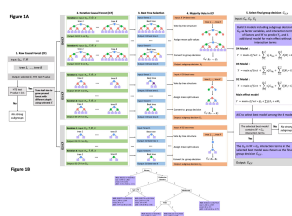
NMR Metabolomics Signatures in Heart Failure: a population-based study Anna Wolska*
Anna Wolska Jungnam Joo Alan T. Remaley James D. Otvos Maureen Sampson Suzette J. Bielinski
Nicholas B. Larson Hoyoung Park Katie Conners Sarah Turecamo Veronique L. Roger

Background: Heart failure (HF) is a poorly understood heterogenous syndrome with persistently
high mortality. Precision phenotyping is needed to improve management and survival. Nuclear
Magnetic Resonance (NMR) spectroscopy enables high-throughput analysis of metabolomics,
suitable for epidemiology research. We hypothesized that metabolomic profiling in a HF community
cohort of optimal clinical relevance would identify novel phenotypes of prognostic importance.

Methods: We performed *NMR LipoProfile*® analysis with the Vantera® Clinical Analyzer on plasma
samples from a HF community cohort. We measured 25 metabolites (large, medium and small
subfractions of triglyceride-rich lipoprotein particles, low- and high-density lipoprotein particles,
ketone bodies, branched-chain amino acids, alanine, glucose, citrate, and GlycA). Unsupervised
machine learning was used to identify metabolomic clusters from NMR data and their association
with mortality was evaluated after stratification for the Meta-Analysis Global Group in Chronic Heart
Failure (MAGGIC) risk score.

Results: We studied 1382 community-dwelling patients with HF [median age 78 years (IQR 68-85);
48.3% women]. Unsupervised machine learning identified 2 metabolomic clusters driven by all 25
NMR variables. Survival was 48.2% (95% CI 45.6%-50.9%) at 5 years and differed by cluster
assignment [5-year survival rate 61.0% (low-risk cluster) vs. 36.1% (high-risk cluster), log-rank *P*-
value<0.001] (Figure). The association was observed across all categories of the MAGGIC risk score
and was particularly notable in the lower MAGGIC risk group [5-year survival rate 86.5% vs. 49.9,
log-rank *P*-value<0.001%] (Figure).

Conclusions: Machine learning applied to NMR data in a HF community cohort identified two
distinct metabolomic profiles. Metabolomic cluster assignment was strongly associated with survival
and improved risk stratification across all strata of the MAGGIC score.

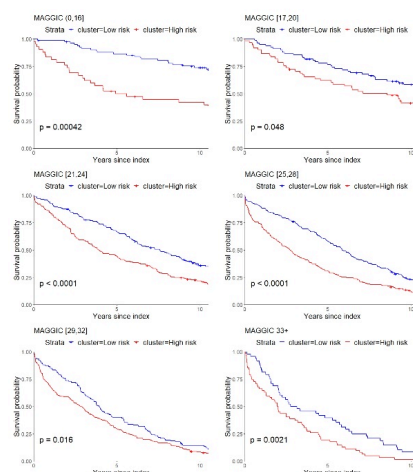Figure : Kaplan-Meier survival curves by cluster assignment in 6
MAGGIC score* risk groups. MAGGIC score* includes age, ejec-
tion fraction, systolic blood pressure, body mass index, creatinine,
New York Heart Association class, sex, current smoking, diabetes,
chronic obstructive pulmonary disease, HF diagnosis > 18 months,
beta-blocker, angiotensin-converting enzyme inhibitor/angiotensin-
receptor blockers.

Big Data/Machine Learning/AI

Machine learning to predict future neighborhood-level overdose risk: Findings from a modeling study to inform overdose prevention in Rhode Island Bennett Allen* Bennett Allen Robert C. Schell Victoria A. Jent Maxwell Krieger Claire Pratty William Goedel Yu Li Brandon D. L. Marshall Jennifer Ahern Daniel B. Neill Magdalena Cerdá

Background

The overdose (OD) epidemic remains a profound health crisis in the United States. Its acceleration since the introduction of illicit synthetic opioids into the drug supply and COVID-19 pandemic underscores the need for efficient targeting and delivery of prevention resources. Machine learning may proactively guide service delivery to maximize reductions in mortality. As part of a randomized trial to test proactive targeting of harm reduction interventions in Rhode Island (RI) neighborhoods, we learned a model with a goal to capture at least 40% of statewide OD mortality by targeting 20% of neighborhoods.

Methods

We used five data sources capturing neighborhood-level indicators in RI: fatal and non-fatal OD; prescription drug distribution; Census demographic and socioeconomic characteristics; health care and social service availability; and commercial land use. Data were available in six-month intervals from 1/1/16 to 6/30/20. To maximize generalizability, we utilized two test periods—7/1-12/31/19 and 1/1-6/30/20—averaging performance across the two periods. Other time periods were training periods. Our model was a stacked ensemble of gradient boost and SuperLearner models, iterated across training periods to predict OD at time t using $t–n$ periods. Hyperparameters were selected using 5-fold cross-validation and MSE. Ensemble weights were derived to obtain final predictions. The primary model evaluation metric was the proportion of test set OD deaths in neighborhoods selected for resource targeting assuming 20% targeting capacity by public health officials.

Results

Our ensemble model successfully targeted neighborhoods capturing 40.2% of OD deaths (MSE=0.22; R^2=0.26) across the two test periods.

Conclusions

Our model predicted neighborhood OD risk using available public health data sources. Findings gesture toward the capacity for machine learning as a promising tool to proactively micro-target public health OD response interventions to areas with highest need.

Big Data/Machine Learning/AI

Investigating combined exposures to air toxics and children's academic achievement: benefits and limitations of an application of data science to children's environmental health research Jeanette A Stingone* Jeanette Stingone

Previous research has found associations between exposure to single air pollutants and children's cognitive health but has often lacked the ability to investigate combined impacts of pollutants. Identifying interpretable associations and interactions within the context of high-dimensional exposure data presents a computational challenge that cannot easily be addressed with standard epidemiologic models. Methods from domains such as data science can be incorporated into our analytic toolbox to address this challenge. Results from these data-driven approaches need to produce interpretable results that can be followed by targeted techniques. The objective of this research is to utilize tree-based methods, such as random forest, to develop an analytic pipeline to discover interpretable combinations of air toxics associated with children's academic outcomes. Residence at birth was used to link EPA data on estimated ambient concentrations of 40 air toxics to an administrative data linkage of public health and education registries for approximately 220,000 children born and raised in New York City. A random forest algorithm was applied to a 1/3 subset of the data in order to generate a collection of regression trees that identify the combinations of air toxics associated with 3rd grade standardized test scores in math and English language arts. Methods to account for confounding and validation of identified combinations were assessed and then compared in a second 1/3 subset, with the remaining data held out for final analyses. Our results suggest that early-life exposure to air toxics is associated with lower test scores but high correlation between pollutants and with social factors remains a challenge for interpretation. Future enhancements of the proposed analytic pipeline, including incorporation of toxicological knowledge of correlated pollutants, will be discussed.

Detecting Spatial and Spatio-Temporal Clusters of Disease Using Stacking Maria
Kamenetsky* Maria Kamenetsky Jun Zhu Ronald Gangnon

Patterns in the grouping of disease across space and time are important to epidemiologists and
health professionals, because they may be indicative of underlying elevated disease risk. In some
cases, elevated risk may be driven by environmental exposures, infectious diseases or other factors
where timely public health intervention could save lives. Our objective is to identify hotspots
(clusters) and map the spatial relative risk gradient of breast cancer in central Japan. Age-
standardized breast cancer incidence counts were collected in 208 municipalities across 5 time
periods from 1975 – 1994. While standard methods are limited to identifying a single correct model,
we develop an approach that stacks all single cluster models into an ensemble of models using
likelihood-based weights. The optimal number of spatio-temporal clusters is identified using
information criteria. Data-driven simulation results show our stacked approach identifies spatio-
temporal clusters while controlling the false positive rate near baseline detection under the null
model with no clusters. We compare methods to calculate cell-wise confidence bounds and find that
model-averaged tail area intervals provide better coverage and narrower confidence widths than
other proposed methods. We identify a single cluster of elevated female breast cancer risk with a
maximum stacked relative risk estimate of 1.18 (95% CI: 0.787, 1.78) comprised of 12 cells in the
cluster center. Stacked estimates in the cluster fell to 1.06 (0.498, 2.21) along the border and to 1.00
(0.358, 2.79) outside of the cluster (*Figure 1*). These results not only identify a cluster, but also
capture the spatial variability of disease risk within the cluster.
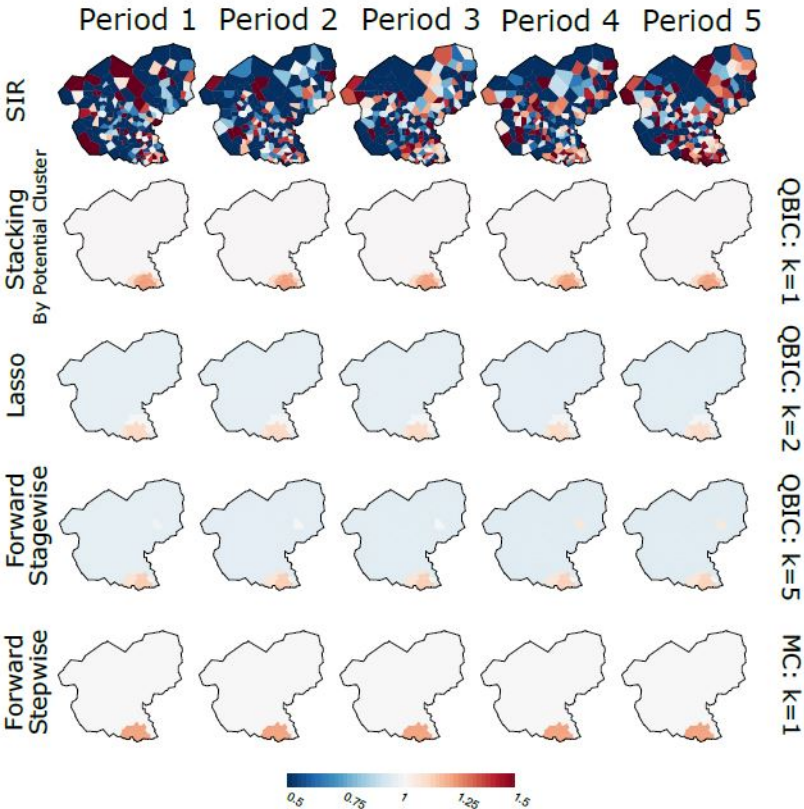

Figure 1: Cluster identification in Japan across four methods. Stacking by potential cluster using QBIC identified a single cluster. All four methods
identified a cluster of elevated relative risk in the southern part of the Saitama prefecture.

Big Data/Machine Learning/AI

Distinguishing the Transparency, Explainability, and Interpretability of Algorithms Georgia Tomova* Georgia Tomova Mark Gilthorpe Gabriela Arriagada Bruneau Peter Tennant

It is often claimed that machine learning will revolutionise health, but much of this hype overlooks some important epistemological and ethical challenges. Although algorithms are excellent at recognising patterns and distinguishing between groups, they are incapable of making precise predictions about *individuals*. Without understanding of the origins and meaning of a dataset, they can reinforce or amplify inequitable decisions, which makes many algorithms poorly suited to informing interventions.

There is consequently a growing interest in making algorithms more transparent, explainable, and interpretable. These terms are often used interchangeably, suggesting they are not sufficiently defined, and their meaning is not well understood. We argue for the following formal definitions based on their distinct scientific aims.

Transparency (*what* is the model?) requires sufficient information on how the model was developed, what variables it includes, why and in what context it is used.
Explainability (*how* does the model work?) is achieved when human beings can provide technical explanations about how the algorithm behaves and computes a specific outcome.
Interpretability (*why* is this outcome determined?) tells us *why* the algorithm determines a certain outcome. It requires transparency, explainability, and knowledge of the context, as well as the meaning of, and causal relationships among, all relevant variables.

The ongoing conflation of these terms has led to many algorithms being used inappropriately, leading to flawed and unjustified ethical decisions. It is especially common for the explanations from theory-free prediction models to be misinterpreted as causally meaningful. We introduce these distinct aims and demonstrate problems with their conflation, using examples from the epidemiological domain, e.g. QRISK and OpenSAFELY. We explain why interpretability requires causal inference and discuss the ethical implications for algorithms built without such insight.

COVID-19 Pandemic

SARS-CoV-2 infection-induced immunity and the duration of viral shedding Hannah Maier*

Hannah Maier Angel Balmaseda Sergio Ojeda Nery Sanchez Miguel Plazaola Roger Lopez Saira Saborio Carlos Barilla Guillermina Kuan Aubree Gordon

Background. As the SARS-CoV-2 pandemic enters its third year, much of the world remains unvaccinated, especially in lower income settings. We investigated the impact of immunity from prior infection on duration of viral shedding.

Methods. We used an ongoing household cohort with an embedded transmission study that closely monitors participants regardless of symptom status. Real-time reverse-transcription polymerase chain reaction (RT-PCR) and Enzyme-linked immunosorbent assays (ELISAs) were used to measure infections and seropositivity, respectively. Blood samples were collected in March and Oct/Nov 2020, and Feb 2021, surrounding the 1st and prior to the 2nd wave. We used accelerated failure time models, allowing for interval and right censoring, to compare shedding times by ELISA positivity status and titer level, by age group.

Results. From the cohort of 2,539 people, there were 446 RT-PCR-confirmed infections between Oct 23, 2020 and Nov 17, 2021. Overall, prior seropositivity was associated with 41% shorter SARS-CoV-2 shedding times, event time ratio (ETR) 0.59 (95% CI: 0.45-0.78). Seropositive mean shedding time was 12.4 days (IQR: 7.2-19.0) versus 20.9 days for seronegative (IQR: 12.2-32.1). This pattern was present in all age groups, 0-9, 10-17, and 18-82 years, but only significant for adults (ETR: 0.47, 95% CI: 0.31-0.71). A 4-fold higher anti-SARS-CoV-2 spike titer was associated with 12% shorter shedding duration (ETR 0.82, 95% CI: 0.82-0.94), with a significant association for adults, and a borderline significant association for children 10-17 years (ETR 0.89, 95% CI: 0.78-1.00).

Conclusions. Prior infection-induced immunity was associated with shorter viral shedding. Although RT-PCR does not indicate viral viability or transmissibility, shorter viral shedding likely leads to lower transmission.

Risk factors for COVID-19 mortality among 326,700 telehealth patients in Bangladesh
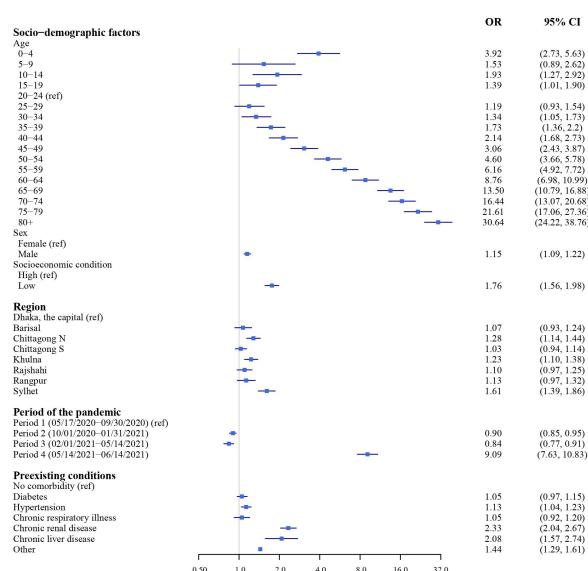
Ayesha Sania* ayesha sania Ayesha S. Mahmud Daniel Alschuler Tamanna Urmi Shayan Chowdhury Seonjoo Lee Shabnam Mostari Kawsar Hosan Sojib Anir Chowdhury Shams el Arifeen

Background: Estimating the contribution of risk factors of mortality due to COVID-19 is particularly important in the context of low- and middle-income countries (LMIC) where vaccination rates are low and public health and clinical resources are limited. The lack of high-quality individual-level data from LMIC has hampered efforts to study relevant risk factors in these settings.

Methods: We used data for 326,700 lab-confirmed COVID-19 patients who participated in a Government provided telehealth service in Bangladesh between May 2020 and June 2021, linked with COVID-19 death data from a national database. We used multivariable logistic regression models to estimate the association between risk factors and mortality, and classification and regression tree models to identify the risk factors that are the most important for clinical decision-making.

Results: This study is one of the largest prospective cohort studies of COVID-19 mortality in LMIC, covering 40% of COVID-19 cases in the country during the study period. We found that being male, being very young or elderly, having low socioeconomic status, chronic kidney and liver disease, and being infected during the latter pandemic period were significantly associated with a higher risk of mortality from COVID-19 (Figure 1). Other significant predictors were severe illness symptoms such as breathing difficulty, fever, and diarrhea. We find that the telehealth doctors' assessment of disease severity was highly predictive of subsequent COVID-19 mortality, underscoring the feasibility of telehealth service.

Conclusions: These findings on the demographic, socioeconomic, and clinical risk factors for COVID-19 mortality can help guide public health and clinical decision-making. Harnessing the benefits of the telehealth system and optimizing care for those most at risk of mortality are the key takeaways from this study.

	OR	95% CI
Socio-demographic factors		
Age		
0–4	3.92	(2.73, 5.63)
5–9	1.53	(0.89, 2.62)
10–14	1.93	(1.27, 2.92)
15–19	1.39	(1.01, 1.90)
20–24 (ref)		
25–29	1.19	(0.93, 1.54)
30–34	1.34	(1.05, 1.73)
35–39	1.73	(1.36, 2.2)
40–44	2.14	(1.68, 2.73)
45–49	3.06	(2.43, 3.87)
50–54	4.60	(3.66, 5.78)
55–59	6.16	(4.92, 7.72)
60–64	8.76	(6.98, 10.99)
65–69	13.50	(10.79, 16.88)
70–74	16.44	(13.07, 20.68)
75–79	21.61	(17.06, 27.36)
80+	30.64	(24.22, 38.76)
Sex		
Female (ref)		
Male	1.15	(1.09, 1.22)
Socioeconomic condition		
High (ref)		
Low	1.76	(1.56, 1.98)
Region		
Dhaka, the capital (ref)		
Barisal	1.07	(0.93, 1.24)
Chittagong N	1.28	(1.14, 1.44)
Chittagong S	1.03	(0.94, 1.14)
Khulna	1.23	(1.10, 1.38)
Rajshahi	1.10	(0.97, 1.25)
Rangpur	1.13	(0.97, 1.32)
Sylhet	1.61	(1.39, 1.86)
Period of the pandemic		
Period 1 (05/17/2020–09/30/2020) (ref)		
Period 2 (10/01/2020–01/31/2021)	0.90	(0.85, 0.95)
Period 3 (02/01/2021–05/14/2021)	0.84	(0.77, 0.91)
Period 4 (05/14/2021–06/14/2021)	9.09	(7.63, 10.83)
Preexisting conditions		
No comorbidity (ref)		
Diabetes	1.05	(0.97, 1.15)
Hypertension	1.13	(1.04, 1.23)
Chronic respiratory illness	1.05	(0.92, 1.20)
Chronic renal disease	2.33	(2.04, 2.67)
Chronic liver disease	2.08	(1.57, 2.74)
Other	1.44	(1.29, 1.61)

CalScope: SARS-CoV-2 Serostatus from Vaccination and Prior Infection in Adults and Children in California May 2021– July 2021 Megha L. Mehrotra* Megha L. Mehrotra Esther Lim Katherine Lamba Amanda Kamali Kristina W. Lai Erika Meza Irvin Szeto Peter Robinson Cheng-ting Tsai David Gebhart Noemi Fonseca Andrew B. Martin Catherine Ley Steve Scherf James Watt David Seftel Julie Parsonnet Seema Jain

Objective: To describe the distribution of SARS-CoV-2 immunity in adults and children from vaccination, prior infection, or both regionally in California.

Methods: CalScope is a repeated cross-sectional population-based serosurvey in 7 counties in California. For the first wave of the study, we invited 200,000 randomly sampled households to enroll up to 1 adult and 1 child between April 20, 2021 and June 16, 2021. We tested all specimen for antibodies against SARS-CoV-2 nucleocapsid and spike proteins, and each participant completed an online survey. We classified participants into serostatus categories: seronegative, antibodies from infection only, antibodies from infection and vaccination, and antibodies from vaccination only. We used causal transportability to generalize our results to each region in California.

Results: 11,161 households enrolled in wave 1 of CalScope, with 7,483 adults and 1,375 children completing antibody testing. As of June 2021, 33% (95%CI [28%, 37%]) of adults and 57% (95%CI[48%, 66%]) of children were seronegative; 18% (95%CI[14%, 22%]) of adults and 26% (95%CI[19%, 32%]) of children had antibodies from infection alone; 9% (95%CI[6%,11%]) of adults and 5% (95%CI[1%, 8%]) of children had antibodies from infection and vaccination; and 41% (95%CI[37%, 45%]) of adults and 13% (95%CI [7%, 18%]) of children had antibodies from vaccination alone. Californians 65 years or older were most likely to have antibodies from vaccine alone (59%; 95%CI [48%, 69%]) and children between 5-11 years old were most likely to have antibodies from prior infection alone (36%; 95%CI [21%, 52%]).

Conclusions: As of June 2021, a third of adults in California and most children were seronegative. Serostatus varied regionally and by demographic group. Wave 2 of CalScope is collecting data through January 2022, and wave 3 is planned for mid-2022.
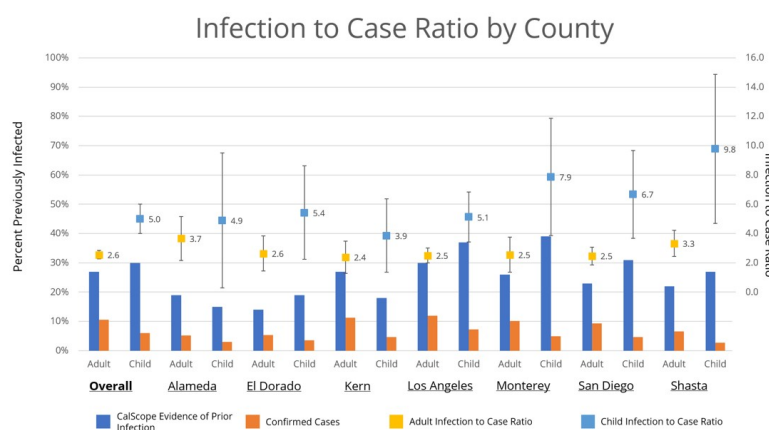

Figure 3. Infection to Case Ratio by County. The infection to case ratio is the ratio of the percent of the population with evidence of prior infection based on antibody test results to the percent of the population with a PCR-confirmed infection in CDPH's COVID-19 surveillance database with an episode date on or before May 8, 2020.

Hospital-based surveillance approximates population seroprevalence of SARS-CoV-2 in the pre-vaccine era Tim Bruckner* Tim Bruckner Daniel Parker Ilhem Messaoudi Vladimir Minin
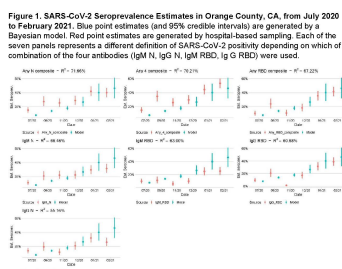
Background: Strategies related to SARS-CoV-2 prevention in the pre-vaccine era would have benefited from knowledge of incidence and prevalence. Given the costly nature, and time-delay, of population-representative studies to estimate these parameters, public health officials instead relied on positive tests and hospitalization rates. The strong selection bias of these surrogate measures, however, calls into question their population validity. We investigated whether, and to what extent, a low-cost and passive hospital-based surveillance approach could approximate seroprevalence of SARS-CoV-2 in the pre-vaccine era.

Objective: Determine whether estimates of SARS-CoV-2 seroprevalence from passively collected, hospital-based serum samples approximate monthly model-based values that require high-cost population-based inputs.

Methods: We retrieved 200 serum samples per month from an ethnically and socioeconomically diverse hospital setting in Orange County, CA, the 6th most populous county in the US. These sera were randomly drawn from all clinical visits. We identified antibody prevalence of IgG and IgM, each for the N, or "spike" protein, and the RBD or receptor-binding-domain (i.e., four antibodies in total). Next, we compared hospital-based SARS-CoV-2 prevalence to that generated from a Bayesian modeling framework (which relied in part on a high-cost population seroprevalence study).

Results: From July 2020 to February 2021, seroprevalence estimated by presence of either IgM N or IgG N antibodies from the hospital-based sera corresponded reasonably well with the Bayesian model's monthly values (R^2= .716).

Conclusion: Carefully conducted surveillance efforts using hospital-based specimens have the potential to yield reasonable population-based seroprevalence estimates of SARS-CoV-2. The low-cost of implementation and real-time availability of results, moreover, should encourage additional efforts to improve hospital-based surveillance of SARS-CoV-2.


Figure 1. SARS-CoV-2 Seroprevalence Estimates in Orange County, CA, from July 2020 to February 2021. Blue point estimates (and 95% credible intervals) are generated by a Bayesian model. Red point estimates are generated by hospital-based sampling. Each of the seven panels represents a different definition of SARS-CoV-2 positivity depending on which of combination of the four antibodies (IgM N, IgG N, IgM RBD, Ig G RBD) were used.

Excess cancer mortality during the COVID-19 pandemic in Chile and Peru Doris Duran* Doris
Duran Renzo Calderon Jay Kaufman

Several countries effected mobility restrictions to control the COVID-19 pandemic, with Peru and
Chile being two of the strictest ones. The effect of this interventions in other health outcomes, such
as cancer death has not been explored.Our aim was to explore cancer mortality trends during the
COVID-19 pandemic in Chile and Peru and compare in-home and hospital deaths.

Mortality data was extracted from Health Statistics (DEIS Chile; SINADEF Peru). We estimated age-
standardized mortality rates (ASMR, with WHO standard population) for all cancer deaths (C00-D48,
ICD-10) for 2018 to 2021, for men and women over 55 years of age, separately. Using the dates for
the strict lockdown's implementation we used an interrupted time series approach to assess the
effect in cancer death both in-home deaths and in hospitals.

Cancer deaths were higher for men in both countries. For both sexes, there was a decreasing overall
trend in Chile, and the opposite in Peru. After the lockdown there was a reduction in the ASMR
trend for women of -0.026(CI95% -0.08,0.02) in Chile and -0.019(CI95% -0.06,0.02) in Peru. For men
an ASMR reduction was only observed in Peru (-0.15 CI95%-0.02,-0.099). For the place of death, in-
home deaths were significantly higher in Chile for both sexes, but particularly for men. There was an
increase for in-home mortality for both countries immediately after the lockdowns (see fig1),
especially for women in Peru (ASMR 14.13 CI95%11.63, 16.98). Consequently, there was an
immediate decrease for in-hospital mortality in both countries with a reduction in the ASMR of -3.64
(CI95% -5.40,-1.87) and -10.81 (CI95% -13.03,-9.60) for women in Chile and Peru respectively, and
of -6.92 (CI95% -9.84,-3.99) and -12.08(CI95%-14.61,-9.54) for men.

During the COVID-pandemic cancer deaths and the place of death was affected by mobility
restrictions. However, the effect is heterogenous, which can be partially explained by covid
incidence and health systems characteristics.
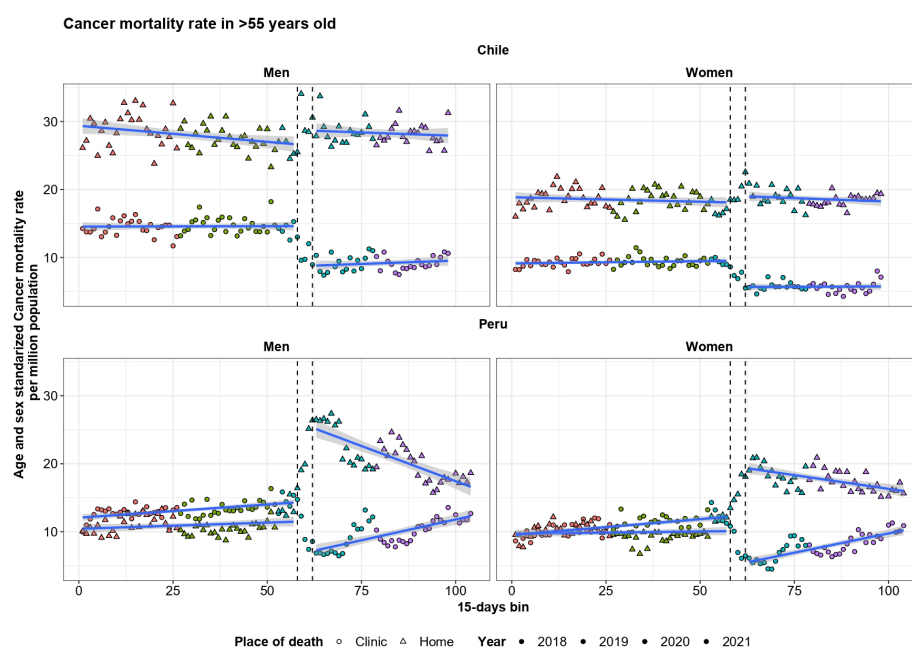
Spatiotemporal Inequalities in COVID-19 Test Positivity Rates in Ontario, Canada from March 2020 to September 2021 Mabel Carabali* Mabel Carabali Aida Parnia Alexandra Blair Laura Rosella Arjumand Siddiqi

Residents of neighbourhoods with greater socioeconomic deprivation and concentration of immigrants and racialized populations in Ontario, Canada have been over-represented among COVID-19 cases. However, little is known about the gradient of COVID-19 risk across continuous measures of area-level disadvantage nor how inequalities vary over time. We used Bayesian spatiotemporal hierarchical mixed-effects models to assess distribution of inequalities in test positivity, by area-level median household income, material deprivation scores, and racial/ethnic segregation index (% of individuals identifying as racialized and recent immigrant). We assessed the presence and magnitude of inequalities using crude and adjusted Relative Concentration Index (RCI), Slope Index of Inequality (SII) and the Relative Index of Inequality (RII) measures. We used individual-level laboratory data of 5.2 million individuals who were tested at least once for SARS-CoV-2 from March 1, 2020, to September 1, 2021, linked to individual-level administrative data and area-level census data. The overall positivity rate for the study period was 5.7%; 12% for recent immigrants and 4.5% for Canadian born or long-term residents. Higher positivity rates were concentrated among areas with lower median household income (RCI=-0.09; 95%CI=-0.13, -0.04) and higher ethnic segregation (RCI= -0.10; 95%CI=-0.16, -0.05), but not according to material deprivation (RCI= 0.04, 95%CI= -0.01, 0.08). SII and RII estimates varied over time. SII and RII results indicate that positivity rates were up to 50 percentage-points higher among areas with highest (versus lowest) ethnic segregation, and up to 20 percentage-points higher in areas with highest (versus lowest) material deprivation. These novel findings describe the gradients of COVID-19 risk across the entire population of Ontario, Canada. However, approaches to account for underreporting and include individual-level socioeconomic data are required.

Racial Inequities in Advice Not To Breastfeed If Using Cannabis Nichole Nidey* Nichole Nidey Adrienne Hoyt-Austin Melissa Chen Brandie Bentley Karen Tabb Chidiogo Anyigbo Christine Wilder Mishka Terplan Jennifer M. McAllister Scott L. Wexelblatt Aaron Murnan Laura R. Kair

Background: In the absence of generalizable evidence on breastfeeding outcomes among people with cannabis use, it is unknown what advice is given to this population. Practice guidelines recommend cessation of cannabis use among pregnant and postpartum people, but separately encourage breastfeeding creating a paradox for providers. Additionally, inequities exist and are linked to experiences of racism in the context of clinical support for breastfeeding and lower breastfeeding rates among Black mother-infant dyads. Therefore, the objective of this study was to examine if prenatal breastfeeding guidance for people using cannabis differs by race and ethnicity.

Methods: The population-based 2017-18 CDC Pregnancy Risk Assessment Monitoring System survey from 9 states was used to assess differences in breastfeeding guidance related to cannabis use among individuals who reported cannabis use three months prior to and/or during pregnancy (weighted n= 51,793). Breastfeeding guidance was based on the following survey question, "During any of your prenatal care visits, did a doctor, nurse, or other health care worker do any of the following things... advise me not to breastfeed my baby if I was using marijuana." The odds of receiving this guidance, by race and ethnicity, were estimated using logistic regression models. Adjusted models included the following covariates: insurance type, prenatal tobacco smoking, maternal age, education, state of residence, delivery year and PRAMS survey weights.

Results: During pregnancy, 36% of our study population reported receiving advice from a prenatal care provider not to breastfeed if they used cannabis, and this advice varied by race and ethnicity. Pregnant non-Hispanic Black people were four times more likely than their pregnant non-Hispanic White peers to be advised against breastfeeding (aOR 4.1, 95% CI 2.1,8.2).

Conclusion: Over one-third of individuals in this study were advised not to breastfeed, and non-Hispanic Black people were disproportionately given this advice. This study provides further evidence of racism in the context of breastfeeding advice and support. Interventions are needed to address racism of healthcare providers and to remedy inconsistencies between conflicting recommendations as to whether postpartum people using cannabis should breastfeed.

Table 1: Odds of Receiving Prenatal Advice Not to Breastfeed When Using Cannabis Among Pregnant People with Self-Reported Prenatal Cannabis Use by Self-reported Race & Ethnicity

	Unadjusted OR (95% CI)	Adjusted† OR (95% CI)
Maternal Race & Ethnicity		
Hispanic	1.7 (0.9, 3.4)	2.0 (1.0, 4.2)
NH American Indian	1.8 (0.7, 4.6)	1.3 (0.6, 3.0)
NH Asian	0.3 (0.1, 1.4)	0.4 (0.1, 2.6)
NH Black	4.2 (2.3, 7.5) ***	4.1 (2.1, 8.2) ***
NH Mixed	2.7(0.8, 8.7)	2.6 (0.8, 8.3)
NH Other	0.3 (0.0, 3.8)	0.2 (0.0, 2.0)
NH White	REF	REF

*=p <.05, ** = p <.01, ***=p <.001, NH = non-Hispanic
†model adjusted for insurance type, state of residence, year of delivery, prenatal smoking, maternal education, maternal age

Associations among adverse childhood experiences, cognitive development, and premature mortality in a U.S. birth cohort Jing Yu* Jing Yu Stephen Gilman

Numerous studies have demonstrated harmful effects of adverse childhood experiences (ACEs) on adult health and mortality outcomes. The developmental mechanisms for these disparities are yet to be delineated. Moreover, most studies examined the cumulative number of adversities, it is not clear whether specific combinations of ACEs are particularly detrimental to child development and long-term health. Using data from the Collaborative Perinatal Project (N=46129), we conducted latent class analysis of 13 ACEs (e.g., neglect, family mental illness, divorce/separation, frequent residential changes, poverty) between birth and age 7, and identified five distinct clustering patterns of ACEs: *Low Adversity* (48% of the sample), *Parental Harshness & Neglect* (4%), *Family Instability* (9%), *Poverty & Crowded Housing* (21%), and *Poverty & Parental Separation* (19%). Children's cognitive development was measured by Wechsler Intelligence Scale for Children at age 7 and mortality status was obtained from the National Death Index (1979-2016). We found that children in *Parental Harshness & Neglect* (Full-Scale IQ=99.16), *Family Instability* (Full-Scale IQ=104.22), *Poverty & Crowded Housing* (Full-Scale IQ=100.33), and *Poverty & Parental Separation* (Full-Scale IQ=99.98) classes all had lower cognitive performance compared to those in the *Low Adversity* class (Full-Scale IQ=106.26). In turn, children's cognitive development was robustly associated with risk of premature mortality (HR=0.81, 95%CI 0.78-0.84), even after controlling for ACE classes and sociodemographic confounders (race, child sex, parental education and employment status, and mother age). The findings suggest that ACEs, especially the clustering of maladaptive parenting behaviors and the two ACE classes related to poverty, significantly undermined children's early cognitive development which could be one developmental mechanism linking these childhood adversities with disparities in adult achievement and health outcomes.

Ethnic Enclaves, Socioeconomic Status And Associations With Obesity Among Latinas

Carola T Sanchez Diaz* Carola Taina Sanchez Diaz Garth Rauscher Caryn Peterson Marian Fitzgibbon Laura Fejerman

Background. Obesity is an important modifiable breast cancer risk factor that disproportionately affects Latinas in the US. As disentangling the notion of enclaves from neighborhood socioeconomic status (nSES) is complex, we took 3 different approaches to conceptualize them and evaluate their association with obesity: weighted sums, Principal Component Analysis (PCA), and Latent Profile Analysis (LPA).

Methods: We used data on n=25,174 Latinas > 40-year-old with at least one mammogram from the Metro Chicago Breast Cancer Registry (2001–2017). Multinomial logistic regressions were estimated to evaluate associations of ethnic enclaves and nSES with obesity using weighted sums and PCA for tract-level enclaves, disadvantage, and affluence. Further, we used LPA to characterize neighborhood composition based on tract indicators of ethnic enclaves, disadvantage, and affluence. We identified four latent profiles, which we labeled as "middling", "disadvantaged", "ethnic enclaves/disadvantaged", and "affluent".

Results: Results from our stratified multinomial regression model, showed a protective association of living in high ethnic enclaves (vs. non-enclaves) with obesity, but only among women living in high disadvantage. In contrast, the first principal component (which was a marker for greater disadvantage and greater enclaves), was associated with greater BMI. In addition, women assigned to the disadvantaged and enclaves' profile also showed higher mean BMI compared to the middling profile, whereas women assigned to the affluent profile had lower mean BMI.

Discussion: Our results highlight the need for researchers to advance the conceptualization of these nSES factors and their interacting influence on health, and serve as a starting point to disentangle causal pathways that may further explain the overarching neighborhood impact on Latinxs' health.

Beyond Black and White: Skin Color and Body Mass Index (BMI) among Women of Childbearing age: The CARDIA Study. Jaime Slaughter-Acey* Jaime Slaughter-Acey Janet Catov Verna M Keith Pamela Schreiner Duke Appaiah

Background Research on racial health disparities often presumes "Black/African American" is a homogeneous racial category. We consider skin color gradations for Black Americans in shaping within-Black and Black-White (B-W) disparities in BMI trajectories for women of childbearing age.

Methods We used data from 2102 (50.8% Black; 49.2% White) women aged 18-30 years enrolled in the CARDIA study, a multicenter, longitudinal study initiated in 1985-1986. BMI was assessed at Year (Y) 0, 2, 5, 7, 10, 15, 20, 25, and 30. Skin color, measured at Y7 by skin reflectometry, was categorized into a 4-level variable: a) Black, dark-brown, b) Black, medium-brown, c) Black, light-brown, and d) White. Linear mixed-effects models adjusting for baseline (Y0) sociodemographics and time-varying smoking and parity were used to assess BMI changes over time.

Results Mean (SD) BMI was 25.6 kg/m^2 [6.5] for Black women and 23.2 [4.4] for White women at Y0. Relative to White, Black women had a higher average BMI (main effect term: =1.81 kg/m^2; SE=0.32 p<0.001), a steeper increase in slope (linear: =0.23 kg/m^2; SE=0.02, p<0.001) that leveled slightly in later years (quadratic: =-0.004 kg/m^2; SE=0.001, p<0.001). For Black women, skin color was related to BMI change over time. Dark-brown, Black women compared to their lighter counterparts had a higher mean BMI, a faster rate of growth, decreasing slightly in later years. The B-W disparity in BMI varied with skin color over time, Figure 1. On average, the B-W gap was greater for dark-skin, Black women at Y0 (=4.52 kg/m^2; SE=0.57, p<0.001) than for medium (=1.37 kg/m^2; SE=0.38, p<0.001) and light (=0.97 kg/m^2; SE=0.46, p=0.037), Black women. Growth rates indicated the B-W gap widened more rapidly for dark-skin, Black women than for their lighter Black peers.

Conclusion Skin color intersects with self-reported race to shape and maintain within-Black and B-W disparities in adiposity among childbearing women during early and middle adulthood.

Figure 1

Mental Health
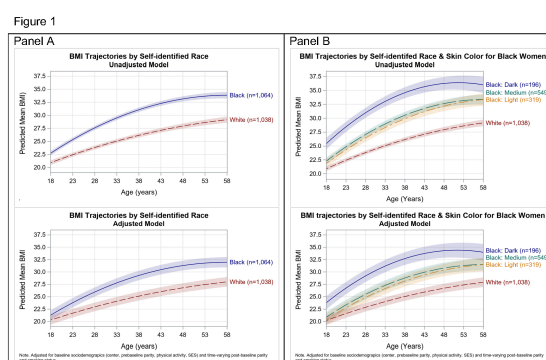
Psychiatric emergencies in Los Angeles County during, and after, initial COVID-19 societal restrictions: an interrupted time-series analysis Tim Bruckner* Tim Bruckner Annie Ro Shutong Huo
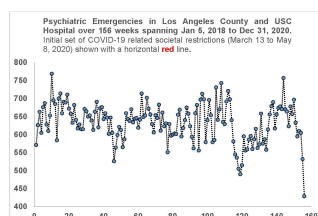
Background: The early stage of COVID-19 led to state-imposed restrictions on population movement, work activity, and social gatherings. Some research finds that psychiatric emergency (ED) visits, one key indicator of population mental health, declined during these restrictions. This work, however, does not control for strong patterning over time in ED visits, does not examine subtypes of ED visits, and does not test whether these visits strongly "rebounded" _after_ the loosening of societal restrictions.

Objective: We analyze, in the largest hospital in the most populous county in the US (Los Angeles, California), two related aims. First, we test whether psychiatric ED visits fall below expected levels during the 1st stage societal restrictions–and second, whether psychiatric emergencies "rebounded" _after_ the loosening of societal restrictions.

Method: We obtained counts of psychiatric ED visits (98,888 total over 156 weeks, Jan 2018 to Dec 2020) from Los Angeles County and USC (LAC+USC) hospital. We applied Box-Jenkins time series methods to identify and remove autocorrelation in psychiatric ED visits before examining their relation with the 1st stage of societal restrictions (i.e., March 13 to May 8, 2020) as well as the subsequent period of relaxed restrictions (i.e., May 8 to Dec 31, 2020).

Results: Psychiatric ED visits fell by 78.13 per week (i.e., 12%) during the 1st stage of societal restrictions (95% CI: 31.10, 125.16). Alcohol use and anxiety disorder accounted for the largest share of the reduction. After the 1st stage of societal restrictions, however, we observe no "rebound" above expected values in psychiatric ED visits overall (coef= -16.89, 95% CI:-57.22, 23.44) or by diagnostic subtype.

Discussion: This pattern of results supports that, whereas psychiatric ED visits substantially fell during the initial societal restrictions, LA did not experience a subsequent psychiatric "pandemic" of urgent visits thereafter.

Psychiatric Emergencies in Los Angeles County and USC Hospital over 156 weeks spanning Jan 5, 2018 to Dec 31, 2020. Initial set of COVID-19 related societal restrictions (March 13 to May 8, 2020) shown with a horizontal red line.

Policing/Incarceration

Neighborhood-level associations between policing and hospitalizations for mental health, substance use, and violent injuries among adolescents and young adults in New York City, 2006 – 2014 Samuel Packard* Samuel Packard Zoe Verzani Finsaas, Megan C. Ruth Shefner Seth Prins Natalie Levy

Background:

Individual-level exposure to aggressive policing is associated with anxiety and post-traumatic stress among adolescents and young adults. Theory and evidence also show that mass criminalization more broadly, such as high neighborhood rates of policing and incarceration, is harmful to the health of communities. During the critical developmental period of adolescence, exposure to mass criminalization may result in more severe health outcomes. To test this hypothesis, we assessed whether rates of policing involving adolescents and young adults were associated with hospital admissions and emergency room visits for mental health, substance use, and violent injury at the neighborhood level.

Methods:

Policing data involving adolescents and young adults aged 10-24 were obtained from the NYC Open Data platform from 2006-2014, including stop-and-frisk encounters, criminal court summons, and arrests (n = 3,323,129). Hospital admissions and emergency department visits were obtained from the Statewide Planning and Research Cooperative System dataset and ICD-9 codes were used to identify psychiatric, substance use, and violent injury diagnoses in the same age group over the same years (n = 2,684,774).

Home address from the hospital data and encounter location from the policing data were geocoded to the ZIP Code Tabulation Area (ZCTA) for each month and matched to socio-economic and demographic variables obtained from the NYC Department of City Planning Open Data. Repeated measures multi-level Poisson models were fit regressing monthly hospitalization rates on policing events with 0-, 1-, 6-, and 12-month lag terms, using ZCTA as a random effect and controlling for area socio-economic and demographic variables.

Results:

Preliminary findings suggest that ZIP-code-level rates of police encounters among adolescents and young adults are positively associated with hospitalizations among the same age group. Model estimates, maps, and sensitivity analyses are forthcoming.

Institutional and socio-cultural determinants of gender differences in major depression and alcohol use disorder in the United States: Results from the Behavioral Risk Factor Surveillance System Daniel Hagen* Daniel Hagen Clare Bambra Danielle Ompad Emily Goldmann

Background:

Major depressive disorder (MDD) and alcohol use disorder (AUD) are leading psychiatric causes of burden of disease in the U.S., with MDD disproportionately affecting women and AUD being considerably more prevalent among men. Theories of health inequalities suggest that political (institutional and socio-cultural) characteristics may impact the magnitude of gender differences in the prevalence of these disorders.

Methods:

Data on depressive symptoms and alcohol use (outcomes) were retrieved for 238,043 participants of the 2006 and 2008 Behavioral Risk Factor Surveillance System (BRFSS) based on the Patient Health Questionnaire (PHQ)-8 and the binge drinking item of the Alcohol Use Disorder Identification Test (AUDIT)-C. Data on 2004/2006 state-level per capita public welfare expenditures were obtained from the U.S. Census Bureau Annual Survey of State Finances (institutional characteristic), and state-level public attitudes towards gender equity were based on public opinion survey data (socio-cultural characteristic). Modified Poisson regression models were estimated separately for both outcomes and exposures, and predictive margins were plotted to visualize interactions of gender with public welfare expenditures and gender equity norms.

Results:

Higher public welfare expenditures were associated with smaller absolute, but not relative, gender differences and lower overall prevalence of AUD, with a difference in predicted probabilities between men and women ranging from 12% in states with lowest to 7% in states with highest expenditures (Figure 1; p=0.006). No such association with gender differences was detected for MDD, and no effect of gender equity norms on gender differences was observed for either outcome.

Conclusion:

Absolute gender differences in the prevalence of AUD in the U.S. appear to be associated with state-level investment in public welfare. Pending replication of these findings, future research should seek to investigate underlying mechanisms.
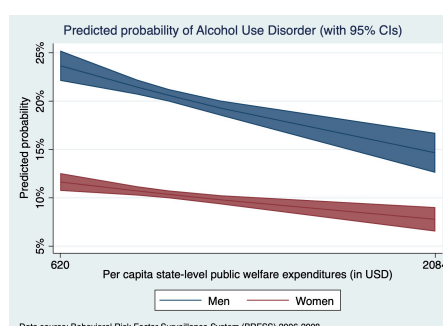
Measuring education inequality and its effect on adolescent mental health Ava Hamilton*

Ava D Hamilton Lisa M. Bates Katherine M. Keyes

Background: Considerable research links income inequality and mental health outcomes. The causal pathway in this relationship due to social comparisons may be particularly salient for adolescents. However, income inequality can be challenging to quantify for adolescents. Adolescent self-reports of parental income may be inaccurate. This project proposes to use an alternative measure of socioeconomic inequality, the EduGini, parameterized by the distribution of self-reported parental education, to estimate the effects of socioeconomic inequality on internalizing symptoms among adolescents.

Methods: Using 2017-2018 Monitoring the Future (MTF) data on 12th graders in the US, we examine the association between parental EduGini and depressive symptoms, self-esteem, and self-derogation. A key strength of MTF is that there are sizable within-school samples. Therefore, we are able to estimate the effects of parental educational inequality on individual adolescent outcomes using a unit of Level 2 aggregation (school) that is highly salient for adolescents.
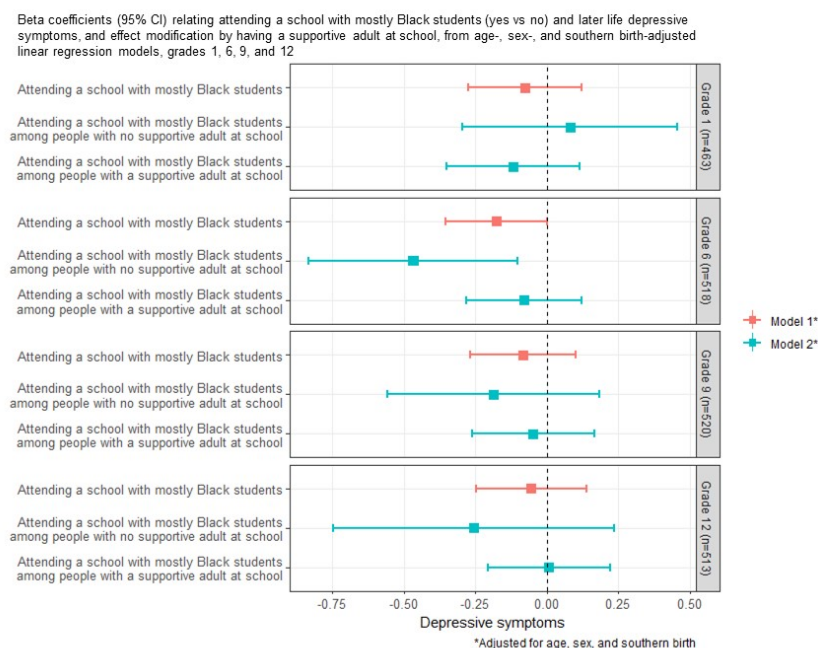
Results: Higher school-level parental EduGini scores were associated with having more symptoms of depression, self-derogation, and low self-esteem when controlling for sex, race, grade, highest level of individual parental education, and urbanity. The results were consistent when looking at the Edu-Gini as a continuous and categorical variable. Compared to students who attended schools in the lowest quartile of parental education inequality, students in the highest quartile of inequality had higher depressive symptoms [OR = 1.43, 95% CI, 1.28-1.60], low self-esteem [OR = 1.27, 95% CI, 1.14-1.41] and high self-derogation [OR = 1.30, 95% CI, 1.16-1.46].

Conclusion: This project aims to provide explicit evidence describing the effect of socioeconomic inequality on adolescent mental health in small geographical locations, which has not been achievable utilizing standard inequality measures such as the Gini coefficient.

School racial/ethnic composition, later-life depressive symptoms, and effect modification by having a supportive adult at school in STAR Taylor M. Mobley* Taylor Mobley Eleanor Hayes-Larson Rachel Peterson Kristen M. George Paola Gilsanz M Maria Glymour Marilyn D. Thomas Lisa L. Barnes Rachel A. Whitmer Elizabeth Rose Mayeda

Prior work indicates that for students of color, attending schools with a higher proportion of non-Latino white students is associated with worse social and health outcomes in adolescence and early adulthood. Proposed mechanisms include lower social support, higher exposure to discrimination, and fewer racially/ethnically concordant teachers/staff. Few studies have examined school racial/ethnic composition and later-life health outcomes, though similar mechanisms are relevant. Participants in the Study of Health Aging among African Americans (STAR), a cohort of community-dwelling Black adults aged 50+ years residing predominantly in Oakland and Richmond, California, were interviewed in 2018-2019 and self-reported school racial/ethnic composition at grades 1 [n=463], 6 [n=518], 9 [n=520], and 12 [n=513]. We assessed the association between attending schools with mostly Black students and later-life depressive symptoms (8-item PROMIS depression score, z-scored to the sample) using age-, sex-, and southern birth-adjusted linear regression models. Further, we examined whether having a supportive adult at school modified this association. In grade 6, attending a school with mostly Black students (range: 30.6% in grade 12 to 53.1% in grade 1) was associated with lower depressive symptoms in later-life (Figure, Model 1), and the association between attending a school with mostly Black students and later-life depressive symptoms was larger for students who did not have a supportive adult at school (Model 2, b=-0.47, 95% CI: -0.83, -0.10 vs b=-0.08, 95% CI: -0.28, 0.12). Our findings, from a cohort where many attended school during the era of desegregation, suggest that attending a school with mostly Black students is associated with mental health benefits that extend into later-life among Black Americans, and attendance of majority Black students may be especially important for Black Americans who do not have supportive adults at school.

Beta coefficients (95% CI) relating attending a school with mostly Black students (yes vs no) and later life depressive symptoms, and effect modification by having a supportive adult at school, from age-, sex-, and southern birth-adjusted linear regression models, grades 1, 6, 9, and 12
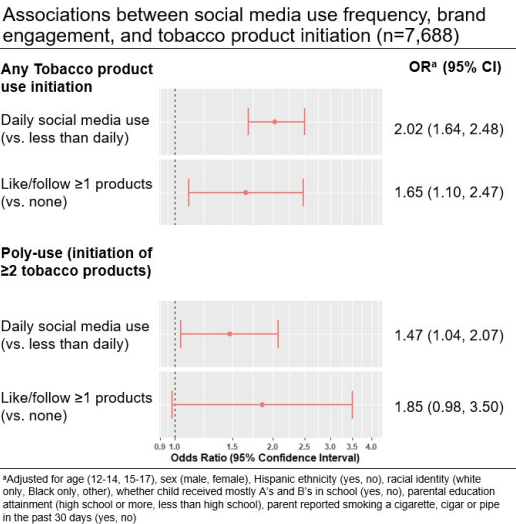
Substance Use

Social media use, tobacco brand engagement, and subsequent tobacco product initiation among youth: Evidence from a nationally representative prospective cohort study Lynsie R. Ranker* Lynsie Ranker Jiaxi Wu Traci Hong Emelia J. Benjamin Aruni Bhatnagar Rose M. Robertson Jessica L. Fetterman Ziming Xuan

Tobacco-related advertising on social media may alter perceived tobacco use norms and risk perceptions among youth. Prior research has predominately focused on cross-sectional associations. We examined associations between measures of social media engagement (daily social media use and liking/following tobacco brands) and odds of tobacco initiation at follow-up, using data from Waves 2 and 3 (2014-2015) of the Population Assessment for Tobacco and Health (PATH) study, a nationally representative sample of youth.

Among PATH youth age 12-17 at Wave 2 with no prior tobacco use (N=7,688), 62% used social media at least daily and 3% reported liking/following one or more of 8 brands on social media: Camel, Marlboro, Newport, Swisher Sweets, Blu, Fin, Vuse, NJOY. Daily social media users (vs. less frequent) tended to be older, female, and received mostly A's/B's in school. Youth engaging with brands on social media (vs. those who did not) tended to be older, female, identify as Black, and have a parent who smoked.

At Wave 3 follow-up, 7.4% of youth reported any tobacco product initiation—most commonly electronic nicotine products (4.8%, e.g., e-cigarettes, vape pens) and cigarettes (2.1%); 2.3% reported initiation of 2+ products (poly-use). Daily social media use (vs. less) was associated with increased odds of any tobacco initiation (adjusted OR, aOR=2.02, 95% CI: 1.64, 2.48) and poly-use (aOR=1.47, 95% CI: 1.04, 2.07). Liking/following any tobacco brand was associated with increased odds of tobacco initiation (aOR=1.65, 95% CI 1.10, 2.47) and poly-use (aOR=1.85, 95% CI 0.98, 3.50). Results were consistent when examining cigarette, electronic nicotine, and cigar initiation separately.

Our findings add to a growing evidence-base describing the exposure of youth to tobacco-related content on social media. Such content—often generated by tobacco companies—may drive youth engagement and subsequent use.

Associations between social media use frequency, brand engagement, and tobacco product initiation (n=7,688)

Any Tobacco product use initiation	OR[a] (95% CI)
Daily social media use (vs. less than daily)	2.02 (1.64, 2.48)
Like/follow ≥1 products (vs. none)	1.65 (1.10, 2.47)

Poly-use (initiation of ≥2 tobacco products)	
Daily social media use (vs. less than daily)	1.47 (1.04, 2.07)
Like/follow ≥1 products (vs. none)	1.85 (0.98, 3.50)

Odds Ratio (95% Confidence Interval)

[a]Adjusted for age (12-14, 15-17), sex (male, female), Hispanic ethnicity (yes, no), racial identity (white only, Black only, other), whether child received mostly A's and B's in school (yes, no), parental education attainment (high school or more, less than high school), parent reported smoking a cigarette, cigar or pipe in the past 30 days (yes, no)

National and state trends in the availability of telehealth services in substance use treatment facilities
George Pro* George Pro Corey Hayes Cari Bogulski Chasmine Flax Brooke E.E. Montgomery Nickolas Zaller

Introduction

Rates of drug-related overdose deaths in rural areas have recently surpassed those in more urban areas. Treatment for substance use disorder (SUD) is effective but uptake remains low, due in part to severe shortages of rural SUD treatment providers. Tele-behavioral health is a promising strategy to increase SUD treatment access for rural residents. Better understanding state-level trends in technology diffusion will help pinpoint geographic locations of high treatment need, low use, and opportunities to expand tele-behavioral health.

Methods

We used the 2018 National Survey of Substance Abuse Treatment Services (N=14,886) to identify treatment facilities that offered tele-behavioral health. We used t-tests to assess differences between national and state telehealth availability, and ANOVA to identify group differences in rurality.

Results

Nationally, only 19% of SUD treatment facilities offered tele-behavioral health, and state means varied widely (e.g., Vermont = 4%, Alaska = 42%). Eleven states demonstrated telehealth percentages significantly higher than the national average ($p<0.05$). States with higher telehealth percentages had the highest proportion of rural residents, but rurality was not significantly different between clusters of states with higher telehealth availability (30% rural), mid telehealth availability (26% rural), and lower telehealth availability (24% rural) ($p=0.62$).

Conclusion

Access to tele-behavioral health services for SUD is low nationally. State-level differences in telehealth availability are stark, with several of the poorest performing states demonstrating telehealth access in less than one in ten facilities. Rural states tended to have more telehealth available than urban states, but the strength of the relationship was weak. Our findings suggest a need for improved access to telehealth services for SUD broadly, as well as in more rural states to most effectively meet the growing demand.

Abstract Figure 1

Percentage of substance use disorder treatment facilities that offer telehealth by state
(N-SSATS 2018; N=14,886 facilities)

Note: National average of substance abuse treatment facilities offering telehealth = 19%
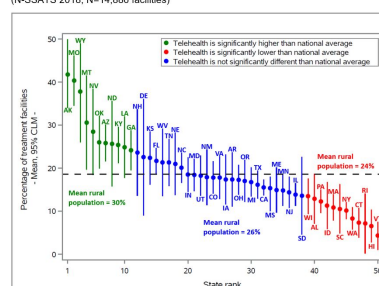
National trends in methamphetamine use and injection: Differences by race/ethnicity and urbanicity Nickolas Zaller* George Pro Corey Hayes Nickolas Zaller

Introduction

Methamphetamine use is increasing in the US, and over 16,000 overdose deaths involved methamphetamine in 2019. While methamphetamine has long been framed as a health burden in predominately White and rural communities, the demographics of people who use methamphetamine may have begun to shift away from this narrative. In addition, little is known about changes in national preferences for injecting methamphetamine, which has implications for increased infectious disease transmission and associated comorbidities.

Methods

We used the Treatment Episode Dataset-Discharges (2010-2019) to identify treatment clients with methamphetamine reported as the primary drug of use. We used logistic regression to model the age-adjusted predicted probability of injection as the primary route of administration over time (versus smoking), stratified by race/ethnicity and location in a core statistical area (core = more urban, non-core = more rural).

Results

The total number of methamphetamine treatment clients increased by 143% between 2010 (n=33,744) and 2019 (n=81,885), and the proportion of non-White clients increased by 38%. Injection increased by 46%, steadily replacing a preference for smoking. The increased rate of injection was strongest among Black clients in core areas (B=0.12, SE=0.01, p<0.0001). The only decrease in injection was observed among American Indian/Alaska Native clients in non-core areas (B=-0.03, SE=0.01, p<0.0001).

Conclusion

Increasing rates of methamphetamine injection pose substantial public health challenges. Drug-related morbidity and mortality will likely continue to parallel this upward trend in methamphetamine injection. To date, the US has only one authorized safe injection site in New York, and medication-assisted treatment for methamphetamine is not available. Considerable resources are needed to strengthen healthcare and safety-net systems to prepare for a continued influx of methamphetamine- and injection-related treatment admissions.

Abstract Figure 1
Predicted probability of injection as the preferred route of methamphetamine administration among methamphetamine treatment clients in the US, 2010-2019 (TEDS-D; N=531,799)
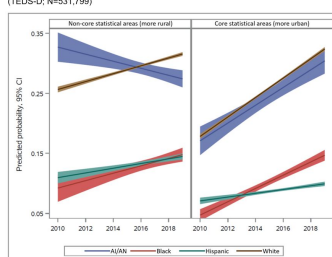
Notes: Models adjusted for client age; AI/AN = American Indian/Alaska Native

Substance Use

Prescription Drug Monitoring Programs and Opioid Overdoses: Variations by Race and Ethnicity Spruha Joshi* Spruha Joshi Victoria Jent Magdalena Cerda

Prescription drug monitoring programs are designed to reduce harms from prescription opioids. However, implementation of PDMPs varies across states, and little is known about what population subgroups may benefit from the heterogeneous programs. We investigated how the relationship between the implementation of two types of PDMPs and rates of fatal overdoses involving prescription opioids and heroin/synthetic opioids varied by race and ethnicity. We implemented ecologic county-level, spatiotemporal study, including 2621 counties in 49 states, in two time periods: 2010-2015 and 2016-2019. We modeled overdose counts using Bayesian hierarchical Poisson models. We defined PDMP as 1) Modern Operational (MO) where PDMP data is accessible to any user (e.g., physician, pharmacist, etc.) authorized by state law to receive it; and 2) Must Query (MQ) where the law mandates prescribers to check a database before prescribing a listed opioid. From 2010–2015, having a MO PDMP compared to no PDMP was associated with lower rates of prescription opioid-related fatal overdose (Risk Ratio(RR)=0.86; 95% credible interval(CI):0.83, 0.89) overall and across racial/ethnic groups. MO PDMP was also associated with lower rates of heroin overdoses for whites, Hispanic, but not for Black people or Other races. From 2016-2019, when stratified by race and ethnicity, both MO and MQ PDMPs were associated with a decrease in prescription opioid overdoses among white people (RR:0.77, 95%CI:0.67, 0.88) and increased risk for Other races (RR:2.18, 95%CI:0.30, 22.85), and no association for Black or Hispanic people. However, MO PDMP was also associated with a decrease in heroin/synthetic opioid overdoses (RR:0.77, 95%CI:0.67, 0.89) for Black people. The impact of PDMPS on opioid-related overdoses varies across opioid type and across racial/ethnic groups. Understanding the impact of PDMPs across racial/ethnic groups is critical step towards achieving equity in reducing harms related to the opioid crisis.

Substance Use

Changes in benzodiazepine misuse in the general U.S. adult population and among prescription opioid users from 2015-2016 to 2018-2019 Julian Santaella-Tenorio* Julian Santaella-Tenorio Magdalena Cerda

Introduction: The rate of overdoses associated with opioid and benzodiazepine use have increased in recent years, with adults ages 18-45 being overrepresented among cases. Despite efforts to reduce the misuse of benzodiazepines, there is limited information on changes in benzodiazepine misuse among people also misusing opioids and the social groups in which this behavior is more frequent.

Methods: We used data from the National Survey on Drug Use and Health to examine changes in the prevalence of past-year benzodiazepine misuse, from 2015-2016 to 2018-2019, in young adults (ages 18-34) and adults 35+. We examined changes in this outcome by frequency of opioid misuse [occasional vs. frequent users (less than 5 times vs. 5 or more times in the past month, respectively)] and by race/ethnicity and sex groups. Logistic regression models were used to examine the factors associated with benzodiazepines misuse in 2018-2019.

Results: In young adults, the prevalence of benzodiazepine misuse decreased by 15.9%, from 4.2% in 2015-2016 to 3.6% in 2018-2019 (p<0.05); this prevalence remained close to 1.2% in adults 35+. In young adults with frequent prescription opioid misuse, benzodiazepine misuse increased by 43.2% in women (from 37% to 53%), by 14.5% in NH-whites (50.4% to 57.7%), and by 158% in Hispanics (from 20.1% to 51.8%) (p<0.01). This prevalence remained close to 49% in NH-blacks with frequent opioids misuse. In adults 35+ with frequent opioid misuse, benzodiazepine misuse did not drastically change in any social group. Results from regression models showed that young adults, NH-whites and those using other substances (e.g., cocaine, methamphetamines) had higher odds of benzodiazepine misuse.

Discussion: Benzodiazepine misuse increased among young women and Hispanics who frequently misuse prescription opioids. Prevention strategies designed to meet their specific needs could help reduce the risk associated with simultaneous use of these substances in these groups.

Is the standard weighting of the Healthy Eating Index appropriate for pregnancy? Julie Petersen* Julie Petersen Ashley Naimi Lisa Bodnar

Background: Adherence to the Dietary Guidelines for Americans, which apply to individuals ≥2 years, is often measured using the Healthy Eating Index (HEI). The HEI comprises 12 equally weighted component scores. Limited empirical basis exists for equal HEI weighting in investigations of health outcomes, including pregnancy.

Objective: We assessed associations between each of the 12 HEI-2010 component scores and pregnancy outcomes. We hypothesized that some HEI components are more important than others for reducing adverse outcomes.

Design: The Nulliparous Pregnancy Outcomes Study: monitoring mothers-to-be was a prospective cohort (U.S. multi-center, 2010-2013). Participants completed a food frequency questionnaire assessing usual periconceptional dietary intake (n=7,880). From these data, we derived the HEI-2010 component scores. Using log binomial regression with inverse probability of missingness weights, we estimated risk differences and robust 95% CIs for the associations between each component score and small-for-gestational age (SGA) birth, preterm delivery, preeclampsia, and gestational diabetes after adjusting for diet pattern, BMI, and total energy intake.

Results: Higher scores for the Total Vegetables and Greens/Beans components were associated with fewer cases of SGA birth, preterm delivery, and preeclampsia. For example, every 1-unit increase in Total Vegetables score was associated with 1.3 fewer SGA cases (95% CI 0.7, 2.0) and 0.7 fewer preterm cases (0.3, 1.1) per 100 births. For preeclampsia, we also observed benefit with higher Seafood/Plant Protein scores. Other components were weakly or not related to these outcomes. For gestational diabetes, most associations were null.

Conclusions: Scores for vegetable components were associated with SGA birth, preterm delivery, and preeclampsia, whereas other components were not. Our findings suggest that traditional equal weighting of the HEI components may not be appropriate for healthy pregnancy outcomes.
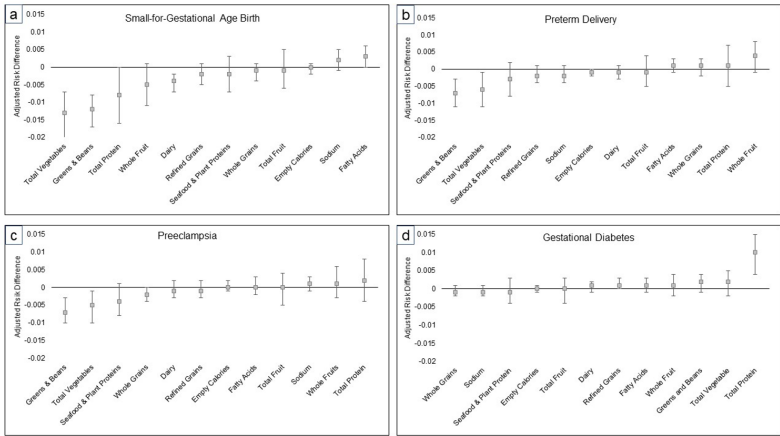

Figure. Risk differences for a 1-unit increase in each of 12 component scores (Total Fruit, Whole Fruit, Total Vegetables, Greens & Beans, Whole Grains, Dairy, Total Protein, Seafood & Plant Proteins, Fatty Acids, Refined Grains, Sodium, and Empty Calories) for each of 4 pregnancy outcomes: a) small-for-gestational age birth, b) preterm delivery, c) preeclampsia, and d) gestational diabetes. Binomial regression models with the identity link adjusted for prepregnancy BMI category, estimated total daily caloric intake, and total HEI-2010 score minus score for the component in question, with one exception. For the fruit and vegetable components (i.e., Total Fruit, Whole Fruit and Total Vegetables, Beans & Greens, respectively) we did not control for the other fruit/vegetable component, given the overlap in the dietary equivalents that contribute to these scores. Data were reweighted to account for missing HEI-2010 data, conditional on measured covariates. Error bars denote 95% robust confidence intervals.

Theory and performance of substitution models for estimating relative causal effects in nutritional epidemiology Georgia Tomova* Georgia Tomova Mark Gilthorpe Peter Tennant

Background:

Experimental substitution analyses in nutrition research are often not practical or sufficiently generalisable and nutritional epidemiology is therefore highly reliant on observational data. The modelling approaches commonly used for estimating relative (substitution) effects are 1) **the 'leave-one-out' model**, where total energy and all dietary components are included as covariates, excluding the nutrient(s) that the exposure should be substituted with; and 2) **the energy partition model**, where all dietary sources are included in the model, without adjustment for total energy. An extension of the energy partition model, termed the **all-components model**, estimates substitutions using the weighted coefficients of dietary covariates. It remains underappreciated that these approaches may not perform equally for estimating substitution effects, and there is limited evidence on whether they produce unbiased estimates.

Methods:

Semi-parametric directed acyclic graphs and data simulations were used to explore the performance of different approaches for estimating the following estimands: 1) the relative causal effect of one nutrient instead of one other, 2) the relative causal effect of one nutrient instead of more than one other, and 3) the average relative causal effect.

Results:

All models perform without bias when the target estimand involves substituting a single exposure with a single other nutrient. However, once the substitution involves more than one dietary component (i.e. estimands 2 and 3), only the all-components model returns unbiased estimates of the causal effects.

Conclusion:

Only the all-components model estimated all estimands without bias; the 'leave-one-out' and energy partition models provided robust estimates only for substituting a single nutrient for a single other. The common practice of simultaneously adjusting for total energy intake and competing foods is likely to deliver obscure relative effect estimands with unclear interpretations.

Comparing food substitution models in nutritional epidemiology: An application for processed red meat and hypertension Conor-James MacDonald* Martin Lajous Conor-James MacDonald Marie-Christine Boutron-Ruault

Nutritional epidemiology analyses that specify specific food substitutions may provide the most relevant results for public health. An analytic approach that recognizes the compositional nature of dietary data by including all components energy in the model rather than total energy intake, and that may potentially be less biased has been proposed (the 'all-components' or partition model). We compare this approach with the 'standard' and 'leave-one-out' methods to assess the impact of processed red meat substitution with fatty fish and vegetables on incident hypertension. In a cohort of 45,771 French women followed for 18 years we evaluated the replacement of one weekly 100 kcal serving of processed red meat with an equivalent serving of the other two foods on hypertension. To estimate substitution effects, we considered the 'standard' model (total energy adjusted), the 'leave-one-out' model, and the 'all-components' model. The substitution in the 'standard' and all-components model was calculated by subtraction of β-coefficients for processed red meat from fatty fish and vegetables. Models were adjusted for risk factors for hypertension that may affect or share common causes with dietary intake. Confidence intervals for food substitutions were generated by bootstrapping. Estimates for replacing a weekly serving of processed red meat with fatty fish for the standard (HRs: 0.95; 95%CI 0.93, 0.97), leave one out (HRs: 0.95, 95%CI 0.91, 0.98), and all-components (HRs: 0.94; 95%CI 0.91, 0.98) models were similar. For replacement of processed red meat with vegetables, the HRs were also similar for all models: standard (HRs: 0.98; 95%CI 0.97, 0.99); leave-one-out (HRs: 0.99; 95%CI 0.98, 1.00); all-components (HRs: 0.98; 95%CI 0.97, 0.99). In this application estimates from alternative approaches did not significantly differ, but the "all-components" and 'leave-one-out' methods explicitly recognize that total energy intake results from the sum of energy containing foods.

Hypothetical diet intervention: Estimating the effect of adherence to the Dietary Approach to Stop Hypertension (DASH) diet on the 22-year risk of heart failure in Swedish men and women Daniel Ibsen* Daniel Ibsen Yu-Han Katalin Alicja

Evidence from randomized trials has found that adherence to the Dietary Approach to Stop Hypertension (DASH) diet lowers blood pressure, which in drug-trials has shown to reduce the risk of heart failure. As there are no long-term trials of the DASH diet, we used the target trial approach to emulate the effect of sustained adherence to the DASH diet on the 22-year risk of heart failure. Men and women aged 45-83 years without previous heart failure, ischemic heart disease, cancer and answered the diet and lifestyle survey in 1997 from the Swedish Mammography Cohort (SMC) and the Cohort of Swedish Men (COSM) were studied. A follow-up questionnaire was sent in 2008-2009 and the women's pre-baseline dietary intake was assessed in 1987. The parametric g-formula was used to estimate the risk of heart failure under sustained adherence to the DASH diet and no dietary intervention (i.e., the usual dietary intake). Adherence to the DASH diet was defined as intake within the ranges of 10 food groups: whole grains, vegetables, fruits, low-fat dairy, red meat, poultry, fish, nuts and legumes, fats and oils, and sweets and added sugar. Incidence of heart failure was ascertained using the Swedish National Patient Register up to 31 December 2019. In total, 31,238 participants were eligible in SMC and 34,939 in COSM at baseline. The 22-year risk of heart failure was 13.0% for adherence to the DASH diet compared with 15.2% with no intervention (risk difference -2.2%, 95% CI -3.9, -0.7%) in SMC and correspondingly in COSM 14.1% vs. 16.2% (risk difference -2.1%, 95% CI -3.5, -0.7%). The risk ratios were 0.85 (95% CI 0.75, 0.95) in SMC and 0.87 (95% CI 0.78, 0.96) in COSM. Our target trial shows that sustained adherence to the DASH diet may reduce the risk of heart failure in a middle-aged and elderly Swedish population.
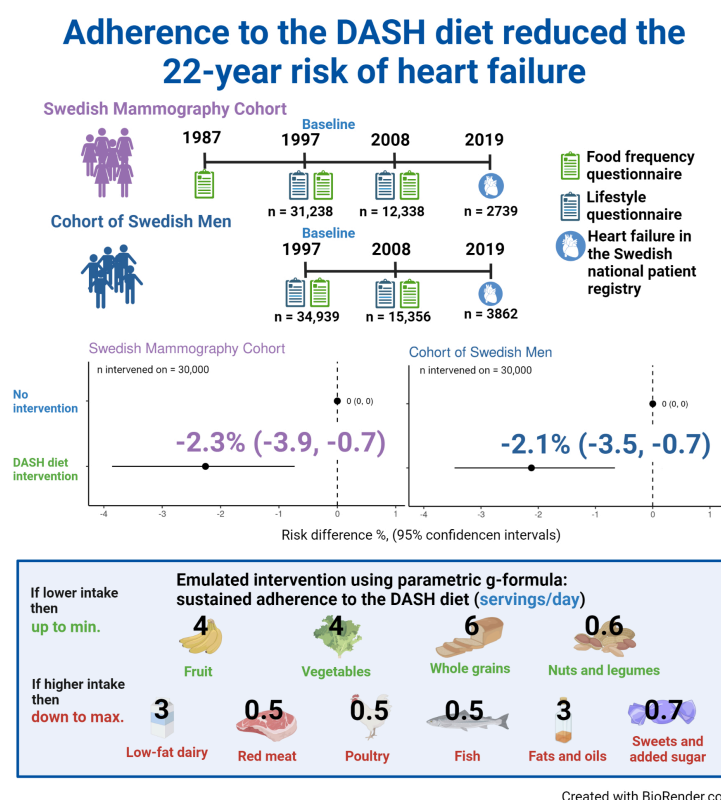
Adolescent appetites, adult growth patterns, and the role of neighborhood conditions: Evidence from a twin/sibling model using Add Health Hyojun Park* Hyojun Park Jesse E. Shircliff

The effect of poor appetite on delayed growth during infancy is well documented, but little is known about the association beyond adolescence. We evaluated whether appetite is prospectively associated with growth patterns during adolescence/adulthood considering neighborhood conditions in a twin/sibling design. Data were from Add Health, a nationally representative longitudinal study of adolescents. After applying exclusion criteria, our study populations of the full and twin/sibling models consisted of 18,625 and 2,612 respondents, respectively. Body mass index (BMI) was calculated from respondents' weights/heights. Appetite was dichotomized as poor or good. Discrete-time models estimated the impact of appetite on sex-specific growth patterns. In the twin/sibling models, the total effect of appetite was decomposed as between-effects and within-effect effects after ruling out unobserved confounders. A priori defined confounders were adjusted for in the full models. A variety of neighborhood-level factors were adjusted for in the twin/sibling models. Survey weights were applied, empirical standard errors obtained, and multiple imputations by chained equation applied for missing data. Only males' poor appetite was negatively associated with the onset of being overweight/obese (AOR: 0.88, 95%CI: 0.70, 0.98) compared to having a good appetite. In the twin/sibling models, both between- and within-effects of a poor appetite were negatively associated with the risk of being overweight/obese (between-effect AOR=0.74, 95%CI: 0.65, 0.87; within-effect AOR=0.81, 95%CI: 0.69, 0.96). The adjusted estimates from twin/sibling models imply that a set of neighborhood characteristics played a critical role in modifying sex-specific growth patterns by appetite. Our findings, sex-specific growth patterns by appetite and the role of neighborhoods during adolescence and adulthood, suggest that this is a also sensitive period in the life course.

Associations between parental BMI and offspring BMI trajectories – potential effect modification by grandparental socio-economic position Christina Dahm* Christina Dahm Jie Zhang Gemma Clayton Kim Overvad Anja Olsen Deborah Lawlor

Background: Prior studies have demonstrated intergenerational transmission of body mass index (BMI), yet the role of socioeconomic position (SEP) in the association between parental-offspring BMI is unclear. We aimed to compare associations between parental BMI and offspring BMI growth trajectories by grandparents' SEP status.

Methods: We used data from the Avon Longitudinal Study of Parents and Children (ALSPAC). Children's weight and height were collected from a variety of sources, including health visitor records, parental reports and measurements taken at clinic visits from age 1 to 18 years old. Mothers reported their own, and their partners', weight and height before pregnancy. Grandparents' SEP was based on attained educational level and categorized as low or high. Multilevel models were used to examine patterns of change in offspring BMI. Three-way interactions between fractional polynomials of age, parental BMI and grandparental SEP were applied, separately for boys and girls.
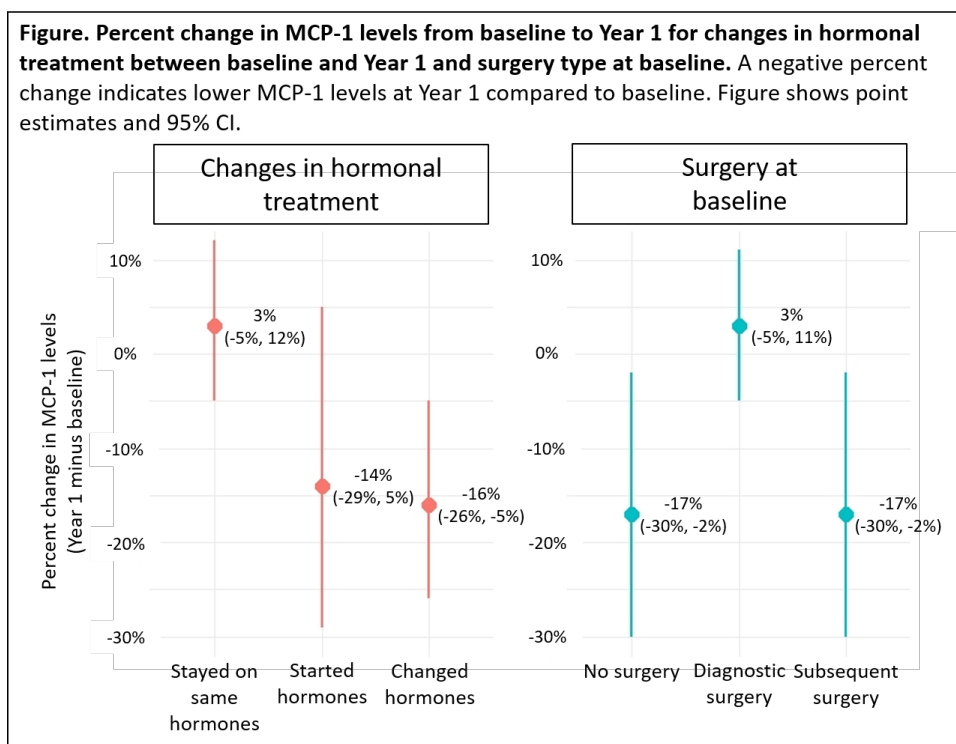
Results: A total of 14,294 (7,321 male and 6,973 female) children who contributed to at least one time point were analysed. The average BMI of offspring whose mothers were overweight or obese (OWOB) was higher throughout childhood and adolescence, compared to those with mothers of normal BMI (Figure). The differences increased with greater age, particularly in female children. Paternal BMI associations were similar from approximately age 9 onwards. For example, the predicted mean BMI at age 15 was 12.71% higher (95%CI: 11.69 to 13.74) with OWOB compared with normal weight mothers whilst it was 7.70% higher (95%CI: 6.78 to 8.63) with OWOB compared with normal weight fathers in the whole sample. These associations remained similar regardless of grandparental SEP status ($P_{interaction}$ = 0.265 maternal side, $P_{interaction}$ = 0.956 paternal side).

Conclusions: The study suggests that parental BMI plays a role in the development of obesity in the successive generations.
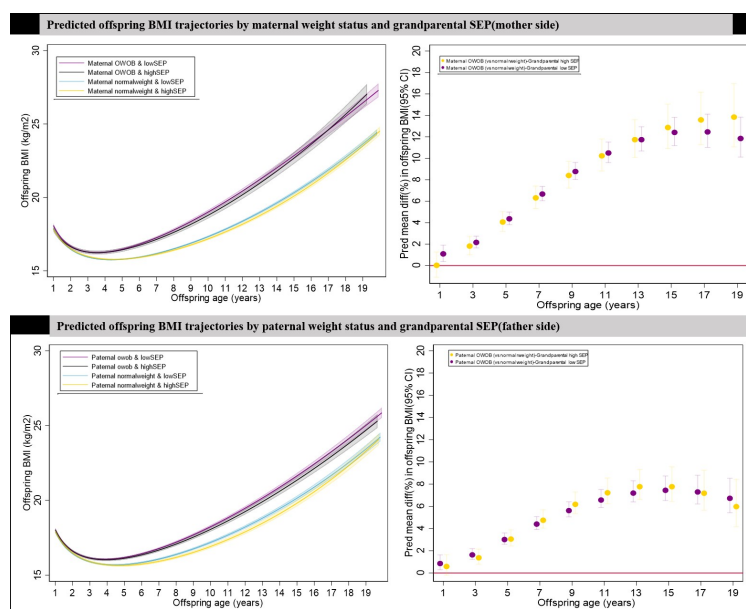
Change in systemic inflammation levels after endometriosis-related treatment Amy L Shafrir* Amy Shafrir Allison F Vitonis Naoko Sasamoto Kathryn L Terry Stacey A Missmer

Endometriosis, a chronic inflammatory condition, affects ~10% of reproductive-aged females. We investigated changes in systemic inflammation one year after endometriosis treatment among adolescent and adult participants of the Women's Health Study: from Adolescence to Adulthood(A2A) cohort, a prospective study in which participants complete questionnaires, provide blood samples, and consent to medical record abstraction. We assayed 11 cytokines and chemokines using multiplex panels from baseline and Year 1 blood samples. Using linear regression, we calculated the percent change(%Δ) in inflammation levels between baseline and Year 1 among participants with surgically-confirmed endometriosis by surgery type at baseline (diagnostic(69%), repeat(15%), no surgery(16%)) and prescription hormonal medication changes between baseline and Year 1 (stayed same(62%), changed type(27%), started(11%)) adjusting for age and analgesic use at baseline. Our analyses included 141 endometriosis participants (median age 17 years). Monocyte chemotactic protein(MCP)-1 levels were 17% (95%CI:-30%, -2%) lower at Year 1 compared to baseline among participants with a repeat surgery at baseline and those without a surgery at baseline (%Δ=-17% (95%CI:-30%, -2%)); however, no change was observed among cases who had a diagnostic surgery at baseline (%Δ=3% (95%CI:-5%, 11%)). Similar results were observed for MCP-4. Additionally, MCP-1 was 16% lower (95%CI:-26%, -5%) at Year 1 compared to baseline for those who changed prescribed hormone type between baseline and Year 1 and 14% lower (95%CI:-29%, 5%) for those who started hormones; there was little evidence of change for those who stayed on the same hormones (%Δ=3%; 95% CI:-5%, 12%). Similar results were observed for interleukin-8. These results suggest that some endometriosis treatments have an impact on inflammation levels, and future work to understand the relationship between change in inflammation and impact on pain symptoms is warranted.

Figure. Percent change in MCP-1 levels from baseline to Year 1 for changes in hormonal treatment between baseline and Year 1 and surgery type at baseline. A negative percent change indicates lower MCP-1 levels at Year 1 compared to baseline. Figure shows point estimates and 95% CI.

Vitamin D and uterine fibroid development: a prospective study Quaker Harmon* Quaker Harmon Stacy Patchel Sheri Denslow Frankie LaPorte Donna Baird

Fibroids are benign tumors with significant morbidity. Black women have a high burden of disease with onset 10 years earlier than White women and 3 times higher rates of hysterectomy. Laboratory investigations and cross-sectional epidemiological studies suggest that vitamin D may offer protection from fibroid development. We assessed the association between repeated measures of serum 25-hydroxyvitamin D [25(OH)D] and fibroid growth, incidence, and loss in the Study of Environment, Lifestyle & Fibroids (SELF). SELF followed 1,610 women self-identified as "African American" or "Black", ages 23-35 from the Detroit, Michigan area with ultrasound every 20 months for 4 visits (5 years). Serum 25(OH)D was assayed at every visit and categorized with clinical cut points: 73% had deficient 25(OH)D (<20ng/ml) at enrollment. Fibroid growth, scaled to 18-months, was estimated for individual fibroids as the difference in log-volume between visits. Women with incident fibroids (n=294) were identified among those who were fibroid free at enrollment (n=1230). Fibroid loss was defined as a reduction in fibroid number between two successive visits. All statistical models used time-varying annual mean 25(OH)D, accounted for within-woman and within-fibroid correlations, and adjusted for time-varying demographic, reproductive, fibroid related and contraceptive factors. Higher 25(OH)D (≥20ng/ml) was associated with a 10% reduction in fibroid growth (95% CI -17, -1) compared to 25(OH)D <20ng/ml. Suggestive associations for fibroid incidence and loss were observed when comparing participants with 25(OH)D ≥30ng/ml at the prior visit to those with 25(OH)D <30ng/ml: fibroid incidence [HR 0.8 (95% CI 0.5, 1.3)] and fibroid loss [RR 1.3 (95% CI 0.9, 1.8)]. The results provide support for the hypothesis that vitamin D can reduce fibroid development, but are limited by the few women with a 25(OH)D measurement ≥30ng/ml (only 8% of measurements).

Vitamin D status and markers of inflammation, iron deficiency, and anemia in a cohort of reproductive-age women 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

Vitamin D may decrease the risk of iron deficiency and anemia by decreasing proinflammatory cytokines, which in turn suppresses hepcidin expression and increases iron bioavailability for erythropoiesis and hemoglobin synthesis. We examined vitamin D status and markers of inflammation, iron deficiency, and anemia in an epidemiologic cohort of women. We used enrollment data from the Study of Environment, Lifestyle & Fibroids, a cohort of 1,693 Black women ages 23-35 years who reside in the Detroit, Michigan area. Among a subset of 1,214 non-pregnant, never smokers, data were available on serum 25-hydroxyvitamin D (25(OH)D), serum C-reactive protein (CRP) (inflammation marker), serum ferritin (SF), and blood hemoglobin (Hgb) concentrations. Since SF is an acute phase reactant, we adjusted SF concentrations for CRP using a recommended regression correction approach. We defined elevated CRP, iron deficiency, and anemia as follows: CRP ≥5 mg/L, adjusted SF<15 μg/L, and Hgb <12 mg/dL; 25(OH)D was categorized in quartiles. Log-binomial regression was conducted to estimate the prevalence ratio (PR) and 95% CI for the association between 25(OH)D quartiles and elevated CRP, iron deficiency, and anemia, adjusting for age, education, passive cigarette smoke exposure, birth in last year, and current hormonal contraceptive method use. We observed a 20% lower prevalence of elevated CRP with higher 25(OH)D concentrations (top vs. lowest quartile: PR 0.80, 95% CI: 0.64, 1.00). The highest quartile of 25(OH)D concentrations (vs. lowest) was associated with a 42% decreased prevalence of iron deficiency (PR 0.58, 95% CI: 0.41, 0.81) and a 39% decreased prevalence of anemia (PR 0.61, 95% CI: 0.47, 0.78). These results are consistent with the proposed role of vitamin D in ameliorating inflammation, iron deficiency, and anemia, and supports further investigation into vitamin D as a potential intervention to improve iron status and anemia in women.

Endogenous hormones in mid-life and later-life subjective memory impairment in women

Sneha Sharma* Sneha Sharma Yu Chen Tess V. Clendenen Fen Wu Yelena Afanasyeva Karen L. Koenig Anne Zeleniuch-Jacquotte

Introduction

Reproductive hormones may impact cognition in women. Recent literature suggests that subjective memory complaints (SMCs) can be an early indicator of cognitive impairment. However, epidemiologic data are mixed, with few prospective studies exploring endogenous sex hormones in relation to later-life SMCs. Assessing this potential association may elucidate an etiology of risk for cognitive impairment in women.

Methods

We included 616 premenopausal and 102 postmenopausal women from the New York University Women's Health Study (NYUWHS), a prospective cohort study with blood samples collected at enrollment (1985-91). At enrollment, women were excluded for use of hormone medications or pregnancy 6 months prior. Women in this study were healthy controls from prior case-control studies who responded to at least one of two follow-up questionnaires (2018-present) featuring 6 questions about SMCs. Multivariate logistic regression was used to estimate ORs and 95% CIs for at least one SMC reported at follow-up in association with baseline hormones, adjusting for age, race, education, original case-control study, and body mass index (BMI) in a separate model.

Results

Baseline androstenedione, testosterone, dehydroepiandrosterone sulfate (DHEAS), and sex hormone binding globulin (SHBG) were measured in premenopausal women; estradiol and estrone were also measured in postmenopausal women. In baseline premenopausal women, there were no associations between hormones/SHBG and SMCs. In postmenopausal women, hormones/SHBG were inversely associated with SMCs: ORs (95% CIs) for SMCs associated with per standard deviation increases in testosterone, estradiol, and SHBG were 0.62 (0.40-0.96), 0.62 (0.38-1.04), and 0.64 (0.41-1.00). The association for SHBG was somewhat attenuated by BMI adjustment, remaining similar for testosterone and estradiol.

Conclusion

Higher postmenopausal testosterone and estradiol is associated with decreased odds of later-life SMCs in women.

Soy-based infant formula feeding and uterine fibroid incidence in a prospective ultrasound study of African American women Christine R. Langton* Christine R. Langton Quaker E. Harmon Kristen Upson Donna D. Baird

Uterine fibroids are highly prevalent, benign tumors and the leading indication for hysterectomy. African American women are disproportionally burdened by fibroids, and few established risk factors have been identified. Exposure to exogenous estrogens during sensitive developmental windows may adversely affect reproductive systems. Soy-based infant formula contains phytoestrogens; in animal studies, postnatal administration of phytoestrogens has demonstrated detrimental effects on uterine development that persists into adulthood including increased fibroid risk in the Eker rat. Limited prior epidemiologic studies also have suggested increased fibroid development with soy formula infant feeding.

We evaluated the association between soy formula feeding and fibroid incidence among African American women aged 23-35 years in the Study of Environment, Lifestyle & Fibroids (SELF). Soy formula was assessed via an early life questionnaire administered to the participant's mother when she was available (89% of analytic sample). A standardized ultrasound examination was conducted during 4 clinic visits over 5 years to detect fibroids ≥0.5 cm in diameter. We used Cox proportional hazards regression to estimate hazard ratios (HRs) and 95% CIs for the association between soy formula feeding and incident fibroids adjusted for early life and adult factors.

Of 1,121 fibroid-free participants at baseline, 150 (13%) were ever fed soy formula as infants and 269 (24%) developed incident fibroids. We did not observe an association between ever being fed soy formula and incident fibroid risk (HR = 1.08; 95% CI: 0.75, 1.54). However, participants fed soy formula within 2 months of birth and for >6 months (n=53) (vs. never fed soy formula), had an elevated risk of fibroid incidence (HR = 1.56; 95% CI: 0.92, 2.65).

Results from this first ultrasound-based, prospective fibroid study add support to prior data suggesting increased fibroid incidence among women fed soy formula early in infancy.

Racial Misclassification of American Indian and Indigenous Americans in Epidemiological and Public Health Research Ceco Maples* Ceco Maples Danielle Gartner

There is speculation that a significant percentage of AI/AN is not included in disease surveillance which leads to an underestimation of disease burden and inadequate resource allocation in/for these groups in the United States. In this study, we investigate the strengths and weaknesses of unused/used solutions proposed by researchers to fix AI/AN racial misclassification in health data. We collected data from published scientific articles using specific criteria: Sex, Age, Race, Chronology, Pathology, Geography, Mode of Racial Classification, and Proposed Solutions. We then looked at each specific study in regard to its limitations and data, the aforementioned criteria, to determine its pros and cons for the best solutions. Most studies use data from larger data sets such as the census and national vital statistics system which are more likely to leave out some AI/AN then links it to AI/AIN specific data sets such as the IHS. Some studies find fixes to misclassification from qualitative routes such as addressing racial profiling in the health system. We found that studies using the data linkage method may have not accounted for all AI/AN due to geography barriers in who their datasets encompass.

Methodological & conceptual considerations when estimating cancer health disparity indicators among small, Native American populations Danielle Gartner* Danielle Gartner Noel Pingatore Shannon Laing

Background: A multi-tribe consortium is addressing cancer health disparities among Michigan (MI) tribes and evaluation of key health indicators is needed to ensure project goals are met, guide decision-making, and satisfy funder requirements. Yet, there are unique concerns for these analyses that necessitate novel conceptual and methodological approaches.

Purpose: To describe our methodological approach and report baseline estimates for key indicators.

Methods: Data are from four tribe-specific, population-level surveillance surveys (modified version of the CDC's American Indian Adult Tobacco Survey) collected from 2015-18. We used random effects models and REML to estimate mean baseline prevalences and standard errors for key indicators. When appropriate, we report tribe-specific estimates rather than group means. All estimates were compared to statewide prevalences from the 2017 MI American Indian (AI) Behavioral Risk Factor Surveillance.

Results: The mean prevalence of current smoking across participating tribes is 50% (95% CI: 46.3-54.3) and the mean prevalence of obesity is 49% (95% CI: 44.4-53.1). Current smoking status among participating tribes is higher than the statewide AI prevalence, while obesity prevalence is comparable. For each tribe, the prevalence of ever having had a colonoscopy/sigmoidoscopy (>50 years) is 65% (95% CI: 52.2-77.0), 76% (95% CI: 65.1-85.9), 85% (95% CI: 77.5-86.8), and 85% (95% CI: 70.4-99.8). The statewide estimate for ever having had a colonoscopy/sigmoidoscopy is compatible with three of four tribe-specific estimates.

Discussion: Status as sovereign nations, and differences in Tribal enrollment size, geographic location and service area, Tribal health system capacity, Tribal enrollment status, and community norms and cultural practices means that care is needed when calculating and interpreting project prevalence estimates. This work overcomes several, but not all, methodological and conceptual challenges.

Mental Health

Family, financial, employment and housing stress: Associations with health among the Indigenous Population of Canada Helen Cerigo* Helen Cerigo Amélie Quesnel-Vallée

Stress created through environmental and social conditions is an important pathway driving both poor mental and physical health. The Indigenous population of Canada faces increased exposure to stress due to a long history of colonialism and discrimination. This structural disadvantage manifests as persistent disparities in employment, education, income, and housing conditions. In this research, we explore a comprehensive set of family, financial, employment and housing stressors and their association with physical and mental health among Indigenous Peoples in Canada. We use the 2017 wave of the cross-sectional Aboriginal People's Survey (APS), which is a representative sample of First Nations people living off reserve, Métis, and Inuit aged 15 and older (n=24,220). In this research, we first develop and validate an inventory of stressors available within the APS among those of working age (25 to 64 years), using confirmatory factor analysis (CFA). We identify a total of 17 stressors, to create an index of stress exposure. To estimate the association between stress exposure and health outcomes ((1) self-reported health; (2) self-reported mental health; (3) presence of disability; and (4) multiple chronic conditions), we fit generalized linear models (GLM) with a Poisson distribution and a log link function with robust standard error to allow for retrieval of relative risks. Finally, we examine health care access, health behaviours and resiliency as potential mediators of the relationship between stress and health. We use the mediation approach for binary mediators using generalized linear model regression, as outlined by Valeri and VanderWeele (2013). Estimates of the direct and indirect effects are reported. Understanding these associations and the stress exposure profile of Indigenous people in Canada will help to target and develop interventions to reduce risk and increase resilience.

Environment/Climate Change

Disability in an American Indian Community: Prevalence, Distribution, and the Role of Polychlorinated Biphenyls Thoin Begum* Thoin Begum Gayle Morse Dedra Buchwald Samuel C. Byrne David O. Carpenter

U.S. Census data show that approximately 40% of Americans over age 65 are affected by disabilities, which is defined as a physical or mental impairment that substantially limits one or more major life activities. Analyses of national data have found the prevalence of disability and associated functional limitations among AI older adults ranges from 20-57%, while they constitute less than 2% of the US population. The indigenous community of the Mohawk Nation at Akwesasne, has faced significant environmental contamination since the 1970s, resulting from historic operations of three aluminum foundries near the reservation. Prior studies among the Mohawk population of New York and Canada have demonstrated that polychlorinated biphenyls (PCBs) are linked to physical health problems. The aim of this study was to investigate associations between disability and PCB exposure, as measured by serum level of PCBs obtained a decade prior, among 109 Native American adults over the age of 50 years. We used the World Health Organization Disability Assessment Schedule II to measure disability. We employed multivariate linear regression to estimate associations between exposure to dioxin-like, estrogenic, mono-ortho, di-ortho, tri-tetra-ortho, low-chlorinated, and total PCBs, adjusted for age, sex, body mass index, and current smoking status. We found that exposure to total PCBs was positively associated with overall disability ($\beta=0.002$, 95% CI: -0.01, 0.01), albeit without statistical significance. We found significant positive associations between exposure to PCBs and the domain of getting along with others, with the greatest association for total PCBs ($\beta=0.07$, 95% CI: 0.02, 0.12). Our results suggest the importance of examining the long-term effects associated with PCB exposure. These results also suggest that exposure assessments of lower-chlorinated PCBs are warranted. Still, a larger and more comprehensive investigation is necessary to more definitively assess the risks.

Casino-based cash transfers and fertility among the Eastern Band of Cherokee Indians in North Carolina: A time-series analysis Parvati Singh, PhD* Parvati Singh Alison Gemmill Tim-Allen Bruckner

Fertility decline remains a key concern among high-income countries. Prior research indicates that income supplementation through unconditional cash transfers (UCT) may correspond with increased fertility. We examine whether a casino-based UCT, in the form of per capita (percap) payments to members of the Eastern Band of Cherokee Indians (EBCI) corresponds with an increase in fertility. We use data from North Carolina vital statistics datasets from 1990 to 2006 and apply time-series analysis methods to examine the relation between specific months of percap payments (exposure) and monthly number
of conceptions that result in live births (outcome) among the EBCI. We control for autocorrelation and monthly counts of births (arrayed by conception cohorts) among white women (ineligible to receive the UCT) in the study region. Results indicate an increase in conceptions that result in live births at 1 and 3 months after percap receipt among EBCI women aged $\geq$ 20 years (exposure month lag 1 coefficient = 1.74, p = 0.03; exposure month lag 3 coefficient = 1.60, p = 0.04). Exploratory analyses indicate that the observed fertility increase concentrates among primiparae (i.e. first-time mothers) EBCI women. We do not find any association between percap payment timing and births to EBCI women aged < 20 years. Our results align with recent work on UCTs and fertility change in the US and support universal income supplementation as a potential mechanism to increase fertility.

Keywords: unconditional cash transfer, Eastern Band of Cherokee Indians, fertility, quasi-experiment, time-series analysis

Opioid prescribing laws and cannabis legalization: what is their synergistic impact on opioid overdose deaths in the current phase of the overdose crisis? Magdalena Cerdá*

Magdalena Cerdá Katherine Wheeler-Martin Emilie Bruzelius Christine Mauro Corey Davis Silvia Martins

State policies to limit overprescribing of opioids, such as mandatory prescription drug monitoring programs (PDMPs) and prescribing limits; and policies to expand access to cannabis, such as medical cannabis legalization (MCL) and recreational cannabis legalization (RCL), have been proposed as promising policy levers in the opioid overdose crisis. We examined the independent and joint effects of PDMPs, prescribing limits, MCL and RCL on opioid overdose deaths in the US from 2010-2014 (modern operational PDMPs and MCL) and 2015-2019 (mandatory PDMPs, prescribing limits, MCL and RCL). We fit Bayesian spatiotemporal models to estimate relative rates of county-level opioid overdose deaths (n=3,109) associated with implementation of these state policies. In 2010-2014, compared to counties in states with neither policy, adoption of modern operational PDMPs alone was associated with a lower rate of opioid overdose deaths (RR: 0.95 (95% CrI: 0.92, 0.99), while MCL alone was associated with higher rates of opioid overdose deaths (RR: 1.28 (1.12, 1.46). Adoption of both policies together (compared to adoption of neither policy) was not associated with overdose death. In contrast, in 2015-2019, adoption of mandatory PDMPs alone (RR: 1.12 (1.09, 1.16)), and RCL alone (RR: 1.09 (1.00, 1.19)) were associated with increased opioid overdose deaths, while MCL alone was associated with decreased overdose deaths (RR: 0.90 (0.87, 0.94)). Joint adoption of mandatory PDMP and RCL (compared to adoption of neither policy) was associated with increased overdose deaths (RR: 1.49 (1.24, 1.78)), while joint adoption of mandatory PDMP and MCL was not associated with overdose deaths. Similar patterns were found for prescribing limits and cannabis legalization. In the current phase of the opioid crisis, when opioid overdoses are driven by illegal opioids, stricter opioid prescribing policies and more expansive cannabis legalization may not lead to a meaningful reduction in overdose death rates.

Associations between medical cannabis laws and treatment for opioid use disorder in the United States, 2004-2017 Sarah Gutkind* Sarah Gutkind Melanie A. Askari Silvia S. Martins Pia M. Mauro

Aim: The evidence linking medical cannabis laws (MCL) and opioid-related overdose mortality and hospitalizations is mixed, and suggests no related reductions in non-medical use of prescription opioids. We estimated the effects of changing cannabis policy on opioid use disorder (OUD) treatment use in the US.

Methods: People ages 12+ participated in the 2004-2017 National Survey on Drug Use and Health. We used the restricted data with state identifiers stratified before/after a 2015 survey re-design (2004-2014, 2015-2017). We distinguished state-years before and after MCL enactment among states with MCL, and states without MCL by 2017. We defined OUD treatment need as meeting criteria for DSM-IV OUD or reporting opioid treatment during the last/current substance use treatment experience in the past year. We estimated the adjusted odds ratios (aOR) of any or specialty OUD treatment among people with OUD treatment need before and after MCL enactment using multi-level logistic regressions with random state intercepts, adjusting for year, sex, age, race/ethnicity, income, urbanicity, and state-level characteristics.

Results: Approximately 9,500 people ages 12+ (0.88%) needed OUD treatment in 2004-14, and 2,200 (0.93%) in 2015-2017. Prevalence of OUD treatment increased from 2004 to 2017. People with OUD treatment need had higher odds of any OUD treatment after MCL enactment in 2004-2014 (aOR=1.16, 95%CI: 0.97, 1.39), and 2015-2017 (aOR=1.22, 95% CI=1.02, 1.46). Higher odds of specialty OUD treatment after MCL enactment in 2004-2014 (aOR=1.26, 95% CI: 0.88,1.79) and 2015-2017 (aOR=1.05, 95% CI=0.75, 1.46) overlapped the null.

Conclusion: People needing OUD treatment had a higher likelihood of receiving OUD treatment following MCL enactment. OUD treatment has been associated with reductions in mortality and improvement in quality of life. This could provide a potential explanation for decreased opioid-related overdose deaths and hospitalizations in some states.

Trends in psychosis-related hospitalizations following cannabis legalization in Colorado

Spruha Joshi* Spruha Joshi Kyle Snyder Bianca Rivera Christian Thurstone Magdalena Cerda Noa Krawczyk

Cannabis is currently the third most used substance worldwide after alcohol and tobacco, with growing legal status in parts of the United States (US). In the US, 36 states allow for medical purposes, and 18 states allow for adult-use purposes. Increasing access to cannabis begets concerns about adverse public health impacts of the legalization of cannabis, including psychotic disorders (PD) and psychosis-like symptoms. We sought to examine trends and characteristics of emergency department (ED) visits and hospitalizations for psychosis before and following changes in the widespread availability of medical and recreational cannabis in Colorado. We utilized an interrupted time-series (ITS) design to examine the change in monthly rates of ED visits and hospitalizations for psychosis overall and psychosis with comorbid cannabis use disorder specifically before and following implementation of the Ogden memo and Colorado 64 Amendment policies using data from the Denver Health System, from 2005-2019 for those aged 12 and older. The overall psychosis with cannabis use disorder hospitalization rate was 25.6 per 100,000 persons before the Ogden memo and 33.2 per 100,000 before legalization but after Ogden memo and increased by 1.30 (95%CI: 0.22, 2.37) each month after the Ogden memo and by 0.40 (95%CI: 0.15, 0.65) each month following legalization. The overall psychosis with cannabis use disorder hospitalization rate was 1.1 per 100,000 persons before the Ogden memo and 1.57 per 100,000 before legalization and increased by 0.42 (95%CI: 0.35, 0.48) each month after legalization. Analysis subset to young adults showed similar patterns but higher rates of psychosis with cannabis use disorder overall. In Denver, we found that overall rates of psychosis-related visits did not increase significantly following either the Ogden memo or legalization. However, the share of psychosis visits with cannabis use disorder increased markedly during this time.

Psychosis and Psychosis with Cannabis Use Disorder Related Hospitalizations, Denver Health System, 2005-2019
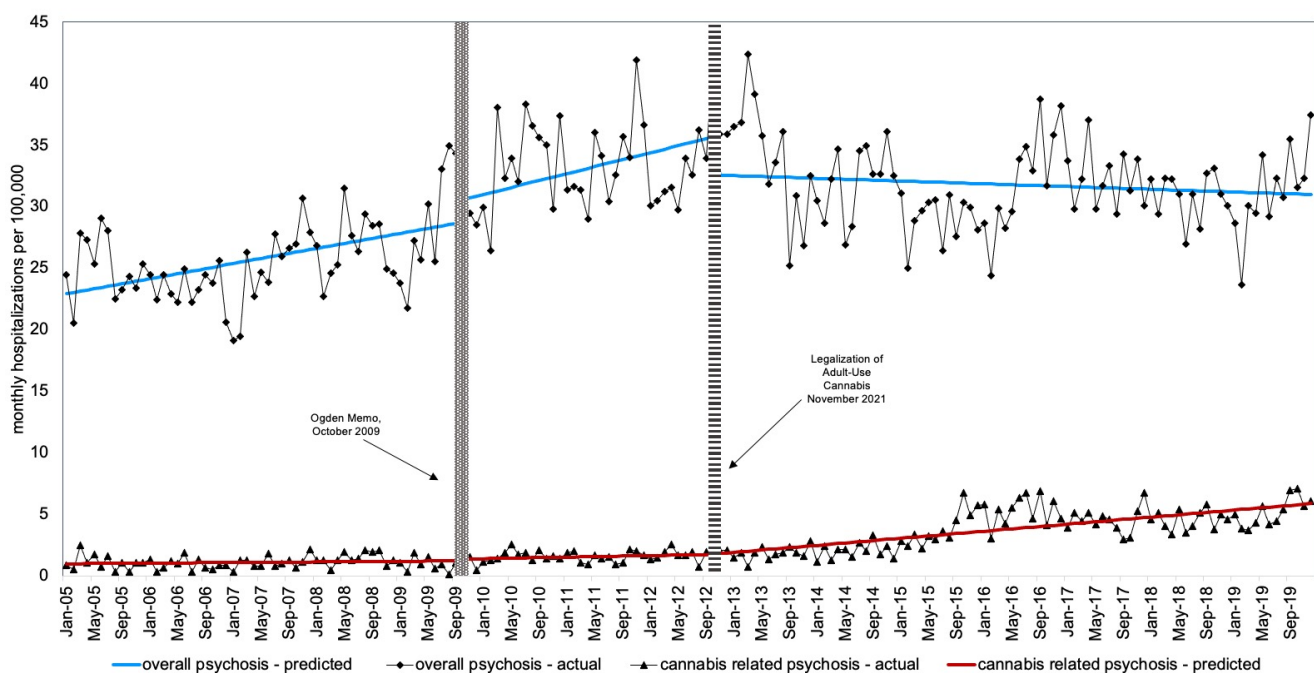
State Cannabis Legalization and Increased Rates of Psychosis Holly Elser* Holly Elser Ellicott C. Matthay Mathew V. Kiang Swapnil Mehta Jong H. Yoon William O. Faustman Keith Humphreys

Background: Psychosis is a potential consequence of cannabis use. Past studies often relied on self-report to measure cannabis use with conflicting results.

Methods: We conducted a state-level panel fixed-effects analysis using a nationwide patient-level commercial and Medicare Advantage claims database, 2003–2017. State cannabis legalization was measured for each state and month based on law type (medical or recreational) and degree of commercialization (presence or absence of dispensaries). Outcomes of interest were rates of psychosis-related claims and outpatient anti-psychotic prescriptions for each state-month. We used negative binomial regression to model outcomes as a function of state cannabis legalization, adjusted for time-varying state-level characteristics and including fixed effects for state, year, and month.

Results: This study included 75,396,344 beneficiaries. Over the study period, 29 states permitted the use of medical cannabis and 11 permitted recreational cannabis. In adjusted models, legalization and commercialization were associated with higher rates of psychosis-related claims in a dose-response manner (compared to no policy: medical, no dispensaries RR=1.17, 95% CI:0.97–1.41; medical, dispensaries RR=1.32, 95% CI:0.99–1.76; recreational, no dispensaries RR=1.61, 95% CI:1.05–2.47; recreational, dispensaries RR=1.66, 95% CI:1.14–2.43). Results for prescribed antipsychotics showed a similar pattern with attenuated magnitude (medical, no dispensaries RR=1.00, 95% CI:0.88–1.14; medical, dispensaries, RR=1.02, 95% CI:0.87–1.20; RR=1.15, 95% CI:0.87–1.53; RR = 1.19, 95% CI:0.93–1.51). Associations were stronger in men, among white and Asian beneficiaries, and those over 55 years.

Conclusion: State cannabis legalization was positively associated with psychosis-related claims, and to a lesser extent with prescribed antipsychotics, with higher rates observed in states permitting recreational cannabis and dispensaries.
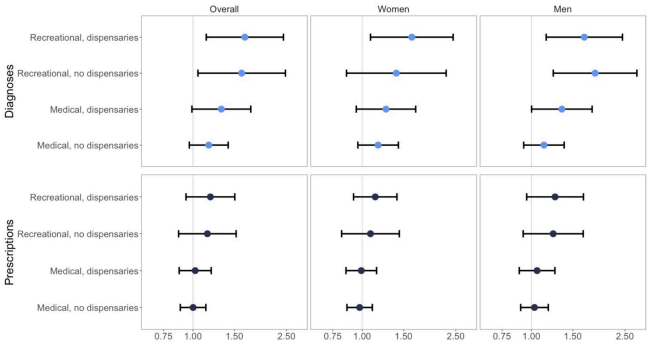

Figure. Adjust results for rates of psychosis-related diagnoses and prescriptions at varying levels of cannabis commercialization overall and by sex, 2003 – 2017. Rate ratios were calculated using negative binomial models with person-months at risk as the offset. Models were adjusted for state-level confounders including percent non-Hispanic Black, non-Hispanic Asian, and Hispanic; percent unemployed and percent renting their home; median income; and the overall claims rate. We included fixed effects for state, year, and calendar month to address spatial and temporal autocorrelation. 95% CI were calculated with robust standard errors to account for repeated observations within states over time.

**Evaluating the impacts of local cannabis policies on cannabis-related calls to the California Poison Control System** Ellicott C. Matthay* Ellicott Matthay Leyla M. Mousli Laura A. Schmidt Dorie E. Apollonio

Background: Prior research documented increases in cannabis-related calls to the California Poison Control System (CPCS) following recreational cannabis legalization. Local governments regulate many aspects of legal cannabis, yet no research has evaluated their effectiveness at preventing dangerous cannabis exposures.

Methods: We collected and coded cannabis policies for all 539 cities and counties in California and linked them to monthly cannabis exposures reported to CPCS, 2010-2020. Using g-computation-based differences-in-differences analyses, we assessed whether local policies were associated with changes in the risk of having 1 or more cannabis-related CPCS calls involving health harms (e.g., vomiting, ataxia, coma) (vs none) after: statewide legalization (November 2016), initiation of retail sales (January 2018), and the COVID-19 shelter-in-place order (March 2020).

Results: Following legalization, 77% of cities banned recreational cannabis outlets. At baseline, the monthly risk of cannabis-related CPCS calls was greater in localities that allowed recreational cannabis outlets by 2021 (0.106) compared to localities that banned them (0.013). In both localities permitting and banning outlets, CPCS calls increased after legalization, increased after retail sales initiation, and declined with the COVID-19 pandemic (Figure). However, increases were substantially larger in localities permitting outlets compared to those banning them (differences-in-differences RD for legalization: 0.080 [95% CI: 0.018,0.141]; retail: 0.030 [95% CI: -0.008,0.062]; COVID-19: -0.014 [95% CI: -0.048,0.026]). Associations were most pronounced for low-severity incidents, children under 13, and ingested products.

Discussion: Local policies restricting recreational cannabis outlets were associated with smaller increases in cannabis-related CPCS calls involving health harms under legalization. Future work will evaluate local policies restricting product types, potency, and packaging.
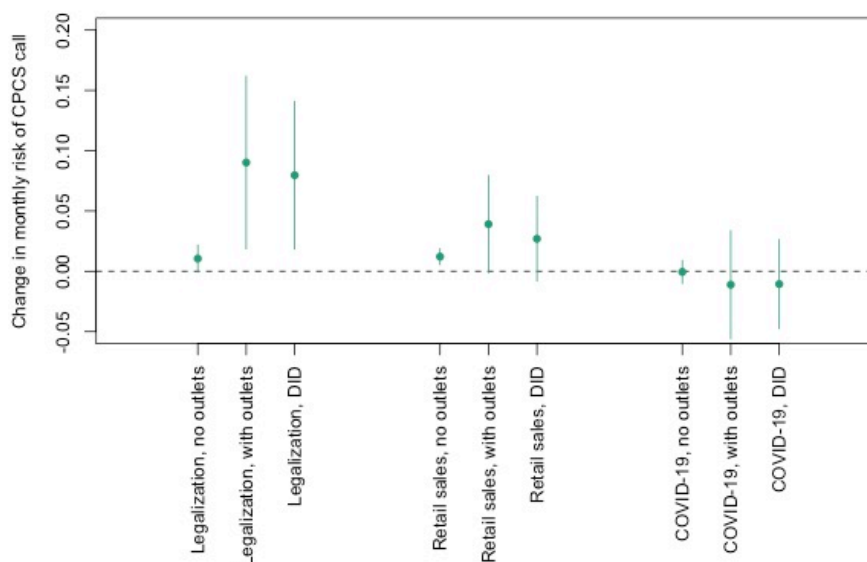
The effect of bye-weeks on injury rates in the Canadian Football League Brice Batomen*

Brice Batomen Caitlin Lee Shane Hoeber Russell Steele Ian Shrier Robert McCormack

Football injuries are common and represent a significant area of interest for teams, clinicians and spectators. Rest periods are considered important for reducing an athlete's risk of injury. We aimed to determine the effect of bye-weeks, which consist of pseudo-random assignment each season of weeks with no practices and games (1 before 2014; 2 during 2014-2017; 3 since 2018), on the Canadian Football League (CFL) injury rate. Using an historical cohort design, we analyzed CFL injury surveillance data between 2011 and 2018. We estimated Incidence Rate ratio (IRR, 95%CI) of game injury events in the week following a bye-week compared to non-bye weeks with conditional Quasi-Poisson regressions to account for overdispersion of events. This was adjusted for bye-week timing, opposing teams, and the number of players at risk as an offset. "*Team-years*" was used as the stratum to account for the differences between teams during the same year. Sensitivity analyses included computing the cumulative injury rate during the 2 and 3 weeks following a bye-week, and adjusting for the possible time varying confounding of "*Available Practice Days*" between games. The IRR including all years was 0.95 (0.86, 1.04) for injury events in the week following the bye-week, 1.02 (0.95, 1.10) for the 2 weeks following the bye-week, and 1.00 (0.94, 1.07) for the three weeks following the bye-week. Sensitivity analysis adjusting for *available practice days* yielded similar results. Results for specific years where there were only 1, 2 or 3 bye-weeks were also similar. Practice injury events were not included as we lacked data for the number of players exposed during practice. Our results suggest that in the CFL, team injury rates after bye-weeks compared to non-bye weeks are minimally reduced if at all. Bye-weeks may benefit mental health and performance outcomes, which were beyond the scope of this study. Further work looking at player injury risk while considering recurrent events is needed.

Impact of Bye weeks at the team level (Game injury events)
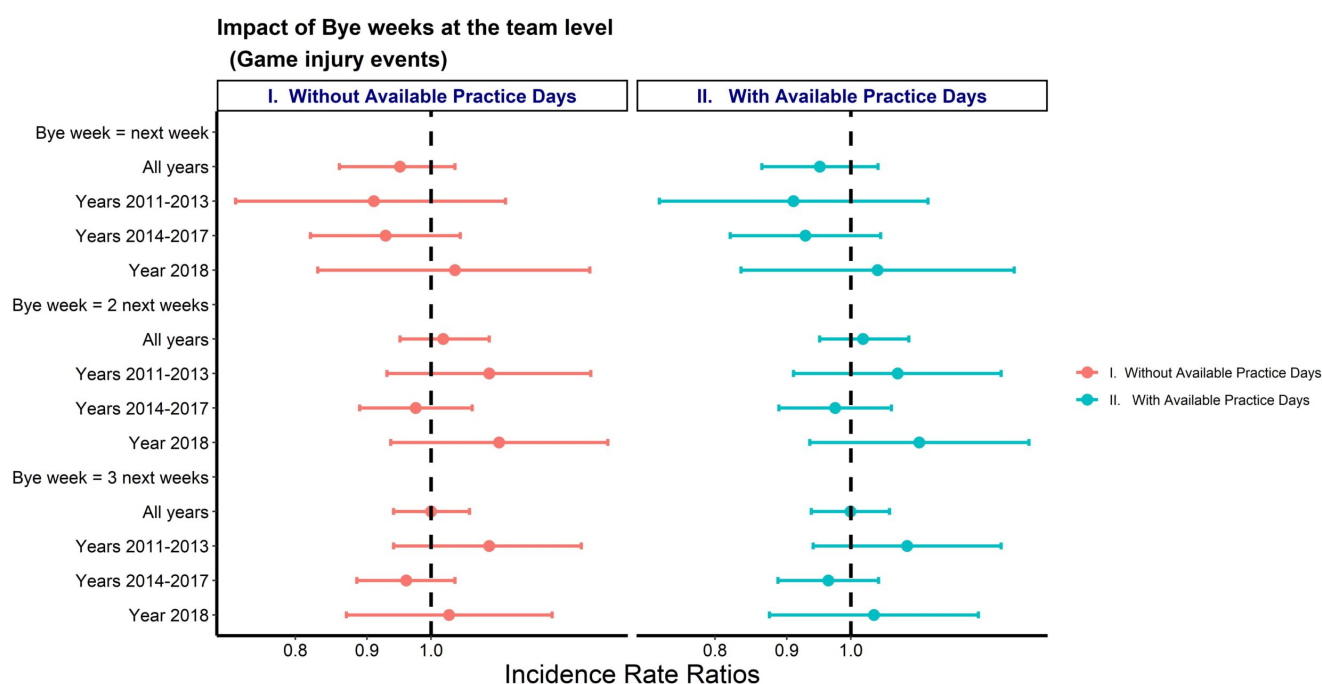
Assessment of Trends and Prevalent Methods of Suicide in Racially Diverse U.S. Adolescents (1999-2019) Victoria A. Joseph* Victoria Joseph Katherine Keyes

Study Objectives: To assess overall suicide trends and prevalent manner of suicide death by sex among racially diverse adolescents ages 10 to 19 in the United States (U.S.) from 1999-2019. **Methods:** Deaths between 1999 and 2019 coded as X60-X84, Y87.0 according to the Tenth Revision of the International Classification of Disease were included from the Centers for Disease Control and Prevention (CDC)'s National Center for Health Statistics Mortality Data on the Wide-ranging ONline Data for Epidemiologic Research (CDC WONDER). Analyses included adolescents aged 10-19, stratified by sex and race. Data were visualized using locally estimated scatterplot smoothing regression curves in SAS version 9.4. Predicted probabilities of proportions of suicide by firearm and suffocation by year by race from logistic regression models were also estimated. **Results**: Suicide rates among adolescents steadily increased from 1999 to 2019 among all racial categories. Suffocation remained the leading cause of suicide deaths overtime among all racial groups of female adolescents. Among Black female adolescents, suffocation accounted for 61% of suicide deaths in 2019. Among Black males, suicide by firearms sharply increased from 2013 to 2019, accounting for 36% of suicide deaths in 2013 and 46% of suicide deaths in 2019. Among White males, suicide by firearms increased at a slower rate accounting for 51% of suicide deaths in 2013 and 52% of suicide deaths in 2019. **Conclusion:** Findings suggest that suicide rates are increasing among American youth. Prevalence of suicide by suffocation is predominant and increasing, especially among non-white youth. One exception is the rapid increase of the proportion of suicide by firearm among Black males. These findings provide crucial information on ways in which suicide prevention efforts should target non-white populations.

Predicted probabilities of suicide by suffocation among female youth 10-19, 1999-2019
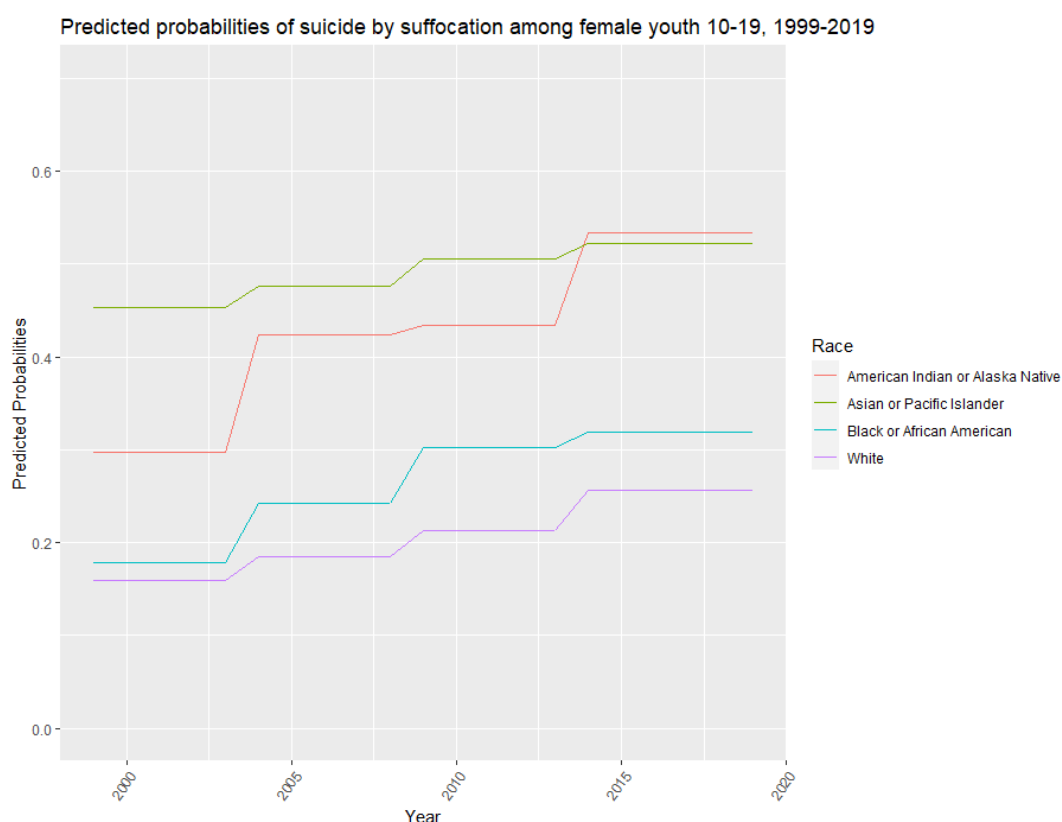
Does domestic violence legislation reduce intimate partner violence? Longitudinal evidence from 23 countries Robin Richardson* Robin Richardson Nuria Rodriguez-Planas Katjana Wiederkehr Lisa M. Bates

Many countries have recently enacted domestic violence legislation, yet the effect of this legislation on intimate partner violence (IPV) is not well-known. In this analysis, we evaluated the effect of adoption of domestic violence legislation on reported IPV across 23 low- and middle-income countries. We linked national-level domestic violence policy data with individual-level IPV data that was collected in population-based, repeated cross-sectional surveys conducted between 2000 and 2020. Presence of IPV was captured with 4 questions about physical abuse (e.g., husband ever slapped you) and 6 questions about partner controlling behaviors (e.g., husband limits contact with friends). We estimated longitudinal associations in logistic regression models that controlled for country, year, individual-level factors (marital status, age, urban or rural location, educational attainment) and time-varying country-level factors (Gini coefficient, gross domestic product, adoption of divorce legislation) and estimated variances that accounted for country-level clustering. Over the study period, 11 countries adopted domestic violence legislation. Among the 555,456 ever-married women included in the study, 26% reported ever experiencing physical abuse by their husband and 57% reported husband controlling behavior. In fully adjusted models, adoption of legislation corresponded to reductions in the prevalence of women reporting physical abuse (PR = 0.88, 95% CI: 0.72, 1.03) and controlling partner behavior (PR = 0.90, 95% CI: 0.80, 1.01), although estimates were imprecise and included the null value. An assessment of effects among specific demographic groups found especially large reductions in partner controlling behavior and physical abuse among women with at least a secondary education. Our results suggest that domestic violence legislation may reduce IPV, especially among more advantaged demographic groups.

Machine Learning Analysis of Handgun Transactions to Predict Firearm Suicide Risk

Hannah Laqueur* Hannah Laqueur Colette Smirniotis Christopher Mccort Garen Wintemute

Background: The purchase of a handgun has been shown to be associated with a substantial increase in suicide risk, and evidence suggests that limiting access to firearms among high risk individuals can be an effective means of suicide prevention. Yet accurately identifying those at risk in order to intervene remains a key challenge.

Methods: Using 4,976,391 handgun transaction records in California (1996–2015), we implement transaction-level random forest to predict firearm suicide risk. We also estimate the relative predictive importance of features in the model via permutation importance.

Results: Firearm suicide within 1 year occurred in 0.066% of handgun transactions. Our model test set AUC was 0.81. Close to 40% of observed firearm suicides were among those transactions classified in the highest risk ventile, with 95% specificity. The model performed particularly well at identifying those at extremely high risk: among the few transactions with a random forest score of 0.99, all were associated with a purchaser who died by firearm suicide within 1 year (16/16); among transactions with a score of 0.95 or higher, 24/49 were associated with a purchaser who died by firearm suicide within a year. Important predictor variables included known risk factors such as older age at first purchase, and previously unreported predictors including distance to dealer and month of purchase.

Conclusions: This is the first study to use firearm transaction records to predict suicide risk. Our results point to the potential utility of such records in identifying high risk individuals to aid suicide prevention efforts via lethal means interventions.

Impact of traffic calming measures on road traffic collisions and injuries: a longitudinal study Brice Batomen* Brice Batomen Marie-Soleil Cloutier Mabel Carabali Brent Hagel Susan Bondy Erica Di Ruggiero

Traffic calming measures (TCMs) which consist of engineering physical modifications to the road network, aim to make the roads safer. Although studies have reported reductions in road crashes and injuries tied to the presence of isolated TCMs, they have been criticized for their pre-post research designs, which can't account for the secular trend in the number of collisions, regression to the mean, collision migration and dispersion. Area-wide approaches are preferable to isolated approaches since they are not limited by collision migration and dispersion. However, previous studies are still limited by their pre-post designs. We assessed the effectiveness of an area-wide approach of TCMs using an historical cohort design. Seven TCMs (e.g., crosswalk, curb extension, diverter, speed bump, etc.) were evaluated in Montreal, Canada from 2012 to 2019; using two units of analysis: intersections and census tracts. The main outcome was serious or fatal collisions. Secondary outcomes were serious or fatal car occupants and pedestrians injuries. Lagged values of the cumulative number of TCMs were used as the independent variable, and we adjusted for the secular trend in outcomes. We estimated Odd ratios (OR), Incidence Rate ratios (IRR) and 95%CI using conditional logistic and Poisson regressions. TCMs were generally implemented in local roads, but most collisions occurred on arterial roads. Overall, TCMs did not affect the study outcomes. However, subgroup analyses of intersections on local roads suggested a 63% reduction in collisions OR:0.27 (0.07, 1.00). At the census tract level, we observed an imprecise 11% reduction in car occupants' fatal and serious injury rates IRR: 0.89 (0.74, 1.06). These results suggest that TCMs reduce serious and fatal collisions on intersections in local roads. Further work addressing the potential time-varying confounding of traffic volume, and the spatial correlation in the data is needed.

Effects of building demolitions on firearm violence in Detroit, Michigan Rose Kagawa* Rose Kagawa Benjamin Calnin Colette Smirniotis Magdalena Cerda Garen Wintemute Kara Rudolph

Rust-belt cities facing economic challenges and rapid depopulation following the 2007-2009 recession often experience high levels of firearm and other forms of violence. Within these cities, violent crime often clusters in neighborhoods affected by high levels of vacant and abandoned housing. Recent research suggests interventions to clean overgrown lots and beautify or remove dilapidated buildings may provide these cities an additional means for preventing violence.

Regression analysis has been a popular method for estimating the effects of these housing remediation interventions on crime. However, traditional regression approaches are challenged because time-dependent confounders -such as foreclosure rates – cannot be controlled for without blocking causal pathways between demolitions and violent crime, our outcome of interest.

This study estimates the effects of building demolition in Detroit, Michigan on the incidence of violent crime using detailed property-level data and longitudinal targeted maximum likelihood estimation. The primary outcomes include violent Crime Index crimes (homicide, rape, robbery and aggravated assault), defined by the Uniform Crime Report. These are considered as a whole and by firearm involvement (excluding rape as weapon involvement is not specified). Drug crimes are included as a secondary outcome. We compare the risk of experiencing each crime type following building demolition in city blocks and block groups to an estimate of the risk had there been no demolition in the 1-3 quarters prior in 2017.

There were more than 2600 total demolitions in about 1700 blocks in 2017 in Detroit. Nearly all demolished buildings were sourced from tax foreclosures. Our estimates suggest the risk for all crime types tested would have been statistically indistinguishable from the observed crime risk had demolitions in the prior 1-3 quarters of 2017 not occurred.

Our results run counter to most previous research on this topic, which tends to show a protective effect of demolition on violent crime. Understanding the cause of these distinct results may be critical to designing and targeting demolition programs.

Figure 1. Demolitions and violent, firearm-involved crimes in Detroit (2017)

Blocks receiving demolition in 2017
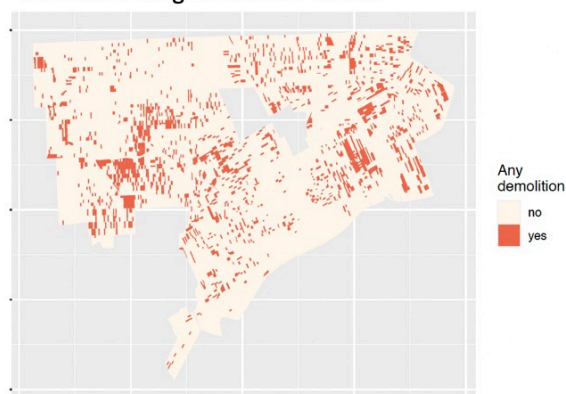
Count of firearm crimes by block in 2017

Understanding the Causal Effect of HIV Prevention Mass Media Campaigns on HIV Incidence: Towards a Refined Analytical Approach Jiajun Lui* Raquel Burgess Esther Luo Tiffany E. Chang José Miguel Aravena Castro Jiajun Luo Zeyan Liew Yusuf Ransome

Background: Inadequate knowledge about the use, availability, and benefits of preventive measures for HIV such as pre-exposure prophylaxis (PrEP) remains a barrier to reducing HIV incidence in America. In particular, a lack of education about HIV prevention may be highest amongst people who are most susceptible to HIV risk due to structural conditions. Mass media campaigns, which disseminate educational content using broadcast, print, and digital media, are an efficient intervention because of their wide reach and low costs. These campaigns aim to improve knowledge, shift attitudes towards preventive measures, and ultimately alter health behaviors to reduce disease incidence.

Problem: However, there is limited evidence of the causal effect of HIV prevention communication campaigns on subsequent HIV incidence. If evidence of a causal relationship could be better established, public health professionals may be able to garner more support and funding for HIV prevention communication programs.

Proposed Solution: In this presentation, we discuss methodological challenges in investigating the relationship between HIV prevention communication and HIV incidence, such as the characteristics of the causal pathway and the difficulty in identifying a valid comparison group. We also review past efforts, including observational studies, randomized controlled trials, and quasi-experimental designs, that aim to characterize the relationship between communication, subsequent changes in health behavior, and HIV incidence. Finally, we propose a new analytic approach to investigate the causal relationship which includes identifying mediating and confounding variables, using non-randomized study designs (i.e., difference-in-differences method), overcoming measurement issues by using variables less prone to bias, and utilizing innovative analytic methods (i.e., mediation analysis; g-computation) to better understand the relationship between prevention communication and HIV incidence.

Patterns of Pre-Exposure Prophylaxis (PrEP) Use in a Population Accessing PrEP in Jackson, Mississippi Erin Chase* Erin Chase Kendra Johnson Mariah Prather Christine Khosropour

Background: Pre-exposure prophylaxis (PrEP) persistence and retention in care is suboptimal in the United States. In the Deep South, a region with high rates of new HIV diagnosis, factors associated with PrEP discontinuation remain unexplored.

Methods: We evaluated data from a clinic-based PrEP program in Jackson, Mississippi. PrEP was offered to patients starting in August 2018. We included patients initiating PrEP by April 2021 and followed patients through August 2021. We considered patients to have disengaged from PrEP if there was a period of at least 30 days without an active PrEP prescription; we defined those restarting PrEP after a 30 day gap as 'stopped and later restarted' and those who did not obtain a new PrEP prescription as 'stopped and did not restart'. Patients without a gap in PrEP prescription were considered 'continuously on PrEP'. Kaplan-Meier methods were used to estimate median time to first PrEP discontinuation, censoring at the end of analysis period. Cox proportional hazards regression was used to examine factors associated with time to first PrEP discontinuation.

Results: 171 patients received an initial 90-day PrEP prescription; 75% were assigned male at birth, 74% identified as Black and 8% were diagnosed with syphilis at baseline. The median time to first discontinuation was 90 days (95% CI=90-114). 22% of patients were continuously on PrEP during the analysis period, 28% stopped and later restarted and 50% stopped and did not restart. From the Cox model, associations with early PrEP stoppage were notable for patients aged 17-24 years vs over 35 (adjusted hazard ratio [aHR]=1.6, 95% CI=0.9-2.6), assigned female vs male (aHR=1.6, 95% CI=1.0-2.5) and living over 25 miles away vs 0-10 miles (aHR 1.89, 95% CI=1.2-3.0).

Conclusions: PrEP persistence was suboptimal, and most patients never refilled a PrEP prescription. Additional interventions tailored to young patients, women, and those living far from providers are needed to improve retention.

Improving Accessibility of HIV Testing Sites Using Location-Allocation Analysis Jessica Webster* Jessica Webster Neal Goldstein Lorna Thorpe Dustin Duncan

As the first step in the HIV care continuum, timely diagnosis is central to reducing transmission of the virus and ending the HIV epidemic. This necessitates adequate testing facilities in locations accessible to individuals living with HIV and unaware of their status, or individuals at risk of becoming infected. Studies have shown that convenience of and distance from a testing site are essential for ease of access to services and educational material. We sought to improve allocation of existing HIV testing sites in Philadelphia, Pennsylvania through location-allocation analyses using publicly available data on HIV prevalence, testing site location, and factors related to risk of infection.

The ArcGIS Location-Allocation analytic tool was used to calculate optimal locations for HIV testing sites using a method that maximizes coverage of facilities based on ZIP code level demand. To target individuals living with HIV and unaware, demand was specified based on percentage of late diagnoses. Driving time and distance from demand points to facilities were used to determine appropriate facility allocation, and a cutoff of 15 minutes driving time was used as a maximum; no threshold was specified a priori for distance.

37 existing facilities were located in 20 (43%) Philadelphia ZIP codes. Our model proposed re-allocating to 22 (47%) ZIP codes when using percent late diagnoses to define demand (Figure). On average, this reallocation would reduce distance to the facilities by 31% and travel time to the facilities by 31% compared to existing locations.

HIV testing should be readily accessible to anyone at risk of infection, and especially to those who may be living with HIV and unaware of their status. Our results propose a wider distribution of HIV testing services across Philadelphia. Reducing the distance and time it takes to reach an HIV testing facility may improve the likelihood of testing, and in turn, increase the percentage of people with knowledge of their status.

Figure. Proposed and existing HIV testing site locations in Philadelphia, Pennsylvania, based on location-allocation analysis using percent late diagnoses within a ZIP code to define demand.
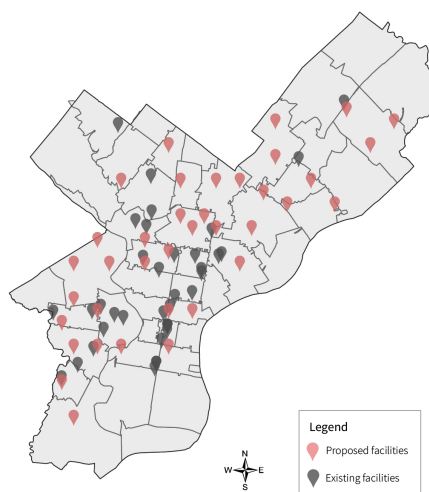
HIV Service Organization Availability in Ending the HIV Epidemic Jurisdictions Jessica
Webster* Jessica Webster Edward Gracely Lorna Thorpe Dustin Duncan Neal Goldstein

The Ending the HIV Epidemic (EHE) initiative's goal of reducing new HIV cases depends upon the
capacity of the health system to prevent, diagnose, and treat infections. Implicit in this goal is the
availability of HIV prevention and treatment services across priority jurisdictions. We sought to
quantify the association between HIV service organizations and HIV burden in EHE priority
jurisdictions.

We linked per capita data on 6 HIV metrics and number of HIV service organizations (n=10,627)
across the 57 priority jurisdictions, which includes 48 counties, the District of Columbia, San Juan
Municipio in Puerto Rico, and 7 entire states. HIV metrics included prevalence, incidence, percent
aware of status, percent linked to care, percent virally suppressed, and percent on pre-exposure
prophylaxis (PrEP). HIV service organizations were categorized as delivering testing or prevention
services (n=10,606) and/or care and treatment services (n=2,500). Linear models were used to
regress the number of HIV service organizations on the various HIV metrics.

Both metrics "percent aware of status" and "percent on PrEP" were positively correlated with per
capita number of testing or prevention organizations adjusting for jurisdiction size (Figure). On
average, states tended to have more testing or prevention organizations compared to the smallest
counties adjusting for HIV metrics. Only the "prevalence" metric was positively correlated with
number of care and treatment organizations adjusting for jurisdiction size. However, on average,
larger counties tended to have fewer care and treatment organizations compared to smaller counties
and adjusting for HIV metrics.

Intuitively this suggests that jurisdictions with better HIV metrics also have more HIV service
organizations, and vice-versa. Paradoxically we found several jurisdictions that had better HIV
metrics also had comparatively fewer organizations, and several that had worse HIV outcomes also
had comparatively more organizations.

Figure. Ecologic plots for HIV testing or prevention service
organizations (per 100,000 people) and their association
with percent aware of positive HIV status **(A)** and percent
prescribed PrEP **(B)**; and plots for HIV care and treatment
organizations (per 100,000 people) and their association
with prevalence of HIV (per 1,000 people) **(C)** for Ending
the HIV Epidemic priority jurisdictions in the U.S. Lines of
best fit and 2 times the standard error of the estimate
(shaded) are shown based on a linear model regressing
HIV service organizations on the individual HIV metrics
adjusting for jurisdiction size.

HIV / STI
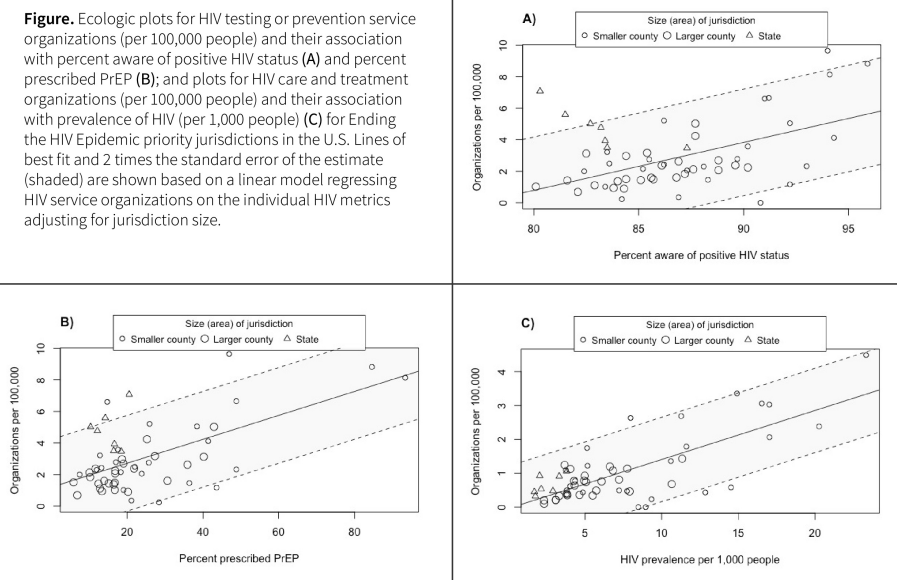
Syndemic Profiles of Human Papillomavirus (HPV) Infection in United States Adults Ashley V. Hill* Ashley Hill Camillia R. Comeaux Brandie D. Taylor Levent Dumenci Abbey B Berenson

Background: Human Papillomavirus (HPV) is prevalent, impacting roughly 40% of the United States population. From 2012-2016, HPV accounted for 79% of cervical, vaginal, vulvar, anal, penile and oropharyngeal cancers and roughly 92% of HPV-related cancers were caused by HPV subtypes targeted by the HPV vaccine. Syndemic factors may influence HPV risk and severity but have not been explored in national cohorts. This study sought to identify syndemics of HPV infection in a nationally representative sample of US adults.

Methods: Data were from 6,004 participants ages 18-59 in the NHANES 2013-2014 and 2015-2016 cycles. Frequencies, percentages, and prevalence ratios of demographic characteristics were calculated for both positive and negative HPV status. A Latent Class Analysis (LCA) examined measures of socioeconomic status, depression, substance use, and sexual behavioral variables. Models were stratified by gender and race/ethnicity and multi-group LCA tested measurement invariance.

Results: HPV prevalence was 43%; prevalence of HPV was higher in non-Hispanic Black (PR=1.55, CI 95% 1.55 – 1.55), unmarried individuals (PR=1.69, CI 95% 1.69 – 1.69), and those from lower socioeconomic backgrounds (PR=1.20, CI 95% 1.20 – 1.20). Among women, the syndemic included oral and anal sex, same sex partners, older sex partners, having another STI, any substance use and depression (Figure 1a). The syndemic for men included oral sex, anal sex, same sex partners and testing positive for other STIs (Figure 1b).

Conclusion: While HPV rates have decreased among US adults, actionable strategies to improve vaccine uptake have stalled. Results confirmed evidence of a unique syndemic related to HPV prevalence and suggest addressing substance use and mental health along with sexual behaviors may reduce HPV infection. Additionally, while targeting 11-12 years old is optimal, increasing vaccination messaging among young adults aged 18-24 may be one immediate strategy to improve uptake.

Running headline: Syndemic Profiles of HPV

Figure 1a. Three Class LCA Solution and Membership Probabilities for Women, NHANES 2011-2016
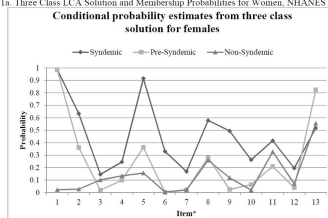
*Item numbers correspond with the following variables: (1) Oral sex; (2) Anal Sex; (3) Same sex partners in past year (1+); (4) Other STI (Chlamydia, HSV or HIV); (5) Ever marijuana use; (6) Ever other drug use; (7) Binge drinking excessive alcohol use; (8) HPV infection; (9) Tobacco use; (10) # of partners in past year (2+); (11) Sex partners 5 years or older (1+); (12) Depression (**females only**); and (13) Age at first sex (<15, ≥15) [**item 12 for male**]

Figure 1b. Three Class LCA Solution and Membership Probabilities for Males, NHANES 2011-2016
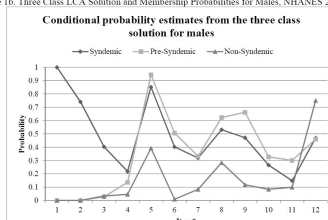
*Item numbers correspond with the following variables: (1) Oral sex; (2) Anal Sex; (3) Same sex partners in past year (1+); (4) Other STI (Chlamydia, HSV or HIV); (5) Ever marijuana use; (6) Ever other drug use; (7) Binge drinking excessive alcohol use; (8) HPV infection; (9) Tobacco use; (10) # of partners in past year (2+); (11) Sex partners 5 years or older (1+); (12) Depression (**females only**); and (13) Age at first sex (<15, ≥15) [**item 12 for males**]

Long term psychotic disorder and chronic kidney disease: a population-based longitudinal descriptive study OU HSIANG HUA* HSIANG HUA OU Sun Chien An Chou Yu Ching

Background: Chronic kidney disease (CKD) is the first leading cancer in Taiwan. Psychotic disorder has been recognized as potential risk factor in developing disease. However, secular trend studies of CKD with psychotic disorder are limited. This descriptive study examined the incidence of CKD with psychotic disorder in a large-scale, population-based Taiwanese cohort.

Methods: From 2000 to 2008, 77,17 new cases with psychotic disorder were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating incidence rates in different sex, age groups and periods. For long term trends, we followed up until December 31, 2013.

Results: The incidence of CKD was 87.54 among psychotic disorder patients per 10,000 person-years. The incidence rate was 80.14 among men and 95.83 among women per 10,000 person-years. The incidence rate of CKD was higher in women. After stratifying age into 5 groups, we found that the incidence rate of psychotic disorder per 10,000 person-years was 36.43 in 20-29 years old, 66.01 in 30-39 years old, 107.44 in 40-49 years old, 132.62 in 50-59 years old and 140.27 in ≥60 years old. Patients have higher incidence rate of CKD when age is increasing. Also, incidence of CKD was 56.59, 103.31, 88.41, 75.77 and 84.25 by visiting 0 time, ≤6 times, 7-32 times, 33-125 times and ≥126 times in psychotic disorder clinical visits respectively.

Conclusion: In the past 14 years, the incidence rate of psychotic disorder had a profound impact on our life. By means of the big data, our finding suggested incidence rate of CKD with psychotic disorder is steadily rising. Thus, the study indicated a positive correlation between psychotic disorder and CKD. The understanding of mechanisms is needed to confirm in the future.

Keywords: Chronic kidney disease (CKD), National Health Insurance Research Database (NHIRD), Psychotic disorder.

Global Health

Association of short-term wealth change with cognitive function among older adults in China, England, Mexico, and the United States, 2012-2018 Tsai-Chin Cho* Tsai-Chin Cho Xuexin Yu Alden L. Gross Yuan S. Zhang Lindsay C. Kobayashi
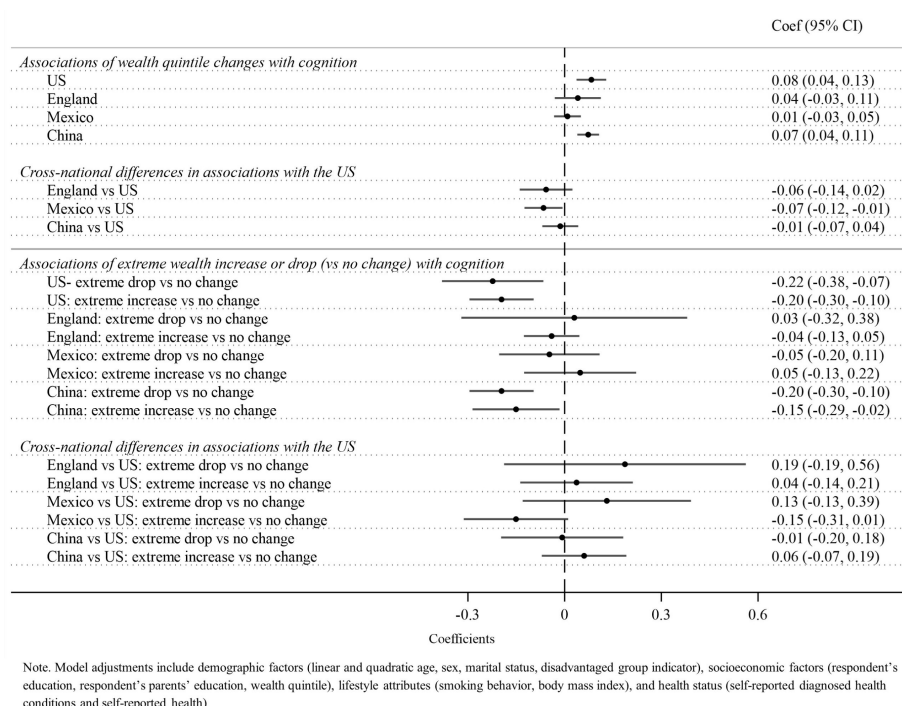
Background: Household wealth is positively associated with later-life cognitive health. However, little is known about the effects of changes in wealth in later life and whether they differ across populations from middle- and high-income contexts. We evaluated the relationships between short-term wealth change and subsequent cognitive function among adults aged ≥65 years in four countries, and whether the association differed by country.

Methods: We used total household wealth data from core interviews of the US Health and Retirement Study (HRS) and its partner studies in China, England, and Mexico. Harmonized cognitive function data were collected in each study's Harmonized Cognitive Assessment Protocol (HCAP) (N=8,175 aged ≥65 years). Wealth change was defined as changes in within-population wealth quintile rank (range: -4 to 4) and extreme wealth shocks of ≥75% increase and ≥75% drop in wealth, over a 3-year period for China and Mexico and a 4-year period for England and the US. Subsequently, harmonized general cognitive performance (GCP) was assessed from the HCAP in each country using factor analysis (mean: 0, standard deviation: 1) of neuropsychological batteries. We used sampling-weighted, multivariable-adjusted linear models to examine associations.

Results: Declining wealth (per quintile) was associated with low GCP factor scores in the US and China, while similar yet non-statistically significant relationships were observed in England and Mexico. Further, associations were weaker in Mexico than in the US. For extreme wealth increases and drops of ≥75%, they were both associated with lower GCP scores in the US and China, but not England or Mexico (Figure 1).

Conclusions: Short-term wealth decreases in later life were associated with poor cognitive health in the US and China but not England and Mexico. The impact of later-life wealth changes on cognitive health may vary by macro-level social and economic structures that require further investigation.

	Coef (95% CI)
Associations of wealth quintile changes with cognition	
US	0.08 (0.04, 0.13)
England	0.04 (-0.03, 0.11)
Mexico	0.01 (-0.03, 0.05)
China	0.07 (0.04, 0.11)
Cross-national differences in associations with the US	
England vs US	-0.06 (-0.14, 0.02)
Mexico vs US	-0.07 (-0.12, -0.01)
China vs US	-0.01 (-0.07, 0.04)
Associations of extreme wealth increase or drop (vs no change) with cognition	
US- extreme drop vs no change	-0.22 (-0.38, -0.07)
US: extreme increase vs no change	-0.20 (-0.30, -0.10)
England: extreme drop vs no change	0.03 (-0.32, 0.38)
England: extreme increase vs no change	-0.04 (-0.13, 0.05)
Mexico: extreme drop vs no change	-0.05 (-0.20, 0.11)
Mexico: extreme increase vs no change	0.05 (-0.13, 0.22)
China: extreme drop vs no change	-0.20 (-0.30, -0.10)
China: extreme increase vs no change	-0.15 (-0.29, -0.02)
Cross-national differences in associations with the US	
England vs US: extreme drop vs no change	0.19 (-0.19, 0.56)
England vs US: extreme increase vs no change	0.04 (-0.14, 0.21)
Mexico vs US: extreme drop vs no change	0.13 (-0.13, 0.39)
Mexico vs US: extreme increase vs no change	-0.15 (-0.31, 0.01)
China vs US: extreme drop vs no change	-0.01 (-0.20, 0.18)
China vs US: extreme increase vs no change	0.06 (-0.07, 0.19)

Coefficients

Note. Model adjustments include demographic factors (linear and quadratic age, sex, marital status, disadvantaged group indicator), socioeconomic factors (respondent's education, respondent's parents' education, wealth quintile), lifestyle attributes (smoking behavior, body mass index), and health status (self-reported diagnosed health conditions and self-reported health)

Circular migration and initial viral suppression among adults living with HIV: a survival analysis of a population-based cohort in rural north-eastern South Africa Rachel Yorlets*
Rachel Yorlets Hae-Young Kim Adrian Dobra Nina Joyce Maxime Inghels Kobus Herbst Dickman Gareta Mark Lurie Frank Tanser

Background: Circular migrants are one of the few remaining high-risk sub-groups within South Africa's generalised HIV epidemic, yet little is known about their HIV care utilisation patterns over space and time. We aim to quantify the effect of migration on the time to achieving initial viral suppression after treatment initiation.

Methods: We use data from 2011–2018 from the Africa Health Research Institute's surveillance system in the high HIV prevalence (> 30%) setting of KwaZulu-Natal province. Our exposure was circular migration events, defined as a person's temporary within-country change of residence from their permanent household; events were measured in frequency, duration, distance, and geo-clustering of destination. Our outcome was initial viral suppression defined as < 1500 viral copies/microliter of blood. Study follow-up began six months after ART initiation ('baseline') and continued until participants achieved suppression, or were censored by death, loss to follow-up, or study end (December 31, 2018). We adjusted for age, sex, education, cohabitation, and socioeconomic index. We used inverse probability-of-censoring weights to adjust for out-selection bias.

Results: Within the analytic sample (n=1,788), at baseline, the mean age was 35, 79% were female, 72% had a secondary education or higher, 81% were married/cohabiting, and the mean socioeconomic index was 2.59. Overall, 58% (n=1029) of the cohort achieved viral suppression: 95% of suppression events occurred among never-migrants, and 5% occurred among one-time migrants (Figure 1). No one with the maximum of two migration events achieved viral suppression. Preliminarily, we found that the hazard of viral suppression was 60% lower for one-time migrants compared to never-migrants, adjusting for confounding.

Discussion: Initial findings suggest that persons who migrate have a higher risk of not achieving initial viral suppression compared to their non-migrant counterparts.

Fig 1: Unadjusted survival estimates by migration event frequency
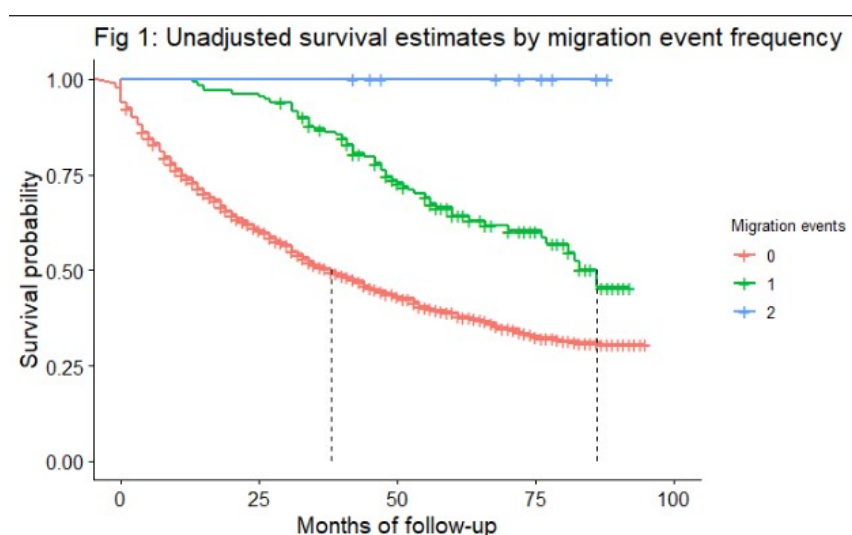
Concordance of diabetes and hypertension among married couples in India: an analysis of nationally representative data Jithin Sam Varghese* Jithin Sam Varghese Shivani Patel

Background: Married couples may share chronic disease risk, and risk clustering may inform interventions. Little is known about risk clustering among couples in India, where chronic diseases are rapidly rising. We investigated spousal concordance in diabetes and hypertension in Indian adults.

Methods: Data were from 57,657 heterosexual married couples (women: 18-49y, men: 21-54y) assessed in the nationally representative National Family Health Survey-IV (2015-16; assessments shown in **Figure**). We estimated the prevalence of concordant diabetes and hypertension, separately, and estimated the prevalence ratio (PR) and 95% CI describing the association of disease status between spouses using survey-weighted Poisson regression with robust standard errors and state fixed effects. Prevalence ratios were also estimated by socio-demographic group: age, rurality, household wealth, and religion.

Results: Nationally, the prevalence of diabetes and hypertension were greater in men (diabetes: 5.4%, hypertension: 27.0%) than women (diabetes: 3.1%, hypertension: 19.8%). The prevalence of concordant diabetes (observed: 0.4%, expected: 0.2%) and concordant hypertension (observed: 9.0%, expected: 5.4%) among spousal dyads was higher than expected by chance alone. Nationally, spouse's disease status was positively associated with own disease for both diabetes (husband's status: PR=1.4 [1.2, 1.6]; wife's status: PR=1.3 [1.2, 1.5]) and hypertension (husband's status: PR=1.7 [1.6, 1.8]; wife's status: PR=1.6 [1.5, 1.6]). Accounting for socio-demographic factors, diabetes status between spouses was positively associated in couples that were mean age <40, bottom 80% of household wealth, rural, and Hindu. Hypertension status between spouses was positively associated across all socio-demographic strata for hypertension (**Figure**).

Conclusion: There is substantial chronic disease concordance in Indian couples. This presents opportunities for novel dyadic preventive and treatment interventions.

Figure: Association of diabetes and hypertension among married couples in India, 2015-16
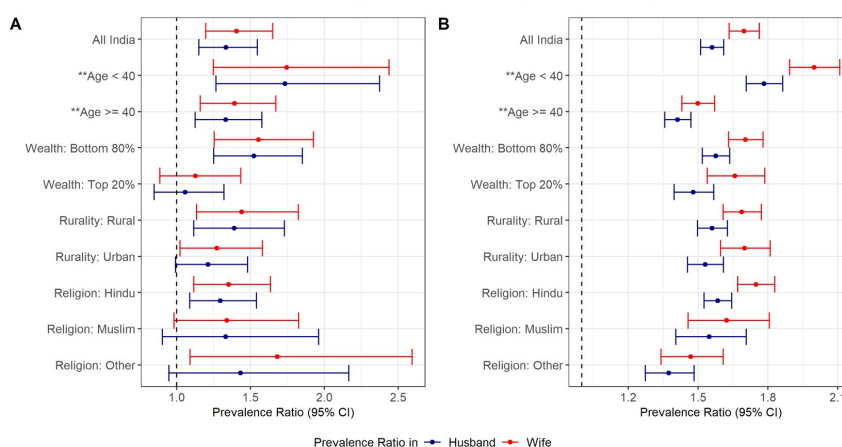
Association of spousal disease status with own disease status for panels A: Diabetes: diagnosed or ≥126/200 mg/dL in fasting/non-fasting (n = 54462); and B: Hypertension: diagnosed or ≥140/90 mmHg (n = 54801).
All models adjusted for individual (age, schooling, body mass index, alcohol and smoking status), partner (schooling, BMI, alcohol and smoking) and household (caste, religion, rurality, wealth quintile) factors and a state fixed-effect. ** Mean age of couple

Longitudinal relationships between childbearing and depressive symptoms in adolescent girls and young women in rural South Africa (HPTN 068 cohort) Helen O. Pitchik* Helen Pitchik Esther O. Chung Nivedita L. Bhushan Kathleen Kahn Francesc Xavier Gómez-Olivé Jennifer Ahern Joanna Maselko Audrey E. Pettifor

Background

Little is known about patterns of depressive symptoms over the prenatal period among adolescent girls and young women (AGYW). We aim to distinguish between pre-pregnancy depressive symptoms and depressive symptom changes postpartum in a longitudinal cohort of AGYW in rural South Africa.

Methods

The study uses data from AGYW enrolled in the HIV Prevention Trials Network 068 study in rural Mpumalanga Province, South Africa. AGYW were assessed up to 6 times between 2012-2019 (age 14-24). Depressive symptoms were measured with Center for Epidemiologic Studies Depression Scale (CES-D). We estimated adjusted mean differences in CES-D scores between AGYW who gave birth during the study period and frequency age-matched controls at three time points: pre-pregnancy (T1), conception to age one (T2), and early childhood (1-5 years old) (T3). Analyses were conducted using parametric g-computation with demographic controls.

Results

The sample includes 706 AGYW with at least three eligible CES-D scores, 37% of whom gave birth during the study period. Preliminary results show that at all time points, AGYW who gave birth during the study had higher CES-D scores than age-matched controls (adjusted mean differences at T1: 1.69 [95%CI: 0.35, 3.01]; T2: 2.23 [1.10, 3.50]; T3: 0.92 [-0.12, 1.84]. In longitudinal analyses, adjusting for CES-D score at T1 to distinguish post-conception depression symptom changes, elevations in CES-D score at T2 and T3 remained, but were attenuated (T2: 1.48 [0.33, 2.67]; T3: 0.62 [-0.35, 1.53].

Conclusion

Among AGYW in South Africa, childbearing was associated with increased depressive symptoms pre-pregnancy and in the first year of life (even after adjustment for pre-pregnancy symptoms). Our results highlight the importance of taking into consideration depressive symptoms pre-pregnancy and also indicate the importance of intervention on depression prior to conception as well as postpartum. Next steps include re-analyzing using censoring weights.

Pharmacoepidemiologic Screening to Identify Drug Interaction Triads: A Real-World Application in Skeletal Muscle Relaxants Users Cheng Chen* Cheng Chen Sean Hennessy Colleen M. Brensinger Emily K. Acton Warren B. Bilker Todd A. Miano Thanh Phuong Pham Nguyen Samantha E. Soprano Charles E. Leonard

Background
Drug interactions are responsible for one-third of all adverse drug events, yet receive little study before a drug's approval. Given the enormous number of drug combinations, high-throughput epidemiologic approaches are needed to identify and prioritize those of potential clinical importance. Skeletal muscle relaxants (SMRs) are commonly co-prescribed with potentially interacting medications that may contribute to iatrogenic unintentional traumatic injury. We utilized real-world healthcare data of SMR users to generate signals of drug triads, i.e., drug-drug-drug interactions (3DIs), associated with traumatic injury.

Methods
Using 2000-19 Optum health insurance data, we conducted thousands of self-controlled case series studies, one for each combination of SMR + concomitant drug (i.e., base pair). Subjects were age ≥16 years with an injury during base pair-exposed observation time, during which we evaluated (as candidate interacting precipitants) all oral medications co-dispensed with the base pair. We used conditional Poisson regression to compare injury rates during base pair observation time exposed vs. unexposed to the candidate interacting precipitant, and calculated confounder-adjusted rate ratios (RRs) with 95% CIs. We accounted for multiple estimation via semi-Bayes shrinkage.

Results
Among 58,478 drug triads examined, 29 were positively associated with injury and therefore deemed potential SMR 3DI signals. Confounder-adjusted RRs ranged from 1.39 (1.01–1.91) for tizanidine + omeprazole + gabapentin (vs. tizanidine + omeprazole) to 2.23 (1.02–4.87) for tizanidine + diclofenac + alprazolam (vs. tizanidine + diclofenac). Most signals are novel yet biologically plausible.

Conclusions
Using high-throughput robust pharmacoepidemiologic methods, we identified 29 SMR 3DIs of potential clinical concern. These hypothesis-generating findings can help target future etiologic investigations of specific SMR drug interactions.
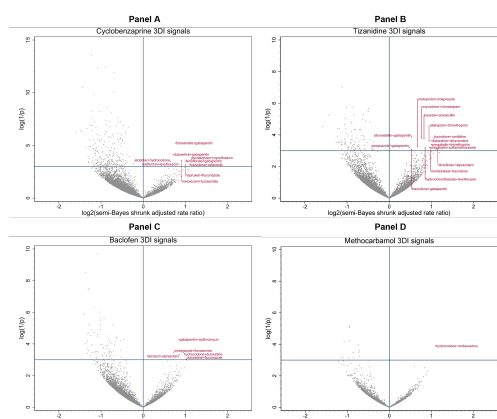
How to win the war of exposure trends in a case-crossover design? An empirical example on the association between phentermine and risk of major cardiovascular events Amir Sarayani* Amir Sarayani Christian Hampp William T. Donahoo Joshua D. brown Almut Winterstein

Obesity is a highly prevalent disease in the US, with few pharmacotherapy options, including phentermine, the most common obesity management drug. There are concerns about phentermine's cardiovascular effects, and no large randomized clinical trial has addressed this knowledge gap. We conducted a case-crossover study in MarketScan® Research Databases (2005-2019) to evaluate the association between short-term phentermine use and major adverse cardiovascular events (MACE). The outcome was defined as acute myocardial infarction, stroke (ischemic or hemorrhagic), or in-hospital cardiovascular death. We identified 325,927 MACE cases with insurance benefits for at least six months before the event. We defined the risk, wash-out, and control windows in two-month increments before the event and considered a study window as "exposed" when at least one day of supply for phentermine was present. We varied window length and changed the exposed definition to prescription fill in sensitivity analyses. Considering the seasonal and temporal trends in phentermine use, we conducted a case-time-control analysis and a case-case-time-control analysis to improve effect estimation. In the primary analysis, 405 cases had exposure to phentermine in any window before MACE (262 acute myocardial infarctions, 133 strokes, 10 in-hospital cardiovascular deaths). The adjusted conditional odds ratio was 0.75 (0.57, 0.98) in the case-crossover analysis, 0.68 (0.50, 0.91) in the case-time-control analysis, and 0.97 (0.55, 1.71) in case-case-time-control analysis. Sensitivity analyses confirmed robustness in primary findings. In this pharmacoepidemiologic study, short-term exposure to phentermine was not associated with a higher risk of MACE. Although case-crossover and case-time-control suggested a protective effect, this is likely due to a temporal trend prior to MACE and residual confounding that were addressed using a case-case-time-control design, but the effect estimate was less precise.
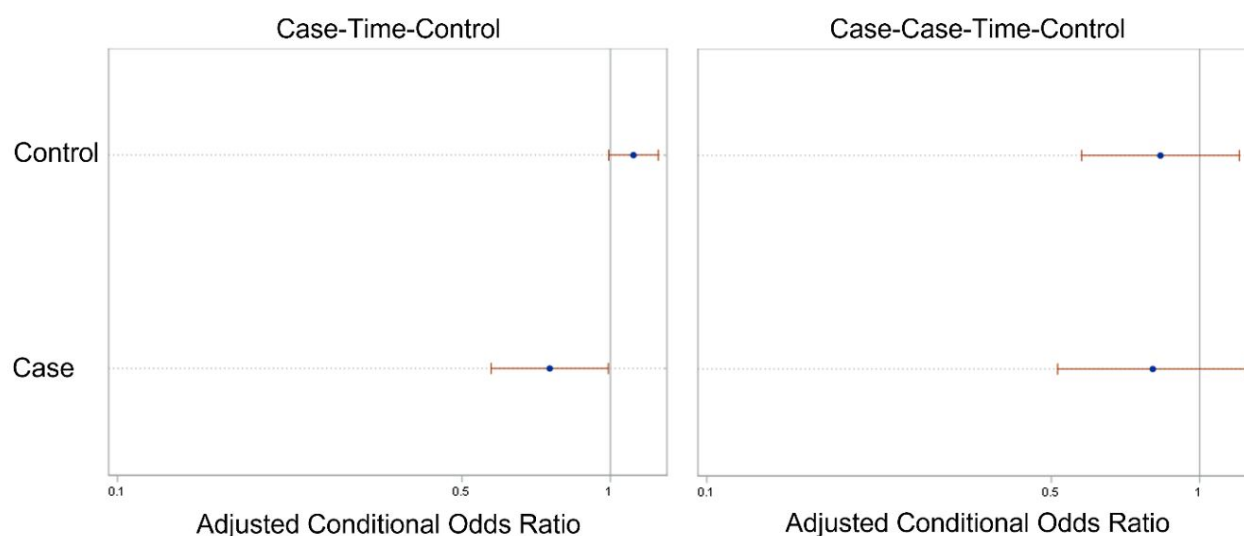

Figure 1. Adjusted Conditional Odds Ratio Stratified by The Case/Control Status in Extended Case-crossover Designs

Association of cognitive enhancers and the risk of incident seizure in patients with dementia: a nationwide population-based study Woo Jung Kim* Woo Jung Kim Junghee Ha Nak-Hoon Son

Background: While individuals with dementia have a high risk of developing seizures, it is unknown whether cholinesterase inhibitors, which are commonly prescribed to treat individuals with dementia, are associated with seizure. This study aims to investigate the risk of incident seizure following the use of cholinesterase inhibitors in patients with dementia.

Methods: A nationwide, nested case-control study was conducted with data from the Korean Health Insurance Review and Assessment Service from 2014 through 2018. A total of 13,767 participants ages 65-95 years with incident seizure were matched for medical comorbidities, and drug exposure for a control group of 39,084 participants. Odds ratios (ORs) and 95% confidence interval (CI) for seizure incidence according to cholinesterase inhibitors use were analyzed using a multivariable conditional logistic regression model.

Results: The study examined the incidence of seizures within one year after receiving cognitive enhancers in patients diagnosed with dementia. Cholinesterase inhibitors use was associated with an increased risk of seizure compared to memantine (aORs [95% CI] for donepezil, 1.11 [1.01-1.22], rivastigmine, 1.31 [1.09-1.57], and galantamine, 1.19 [1.01-1.41]). However, stratification by age and sex, and sensitivity analysis to different drug exposure times did not exhibit significant association between cholinesterase inhibitors use and late-onset seizure.

Conclusions: Our findings suggest that there is no immediate increase in the risk of seizure with cholinesterase inhibitors use; however, it did increase the risk of the seizure in dementia patients after one year of continued medication intake. This suggests that it is more likely to be the result of degenerative changes due to the progression of dementia rather than the effects of the medication itself.
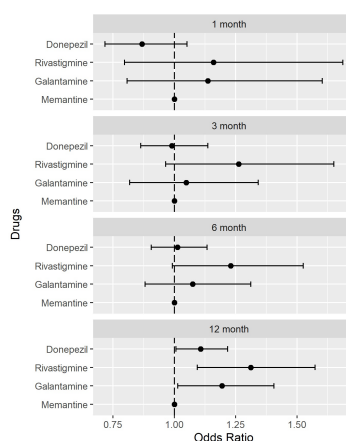
Impact of oral anticoagulant class on adherence in patients with atrial fibrillation: A 23-year population-based cohort study in Canada Peter Loewen* Shahrzad Salmasi Abdollah Safari Mary A. De Vera Tanja Högg Larry D. Lynd Mieke Koehoorn Arden R. Barry Jason G. Andrade Marc Deyell Kathy Rush Yinshan Zhao

Background

Studies measuring OAC adherence in AF patients have suffered from short follow-up times, inability to account for frequent medication switches and have excluded warfarin. Our objective was to compare AF patients' long-term adherence between OACs and identify the impact of taking direct oral anticogulants (DOAC) versus vitamin K antagonists (VKA) on adherence, while accounting for switching.

Methods

Using linked, population-based administrative data containing physician billings, hospitalization and prescription records of 4.8 million British Columbians (1996-2019), incident adult cases of AF were identified. Primary measure of adherence was proportion days covered (PDC). Consecutive rolling windows of 90 day in length were created for each patient starting from their first OAC prescription fill date until the end of their follow-up time. PDC for each of the 90-day-long rolling windows were calculated. If a person permanently discontinued their medication, they were given a PDC of 0 for all subsequent rolling windows after their last supply ran out, until the end of their follow-up period. As such, both poor execution and non-persistence were measured simultaneously. Patient's average adherence over follow-up was obtained by calculating the mean of PDC values of all their windows during follow-up. Changes in adherence over time and the association between drug class and adherence were assessed using generalized mixed effect linear regression model with both adherence and drug class treated as time-varying covariates.

Results

Study sample comprised of 30,264 AF patients [mean age: 72.2(SD11.0), 44.6% Female] with mean follow-up of 7.7(4.8) years. A majority were initiated on warfarin (69.7%), with mean CHA_2DS_2-VASc score of 2.94 (SD1.4). Mean PDC for our cohort was 0.71(SD0.27) with 51% considered non-adherent (PDC<0.8). 40.20% of the cohort experienced OAC switches, most of them being between-class switches. Adherence dropped over time with the greatest decline in the first two years after therapy. After controlling for all other confounders, taking VKA compared to DOAC was, on average, associated with a 1-day decrease in number of days of medication taking per year.

Conclusion

Adherence to OACs in patients with AF was well below the conventional threshold of 80%, with less than half of the patients taking these medications as prescribed. Adherence dropped over time, particularly in the first two years after therapy initiation. Switching was common. Drug class had no meaningful impact on medication adherence.

Pharmacoepidemiology

Comparative risk of opioid overdose with concomitant use of prescription opioids and skeletal muscle relaxants Nazleen Khan* Nazleen Khan Katsiaryna Bykov Michael Barnett Robert Glynn Seanna Vine Joshua Gagne

The concomitant use of prescription opioids and skeletal muscle relaxants has been associated with opioid overdose, but little data exist on the head-to-head safety of these drug combinations. The objective of this study was to compare the risk of opioid overdose among patients on long-term opioid therapy who concurrently initiate skeletal muscle relaxants. We conducted a new user, active comparator cohort study spanning 2000 to 2019 using healthcare utilization data from four US commercial and public insurance databases. Individuals were required to have at least 180 days of continuous enrollment and at least 90 days of continuous prescription opioid use immediately before and on the date of skeletal muscle relaxant initiation. Exposures were the concomitant use of prescription opioids and skeletal muscle relaxants, and the main outcome was the hazard ratio (HR) and bootstrapped 95% confidence interval (CI) of opioid overdose resulting in an emergency visit or hospitalization. The primary analysis quantified opioid overdose risk across seven prescription opioid-skeletal muscle relaxant therapies and a negative control outcome (sepsis) to assess potential confounding by unmeasured illicit opioid use. Secondary analyses evaluated two- and five-group comparisons in patients with similar baseline characteristics; individuals without prior recorded substance abuse; and subgroups stratified by baseline opioid dosage, benzodiazepine co-dispensing, and oxycodone or hydrocodone use. The weighted HR of opioid overdose relative to cyclobenzaprine was 2.52 (95% CI 1.29-4.90) for baclofen; 1.64 (95% CI 0.81-3.34) for carisoprodol; 1.14 (95% CI 0.53-2.46) for chlorzoxazone/orphenadrine; 0.46 (95% CI 0.17-1.24) for metaxalone; 1.00 (95% CI 0.45-2.20) for methocarbamol; and 1.07 (95% CI 0.49-2.33) for tizanidine in the 30-day intention-to-treat analysis. Findings were similar in the as-treated analysis, two- and five-group comparisons, and in patients without prior recorded substance abuse. None of the therapies relative to cyclobenzaprine were associated with sepsis, and no subgroups indicated increased risk of opioid overdose. The concomitant use of prescription opioids and baclofen relative to cyclobenzaprine is associated with opioid overdose. Clinical interventions may focus on prescribing alternatives in the same drug class or providing access to opioid antagonists if treatment with both medications is necessary for pain management.

**Estimation of the public health impact of COVID-19 vaccination in California** Sophia Tan*
Sophia Tan Hailey Park Isabel Rodríguez-Barraquer George Rutherford Kirsten Bibbins-Domingo
Robert Schechter Nathan C. Lo

Introduction: Despite widespread vaccination against COVID-19 in the United States, there are
limited data quantifying the public health impact of vaccination. We estimated the number of
COVID-19 cases, hospitalizations, and deaths averted due to COVID-19 vaccination in California.

Methods: The California Department of Public Health (CDPH) provided person-level data on
COVID-19 cases and vaccine administration from January 1, 2020 to October 16, 2021. We applied a
statistical model that estimated the relationship of COVID-19 cases in the pre-vaccine era between
the unvaccinated age group (<12 years) and vaccine-eligible groups (≥12 years) to COVID-19 case
data after the start of vaccination to predict the number of COVID-19 cases that would have
occurred in the vaccine era in absence of vaccination. Averted cases was defined as the difference
between predicted number of COVID-19 cases in absence of vaccination and observed COVID-19
cases. We developed a second independent model that estimated the number of vaccine-averted
COVID-19 cases using published data on COVID-19 vaccine effectiveness and administration. We
estimated averted COVID-19-related hospitalizations and deaths by applying measured
hospitalization and case fatality rates.

Results: There were 4,585,248 confirmed COVID-19 cases in California, during which 27,164,680
individuals received at least 1 dose of a COVID-19 vaccine (79.5%). We estimated that 1,523,500
[95% PI (976,800-2,230,800)] COVID-19 cases were averted by vaccination and there was a 34%
[95% PI (25-43)] reduction in cases. We estimated 70,100 [95% PI (49,880-96,410)] hospitalizations
and 17,500 [95% PI (12,530, 24,410)] deaths were prevented due to vaccination. Our alternative
model identified comparable findings.

Conclusion: Our analysis provides robust evidence on the public health impact of COVID-19
vaccination in the United States.

Averted COVID-19 cases, hospitalizations, and deaths due to COVID-19 vaccination in California
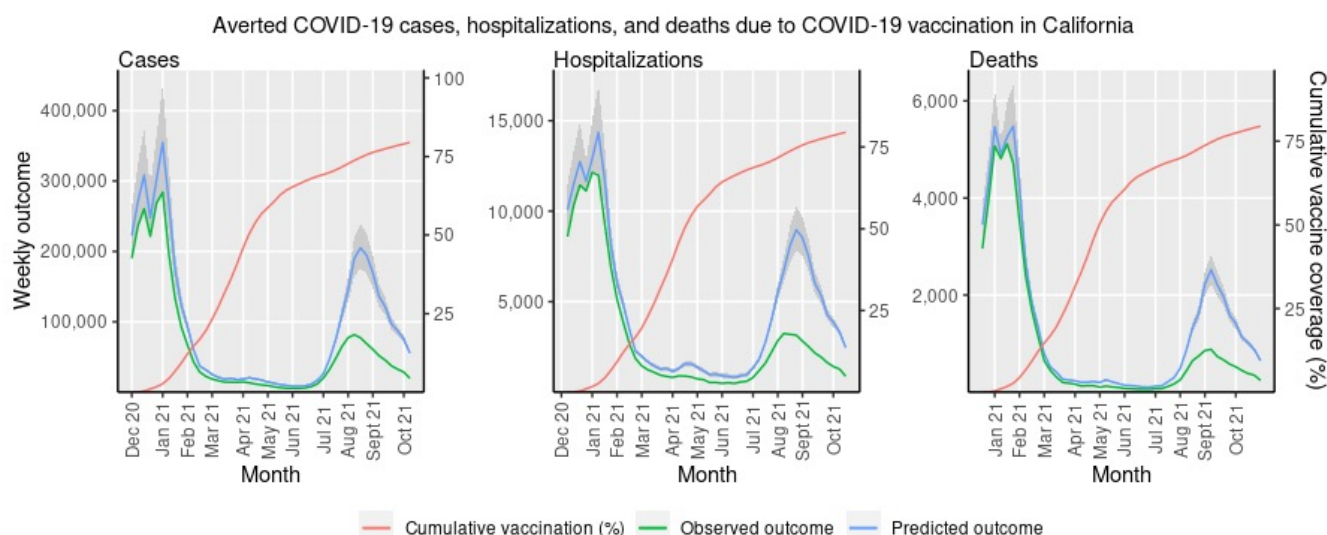
Waning of mRNA-based COVID-19 vaccine effectiveness against SARS-CoV-2 symptomatic infection in California: a test-negative design case-control study Kristin Andrejko* Kristin Andrejko Joe Lewnard

Background: Concerns about the duration of protection conferred by COVID-19 vaccines have arisen following their implementation in real-world contexts. However, time-varying biases may contribute to the appearance of waning vaccine effectiveness (VE) in epidemiologic studies, potentially hindering interpretation of estimates.

Methods: We enrolled adult participants residing in California in a matched, test-negative design case-control study to estimate VE of mRNA-based COVID-19 vaccines between 23 February and 5 December, 2021. We calculated VE against symptomatic COVID-19 from the adjusted odds ratio (aOR) of prior vaccination at differing time intervals, estimated via conditional logistic regression. We undertook analyses within the full sample as well as subgroups stratified by age and presence of comorbid conditions. We used data from case-based surveillance, and case-to-infection ratios inferred from a population-based serological study, to quantify the potential contribution of depletion-of-susceptibles bias to time-varying VE estimates.

Results: Pooled VE of BNT162b2 and mRNA-1273 against symptomatic SARS-CoV-2 infection was 91.3% (95% confidence interval: 83.8,95.4%) at 14 days after second-dose receipt and 50.8% (31.2-75.6%) at 7 months (absolute difference in VE: 40.2% [17.5-73.7%]). Depletion of susceptibles contributed minimally to time-varying VE; correcting for depletion-of-susceptibles bias, we estimated VE was 53.2% (23.6, 71.2%) at 7 months. Point estimates suggested greater reductions in VE among individuals >50 years of age (vs. younger individuals) and individuals with comorbid conditions (vs. immunocompetent individuals without comorbid conditions).

Conclusions: While mRNA-based vaccines remain effective against COVID-19 at least 7 months after second-dose receipt, waning VE supports the consideration of complementary public health interventions, including administration of additional doses, to mitigate SARS-CoV-2 circulation in the community.
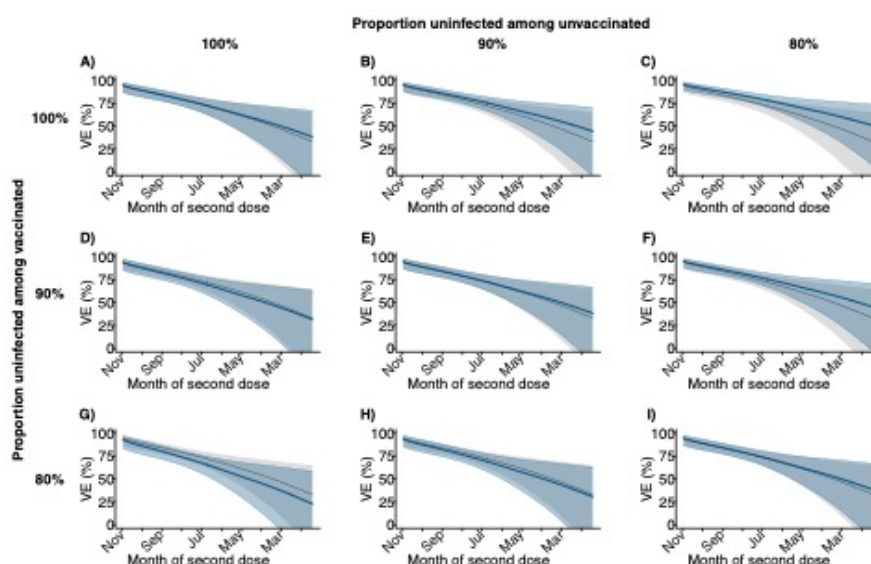
SARS-CoV-2 seroprevalence: demographic and behavioral predictors of seropositivity among college students in the Southern US Karen Diepstra* Karen Diepstra Brooke W. Bullington Lakshmanane Premkumar Bonnie E. Shook-Sa Corbin Jones Audrey Pettifor

Background: Young adults, especially those living in or around congregate settings such as universities, are particularly at risk of acquiring and transmitting SARS-CoV-2. We examined SARS-CoV-2 seroprevalence and the association of seropositivity with demographic, geographic, and behavioral predictors among undergraduate college students.

Methods: All UNC-CH undergraduate students enrolled in the Fall 2020 semester were invited to participate in the Heelcheck study; participants were weighted to the UNC-CH undergraduate population using raking methods. We estimate SARS-CoV-2 seroprevalence at study entrance (11/12/2020-12/10/2020) and bivariable associations using log-binomial regression.

Results: SARS-CoV-2 seroprevalence was 7.3% (95% confidence interval (CI): 5.4%-9.2%) at baseline. Compared to students who were living off-campus in the Chapel Hill/Carrboro area (CH) for the Fall 2020 semester (8.6% seroprevalence), students who never returned to CH had lower seroprevalence (1.9%, prevalence ratio (PR), 95% CI: 0.22, 0.06-0.81), whereas students who started the semester on-campus and moved to off-campus CH housing had 18.9% seroprevalence (PR, 95% CI: 2.21, 1.04-4.72) and students who spent the semester living in a Sorority/Fraternity house had 46.8% seroprevalence (PR, 95% CI: 5.47, 2.62-11.46). Those who predicted they would join an indoor party unmasked had 3.8 times the seroprevalence of those who indicated they would not attend (PR, 95% CI: 3.80, 1.58-9.16). Compared to students who disagreed with the statement "…I am not going to let COVID-19 stop me from having fun…", those who agreed had higher seroprevalence (14.0% versus 5.7%; (PR, 95% CI: 2.45, 1.13-5.32)).

Conclusions: Increased seroprevalence was associated with congregate living and participation (actual or endorsed) in social activities. During pandemics, universities must create safe socializing opportunities while minimizing transmission.

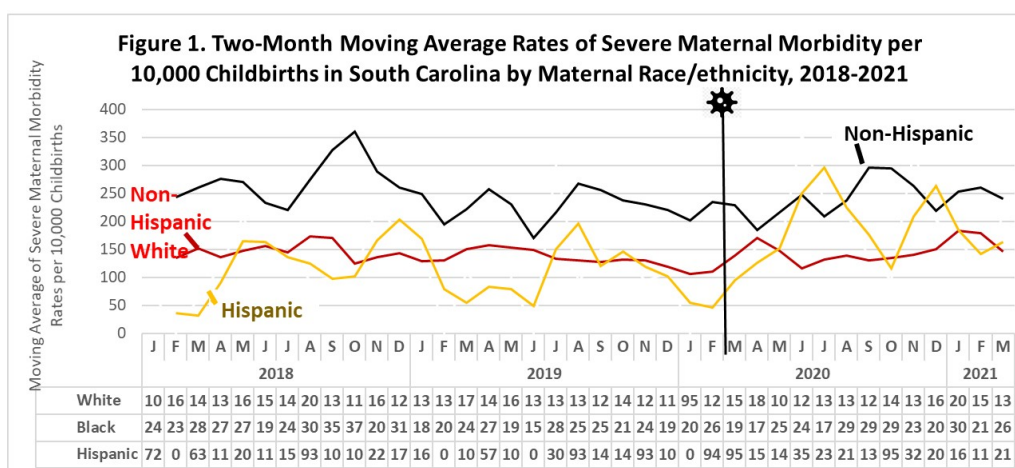**Impacts of COVID-19 Pandemic on Racial/Ethnic Disparities in Severe Maternal Morbidity: Data from the South Carolina COVID Cohort** Jihong Liu* Jihong Liu Peiyin Hung Jiajia Zhang Berry Campbell Bankole Olatosi Yiwen Shih Chen Liang Xiaoming Li

Background: Severe maternal morbidity (SMM)—life-threatening childbirth complications—has been rising in the US before the COVID-19 pandemic. This study aimed to understand the impact of SARS-CoV-2 infection and the COVID-19 pandemic on SMM and racial disparities in SMM.

Methods: Data came from the South Carolina (SC) COVID-19 Cohort, novel linkages of statewide COVID testing, vital records, and health utilization data for all women giving birth during pre-pandemic (01/2018-02/2020) (n=106,331 births to 102,327 women) and peri-pandemic (03/2020-03/2021) (n=65,077 births to 53,235 women) periods. ICD-10 and DRG codes were used to identify delivery records and ICD-10 codes for SMM using CDC definitions. Multilevel logistic regressions with random effects at facility level were used to examine the differences in SMM by pandemic period, COVID-19 status, and race/ethnicity.

Results: The SMM rates in SC slightly increased during peri-pandemic vs. pre-pandemic time (183.9 vs 177.7 SMM per 10,000 births, p=.13). Compared to non-Hispanic (NH) whites, NH Blacks and NH others experienced 1.8 times higher odds of SMM (95 CI: 1.4, 2.4 and 1.2, 2.7, respectively), while Hispanics-whites had no differences in SMM. Racial disparities in SMM did not change significantly by pandemic period. Compared to women without COVID, women with lab-confirmed/probable COVID diagnosis had 2.4 times higher odds of SMM (95% CI: 1.5, 3.8) while women whose first COVID diagnosis occurred during the third trimester or at childbirth had 2.8 and 2.2 times higher odds of SMM (95% CI: 1.1, 7.2 and 1.1, 4.7), respectively.

Conclusions: During the first year of the pandemic, SMM rates increased slightly at the SC population level. Racial disparities in SMM persisted, showing no signs of larger racial disparities during the pandemic. COVID infections especially among women diagnosed in third trimester or at childbirth increased risks for SMM.

Figure 1. Two-Month Moving Average Rates of Severe Maternal Morbidity per 10,000 Childbirths in South Carolina by Maternal Race/ethnicity, 2018-2021

	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M	A	M	J	J	A	S	O	N	D	J	F	M
				2018												2019												2020											2021	
White	10	16	14	13	16	15	14	20	13	11	16	12	13	13	17	14	16	13	13	13	12	14	12	11	95	12	15	18	10	12	13	13	12	14	13	16	20	15	13
Black	24	23	28	27	27	19	24	30	35	37	20	31	18	20	24	27	19	15	28	25	25	21	24	19	20	26	19	17	25	24	17	29	29	29	23	20	30	21	26
Hispanic	72	0	63	11	20	11	15	93	10	10	22	17	16	0	10	57	10	0	30	93	14	14	93	10	0	94	95	15	14	35	23	21	13	95	32	20	16	11	21

COVID-19 Pandemic

Tenofovir disoproxil and COVID-19 outcomes in men with HIV Guilin Li* Guilin Li Lesley S. Park Sara Lodi Roger Logan Emily J. Cartwright Lydia Aoun-Barakat Juan P. Casas Romero Barbra A. Dickerman Christopher T. Rentsch Amy C. Justice Miguel A. Hernán

Recent observational studies suggest that tenofovir disoproxil (TDF) may have antiviral potential against severe COVID-19. TDF may interfere with the SARS-CoV-2 RNA-dependent RNA-polymerase and is inexpensive and safe.

We included men living with HIV on antiretroviral therapy (ART) in the Veterans Aging Cohort Study (VACS) who on February 1, 2020 or later were 18 years or older, virologically suppressed, had HIV lab results in the previous 12 months, no history of CD4 count < 50 cells/µL, and no prior COVID-19 diagnosis or vaccination. We compared the adjusted risks of documented SARS-CoV-2 infection, COVID-19-related hospitalization and intensive care unit (ICU) admission by baseline ART regime: tenofovir alafenamide (TAF)/emtricitabine (FTC), TDF/FTC, abacavir (ABC)/lamivudine (3TC), and other. We fit pooled logistic regression models to estimate the risk of each outcome standardized by demographic factors, HIV lab results, clinical measurements, calendar time and history of comorbidities.

Among 20,494 eligible individuals, 62% were on TAF/FTC, 5% on TDF/FTC, 18% on ABC/3TC, and 15% on others. The baseline characteristics were similar, except for prevalence of chronic kidney disease being lowest for TDF/FTC. There were 1,011 documented SARS-CoV-2 infections, 291 COVID-19-related hospitalizations and 89 ICU admissions. Compared with TAF/FTC, the estimated 12-month risk ratio (95% CI) of documented SARS-CoV-2 infection was 0.65 (0.43, 0.90) for TDF/FTC, 1.05 (0.89, 1.23) for ABC/3TC, and 0.87 (0.71, 1.04) for others. The corresponding risk ratios for COVID-19 hospitalization were 0.38 (0.01, 0.79), 1.13 (0.82, 1.52), and 1.15 (0.84, 1.56). The risk of COVID-19 ICU admission was lowest for TDF/FTC, but the estimates were very imprecise.

Our study suggests that in men living with HIV, TDF/FTC may provide protection against COVID-19-related events. Randomized trials are needed to investigate the effectiveness of TDF against COVID-19 in the general population.

Paid sick leave and COVID-19 vaccination Coverage: A longitudinal analysis of 37 large US cities Alina Schnake-Mahl* Alina Schnake-Mahl Gabriella O'Leary Pricila Mullachery Ana Diez Roux Jennifer Kolker Alexandra Skinner Julia Raifman Usama Bilal

Background: The presence of paid sick leave (PSL) may influence an individual's decision to get vaccinated, by providing paid time-off to receive vaccines and to recover from potential vaccine side effects. Nearly 24% of the US worker population has no access to PSL. We examine the association between city-level PSL policies and COVID-19 vaccination coverage and inequities in coverage in 37 of the largest US cities in 2021.

Methods: Using county-level vaccination and PSL policy data from 37 US cities we estimated the association between PSL city-level policies and vaccination coverage (ages 18-65) using a negative binomial model, stratified by period (January-March, April-October, November-January 3rd, 2022). We compared cities with mandated PSL vs not, controlling for city political lean and social vulnerability. We repeated the analysis using coverage in the population aged 65+ as a negative control.

Results: In the 37 cities, a total of 43,368,491 individuals aged 18-65 were fully vaccinated between January 1st,2021 and January 3rd, 2022. Among the 18-65 population, having a city PSL policy was associated with 14% (IRR=0.86; 95% Confidence Interval (CI): 0.80, 0.93) higher vaccination coverage than cities without a PSL policy, after adjusting for political lean and vulnerability. This association was stronger in the early months of rollout (20% in January-March). There was no association between PSL and vaccination coverage for the 65+ population (negative control) (IRR=0.99; CI: 0.93,1.05).

Conclusion: Paid sick leave policies are associated with higher rates of COVID-19 vaccination coverage. Policies to increase access to paid sick leave may help increase vaccination coverage, particularly in the most vulnerable neighborhoods.

Did expanding the dental therapist workforce improve access to dental care? A synthetic control analysis Hawazin Elani* Hawazin Elani Elizabeth Mertz Ichiro Kawachi

Background: Currently 13 states have expanded their dental workforce by adopting dental therapists. To date there has been no evaluation of the impact of this policy on dental care utilization.

Objectives: To assess changes in dental care utilization in Minnesota after the adoption of dental therapy in 2009.

Methods: We analyzed data from the Behavioral Risk Factor Surveillance System from 2006 to 2018. We used a synthetic control method to compare changes in dental use in Minnesota compared to a synthetic control of non-adopting states. We examined changes among adults overall as well as among low-income population including Medicaid eligible adults. In addition, we conducted subgroup analysis to assess whether the policy differentially impacted minority adults. Our outcome was self-reported indicator for whether a respondent had visited a dentist or a dental clinic in the past 12 months. Our analysis included 2,613,716 adults aged 18 and older.

Results: The proportion of adults visiting a dentist prior to the authorization of dental therapists in Minnesota was 76.2% (95%CI 75.0, 77.4) in the full sample, 61.5% (95%CI 58.4.0, 64.6) in low-income adults, and 58.4% (95%CI 53.0, 63.5) among Medicaid eligible adults. In the low-income sample, we found that authorizing dental therapists in Minnesota was associated with an increase of 7.3 percentage points (95%CI 5.0, 9.5) in dental care use, a relative increase of 12.5% (95%CI 8.6, 84 16.4). Among Medicaid eligible adults, the adoption of the policy was associated with an increase of 6.2 percentage points (95%CI 2.4,10.0), a relative increase of 10.5% (95%CI 3.9, 17.0). In the subgroup analysis, the policy was associated with increase in dental visits among White adults with no corresponding increases among racial and ethnic minorities in the low-income and Medicaid population (Low-income sample: 10.8 percentage points; 95%CI 8.5, 13.0, Medicaid sample: 13.5 percentage points; 95%CI 9.1,17.9).

Conclusions: Expanding the dental workforce to include dental therapists in Minnesota show associated improvements in access to dental care among low-income populations.

The Affordable Care Act dependent coverage provision and unintended pregnancy Colleen L. MacCallum-Bridges* Colleen MacCallum-Bridges Robert Kaestner Zhehui Luo Claudia Holzman Tim Bruckner Claire E. Margerison

Background: Nearly 50% of pregnancies in the US are unintended (mistimed or unwanted), and these pregnancies disproportionately impact younger and lower income women. The Affordable Care Act dependent coverage provision (hereafter "the provision") required that insurance plans cover dependents up to age 26, increasing access to health insurance coverage and contraceptives for young women. This had potential to reduce unintended pregnancies. The impact of this policy may have differed by dependent income level as those with lower income were less likely to be insured and thus more likely to benefit.

Objective: Estimate the association between the provision and unintended pregnancy, overall and by dependent income level.

Methods: We used data from the National Survey of Family Growth, cycles spanning 2006-2015. We estimated the impact of the provision on unintended pregnancy using an event study approach to compare trends in unintended pregnancy between those eligible to benefit (ages 18-25) and those ineligible to benefit (ages 26-44). We used 2007-2009 as the reference period, and we estimated unadjusted and adjusted associations overall and within income subgroups [<100% of the federal poverty level (FPL), 100-399% FPL, ≥400% FPL].

Results: There was no evidence of an association overall. However, among those with income <100% FPL, the provision was associated with an 8.7 (95% CI:3.8, 13.6) percentage point decrease in unintended pregnancy between 2007-2009 and 2012-2014. Prior to the provision, the annual prevalence of unintended pregnancy among this group was 15%. Thus, the observed association is a decrease of >50%. No evidence of an association was found among other income groups.

Conclusion: Following the provision, a large decline in unintended pregnancy was observed among low-income women <26 years old. Additional work is needed to understand the interaction between parental and dependent income level and its implication for health equity.

Prevalence[1] of unintended pregnancy over the study period, by eligibility[2] and income level
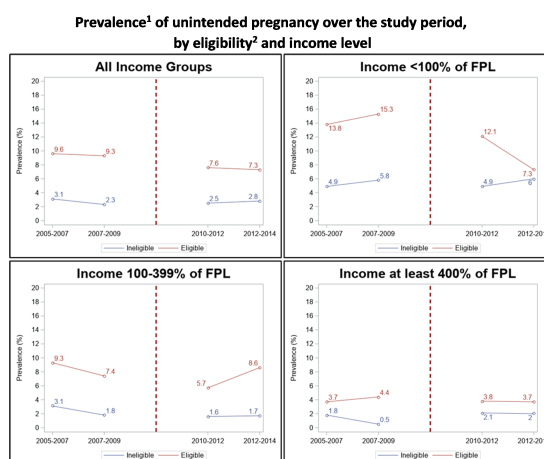
Red dashed line indicates implementation of the Affordable Care Act (ACA) dependent coverage provision. The ACA was signed into law in March 2010 and the provision became effective in September 2010.
FPL = Federal poverty level
[1] Percent of respondents reporting at least one unintended pregnancy in the period
[2] Eligible: < 26 years old, Ineligible: ≥26 years old

Impact of a statewide livestock antibiotic use policy on resistance in human urinary tract infection: a synthetic control analysis Joan Casey* Joan Casey Sara Tartof Meghan Davis Keeve Nachman Lance Price Cindy Liu Alice Pressman Gabriel Innes

Background: On January 1, 2018, California's Senate Bill 27 (SB27) went into effect, banning regular pattern use of antibiotics in food-producing animals and any antibiotic use without a veterinarian's prescription. We aimed to determine if SB27 resulted in decreased antimicrobial resistance from *E. coli* isolated from human infections.

Methods: We used U.S. nationwide monthly state-level data from Becton Dickinson, and Co. spanning January 1, 2013 to June 30, 2021 on antibiotic-resistance patterns of *E. coli* isolated from urinary tract infection (UTI). Tested antibiotic classes included aminoglycosides, extended-spectrum cephalosporins (ESC), fluoroquinolones, and tetracyclines. Counts of tested and non-susceptible (resistant and intermediate, hereafter resistant) UTIs were available by sex, age group (<65, 65+), month, and state. We applied a synthetic control approach to estimate the causal effect of SB27 on UTI susceptibility patterns. Our approach created a synthetic California based on a composite of other states without the policy change and contrasted its counterfactual post-policy trends with the observed post-policy trends in California.

Results: We included 7.1 million UTIs, 90% among women, across 35 states. From 2013–2017, the median (interquartile range) resistance percentages in California were 11.9% (87.4, 17.6), 13.8% (5.8, 20.0), 24.6% (9.6, 36.4), 7.9% (2.1, 13.1), for aminoglycoside, ESC, fluoroquinolones, and tetracyclines, respectively. SB27, implemented in January 2018, was associated with a 7.1% reduction in ESC resistance (p-value for joint null: <0.01), but no change in resistance to aminoglycosides, fluoroquinolones, or tetracyclines.

Conclusion: State-level agricultural policy has the potential to alter antibiotic-resistant infections on the population level.
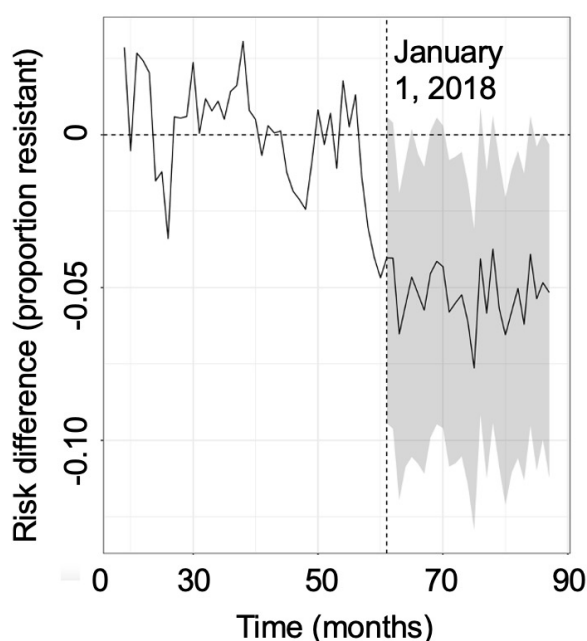
Using machine learning to predict suicide one year after discharge from a somatic hospitalization in Denmark Vijaya L. Seegulam* Vijaya Seegulam Péter Szentkúti Erzsébet Horváth-Puhó Anthony J. Rosellini Tammy Jiang Timothy L. Lash Henrik T. Sørensen Jaimie L. Gradus

Introduction. Suicide remains one of the leading preventable causes of death globally. While the elevated suicide risk after psychiatric hospitalization has been studied extensively, suicide risk after a somatic (i.e., physical health) hospitalization is still poorly understood.

Methods. Using population based Danish registries, we conducted a case-cohort study. Cases were all individuals who died by suicide within one year of a somatic hospitalization (n=4,563) and the comparison subcohort was a 5% random sample of individuals in Denmark who had their first hospital admission for a somatic condition (n=177,664) between January 1, 1995 and December 31, 2015. We used random forests, built with 1000 trees with a minimum of 10 observations needed to attempt a split, to determine the most important predictors of suicide following somatic hospitalization from 2,563 time-varying predictor variables spanning domains of demographics, medications, somatic and psychiatric diagnoses. These analyses were stratified by sex.

Results. Psychiatric disorders were most important to suicide prediction, even within this sample of persons hospitalized for somatic conditions. For women, top 10 variables in the variable importance plot were all related to psychiatric diagnoses (e.g., alcohol-related disorders, reactions to severe stress, major depression). For men, many physical health conditions also appeared important to suicide prediction in addition to psychiatric diagnoses. Among the top 10 variables in the variable importance plot were influenza, injuries to the head, nervous system surgeries, and cerebrovascular diseases.

Conclusion. Effective prevention of suicide following a somatic hospitalization may require comprehensive consideration of multiple factors for men and women. For men in particular, it is critical to look beyond psychiatric diagnoses and further evaluate physical health diagnoses and conditions as potential predictors of suicide risk.

Identifying homelessness from EMRs: standard and custom approaches Paulina Kaiser*
Paulina Kaiser Olivia Pipitone Anita Earl Miranda Miller

Using data from electronic medical records (EMRs) can be challenging for research at the intersection of clinical and social determinants of health. At a community-based regional healthcare system in suburban/rural Oregon, we created an EMR-based registry using standard and custom documentation to identify homeless patients. With input from clinic care coordinators, hospital discharge planners, clinical social workers, and community partners, we identified six ways in which homelessness is captured in the EMR (Epic): 1) encounter diagnosis of homelessness (Z59.0) in the past year; 2) diagnosis of homelessness (Z59.0) active on the patient's problem list; 3) current address is listed as 'homeless' or matches a curated list of social service agencies; 4) social history documentation of home environment is 'homeless' (in the past year); 5) residence type on care management facesheet is 'homeless' (in the past year); and 6) documented housing status is 'homeless shelter' or 'street' (in the past year). In January 2022, 1,256 patients met one or more of these criteria. Most (66.5%) were identified by address (53.9% with an address of 'homeless' and 12.6% with an address affiliated with a social service agency). Only 28.3% of patients identified as homeless had a documented diagnosis of homeless (17.1% encounter diagnosis, 2.9% problem list, 8.3% both). Patients with a diagnosis of homelessness were older (mean age 50.2 vs 44.1, p<0.001) and more likely to have Medicaid coverage (79.8% vs 61.4%, p<0.001). After adjusting for age, payor, and major comorbidities, patients with a diagnosis of homelessness had 1.5 times higher odds of having 1+ hospitalizations in the past year than patients without a diagnosis of homelessness (95% CI 1.1, 2.1). ICD-10 codes for homelessness are underutilized but capture a subpopulation at high risk; knowledge of custom documentation methods can help identify a broader population with housing-related social needs.

Statistical methods to impute missing race and ethnicity information in routinely collected data sources: investigating COVID-19 outcome disparities in Holyoke, Massachusetts Sara Sauer* Sara Sauer Isabel Fulcher Wilfredo Matias Ryan Paxton Jack Zhu Francisco Molano Atany Nunez Marisol Rosa Louise Ivers Molly Franke

Routinely collected testing and case reporting data are crucial resources for informing targeted public health response to the ongoing COVID-19 pandemic. A growing body of research using these data sources has found that Black, Hispanic, and other marginalized communities have borne a disproportionate burden of COVID-19, with higher rates of infection, hospitalization, and death. However, many of these studies have been limited due to incomplete information on race and ethnicity. Recent research investigating disparities typically exclude participants with missing information or group them into an "Unknown" category for analysis. Excluding or grouping individuals will bias estimates when comparing rates by race and ethnicity if information is not missing completely at random. In this paper, motivated by an overarching goal to quantify disparities in rates of SARS-CoV-2 infection and COVID-19-related hospitalization or death by race and ethnicity in Holyoke, Massachusetts, we evaluate different strategies for handling missing race and ethnicity data. In particular, we consider a resource intensive strategy of additional data collection through telephone surveys to recover missing information on race and ethnicity, as well as three imputation methods: 1) Bayesian Improved Surname Geocoding (BISG), which uses individuals' surnames and census tract to impute race and ethnicity, 2) multiple imputation by chained equations (MICE), and 3) population-calibrated multiple imputation (PCMI), which uses the population distribution of the missing variable to calculate an adjustment to the imputation model. We investigate the performance of each method over a range of missingness mechanisms and ultimately provide recommendations for researchers faced with missing information on race and ethnicity from similar data sources. Finally, we compare rates of infection, hospitalization, and death, by race and ethnicity among Holyoke residents using each of the discussed strategies.
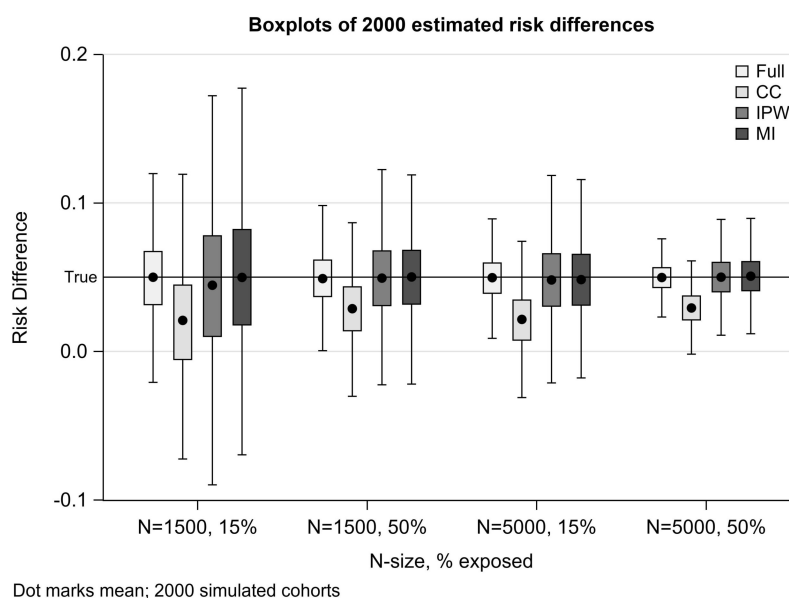
Nonmonotone missing data: inverse probability weights or multiple imputation? Rachael K. Ross* Rachael Ross Stephen R. Cole Daniel Westreich Julie L. Daniels Jeffrey S.A. Stringer Jessie K. Edwards

Inverse probability weighting (IPW) for missing data is challenging to implement when missingness is nonmonotone. We explore the potential for a new estimator, the unconstrained maximum likelihood estimator (UMLE) for IPW, to overcome this challenge. We compared IPW UMLE and multiple imputation (MI) in weighted time-fixed marginal structural models.

We simulated data with a binary exposure, a binary outcome, and 3 confounders. We varied sample size, percent exposed, and the true causal risk difference (RD). We simulated missing data (missing at random) yielding 50% complete cases. We implemented 4 analyses: full data (without missingness), complete case analysis (CC), IPW UMLE, and MI by chained equations. In each, we used IPW to address confounding and obtained robust standard errors. In UMLE, the model used to estimate the treatment weights was weighted by the missingness weights; the final weight was the product of the two weights. For MI, we imputed 20 times. We also implemented analysis in motivating data from a prospective cohort of 1447 pregnant women.

The figure shows boxplots of estimates from 2000 simulated cohorts for each analysis where the true RD was 0.05 (results were similar for RD 0). CC was biased in each scenario. MI had negligible bias. UMLE also had negligible bias; however, bias increased slightly at N=1500 with 15% exposed. At N=5000, 50% exposed, UMLE and MI were equally precise. As sample size and percent exposed declined, MI was slightly more precise (empirical standard error difference 0.002). MI implementation was >13 times slower than UMLE in SAS.

IPW UMLE performed well and was easy to implement in SAS and R. Though less precise at smaller sample sizes, IPW is a viable alternative, with different modeling assumptions, to MI for nonmonotone missingness. Some argue that it is easier to correctly specify the models for IPW than for MI. Faster implementation of IPW is attractive in large datasets or when bootstrap is needed.

Boxplots of 2000 estimated risk differences

Dot marks mean; 2000 simulated cohorts

Methods/Statistics

Missing Data Interpolation among Cohorts with Disparate Covariate Information in the ECHO-wide Cohort Amii Kress* Amii Kress Ekaterina Smirnova Yongqi Zhong Xuejuan Ning Rasha Alsaadawi Jordan Kuiper Mingyu Zhang Lisa Jacobson Bryan Lau

The Environmental influences on Child Health Outcomes (ECHO)-wide cohort (EWC), a nation-wide collaborative cohort study, combines 69 pediatric cohorts to study child health outcomes. The independent cohort studies (ICS) differ with respect to original study design, sampling strategy, primary outcomes of interest, and data elements collected. The ICS differences in data collection cause methodological issues in harmonizing extant data, and results in disparate covariate information in ECHO-wide analyses, since some cohorts may not have collected all variables of interest for an analysis. This issue is not addressed well in the literature as most consortium cohort studies consist of studies with similar disease-based outcomes (e.g., Alzheimer's, HIV) with comparable exposure and covariate data. Traditional approaches for cohort-level missing confounder data include dropping variable(s) with missing data resulting in potential residual confounding bias; excluding cohorts missing entire data elements for the analysis, reducing the sample size, precision, and possibly generalizability; and/or using traditional missing data imputation approaches. Existing methods for dealing with disparate covariate data across cohorts, (e.g., generalized meta-analysis) assume that the underlying joint distributions are the same. This assumption is difficult to test and may be violated. We developed a machine learning approach, combining unsupervised random forests to obtain distances between observations within and across cohorts, hierarchical clustering to identify sub-groups of cohorts, and then test whether covariate distributions provide evidence differences in joint distributions. The performance of these methods was tested using an extensive set of simulations which indicated that the algorithm correctly identifies the cohort subgroups.

Overcoming Data Gaps in Life Course Epidemiology Using Probabilistic Matching Across Cohorts Katrina Kezios* Katrina Kezios Scott Zimmerman Kara Rudolph Sebastian Calonico Maria Glymour Adina Zeki Al Hazzouri

Research on early- and mid-life determinants of later life health is often hampered by the absence of studies with life course or long-term prospective follow-up. Innovative methods are needed to estimate the effects of early- and mid-life factors on late-life outcomes in studies with shorter follow-up periods, especially those beginning in older age. Here, we evaluate a method to create a synthetic life course cohort. Specifically, we conduct a simulation study where individuals from one dataset containing information on an early-life exposure (V) are matched to individuals from another data set containing information on a later-life outcome (Y) based on variables (W,M,W2) common to both datasets. We explore various scenarios for causal models, represented in DAGs (Figure 1), where we vary both the matching variable(s) and caliper of the match. For each DAG, we first calculated the true causal effect of V on Y, and then enumerated the assumptions under which it could be identified using the rules of do-calculus and the above two data set approach. We then simulated data based on each causal model, where each individual in the early-life cohort was matched to individuals in the late-life cohort using a many-to-many match. We estimated the effect of V on Y using a correctly specified regression model on each synthetic cohort in 5000 simulation iterations, accounting for clustering due to multiple matches per person, and calculated bias as the average estimate minus the true effect. Finally, we compared the bias as we varied the match quality (e.g., caliper width). As would be expected based on theory, and confirmed through simulation, in scenarios when the set of matching variables included all variables along all pathways linking V to Y, the synthetic cohort yielded unbiased estimates when high-quality matches were found. Methods based on merging cohorts, when conducted carefully, provide opportunities to evaluate early- and mid-life determinants of late life health.

Figure 1. Simulation models and matching variables
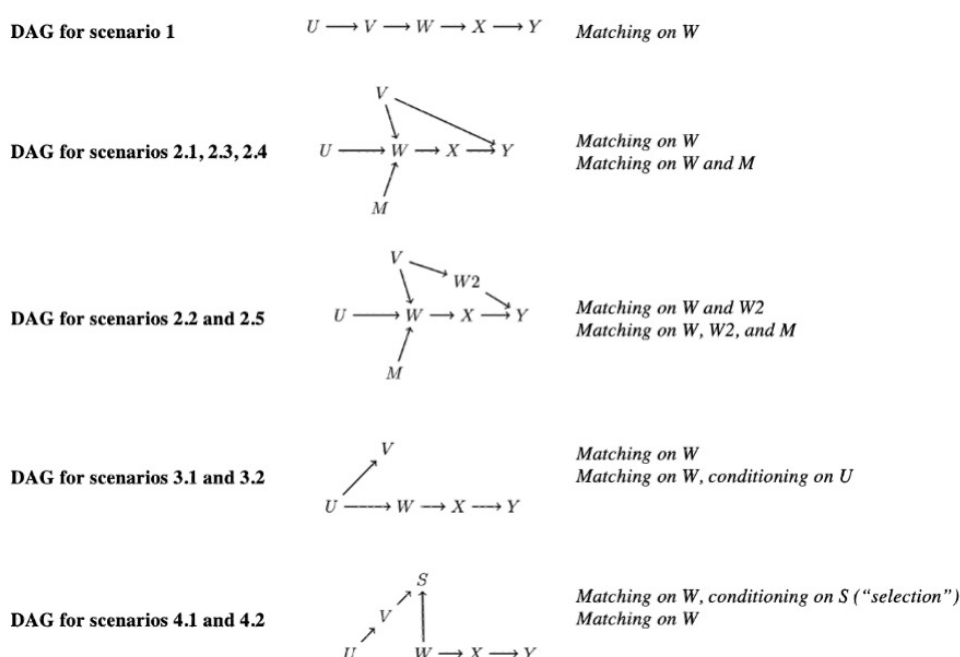
An algorithmic approach for establishing statistical convergence of the pooled treatment effect in meta-analysis Hayley Belli* Hayley Belli Zhongyang Ma Ellen Caniglia Andrea Troxel Scott Braithwaite

Meta-analysis is an approach used in clinical research to pool treatment effects across multiple studies into a single effect size. The individual studies included in a meta-analysis however may be highly variable in the directionality or magnitude of their independent treatment effects. While meta-analyses aim to include only studies implementing robust methodology or shared study characteristics to improve the accuracy of their population-level estimates, it can be challenging to identify whether the pooled meta-analysis estimate is in fact converging towards the true population-level effect size. In this presentation, we discuss an approach that utilizes both the total number and variability of individual studies to determine when the pooled effect size from a meta-analysis has converged towards the true population effect. We first present the methodology of the developed convergence algorithm. We then discuss example applications, specifically focusing on randomized controlled trials measuring changes in low-density lipoprotein cholesterol. We explore 3 interventions: low-intensity statins (n=55 studies), high-intensity statins (n=12), or ezetimibe (n=34), each compared to placebo. Studies were selected based on a PubMed search and consistent inclusion/exclusion criteria. For each of the 3 cases, independent study effect sizes were directly extracted or calculated from data in the publications. The convergence algorithm was first applied to the studies in their chronological order by publication date. We then performed a sensitivity analysis by generating random permutations of the order in which studies were included in the algorithm. We experimented with the number of studies (1-7) included in a moving average look back window. Results found the study stopping index to lie within 7.8-26.2% of the true underlying pooled effect-size. Future work will aim to increase algorithm accuracy, as well as develop software to improve algorithm usability among researchers.

How the Choice of Effect Measure Influences Minimally Sufficient Adjustment Sets for External Validity Michael Webster-Clark* Michael Webster-Clark Alexander P. Keil

Epidemiologic research generalizing or transporting effect estimates from a study population to a target population often suggests conditioning on all effect measure modifiers (EMM) on the scale of interest. EMM is well known to be scale dependent, but there is also a rich literature on the nuances of EMM and collapsibility that is often neglected when considering external validity. More specific characterization of EMM and the mathematical nuances of the effect measure of interest may yield additional insight into minimally sufficient variable sets for achieving valid target population estimates.

First, we defined two types of EMM: marginal EMM, where the (unconfounded) effect on the scale of interest differs across levels of a variable; and second, conditional EMM, where the effect differs across levels of a variable conditional a set of other variables. Based on these EMM types, we placed variables in **Class 1** (conditional and marginal EMM), **Class 2** (marginal, but not conditional EMM), or **Class 3** (neither marginal nor conditional EMM, still associated with the outcome) on a given scale. We used a simulation study to verify mathematical expectations about variables required to estimate externally valid treatment effects on three scales.

Our analyses showed that **Class 1** variables were sufficient to achieve a valid estimate of the RD in a target, while a valid RR required **Class 1** and **Class 2** and a valid OR required **Class 1, Class 2,** and **Class 3** (in other words, all variables associated with the outcome). Clearly, a richer definition of EMM is needed to identify minimally sufficient adjustment sets for external validity for specific effect measures. While this does not imply that fewer variables are required to transport the RD than the RR (because variables may modify effects on only one scale), it does have implications for identifying key EMMs for adjustment.

Role of Citizenship and Immigration Status on Cardiometabolic Health among United States Hispanic/Latino Adults from the HCHS/SOL study Hridya C. Rao* Hridya Rao Lindsay Fernandez-Rhodes Aida Giachelloa Martha L. Daviglus Carmen R Isasi Gregory A. Talavera Linda C. Gallo Sandra S. Albrecht Krista M. Perreira

Compared to US-born citizens of non-Hispanic origin, Hispanic/Latino adults face a higher burden of cardiometabolic risk (CMR). Among those who are foreign-born, US citizenship and immigration status may relate to differential weathering and cardiometabolic outcomes. We utilized data on US citizenship and immigration status [i.e., US-born citizen (UBC), foreign-born naturalized citizen (FBC), non-US citizen documented immigrant (NCD), and non-US citizen undocumented immigrant (NCU)] and Metabolic Syndrome (MetS; using clinical criteria defined by the National Cholesterol Education Program Third Adult Treatment Panel criteria) from Visit 2 (2014-17) of the community-based Hispanic Community Health Study/Study of Latinos (HCHS/SOL; n=11623, age 22-82). Complex sampling weighted logistic regression models were adjusted for age, age^2, gender, site, and Hispanic/Latino background. Compared to FBC, UBC (OR=1.26, 95% CI=1.02-1.56) and NCD (OR=1.24, 1.08-1.44) individuals had higher odds of MetS. FBC and NCU individuals did not differ significantly. Additional adjustments for income, education, age at immigration, language preference, and Short Acculturation Scale for Hispanics-Social & Ethnic Relations subscale, reduced the odds ratio for MetS for UBC (OR=1.11, 0.83-1.48), and slightly increased the odds ratio for NCD (OR=1.25, 1.07-1.45), as compared to FBC. Adjusting for sociocultural factors, significantly reduced the difference between UBC and FBC individuals, but increased the difference between NCD and FBC individuals, implying that either the benefits of citizenship or some other unmeasured factors may explain this association. In future work, we will consider how healthcare coverage, utilization, and healthy lifestyle factors may act as mediators. Our findings from the HCHS/SOL communities suggest that immigration status may be an important social determinant of CMR in Hispanic/Latino adults.

How do social and environmental neighborhood exposures jointly contribute to cardiometabolic health?
Noemie Letellier* Noemie Letellier Steven Zamora Jiue-An Yang Dorothy Sears Marta Jankowska Tarik Benmarhnia

Introduction

The evidence linking environmental determinants with cardiometabolic health is growing and may contribute to explain health inequalities. We examined whether environmental characteristics were associated with insulin resistance, hypertension, obesity, diabetes, and metabolic syndrome, considering the environmental characteristics individually and as joint exposures.

Methods

Among the Community of Mine study, in San Diego County, insulin resistance, hypertension, BMI, diabetes, and metabolic syndrome were measured. Seven environmental characteristics (economic, education, health resources, neighborhood conditions, transportation, social and clean environment) were assessed at the census tract level of residence. Generalized estimating equation models were performed to estimate β or relative risk (RR) and 95% confidence intervals (CIs) between each of the seven environmental characteristics and cardiometabolic outcomes. Quantile g-computation was used to examine the association between the joint effect of a simultaneous increase in all environmental determinants and cardiometabolic outcomes.

Results

Among 570 participants (mean age: 58.8), environmental economic, educational and health resources were individually associated with insulin resistance, diabetes, obesity, and metabolic syndrome. In the mixture analyses, a quartile increase in all positive environmental characteristics was associated with decreasing insulin resistance (β, 95%CI: -0.09, -0.18 to 0.01), risk of diabetes (RR, 95%CI: 0.59, 0.36 to 0.98) and obesity (RR, 95%CI: 0.81, 0.64 to 1.02). The environmental characteristics with the largest contributions were health care access, economic and educational resources.

Conclusion

Our analysis suggests that various environmental determinants synergistically contribute to cardiometabolic health and that analyzing such determinants independently may not fully capture the potential health benefits associated with social and environmental policies.

A National Assessment of the Contribution of Social Factors in Racial Disparities in Ideal Cardiovascular Health Nicole Fields* Nicole Fields Daesung Choi Shivani Patel

Background: Cardiovascular health (CVH) in Black adults, particularly Black women, has lagged behind that of White adults for decades. We examined the role of key policy-amenable social factors in observed racial disparities in ideal CVH by gender.

Methods: We utilized data from the National Health and Nutrition Examination Survey 2011-2018 cycles to assess disparities in ideal CVH between Black and White adults (N=8,047). Ideal CVH was defined using a score (range: 0-14; 14 optimal) derived by the American Heart Association based on 7 metrics: smoking, diet, body mass index, physical activity, total cholesterol, blood pressure, and HbA1c. We utilized decomposition analysis to assess the impact of equalizing the distribution of college education, income to poverty ratio (IPR), and food security on racial disparities in CVH.

Results: Black adults, compared to White adults, were less likely to be college educated (20.5% v 37.4%) and food secure (75.9% v 88.4%) and had lower IPR (2.33 v 3.37). CVH scores were lowest in Black women (M=7.84, SD=0.06) and highest in White men (M=8.49, SD=0.06). In women, the Black-White CVH disparity was -0.59 (95%CI: -0.75, -0.44); equalizing levels of college education, income, and food security across race was associated with a 47% potential reduction in the CVH disparity (absolute reduction: -0.28; 95%CI: -0.37, -0.18). In men, equalizing levels of these social factors was associated with a 31% reduction (absolute reduction: -0.12; 95%CI: -0.20, -0.04). After age-adjustment, social factors were no longer associated with reductions in the Black-White disparity in women or men.

Conclusions: While Black Americans lag behind White Americans in socioeconomic status and food security, these factors play a negligible role in the CVH racial disparity after accounting for age. Novel factors, such as structural racism, may offer further insight into the origins and intervention strategies to address disparities.

Figure 1. The Contribution of Social Factors to Racial Disparities in Ideal Cardiovascular Health by Gender

	Black Women (ref=White Women)[a]		Black Men (ref= White Men)[b]	
	Absolute Disparity (95% CI)		Absolute Disparity (95% CI)	
Total Initial Disparity in Ideal CVH Score[c]	-0.59 (-0.75, -0.44)		-0.39 (-0.56, -0.23)	
	Absolute Reduction in Disparity (95% CI)	% change from total initial	Absolute Reduction in Disparity (95% CI)	% change from total initial
Explained Disparity in Ideal CVH Score Individual Social Factors[d]				
College Education	**-0.17 (-0.23, -0.11)**	28.8%	**-0.15 (-0.21, -0.10)**	38.5%
Income to poverty ratio	**-0.25 (-0.34, -0.17)**	42.4%	-0.04 (-0.11, 0.03)	10.3%
Food Security	**-0.08 (-0.11, -0.04)**	13.6%	-0.04 (-0.09, 0.001)	10.3%
Combined Social Factors[e]	**-0.28 (-0.37, -0.18)**	47.5%	**-0.12 (-0.20, -0.04)**	30.8%
Age-adjusted Combined Social Factors[f]	-0.04 (-0.15, 0.07)	6.8%	-0.004 (-0.11, 0.10)	1.0%

[a]$N_{Black\ women}$ = 1,482; $N_{White\ women}$ = 2,628

[b]$N_{Black\ men}$ = 1,363; $N_{White\ men}$ = 2,574

[c]Initial disparity is the unadjusted differences between Black and white adults.

[d]Explained disparities are derived as coefficients obtained from three separate decomposition models that equalized education, income, food security levels, respectively, across race.

[e]Explained disparities are derived as coefficients obtained from a decomposition model that equalized education, income, food security levels across race.

[f]Explained disparities are derived as coefficients obtained from a decomposition model that equalized education, income, food security, and age levels across race.
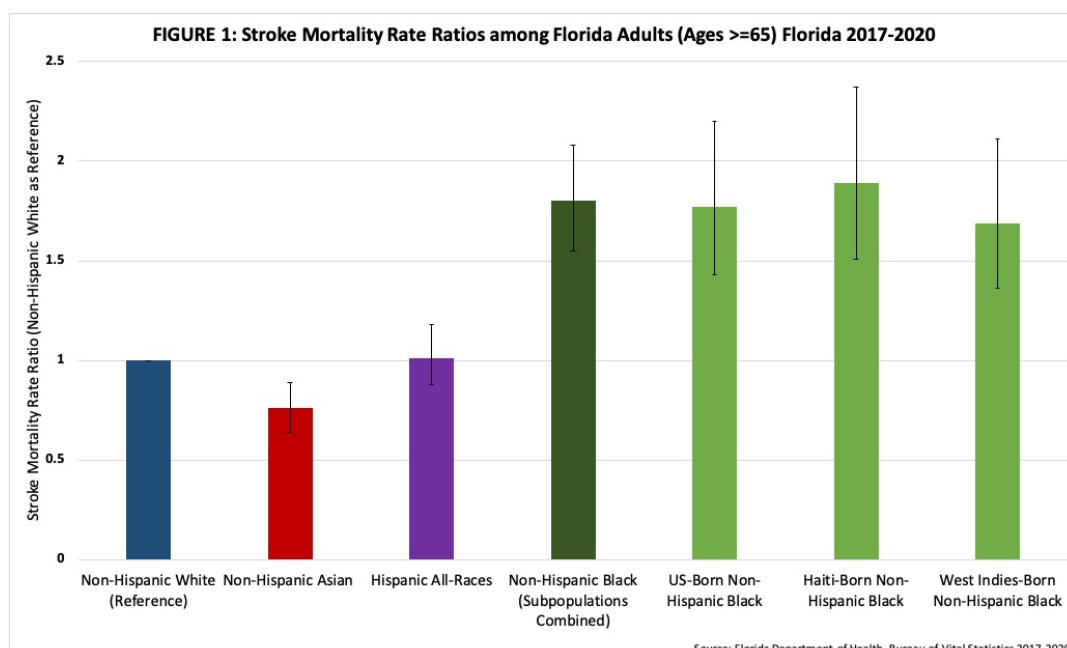
Cardiovascular

Stroke Mortality in Black Populations in Florida Karlon Johnson* Karlon Johnson WayWay
Hlaing Paulo Pinheiro

Background: Non-Hispanic Blacks are the racial-ethnic group most afflicted by stroke mortality.
Disparities in stroke mortality for subpopulations of African descent, who have varying stroke risk
factor prevalences, have never been studied in the US.

Methods: We utilized 2017-2020 population denominators from the American Community Survey to
match corresponding numerator data from the Florida Department of Health Bureau of Vital
Statistics. We computed the age-adjusted and sex-specific stroke mortality rates in adults 65 years
and older. We utilized negative binomial regression to calculate mortality rate ratios (MRRs) for
comparisons between different racial ethnic groups: (1) four race-ethnic groups: Non-Hispanic
Whites (reference group), Non-Hispanic Blacks, Non-Hispanic Asians, and Hispanics; and (2) three
Non-Hispanic Black subpopulations by nativity (US-, Haitian-, and West-Indies-Born). Age- and sex-
adjusted MRRs, were also calculated to evaluate differences within the three subpopulations, with
US-Born Blacks as the reference group.

Results: In our study population of 55,806 stroke deaths, mortality rates were the highest for non-
Hispanic Black males (66.7) and females (58.9) per 100,000 persons compared to non-Hispanic
White (38.8 and 39.8 per 100,000 for males and females respectively). Compared to the referent
non-Hispanic White group, Non-Hispanic Blacks had a higher stroke (MRR 1.80; 95% CI 1.55-2.08)
(**FIGURE 1**). All three nativity-specific non-Hispanic Black subpopulations had similarly high MRRs
[1.77 (95% CI 1.43-2.20), 1.89 (95% CI 1.51-2.37), and 1.69 (95% CI 1.36-2.11) for US-Born, Haiti-
Born, and West Indies-Born Non-Hispanic Blacks respectively].

Conclusion: Striking similarities in stroke mortality rates, despite differences in prevalence of risk
factors, call for increased research on vulnerabilities of Non-Hispanic Black subpopulations for
stroke and the development of more effective and culturally appropriate prevention strategies.

FIGURE 1: Stroke Mortality Rate Ratios among Florida Adults (Ages >=65) Florida 2017-2020

Source: Florida Department of Health, Bureau of Vital Statistics 2017-2020

Heightened Cardiovascular disease risk increase byassociated with PTSD is more prominent in patients with lower socioeconomic position: longitudinal evidences from a representative nationwide longitudinal database. Kwanghyun Kim* Kwanghyun Kim Ye Jin Jeon Jennifer A. Sumner Sun Jae Jung

Introduction: Substantial evidence indicates that posttraumatic stress disorder (PTSD) is linked to incident cardiovascular disease (CVD). We aimed to research sociodemographic heterogeneities in the association between PTSD and CVD.

Methods: Medical insurance claim records of patients with PTSD who were diagnosed in 2004-2018 (N=109,235) were recruited from Korean National Health Insurance Database (NHID). Patients aged 18 or younger at PTSD diagnosis (N=35,067), diagnosed with CVD before PTSD (N=2,493), and with erroneous records for insurance eligibility (N=5) were excluded, leaving 71,670 patients for final analyses. Age-, sex-, and enrollment year-matched 1:4 controls without PTSD diagnosis were recruited from general population registered at NHID. Monthly insurance premium was used as a surrogate variable for socioeconomic position. Time-dependent Cox regression models were used to estimate hazard ratios of PTSD on incident acute coronary syndrome, incident stroke, and cardiovascular mortality. Stratified analyses by age, sex and insurance premium were conducted to test heterogeneities in association.

Results: PTSD was associated with increased risk for acute coronary syndrome, hemorrhagic stroke, and cardiovascular mortality. PTSD was positively associated with ischemic stroke in men, but not in women. Elevated risk of cardiovascular diseases was more prominent in patients with PTSD aged 19-39 years than their older counterparts. Patients with a lower insurance premium, particularly male patients, showed a greater increase of CVD risks.

Discussion: Patients with PTSD showed higher risk for CVD than patients without PTSD. Younger patients and patients with lower socioeconomic position, especially men, are more likely to suffer from negative cardiovascular consequences associated with PTSD.
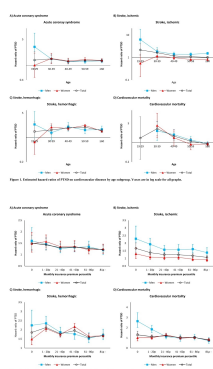
Cardiovascular

A national profile of cardiovascular disease deaths in the United States: The impact of community economic distress George Pro* George Pro Clare Brown Brooke E.E. Montgomery Nickolas Zaller

Introduction

Cardiovascular disease (CVD) is the leading cause of preventable death in the US, contributing to around 25% of all deaths. While many individual-level factors are known to influence CVD risk, less is known about how community-level economic distress may affect CVD burden. Better understanding local economies may help inform programmatic decision making to focus resource allocation and policies towards factors that have the greatest impact on CVD mortality.

Methods

Data from CDC Wonder was used (2017-2019) to identify CVD deaths at the county level (per 100,000) (n=3,048). The Distressed Communities Index (pooled 2015-2019) was used to identify county level indicators of economic distress, including education, unemployment, housing vacancy, income, employment changes, and establishment changes. We used linear regression to model log-transformed CVD death rates, predicted by all distress items and adjusted for race/ethnicity.

Results

From 2017-2019, the mean county CVD death rate was 468 per 100,000 and varied from 98 (Pitkin, CO) to 1,203 deaths per 100,000 (Alpine, CA). Of the indicators of economic distress, poverty was most strongly associated with CVD death ($\beta = 0.014$, SE = 0.001, $p < 0.001$). The average county-level poverty rate nationally was 15.2%, which ranged from 2.8% (Morgan, UT) to 55.5% (Todd, SD). Of the 1,013 counties in the highest quintile of poverty rates, 608 (60%) were also in the highest quintile for CVD deaths. These counties were largely concentrated in the US South (Figure 1).

Conclusion

CVD deaths varied significantly across counties, with higher levels of poverty being associated with higher rates of CVD deaths, illustrating a disproportionate health burden among low-income counties. Our findings suggest that promoting access to capital and wealth accumulation may lower CVD rates in poor and Southern counties.

U.S counties with a high proportion of the population in poverty and a high rate of CVD deaths, 2015- 2019

Counties with high % of poverty and high rate of CVD death
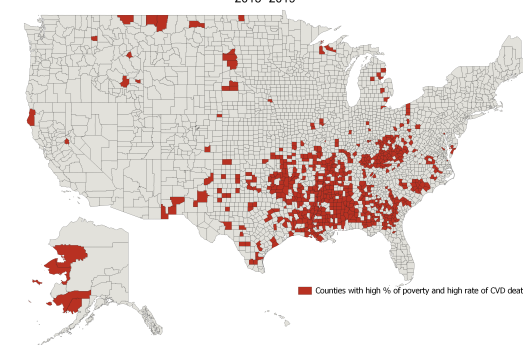
Temporal Trends in COVID-19 Vaccine Uptake by Occupational Group Garret M Guthrie*

Garret Guthrie Paul K Henneberger Jean M Cox-Ganser Caroline P Groth

Background: Limited work has been done to understand COVID-19 vaccine uptake by occupation. Our objective was to describe temporal trends in occupation-specific vaccination percentages during the COVID-19 pandemic in 2021.

Methods: We used data collected January-July 2021 by the daily Facebook/Delphi Group US COVID-19 Trends and Impact Survey. Survey respondents were Facebook users ≥18 years who reported working for pay in the last 4 weeks and answered the question "Have you had a COVID-19 vaccination?" Respondents reported their occupation by selecting a category based on the US Bureau of Labor Statistics 2018 Standard Occupational Classification (SOC) system. Vaccination percentages were calculated for 23 SOC major occupational groups and plotted by month. These percentages were weighted to adjust for non-response and to resemble the US general population.

Results: Vaccination percentages increased over time for all 23 major occupational groups, starting with a median of 6.3% in January 2021 and ending with 82.5% in July 2021. Healthcare Practitioners and Technicians, Healthcare Support, Community and Social Service, and Protective Service had the highest percentages (≥25%) in January, and all were above the median in July except for Protective Service (68.5%). Across all workers, the largest vaccination percentage point increase occurred March to April (+23.9%), a time when 18 of the 23 SOC groups experienced their largest increase. Three SOC groups had low month-to-month increases in vaccination percentages and by July had the lowest values: Farming, Fishing and Forestry (60.4%), Installation, Maintenance and Repair (59.0%), and Construction and Extraction (52.4%).

Conclusion: Our results suggest that workers in some SOC groups fell behind in vaccine uptake and may benefit from vaccine acceptance promotion activities.

Figure Title: Trends in COVID-19 vaccine uptake by major occupational group during 2021

Occupational
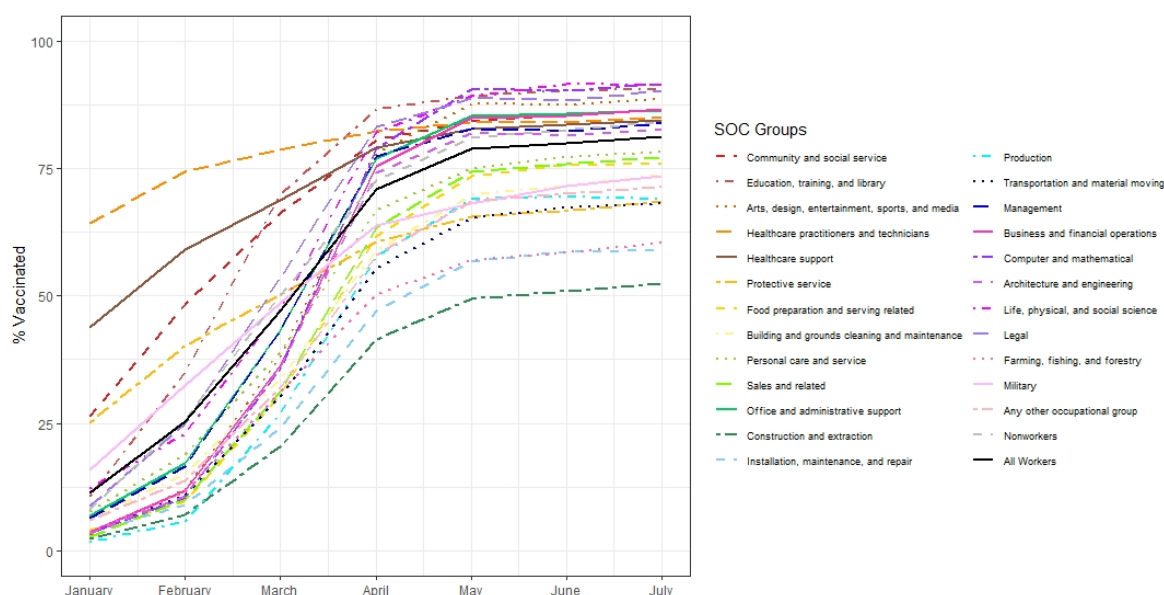
Metalworking fluids and cancer incidence in the United Autoworkers – General Motors cohort Hilary Colbeth* Hilary Colbeth Kevin Chen Sally Picciotto Sadie Costello Ellen A. Eisen

Objective Increased risks of mortality due to specific cancers have been consistently reported in relation to mineral oil-based metalworking fluid (MWF) exposure. We broadly examined cancer *incidence* and MWF exposure in the United Autoworkers-General Motors cohort. Based on previous work, we studied melanoma, leukemia, non-Hodgkin lymphoma and cancers of the colon, rectum, pancreas, esophagus, stomach, larynx, lung, breast, prostate, kidney, and bladder.

Methods The cohort includes 39,132 workers followed for cancer incidence in Surveillance, Epidemiology, and End Results Program (SEER) and Michigan cancer registries, from 1973-2015. Cox models with categorical variables for lagged cumulative exposure to each MWF type (straight, soluble, and synthetic) yielded adjusted hazard ratios (HR) estimates, using no exposure as the referent. Penalized splines were fit to examine the shape of the exposure-response relationships.

Results There were 7,809 cases of interest. Oil-based straight and soluble MWFs were each modestly associated with all cancers combined. Several specific cancers were associated with higher levels of straight MWF exposure, including stomach (HR: 1.54; 95% CI: 1.01-2.35) and kidney cancer (HR: 1.59; 95% CI: 1.09-2.31), as well as esophageal, rectal, bladder, and female breast. Soluble MWF was associated with non-Hodgkin lymphoma and prostate cancer, with HRs elevated to 1.70 (95% CI: 1.13-2.54) and 1.28 (95% CI: 1.10-1.49), respectively. Increasing exposure to water-based synthetic fluids was associated with increased risks of rectal and prostate cancers. Results for colon and lung cancers were null in all analyses.

Conclusions Our results are consistent with prior reports from this cohort and provide updated evidence for associations between each MWF and several cancers, particularly digestive and urinary tract cancers. These HRs do not address potential downward bias from the healthy worker survivor effect which may be necessary in targeted analyses.

Self-reported obstructive airway disease in WTC-exposed firefighters compared with non-WTC-exposed firefighters Alexandra Mueller* Alexandra Mueller Ankura Singh Mayris P. Webber Charles B. Hall David J. Prezant Rachel Zeig-Owens

Background

Firefighting has been associated with respiratory conditions, both nationally and internationally. Among firefighters, rescue/recovery work at the World Trade Center (WTC) on 9/11/01 is associated with obstructive airway disease (OAD) including diagnoses of asthma, emphysema/chronic obstructive pulmonary disease (COPD), and bronchitis. The degree to which routine, non-WTC firefighting exposures contribute to the WTC-exposure-OAD relationship is unknown.

Objective

To compare self-reported OAD diagnoses in WTC-exposed firefighters from the Fire Department of the City of New York (FDNY) to those from a cohort of non-WTC-exposed firefighters from other cities.
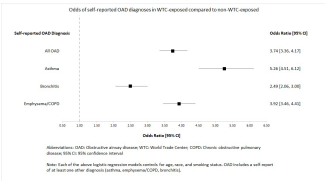
Methods

10,803 WTC-exposed male FDNY firefighters who receive routine monitoring and 3,129 non-WTC-exposed male firefighters from Chicago, Philadelphia, and San Francisco who were actively employed on 9/11/01 and completed a health questionnaire were included in analyses. Logistic regression estimated ORs of self-reported OAD diagnoses in WTC-exposed to non-WTC-exposed firefighters, adjusting for age, race, and smoking status.

Results

WTC-exposed firefighters were slightly younger on 9/11 on average (Mean±SD=40.0±7.7 vs. 43.6±8.9) and less likely to report ever smoking (32.3% vs. 43.7%) compared to non-WTC-exposed firefighters. All WTC-exposed firefighters (100%) had a recent medical visit through the WTC Health Program; nearly 90% of non-WTC-exposed firefighters had seen a medical professional within the year prior to data collection. Odds of self-reported OAD diagnoses were 3.7 times greater in WTC-exposed compared to non-WTC-exposed. Odds of self-reported asthma were over five times greater in those WTC-exposed (Figure).

Conclusion

Odds of all self-reported OAD diagnoses were greater in WTC-exposed compared to non-WTC-exposed after adjusting for covariates. While asthma and other OAD are known occupational hazards of firefighting, WTC exposure significantly compounded these adverse respiratory health effects.

Methods to Quantify Longitudinal Ototoxicant and Noise Exposure in Military Workplaces from Self-Reported Histories Kelly Reavis* Julieta Scalo Leslie Grush Samrita Thapa Emily Thielman Kathleen Carlson James Henry Kelly Reavis

Occupational noise exposure is a well-established risk factor for hearing loss and tinnitus, and there is a growing body of evidence to document ototoxicity due to occupational chemical exposures. The evidence suggests that chemical ototoxicants may potentiate noise-induced auditory damage, but the interaction of these two risk factors is poorly characterized. A particular challenge for estimating combined exposure effects is that individual trajectories for both noise and chemical exposure can vary greatly in terms of source, duration, frequency, and prophylaxis. Timing is an additional complication; risk levels likely differ between contemporaneous and asynchronous exposures. We present data from 940 Service members (503 recently separated, 437 currently serving) participating in the Noise Outcomes in Servicemembers Epidemiology (NOISE) study, a collaboration between the Veterans Affairs National Center for Rehabilitative Auditory Research and the Department of Defense Hearing Center of Excellence. Baseline assessments include an extensive audiometric and tinnitus (if present) evaluation as well as a comprehensive self-reported history to document occupational noise and chemical exposures (using the Lifetime Exposure to Noise and Solvents Questionnaire, LENS-Q). Exposure data were examined descriptively. Most participants reported some noise exposure (n = 890; 94.7%) and about one third reported chemical exposures (n = 292; 31.1%), mostly concurrent with noise (n = 289, 30.1%). For both noise and chemicals, exposure times ranged from 1 to 40 years, with a median duration of 7 years (interquartile range = 10). Among those who reported exposure to chemical ototoxicants, the most frequently reported ototoxicants were burn pits (42.5%), carbon monoxide (19.8%), lead (11.8%), and welding fumes (10.5%). Notably, for most participants who reported concurrent noise and chemical exposures, the overlaps were fragmented; start and end times, total duration, and total number of concurrent noise sources and ototoxicants varied over time. Detailed exposure data, including types of noise or chemicals, duration in years, daily frequency, and use of protective equipment over time and for each exposure, are presented at the individual level and in summary. We discuss methods for modeling this dynamic, complex landscape of occupational exposures over time. These methods have important implications for designating noise and ototoxicant hazards in military and other hazardous workplaces, refining environmental controls, and assessing and improving occupational auditory health outcomes

Associations between occupation-related factors and vitamin D deficiency: findings from the National Health and Nutrition Examination Survey, 2005-2010 Raquel Velazquez-Kronen*

Raquel Velazquez-Kronen Leslie A. MacDonald Amy E. Millen

Background: Vitamin D deficiency is highly prevalent worldwide; however, few large population-based studies exist that have examined occupational risk factors.

Objective: We examined the association between shift work, hours worked per week (hrs/wk), outdoor work exposure, occupation group, and vitamin D status in the U.S. working population.

Methods: This cross-sectional study included 8,601 workers aged ≥16 years from the 2005-2010 National Health and Nutrition Examination Survey cycles. Based on recommendations from the Institutes of Medicine and Endocrine Society, serum 25(OH)D concentration in nanomoles per liter (nmol/L) was categorized as sufficient (≥75), insufficient (50-<75), moderately deficient (30-<50), and severely deficient (<30). Job characteristics from the Occupational Information Network were used to determine whether work involved outdoor exposure. Age-adjusted multinomial logistic regression was used to examine associations between work-related factors and vitamin D status.

Results: Shift workers had higher odds of severe vitamin D deficiency compared to day workers (odds ratio [OR]:1.64, 95% confidence interval [CI]:1.22-2.19), with the association being greatest for night workers (OR:2.38, 95% CI:1.51-3.75). Compared to those employed in white-collar occupations, those in natural resources were less likely to be deficient (OR:0.31, 95% CI:0.19-0.52) while those in production were more likely to be deficient (OR:2.25, 95% CI:1.48-3.43). Those working ≥60 hrs/wk had higher odds of moderate deficiency compared to those working <20 hrs/wk (OR:1.61, 95% CI:1.21-2.14). Those working outdoors <1 hour were more likely to be severely deficient than those working outdoors ≥2 hours (OR:1.95, 95% CI:1.40-2.71). Associations were robust to adjustment for vitamin D supplementation and dietary intake.

Discussion: Work-related factors were highly associated with vitamin D status. Night and indoors workers may benefit from vitamin D screening and supplementation.

The prevalence of endometriosis and work-related exposures: The Environmental Health Study for Western New York – a prospective cohort study Maggie Fuzak* Maggie Fuzak Dr. Matthew Bonner Dr. Lina Mu Dr. Denise Feda Dr. James Olson Dr. Laurene Tumiel-Berhalter

Endometriosis is a chronic disease with few known risk factors beyond reproductive factors. However, emerging evidence indicates that environmental and occupational exposures, some which are hormonally active, may be important because endometriosis is an estrogen-dependent disease. In 2018, we enrolled 13,306 adults aged 18 years and above as part of the EHS4WNY a prospective cohort study designed to investigate industrial pollution and adult chronic diseases. Online and mailed, baseline self-administered questionnaires ascertained information on demographics, lifestyle factors, personal and family medical history, and selected work-related chemical exposures. Our analyses included 7,617 females. Prevalence ORs (95% CI's) were calculated with logistic regression, adjusting for age, menopausal status, age at menarche, and if ever pregnant. 508 (7.59%) participants reported a prior endometriosis diagnosis. The prevalence OR for endometriosis and workplace asbestos exposure was 1.55 (1.17-2.10) as compared with women who had no such exposure. Workplace exposure to chemicals/acids/solvents (OR=1.48; 1.20-1.82) and formaldehyde (OR=1.70; 1.18-2.44) were also associated with prevalent endometriosis. We did not see any association between endometriosis and coal or stone dusts, coal tar/pitch/asphalt, diesel engine exhaust, dyes, gasoline exhaust, pesticides/herbicides, textile fibers/dusts/wood dust, or x-rays/radioactive materials. While necessarily preliminary, the prevalence odds ratios for workplace exposures to chemicals/acids/solvents and formaldehyde and endometriosis were consistent with prior literature. Although to our knowledge, a positive association between workplace asbestos exposure and prevalent endometriosis has not been reported in the literature.

Childhood adversity and mental health outcomes among post-secondary students: A longitudinal study Asmita Bhattarai* Asmita Bhattarai Nathan King Kamala Adhikari Gina Dimitropoulos Dan Devoe Jin Byun Melanie Li Daniel Rivera Simone Cunningham Andrew GM Bulloch Scott B Patten Anne Duffy

Background:

Mental health concerns are common among post-secondary students and may be further elevated among those with childhood adversity. This study examined the association between childhood adversities and mental health outcomes among Canadian post-secondary students.

Methods:

The Queen's University Student Well-Being and Academic Success Survey surveyed cohorts of first year entering undergraduate students in Fall 2018 (n=2,994) and 2019 (n=2,949) and followed them through surveys in Spring 2019, Fall 2019, and Spring 2020. At baseline, students reported childhood physical abuse, sexual abuse, peer bullying, and parental separation/divorce. Surveys collected repeated data on anxiety (GAD-7) and depressive symptoms (PHQ-9), non-suicidal self-harm, and suicidal thoughts/attempts (C-CSSR), along with psychosocial and lifestyle variables. Repeated measures logistic regression, using Generalized Estimating Equations (exchangeable covariance) was used to characterize the association between childhood adversities and mental health outcomes.

Results:

Adjusting for known confounders (age, gender, ethnicity, familial mental illness, and parental education status), any childhood abuse (OR 2.89; 95%CI 2.58,3.23) and parental separation/divorce (OR 1.29; 95%CI 1.12,1.50) were significantly associated with a composite indicator of mental health outcomes (either PHQ-9 score ≥10 or GAD-7 score ≥10 or suicidality or self-harm). The association with child abuse weakened when adjusted for perceived stress, self-esteem, and insomnia (OR 2.05; 95%CI 1.80,2.34), and that with parental divorce weakened when adjusted for self-esteem (OR 1.17; 95%CI 1.00,1.36).

Conclusion:

Students with childhood adversity may be at high risk of adverse mental health and may benefit from a better understanding of how and when to seek support for their mental health. Student welfare services may benefit from including childhood adversity-informed interventions among students seeking mental health support.

Mental Health

Effect modification of transgender identity on relationship between adverse childhood experiences and depressive disorders in US adults using the BRFSS 2020 survey Sivasankar Balakrishnan* Sivasankar Balakrishnan Ann Weber

Introduction

Transgender (trans) adults have higher odds of mental illness, such as depression, compared to cisgender (cis) adults. Adverse childhood experiences (ACE) have been linked to higher odds of adult depression, especially in trans adults. Biological sex has also been linked to depression and shown to synergistically modify the effect of ACE on depression. The purpose of this study was to access the effect modification of the relationship between ACE and depressive disorders (DD) by trans identity, after accounting for birth sex.

Methods

A nationally representative sample of 214 trans and 53,769 cis US adults was retrieved from the 2020 Behavioral Risk Factor Surveillance System survey. ACE, trans identity, and presence of DD were self-reported. ACE was categorized into three groups by the number experienced: 0, 1-2, and 3+. The sample was stratified by birth sex. Adjusted, weighted logistic regressions were used to assess whether trans identity modified the effect of ACE on DD in each stratum.

Results

80% of trans compared to 64% of cis adults had experienced at least one ACE. The reference group was cis adults with no ACE. Among adults born female with 1-2 ACE, trans adults had higher odds of DD (aOR=8.69, 95% CI 1.51-49.91) compared to cis adults (aOR=1.89, 95% CI 1.68-2.25). Similar results were found in adults born female with 3+ ACE (trans: aOR=32.18, 95% CI 2.75-377.14; cis: aOR=4.02; 95% CI 3.36-4.80). CIs for trans adults in each stratum were large due to low sample size (trans male at birth=106; trans female at birth=108).

Conclusion

There is evidence of the synergistic effect modification of the relationship between ACE and DD by trans identity among US adults born female. Future studies should aim to collect more data on ACE in trans adults and better understand the mechanisms behind this synergistic interaction. Healthcare providers should consider the interaction of ACE and trans identity when diagnosing and treating trans patients for DD.

Pre-pandemic psychological resilience to trauma and changes in sleep and physical activity during COVID-19 among current and former female healthcare workers Laura Sampson*

Laura Sampson Kristen M. Nishimi Karmel W. Choi Yiwen Zhu Arielle Scoglio Qi Sun Eric B. Rimm Laura D. Kubzansky Karestan C. Koenen

The COVID-19 pandemic has resulted in high levels of distress, especially among healthcare workers and women. This distress may exacerbate maladaptive health behaviors like decreased physical activity and shorter sleep duration. Positive pre-pandemic mental health, including psychological resilience to prior trauma, may offset such behavior changes. We collected data from 18,000 current or former female nurses in the Nurses' Health Study II using pre-pandemic surveys in 2017-2019 and COVID-19-related surveys during 2020. Among women with trauma history (n=14,667), we created a 6-level categorical measure of pre-pandemic resilience to prior trauma by cross-classifying higher versus lower trauma burden (measured in 2019) by unfavorable, adequate, and favorable psychological health (measured in 2017-2019), where psychological health was defined by levels of both distress (post-traumatic stress disorder, depression) and emotional well-being (optimism, purpose, life satisfaction). On the May 2020 survey, 16.7% reported getting less sleep and 43.6% reported getting less physical activity since the start of the pandemic. Among current frontline healthcare workers (23.2% of the sample), these proportions were similar at 20.4% and 41.5%, respectively. Relative to women characterized as being most resilient (favorable psychological health despite higher trauma), only women with lower trauma and favorable prior psychological health had lower risk of getting less sleep (RR: 0.76; 95% CI: 0.69, 0.85) and less physical activity (RR: 0.94; 95% CI: 0.90, 0.99) during the pandemic. Women with higher trauma and unfavorable psychological health had the highest risk for both outcomes (see figure). No differences in these relationships by frontline healthcare worker status was observed. Higher pre-pandemic resilience may protect against worsening health behavior during the pandemic among current and former female healthcare workers, which could have long-term health implications.

Figure. Natural logs of adjusted risk ratios for pre-pandemic psychological resilience (2017-2019) in relation to reporting less sleep since the start of the COVID-19 pandemic (2020), among 14,667 women with trauma history in the Nurses' Health Study II. [a]
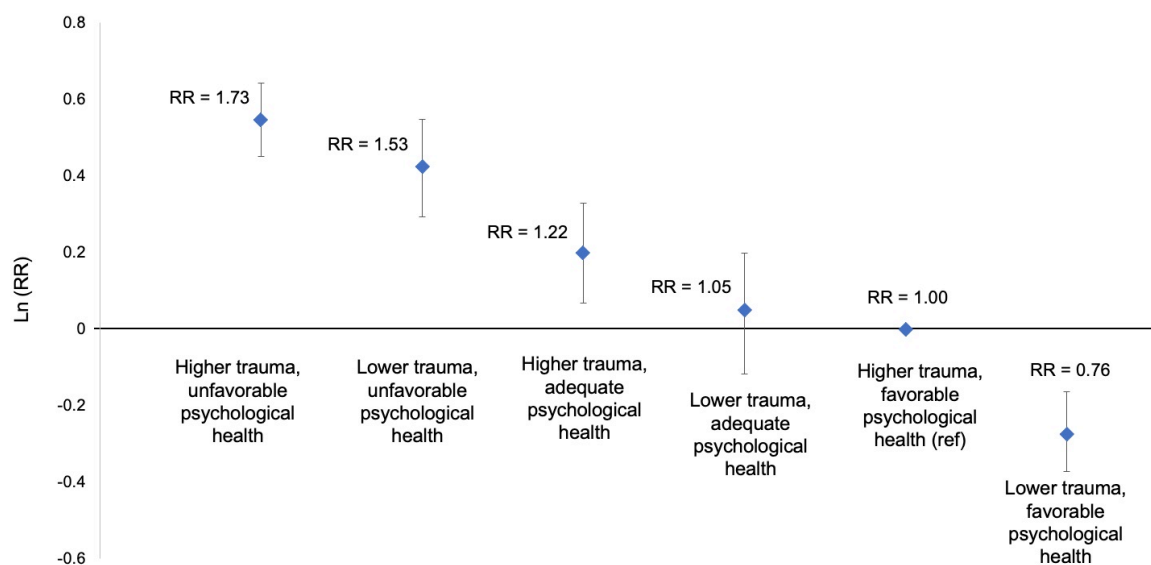
[a] Ln = natural log. RR = risk ratio. Models are adjusted for age, race, education, marital status, chronic conditions, living arrangement, and quartile of census tract median income. Trauma was assessed with a modified version of the Brief Trauma Questionnaire.

The association between adverse childhood experiences and adulthood obesity on stressors and the perceived consequences of the COVID-19 pandemic: A longitudinal study using the Canadian Longitudinal Study on Aging (CLSA) Vanessa De Rubeis* Vanessa De Rubeis Andrea Gonzalez Margaret de Groh Ying Jiang Urun Erbas Oz Jean-Eric Tarride Nicole E. Basta Susan Kirkland Christina Wolfson Lauren E. Griffith Parminder Raina Laura N. Anderson

Adverse childhood experiences (ACEs) and obesity are established risk factors for chronic stress in adulthood, thus it is possible these factors may also impact stress during the pandemic. The objectives of this study were to evaluate the associations between ACEs, obesity, and measures of stress during the pandemic and to determine if the association between obesity and stress was modified by ACEs. A longitudinal study was conducted among adults aged 50-96 years from the Canadian Longitudinal Study on Aging (CLSA) who participated in the COVID-19 Questionnaire Study (n=23,972). ACEs and obesity were measured pre-pandemic (2015-2018) and study outcomes (number of stressors and negative perceived consequences of the pandemic) were measured at COVID-19 Exit Survey (Sept-Dec 2020). Adjusted risk ratios (RRs) and 95% confidence intervals (CIs) were estimated for the associations between both ACEs and obesity, and study outcomes using Poisson and binomial regression. Effect modification by ACEs was assessed on the additive and multiplicative scales. ACEs were strongly associated with all outcomes. For instance, those with 4-8 ACEs, compared to none, were at an increased risk of an additional stressor (adjusted RR=1.53, 95% CI: 1.43-1.63) and perceiving the consequences of the pandemic as negative or very negative (adjusted RR=1.31; 95% CI: 1.18-1.46). Obesity was also associated with increased resource-related stressors (class III severe obesity versus normal weight adjusted RR=1.38; 95% CI: 1.25-1.53) and health-related stressors (class III severe obesity versus normal weight adjusted RR= 1.25; 95% CI: 1.12-1.39). There was limited evidence of interactions on the additive and multiplicative scales. Both ACEs and adult obesity were strongly and independently associated with increased stressors and negative perceived consequences of the pandemic. Experiences across the life course should be recognized when evaluating the consequences of the COVID-19 pandemic.

Association between adverse childhood experiences and later life allostatic load in UK Biobank female participants Debbie Jakubowski* Debbie Jakubowski Caryn Peterson Jiehuan Sun Kent Hoskins Garth Rauscher Maria Argos
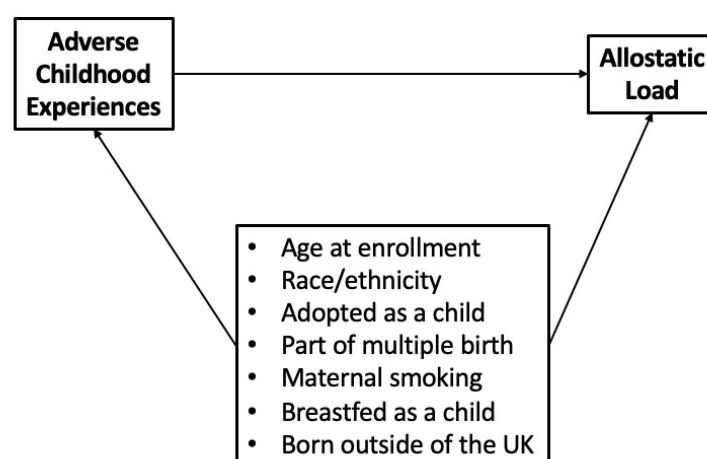
Background: Adverse childhood experiences (ACEs) during key developmental periods have been shown to impact long-term health outcomes. ACEs include psychological, physical or sexual abuse, neglect, and more. ACEs have been linked with an increase in poor health behavior such as smoking and alcohol consumption, and may also influence epigenetic changes, inflammatory response, metabolic changes, and allostatic load (AL). We sought to explore associations between ACEs and later life AL in female participants in the UK Biobank.

Methods: The UK Biobank is a multisite cohort study capturing lifestyle, environment, exposure, health history, and genotype data on individuals in the UK. ACEs were assessed from the Childhood Trauma Screener, which measures abuse and neglect across five items. Biological measures at enrollment were used to construct AL, including measures of metabolic, inflammatory, and cardiovascular function. Females with a cancer diagnosis prior to enrollment were removed as it may influence AL. Linear regression models were used to assess the association between ACEs and AL, accounting for a priori confounders.

Results: A total of 47,545 females with complete data were analyzed, with a median age at enrollment of 54 years (range 40 to 70 years.) Among the study sample, 79.2% reported no ACEs, and 2.7% reported three or more (range 0 to 5.) AL ranged from 0 to 9 with a mean score of 2.6 (SD 1.3.) After adjusting for confounders, there was no observed association of AL for each additional ACE reported (beta=0.0, 95% CI: -0.02 to 0.02.). Similar results were observed when assessing individual ACE components.

Conclusions: This analysis found no association between reported ACEs and later life AL in females. These results add to current literature with varied findings. Future incorporation of early life socioeconomic factors should be explored.

Directed Acyclic Graph

Adverse childhood experiences moderate the impact of disaster trauma on cognitive disability. A natural experiment from the 2011 Great East Japan Earthquake and Tsunami

Sakurako Okuzono* Sakurako Okuzono Koichiro Shiba Slopen Natalie Aki Yazawa Ichiro Kawachi

Little is known about the sources of population heterogeneity in long-term adverse health consequences following exposure to disaster-related trauma. We examined whether adverse childhood experiences (ACEs) potentiate the association between disaster-related traumas and subsequent cognitive disability among survivors. We used a prospective cohort study of older adults (≥65 years) who survived the 2011 Great East Japan Earthquake. The baseline survey predated the disaster by 7 months. Participants were free of cognitive disability before the disaster (n=602) and completed the 2013 and 2016 post-disaster surveys. Participants retrospectively reported on disaster-related traumas (home loss, relocation, loss of relatives/friends/pets, job loss, and worsening economic condition). ACEs were assessed in 2013 and categorized into binary (≥2 ACEs vs. < 2 ACEs). Cognitive disability levels (range: 1-8) in 2016 were obtained via in-home assessment by a trained investigator. After adjusting for pre-disaster characteristics using a doubly-robust Targeted Maximum Likelihood Estimation combined with machine learning algorithms (SuperLearner), home loss and relocation were associated with greater cognitive disability. Among individuals with more ACEs, home loss was associated with even higher cognitive disability levels relative to the association among those with fewer ACEs. Loss of friends and pets were both associated with higher cognitive disability levels, but only among those reporting more ACEs. Loss of friends and pets were associated with higher cognitive disability levels only among those with more ACEs. Our findings suggest that a history of ACEs may increase vulnerability for developing cognitive disability following exposure to specific types of disaster-related traumas.
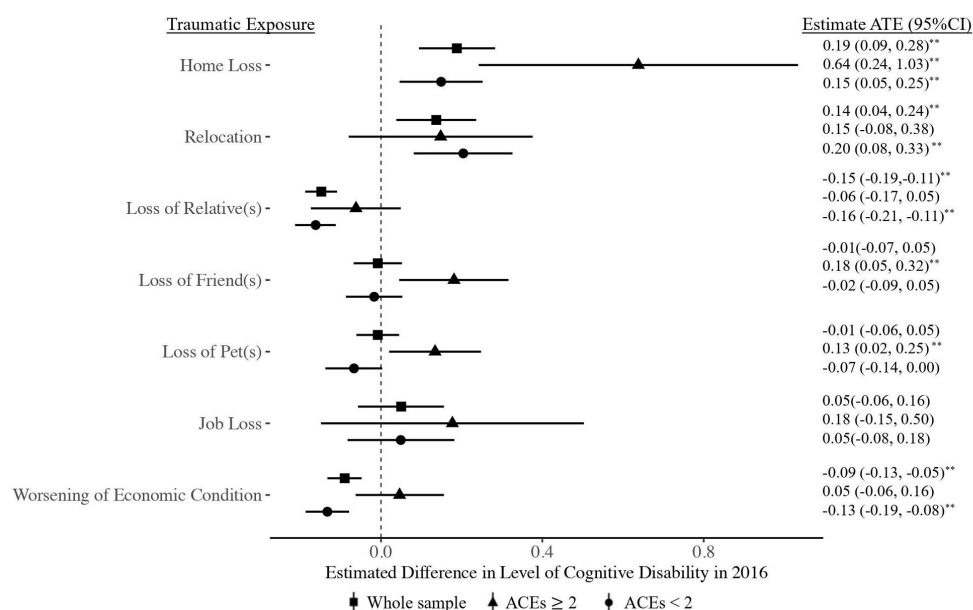

Figure . Association Between Disaster-Related Traumatic Experiences and Levels of Cognitive Disability in 2016 by Adverse Childhood Experiences Status.
Average Treatment Effect (ATE) of the disaster-related traumatic experiences were estimated via the doubly-robust targeted maximum likelihood estimation (TMLE). We used the SuperLearner to fit the models flexibly using generalized linear models. Levels of certified cognitive disability ranged from 1(no cognitive disability) to 8 (need treatment). Hence, larger effect estimate indicates greater levels of cognitive disability. We adjusted for age, gender, marital status, equivalized income, educational status, employment status, IADL (Instrumental Activity of Daily Living, depressive symptoms assessed with the Geriatric Depression Scale, chronic condition, current alcohol consumption, and current smoking status from the baseline wave (2010). To examine the effect modification by ACEs, we stratified by ACEs status (<2 or ≥2) via bootstrapping with 1,000 replications. Binary status of ACEs was created from total number of ACEs (ranging 0 to 8).
**p<0.05

Aging

Life Course Food Insecurity Among Older Adults Predicts Elevated Subsequent Dementia Risk Suzanna Martinez* Haobing Qian Anusha Vable Aayush Khadka Maria Glymour

Background: Dementia is a leading cause of death in the U.S. Persistent food insecurity across life course is a potential determinant of dementia risk. Food insecurity is modifiable and can be alleviated through federal state and local levels. Yet there are few studies examining the relationship between food insecurity and Alzheimer's Disease and Alzheimer's Related Dementias (AD/ADRD).
Objective: We aimed to investigate the relationship between food insecurity and dementia risk from 2014 to 2018 among US adults aged 55 years or older.
Methods: We used a subsample of Health Retirement Study (HRS)respondents who participated in a 2013 Health Care and Nutrition Study (N=5496 in 2014, N=4941 in 2016, N=3766 in 2018 with complete demographic information out of total of 8071). The exposure is food insecurity. We constructed a binary indicator and 3-level categorical variable based on USDA based on 6-item U.S. Household Food Security Survey Module as high and marginal food security (reference group), low food security and very low food security. The outcome measure was dementia risk. It is an algorithmically defined dementia probability score (ranging from 0 to 1). We fit a Generalized Estimation Equation with a logit link adjusting for age, age at baseline, gender, race/ethnicity, marital status, socioeconomic status in 2012 including education, income and wealth, parental education, birthplace, and parental education which precedes the exposure in 2013.
Results: Higher food insecurity predicts higher dementia risk. We found being food insecure is associated with a 0.48 increase in the log odds of dementia probability relative to being food secure, conditional on covariates (β=0.48,OR=1.62, 95% CI:0.23,0.72); being low food secure is associated with a 0.45 increase in the log odds of dementia probability (β=0.45, OR=1.57, 95% CI: 0.15,0.75), and being very low food secure is associated with a 0.51 increase in the log odds of dementia probability (β=0.51, OR=1.67, 95% CI: 0.17,0.85), relative to being food secure respectively. Effect modification results also show differences in food insecurity effects by gender. Female reduced the negative effects of food insecurity (binary indicator specification).
Conclusion: Food insecurity in older adulthood predicts later dementia risk. Higher level of food insecurity is associated with higher dementia risk. The effects also vary by gender.

Prevalence of depression and anxiety among older Americans with hearing loss before and during the COVID-19 pandemic Hua Ou* Hua Ou Chuan-Ming Li Howard Hoffman

OBJECTIVES.

To determine the prevalence of depression and anxiety among older Americans with hearing loss before and during the COVID-19 pandemic.

METHOD.

We analyzed the National Health and Aging Trends Study (NHATS), a nationally representative survey of Medicare beneficiaries conducted annually since 2011. Hearing loss was evaluated using Yes/No responses to any hearing trouble questions. Depression and anxiety were assessed using the Patient Health Questionnaire for Depression (PHQ-2) and Generalized Anxiety Disorder Screener (GAD-2), with reference period "previous 30 days." We applied a cut-off score of three for both depression and anxiety. A total of 4,389 participants (aged ≥ 65 yrs; female 56.0%) completed both Round 9 (2019) and 10 (2020). Multivariable logistic regression models were adjusted for demographic factors and comorbidities.

RESULTS.

In 2019, the prevalence of depression and anxiety was 5.1% (95%CI: 4.3-5.8%) and 5.0% (95%CI: 4.2–5.9%), respectively. Both prevalence increased slightly in 2020, with depression at 5.7% (95%CI: 4.9–6.4%) and anxiety at 5.5% (95%CI: 4.5–6.5%). Prevalence of hearing loss was 29.3%, representing 9.6 million older adults in the US. Depression increased from 5.8% (95%CI: 4.3-7.2%) in 2019 to 8.0% (95%CI: 6.3-9.7%) in 2020 among people with hearing loss, while anxiety increased from 5.3% (95%CI: 4.0-6.6%) to 7.6% (95%CI: 5.8-9.3%).

Hearing loss was significantly related to a higher risk of depression among older adults in both unadjusted (OR 1.7; 95%CI: 1.2–2.5) and adjusted multivariable analyses (OR 1.5; 95%CI: 1.01–2.1). For anxiety, hearing loss was a significant risk factor using unadjusted OR 1.5 (95%CI: 1.1–2.1), however, not significant as adjusted OR 1.4 (95%CI: 0.96–2.0).

CONCLUSIONS.

Given the high prevalence of hearing loss and its association with depression and anxiety, the provision of integrated mental health and hearing care to older adults with hearing loss during and after the COVID-19 pandemic is essential.
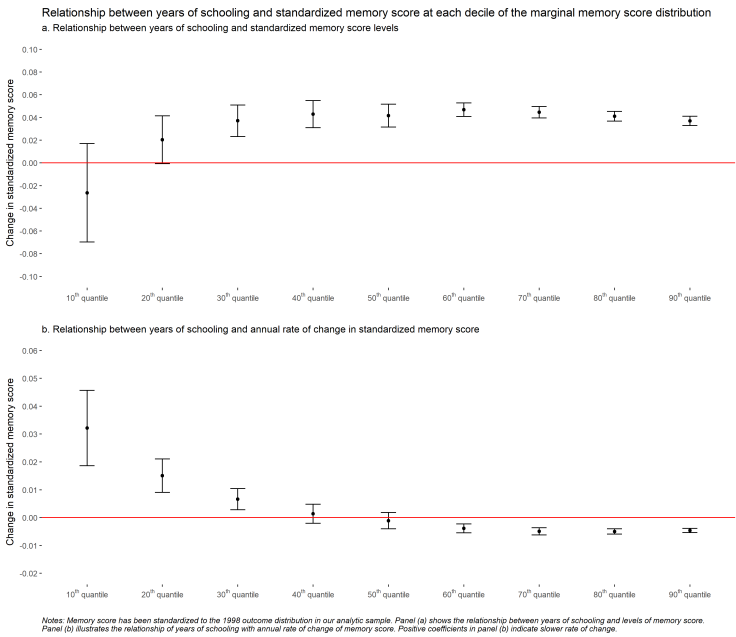
Racial difference in midlife employment-poverty histories and health: An application of sequence analysis Peiyi Lu* Peiyi Lu Katrina Kezios Adina Zeki Al Hazzouri

In the US, Black adults encounter more barriers in the job market and earn less compared to White adults. Such structural disadvantages can accumulate over the lifecourse and contribute to racial health disparities in older age. However, disparities in the combined employment and poverty histories for Black and White Americans and their implications for later health outcomes are not fully understood. This study characterized the employment-poverty histories for Blacks and Whites in middle-age, and examined their association with health in later life. Our sample included respondents who were born in 1948-1953 and enrolled in the 2004 Health and Retirement Study (=555, =2,209). We used sequence analysis to group respondents with similar employment-poverty trajectories from 2004 to 2016. Next, using regression and survival models, we estimated the association between employment-poverty trajectories and several health measures (self-reported health, depressive symptoms, and cognition, mortality) in 2018 (mean age = 67.11, SD=1.75). Three trajectories were identified for Black and White respondents, separately. For Black respondents, 23.06% experienced the "double jeopardy" of both employment and financial fluctuations in 2004-2016. Among this group, worse cognition (β=-0.37, 95%CI=-0.59, -0.16) and higher mortality risk was observed compared with their employed and not poor counterparts. To contrast, none of the White respondents experienced poverty risk over this period, even when employment fluctuations were present. Among White Americans, those with employment fluctuations had higher risk of poor health (RR= 1.10, 95%CI=1.04, 1.15) and elevated depressive symptoms (RR=1.06, 95%CI=1.01, 1.12), worse cognition (β=-0.21, 95%CI=-0.30, -0.12) and higher mortality risk than their employed counterparts. For both Black and White respondents, having employment fluctuations was associated with worse health, especially cognition. The observed association for cognition was strongest among the group of Black Americans who experienced the "double jeopardy" of both employment fluctuations and poverty. These findings highlight the importance of enhancing employment stability and suggest that additional programs to reduce poverty risk are especially needed for Black Americans.

More years of education predicts slower memory decline at the lower quantiles of the outcome distribution, but faster decline at the upper quantiles in the Health and Retirement Study cohort: An unconditional quantile regression analysis Aayush Khadka*

Aayush Khadka Haobing Qian M. Maria Glymour Elizabeth Rose Mayeda Willa D. Brenowitz Anusha M. Vable

Higher educational attainment predicts higher cognition levels across all ages, but the effect on rate of cognitive decline in later-life, a predictor for mild cognitive impairment and dementia, is not clear. Nearly all prior research has focused on differences in average cognitive test scores. Little is known about the education-cognition relationship at different quantiles of the cognitive function distribution. We investigated the relationship of education with memory levels and decline at each decile of the marginal memory distribution among individuals 65 years and older in the Health and Retirement Study from 1998 onward (N=23,881; 117,403 person-wave observations).

We defined educational attainment as the total number of years in school. Our outcome was a previously validated composite memory score that combined direct and proxy memory assessments. We standardized the memory score to the 1998 outcome distribution. We used unconditional quantile regressions to estimate the education-memory relationship at each decile of the marginal outcome distribution while controlling for individual-level, baseline confounders and accounting for differential loss to follow-up using inverse probability of censoring weights. Higher years of education predicted higher memory levels except at the 10th (worst) quantile of the marginal memory score distribution. Higher years of education also predicted slower annual memory decline at the 10th-30th quantiles (e.g., at the 10th quantile, $\beta = 0.03$, 95% CI: 0.02, 0.05) and a small but faster decline at the 60th-90th quantiles (e.g., at the 90th quantile, $\beta = -0.005$, 95% CI: -0.005, -0.004). Our results show that education is positively associated with higher memory levels at almost all quantiles of the outcome distribution. Our results also suggest that more years of schooling may slow memory decline for those at the lower tail of the memory distribution, but the reverse association may prevail for people with high memory scores.

Relationship between years of schooling and standardized memory score at each decile of the marginal memory score distribution
a. Relationship between years of schooling and standardized memory score levels

b. Relationship between years of schooling and annual rate of change in standardized memory score

Notes: Memory score has been standardized to the 1998 outcome distribution in our analytic sample. Panel (a) shows the relationship between years of schooling and levels of memory score. Panel (b) illustrates the relationship of years of schooling with annual rate of change of memory score. Positive coefficients in panel (b) indicate slower rate of change.

Aging

**Pathways explaining racial/ethnic disparities in incident all-cause and Alzheimer's Disease dementia among older US men and women** MAY A. BEYDOUN* MAY BEYDOUN Jordan Weiss Hind A. Beydoun Marie T. Fanelli-Kuczmarski Sharmin Hossain Ziad W. El-Hajj Michele K. Evans Alan B. Zonderman

Background: Racial disparities in Alzheimer's Disease (AD) and all-cause dementia incidence may exist differentially among men and women, with unknown explanatory mechanisms.

Methods: A retrospective cohort study examining all-cause and AD dementia incidence was conducted linking third National Health and Nutrition Examination Surveys (NHANES III) to Centers for Medicare and Medicaid Services-Medicare data over ≤26y of follow-up (1988-2014). Cox regression and generalized structural equations models (GSEM) were constructed among men and women aged≥60y at baseline (N=4,592). Outcomes included onset ages of all-cause and AD dementia, while the main exposures were race/ethnicity contrasts (RACE_ETHN). Potential mediators (z-scores), included socio-economic status (SES), lifestyle factors [dietary quality (DIET) nutritional biomarkers (NUTR), Physical Activity (PA), social support (SS), alcohol (ALCOHOL), poor health or HEALTH, poor cognitive performance or COGN. In addition to RACE_ETHN, baseline age, sex, urban-rural, household size and marital status were exogenous covariates in the GSEM and potential confounders in Cox models.

Results: Non-Hispanic Black women had higher risk of DEMENTIA versus Non-Hispanic White (NHW) women in GSEM, consistently with Cox models (Age-adjusted model: hazard ratio (HR)=1.34, 95% confidence interval (CI): 1.10-1.61). This total effect of this RACE_ETHN contrast in women was explained by four main pathways: (1) RACE_ETHN–> poor cognitive performance (COGN,+)–>DEMENTIA(+); (2) RACE_ETHN à SES(-)–>COGN(-)–>DEMENTIA(+); (3) RACE_ETHN –> SES(-) à physical activity (PA,+))–> COGN(-)–>DEMENTIA(+); (4) RACE_ETHN à SES(-) –> DIET(+)) –> COGN(-)–>DEMENTIA(+). A reduced AD risk in Mexican-American (MA) women vs. NHW women upon adjustment for SES and downstream factors (HR=0.53, 95%CI: 0.35-0.80). For the Non-White vs. NHW contrast in incident DEMENTIA, pathways involved lower SES increasing cognitive deficits which then directly increases DEMENTIA or indirectly through lifestyle factors.

Conclusion: Socio-economic and lifestyle factors explaining disparities between NHB and NHW in dementia onset among women are important to consider for future observational and intervention studies.
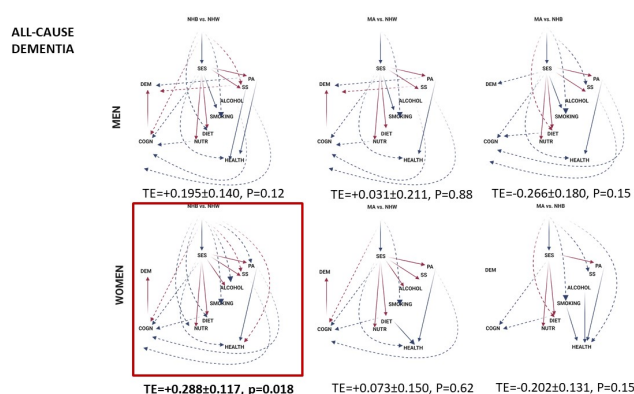
The Impact of Attending Historically Black Colleges and Universities on Cognitive Decline in Late-life Black Adults: A Longitudinal Analysis in the KHANDLE and STAR cohorts

Harmon Khela* Marilyn Thomas Camilla Calmasini Harmon Khela Taylor Mobley Elizabeth Rose Mayeda Christina Mangurian Lisa L. Barnes Paola Gilsanz Rachel A. Whitner M. Maria Glymour

Cognitive decline (e.g., Alzheimer's Disease) disproportionately impact older Black adults, yet there is limited research on drivers of cognitive decline among Black adults. Although education is linked to improved cognitive outcomes regardless of race, schooling is a heterogeneous experience: it is vital to evaluate educational experiences that distinctly impact Black Americans. Attendance at Historically Black Colleges and Universities (HBCUs) is a promising and unexplored mechanism that may influence later life cognition among Black adults.

We used data from the Study of Healthy Aging in African Americans (STAR) and the Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE), two cohorts of long-term Kaiser Permanente healthcare members. Executive function (EF) and verbal memory (VM) were assessed by the Neuropsychological Assessment Scales (3 waves each 14 months apart). HBCU attendance (yes/no) was self-reported. We fit linear mixed-effects models with random intercept adjusted for study factors (e.g., years since baseline, practice effects), participant predictors (e.g., baseline age, gender, academic support), and a time by HBCU attendance interaction term to evaluate differences in cognitive decline rates.

Among 710 Black participants, the average age was 70 (SD=8.4), and 8.2% attended an HBCU. HBCU attendance was not associated with EF [β_{EF}=-0.03 (-0.27,0.21)] or VM [β_{VM}=-0.01 (-0.25,0.23)] at baseline, nor with rate of change in VM [β_{VM}=0.00 (-0.09,0.10)]. However, HBCU attendance was marginally associated with rate of change in EF [β_{EF}=0.04 (-0.03,0.11)] (Fig 1).

 HBCU attendance was not associated with cognitive decline, however confidence intervals were too wide to rule out important benefits or harms. Harmonized analyses with studies including other aspects of HBCUs (e.g., prestige) are likely needed. Research on late life health outcomes should incorporate race-based experiences that may differentially offer protective advantages to Black adults.
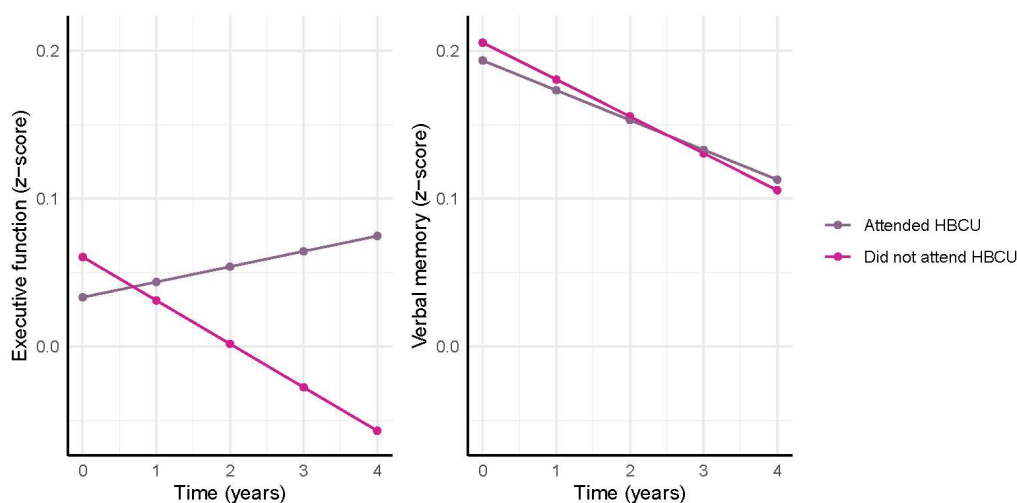
Indirect effects of statin initiation on Alzheimer's disease and related dementias mediated by LDL cholesterol: Comparing definitions of L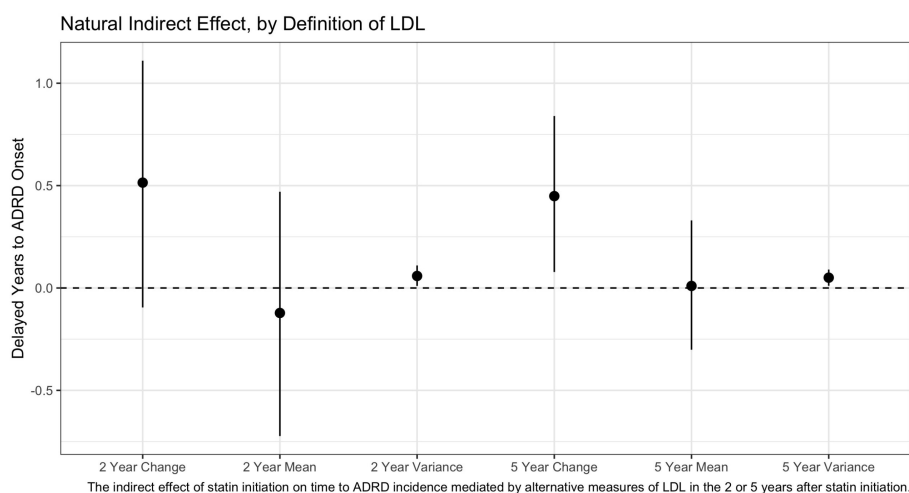DL change in electronic health records Erin Ferguson* Erin Ferguson Scott C Zimmerman Chen Jiang Vidhu Choudhary Kaitlin Swinnerton Thomas Hoffmann Eleanor Hayes-Larson Aline D Folle Elizabeth Rose Mayeda Ronald Krauss Catherine Schaefer M Maria Glymour

Introduction: Changes in low density lipoprotein (LDL) cholesterol induced by statin use may reduce Alzheimer's disease and related dementia (ADRD) risk, but research is methodologically difficult. We evaluated indirect effects of LDL changes after statin initiation on ADRD risk in the unique Kaiser Permanente Northern California (KPNC) Research Program on Genes Environment and Health Cohort, comparing 6 ways of characterizing LDL changes.

Methods: Analyses included KPNC health plan members who completed a survey around 2007 and had no prior history of statin use or ADRD, with follow-up through 2019 (n=113,753). At statin initiation (first prescription), participants were age-matched to 6 individuals who had not initiated statins. Mediator LDL variables (mean, variance, and change between last LDL prior to initiation and mean mediator LDL) were defined over a 2 or 5 year "mediation period" after statin initiation. To avoid immortal time bias, follow-up began after this period, limited to participants without ADRD diagnosis or censoring events during the mediation period. Weibull survival models for incident ADRD were censored at death or end of membership or study period. We estimated the natural indirect effect of changes in LDL induced by statin initiation on time to ADRD, with adjustment for race, sex, education, marital status, income, nativity, self-reported health, diabetes, smoking, and CVD history at baseline.

Results: Statin initiation reduced 2- and 5-year mean LDL (average 5-year decrease of 42.7 mg/dL [SD=25.5]) and increased LDL variance. The indirect effects of statin initiation on ADRD mediated by changes in LDL were small (Figure). For example, the change in 5-year mean LDL delayed expected time to ADRD onset by 0.45 years (95%CI: 0.08-0.84).

Conclusions: Small estimated indirect effects of statin initiation on ADRD incidence were sensitive to the definition of LDL used. Findings should be cautiously interpreted given possible unmeasured confounders.

Natural Indirect Effect, by Definition of LDL

The indirect effect of statin initiation on time to ADRD incidence mediated by alternative measures of LDL in the 2 or 5 years after statin initiation.

LATEBREAKER

Aging

An evaluation of selection processes into US Alzheimer's Disease Centers Sindana Ilango*
Sindana Ilango Yuan Zhang Eleanor Hayes-Larson Katrin Wolfová Ryan Andrews Melinda Power
Alden Gross

Background: A challenge in identifying determinants of Alzheimer's disease and related dementias
(ADRD) is the lack of population-representative data. Understanding the selection process into a
sample is important in thinking about whom the estimates might apply to and how they might differ
from a target population of interest. The National Alzheimer's Coordinating Center (NACC), is one of
the largest resources of cognitive, neuroimaging, and pathology data on ADRD. Although NACC is
often analyzed in aggregate, it is composed of data from many Alzheimer's Disease Centers (ADRCs)
across the United States; heterogeneity in selection processes and sample composition across
centers may affect measures of association and interpretation of results from the dataset in
aggregate.

Methods: Our objective of this study was to describe the sample composition of ADRCs. We used
linear regression models to estimate the effects of demographic and socioeconomic characteristics
on cognitive, imaging, and neuropathological outcomes in the four centers with largest sample size.

Results: We found that the relationship between demographic and socioeconomic characteristics
(e.g., race/ethnicity, age, and education) and cognitive performance varied across centers. For
example, race/ethnic minorities were associated with worse cognitive performance in some centers
(β= -1.96, SE=0.27) and not others (β=0.27, SE=0.58).

Conclusions: Estimates of associations between known risk factors and cognitive outcomes varied
substantially across centers within NACC. Efforts to generalize/transport NACC findings to target
populations should consider center-specific selection and sample compositions.

Development of a model to predict psychotherapy response for depression among Veterans

Hannah N. Ziobrowski* Hannah Ziobrowski Ruifeng Cui Eric L. Ross Howard Liu Victor Puac-Polanco Brett Turner Lucinda B. Leung Robert M. Bossarte Corey Bryant Wilfred R. Pigeon David W. Oslin Edward P. Post Alan M. Zaslavsky Jose R. Zubizarreta Andrew A. Nierenberg Alex Luedtke Chris J. Kennedy Ronald C. Kessler

Background: Less than half of patients with major depressive disorder (MDD) respond to psychotherapy. Pre-emptively informing patients of their predicted likelihood of responding could be used as part of a patient-centered treatment decision-support plan. Such an approach could help patients who are unlikely to respond to psychotherapy receive alternative treatments sooner, thereby reducing costs to patients and healthcare systems.

Methods: This prospective observational study examined a national sample of 807 patients beginning psychotherapy for MDD at the Veterans Health Administration. Patients completed a self-report survey at baseline and 3-months follow-up (data collected 2018-2020). A machine learning model to predict psychotherapy response at 3 months was developed using baseline survey, administrative, and geospatial variables in a 70% training sample. Model performance was then evaluated on the remaining 30%. We compared an ensemble machine learning method, Super Learner, to a simpler lasso method.

Results: 32.0% of patients overall responded to treatment after 3 months. A lasso model performed slightly better than the ensemble model. This lasso model had an area under the receiver operating characteristic curve of 0.652 (standard error=0.038) in the test sample. Fifty percent of patients in the top tertile of the predicted risk distribution responded to psychotherapy compared to <25% of other patients. This model selected 43 predictors, of which nearly all were self-report variables.

Conclusions: Patients with MDD could pre-emptively be informed of their likelihood of responding to psychotherapy using a prediction tool based on self-report data. This tool could meaningfully help patients and providers in shared decision-making.

LATEBREAKER

Big Data/Machine Learning/AI

Ensemble-Epidemiology to Contextualize Healthy Aging: Overcoming Genetic Risk for Type 2 Diabetes and Kidney Disease in UKBB Alexis Garduno* Alexis Garduno

Ensemble modeling with unsupervised learning may contextualize an individual (capacity, environment, and experience) and their risk for diabetes/healthy aging, as with our study of 391,135 UKBB subjects. After Box-cox scaling and data reduction, principal components (PCs) were selected using total variance explained (var). K-means, mixtures of gaussian, and spectral clustering were performed on PCs. Logistic regression modeled associations between contextual-health clusters with type 2 diabetes (T2D), chronic kidney disease (CKD), and kidney disease (KD) after adjustment for gender, age, an insulin polygenic risk score (IR-PRS), and continental PCs, in the overall and T2D-stratified sample, and we tested for a PRSxCluster interaction. Four behavioral PCs (BPC) were selected for more physical activity (PC1), more smoking (PC2), less vigorous activity and longer sleep duration (PC3), and lower activity, less smoking, and sleep (PC4, var=80%). Two SES PCs (SPC) reflected greater poverty and less education (PC1), and PC2 represented less work hours (var=69%). From k-means, cluster 0 reflected lower activity (PC1=-0.81, PC2=0.43), more tobacco usage (PC4=0.39), and more deprivation (SPC=0.97); cluster 1 reflected higher vigorous and moderate activity (PC1=1.76); cluster 2 reflected lower vigorous activity (PC=-1.01), lower tobacco use (PC4=-0.13), and lower deprivation (SPC=-0.65). Clusters 0 and 2 (ref=C1) were positively associated (p<0.0001) with T2D and KD outcomes (OR,C2-T2D: 2.05 (95%CI: 1.76-2.40); OR,C2-CKD: 2.05 (95%CI: 1.76-2.40); OR-C2-Micro: 1.43 (95%CI: 1.38-1.49). Cluster-KD associations were not attenuated after stratifying by T2D. For those with T2D, we detected some slight evidence of PRSxCluster interactions although showing consistent negative interactions (PRS-Micro, p=0.049); similar trends were seen in the total sample and non-diabetics. We found that associations between IR-PRS and T2D/KD were modifiable by healthy contextual factors.
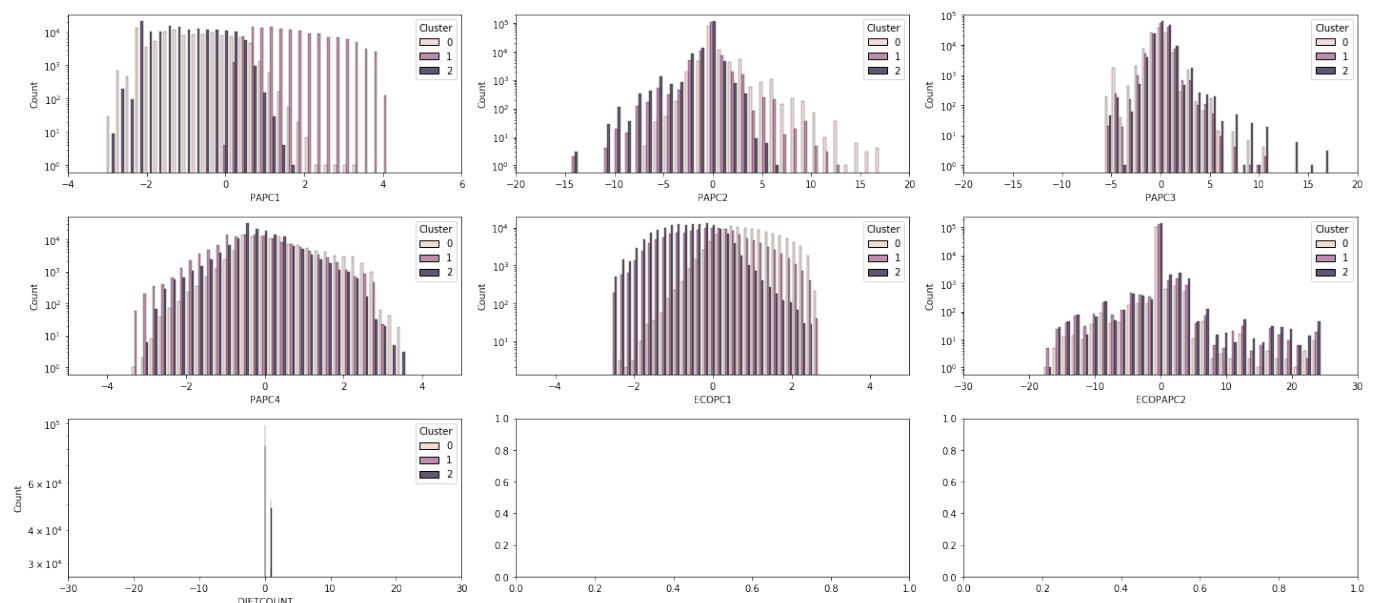
LATEBREAKER

Big Data/Machine Learning/AI

Increased Discussion of Smoking Fentanyl in Online Opioid Forums Alexander Preiss*

Alexander Preiss Georgiy Bobashev

Background

Recent studies have shown that some communities of people who use opioids are transitioning from injecting heroin to smoking fentanyl. This transition may reduce harm by reducing risk of blood-borne virus transmission and/or overdose. However, it is unknown whether this transition is widespread.

Methods

Reddit is a social media platform comprised of communities called subreddits, which organize content based on interest. We secured ~4 million posts and comments from two opioid-focused subreddits: *r/opiates* and *r/OpiatesRecovery*. We developed an information extraction tool that uses natural language processing to identify content discussing a given topic. The tool uses FastText word embeddings to conduct keyword expansion, then uses regular expressions to search content for expanded keyword sets. We used this tool to measure trends from 2016 to 2021 in the proportion of discussions mentioning fentanyl that also mentioned smoking. We conducted a qualitative analysis of a sample of 100 comments from 2021 to better understand the context in which fentanyl and smoking were discussed.

Results

The proportion of comments, posts, and authors mentioning fentanyl that also mentioned smoking increased sharply through 2019 and plateaued through 2020 and 2021, as shown in Figure 1. Of the sample of 100 comments from 2021, 76 explicitly discussed smoking fentanyl.

Conclusion

Smoking fentanyl appears to be a widespread trend in this online community. Social media discussion trends might not correlate exactly with prevalence but provide a useful complement to other forms of surveillance. The high percentage of identified comments which explicitly discuss smoking fentanyl suggests that our information extraction approach is effective. Further analysis of these posts and comments could help build our understanding of how fentanyl is smoked and its effects.

Figure 1: Change in the proportion of authors, comments, And posts mentioning fentanyl that also mentioned smoking
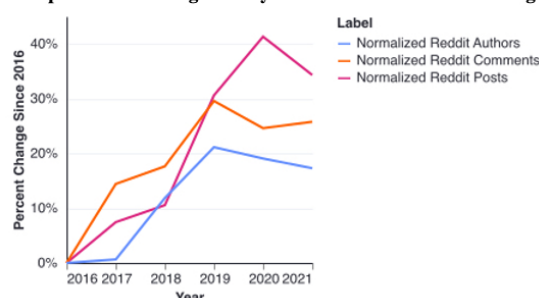
Stage of cervical cancer diagnosis by immigrant and screening status: a population-based retrospective cohort study in Ontario, Canada Geetanjali D Datta* Geetanjali Datta Hong Lu Alexander Kopp Samantha Lee Marie-Helene Mayrand Rachel Kupets Aisha Lofters

Background: Despite improvement in screening and HPV vaccination, cervical cancer is the 4th most frequent cancer among Canadian women aged 15 to 44 years. Poor staging data quality has hindered research on cancer stage and related inequalities. However, significant improvements have been made since 2012 which permit more complete assessment of stage differences.

Objective: To assess stage of cervical cancer diagnosis by immigrant and screening status.

Methods: Multiple linked health-administrative databases were used to create a census of Ontarians who were diagnosed with cervical cancer between April 1, 2012 and March 31, 2020 (sampling size=3, 402). We calculated descriptive statistics and implemented Poisson models to compare stage at diagnosis [early-stage (stage 1 and 2) vs late-stage (stage 3 and 4)] between immigrants and long-term residents (i.e. those who arrived in Ontario before 1985, the earliest date immigration data are available).

Results: Overall 29% of cervical cancer patients were diagnosed with late-stage disease. Among women diagnosed at early-stage 18% were not screened in the 3 years preceding diagnosis. In contrast, 48% of women diagnosed with late-stage disease were not screened in the 3 years preceding diagnosis. Additionally, 5% of those diagnosed with early-stage and 19% diagnosed with late-stage disease had never been screened. A similar proportion (26% vs 30%) of immigrants were diagnosed with late-stage disease in comparison to long-term residents and unadjusted models were not statistically significant (RR: 0.9, 95% confidence interval: 0.7-1.0). Differences remained null in models adjusting for age, area-level income, co-morbidities, healthcare utilization, and physician characteristics.

Conclusion: No differences in cervical cancer stage of diagnosis was observed between immigrants and long-term residents. Efforts should be made to increase screening among those who have never been screened, regardless of immigrant status.

The association between irritable bowel syndrome, inflammatory bowel diseases, and all-cause and cause-specific mortality Fangyu Li* Fangyu Li Carrie R. Daniel Shreela V. Sharma Eric L. Brown Ruosha Li Rashmi Sinha Qing Lan Maki Inoue-Choi Emily Vogtmann

Background: Irritable bowel syndrome (IBS) and inflammatory bowel diseases (IBD) are two of the most common functional gastrointestinal (GI) disorders. IBS is characterized by a group of GI symptoms, while IBD presents as chronic relapsing inflammation of the GI tract. Given the sparse data regarding risk of death in individuals with these two GI conditions, we explored the association between IBS, IBD, and all-cause and cause-specific mortality.

Methods: The UK Biobank is a large, population-based, prospective cohort study which recruited participants from 2006 to 2010 and includes follow-up for mortality through 2021. After excluding people with a history of large bowel resection or colostomy, a total of 501,166 participants were available for analysis. We defined our primary exposure of IBS/IBD via self-reported questionnaire or inpatient diagnosis prior to baseline and identified deaths through linkage to the UK National Health Service. We estimated hazard ratios (HR) and 95% confidence intervals (CI) for all-cause and cause-specific mortality in multivariable Cox proportional hazards models adjusted for socio-demographics, behavioral, and medical factors.

Results: A total of 12,411 (2.5%) participants reported a history of IBS and 4,708 (0.9%) reported a history of IBD. After a median follow-up of 12.6 years, having IBS at baseline was associated with lower risk of all-cause mortality (HR=0.91, 95% CI=0.84-0.98) and cancer-specific mortality (HR=0.88, 95% CI=0.79-0.98) while IBD was associated with increased all-cause mortality (HR=1.44, 95% CI=1.32-1.58) and cancer-specific mortality (HR=1.37, 95% CI=1.20-1.56). Neither having IBD nor IBS were associated with mortality risk for cardiovascular or respiratory diseases.

Conclusion: In this large-scale, prospective cohort study, we found that having IBS was inversely associated with all-cause and cancer-specific mortality while having IBD was associated with increased all-cause and cancer-specific mortality.

Driver gene genomic alterations associated with pancreatic cancer prognosis. David Adeleke* David Adeleke Rick Jansen

Background: Combining simple somatic mutations (SSM) and copy number variations (CNV) to the best of our knowledge has not been jointly associated with pancreatic cancer (PACA) prognosis. This study applied a bioinformatics approach to identify six driver genes and develop a polygenic risk score that incorporates the potential joint effects of the co-occurrence of CNV and SSM alterations on PACA prognosis.

Methods: Pancreatic cancer SSM, CNV, and clinical data were downloaded from The International Cancer Genome Consortium portal. The top 6 commonly mutated genes were identified based on the pattern of the oncoplot from the SSM and CNV. The associations between the samples' CNV types, SSM, and survival were measured using Cox proportional-hazards model (CoxPh). The Protein Variation Effect Analyzer was used to assign scores to the functional consequence of SSM within each gene. These scores were multiplied by the corresponding gene CNV burden and summed for each sample to generate the polygenic risk score. These scores were grouped into tertiles (A, B, and C), and associations between the risk score tertiles, disease status at last follow-up, and prognosis were assessed using CoxPh and ANOVA.

Results: KRAS, TP53, TTN, SMAD4, MUC16, and CDKN2A were identified to be the commonly mutated genes, and KRAS, TP53 SSMs were significantly associated with poor prognosis in PACA ($p<0.05$, HR= [1.51, 1.23]). Copy number loss of heterozygosity significantly associated with better prognosis in KRAS, TP53, SMAD4, and CDKN2A genes ($p<0.05$; HR= [0.64, 0.43, 0.13, 0.17]) and poorer prognosis in MUC16 gene ($p<0.05$ HR=6.01). The polygenic risk score, but not the single gene SSM or CNV scores, showed statistically significant association with survival ($p < 0.01$, HR=0.67), and disease status ($p < 0.01$).

Conclusion: This study showed that polygenic score that incorporates joint CNV and SSM for driver genes offers better PACA prognosis than individual score.

Cancer

Effect of testosterone on breast cancer in European and East Asian women Kezhen Fei*

Kezhen Fei C. Mary Schooling

Background: Testosterone is an effective treatment for women with low sexual desire, whose long-term safety is not well understood. Observationally, testosterone increases the odds of breast cancer, including in a mendelian randomization (MR) study of women of European descent. Whether this effect replicates and extends to other ethnicities is unknown and was examined here.

Methods: Established genetic instruments for total testosterone from the UK Biobank were applied to the largest genome wide association study (GWAS) of breast cancer (cases=122,977, controls=105,974) and estrogen positive breast cancer (cases=69,501, controls=105,974) in Europeans and of breast cancer in East Asian women (cases=5,552, controls=89,731), with body mass index as a positive control outcome in East Asian women.

Results: A genetically predicted 1 standard deviation (s.d.) higher testosterone was positively associated with breast cancer in European women odds ratio (OR)=1.15 (95% confidence interval (CI) 1.07, 1.24), and with estrogen positive breast cancer OR=1.19 (95% CI: 1.12, 1.27). In East Asians, 1 s.d. higher testosterone was associated with the positive control outcome of BMI (n=108,757) in East Asian women 0.07 standard deviation higher (95% CI: 0.03, 0.12) as expected. Testosterone was also positively associated with breast cancer in East Asian women (OR=1.08, 95% CI: 1.03, 1.41)

Conclusion: Use of testosterone in women may increase the risk of breast cancer. Whether testosterone operates by increasing estrogen, which is known to cause breast cancer, might be worth investigating to clarify the causal pathway and identify any other consequences of testosterone use in women as a treatment for low sexual desire or for use by transgender men.

Evaluation of ethno-racial differences in cancer incidence among World Trade Center (WTC) Exposed Rescue and Recovery Workers David Goldfarb* David Goldfarb Rachel Zeig-Owens Charles B. Hall Dana Kristjansson Amy Kahn Baozhen Qiao Maria Schymura Mayris Webbet Christopher Dasaro Moshe Shapiro Andrew Todd David Prezant Paolo Boffetta Jiehui Li Robert Brackbill James Cone Janette Yung

Background: Three independent cohort studies have reported associations between WTC exposures and cancer, as has our study in a combined, de-duplicated cohort of 69,102 WTC rescue/recovery workers. Ethno-racial differences in cancer incidence are yet to be explored.
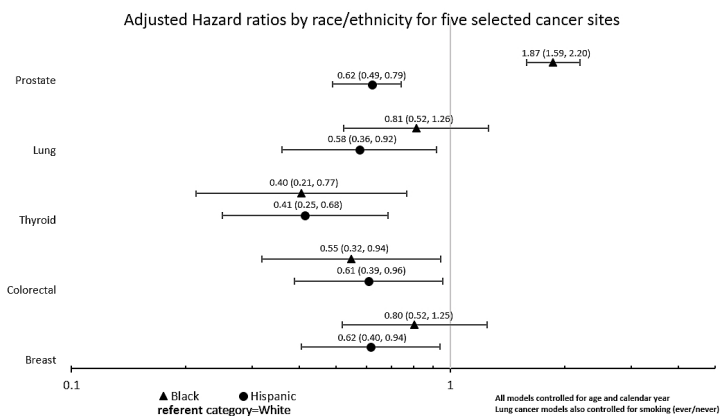
Objective: To evaluate cancer incidence differences for five cancer sites among White, Black and Hispanic WTC-exposed rescue/recovery workers.

Methods: The primary exposure of interest was race/ethnicity. Outcomes were incident prostate, lung, thyroid, colorectal and female breast cancers. Person-time accruals began six months after enrollment into a WTC cohort and ended at death or 12/31/15. Data were obtained via linkages with 13 state cancer registries. Poisson regression was used to estimate hazard ratios between ethno-racial groups, controlling for age, calendar year and sex (where appropriate). Secondary analyses compared rates to the New York State (NYS) population stratified by race/ethnicity.

Results: White, Black and Hispanic participants contributed 473,967; 60,646; and 101,829 person-years of follow-up, respectively. In our internal analysis, Blacks had a significantly higher prostate cancer risk and reduced thyroid and colorectal cancer risk when compared to White participants. Hispanics had a lower risk for the five selected cancers.

When compared to NYS data, Blacks had a significantly elevated hazard for prostate cancer (HR=1.22; 95% CI=1.05-1.40) and a lower hazard for lung (HR=0.47; 95% CI=0.31-0.71) and colorectal cancers (HR=0.37; 95% CI=0.22-0.62); Hispanic participants had a lower hazard for lung (HR=0.59; 95% CI=0.37-0.92) and colorectal cancers (HR=0.53; 95% CI=0.34-0.81).

Conclusions: Aside from prostate cancer, rates for Black and Hispanic participants were lower for selected sites among WTC-exposed participants. Continued follow-up and ascertainment of differences in screening will be important future work for evaluating the cancer burden among minority subgroups in this cohort.

Adjusted Hazard ratios by race/ethnicity for five selected cancer sites

Prostate — 0.62 (0.49, 0.79); 1.87 (1.59, 2.20)
Lung — 0.81 (0.52, 1.26); 0.58 (0.36, 0.92)
Thyroid — 0.40 (0.21, 0.77); 0.41 (0.25, 0.68)
Colorectal — 0.55 (0.32, 0.94); 0.61 (0.39, 0.96)
Breast — 0.80 (0.52, 1.25); 0.62 (0.40, 0.94)

▲ Black ● Hispanic
referent category=White

All models controlled for age and calendar year
Lung cancer models also controlled for smoking (ever/never)

Association between thyroid disease and risk of breast cancer in the Sister Study Rina Yarosh* Rina Yarosh Jennifer M.P. Woo Katie O'Brien Dale P. Sandler

Background: Thyroid disease and its treatments may be associated with breast cancer (BC) risk, but there are few studies and results are inconsistent. We assessed the associations of hyper- and hypo- thyroid disease (TD) and BC overall and by menopause status at diagnosis.

Methods: Data were from the Sister Study, a U.S.-based cohort of 50,884 women enrolled in 2003-2009. Participants were aged 35-74 years and BC free at baseline. Information on TD and treatments was self-reported at baseline and follow-up. We evaluated risk of BC in relation to TD diagnosed both prior to enrollment and during follow up using time-varying Cox proportional hazards models to estimate HRs and 95% CIs.

Results: At enrollment 2,096 participants reported hyper- and 7,434 reported hypo-TD. Over a median of 9 years of follow up, 3,999 women developed BC. After adjustment for covariates, hyper-TD was associated with overall (HR 1.1, CI 1.0, 1.3) and premenopausal BC (HR 1.4, CI 1.0, 2.0). Associations with hyper-TD appeared driven by radioactive iodine treatment; with a HR of 1.4 (CI 1.1, 1.8) with known radioactive iodine vs. no TD. Postbaseline, 1,549 participants reported incident hyper-TD. In time varying analysis, the HR for hyper-TD vs. no TD was 1.5 (CI 1.3, 1.7) Hyper-TD was more strongly associated with premenopausal BC (HR 2.2, CI 1.6, 3.1), but was also associated with increased risk for postmenopausal BC (HR 1.4, CI 1.2, 1.6). Pre-baseline hypo-TD was not associated with BC (HR 1.0, CI 0.7, 1.3). Postbaseline, 6,412 participants reported incident hypo-TD increasing the HR to 1.6 (CI 1.5, 1.7). The HR for premenopausal BC was highest (HR=2.1, CI 1.7, 2.6) but was also elevated for postmenopausal BC (HR 1.5, 1.4, 1.7).

Conclusion: Both hyper- and hypo- TD are risk factors for BC, however underlying mechanisms may differ. Understanding the increased risk of BC for women diagnosed with TD may be important for the clinical management of TD and BC screening in this population.

Cancer mortality rates by racial/ethnic groups in the United States, 2018–2019 Anika T. Haque* Anika Haque Amy Berrington de González Yingxi Chen Maki Inoue-Choi Wayne Lawrence Qianlai Luo Jennifer Mcgee-Avila Jacqueline Vo Neal Freedman Meredith S. Shiels

Background: In 2018, the National Center for Health Statistics released single-race mortality data, resulting in the disaggregation of Native Hawaiians and Pacific Islanders (NHPI) from Asians for the first time. We estimated US mortality rates across cancer type by race/ethnicity, sex and age.

Methods: Age-standardized cancer mortality rates and RRs by race/ethnicity, sex and age were estimated with data from Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research. We analyzed data for individuals aged 20-84 in the following racial/ethnic groups: Hispanic/Latino all races (Latino), and non-Hispanic White, Black, Asian and NHPI.

Results: During 2018-2019, lung cancer caused the largest number of cancer deaths among men in each racial/ethnic group, and among Asian and White women. Breast cancer was the most common cancer death among Black, Latino, and NHPI women. Black men and women had the highest cancer death rates (258.9 and 185.7/100,000). Compared to White men and women, we observed lower death rates for nearly all cancer types among Asian men and women (RRs 0.08-0.76 and 0.11-0.71) and Latino men and women (RRs 0.23-0.89 and 0.28-0.93). NHPI individuals had higher death rates than Asian individuals for nearly every cancer type. Black individuals had the highest cancer death rates among 60-79 and 80-84-year-olds (693.7 and 1289.0/100,000), NHPI individuals had the highest cancer death rates among 20-39 and 40-59-year-olds (19.5 and 126.2), and Asian individuals had the lowest cancer death rates across every age group.

Conclusion: There are striking racial/ethnic disparities in cancer death rates in the US with the highest death rates for most cancer sites in NHPI or Black men and women. Separating NHPI and Asian individuals reveals a stark difference in cancer mortality patterns. Policies aimed at equitable cancer prevention and early detection/treatment are needed to reduce cancer mortality disparities.

Age-Standardized Cancer Death Rates by Race and Ethnicity Between 2018 and 2019 in the U.S. for the 5 Most Common Types of Cancer Death in Men and Women
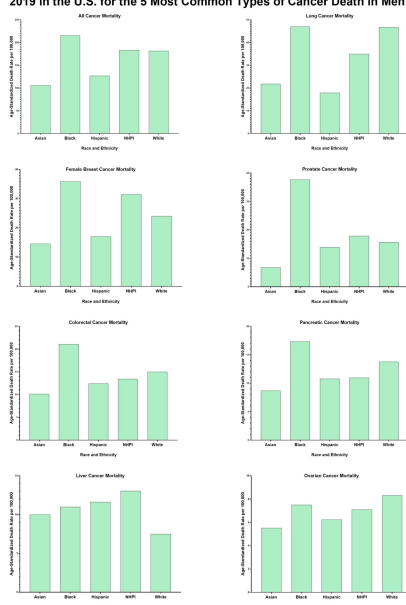
Cancer

Factors influencing the Black-White race disparity in patient reported outcomes (PROs) among elderly female breast cancer patients in the SEER-MHOS database Kendra Krebsbach* Kendra Krebsbach Chloe Stallion Keith Dookeran

Multivariable generalized linear regression models with predictive margins [risk differences (RD) with 95% confidence intervals (CI)] were used to estimate the Black-White race disparity in physical and mental health PROs [Physical and Mental Component Summary T-Scores (PCS/MCS: are linear transformation of the 0-100 possible range scoring for 8 Veterans RAND 12 Item Health Survey (VR-12) sub-scales, with mean of 50 and standard deviation (SD) of 10, normed to the US population)] among elderly female patients, with newly diagnosed breast cancer (BC) between 2010-2015 in the Surveillance, Epidemiology and End Results-Medicare Health Outcomes Survey (SEER-MHOS) database (a cancer registry that provides value health-related quality of life information on patients enrolled in Medicare Advantage). Fully specified models were adjusted for age, BMI, marital status, SES factors [household income (HHI) and education level], comorbid disease [smoking status, presence of diabetes and hypertension] and tumor factors [grade, stage and subtype]. Our sample consisted of 11,765 White and 1,988 Black women. Compared with White, Black women were more likely to be younger, single and current smokers; have higher BMI; have diabetes and hypertension; with lower HHI and education level; and have tumors with higher grade, more advanced stage, and triple-negative subtype (compared with luminal A); and have worse BC-specific mortality (all $p<0.05$). Both crude PCS (RD: -4.26; CI: -4.87, -3.65) and MCS (RD: -3.79; CI: -4.37, -3.22) scores were worse for Blacks; however, these differences were not evident in fully specified models [PCS (RD: -0.12; CI: -1.25, 1.02); MCS (RD: 0.84; CI: -0.29, 1.96)]. Stratified analysis by tumor stage and subtype also did not show evidence of effect modification. Our findings suggest that observed PRO disparities between elderly Black and White women with BC in SEER-MHOS data are likely due to confounding by SES and comorbid disease, rather than tumor factors.

LATEBREAKER

Cancer

Exercise Adherence in a Randomized Controlled Trial of Exercise on Quality of Life in Ovarian Cancer Survivors Anlan Cao* Anlan Cao Brenda Cartmel Fang-Yong Li Linda T. Gottlieb Maura Harrigan Jennifer A. Ligibel Radhika Gogoi Peter Schwartz Melinda L. Irwin Leah M. Ferrucci

Background: Exercise can improve quality of life and depression in women with ovarian cancer. However, factors associated with increasing physical activity levels in ovarian cancer survivors remain unknown. We explored factors associated with better exercise adherence among post-treatment ovarian cancer survivors in the Women's Activity and Lifestyle Study in Connecticut (WALC) randomized controlled trial.

Methods: Women randomized to the WALC exercise arm (N=74) were included in this analysis. Women were sedentary (≤90 mins/wk) and post-treatment for ovarian cancer at enrollment. The intervention included 25 telephone-based exercise counseling sessions over 6 months with a certified cancer exercise trainer. Adherence was defined as meeting the 150 min/wk moderate/vigorous intensity intervention exercise goal. We evaluated factors associated with exercise adherence and duration using multivariate logistic and linear regression.

Results: Women were on average 57.3±8.8 years old and 1.7±1.0 years since diagnosis. The mean exercise time over the 6 months was 166.0±66.1 min/wk, 64.9% of women met the exercise goal and on average women attended 22.8±3.6 counseling sessions. No cancer recurrence during the study (P<0.01) and greater counseling session attendance (P<0.01) were related to meeting the exercise goal. Greater counseling session attendance (P<0.01), higher baseline exercise level (P<0.01), and receiving clinical care at a main study recruitment site (P=0.04) were associated with greater exercise duration.

Conclusion: The majority of ovarian cancer survivors in this trial were able to meet the exercise goal and attendance to counseling sessions was high. Attending more counseling sessions and no cancer recurrence during the study were associated with meeting the exercise goal. More research is needed to understand the ideal counseling level for ovarian cancer survivors to attain exercise goals.

LATEBREAKER

Cancer

Adjuvant radiation therapy and health-related quality of life among older women with early-stage endometrial cancer: An analysis using the SEER-MHOS linkage Jihye Park* Jihye Park Erin E. Kent Jennifer L. Lund Chelsea Anderson Andrew F. Olshan Wendy R. Brewster Hazel B. Nichols

Background: Radiation therapy (RT) has been associated with decreased health-related quality of life (HRQOL) in clinical trials of early-stage endometrial cancer (EC), but few studies have examined the association in real-world settings. We assessed HRQOL associated with adjuvant RT for older women with early-stage EC within a large U.S. national population-based registry resource.

Methods: The Surveillance Epidemiology and End Results and the Medicare Health Outcomes Survey linkage (1998-2017) was used to identify women with early-stage EC aged≥65 years at survey who received surgery and were diagnosed ≥1-year prior (n=1,140). HRQOL was evaluated with the 36-item Short Form Health Survey (SF-36) until 2006 and the Veterans RAND 12-Item Health Survey (VR-12) post 2006; scores were pooled and harmonized. Mean T-scores were estimated to compare HRQOL across treatment groups: surgery alone, adjuvant external beam radiation therapy (EBRT), or adjuvant vaginal brachytherapy (VBT). Ordinary least squares regression was used to estimate difference in means and 95% confidence intervals (CIs) comparing treatment groups after accounting for measured confounders using propensity score weighting.

Results: Overall, RT was not associated with physical health (mean difference [MD], 0.97; 95% CI, -1.13 to 3.07) or mental health (MD, -0.78; 95% CI, -2.60 to 1.05) relative to surgery alone. In analyses by RT type, adjuvant VBT was associated with better general health on the SF-36/VR-12 subscale (MD, 3.59; 95% CI, 0.56 to 6.62) relative to surgery alone. No statistically significant associations were observed for adjuvant VBT and physical or mental health, or for adjuvant EBRT and any HRQOL domain.

Conclusions: Our results, based on a national data resource, suggest that adjuvant RT was not associated with worse HRQOL profiles among older women with early-stage EC.

Occupational Pesticide Use and Colon and Rectal Cancer in the Agricultural Health Study, 1993-2017

Gabriella Andreotti* Gabriella Andreotti Richard Remigio Dale P. Sandler Rashmi Sinha Patricia Erickson Stella Koutros Jay H. Lubin Paul S. Albert Won Jin Lee Christine G. Parks Jonathan N. Hofmann Laura E. Beane Freeman

Background: Pesticides, a diverse set of chemicals, may be associated with colon and rectal cancers. **Objective:** With over 20 years of follow-up in the Agricultural Health Study, we investigated associations between use of individual pesticides and incident colon and rectal cancer. **Methods:** Among 54,342 male applicators, there were 621 colon and 284 rectal cancer cases diagnosed between enrollment (1993-1997) and end of follow-up (2014-2017). We calculated rate ratios (RRs) and 95% confidence intervals (CI) of colon and rectal cancer incidence using multivariable Poisson regression adjusting for potential confounding factors. We evaluated exposure-response for 44 pesticides and ever use of 50 pesticides stratified by age of diagnoses. **Results:** Compared to never users, we observed statistically significant increased risks of colon cancer among the highest users of the herbicides EPTC (RR=1.70, 95%CI 1.09-2.65, p_{trend}=0.03) and chlorimuron ethyl (RR=1.97, 95%CI=1.22-3.18, p_{trend}=0.003), and the insecticide lindane (RR=2.04, 95%CI 1.15-3.64, p_{trend}=0.01). We also found increased risks of colon cancer diagnosed before age 50 (n=37) associated with ever used the herbicides alachlor (RR=2.3, 95%CI 1.18-4.46) and butylate (RR=2.43, 95%CI 1.22-4.83), and the insecticides chlordane (RR=3.5, 95%CI 1.5-7.50), dichlorvos (RR=3.02, 95%CI 1.15-7.89), fonofos (RR=3.49, 95%CI 1.71-7.11), and aldicarb (RR=4.81, 95%CI 1.94-11.97). Increased risk for rectal cancers diagnosed before age 50 (n=30) was associated with the herbicides 2,4,5-T (RR=2.88, 95%CI 1.07-7.74) and petroleum oil (RR=2.82, 95%CI 1.37-6.21), and the insecticides chlordane (RR=3.69, 95%CI 1.54-8.86), lindane (RR=4.14, 95%CI 1.85-9.25), malathion (RR=2.99, 95%CI 1.25-7.15), and permethrin for animals (RR=2.74, 95%CI=1.10-6.88). **Conclusions:** In this prospective evaluation, we found evidence of increased incidence of colon and rectal cancers with several pesticides, and that associations may vary by age of diagnosis.

Cardiovascular

Exposure to indoor and outdoor artificial light at night in relation to hypertension risk among women Yong-Moon ("Mark") Park* Yong-Moon ("Mark") Park Chandra L. Jackson Rena R. Jones Alexandra J. White Clarice R. Weinberg Dale P. Sander

Background: Although light exerts an influential amount of control over neuroendocrine functions heavily involved in blood pressure (BP) regulation, the relationship between artificial light at night (ALAN) exposure and high BP is not well understood.

Objective: To determine whether indoor or outdoor ALAN is associated with the prevalence and risk of hypertension.

Methods: After excluding women who were shift workers or slept during the daytime or who had a history cardiovascular disease, we included 42,343 Sister Study participants (aged 35 to 74 years) enrolled between 2003-2009 and followed through September 2019. Self-reported indoor ALAN while sleeping was categorized at enrollment as no light, small nightlight in the room, light outside the room, and light or television on in the room. Outdoor ALAN was measured by linking geocoded enrollment addresses with satellite imagery from the U.S. Defense Meteorological Satellite Program. Generalized log-linear models with robust error variance and Cox proportional hazard models were used to estimate prevalence ratios (PR), hazard ratios (HR), and 95% CI, adjusting for confounders including geospatial characteristics.

Results: Having any indoor ALAN exposure while sleeping was associated with higher systolic and diastolic BP (both P<.01), and prevalence of hypertension at baseline (PR1.06; 95% CI 1.01-1.12). Compared with no ALAN while sleeping, indoor ALAN was also associated with incident hypertension, with a HR of 1.11 (95% CI 1.01-1.22) for any ALAN exposure and 1.19 (95% CI 1.05-1.34) for sleeping with a television or a light on in the room. Results were unchanged in analyses accounting for sleep duration and quality, diet, and physical activity. Even among those reporting light from outside the room, outdoor ALAN was not associated with hypertension after adjusting for other geospatial measures.

Conclusions: Exposure to indoor-sourced ALAN while sleeping may be a risk factor for development of hypertension.

Association of a genetic risk score with prevalent coronary heart disease in the Hispanic Community Health Study/Study of Latinos (HCHS/SOL) cohort Christina G Hutten* Christina G Hutten Ramon Durazo-Arvizu Molly Scannell Bryan Liana Preudhomme Krista M Perreira Gregory A Talavera Sylvia Wassertheil-Smoller Jiehuan Sun Victoria Persky Tamar Sofer Martha L Daviglus Maria Argos

Background: Coronary heart disease (CHD) is one of the leading causes of death for the Hispanic/Latino population living in the United States (US). Genetic risk scores (GRS) have been used in populations of European ancestry to identify those at higher risk for CHD events.

Objectives: This study evaluates a GRS with prevalent CHD in a Hispanic/Latino cohort.

Methods: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) is a prospective study that enrolled 16,415 Hispanic/Latino adults aged 18-74 years from four US communities in 2008-2011. We assessed the association between a 71-SNP GRS and prevalent CHD among 9,030 HCHS/SOL participants with complete data and consent to conduct genetic research. Prevalent CHD was defined as self-reported physician diagnosis or evidence of electrocardiographic abnormalities indicative of CHD. We considered unweighted (sum of trait-increasing alleles), European-weighted, and Latino-weighted GRS. European and Latino weights were derived from a prior publication employing this GRS (Ke et al. 2018). Logistic regression was used to derive ORs and 95% CIs for the association between the GRS and prevalent CHD, adjusted for a priori confounders and accounting for survey weights.

Results: Among participants, 7.3% had prevalent CHD. The odds of prevalent CHD was 40% higher for the highest quintile of the Latino-weighted GRS (OR 1.40, 95% CI 1.09, 1.80) compared to the lower four quintiles combined. Stratified analyses to explore heterogeneity by background group showed those in the Cuban (OR 1.97, 95% CI 1.26, 3.08) and Central American (OR 2.70, 95% CI 1.17, 6.25) background groups had increased odds of prevalent CHD when comparing the highest quintile of the Latino-weighted GRS to all other quintiles. Results were comparable using the other GRS constructs.

Conclusion: Additional studies are needed to evaluate and optimize risk prediction of CHD based on cumulative genetic risk in the Hispanic/Latino population.

Cardiovascular

Carotid intima-media thickness in adults with and without psoriasis – a nested case-control study from baseline data of ELSA-Brasil cohort Isabela M. Bensenor* William Tebar Itamar S. Santos Vandrize Meneghini Márcio Sommer Bittencourt Paulo A. Lotufo Isabela M. Bensenor

Introduction: The association between carotid intima-media thickness (cIMT) and psoriasis (PSO) is not consensual in literature. Previous studies considered different PSO cases recruited in dermatologic outpatient clinic or general population, but no information is available for workers.

Objective: The present study compared cIMT levels in individuals with and without PSO in a cohort of civil servants and analyze its association with the disease.

Methods: Data from 10,530 participants of the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) were analyzed. PSO cases, treatment and disease duration were identified based on medical diagnosis informed by the participants at the baseline data collection. A paired group without PSO was identified by propensity score matching among all the participants without PSO (4 per case, n=648). Mean cIMT values and cIMT above 75th percentile was considered for continuous and categorical analysis, respectively.

Results: PSO prevalence in the sample was 1.54% (n=162). Only 7 PSO participants reported the use of medications for treatment (4.3%). CIMT was higher in men than in women independently of PSO (p<0.01). No difference in cIMT values was observed between participants with PSO and matched participants or overall sample. Regression models showed no association of PSO with linear increment of cIMT (vs. overall sample: β=.003, p=.690; vs. matched controls: β=.004, p=.633) neither with increased chance of having cIMT above 75th percentile (vs. overall sample: OR=1.06, p=.777; vs. matched controls in binary logistic regression: OR=1.19, p=.432; and conditional regression: OR=1.31, p=.254). No relationship was observed between disease duration and cIMT (β=.000, p=.627).

Conclusion: PSO participants did not have higher cIMT values than matched controls and overall sample and no relationship between PSO and cIMT was observed. However, prospective investigation is still needed in this wide cohort of civil servants.
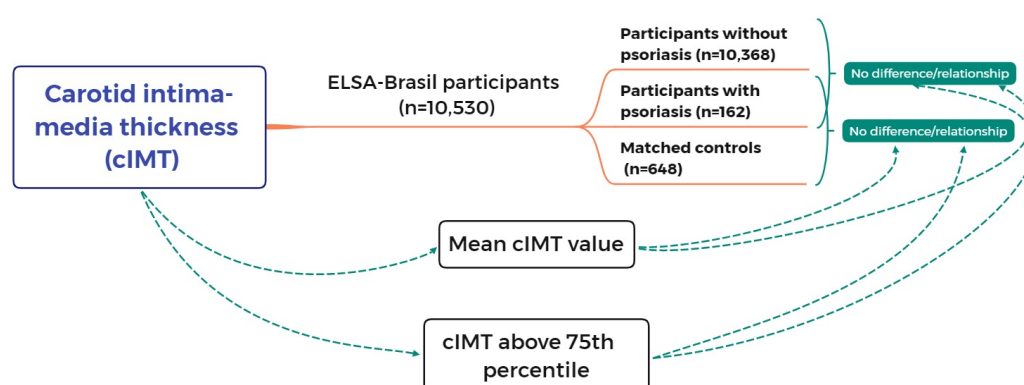
Circulating leukocyte composition reflects hypertension prevalence and risk Jacob Kresovich* Jacob Kresovich Zongli Xu Katie O'Brien Clarice Weinberg Dale Sandler Jack Taylor

Hypertension may precede various health conditions, including stroke, heart failure, and dementia. The development and consequences of hypertension involve multiple biological systems and may include changes in immune function. Epidemiologic studies suggest concentrations of proinflammatory cytokines are higher in those with hypertension. Others report that the number of circulating white blood cells, or leukocytes, is associated with hypertension incidence. Whether hypertension is related to distinct leukocyte subsets, including those from the lymphoid (i.e., natural killers, T and B lymphocytes) or myeloid lineages (i.e., monocytes and granulocytes), is not known. Here, we estimate circulating proportions of six leukocyte subsets by deconvoluting cell-type-specific DNA methylation patterns to describe how the composition of circulating immune cells is associated with prevalent and incident hypertension. Among 4,176 women enrolled in the Sister Study with available whole blood DNA methylation data, 1,430 had high blood pressure or reported hypertension medication use at baseline. Within 16 years of follow-up, an additional 417 women self-reported an incident hypertension diagnosis. In models accounting for confounders and incorporating inverse-probability of selection weights, four lymphocyte proportions were inversely associated with hypertension prevalence (cytotoxic T cell, OR: 0.89, 95% CI: 0.80, 0.99; helper T cell OR: 0.91, 95% CI: 0.83, 1.01; natural killer OR: 0.86, 95% CI: 0.76, 0.96; B cell OR: 0.88, 95% CI: 0.78, 0.99), whereas the granulocyte proportion was positively associated with hypertension prevalence (OR: 1.20, 95% CI: 1.08, 1.33). Higher circulating B lymphocyte proportion was associated with the incidence of new-onset hypertension (HR: 1.12, 95% CI: 0.99, 1.27). By clarifying the extent to which leukocyte subsets become altered relative to diagnosis timing, we show that hypertension is related to adaptive and innate immune defenses.

The causal effect of statin prescription in routine care on health outcomes: applying a regression discontinuity approach to large-scale electronic health record data Julia Lemp*
Christian Bommer Dominik Jockers Sebastian Vollmer Till Bärnighausen

Aim: Clinical guidelines recommend statin prescription for patients with an elevated cardiovascular disease (CVD) risk. Despite demonstrated efficacy in randomized controlled trials, evidence from clinical practice is limited. We employed a regression discontinuity (RD) approach to determine the real-world effect of statin prescription on preventing mortality and hospitalizations.

Methods: We retrospectively analyzed a cohort of 671,896 adult patients in UK primary care with measured CVD risk between 01/01/1998 and 12/31/2014. Endpoints included all-cause mortality and (emergency) hospitalizations as well as mortality and hospitalizations due to stroke and heart disease. We estimated the complier average causal effect of statin prescription within 30 days of CVD risk assessment, using an RD approach and exploiting the fact that guidelines recommended statins if a patient's 10-year CVD risk exceeded 20%. Mortality was assessed within five and ten years, and hospitalization within one year and five years of follow-up after the first relevant CVD risk assessment. We additionally analyzed a subsample of patients attending practices with above-average guideline adherence ("guideline-adhering practices").

Results: We observed a statistically significant increase in the probability of statin prescription at the CVD risk score threshold both in the full sample (effect size: 3.85 percentage points, p-value < 0.001) and the subsample of patients attending guideline-adhering practices (effect size: 8.57 percentage points, p-value < 0.001). We found no statistically significant impact on any of the mortality and hospitalization outcomes.

Conclusion: Despite the efficacy of statin treatment in trials, our effectiveness study using real-world clinical data did not reveal benefits of statin prescription on mortality and hospitalization outcomes. The results indicate that additional action may be necessary to ensure that the full benefits of statins are realized in routine care.

Probability of statin prescription and CVD risk

Panel A: full sample   Panel B: guideline-adhering practices
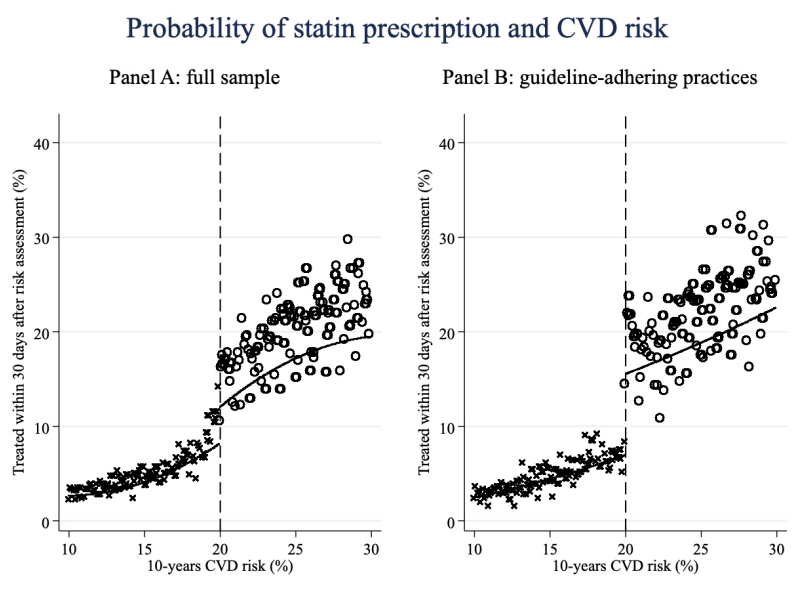
Causal Inference

Causality within the American firearm ecosystem: Exploring the effects of time series' resolution on the inference of causal relationships Roni Barak Ventura* Roni Barak Ventura Maurizio Porfiri

Mass shootings are a serious public health issue in the US, where more such events take place than anywhere else in the world. Although mass shootings account for a small fraction of firearm-related harms in the US, they play an important role in shaping the public's opinion about firearm regulation. In the wake of these events, heated debates about the relationships between firearm prevalence and mass shootings are often broadcast through the media: some advocate for restricting firearm ownership and others for empowering people with firearms to reduce mass shootings through deterrence and self-protection. In the past, we investigated the interplay between mass shootings, firearm ownership, and media coverage of firearm-related topics. We collected data on mass shootings from Mother Jones and the Washington Post, as well as the number of firearm background checks registered by the FBI National Instant Criminal Background Check System, and the number of articles on firearm violence and firearm regulation published by the New York Times and Washington Post from ProQuest. Limited by the availability of data from the FBI, we generated time series for each variable with a monthly resolution. We employed the information-theoretic notion of transfer entropy to infer causal relationships between those variables. Recently, the FBI released a daily times series of background checks on a national level which opens the door for additional analyses with enhanced statistical power that we present herein. Alongside increased time resolution, we expanded our data set on media output to include a wider range of news outlets from across the country. Working with this new dataset, we revisit the conclusions of our previous work, specifically focusing on the role of media output on either firearm regulation or shootings on firearm prevalence.

Causal Inference

Learning the potential effects of selective interventions based on real-world data Helene Charlotte Wiese Rytgaard* Amalie Lykkemark Møller Julie Andersen Christian Torp-Pedersen Thomas Alexander Gerds

Selective interventions typically aim at improving treatment access or health behavior to reduce risk of adverse health outcomes among high-risk patients. High-risk patients are commonly identified by social exposures such as race, residential area, and income. Mediation analysis has been a common estimation tool, but it is not designed to capture effects of interventions targeting only a part of the population.

In this paper, we define and estimate the causal effects of hypothetical selective interventions in real-world data using a modified targeted minimum loss-based estimator. We illustrate the methods using two examples of hypothetical interventions aimed at reducing mortality among low-income heart failure patients. In addition, we demonstrate how effects change when we vary the cut-offs, e.g., in income, that define the high-risk population. This could be an important tool for policymakers.

The first example is a combined intervention where the medical treatment is free of charge and a patient education program is initiated for low-income heart failure patients. The target parameter is the potential mortality reduction among low-income patients if they had the same chance of medical treatment as high-income patients. For the second intervention, it is mandatory for hospitals to provide a medical supply to low-income patients along with the educational program. The target parameter is the change in mortality among low-income patients if everyone received medical treatment. Under assumptions including exchangeability, consistency, and positivity, both parameters have a causal interpretation. Importantly, the first parameter poses assumptions of exchangeability between the high-risk characteristic, income, and the intermediate, access to medication, which might not always be reasonable. This assumption is not needed for the second parameter. Considering the assumptions is important when defining the hypothetical intervention if the goal is a causal interpretation.

Effect of treatment in specialized pediatric oncology care on 5-year survival in adolescents with acute lymphoblastic leukemia: A quasi-experimental study Margrietha van der Linde*

Margrietha van der Linde Nikki van Leeuwen Frank Eijkenaar

The most common form of pediatric cancer is Acute Lymphoblastic Leukemia (ALL), which is also the most common form of cancer-related mortality under the age of twenty. Survival rates of adolescents with ALL are lower compared to pediatric ALL patients. In part, this might be caused by differences in care provision and treatment setting as children are generally treated in specialized pediatric oncology care settings whereas adolescents are treated in adult oncology settings. This study aims to assess the causal effect of being treated in specialized pediatric oncology settings on 5-year survival for adolescent ALL patients in the Netherlands. We used nationwide registry data (2004-2013) on 472 ALL patients aged between 10-30 years. A fuzzy regression discontinuity design, allowing identifying causal inference in observational data, was applied to estimate treatment effects of being treated in specialized pediatric oncology care compared to regular oncology settings using 2-stage least squares regression with treatment assignment threshold set at 17 years and 7 months old, adjusting for sex, age at diagnosis and immunophenotype. We found a risk difference of 0.419 (95% CI= -0.0686; 0.907), meaning a 41.9 percentage point higher probability of surviving 5 years after diagnosis for ALL patients treated in specialized pediatric oncology care settings. Our results suggest that treatment of adolescent ALL patients in specialized pediatric oncology settings should be considered and/or collaboration between pediatric and adult oncology should be stimulated.
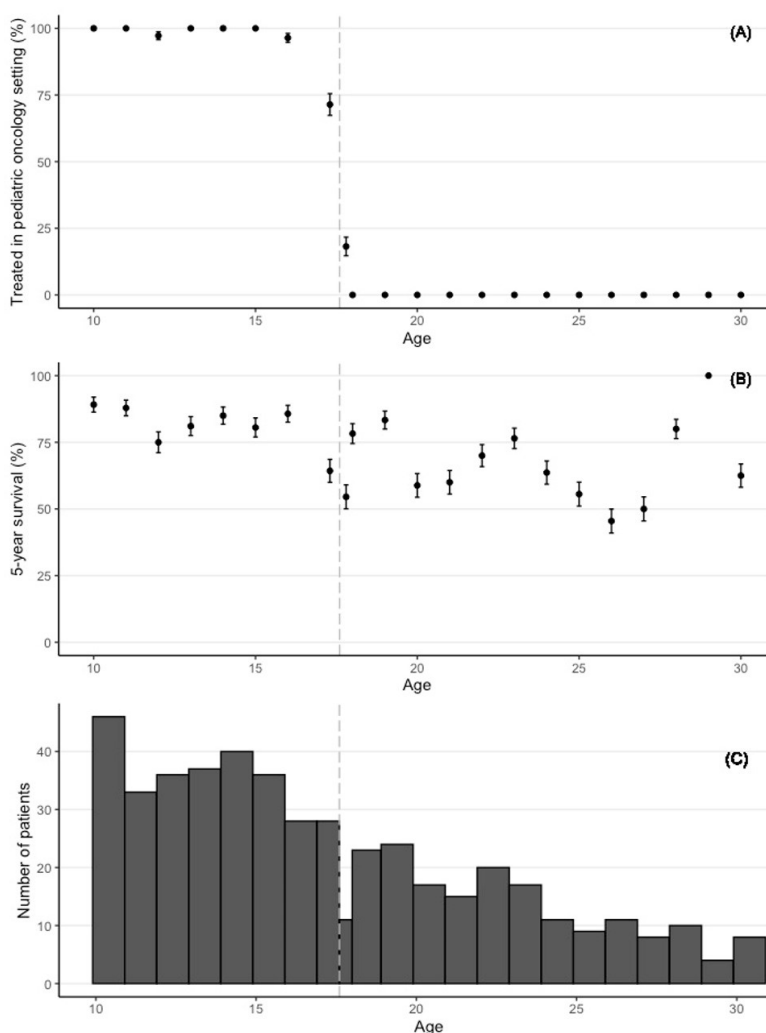
An improved estimator of survival in the presence of the healthy worker survivor effect and left truncation Kevin Chen* Kevin Chen Monika Izano Ellen Eisen

Background: The United Autoworkers-General Motors cohort includes workers hired from 1938 to 1985, but cancer incidence reporting did not start until 1973. In the presence of the healthy worker survivor effect (HWSE), the left-truncated subset still alive in 1973 is not representative of the cohort at hire, our target population. To address this bias, we conducted simulations following Izano (2017) and evaluated two estimators for 20-year survival curves under hypothetical interventions on exposure.

Methods: We specified a data-generating function compatible with left truncation in the presence of the HWSE for 20 years of follow-up under five scenarios. Following the base case (Scenario 1), we varied parameter values to increase cancer-related mortality, susceptibility to exposure-related cancer, and time-varying confounding. We considered two interventions in each scenario: always exposed while at work and never exposed. Both interventions enforced no censoring or competing risks. We generated true survival curves in large samples (N = 500,000) by deterministically applying the interventions and removing left truncation. We estimated the expected value and bias for the inverse probability of treatment-weighted Kaplan-Meier (WKM) and the Aalen-filtered WKM (AWKM) estimators by summarizing results from 250 replicates of left-truncated small-sample simulations (N = 50,000).

Results: Survival curves for the two interventions in each of the five scenarios are presented in the figure. Across all scenarios, true survival (solid line) was poorer when always exposed than when never exposed. In all scenarios, we can see that the average WKM curves (dotted line) were farther away from the true curves than the average AWKM curves (dashed line), which consistently exhibited low bias.

Conclusions: We have demonstrated that the AWKM is less biased than the WKM when estimating survival using left-truncated data in the presence of the HWSE and recommend its application in real data.
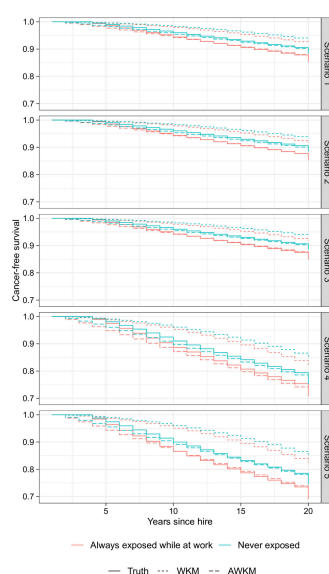
COVID-19 pandemic impact on trajectories in cardiometabolic health, physical activity and functioning among adults from the 2006-2020 Health and Retirement Study Hind A. Beydoun* Hind Beydoun May Beydoun Rana S. Gautam Brook T. Alemu Jordan Weiss Sharmin Hossain

Objectives: To evaluate the impact of the COVID-19 pandemic on trajectories in cardiometabolic health, physical activity and functioning among U.S. older adults, overall and according to selected baseline socio-demographic characteristics. **Methods:** We performed secondary analyses using longitudinal data on 1,372 participants from the 2006-2020 Health and Retirement Study. Pre-post COVID-19 pandemic was examined in relation to body mass index (BMI), number of cardiometabolic risk factors and/or chronic conditions, physical activity, Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) using mixed-effects regression models and group-based trajectory models. **Results:** The COVID-19 pandemic was associated with significantly increased BMI (β=1.39, 95% CI: 0.82, 1.96). Furthermore, the odds of having at least one cardiometabolic risk factor and/or chronic disease increased pre-post COVID-19 onset (OR 1.16, 95% CI: 1.04, 1.31), whereas physical functioning worsened pre-post COVID-19 onset (ADL: β=1.11, 95% CI: 0.96, 1.27; IADL: β=0.59, 95% CI: 0.46, 0.72). The pre-post COVID-19 period (2018-2020) showed a stable group of trajectories, with low, medium and high levels of the selected health indicators. Health disparities according to sex, race/ethnicity, educational level, work status and total wealth are highlighted. **Conclusions:** The COVID-19 pandemic appears to worsen cardiometabolic health and physical functioning among U.S. older adults, with clusters of individuals defined by selected socio-demographic characteristics experiencing distinct trajectories pre-post COVID-19 pandemic.
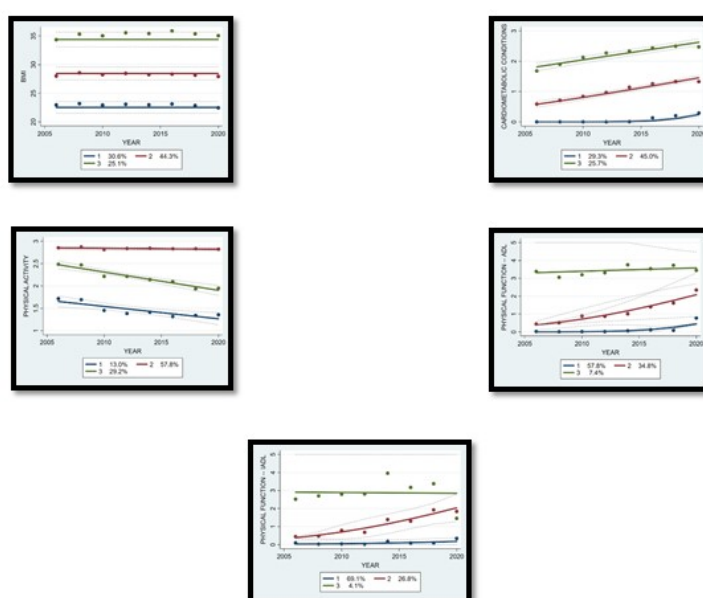
COVID-19 surveillance in the Flemish school system: development of systematic data collection within the Public Health School System and descriptive analysis of cases reported between October 2020 and June 2021 Joanna Merckx* Joanna Merckx Jonas Crèveceour Kristiaan Proesmans Naïma Hammami Hilde Denys Niel Hens

Background

The age distribution of recorded SARS-CoV-2 cases in schools reflects community transmission while being shaped by age-specific testing and interventions. A case-surveillance system was introduced within the Flemish school and health-prevention network. We present epidemiological data of in-school reported cases based on the system, in conjunction with testing and community cases.

Methods

We describe the development of the surveillance system and provide the number of reported cases and standardized rates per grade from October 2020 to June 2021. We calculate absolute and relative differences between incidence cases by grade of primary (grades 1-6) and secondary school (grades 7-12) and compare to grades 7-8, relating them to infection prevention interventions. Cumulative population incidences (IP) stratified by age, province and social-economic status (SES) of the school population are presented.

Results

A total of 59,996 COVID-19 cases were reported in the school surveillance system, with the highest population adjusted IP in grade 11-12 (7.39% (95%CI 7.24-7.53)) and ranging from 2.23% to 6.25% from pre-school through grade 10. Age-specific reduction in in-person teaching and mask introduction, are temporally associated with decreases in incident cases. Lower pupil SES is associated with increased cumulative cases (excess 2,739/100,000 pupils). Community testing volumes varied more for children, with overall higher child test-positivity. Holidays influence system performance, however efficiency reached >75% after further automation and integration in existing structures.

Conclusion

Integration of surveillance within a school health system is feasible, provides epidemiological data and should be part of public health. The relationship towards community transmission needs careful evaluation because of age-different testing. Case incidence within schools follows an age gradient mitigated through grade specific interventions, while differences by SES remain.

Association between inflammatory markers and symptoms during the acute phase of COVID-19 in a non-hospitalized population Sarah A. Goldberg* Sarah Goldberg Scott Lu Khamal A. Anglin Michelle C. Davidson Jesus Pineda-Ramirez Mariela D. Romero Paulina R. Rugart Sujata Mathur Kevin C. Donohue David V. Glidden Michael J. Peluso Jeffrey N. Martin J. Daniel Kelly

Background Although inflammatory markers and symptoms are independently well documented during acute SARS-CoV-2 infection, the causal role of inflammation on COVID-19 related symptoms is poorly understood among non-hospitalized, infected individuals. **Methods** Find-COVID is an observational, longitudinal cohort study designed to examine the natural history of SARS-CoV-2 infection in individuals who are PCR-positive for SARS-CoV-2 and living in San Francisco from Sept 2020 to April 2021. We conducted weekly blood draws and symptom checklists over a 28-day period. Blood samples were tested for inflammatory markers (IL6, IL10, TNF-□, IFN-□, IFN-ɣ, MCP1, IP10, IgG, N-protein, NFL and GFAP) and considered our exposure variable. Daily symptom data was used to create the outcome variable. Given that the infectious period is less than 14 days, we restricted analyses to the infectious period and fit regression models to examine the association between the highest level of each inflammatory maker and number of symptoms. We performed a neurological-specific analysis of markers and symptoms. **Results** Our analysis cohort included 60 unvaccinated individuals. They reported a median symptom count of 11 (IQR 7-14). Participants with a higher symptom count were more likely to have elevated levels of IL6 ($\beta = 0.23$, $p = 0.02$), IL10 ($\beta = 0.13$, $p = 0.03$), TNF-□ ($\beta = 1.5$, $p < 0.01$), IFN-□ ($\beta = 0.94$, $p < 0.01$), IFN-ɣ ($\beta = 0.23$, $p < 0.01$), MCP1 ($\beta = 0.03$, $p < 0.01$), and N-protein ($\beta = 0.007$, $p = 0.04$). Individuals who had a higher neurological symptom count were more likely to have elevated levels of GFAP ($\beta = 0.006$, $p < 0.01$), but not NFL. **Conclusions** In this longitudinal cohort of individuals with acute COVID-19, we found an association between level of inflammatory markers and symptoms, including a neurological-specific relationship. Future research will examine the relationship between specific inflammatory markers and select symptoms to unpack the biological mechanisms of symptoms.

COVID-19 Pandemic

Symptoms of Depression and Anxiety, and Unmet Healthcare Needs in Older Adults during the COVID-19 Pandemic: a Cross-Sectional Study from the Canadian Longitudinal Study on Aging Jayati Khattar* Jayati Khattar Laura N. Anderson Vanessa de Rubeis Margaret de Groh Ying Jiang Aaron Jones Nicole E. Basta Susan Kirkland Christina Wolfson Lauren E. Griffith Parminder Raina

The COVID-19 pandemic disrupted access to healthcare services in Canada. Research has found that people with depression and anxiety symptoms are more likely to report unmet healthcare needs. Our study objective was to examine if mental health was associated with perceived access to healthcare during the pandemic. A cross-sectional study was conducted using data from 23,972 participants (aged 50-96) in the Canadian Longitudinal Study on Aging COVID-19 Exit survey (Sept–Dec 2020). We used logistic regression to estimate how depression and anxiety, defined using scores of ≥10 on the Center for Epidemiologic Studies Depression Scale and Generalized Anxiety Disorder score respectively, were associated with the odds of: 1) any challenges accessing healthcare, 2) not going to a hospital or seeing a doctor when needed, 3) experiencing barriers to COVID-19 testing. Models were adjusted for sex, age, region, urban/rural, racial background, immigrant status, income, marital status, work status, chronic conditions, and pre-pandemic unmet needs. Depressive (adjusted OR=1.96; 95% CI=1.82, 2.11) and anxiety symptoms (adjusted OR=2.33; 95% CI=2.04, 2.66) were associated with increased odds of challenges accessing healthcare. A statistically significant interaction with sex suggested stronger associations in females. Symptoms of depression (adjusted OR=2.88; 95% CI=2.58, 3.21) and anxiety (adjusted OR=3.05; 95% CI=2.58, 3.60) were also associated with increased odds of not going to a hospital or seeing a doctor when needed. Lastly, depressive (adjusted OR=1.99; 95% CI=1.71, 2.31) and anxiety symptoms (adjusted OR=2.01; 95% CI=1.58, 2.56) increased the odds of reporting barriers to COVID-19 testing. Depression and anxiety symptoms were strongly associated with perceived unmet healthcare needs during the COVID-19 pandemic. Interventions to improve healthcare access for adults with depression and anxiety during the pandemic may be necessary.
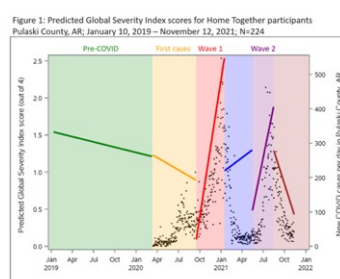
The impact of successive waves of daily COVID-19 cases on the mental health of homeless women with young children: Lessons learned for future program planning with vulnerable populations Brooke EE Montgomery* Brooke EE Montgomery George C. Pro Isis D. Martel Jessica Burnham Ruthie Hokans Jaime Stacker Jennifer McClane Nick Zaller Ben Goodwin

Introduction. Successive waves of COVID-19 threaten mental health, especially for vulnerable populations. *Home Together* (*HT*) is a program in Pulaski County, AR that provides case management to homeless women who have a diagnosed mental health condition and a child younger than 6yrs. Better understanding of how sharp increases in daily COVID cases affect mental health burden may inform future interventions designed to mitigate adverse mental health consequences during crises.

Methods. We used the 18-item Likert-scale (0–4) Brief Symptom Inventory to assess mental health symptom severity (i.e., Global Severity Index (GSI) score) among women entering *HT* between 1/2019 and 11/2021 (N=224). We used simple linear regression to derive the predicted GSI score over time. We used publicly-available COVID data to determine the number of new daily cases and define outbreak waves in Pulaski County.

Results. Over the study period, the mean GSI score was 1.29 and the mean daily case count was 99 (min=0, max=547). Predicted GSI scores were closely aligned with daily COVID cases during Waves 1 and 2 (Fig 1). In Wave 1 (9/1/2020–1/1/2021), daily COVID cases increased by 1800% (from 28 to 547 daily cases) while there was a corresponding increase in predicted GSI scores of 2700% (from 0.09 to 2.54). A similar relationship was observed during Wave 2 (5/2021–8/2021). The most notable downward trend followed the Wave 2 spike (8/2021–11/2021), when COVID cases decreased by 95% (from 347 to 28 cases) and were paralleled by a 67% decrease in predicted GSI scores (from 1.29 to 0.43).

Conclusion. We identified a strong relationship between mental health symptoms and the overall pattern of the pandemic, such that increases in COVID cases were followed nearly identically by increases in self-reported symptoms of poor mental health. As waves and outbreaks are expected to continue indefinitely, decision-makers must adjust their efforts to address the cyclical and persistent nature of this pandemic.

Figure 1: Predicted Global Severity Index scores for Home Together participants
Pulaski County, AR; January 10, 2019 – November 12, 2021, N=224

Evaluating reasons for non-compliance with stay-at-home recommendations during the outbreak of SARS-Cov-2 in Mexico City: one year of daily SMS surveys Susana Lozano-Esparza* Susana Lozano-Esparza Priscilla Espinosa-Tamez Hector Lamadrid-Figueroa Marion Brochier Martín Romero Sergio Bautista-Arredondo Martin Lajous

Objective: To monitor reasons for non-compliance with stay-at-home recommendations during the COVID-19 pandemic in Mexico City using daily SMS surveys.

Methods: Between May 5th, 2020 and May 4rd, 2021, we estimated the weekly average outings for work and social gatherings as a proportion of all outings from surveys sent to a daily random sample of 30,000 mobile phones. We estimated the average proportions and 95% prediction intervals (95%PIs) using log-linked negative binomial regression and sampling weights based on household size distribution. We explored results according to the local epidemiological risk traffic light system established by the government (Lock-down May 4th-May 31st; Red 1, June 1st-June 28th; Amber 1, June 29th-December13th; Red 2, December 14th-February 14th, 2021; Amber 2, February 15th-May 3rd, 2021) and COVID-19 hospitalizations (publicly available data). We also stratified data by age of the respondent.

Results: Outings for work were frequent during Lock-down (63.2% 95%PI 62.3, 64.1) and increased and stabilized as epidemiologic risk and hospitalizations increased. Non-compliance due to social gatherings increased from 4.2% (95%PI 3.8, 4.6) in Lock-down and peaked in mid-November (7.2%; 95%PI 7.0, 7.4). As hospitalization rose in December, social gatherings declined but later resumed as epidemiologic risk lowered. Outings because of work or social gatherings decreased with the age of the respondent. At the height of hospitalizations during high epidemiological alert, non-compliance due to social gatherings was almost 50% higher when the respondent was <24 years relative to ≥65 years

Conclusions: Outings for work increased after Lock-down and remained stable thereafter. Non-compliance due to social gatherings appeared to be responsive to epidemiologic risk and COVID-19 hospitalizations. Compliance with stay-at-home directives appeared to be lower when respondents were young adults.

Figure. Percentage (95% prediction intervals) of non-compliance to stay-at-home guidance due to work and social gatherings and daily COVID-19 hospitalizations in Mexico City from May 4th, 2020 through May 3rd, 2021*
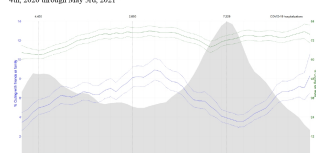
*Percentage of non-compliance due to work (green) and social gatherings (blue) adjusted for seasonality (12-, 6-, 4-, and 1-month periods). Dashed lines represents 95% prediction intervals. The area in gray represents the daily number of COVID-19 hospitalizations. We imputed the proportions for 58 days where data was unavailable using the mean of adjoining days.
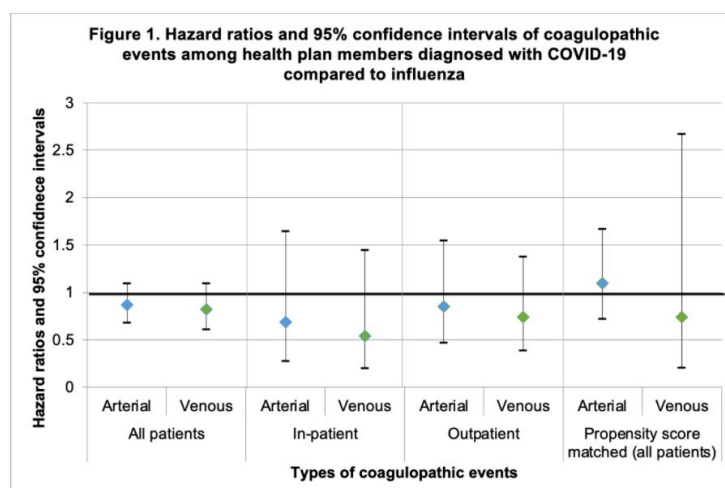
The role of real-world data in combating COVID-19 and understanding the natural history of coagulopathy. Etienne Holder* Etienne Holder Alexandra Muir Aleah Peffer Quinn Johns Claire Cravero Mark Cullen

Background: Since the Coronavirus disease 2019 (COVID-19) pandemic began in December 2019, the U.S. alone has experienced over 50.1 million cases and more than 797 thousand deaths due to COVID-19. As morbidity and mortality due to COVID-19 continues to rise, the necessity to better quantify the burden of disease is paramount. The current study aimed to investigate the rate of coagulopathic events following COVID-19 compared to influenza infections.

Methods: We utilized medical and pharmacy claims data provided by Symphony Health to examine the association between COVID-19 diagnosis and time to a coagulopathic or thrombotic event. These data were made available through the COVID-19 Research Database which provides pro-bono de-identified healthcare data to empower research and analytics on COVID-19. The earliest diagnosis of COVID-19 on a medical claim between April 1, 2020, and November 30, 2020 was used as an indication of infection indicated by ICD-10 codes. For our main analyses, we examined the time to coagulopathic events comparing COVID-19 to influenza using cox proportional hazards regression modeling across the study population and stratified by place of service (in-patient vs. outpatient). Propensity score matching was used to attain covariate balance. Hazard ratios (HR) and 95% confidence intervals (CI) were reported.

Results: Overall, a 26% non-statistically significant reduction in risk was observed and more so for venous events in the in-patient setting (HR=0.54, 95% CI=0.20-1.45) as compared to the outpatient setting (HR=0.74, 95% CI=0.39-1.38). Propensity score matched, cox proportional hazards models demonstrated a non-statistically significant 10% increase in risk of arterial thrombosis after additional adjustment for place of service (HR=1.10, 95% CI=0.72-1.67).

Conclusion: In this large, U.S.-based prospective cohort study using real world data, we found a non-statistically significant association between COVID-19 and coagulopathic or thromboembolic events, in a 90-day period, compared to influenza after adjusting for relevant risk factors. This outcome is likely due to our small number of events observed during our study timeframe. With greater power, we may be able to elucidate these findings more fully.

Figure 1. Hazard ratios and 95% confidence intervals of coagulopathic events among health plan members diagnosed with COVID-19 compared to influenza

Gender and Sexual Identity Disparities in COVID-19 Coping Patterns Laura Houghtaling*
Laura Houghtaling Wendy Manning Miranda Berrigan Claire Kamp Dush

The COVID-19 pandemic has had a profound impact on all Americans. There is still limited research on how we are coping, especially among sexual and gender minority populations. We examine the prevalence of negative and positive Covid-19 coping behaviors comparing monosexual and non-monosexual adults; LBG and non-LGB adults; and adults in different-gender and same-gender couples using the National Couples' Health and Time Study (NCHAT) dataset (N=3,638). NCHAT provides a rich and unique opportunity to explore experiences of sexual and gender minority (SGM) populations during the COVID-19 pandemic through a nationally representative population-based sample of married or cohabitating adults aged 20-60 years with oversamples of racial, ethnic, and sexual minorities. Using Poisson regression models adjusted for relevant sociodemographic controls, we find identifying as non-monosexual OR identifying as bisexual, gay, lesbian or other increases the number of negative coping behaviors regardless of couple type. Based on the minority stress model, we would expect to see more deleterious health behaviors among sexual minority populations due to excess stress attributable to stigma and discrimination. We also find that non-monosexual adults in a different-gender couple; bisexual adults in a different-gender couple and other identity adults in a different-gender couple report the greatest number of negative coping behaviors compared to same-gender couples of all sexual identities. When examining positive coping behaviors, we do not find any measurable differences by couple type, sexual identity or sexual/romantic attraction. We compare COVID-19 coping patterns by population characteristics using an adjusted Wald test for categorical variables in Table 1.

Table 1. Description of the study population by mean number of positive and negative COVID-19 coping behaviors (n=3,638)

	Positive Coping Behaviors			Negative Coping Behaviors			Total
	Weighted mean	SE	$p^\dagger$	Weighted mean	SE	$p^\dagger$	Unweighted sample size (n)
Sexual identity			0.83			<0.001	
Exclusively Heterosexual	3.26	0.047		1.74	0.03		2,017
Exclusively Gay or Lesbian	3.24	0.095		2.11	0.051		736
Bisexual	3.12	0.16		2.72	0.11		515
Other Identity	2.69	0.22		2.94	0.24		370
Sexual and/or Romantic Attraction			0.64			<0.001	
Monosexual	3.26	0.047		1.75	0.029		2,786
Non-monosexual	3.2	0.12		2.71	0.087		752
Couple Type			0.11			<0.001	
Different-gender	3.25	0.046		1.78	0.031		2,498
Same-gender	3.44	0.11		2.13	0.072		993
Gender			<0.001			0.062	
Man/Trans Man	2.95	0.064		1.72	0.045		1,784
Woman/Trans Woman	3.54	0.066		1.84	0.041		1,756
Education level			0.28			<0.01	
Bachelor's degree or higher	3.38	0.058		1.79	0.039		2,049
Some college or associate's	3.23	0.078		1.92	0.065		948
Less than HS, HS degree or GED	3.09	0.11		1.66	0.053		640
Race/ethnicity			<0.01			0.2	
NH White	3.2	0.065		1.77	0.042		2,245
NH Black	3.63	0.11		1.87	0.068		335
NH Asian	2.98	0.11		1.62	0.085		209
Hispanic	3.34	0.075		1.83	0.056		584
NH Multiracial	3.26	0.16		1.93	0.12		206
NH Other race	2.86	0.37		1.8	0.21		57
Employment Status			0.1			0.032	
Full or part time	3.21	0.049		1.75	0.034		2,840
Unemployed or furloughed	3.36	0.084		1.89	0.057		794
Foreign Born			0.14			<0.001	
Born in the US	3.27	0.048		1.82	0.032		3,274
Born outside the US	3.09	0.12		1.53	0.068		342
Marital status			0.039			<0.001	
Legal marriage	3.28	0.056		1.69	0.031		2,287
Civil union or similar	3.34	0.13		1.78	0.12		523
Partnered	3.05	0.096		2.22	0.076		824
TOTAL sample	**3.25**	**0.046**		**1.79**	**0.03**		**3,638**

Positive coping behaviors include the following: 1) Take a break from news or social media; 2) Exercising or walking; 3) Praying or meditating; 4) Getting plenty of sleep; 5) Connecting with friends or family; 6) Connecting with religious community; 7) Connecting with mental or physical health care provider

Negative coping behaviors include the following: 1) Watching or streaming TV or gaming; 2) Smoking or vaping; 3) Drinking alcohol; 4) Using drugs; 5) Eating more food than usual; 6) Eating less food than usual; 7) Cutting or self-injury

†Statistically significant difference by population characteristic determined using adjusted Wald F-test for categorical variables

COVID-19 Infection and Sleep Health among a Nationally Representative Diverse Sample of U.S. Adults: COVID-19's Unequal Racial Burden Survey, 2020-2021 Dana Alhasan* Dana Alhasan Symielle A. Gaston Paula D. Strassle Anita L. Stewart Eliseo J. Pérez-Stable Anna María Nápoles Chandra L. Jackson

Minoritized racial/ethnic groups are more likely than Whites to contract COVID-19, likely exacerbating sleep disparities and thus overall health disparities. Yet, few studies have examined COVID-19 and sleep health associations by race/ethnicity. We conducted an online survey of Asian, Black, Latino (English and Spanish-speaking), and White adults (1000 each), and American Indian/Alaska Native (AI/AN), Native Hawaiian/Pacific Islander (NH/PI), and multiracial adults (500 each) from 12/2020-2/2021 (N=5500). Eligible participants were proximity matched and weighted to a target sample from the 2018 American Community Survey, generating nationally representative cohorts within each racial/ethnic group. We estimated overall and racial/ethnic-specific cross-sectional associations between COVID-19 and sleep health. COVID-19 infection (confirmed, probable, suspected) was classified based on self-report and using WHO definitions. Sleep dimensions included fair/poor sleep quality, non-restorative sleep, sleep problems, and difficulty falling asleep. Poisson regression with robust variance estimated PRs while adjusting for sociodemographic and clinical characteristics. Among 4,726 eligible participants, 24% had a COVID-19 infection. Among those with fair/poor sleep quality (18.2%), prevalence was highest among White (3.6%), Black (3.0%), and Latino (2.9%) adults. COVID-19 versus no infection was associated with a higher prevalence of sleep problems (1.13 [1.08-1.17]) and difficulty falling asleep (1.15 [1.11-1.19]). Associations between COVID-19 versus no infection and difficulty falling asleep were stronger among Latino (1.27 [1.15-1.39]), NH/PI (1.23 [1.09-1.38]), AI/AN (1.12 [1.08-1.33]), and Black (1.12 [1.03-1.23]), compared to White adults (0.99 [0.0.90-1.08]). Future research should longitudinally assess COVID-19 (including severity) and sleep, and mitigation strategies should prioritize minoritized racial/ethnic groups who are disproportionately impacted by COVID-19.
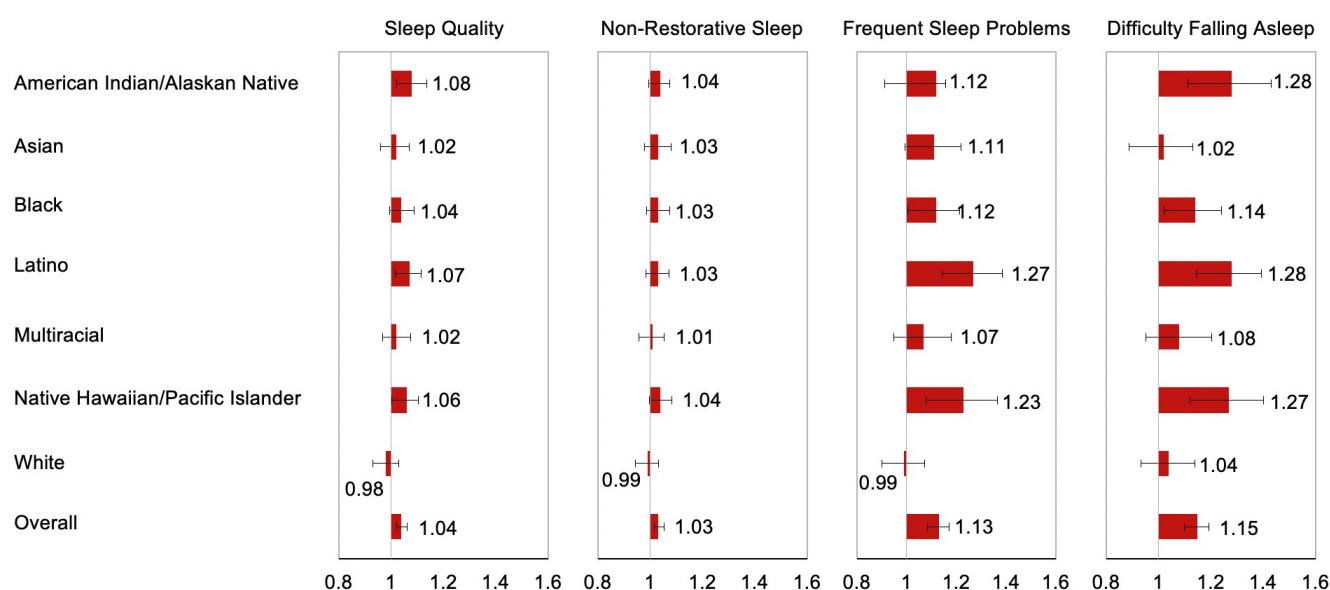
Immune response to SARS-CoV-2 in pregnant and non-pregnant women following infection

Marni B. Jacobs* Marni B. Jacobs Holly Valentine Celestine Magallanes Sierra Adkins Sydney C. Morgan Abbas Hakim Peter DeHoff Louise C. Laurent Priyadarshini Pantham

During pregnancy, the immune system undergoes adaptations to prevent fetal rejection. For certain pathogens, these adaptations cause increased disease susceptibility and altered immune response following infection. Recent research suggests that pregnant women are at higher risk for severe COVID-19 disease compared to non-pregnant patients. However, it is unclear whether this increased risk is associated with differences in immune response to infection. The present study assesses whether humoral immune response to SARS-CoV-2 is affected by pregnancy. Pregnant women with a positive SARS-CoV-2 test (n=20) were matched in a 1:2 ratio with non-pregnant reproductive aged women (n = 40) on number of days post-positive test at the time of blood sample. The final study population included 71 samples from 59 patients (1 vaccinated control excluded). Mean immunoglobulin G (IgG) and immunoglobulin M (IgM) levels to SARS-CoV-2 proteins were compared between groups using generalized estimating equations to account for repeated measures in some participants. Levels were log transformed prior to analysis and are reported in arbitrary units (a.u.). Median number of days post-positive at the time of sampling was 6 (range 2-97). No significant differences in mean age (29.6 vs. 26.9 years), ethnicity (40% Hispanic vs. 41%), or race (55% white vs. 37%) were noted between groups. No differences in mean antibody levels were seen between pregnant and non-pregnant groups (Figure 1). Results were similar when stratified by trimester of infection. Additionally, no differences were noted in IgG or IgM trajectories over time between groups. Overall, results suggest that humoral immune response following SARS-CoV-2 infection does not differ in pregnant women compared to their non-pregnant counterparts. While this study is small, findings should reassure patients and healthcare providers that pregnant patients appear to mount an appropriate immune response to SARS-CoV-2 following infection.
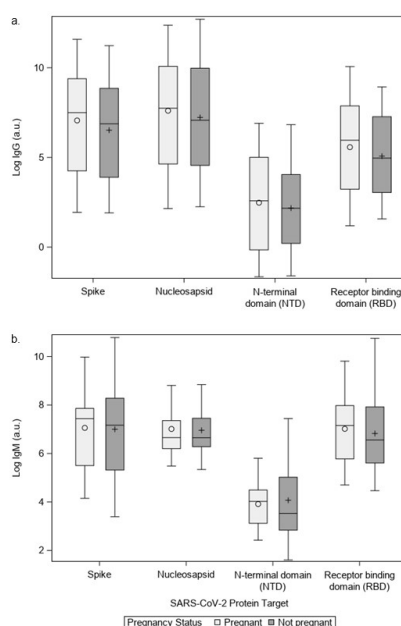

Figure 1: (a) Immunoglobulin G (IgG) and (b) immunoglobulin M (IgM) levels to SARS-CoV-2 proteins in pregnant and non-pregnant patients following SARS-CoV-2 infection

Adoption of Go.Data as a digital tool for contact tracing in the context of COVID-19 in the Americas; case studies in practice Cristina Valencia* Cristina Valencia Giovanna Jaramillo-Gutierrez Sara Hollis Analia Rearte Paula Rosin Fernando Gassino Silvia Morreale Lorena Gobern Antonio Paredes Evelyn Balsells Pablo Galindo Marc Rondy Liz Parra Oliver Mazariegos Amy Young Aaron Miri Daniel Iken Emily James Emily James Angel Rodriguez

Background:

In the Americas, a range of digital contact tracing tools have been used to enhance COVID-19 outbreak response. Go.Data, an outbreak investigation tool developed by the World Health Organization, may accelerate the capacity for countries to operationalize and tailor contact tracing operations. To capture best practices, we present three case studies on the successful implementation of Go.Data in the Americas.

Methods:

We conducted in-depth interviews with members from three Go.Data implementation teams : two at national level (Argentina and Guatemala) and one at institutional level (The University of Texas, USA). We reviewed the epidemiological context of the COVID-19 outbreak response before and after Go. Data adoption including the processes undertaken for its implementation. Interviews were transcribed using NViVo, the analysis was descriptive.

Results:

All three teams implemented Go.Data as a first contact tracing tool at early stages of the pandemic, all with sizeable and multi-disciplinary dedicated staff. Through a container technology infrastructure, Argentina made Go.Data accessible to its provinces and its utilization was optional for local and provincial teams. Guatemala's Go.Data implementation required strong health systems interoperability between stakeholders from the Ministry of Health and municipalities to enable case and contact detection and monitoring. The University of Texas utilized Go.Data key performance indicator (KPI) outputs to inform a reactive testing strategy to complement contact tracing activities and integrated data from both on and off-campus testing sites.

Conclusions:

A tailored approach including sizeable multi-disciplinary teams, a dedicated technology infrastructure, health systems interoperability and embedment of the tool in the continuum of surveillance activities are necessary to sustain the adoption of Go.Data in the Region of the Americas.

Trends in Domestic Violence and Firearm Domestic Violence During COVID-19 in Six US Cities Elizabeth Tomsich* Elizabeth Tomsich Julia Schleimer Garen Wintemute Chris McCort

Introduction: The COVID-19 pandemic may be associated with increased risk for domestic violence and firearm domestic violence.

Methods: We examined trends in domestic violence (DV) and firearm DV in 6 US cities during the pandemic using Poisson or negative binomial regressions. We used binomial regressions to assess trends in firearm domestic violence as a proportion of domestic violence.

Results: Findings varied across outcomes and cities. As one of the first studies to examine firearm DV, results demonstrate that certain cities, such as Los Angeles and Nashville, observed no increase in trend in DV compared with trends prior to the stay-at-home order, yet trends in firearm DV and/or firearm DV as a proportion of DV increased.

Conclusions: Consistent with prior research on DV generally, we found substantial variation between jurisdiction in the association between the onset of stay-at-home orders and DV, firearm DV, and firearm DV as a proportion of DV.

Comparing Faculty and Staff Contacts with Two Different Teaching Styles During the COVID-19 Pandemic Stephanie Sikavitsas Johnson* Stephanie Johnson Katelin C Jackson Matthew S Mietchen Eric T Lofgren

As the COVID-19 pandemic enters its third year, universities have altered their teaching based on local and state guidelines. While many campuses had an online class delivery and work from home system for the 2020-2021 school year, as vaccinations and boosters became available many have switched back to in-person teaching and work for the 2021-2022 year. We wanted to understand how the different delivery systems affected faculty and staff contact patterns. We conducted an anonymous, voluntary online survey for faculty and staff of a PAC-12 school on their contact patterns with those both within and outside the university during the two delivery systems. Participants for each survey period were asked in general terms about the individuals they've encountered, the type and location of the interactions, and what COVID-19 precautions were taken.

We analyzed 271 responses for the online delivery period and 66 for the in-person period. For online delivery, employees had a median of 3 contacts/respondent (IQR 1-4). For in-person, there was a median of 8 contacts/respondent (IQR 3-23). During online delivery, 51% of reported contacts happened at home and 19% at work, compared to in-person of 37% and 39%, respectively. For online delivery, immediate family relations (43%) were the primary type of contact compared to in-person, where the largest interactions were with colleagues and students (37%). 56% of online delivery interactions had the respondent unmasked, compared to 48% of in-person delivery interactions ($p=0.03$).

These results show contacts increase as universities have employees back on campus. While family was the primary type of contact reported for online, the in-person split the type, if not number, between work and family contacts. The rise in employee contacts suggests a potential increase in student-employee and employee-employee transmissions as new, more transmissible variants arise and employees are having greater contact than at the start of the pandemic.

COVID-19 Testing, Vaccination Intentions, and Uptake among Youth and Young Adults: Disparities in Sexual, Gender, and Racial/Ethnic Minority Populations Jiayi Xu* Jiayi Xu Megan M Ruprecht Joseph Choi Gregory Phillips II

The COVID-19 pandemic continues to have a disproportionate impact on sexual and gender minority (SGM) youth and young adults (YYA), likely due to minority stress theory. Early research found SGM YYA experienced elevated rates of homelessness, unemployment, loss of healthcare, and familial rejection, all factors associated with COVID-19 infection and morbidity. COVID-19 testing and vaccination are currently the best strategies for prevention, yet little is known about differences in intentions and uptake between SGM YYA and their cisgender heterosexual peers. To explore potential differences, we conducted the YYA COVID-19 Study between 2/2021 and 2/2022. The study was a national, cross-sectional online survey (n = 933, mean age = 20.1) focused on recruiting diverse YYA ages 14-24. COVID-19 testing, vaccination, and vaccination intentions were compared among participants based on age, race/ethnicity, sexual identity, and gender modality/identity. Most YYA tested for COVID-19 (76.2%), but the only difference was seen by age (Table). More than two-thirds of participants received at least one shot (69.5%), and differences were seen by age and race/ethnicity. Finally, most unvaccinated participants (82.8%) indicated they were likely to get vaccinated. Combining vaccination uptake and intention in a single variable, we saw several significant differences. Of most relevance, Black and straight individuals were significantly more likely to report being unvaccinated and unwilling to get vaccinated. We also examined the impact of time on vaccine uptake; results showed that participants were 40% more likely to get vaccinated each subsequent month after 2/2021. Our study gives a fuller picture of how the pandemic has differentially affected COVID-19 testing and vaccination among SGM YYA, and provides critical information for health institutions to prioritize vaccine distribution equity, and to ensure SGM YYA are not left out of vaccination information and distribution campaigns.

Table: Differences in COVID-19 Testing, Vaccination, and Vaccination Uptake by Demographics (n = 933).

Demographics	N (%)	Tested for COVID-19			Received a COVID-19 vaccine			Vaccine Uptake*				
		Yes	No	Chi-Squared p-value	Yes	No	Chi-Squared p-value	Fully vaccinated	Partially vaccinated	Not vaccinated but likely to get vaccinated	Not vaccinated and not likely to get vaccinated	Chi-Squared p-value
Age, Years				<0.001			<0.001					<0.001
14-17	143 (15.33)	79 (55.24)	64 (44.76)		69 (48.25)	74 (51.75)		57 (39.86)	12 (8.39)	57 (39.86)	17 (11.89)	
18-21	463 (49.62)	369 (79.70)	94 (20.30)		328 (70.84)	135 (29.16)		258 (55.72)	70 (15.12)	122 (26.35)	13 (2.81)	
22-24	327 (35.05)	263 (80.43)	64 (19.57)		251 (76.76)	76 (23.24)		210 (64.22)	41 (12.54)	57 (17.43)	19 (5.81)	
Race/Ethnicity				0.344			<0.001					<0.001
Asian	67 (7.18)	49 (73.13)	18 (26.87)		39 (58.21)	28 (41.79)		28 (41.79)	11 (16.42)	28 (41.79)	0 (0.00)	
Black	163 (17.47)	115 (70.55)	48 (29.45)		120 (73.62)	43 (26.38)		108 (66.26)	12 (7.36)	29 (17.79)	14 (8.59)	
Latinx	282 (30.23)	217 (76.95)	65 (23.05)		224 (79.43)	58 (20.57)		186 (65.96)	38 (13.48)	47 (16.67)	11 (3.90)	
Multiracial	119 (12.75)	90 (75.63)	29 (24.37)		88 (73.95)	31 (26.05)		82 (68.91)	6 (5.04)	23 (19.33)	8 (6.72)	
Native American/American Indian or Alaska	100 (10.72)	82 (82.00)	18 (18.00)		76 (76.00)	24 (24.00)		70 (70.00)	6 (6.00)	16 (16.00)	8 (8.00)	
White	202 (21.65)	158 (78.22)	44 (21.78)		101 (50.00)	101 (50.00)		51 (25.25)	50 (24.75)	93 (46.04)	8 (3.96)	
Sexual Identity				0.476			0.535					0.014
Asexual	45 (4.82)	31 (68.89)	14 (31.11)		29 (64.44)	16 (35.56)		21 (46.67)	8 (17.78)	16 (35.56)	0 (0.00)	
Bisexual/Pansexual	328 (35.16)	257 (78.35)	71 (21.65)		229 (69.82)	99 (30.18)		191 (58.23)	38 (11.59)	86 (26.22)	13 (3.96)	
Gay/Lesbian	218 (23.37)	169 (77.52)	49 (22.48)		160 (73.39)	58 (26.61)		127 (58.26)	33 (15.14)	51 (23.39)	7 (3.21)	
Queer	134 (14.36)	97 (72.39)	37 (27.61)		92 (68.66)	42 (31.34)		68 (50.75)	24 (17.91)	34 (25.37)	8 (5.97)	
Straight	208 (22.29)	157 (75.48)	51 (24.52)		138 (66.35)	70 (33.65)		118 (56.73)	20 (9.62)	49 (23.56)	21 (10.10)	
Gender Modality/Identity				0.866			0.430					0.376
Cis Man/Boy	171 (18.33)	131 (76.61)	40 (23.39)		121 (70.76)	50 (29.24)		102 (59.65)	19 (11.11)	41 (23.98)	9 (5.26)	
Cis Woman/Girl	428 (45.87)	325 (75.93)	103 (24.07)		304 (71.03)	124 (28.97)		254 (59.35)	50 (11.68)	99 (23.13)	25 (5.84)	
Non-binary Not Trans	42 (4.50)	35 (83.33)	7 (16.67)		32 (76.19)	10 (23.81)		25 (59.52)	7 (16.67)	7 (16.67)	3 (7.14)	
Non-binary Trans	108 (11.58)	81 (75.00)	27 (25.00)		76 (70.37)	32 (29.63)		54 (50.00)	22 (20.37)	28 (25.93)	4 (3.70)	
Questioning	75 (8.04)	54 (72.00)	21 (28.00)		47 (62.67)	28 (37.33)		39 (52.00)	8 (10.67)	25 (33.33)	3 (4.00)	
Trans Man/Boy	82 (8.79)	65 (79.27)	17 (20.73)		52 (63.41)	30 (36.59)		39 (47.56)	13 (15.85)	27 (32.93)	3 (3.66)	
Trans Woman/Girl	27 (2.89)	20 (74.07)	7 (25.93)		16 (59.26)	11 (40.74)		12 (44.44)	4 (14.81)	9 (33.33)	2 (7.41)	
Total	933	711 (76.21)	222 (23.79)		648 (69.45)	285 (30.55)		525 (56.27)	123 (13.18)	236 (25.29)	49 (5.25)	

* Vaccination uptake is a constructed variable using responses to questions about vaccine intention and vaccine receipt.

Phenome-Wide Association Study of COVID-19 in the Colorado UCHealth System Lauren Vanderlinden* Lauren Vanderlinden Nicholas Rafaels David Mayer Kathleen Barnes Christopher Gignoux Randi Johnson

Pre-existing health conditions may associate with risk of COVID-19. To identify these risk factors, we performed a Phenome-Wide Association Study (PheWAS) using electronic health records (EHR) from a COVID-19 Data Mart maintained by the Colorado Center for Personalized Medicine (>1.4 million patients of the UCHealth health care system) using patients active in UCHealth prior to the pandemic (≥3 face-to-face visits in January 2015 to January 2020) and who were tested for COVID-19 at UCHealth (N=313,981) up to January 2022. Testing was determined using labs. 51,427 patients tested positive (16%), as determined by the ICD-10 diagnosis code U07.1. Pre-existing conditions were determined using the PheWAS R package to calculate phecodes from healthcare encounters during the pre-pandemic period. For each condition, we compared patients with at least two occurrences of the phecode during the pre-pandemic period to patients with no occurrences of the phecode during the same period. 1,816 distinct pre-existing conditions had sufficient sample size (≥20 patients with the condition) and tested for association with COVID-19 using logistic regression adjusted for age, sex, and race/ethnicity. We identified 166 pre-existing conditions associated with COVID-19 after Bonferroni correction (P<0.05). A higher proportion of respiratory pre-existing conditions were associated with COVID-19 (32%) compared to metabolic (15%), and other conditions (Chi-squared P = 1.1e-12). Prior viral pneumonia conferred the greatest risk for testing positive for COVID-19 (OR=37.4, 95%CI: 29.3-48.4). However, results indicated an inflated number of associations (λ=2.7). Results were similar with additional adjustment for health care utilization. Diagnosis of a pre-existing condition and testing positive for COVID-19 may both be related to study selection which could lead to selection bias, as is common in EHR-based investigations. Further quantitative bias analyses should be performed to validate results.

Are We Safe After COVID-19 Vaccination? Hongshuo Wei* Hongshuo Wei Quinn Michael Monson Summer Michelle Nichols Eva Ann Larson Xiaoling Wang

BACKGROUND: As COVID-19 pandemic continues, it becomes clear that the virus probably will not completely go away. Although CDC has stated that fully vaccinated people can go back to normal social activity, this recommendation changes with the waves of the pandemic and the definitions of fully vaccination, resulting in different responses in the population. The questions we are asking are whether increased social activity is linked with the risk of COVID-19 contraction and what are the key factors associated with people's decision about what lifestyle they choose.

METHODS: We conducted an online survey using a 21-question questionnaire on fully vaccinated volunteers. Main questions include type of vaccine, COVID-19 infection status, number of comorbidities, numbers of social activities and satisfaction with current lifestyle, etc. Social activity includes shopping, sports activities/going to gym, family gathering, in-person learning or working, volunteering as a group, leisure activities (dining out, going to bar, etc.), traveling with friends or taking flight, and religious activities.

RESULTS: A total of 1002 participants submitted valid survey data with a mean age of 51.6 (SD=14.6) and 73.8% being females. Out of these participants, 221 contracted COVID after vaccination. In comparison with the participants that did not contract COVID, this population had a significantly higher level of social activity (4.14 +/- 1.99 vs. 3.87+/-2.12, P=0.048). A clear trend was also observed when participants were divided into 3 groups based on different levels of social activity. 15.8% of people contracted COVID-19 in those with 0 to 2 social activities, while 22.7% in those with 3 to 5 social activities, and this number was up to 25.2% in those with 6-8 social activities, P<0.001. Multivariate regression analysis showed that participants with more comorbidities were less likely (p<0.001), while participants with previous COVID infection (P=0.035) were more likely to choose a high level of social activity. On the other hand, participants with more social activities are more satisfied with their current lifestyle (P<0.001)**,** while those with less social activities do feel lonely, want more activities, or wish more people vaccinated for them to feel safe to go out.

CONCLUSION: Higher level of social activities is associated with the risk of COVID-19 contraction. Comorbidities and previous COVID-19 infection are key factors when people decide what level of social activity they are comfortable with.

LATEBREAKER

COVID-19 Pandemic

Trends and factors associated with change in COVID-19 vaccination intent among residents and staff in six Seattle homeless shelters, March 2020 to August 2021 Sarah Cox*

Sarah Cox Julia H. Rogers Nicholas B. Thuo Ashley Meehan Amy C. Link Natalie K. Lo Brian J. Manns Eric J. Chow Morhaf Al Achkar James P. Hughes Melissa A. Rolfes Emily Mosites Helen Y. Chu

Introduction: Achieving high COVID-19 vaccination coverage in homeless shelters is critical in preventing morbidity, mortality, and outbreaks, however, vaccination coverage remains lower among people experiencing homelessness than the general population.

Methods: We conducted a cross-sectional study to retrospectively describe attitudes and identify factors associated with change in COVID-19 vaccination intent among shelter residents and staff during March 2020 and August 2021. To identify factors associated with change in COVID-19 vaccine intent becoming more positive overall compared to other attitudes, we utilized a Poisson model to calculate Risk Ratios with robust standard errors, adjusting for confounding by shelter site and demographic variables determined *a priori*.

Results: From July 12 – August 2, 2021, 97 residents and 20 staff participated in surveys across six shelters in Seattle King County, Washington. Intent to be vaccinated against COVID-19 increased from 45.3% (n=53) when recalling attitudes in March 2020 to 74.4% (n=87) as of August 2021, and was similar among residents and staff. Many participants (43.6%, n=51) indicated feeling increasingly accepting about receiving a COVID-19 vaccine since March 2020, while 13.7% (n=16) changed back and forth, 10.3% (n=12) became more hesitant, and 32.5% (n=38) had no change in intent. In the model examining the relationship between becoming more positive about receiving a COVID-19 vaccine compared to all other attitudes (n=116), we found a 57.2% increase in vaccine acceptability (RR 1.57; 95% CI: 1.01, 2.45) among those who reported worsening mental health since the start of the pandemic.

Conclusions: Findings highlight opportunities to improve communication with residents and staff about COVID-19 vaccination and support a need for continued dialogue and a person-centered approach to understanding the sociocultural complexities and dynamism of vaccine attitudes at shelters.

Figure 1. COVID-19 vaccination intent among shelter residents and staff, March 2020 – August 2021 (N=117)
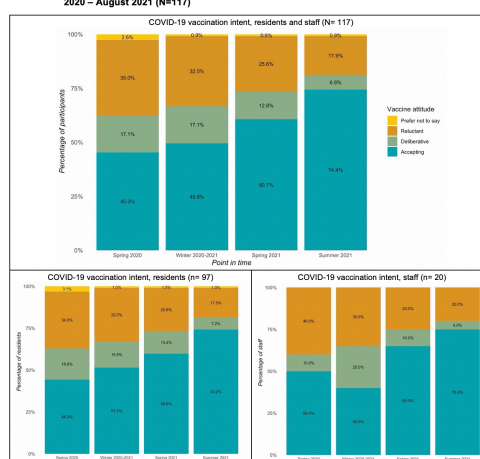
LATEBREAKER

COVID-19 Pandemic

Enduring the "slow burn" in rural America: estimating pandemic dynamics by rurality

Lindsey M. Filiatreau* Lindsey M. Filiatreau Banson Fox Aaloke Mody Elvin H. Geng

Heterogeneity in the severity of the COVID-19 pandemic (e.g., cases, hospitalizations, and deaths) has been widely documented. However, finer epidemiological characterization of pandemic dynamics such as transmission intensity over time and geography could provide insights into community-level behavioral responses.

We introduce the concept of "pandemic sustainability" as the total time spent with an effective reproductive number (i.e., "R") above 1, "pandemic burden" as the area under the curve when R is plotted over time (accounting for height of the curve and time), and "pandemic responsiveness" as the decay time of transmission after each wave in which R is greater than one to when it first recedes below one. Using county-level COVID-19 case data from Johns Hopkins Center for Systems Science and Engineering and R-package EpiEstim, we estimate R each day between March 1, 2020 and March 1, 2022 to examine these parameters in the United States, stratified by rurality.

The median county-level value of pandemic burden was 861 (IQR 834-903) and 990 (IQR 906-1205) in urban and rural counties, respectively. Median county-level value of pandemic sustainability was 397 (IQR: 381-414) and 430 (IQR 404-470) days in urban and rural counties, respectively. Responsiveness during the first wave of the pandemic was greater in urban (40 days) versus rural settings (62 days) while it varied in subsequent waves.

Greater pandemic responsiveness was observed in urban versus rural settings while the converse was true for pandemic burden and sustainability. The rapid movement of each variant through urban locales presented recurrent opportunities for urban healthcare systems to recover. Conversely, the prolonged periods of moderately high transmission in rural settings yielded fewer opportunities for recovery. These differences have important implications for achieving equitable health outcomes across geographies and should be used to inform future pandemic response efforts.
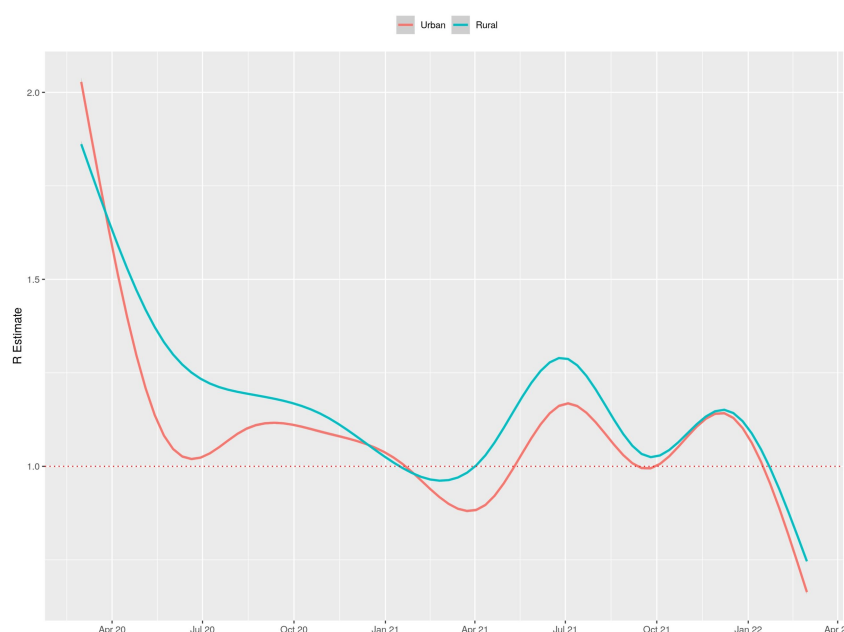
Diabetes

Association of income variability and income drops with incident cardiovascular disease in individuals with type 2 diabetes: a nationwide population-based cohort study in South Korea Yong-Moon ("Mark") Park* Yong-Moon ("Mark") Park Hong Seok Lee Tali Elfassy Clare C. Brown Benjamin C Amick Seong-Su Lee Kyungdo Han

Background: Cardiovascular disease(CVD) is the leading cause of death in people with type 2 diabetes(T2D). While there is a substantial literature on how CVD risk differs by income, little is known about whether income change is associated with CVD risk among those with T2D.

Methods: Using nationally representative data from the Korean Health Insurance Service database, 1,531,523 adults with T2D aged 30 to 64 years and without a history of CVD were enrolled between 2009-2012 and followed for CVD through December 2018. Actual income data were not available and income levels were determined based on annual health insurance premiums, which were provided using 20 quantiles for each of the five years preceding the participant's enrollment. Individual's variability of income quantile over time was measured using variability independent of the mean(VIM), which was calculated by transforming standard deviation using nonlinear regression analysis. VIM was categorized into quartiles with higher quartiles representing higher variability. Income drop was defined as a decrease ^{3}25% in income quantile. Presence of a drop was measured at two time points: 1) two years prior to enrollment vs enrollment and 2) four vs two years prior to enrollment. Multivariable Cox proportional hazards regression was used to estimate hazard ratios(HR) for incident CVD and for individual CVD outcomes separately, adjusting for sociodemographic factors, comorbidities, diabetes duration, and diabetes treatment.

Results: High income variability over time was associated with increased risk of CVD (HR$_{\text{highest vs. lowest quartile}}$ 1.13, 95%CI 1.11-1.15; P$_{\text{trend}}$<0.001). More income drops (2 vs. 0 drops) were also associated with increased CVD risk (HR 1.13, 95%CI 1.08-1.81), with the greatest impact among younger adults (<45years) and men, as well as CVD death (HR 1.45, 95%CI 1.26-1.67).

Conclusions: Among Korean adults with T2D, high income variability and income drops were associated with increased risk of CVD.

Neurocognitive outcomes among adults exposed to in utero pre-gestational diabetes – follow-up from a diabetes program project grant conducted between 1978 and 1995

Katherine Bowers* Katherine Bowers Katherine Bowers Jane Khoury Rhonda Szczesniak Krishna

Exposure to maternal diabetes *in utero* increases the risk in the offspring for metabolic disturbances, including obesity and diabetes and for cardiovascular disease, and may additionally increase the risk for cognitive impairment and poor behavioral outcomes. The Transgenerational Effect on Adult Morbidity Study (The TEAM Study) was initiated to evaluate young adult metabolic, cardiovascular and neurologic outcomes in offspring of mothers with pregestational diabetes mellitus who participated in a Diabetes in Pregnancy (DiP) Program Project Grant between 1978 and 1995. The DiP Study collected medical and obstetric data across pregnancy. At the study visit TEAM participants undergo a comprehensive medical examination to evaluate multiple outcomes including biomarkers of disglycemia, as well as nephrotic, cardiovascular and neurologic indicators. Neurocognition was assessed using the Wechsler Abbreviated Scale of Intelligence (WASI)-II. Utilizing up to six daily glucose measures, profiles of temporal glucose levels and excursions were estimated utilizing cubic B-splines. Sparse functional principal component analysis (fPCA) for longitudinal data was used to obtain univariate scores based on the first fPC. Each mother's score was used to assign her profile into exactly one of three groups. Subscale and composite T-Scores from the WASI-II were compared across maternal glucose profiles using descriptive and regression analyses. *Results*. Profiles were available for a subset of TEAM participants (n=75). WASI-II composite T scores and percentile ranks varied across maternal glucose profiles. Lower offspring cognitive scores and ranks were identified among a maternal profile defined by high mean and high variability of glucose across pregnancy. Additional analyses include identification of potential mediators (e.g. birth timing and weight at birth) and effect modifiers (e.g. postnatal experiences).

Characterizing the Risk of Type 2 Diabetes Mellitus by Gestational Diabetes: The NYC APPLE Cohort Katharine McCarthy* Katharine McCarthy Shelley Liu Luciana Vieira Victoria Mayer Teresa Janevic

Diverse population-based data on the progression to Type 2 Diabetes (T2DM) by a gestational diabetes mellitus (GDM) pregnancy are lacking. We estimate the population-based risk of T2DM by GDM status and race/ethnicity with the A1c in Pregnancy and Postpartum Linkage for Equity (APPLE) cohort, a multiethnic retrospective cohort in New York City (NYC). We used a systematic match algorithm to identify unique women who gave birth between 2009 and 2011 and were followed for up to eight years postpartum using linked NYC birth record, hospital discharge and A1c diabetes registry data. Differences in time to T2DM by GDM status were assessed using Cox regression, adjusting for sociodemographic and clinical factors. We tested for effect measure modification between GDM status and race/ethnicity using tests for interaction and stratification. Models were generalized to accommodate non-proportional hazards by GDM by allowing interaction with time and through stratification by postpartum time interval. We applied a quantitative adjustment for bias due to disease misclassification using probabilistic bias analysis, hypothesizing non-GDM women may be less closely monitored and more likely to be underdiagnosed for T2DM. The cumulative incidence for T2DM was 8.2% and 0.5% among women with and without GDM, respectively. The adjusted hazard ratio (aHR) for the risk of GDM on developing T2DM was 15.7 (95% Confidence interval (CI) 13.9, 17.8) in the overall cohort and varied only slightly by race/ethnicity. When stratified by time, we found risk was highest in the first year following birth (aHR 17.2, 95% CI: 14.8, 20), and decreased with time to (aHR: 7.8, 95%CI: 6.2, 9.9) at 5-9 years postpartum. Under diagnosis of T2DM among women without GDM could reduce estimates by only one-third. Results demonstrate stark differences in the risk of T2DM by GDM which persist after accounting for diagnostic bias. These findings call for improved T2DM prevention in the postpartum period.

Relationship Between Blood Manganese Levels and Elevated Triiodothyroxin Measures in Adolescents and Adults in the National Health and Nutrition Examination Survey (NHANES 2011-2012) Victor Florez* Victor Florez Amy Kalkbrenner

Manganese (Mn), while a nutrient, can be deleterious at high levels, and may affect thyroid hormone (TH) homeostasis through direct dysregulation of the thyroid gland, or indirectly via dopaminergic control. Prior research suggests links between Mn and TH. Our goal was to deepen the knowledge of modifiable environmental factors, specifically Mn, that may contribute to negative functioning of triiodothyroxine (TT3), the last hormone in TH pathways and part of the diagnosis of hyperthyroidism (>180 ng/dL of serum).

We included 1923 persons aged >12 from NHANES (2011-2012) after excluding 44 with liver problems (for whom Mn levels are impacted), where 43 (2.23%) had clinically high serum TT3 levels detected by competitive binding immunoenzymatic assay (TT3 sample mean 118.06±24.66 ng/dL). Whole blood Mn was determined using inductively coupled plasma mass spectrometry. Mn was log2 transformed because it yielded a better predictive ability (lowest AICC) with TT3 versus continuous, quadratic, dichotomous, and 5-category codings. We estimated OR (logistic regression) of high TT3 and also examined impact on continuous TT3 (linear regression), adjusting for age, smoking, gender, urinary iodine/creatinine, and serum zinc (Zn). We investigated whether Zn modified this relationship, given overlapping metabolic pathways between Mn and Zn, using a cross product term with Zn dichotomized at 80.8 μg/dL.

For every doubling of Mn, TT3 was on average 3.7 ng/dL higher (95% CI of 1.7, 5.7) and the risk of having high TT3 was elevated, but with CIs including the null value of no association (OR=1.58; 95% CI= 0.81-3.07) that was not modified by Zn (interaction p=0.20).

Our results add to a literature showing that Mn exposure may lead to elevated TT3, even in adolescence and adulthood and with concurrent Mn (where blood Mn half-life is 10-42 days). Longitudinal studies of earlier life stages are indicated given expected greater sensitivity of TH to Mn at earlier developmental periods.

The prevalence of selected adult chronic conditions in the Environmental Health Study for Western New York (EHS4WNY): A prospective cohort study Matthew Bonner* Matthew Bonner Denise Feda Tammy Milillo Lina Mu Laurene Tumiel Berhalter James Olson

The EHS4WNY is a prospective cohort study designed to investigate exposure to industrial pollution and adult chronic diseases in several highly industrialized communities in Western New York. Specifically, these communities were exposed to coke oven emissions as well as other common and ubiquitous industrial pollutants, including benzene and polycyclic aromatic hydrocarbons. Starting in 2018, we enrolled 13,306 adults aged 18 years and above who currently or formerly resided in these communities using mailed and online self-administered questionnaires. The questionnaire ascertained information about demographics, residential history, personal and family medical histories, work histories, and life-style factors, including diet, smoking and alcohol intake. We calculated prevalence proportions and 95% CIs for selected self-reported medical conditions at baseline to describe the burden of these diseases in these communities. Among the 13,306 cohort members, the mean age of the cohort is 52.5 (SD=17.7) years, the major of the members are female (n= 7,617;58.9%), and the majority self-reported as White (n = 11,908; 91.7%). Overall, nearly 62% of the cohort reported at least one medical condition. The most common conditions are hypertension (30.0 per 100; 95% CI =29.1-30.7), high cholesterol (26.6 per 100; 95% CI =25.8-27.4), and obesity (18.0 per 100; 95% CI = 17.3-18.7). In contrast, there is a relatively low prevalence of clinical events such as myocardial infarction (3.3 per 100; 95% CI =3.0-3.6) and lung cancer (0.8 per 100; 95% CI= 0.6-1.0). The leading self-reported medical conditions were cardiovascular disease risk factors and this is consistent with the leading causes of mortality and morbidity in Western New York. While this analysis does not explore whether industrial pollution is associated with these diseases, the results set the stage for further investigating such associations using incident disease data.

Portable Air Cleaner Use Is Associated With Lower Blood Pressure In Adults With Hypertension Sharine Wittkopp* Sharine Wittkopp Elle Anastasiou Jordan Ramsaywak Albert Tovar Emily Gill Terry Gordon Lorna E. Thorpe Jonathan D. Newman

Background: Exposure to fine particulate matter air pollution ($PM_{2.5}$) is associated with cardiovascular risk, including short-term increases in systolic blood pressure (SBP). Studies show that portable air cleaners (PACs) with high efficiency particulate air (HEPA) filters reduce $PM_{2.5}$ and lower SBP. However, the effects of PACs on SBP among adults with hypertension (HTN) remain unclear. We hypothesized that continuous bedroom PACs would reduce $PM_{2.5}$ exposure and morning (AM) home SBP .

Method: We performed a pilot randomized, double-blind, sham-controlled trial to test the effect of PAC use on AM SBP and $PM_{2.5}$ levels. We enrolled 20 non-smoking adults with self-reported HTN living in New York City public housing; untreated normotensive participants or those with an average SBP>160 mmHg were excluded. We collected self-reported demographic and clinical data, provided home BP monitors and low-cost $PM_{2.5}$ sensors, and randomized participants 1:1 to active vs. sham PAC (HEPA filter removed). After a 4-day post-randomization run-in, eligible participants were instructed to turn on PACs and measure AM SBP for 10 days. We calculated means (± standard deviations) and used independent t-tests to compare mean $PM_{2.5}$ and AM SBP for active vs. sham PACs over 10 days.

Results: We included 20 non-white adults, 70% female, with mean age 55 (±14) years, BMI 33.7 (±6.2) kg/m^2; 65% had HTN for >10 years, and 85% reported antihypertensive use. During the intervention, $PM_{2.5}$ was lower for active vs sham (8.2±1.4 vs 15.2±1.1 μg/m^3, p<0.001) but did not significantly differ during run-in (8.7±2.0 vs 9.2±1.7 μg/m^3, p=0.30). Intervention period SBP was significantly lower for active vs sham (128.8 ± 11.8 vs 135.2 ± 12.8 mmHg, p=0.002) but did not significantly differ during run-in (134.2 ± 13.6 vs 136.3 ± 10.2 mmHg, p=0.52), Figure 1.

Conclusion: In a cohort of 20 non-smoking adults with HTN, PAC use is associated with significantly lower $PM_{2.5}$ and AM SBP over a 10-day intervention period.

Figure 1. Average systolic blood pressure during study period
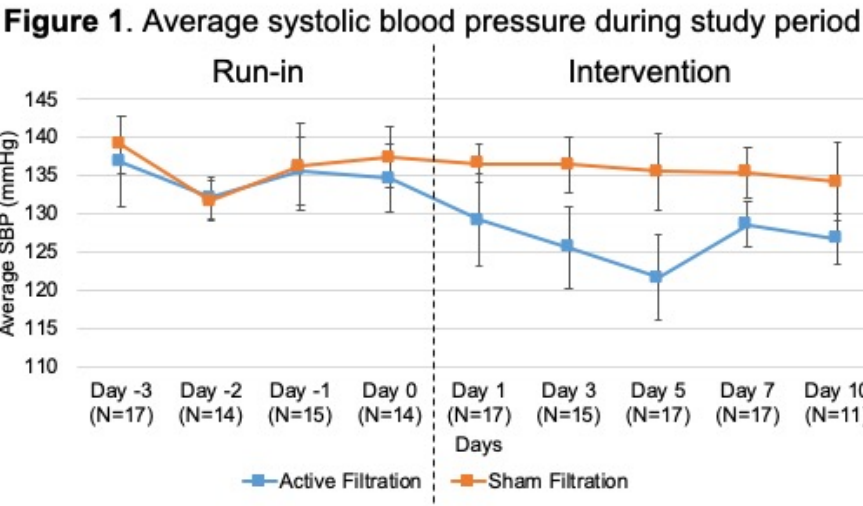
Pesticide exposure, general intellectual ability, and executive functions in school-age children from Montevideo, Uruguay Danelly Rodriguez* Danelly Rodriguez James Olson Gabriel Barg Elena Queirolo Nelly Mañay Katarzyna Kordas

Background: Pyrethroid and chlorpyrifos are commonly used pesticides. The developing brain (infancy to school-age) is especially susceptible to toxic effects of pesticides because the nervous system is specifically targeted. Few studies have examined the relationship between multiple pesticides, general intellectual ability, and executive functions (EF) in school-age children.

Methods: In this cross-sectional study 357 children aged ~7 years were enrolled between 2009 and 2013; 236 had complete data on relevant variables. Chlorpyrifos metabolite 3,5,6-trichloro-2-pyridinol (TCPy) and pyrethroids metabolite 3-phenoxybenzoic acid (3-PBA) were measured in first void urine samples, adjusted for urinary creatinine. General intellectual ability was assessed using the Woodcock-Muñoz battery. EF were evaluated with the Stockings of Cambridge, Intra-dimensional/extra-dimensional shift task, and Spatial Span tests from the Cambridge Neuropsychological Test Automated Battery. Urine samples and cognition were typically measured within a 2-week period. Generalized linear models assessed the association between log-transformed pesticide metabolites (separately and combined) and cognitive measures, adjusting for age, sex, maternal education, HOME Inventory score, school clusters, hemoglobin, and blood lead.

Results: In separate covariate-adjusted models, children with higher log-transformed TCPy and 3-PBA levels had somewhat shorter Spatial Span (β [95% CI]: TCPy -0.15 [-0.35, 0.05], and 3-PBA -0.04; [-0.20, 0.12]). These associations did not reach statistical significance. When modeled together, the metabolites were not associated with any of the endpoints.

Conclusions: We observed no significant associations between pesticide exposure and EF in school-age children, possibly due to modest sample size. EF underpin children's learning and behavior; therefore, additional studies are needed to determine the effect of pesticide exposure on these cognitive domains.

Acute ambulatory blood pressure response to short term black carbon exposure: the MobiliSense sensor-based study Sanjeev Bista* Sanjeev Bista Basile Chaix

Documented relationships between black carbon (BC) exposure and blood pressure (BP) have been inconsistent. Very few studies used residential outdoor BC exposure measurements considering time-activity data and ambulatory BP in the general population, and none adjusted for personal noise exposure, a major confounder. Our study addresses these gaps in a study of 245 participants living in the Grand Paris region. Personal exposure to BC was monitored for 2 days using microaethalometers. Ambulatory BP was measured every 30 minutes after wake time using Arteriograph 24 (n =6772). Mixed effect models with a random intercept at the individual level and time-autocorrelation structure adjusted for personal noise measurements were used to evaluate the associations between BC exposure (averaged from 5-minutes to 1-hour before each BP measurement) and BP. To increase the robustness of findings, we eliminated confounding by unmeasured time-invariant personal level variables, by modelling the associations with fixed-effect models as well. All models were adjusting for potential confounders and short term time trends. Results from mixed models show that a 1-µg/m^3 increase in 5-minutes averaged BC exposure was associated with an increase of 0.57 mm Hg in ambulatory systolic blood pressure (SBP) (95% CI: 0.30, 0.83) and with an increase of 0.36 mm Hg in diastolic blood pressure (DBP) (95% CI: 0.14, 0.58). The slope of the exposure-response relationship gradually decreased for both SBP and DBP with the increase in the averaging period of BC exposure from 5-minutes to 1 hour preceding each BP measurement. Findings from the fixed-effect models were consistent with these results. We found evidence of a relationship between BC exposure and acute increase in ambulatory SBP and DBP after adjustment for personal noise exposure, with potential implications for the development of adverse cardiovascular outcomes.
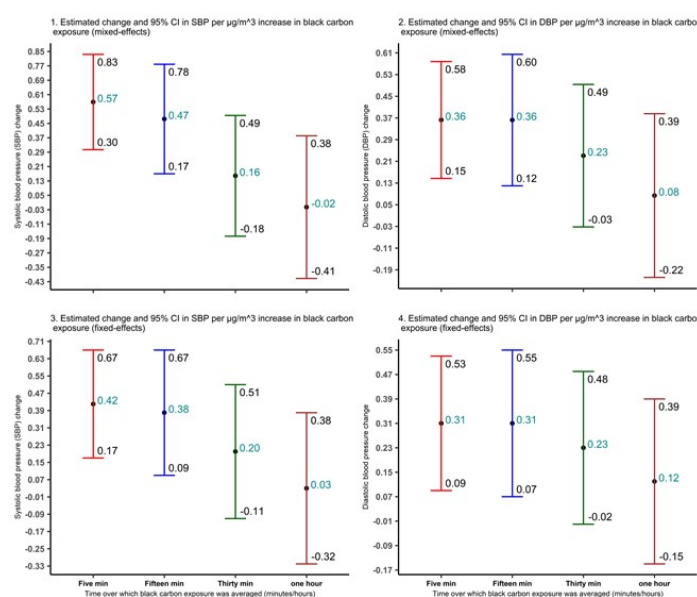
MobiliSense Study, 245 participants, 6772 ambulatory BP measurements
All Models were adjusted for noise, physical activity, temperature, relative-humidity, proportion of time spent in different contexts (home, motorized vehicle and non-motorized vehicles, other places), week Vs weekend, living standard of places where the BP measurements were taken and short-term time trend.
Mixed models were additionally adjusted for residence area, age, sex, household income per member, education, employment, monthly alcohol consumption, body mass index, and living standard of residence area.

Associations of per- and polyfluoroalkyl substance concentrations and fibroid changes across pregnancy: NICHD Fetal Growth Studies – Singletons cohort

Susanna Mitro* Susanna D. Mitro Rajeshwari Sundaram Germaine M. Buck Louis Shyamal Peddada Zhen Chen Kurunthachalam Kannan Jessica L. Gleason Cuilin Zhang Katherine L. Grantz

Background: Uterine fibroids are common, hormonally responsive benign tumors that often undergo volume changes in pregnancy for unknown reasons. Because per- and polyfluoroalkyl substances (PFAS) may disrupt hormonal signaling, they might affect fibroid growth. We assessed associations between PFAS concentrations and fibroid changes in pregnancy.

Methods: We analyzed 7 PFAS, including perfluorohexanesulfonic acid (PFHxS), perfluorooctanesulfonic acid (PFOS), perfluorodecanoic acid (PFDA), and perfluoroundecanoic acid (PFUnDA), quantified in blood collected at 10-13 weeks gestation from 2221 women. Sonographers recorded fibroid number and volume of the 3 largest fibroids during 1-6 ultrasounds at gestational weeks 10-41. We used generalized linear mixed models with random intercepts and assessed associations of $\log_2$-transformed PFAS and changes in fibroid number and total volume, adjusted for race/ethnicity, body mass index, age, and education. Volume analyses were stratified by total volume at first visualization (equivalent to a <1cm (small), 1-<3cm (medium), or ≥3cm (large) diameter fibroid).

Results: Fibroid prevalence was 9.2% (n=204 women). PFAS were not associated with fibroid number changes, but were associated with volume changes, dependent on starting total volume. Among women with small fibroid volume, PFAS were associated with fibroid growth: doublings in PFHxS and PFOS were associated with 3.6% (95%CI: 0.2, 7.0) and 5.2% (95%CI: -0.4, 11.1) greater fibroid growth, respectively. Among women with medium fibroid volume, PFAS were associated with fibroid shrinking: doublings in PFOS, PFDA, and PFUnDA were associated with 1.9% (95%CI: 0.4, 3.3), 1.2% (95%CI: 0.1, 2.4), and 1.4% (95%CI: 0.4, 2.8) greater volume decreases, respectively. PFAS were not significantly associated with volume change among women with large fibroid volume (Figure).

Conclusion: Certain PFAS were associated with fibroid volume changes during pregnancy, varying by initial fibroid volume.
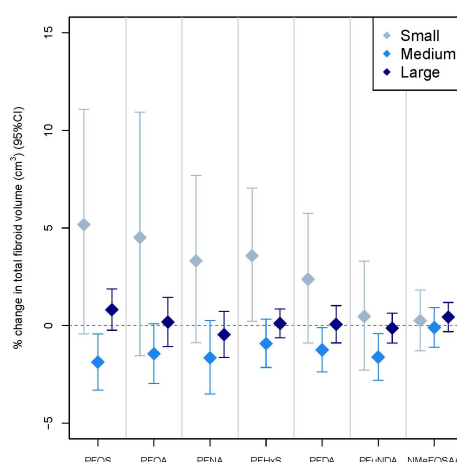
A Nested Case-Control Study of Prenatal Organophosphate Esters and Preschool ADHD in the Norwegian Mother, Father, and Child Cohort Study (MoBa) Amber M Hall* Amber Hall Amanda Ramos Samantha SM Drover Giehae Choi Alexander P. Keil David B. Richardson Chantel L. Martin Andy Olshan Gro Villanger Ted Reichborn-Kjennerud Pal Zeiner Kristin Overgaard Amrit Sakhi Cathrine Thomsen Heidi Aase Stephanie M. Engel

Background: Organophosphate esters (OPEs) are ubiquitous chemicals that have been linked to attention-deficit/hyperactive-disorder (ADHD) in childhood and ADHD-like symptoms in preschoolers. OPE exposure is increasingly prevalent as a replacement for other regulated chemicals. We assessed the impacts of prenatal OPE exposures on clinically-assessed ADHD in preschoolers.

Methods: In this nested case-control study within the Norwegian Mother, Father and Child Cohort, 260 preschool ADHD cases were identified using the Preschool Age Psychiatric Assessment and compared to a birth-year-stratified random sample of 549 children. We measured diphenyl phosphate (DPhP), di-n-butyl phosphate (DnBP), bis(2-butoxyethyl) phosphate (BBOEP), and bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) in maternal urine collected at 17 weeks' gestation. Due to low detection, BBOEP and BDCIPP were categorized. DPhP and DnBP values <level of detection (LOD) and missing covariate data were imputed. DPhP and DnBP were analyzed as quartiles and a log10 linear term. We estimated multivariable adjusted odds ratios (ORs) using logistic regression, and examined effect measure modification (EMM) by child sex using an augmented product term approach.

Results: Mothers in the 3rd DnBP quartile had 1.71 times the odds of having a child with preschool ADHD compared to the 1st quartile (95%CI: 1.13, 2.58). A similar trend was observed for log10 DnBP and preschool ADHD [OR: 1.30; 95%CI: 0.86, 1.97)]. Mothers with BDCIPP ≥LOD but <level of quantification had 1.39 times the odds of having a child with preschool ADHD compared to those with BDCIPP <LOD (95%CI: 0.83, 2.31). Girls had lower odds of preschool ADHD with increasing BBOEP exposure, however boys did not. [Girls: log10 OR: 0.55 (95%CI: 0.37, 0.93); Boys: log10 OR: 1.25 (95%CI: 0.74, 2.11); p=0.01]. No other notable trends were observed.

Conclusions: We found a modest and imprecise, increased odds of preschool ADHD with higher exposure to DnBP and BDCIPP.
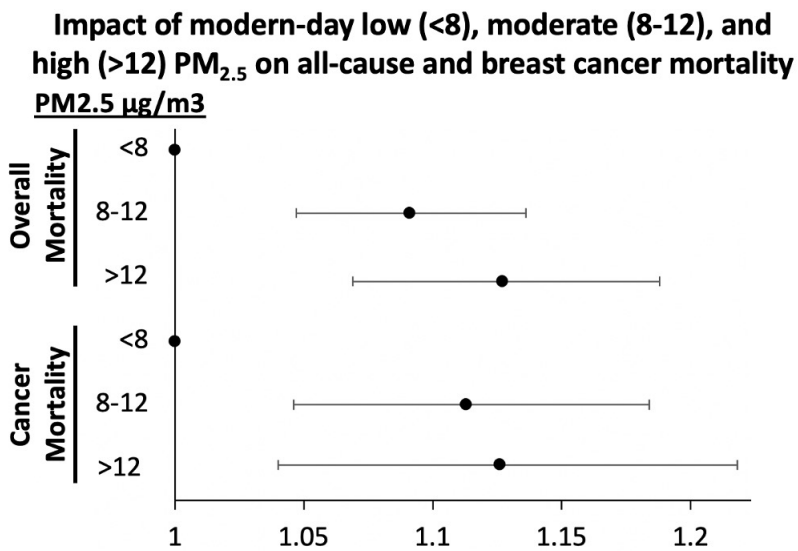
Environment/Climate Change

The effectiveness of a text messaging intervention trial to conserve healthy fish consumption and reduce mercury contaminants in reproductive age Chicago Asian women

Mariam Oladosu* Mariam Oladosu Susan Buchanan Jing Zhang Noel Chavez Sally Freels Kyeezu Kim Mary Turyk

Hg exposure during pregnancy can impact cognition, memory, attention, language, fine motor skills, and visual spatial skills in offspring. There is a high prevalence of elevated mercury (Hg) levels among Asian communities, attributable to frequent fish consumption. A controlled, cluster-randomized, 6-month intervention trial was conducted to decrease consumption of fish with moderate to high mercury levels and/or very frequent fish consumption and to reduce hair Hg levels. Reproductive age Asian women were recruited with the help of community organizations serving the Chinese, Vietnamese, and Korean communities in Chicago. The control group (n = 131) received general nutrition text messages, while the intervention group (n = 154) received text messages on risks and benefits of fish consumption, with advice tailored to the Chicago Asian communities based on a prior community assessment. Outcomes were hair Hg measurements and rates of fish consumption. Non-parametric tests compared treatment groups at baseline and six months and the effect of the intervention on outcomes was tested using longitudinal linear models with random effects for cluster. Geometric mean hair mercury decreased 16% in the intervention group and increased 2% in the control group (p=0.04). In Chinese women, hair Hg decreased 9% in both treatment groups, while in Korean women hair Hg decreased 27% in the intervention and increased 10% in the control group (p=0.04). The rate of ingestion of moderate and high mercury fish (g/day) decreased 50% in the intervention and 35% in the control group (p = 0.15). Our findings suggest that in reproductive age Asian American women, a text messaging intervention providing information on healthy fish consumption and health risks of contaminated fish consumption decreased hair mercury levels, but efficacy differed by Asian ethnicity.

Association between air pollution and mortality among older women with breast cancer in the US Benjamin Bates* Benjamin Bates Rachel Nethery Elisa Bandera Soko Setoguchi

Background: Historically high levels of particulate matter ($PM_{2.5}$) (mean >12mg/m^3) have been associated with breast cancer (BC) mortality. We evaluated risk of all-cause and BC-specific mortality among a geographically diverse cohort of older women with BC exposed to modern-day lower $PM_{2.5}$ levels. **Methods:** Using SEER-Medicare data linked with a high-resolution predictive $PM_{2.5}$ model by residence zip code (2007-2016), we designed a cohort of women ≥ 66 years with incident stage I-IV BC and assessed $PM_{2.5}$ exposure, categorized as <8 (low), 8-12 (moderate) and >12 (high), during the year prior to the BC diagnosis. We assessed BC and all-cause mortality within 5 years of BC diagnosis (ending at Dec 31, 2017 and 2018, respectively). We fit multivariable Cox proportional hazard models to assess effects of $PM_{2.5}$ exposure, adjusting for individual-level characteristics (demographics, tumor characteristics, comorbidities), neighborhood features, and state. **Results:** Among 85,844 women (mean age 75 years, 82% white, 52% stage I, 32% stage II, 8.9% stage III, 7.1% stage IV), the mean $PM_{2.5}$ exposure was 9.2mg/m^3, with 36%, 50%, and 14% exposed to low, moderate, and high $PM_{2.5}$, respectively. Mean $PM_{2.5}$ exposure for Black (10.2mg/m^3), Asian (9.9mg/m^3), and Hispanic (9.7mg/m^3) women were greater than the cohort mean. We observed 19,760 all-cause and 9,257 BC deaths during follow-up of 335,870 and 308,691 person-years (py), respectively. Incidence rates (per 1,000 py) were 51, 61, and 66 for all-cause and 25, 31, and 33 for BC mortality in low, moderate, and high $PM_{2.5}$, respectively. For BC mortality, the HRs for moderate and high $PM_{2.5}$ were 1.11 (1.05-1.18) and 1.13 (1.04-1.22), respectively. Similar HRs were present for all-cause mortality (Figure). **Conclusion:** Modern-day $PM_{2.5}$ levels were associated with all-cause and BC mortality among older women with BC, even at levels below US national standards. Further research should consider specific mechanisms for the increased mortality.

Impact of modern-day low (<8), moderate (8-12), and high (>12) PM$_{2.5}$ on all-cause and breast cancer mortality

LATEBREAKER

Environment/Climate Change

Gene-Gene and Gene-Environment Interactions in relation to Blood Aluminum Concentrations of Jamaican Children Mohammad H. Rahbar* Mohammad H. Rahbar Maureen Samms-Vaughan Yuansong Zhao Sepideh Saroukhani Jan Bressler Manouchehr Hessabi Megan L. Grove Sydonnie Shakspeare-Pellington Katherine A. Loveland

Aluminum (Al) is a metallic toxicant at high concentrations after natural or unnatural exposure. Dietary intake is considered as the main source of aluminum exposure in children. We used data from 366 typically developing (TD) children (ages 2–8 years) who participated as TD controls in an age- and sex-matched case-control study in Jamaica. We investigated additive and interactive associations among environmental factors and children's genotypes of glutathione S-transferase (GST) genes (*GSTT1*, *GSTM1*, *GSTP1)*, in relation to having a detectable level of blood aluminum concentration (BAlC) of >5 µg/L. Findings from our interactive multivariable logistic regression models revealed that consumption of string beans was associated with about 3.5 times higher odds of having a detectable BAlC, while consumption of green banana and parental education level was associated with 50% lower odds of having a detectable BAlC in TD children (all *P* 0.02). In addition, we found that among children with the Ile/Ile genotype of *GSTP1* Ile105Val, children who consumed sea water fish had higher odds of having a detectable BAlC compared to children who did not eat such food using either dominant or co-dominant models [OR (95% CI) = 2.90 (1.11, 7.60), *P* = 0.03; and OR (95% CI) = 2.94 (1.13, 7.70), *P* = 0.03, respectively]. Furthermore, we observed a significant interaction between *GSTT1* and *GSTM1*. Specifically, among children with DD genotype in *GSTM1*, the odds of having a detectable BAlC was lower in children with DD genotype in *GSTT1* than those with I/I or I/D genotype [OR (95% CI) = 0.25 (0.09, 0.72), *P* = 0.01]; among children with DD genotype in *GSTT1*, the odds of having a detectable BAlC was lower in children with DD genotype in *GSTM1* than those with I/I or I/D genotype [OR (95% CI) = 0.22 (0.08, 0.64), *P* = 0.005]. Since this is the first study from Jamaica that reports such findings, replication in other populations is warranted.

Genetics

Negative control outcome adjustment to reduce unmeasured confounding in epigenome-wide studies: An application to assisted reproductive technologies and placental epigenomics Jonathan Huang* Jonathan Huang

Background: Prevailing epigenomic epidemiologic methods poorly handle confounding, often including only a few common covariates across genome-wide regressions. This leaves open broad possibilities of unmeasured and differential confounding between regions. Reproductive studies are threatened by unmeasured, underlying parental health status. Specific mechanistic hypotheses, e.g. if effects of *in vitro* fertilization (IVF) on offspring are mediated by DNA methylation (DNAm) of certain tissues, may facilitate the use of negative control approaches.

Methods: We assayed fetal- and maternal- facing placental DNA methylation (Illumina EPIC) for 200 offspring (70 IVF, 130 spontaneous conception) within a longitudinal parent-offspring cohort. Despite common ontology, DNAm of fetal-facing tissues may directly reflect IVF-related fetal programming, while DNAm of maternal-facing tissues may capture a broader maternal milieu, proxying unmeasured maternal confounders. In epigenome-wide analyses, we regress fetal-facing CpG beta-values on IVF status, cell composition, and plate position. We compare this to analyses additionally adjusted for corresponding maternal-facing CpG beta values as control outcomes. We have previously demonstrated in simulations that direct adjustment outperforms other approaches when identification conditions are not satisfied.

Results: Consistent with past work, we show shrinkage of effect sizes and t-statistics, particularly top hits, upon adjusting for putative negative controls (e.g. N with $P < 0.01$ among first 10k sites decreased from 125 to 74). Adjustments reduced FDR-corrected differentially methylated regions by ~50%. Q-Q plots of control-adjusted models were also less skewed.

Discussion: Despite the strong potential for unmeasured and differential confounding in omic-wide studies, there have been few scalable solutions. If appropriate tissues can be identified, negative control approaches may be a potentially useful tool for observational research.
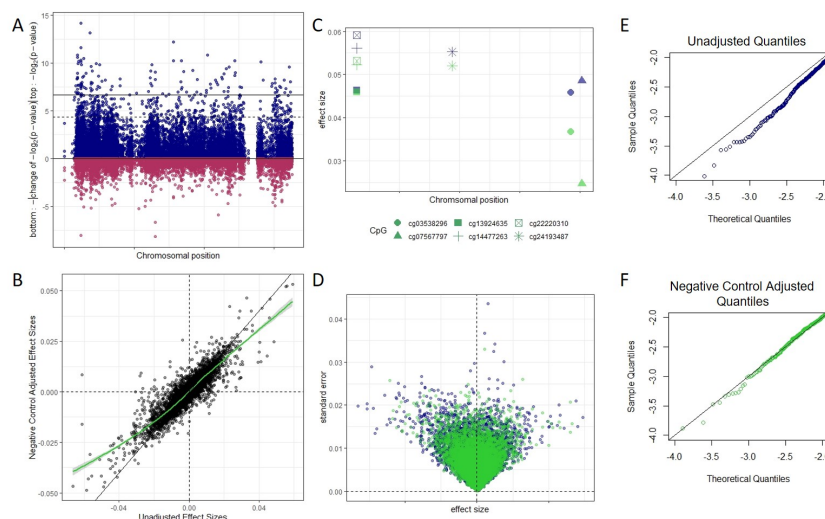
Figure 1. Changes in effect sizes and test statistics upon adjustment for negative control DNA methylation sites. (A) S-values (*navy*) and absolute change in S-values (*maroon*) after adjustment generally greater for larger S-values; (B) shrinkage of effect sizes (*green*) after adjustment; (C) effect size shrinkage of a few top hits before (*navy*) and after (*green*) adjustment; (D) volcano plot showing more precise estimates after (*green*) adjustment; (E) test statistic quantiles prior to adjustment (*navy; enlarged section*); (F) test statistic quantiles after adjustment for complementary DNAm (*green; enlarged section*)

Helicobacter pylori infection and lung cancer: a population-based longitudinal descriptive study Shun Yi, Wang* Shun Yi Wang Chien An Sun Yu Ching, Chou

Shun-Yi Wang[1], Chien-An Sun[2], Yu-Ching Chou[1*]

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Background: Lung cancer is the third leading cancer in Taiwan. *Helicobacter pylori* infection has been recognized as potential risk factor in developing disease. However, secular trend studies of Lung cancer with *Helicobacter pylori* infection are limited. This descriptive study examined the incidence of Lung cancer with *Helicobacter pylori* infection in a large-scale, population-based Taiwanese cohort.

Methods: From 2000 to 2008, 3,936 new cases with *Helicobacter pylori* infection were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating incidence rates in different sex, age groups and periods. For long term trends, we followed up until December 31, 2013.

Results: The incidence of lung cancer was 15.56 among *Helicobacter pylori* infection patients per 10,000 person-years. The incidence rate among men and women with *Helicobacter pylori* infection was respectively 17.57, 13.03 per 10,000 person-years. The incidence rate of lung cancer was higher in men. After stratifying age into 5 groups, we found that the incidence rate of lung cancer per 10,000 person-years was 7.31 in 40-49 years old, 21.8 in 50-59 years old and 33.57 in ≥60 years old (there's no lung cancer cases among 20-29 years old and 30-39 years old patients). Patients have higher incidence rate of lung cancer when age is increasing. Also, incidence of lung cancer was 10.44, 12.88, and 16.69 by visiting 0 time, ⬚2 times, >2 times in *Helicobacter pylori* infection clinical visits respectively.

Conclusion: In the past 14 years, the incidence of lung cancer had a profound impact on our life. By means of the big data, our finding suggested incidence rate of lung cancer with *Helicobacter pylori* infection is steadily rising. Thus, the study indicated a positive correlation between *Helicobacter pylori* infection and lung cancer. Future investigations are necessary to validate the kinds of conclusions that can be drawn from this study.

Keywords: Lung cancer , National Health Insurance Research Database (NHIRD), *Helicobacter pylori* infection.

Assessing cause of death specific perioperative mortality ratios in high-, middle-, and low-income countries: a systematic review and multilevel meta-regression protocol Kevin McIntyre* Kevin McIntyre Dr. Janet Martin Dr Saverio Stranges Dr Daniel Lizotte Dr Ava John-Baptiste Dr Yun-Hee Choi Jessica Moodie

There has been very little work done to systematically investigate the causes of perioperative mortality in a global context. This project proposes a systematic review and meta-analysis of surgical literature to identify trends of perioperative mortality and key causes of death among three indicator surgeries: Caesarean section, laparotomy, and the treatment of open fractures.

Five databases will be searched using a search strategy developed alongside a medical librarian. The resulting articles will be uploaded into the DistillerSR review management software to be screened by title and abstract against pre-specified criteria by a single author. Included articles will then undergo full text screening against pre-specified criteria performed by two authors independently and included based upon consensus where they will undergo data extraction in duplicate from a pre-specified data extraction form.

The data extracted will include items such as the number of patients undergoing surgery, number experiencing perioperative mortality, causes of death, which country the study was conducted in, what year the procedure was done, the corresponding human development index value, average age of the patients, proportion of emergency cases, proportion of females, average American Society of Anesthesiologists Score, proportion of COVID-19 positive patients, and recorded follow-up time.

These variables will be used to fit a three-level multilevel meta-regression model with patients nested within studies nested within countries. Such a model accounts for the impact of clustering that is inherent with this complex data structure while also adjusting for covariates. This method will be used to assess perioperative mortality overall as well as for each cause of death. Thus, this project aims to identify key causes of perioperative mortality globally which will provide evidence to guide future research into interventions to reduce perioperative mortality.

Prevalence and Mortality among Children with Anorectal Atresia: A Multi-Country Analysis

Vijaya Kancherla* Vijaya Kancherla Manasvi Sundar Lucita Tandaki Anke Lux Marian K Bakker Jorieke EH Bergman Eva Bermejo-Sanchez Mark Canfield Saeed Dastgiri Marcia L Feldkamp Miriam Gatt Boris Groisman Paula Hurtado-Villa Kärin Kallén Danielle Landau Nathalie Lelong Jorge Lopez-Camelo Laura Elia Martinez Pierpaoloa Mastroiacovo Margery Morgan Osvaldo M Mutchinick Amy E Nance Wendy N Nembhard Anna Pierini Antonin Šípek Erin Stallings Elena Szabova Giovanna Tagliabue Wladimir Wertelecki Ignacio Zarante Anke Rissman

Anorectal atresia is a common birth defect of the gastrointestinal tract characterized by complete or partial absence of the anorectal canal at birth. Affected individuals require repeated surgeries and multidisciplinary care, which are associated with high healthcare costs. Mortality among cases is not well examined in large birth defects registry studies; previous knowledge on mortality and survival is mostly drawn from hospital-based case cohorts with relatively small samples. We conducted a retrospective cohort study using data from 24 population- and hospital-based birth defects surveillance programs affiliated with the International Clearinghouse for Birth Defects Surveillance and Research (ICBDSR) from 18 countries and for births from 1974-2014. We estimated pooled and program-specific total prevalence per 10,000 total births. Poisson regression was used to assess time trends in prevalence from 2001-2012 when most programs contributed data. We calculated selected age-specific proportions of deaths, stratified by case status. Results showed that the pooled total prevalence of anorectal atresia was 3.26 per 10,000 total births (95% Confidence Interval = 3.19, 3.32) for birth years 1974-2014. About 60% of cases were multiple or syndromic. Prevalence of multiple, syndromic, and stillborn cases decreased from 2001-2012. The first week mortality proportion was 12.5%, 3.2%, 28.3%, and 18.2% among all, isolated, multiple, and syndromic cases, respectively. In conclusion, our descriptive epidemiological findings contribute to our understanding of geographic variation in the prevalence of anorectal atresia and can be used to plan needed clinical services. Future studies should explore factors influencing prevalence and mortality among individuals with anorectal atresia.

Health Disparities

Factors influencing national race/ethnicity disparity of Neonatal Abstinence Syndrome (NAS) Marina Feffer* Marina Feffer Keith A Dookeran Kyla M Quigley Phoebe E Troller Chariya A Christmon Janine Y Khan

Few studies have examined factors influencing the rates of NAS observed among newborns in the U.S.

Cross-sectional U.S. data from the Agency for Healthcare Research and Quality, Healthcare Cost and Utilization Project Kids' Inpatient Database for 2016 and 2019 cycles were used to estimate NAS prevalence, excluding iatrogenic cases, among newborns ≥ 35 weeks gestational age. Multivariable generalized linear regression models with predictive margins were used to estimate White-Black and White-Hispanic NAS disparities, reported as risk differences (RD) with 95% confidence intervals (CI). Models were adjusted for sex, payer (Medicaid/Private), income (ecologic quartiles), and hospital size (large/medium/small), hospital type (urban non-teaching/urban teaching) and region (Northeast/Midwest/South/West).

The weighted sample prevalence of NAS was 1.14% (n=7721/677721) and did not differ over cycles. In fully specified models, NAS among Whites was 2.6% (CI: 2.69, 2.76) higher than Blacks and 2.7% (CI: 2.60, 2.72) higher than Hispanics. Effect modification was evident by payer, hospital region, and income. NAS risk was 5.0% higher among Whites on Medicaid (CI: 4.89, 5.10) compared to Whites on Private insurance (RD: 0.6%; CI: 0.51, 0.67), Blacks with either payer (RD: 1%; CI: 0.85, 1.16; RD: 0.24%; CI: 0.02, 0.46), or Hispanics with either payer (RD: 0.86%; CI: 0.71, 0.99; RD: 0.17%; CI: -0.02, 0.37). NAS risk was 3.2% higher among Whites in the Northeast region compared to both Blacks and Hispanics (CI: 3.02, 3.31). NAS risk was 3.1% higher among Whites in the lowest income quartile (CI: 2.94, 3.22) than Blacks (RD: 0.67%; CI: 0.48,0.86) and Hispanics (RD: 0.63%; CI: 0.44, 0.82) in the same quartile, and all subgroups in other quartiles.

Compared to Blacks and Hispanics, Whites on Medicaid, in the lowest income quartile, and in the Northeast U.S. were found to have the highest rates of NAS. Further research is needed to explain this low socioeconomic status (SES) disparity.

Trends in Racial and Ethnic Differences in Perceived Unmet Need for Adult Mental Health Treatment: Results from the 2005-2020 National Survey on Drug Use and Health Navdep Kaur* Navdep Kaur Precious I. Esie Katherine M. Keyes

Introduction

In the past two decades, rates of mental health treatment increased in the US, yet gaps between racial/ethnic groups persisted; it is unclear whether these gaps persist due to lower perceived need. We assessed trends in perceived unmet need for mental health treatment by racial/ethnic group from 2005-2020 among people with past-year major depressive episode (MDE), serious psychological distress (SPD), or severe mental illness (SMI).

Methods

The 2005-2020 National Survey on Drug Use and Health included participants with past-year MDE (n=49,441) and SPD (n=88,366), and with past-year SMI in 2008-2020 (n=25,038). We modeled past-year perceived unmet need using linear risk regressions and included an interaction term between the study year and race/ethnicity (Black/African American, Hispanic, or Asian/Pacific Islander/Native Hawaiian group [Asian/PI/NH] vs. white group). We derived predicted probabilities from these models.

Results

From 2005-2020, perceived unmet need increased from 5.4% to 7.9%. Among people with MDE, increases in unmet need were faster for Hispanic compared to white people (interaction RR=1.02, 95%CI: [1.01, 1.04]), and predicted probabilities were similar across groups. Among adults with SPD, unmet need increased faster for Hispanic (interaction RR=1.03, 95%CI: [1.01, 1.04]) and Asian/PI/NH (interaction RR=1.05, 95%CI: [1.02, 1.08]) compared to white people, and predicted probabilities across groups converged in recent years. Among adults with SMI, unmet need increased at a faster rate for Hispanic compared to white people (interaction RR=1.04, 95%CI: [1.01, 1.06]), and predicted probabilities across groups converged in recent years.

Discussion

Perceived unmet need is either similar or higher among marginalized groups compared to white people, with Hispanic people emerging as a particularly underserved group. Moreover, disparities in mental health treatment persist, suggesting that additional barriers to treatment remain.

Predicted probabilities of unmet need for mental health treatment in the past year by race/ethnicity
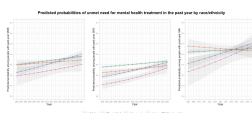
Public Health Funding and Influenza Vaccine Coverage in Ontario, Canada Jo Lin Chew* Jo Lin Chew Brendan Smith Roman Pabayo

Background

Public health funding has a positive impact on population health outcomes. Currently, few studies have focused on the potential role of public health funding in reducing health inequities in flu (influenza) vaccine uptake. The study objectives were to: 1) estimate the association between public health funding and flu vaccine uptake among individuals aged 12 and older across 34 public health units (PHUs) in Ontario, Canada; and 2) determine whether any observed associations were heterogeneous across income groups.

Methods

We conducted a cross-sectional study using data from the 2013 Canadian Community Health Survey, a population-representative survey that collects health information at the PHU level (n=38,739). Public health funding (per capita) was measured using the approved funding for mandatory programs in 2013 for all PHUs and the 2011 Canadian Census Population Estimates. Income was defined as total household income in 2013. We used multilevel modelling to estimate the association between public health funding and self-reported flu vaccine uptake, adjusting for sex, age, marital status, immigration, education, and economic deprivation. A cross-level public health funding by household income multiplicative interaction term was tested.

Results

Public health funding was not associated with being unvaccinated in the population average model (OR: 1.00; 95% CI: 0.94, 1.07). However, a cross-level interaction between public health funding and income revealed that public health funding is protective among those from the lowest income group. For every standard deviation increase in public health funding, there is a decreased likelihood of being unvaccinated among individuals who earn less than 20,000 CAD (OR: 0.88; 95% CI: 0.75, 1.02) but not among other income levels in the fully adjusted model.

Conclusions

Public health funding was found to benefit individuals from low-income households, demonstrating potential to decrease health inequities in flu vaccine uptake.
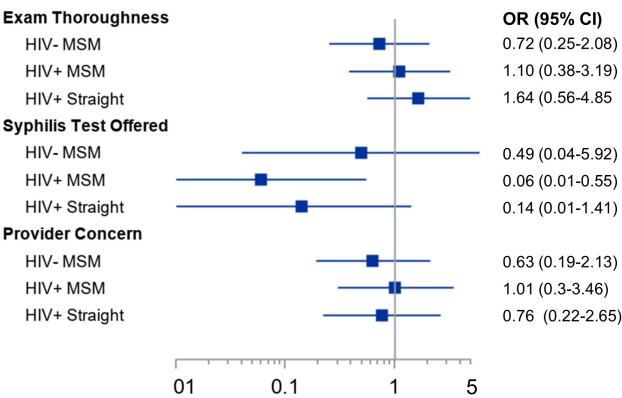
Can't Fix What You Can't See: Measuring Healthcare Discrimination with an Experimental Audit Approach M Kumi Smith* M Kumi Smith Danyang Luo Siyan Meng Krystal Zhang Yunqing Fei Ligang Yang Bin Yang Joseph D Tucker Chongyi Wei Benny L Joyner Sean Y Sylvia

Introduction: Discrimination experienced by patients in healthcare settings harms health by subjecting them to suboptimal care, harmful delays, and by discouraging future care seeking. Though widely reported, objective measures remain elusive due to social desirability bias and the complexities of individual encounters. We conducted an experimental audit in Chinese clinical settings to measure the impact of homophobia, HIV stigma, and their intersection on quality of sexual healthcare.

Methods: Trained standardized patients (SP) presented with classic complaints of post-primary syphilis at sexual health clinics, in which their HIV status and sexual orientation (men who have sex with men [MSM] vs. not) was randomly varied across visits. Providers consented to visits in advance but were not told when they would happen to minimize the Hawthorne effect. SPs reported on provider performance after each visit using a standardized checklist. Associations between presented scenarios and 3 key performance indicators were estimated using generalized linear mixed models.
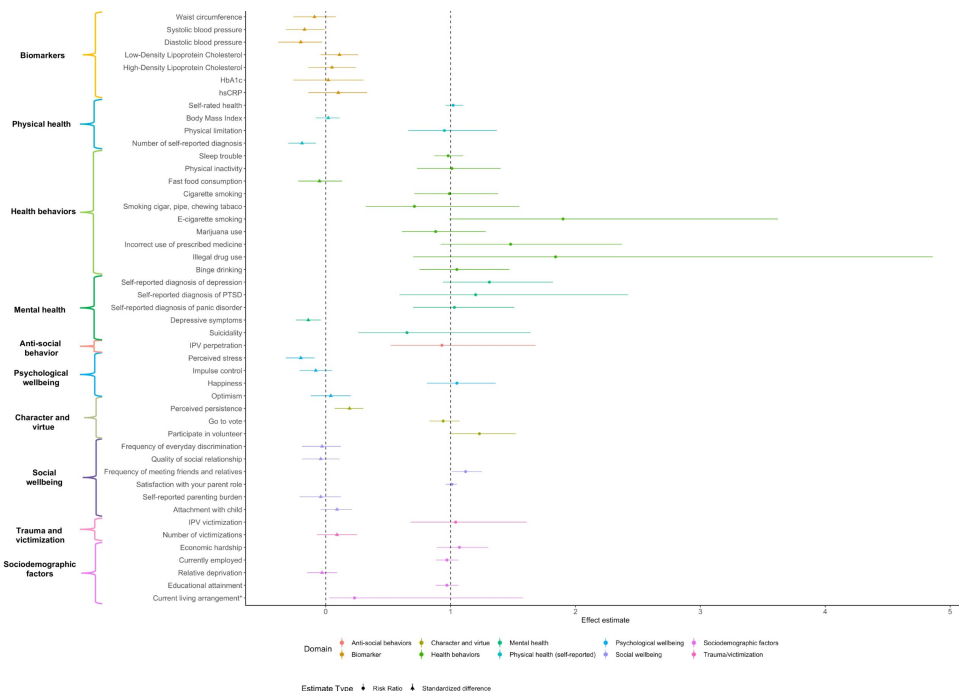
Results: 123 visits were conducted with 41 providers in 17 clinics. Compared to the referent scenario of an HIV negative straight man, every other scenario received less thorough patient exams, were less likely to be offered a syphilis test, or to receive care in which providers showed less concern. All estimates except for lower odds of being offered syphilis test for HIV positive MSM (OR, 0.06; 95% CI, 0.01-0.55) lacked precision.

Discussion: We documented preliminary evidence of poorer care quality across nearly all presented case scenarios, suggesting that discrimination against HIV status, same sex behaviors, and their intersection may erode healthcare quality in this setting. Findings will help inform design of a provider interventions to be evaluated as part of a randomized trial. Our approach can also guide investigations of discrimination of other commonly stigmatized attributes (e.g. race, gender).

	OR (95% CI)
Exam Thoroughness	
HIV- MSM	0.72 (0.25-2.08)
HIV+ MSM	1.10 (0.38-3.19)
HIV+ Straight	1.64 (0.56-4.85
Syphilis Test Offered	
HIV- MSM	0.49 (0.04-5.92)
HIV+ MSM	0.06 (0.01-0.55)
HIV+ Straight	0.14 (0.01-1.41)
Provider Concern	
HIV- MSM	0.63 (0.19-2.13)
HIV+ MSM	1.01 (0.3-3.46)
HIV+ Straight	0.76 (0.22-2.65)

Residential instability during childhood and adulthood health and wellbeing: Outcome-wide study
Sakurako Okuzono* Sakurako Okuzono Renae Wilkinson Natalie Slopen

Prior research suggests that residential instability during childhood and adolescence can have long-term impacts on health and wellbeing. However, previous studies have focused on a limited set of outcomes and paid less attention to identifying a robust comparison group to support strong causal inference. To address these knowledge gaps, using the National Longitudinal Study of Adolescent to Adult Health, we examined the associations between residential instability during adolescence and 49 indicators of adult health and wellbeing using an outcome-wide design. We defined residential instability as 2 or more moves between Waves I and II (i.e., ages 13-18 years). Based on the theories on multidimensional wellbeing, we assessed outcomes at ages 33-43 years (i.e., Wave V) in eight domains: physical health, health behaviors, psychological distress, anti-social behaviors, psychological wellbeing, social wellbeing, trauma/victimization, and sociodemographic factors. To address potential confounding and reverse causation, we used Wave I to obtain information on covariates, including pre-exposure values of the outcome variables. We used doubly-robust targeted maximum likelihood estimation to estimate the population average treatment effects (ATEs) and minimize bias due to model misspecification. To estimate the average treatment effect among the treated (ATTs), we used propensity score matching (PSM) analysis. When estimating ATEs, residential instability was associated with certain outcomes (e.g., fewer self-reported physician-diagnosed conditions). However, all associations disappeared when we estimated ATTs via PSM, suggesting that convention models are underspecified and produce misleading results due to unobserved confounding. Our results suggest that residential instability in adolescence does not lead to worse health and wellbeing in adulthood, but rather, outcome differences between groups are due to pre-existing differences prior to residential instability.

Figure 1. Association Between Residential Instability and Health and Wellbeing.
Average Treatment Effect (ATE) of the residential instability was estimated via the doubly-robust targeted maximum likelihood estimation (TMLE). We adjusted for pre-exposure variables (i.e., parental report of child's health condition, self-rated health, body mass index, sleep trouble, physical inactivity, cigarette smoking, binge drinking, marijuana use, illegal drug use, suicidality, depressive symptoms, optimism, happiness, impulsive control) and covariates (i.e., child age, child sex, child race/ethnicity, child nativity, household structure, geographical region, health insurance status, household income, household welfare receipt, smoker in household, parent's age, parent's race/ethnicity, parental nativity, parental high school graduation, parental romantic relationship, parental employment status, pubertal development, parental self-rated health, parental functional limitation, parental obesity, parental alcoholism, delinquency, personal control, educational future orientation, life satisfaction, academic achievement, parental happiness, parental participation in social groups, religious participation, school connectedness, parental assessment of parent-child relationship, quality of relationships, neighborhood connectedness, neighborhood satisfaction, neighborhood social capital, quality of neighborhood environment), and estimated Risk Ratio for binary outcomes and standardized difference for continuous outcomes.
* Current living arrangement was assessed by asking, "where do you live now?" Participants select their response from the following options (Your own place, your parent's home, another person's home, group quarters, homeless, other). Living in your own place and parent's home was treated as having a stable living arrangement.

Telemedicine Utilization among Patients with Multiple Sclerosis in the US Veterans Health Administration: 2010-2020 Hoda S. Abdel Magid* Hoda Abdel Magid Shan Jin William J. Culpepper Lorene M. Nelson Mitchell T. Wallin

Importance: Telemedicine may help to bridge the specialty care access gap for patients with MS (PwMS) restricted by distance or disability.

Objectives: To assess the frequency and longitudinal patterns of telemedicine utilization among PwMS and controls.

Design: Population-based nested case-control study

Setting: Veterans Health Administration (VHA), January 1, 2010 – December 31, 2020.

Participants: MS case and control participants by year: 2010: 19,387/86,379; 2016: 19,752/88,535; and 2020: 16,451/78,315. MS cases and controls were individually matched on sex, age, and VA service region (VISN).

Exposure: Telemedicine encounter codes were used to identify telemedicine utilization among MS cases and controls in the VHA for 2010, 2016, and 2020. Telemedicine encounters were categorized according to mode (video, phone, supplementary remote) and type of care provided.

Covariates: Age, sex, race, ethnicity, urban/rural status, and zip code were retrieved from VHA.

Results: Patients in the VHA have had increasing utilization of telemedicine over the past decade. Among PwMS, mean telemedicine encounters increased steadily from 2010 to 2020 (5.6 to 10.5 encounters/patient, respectively). Across all years, MS cases were significantly more likely than controls to utilize telemedicine. The odds ratios (95% confidence Interval (CI)) of any telemedicine utilization comparing MS cases to controls in 2010, 2016, and 2020, respectively were: 1.5 (CI: 1.3-1.5), 1.9 (CI: 1.8,-2.0), and 1.7 (CI: 1.6-1.8). Compared to non-Hispanic White Veterans, non-Hispanic Black Veterans were more likely to utilize telemedicine (Adjusted OR=1.5; (CI: 1.40-1.60)). The most common and least common modes of telemedicine among cases and controls were telephone and supplementary remote, respectively. States with the highest increases in telemedicine utilization were AL, CA, CO, FL, GA, KS, IL, NY, and SC. PwMS tended to live in counties with more adverse social determinants of health compared with controls.

Conclusion: PwMS were significantly more likely to use telemedicine than their matched controls. There were significant increases in telemedicine utilization between 2010 and 2020. Future work is needed to assess the determinants of telemedicine utilization.

Mean Telehealth Utilization in the Veterans Health Adminstration
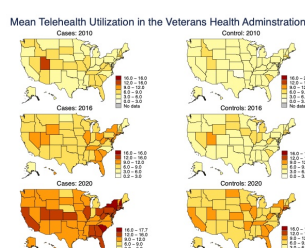
The effect of racial/ethnic disparity on time to treatment and survival in breast cancer patients: a systematic review Parisa Mokhtari Hesari* Parisa Mokhtari Hesari

Background and objective: researches on racial disparity in breast cancer is of valuable importance to provide information for health authorities to implement efficient strategies at the population-level. It seems that time to treatment can be considered as an indicator of breast cancer survival disparity. This review aimed to address effect of racial difference on time to treatment and breast cancer survival disparity.

Methods: a comprehensive search was conducted in Medline (PubMed), Embase, Web of science and Cochrane systematic review to find publications on keywords including race, time to treatment (e.g., surgery, chemotherapy, hormone therapy), survival and breast cancer. The PRISMA guideline was used, and risk of bias was assessed. The common eligibility criteria of all included studies were considered in this review. Causal DAGs were built to understand causal relationship and possible biases in included studies. In general, to report the result of studies, two approaches were considered in the present review: first, time to treatment was considered as an outcome and second, its role as an effect modifier along with other covariates was assessed.

Results: a total of 379 articles was found. After removing duplications and screening the studies, 58 full texts were analyzed in-depth. Based on the inclusion criteria, 21 studies were evaluated for this review. Despite large sample sizes of included studies, external validity was violated in a few studies. As a result, spars bias was occurred as there was lack of data in certain categories of race or in specific form of treatment. Moreover, selection bias was the most frequent systemic error as most retrospective cohort studies used administrative data. Studies showed that there is a significant difference in prolonged time to treatment in African American patients compared to Whites. Studies on race and prolonged time to treatment (i.e., modifier) found statistically significant difference in overall survival of Black patients compared to Whites. Although, in early-stage breast cancer, a significant racial disparity was observed between White and Black patients in time to all treatment modalities, it is required to adjust for other causes such as tumor subtype and nodal stage. Finally, the importance of considering specific race/ethnicity (e.g., African American ethnicity) as an independent predictor of poor breast cancer survival was highlighted in the literature.

Conclusion: although delay to treatment can mitigate survival in breast cancer patients of certain race/ethnicity groups, considering other essential unobserved confounders is of importance to detect precise magnitude of race effect. Overall, studies on racial disparity in breast cancer suffer from unmeasured confounders and causal questions. Therefore, further studies are required to assess causes of prolonged time to treatment modalities on poor survival in minority population.

Keywords: racial disparity, survival disparity, time to treatment, breast cancer.

Vicarious Structural Racism and Infant Health Disparities in Michigan: The Flint Water Crisis Kristi Allgood* Kristi Allgood Jasmine Mack Nicole Novak Cleopatra Abdou Nancy Fleischer Belinda Needham

Building on nascent literature examining the health-related effects of vicarious structural racism, we examined indirect exposure to the Flint Water Crisis (FWC) as a predictor of birth outcomes in Michigan communities outside of Flint, where residents were not directly exposed to lead-contaminated water. Using linear regression models, we analyzed records for all singleton live births in Michigan from 2013-2016, excluding Flint births. First, we determine whether birthweight (BW), gestational age (GA), and size-for-gestational-age (SzGA) decreased following the highly-publicized January 2016 emergency declaration in Flint. Then, we determine if birth outcomes were lower among babies born to Black mothers, but not among babies born to White mothers. In adjusted regression models BW and SzGA were lower for babies born to both Black and White mothers in the 37 weeks following the emergency declaration compared to the same 37-week periods in the previous three years. There were no racial differences in the associations of exposure to the emergency declaration with BW or SzGA. Among infants born to Black mothers, GA was 0.06 weeks lower in the 37-week period following the emergency declaration versus the same 37-week periods in the previous three years (95% CI: -0.10, -0.01; p=0.008), while there was no change in GA for infants born to White mothers following the emergency declaration (95% CI: -0.01, 0.03; p=0.5291). The FWC, which was widely attributed to structural racism, appears to have had a greater impact, overall, on outcomes for babies born to Black mothers. However, given the frequency of highly publicized examples of anti-Black racism over the study period, it is difficult to disentangle the effects of the FWC from the effects of other racialized stressors.

A vegetables, oils, and fruit dietary pattern during late pregnancy is linked to lower risk of adverse birth outcomes in a predominantly low-income Hispanic/Latina pregnancy cohort in Los Angeles: the Maternal And Developmental Risks from Environmental and Social Stressors (MADRES) cohort study Luis Enrique Maldonado* Luis E. Maldonado Shohreh F. Farzan Claudia M. Toledo-Corral Genevieve F. Dunton Rima Habre Sandrah Proctor Eckel Mark Johnson Tingyu Yang Brendan H. Grubbs Deborah Lerner Nathana Lurvey Thomas Chavez Carrie V. Breton Theresa M. Bastain

Background: Prenatal dietary patterns (DPs) have been linked to birth outcomes, but studies examining these relationships among socioeconomically disadvantaged populations in the US are lacking. **Methods:** Women in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) study (n=465)—an ongoing, prospective pregnancy cohort of predominantly low-income Hispanic/Latina women in Los Angeles—completed up to two 24-hour dietary recalls in the third trimester of pregnancy. We identified prenatal DPs via factor analysis and evaluated their associations with birth weight and gestational age at birth (GA) z-scores, separately, using linear regression and premature birth, small-for-gestational age (SGA), and large-for-gestational-age (LGA) using logistic regression, adjusting for maternal age, pre-pregnancy BMI, birth order, energy intake, education, and the other DP. We additionally tested interaction terms between prenatal DPs and maternal diabetes status (none, gestational [GDM], chronic) in separate models. We adjusted for multiple comparisons using false discovery rate. **Results:** We identified two prenatal DPs: solid fats, refined grains, and cheese (SRC); and vegetables, oils, and fruit (VOF). Comparing highest-to-lowest quartiles, the VOF DP was significantly associated with greater birth weight (β=0.40, 95% CIs: 0.10, 0.70; P_{trend}=0.011), GA (β=0.32, 95% CIs: 0.03, 0.61; P_{trend}=0.036) and lower odds of premature birth (OR=0.31, 95% CIs: 0.10, 0.95; P_{trend}=0.049) and SGA (OR=0.18, 95% CIs: 0.06, 0.58; P_{trend}=0.028). Only among women with GDM, a 1-SD score change in the SRC prenatal DP was significantly associated with lower birth weight (β=-0.20, 95% CIs -0.39, -0.02; $P_{interaction}$=0.040; **Figure 1**). **Conclusion:** Among low-income Hispanic/Latina pregnant women, greater adherence to the VOF prenatal DP may lower risk of premature birth and SGA, while adherence to the SRC DP may adversely affect newborn birth weight among mothers with GDM.

Visual gender nonconformity, discrimination, and posttraumatic stress disorder symptoms in a probability sample of U.S. transgender adults Ilan H. Meyer* Mai-Han Trinh Sari L. Reisner Dougie Zubizarreta Jarvis T. Chen Karestan C. Koenen

Background. Discrimination contributes to mental health inequities among transgender and gender diverse (TGD) populations, but few studies have examined its role in relation to posttraumatic stress disorder (PTSD). Moreover, comparative studies assessing differences in PTSD between TGD and cisgender populations are limited.

Objectives. To estimate associations between TGD identity and PTSD symptoms and quantify how everyday discrimination mediates the relationship between visual gender nonconformity (VGNC) and PTSD symptoms among TGD people.

Methods. We analyzed the U.S. Transgender Population Health Survey, a cross-sectional national probability sample of 272 TGD and 1,125 cisgender adults recruited April 2016–December 2018. Data were collected on VGNC, with an item adapted from the National Transgender Discrimination Survey; everyday discrimination, with the Everyday Discrimination Scale; and PTSD symptoms, with the Primary Care PTSD Screen for DSM-IV. We estimated prevalence ratios for the association between TGD vs. cisgender identity and probable PTSD, defined as PTSD symptom score ≥ 3 out of 4, using Poisson models with robust variance. Under the causal mediation framework, we decomposed the effect of VGNC on continuous PTSD symptom score into the natural direct effect and the natural indirect effect through everyday discrimination.

Results. TGD people had twice the prevalence of probable PTSD compared with cisgender people, adjusting for age, race, and census region (prevalence ratio: 2.00; 95%CI: 1.50–2.66). Though the total effect of VGNC on PTSD symptom score within the TGD sample was nonsignificant (mean difference: 0.40; 95%CI: -0.10–1.01), 69% of the total effect of VGNC was mediated by everyday discrimination, with a natural indirect effect of 0.28 (95%CI: 0.00–0.60).

Conclusions. Clinical practice interventions considering everyday discrimination in PTSD treatment, and policies protecting against discrimination, are needed to promote TGD mental health.

Figure 1. Directed acyclic graph for mediation analysis, TransPop, United States, April 2016 – December 2018
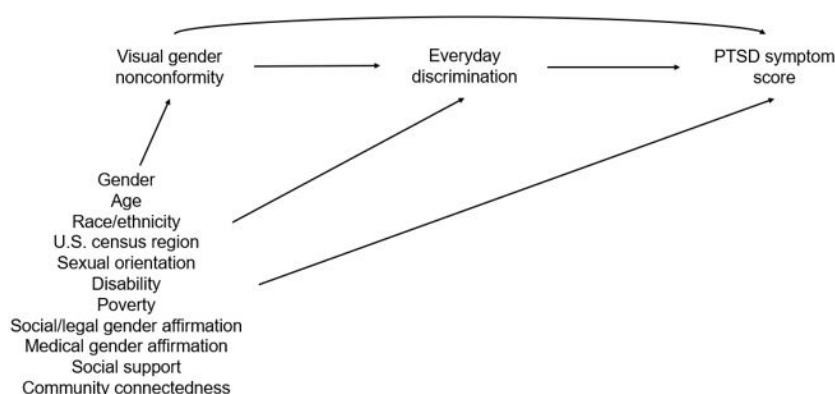
Dismantling the monolith — ethnic origin, racial identity, and major depression among US-born Black Americans Precious Esie* Precious Esie Lisa Bates

The "Black-white depression paradox" has been the topic of extensive research toward understanding why Black Americans have a lower prevalence of major depressive disorder (MDD) relative to white Americans, yet far less research has explored causes of within-racial variation; namely, why US-born Caribbeans have higher levels of MDD relative to African Americans. Research suggests racial identity among Black Americans – specifically, African Americans – may explain the apparent race "paradox" in MDD. Less is known about how racial identity functions within Black Americans with recent immigrant origins. We examined the extent to which differential effects of racial identity on MDD by ethnic origin explain the elevated prevalence among US-born Caribbeans relative to all other US-born Black Americans.

Data were drawn from the National Survey of American Life, the largest nationally representative study of Black mental health. Log-binomial models assessed effect modification of ethnic origin (Caribbean, non-Caribbean) the relationship between racial identity and MDD. We used four indicators of racial identity in separate models — closeness to Black people, importance of race to one's identity, belief that one's fate was shared with other Black people, and Black group evaluation.

We found support that rather than being protective, shared fate was positively associated with MDD for US-born Caribbeans (RR=3.43) and not associated with MDD for non-Caribbeans. Models also suggested importance of race to one's identity and Black group evaluation were detrimental for Caribbeans, yet protective for non-Caribbeans. Closeness appeared to be protective for both groups.

This analysis examined the role of racial identity in explaining the heightened prevalence of MDD among US-born Caribbeans compared to US-born non-Caribbeans. Findings provide new insight into the role of racial identity on MDD and contribute to the scant literature disaggregating the US Black population.
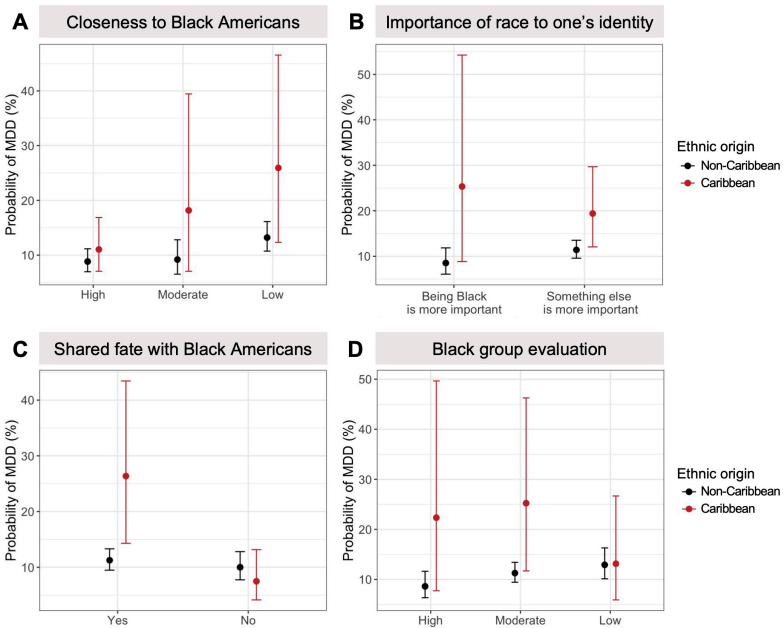
LATEBREAKER

Health Disparities

The association of sleep disturbance and sleep apnea with complex multimorbidity among Chinese and Korean Americans Sunmin Lee* Sunmin Lee Soomin Ryu Grace E. Lee Susan Redline Ichiro Kawachi

Objectives: A new concept called complex multimorbidity (CMM) provides a more reliable measure of disease burden than multimorbidity based on a simple count of diseases, by categorizing diseases by the body system they affect. This study aims to examine associations between sleep measures and CMM among Chinese and Korean Americans in the United States.

Methods: In this cross-sectional study of 400 Chinese and Korean Americans, sleep disturbance was measured using the 8-item Patient Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance scale. Participants with a standardized T-score ≥55 were categorized as having a sleep disturbance. Participants with positive scores on ≥2 subcategories of three subcategories of the Berlin questionnaire were categorized into high risk for sleep apnea. Complex multimorbidity was defined as the coexistence of ≥3 body system disorders. Logistic regression analyses were conducted to examine the associations between sleep measures and CMM, adjusting for sociodemographic variables.

Results: Nineteen percent of the participants had sleep disturbance, and 12.5% were at high risk for sleep apnea. In adjusted logistic regression models, individuals with sleep disturbance had 2.55 times the odds of having CMM (95% confidence interval (CI): 1.10-5.91), whereas individuals with a high-risk of sleep apnea had 1.24 times the odds of having CMM (95% CI: 0.43-3.56).

Conclusions: This is the first U.S.-based study to examine the association between sleep measures and CMM. Although sleep disturbances and sleep apnea are amenable to treatment and interventions, there is a high prevalence of unrecognized and under-treated sleep problems, particularly among Asian Americans. Findings suggest a need for public health interventions to increase awareness of the importance of sleep among health care providers and the public and to educate the public about the causes, signs, and treatment of sleep disturbance and sleep apnea.

LATEBREAKER

Health Disparities

Longitudinal neighbourhood socioeconomic status and risk of premature death Emmalin
Buajitti* Emmalin Buajitti Laura C. Rosella

Background

Though area-level socioeconomic (SES) inequalities in premature death have widely reported, few
studies have considered time-dependent neighbourhood exposures; this may be due to limited access
to longitudinal residential data. We sought to leverage comprehensive data linkages in Ontario,
Canada to capture neighbourhood SES gradients in premature injury mortality, overall and for injury
deaths, which have a more direct path from exposure to outcome.

Methods

We identified Canadian Community Health Survey (CCHS) respondents, aged 18 to 74, who were
interviewed between 2000 and 2012 (n=158,074). We captured neighbourhood income quintile at
interview, and each subsequent year, using encounter-based postal code records from Ontario's
single-payer health care system. Deaths were identified from vital statistics data; injury deaths were
defined based on ICD-10 codes (V01-Y98). Respondents were followed until December 31st, 2018,
age 75, emigration, or death.

We used cause-specific Cox models to quantify neighbourhood SES gradients in premature death.
Time-independent models included neighbourhood SES at survey; time-dependent models included
up to 20 annual measures. Fully adjusted models included age, sex, year of survey, education,
immigrant status, self-rated health, smoking, physical activity, and alcohol use.

Results

Almost all (99.1%) CCHS respondents had complete neighbourhood income. Time-dependent models
showed a neighbourhood SES gradient for both outcomes (Fig 1). Time-dependent Cox models found
larger gradients compared to time-independent models, although confidence intervals were wide
and overlapped for both. Differences between time-independent and time-dependent models were
greater for injury deaths.

Conclusion

Longitudinal postal code information enables robust estimation of neighbourhood SES gradients.
Our findings suggest that time-dependent exposure measures may be more sensitive for detecting
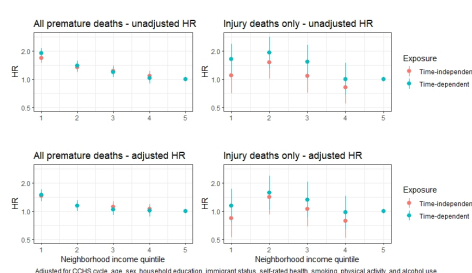associations with short-latency outcomes.

**Figure 1. Hazard ratios (HR) for neighborhood income quintile, Ontario CCHS
respondents ages 18 to 74, 2000 to 2012 (n=158,074).**

Health Services/Policy

Team-based primary care and medication management in Canadian seniors: a cross-provincial analysis Nichole Austin* Nichole Austin David Rudoler Erin Strumpf Sara Allin Caroline Sirois Rick Glazier

Background: Team-based primary care reforms aim to streamline care coordination by involving multiple health professionals in patient care. This may ultimately improve medication management, particularly for seniors who are intensive users of medications with multiple points of contact with the healthcare system. However, little is known about this association. This study compares sociodemographic and prescribing trends in team-based vs. traditional primary care models in Ontario and Quebec between 2006 and 2018.

Methods: We constructed two provincial cohorts using population-level health administrative data. Our primary exposure was enrollment in a team-based model of care. Key endpoints included adverse drug events and potentially inappropriate prescriptions. We plotted prescribing trends across the observation period (stratified by model of care) in each province. We used standardized mean differences to compare seniors' characteristics and prescribing endpoints.

Results: Enrollment in team-based models increased steadily since the time of policy implementation. Despite early differences, the sociodemographic profile of seniors in team-based and traditional models of care became increasingly similar over time. All key endpoints were more common among team-based patients in Quebec and Ontario, but trends in most adverse events declined over the observation period, regardless of enrollment status (e.g., the proportion of Quebec patients with overlapping opioid and benzodiazepine prescriptions declined by ~40% from 2006 to 2018, regardless of model of care).

Discussion: Early sociodemographic differences in these patient populations gradually diminished over time in both provinces. Most adverse prescribing endpoints also declined steadily over time, and the rate of change was similar regardless of enrollment status. Additional work is required to assess whether exposure to team-based models impacts medication management in seniors.

The association of physician characteristics on prescribing of benzodiazepines among older adults
Fiona Chan* Fiona Chan Maria-Teresa Moraga Nadyne Girard Robyn Tamblyn

Benzodiazepines and Z-drugs (BDZ) are associated with risk of falls and cognitive impairment among older adults, thus are considered potentially inappropriate medications (PIMs). However, despite guidelines advising against their use particularly for insomnia and delirium, they remain the most utilized PIM. While physician's age, sex, and location are known predictors of PIM prescribing, it has been postulated that culture, clinical competency, and communication skill are also important factors. This study examined the relationship between physician characteristics – chiefly, country of origin, clinical and communication competency – on prescribing of BDZ. For our cohort of all international medical graduates (IMGs) licensed in the US between 1998-2004, we obtained their competency assessment scores at licensure. Linking these IMGs to Medicare patients they encountered in 2014-15, we analyzed their outpatient visit and drug dispensations records. Overall, 5,153 of our 6,199 study IMGs with a specialty in primary care or internal medicine, diagnosed 57,648 patients over 65 years old with insomnia or delirium at an ambulatory visit. Of these, 17,739 (30.8%) patients were prescribed a BDZ by 3,335 (64.7%) of our study physicians. In our multivariate GEE logistic regression models, accounting for physician-level clustering, white patients and those aged 65-70 are more likely to use BDZ. Physicians who are male, who practice internal medicine, or with citizenship in the United Kingdom are less likely to prescribe BDZs. Across all individual and composite measures of clinical competency and communication ability, only diagnosis and management ability among male physicians was found to decrease the risk of BDZ prescribing. Given strong associations by sex and citizenship, and well-documented differences in medical treatment among physician and patients of discordant sex and race, it would be important to understand if inequities exist in certain patient-physician pairs.

Table 1 - The association between physician characteristics and the odds of prescribing of benzodiazepine/Z-drug (BDZ) within 30-days of a diagnosis for insomnia or delirium. 5153 International Medical Graduates diagnosed 57,648 US Medicare patients, of whom 17,739 (30.8%) received a BDZ from 3,335 (64.7%) physicians.

Characteristic	Odds of Prescribing a BDZ			
	N Patients (%)	N Patients with BDZ (%)	OR (95% CI)	P-Value
Physician Gender				
Female	21,962 (38.1)	6,820 (38.5)	Reference	
Male	35,686 (61.9)	10,919 (61.5)	0.86 (0.80-0.93)	0.0003
Citizenship				
United Kingdom	563 (1.0)	131 (0.7)	Reference	
Africa	2,678 (4.7)	699 (3.9)	1.15 (0.85-1.56)	0.3695
Asia	9,915 (17.2)	3,111 (17.5)	1.70 (1.28-2.26)	0.0002
Canada	372 (0.7)	94 (0.5)	1.22 (0.79-1.89)	0.3743
Central America/Caribbean	2,855 (5.0)	995 (5.6)	1.84 (1.35-2.50)	0.0001
Europe	3,865 (6.7)	1,178 (6.6)	1.46 (1.09-1.95)	0.0117
India	13,774 (23.9)	3,953 (22.3)	1.37 (1.04-1.82)	0.0274
Mexico	417 (0.7)	108 (0.6)	1.46 (0.92-2.32)	0.1086
Middle East	4,874 (8.5)	1,566 (8.8)	1.65 (1.23-2.21)	0.0009
Missing	259 (0.5)	63 (0.4)	1.36 (0.77-2.40)	0.2858
Oceania	74 (0.1)	24 (0.1)	1.26 (0.67-2.37)	0.4748
Pakistan	3,234 (5.6)	835 (4.7)	1.25 (0.92-1.69)	0.15
Russia	2,110 (3.7)	748 (4.2)	1.64 (1.17-2.29)	0.0036
South America	1,926 (3.3)	636 (3.6)	1.52 (1.10-2.09)	0.0108
United States	10,732 (18.6)	3,598 (20.3)	1.62 (1.22-2.15)	0.0008
Physician Specialty				
Primary care	26,768 (46.4)	8,780 (49.5)	Reference	
Internal Medicine	30,880 (53.6)	8,959 (50.5)	0.74 (0.69-0.79)	<0.0001
Diagnosis & Management Score[1] - mean (SD)	16.52 (20.9)	16.66 (21.1)	1.00 (1.00-1.00)	0.5016
Diagnosis & Management Score[1] x Gender - mean (SD)				
Female	15.05 (20.0)	14.82 (19.9)	Reference	
Male	17.42 (21.4)	17.81 (21.8)	1.00 (1.00-1.01)	0.0361

[1] Per 10% increase in score

Average Treatment Effect of the Medicaid Expansion Program on Cardiovascular Disease Mortality over Time by States, Sex and Race/Ethnicity: A Generalized Synthetic Control Approach Roch Nianogo* Roch Nianogo Fan Zhao

Background: Cardiovascular Diseases (CVD) affect the socially and economically disadvantaged populations—the underserved racial/ethnic minorities and low-income subpopulations. Recent studies have suggested that the Affordable Care Act Medicaid Expansion Program (MEP) policy enacted in 2014 has resulted in a reduction in overall cardiovascular disease (CVD) mortality in the U.S. However, such findings did not separate the beneficial effects of the policy over time, by state, sex and race/ethnicity. Knowledge of which is paramount to tailoring interventions for sub-populations that needed it the most. **Objective**: We set out this study to investigate the impact of the MEP on the CVD mortality over time by states, sex and race/ethnicity. **Methods**: Data from the Behavioral Risk Factor Surveillance System and the Centers for Disease Control and Prevention Wide-ranging Online Data for Epidemiologic Research were used. We implemented the generalized synthetic control method, an extension of the traditional synthetic control method which has been shown to be more precise than the former and less prone to bias compared to the Difference-in-Difference methods. **Results**: We found that the MEP appears to have a highly heterogenous impact on the CVD mortality over time. The overall average treatment effect in terms of the mean difference (MD) of the MEP on CVD mortality per 100,000 people for all states were -5, 95%CI (-10, -1) in 2014 and -5, 95%CI (-11, 0) in 2018; for Blacks: 5, 95%CI (-14, 21) in 2014 and -2, 95%CI (-24, 21) in 2018; for Whites: -4, 95%CI (-9, 1) in 2014 and -3, 95%CI (-9, 4) in 2018; for Men: -3, 95%CI (-10, 5) in 2014 and 0, 95%CI (-8, 9) in 2018; for Women: -6, 95%CI (-9, -3) in 2014 and -7, 95%CI (-12, -2) in 2018. Some states such as Delaware but not others have seen some beneficial effects of the MEP in 2018 among women: -29, 95%CI (-53, -5). **Conclusion**: This study provides insights on where, when and for whom, the policy appears to have a beneficial effect which in turn can allow scientists and policymakers to investigate further into factors that promote such effects in the hopes of scaling what works to the rest of the U.S.

Impact of the Medicaid Expansion on CVD mortality, female, 2018 (t+4)
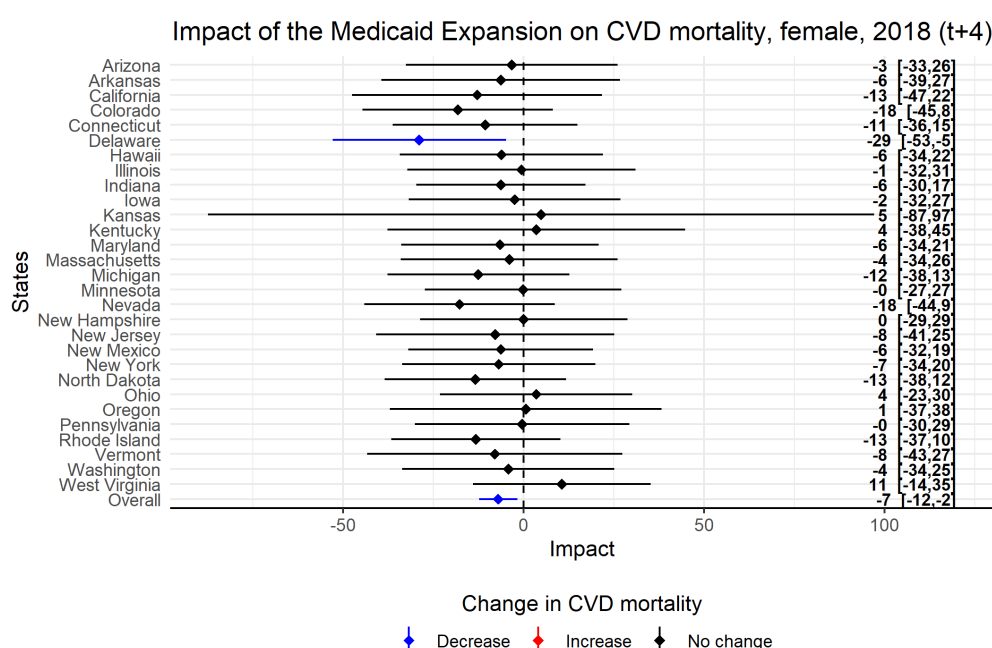
Trends in risk of lung cancer among people living with HIV in the United States Cameron
Haas* Cameron Haas Meredith Shiels Marie-Josephe Horner Eric Engels Neal Freedman Qianlai Luo
Susan Gershman Baozhen Qiao Ruth Pfeiffer

Background: Lung cancer is the most common non-AIDS-defining cancer in people living with HIV
(PLWH) and the risk is elevated compared to the general population, for whom rates have declined.
We investigated trends in excess risk and cumulative incidence of lung cancer among PLWH within
age groups.

Methods: We used data from the HIV/AIDS Cancer Match study during 2001-2016 to estimate risk
of lung cancer in PLWH and to make comparisons to the general population in the United States. We
estimated the average annual percentage change (AAPC) using multivariable Poisson regression.
Within age groups, we calculated standardized incidence ratios (SIRs) and excess absolute risks
(EAR) of lung cancer. We estimated the 5-year cumulative incidence of lung cancer, non-Hodgkin
lymphoma, and Kaposi's sarcoma (two AIDS-defining cancers) from 2011 using the Nelson-Aalen
estimate.

Results: There were 3,426 lung cancers in 4,310,304 person-years of follow-up for PLWH in the U.S.
in 2001-2016. Incidence of lung cancer declined 6% per year among PLWH (95% confidence interval
[CI]=-7% to -5%), with greater declines among younger age groups. During 2013-2016, risk of lung
cancer among PLWH was 1.7 times higher than the general population for 20-39 year-olds (95%
CI=0.55-3.97) and 2.0 times higher for 40-49 year-olds (95% CI=1.51-2.67) and EARs were greatest
among those 70+ years of age (67.0, 95% CI=-47.0-209.8 per 100,000 person-years). The 5-year
cumulative incidence for lung cancer surpassed that of Kaposi's sarcoma and non-Hodgkin
lymphoma for PLWH ages 50 years and older (**Figure**).

Conclusion: The risk of lung cancer has decreased for younger PLWH but remains a significant
excess burden among those 50 years and older, for whom there is a considerable excess risk in this
population that may possibly be explained by a higher prevalence of smoking. For the growing
proportion of PLWH living beyond 50 years old, lung cancer risk is higher than the most common
AIDS-defining cancers.

Figure: Within age group 5-year cumulative incidence of lung cancer, non-Hodgkin lymphoma,
and Kaposi's sarcoma in people living with HIV in the United States using a time origin of 2011

Blue = Lung cancer
Green = non-Hodgkin lymphoma
Red = Kaposi's sarcoma
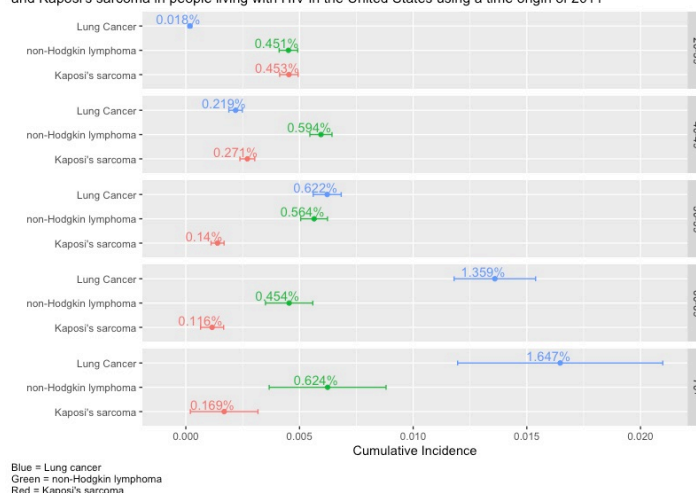
Rapid impact of "Treat All" on population-level viral suppression in older adults living with HIV: pre- and post- cross-sectional analysis conducted in Lesotho Domonique Reed*
Domonique Reed Pich Seekaew Matt Lamb Tiffany Harris Qixuan Chen Jessica Justman

Older adults account for an increasing proportion of people living with HIV (PLWH) yet details about HIV viral suppression (VS) in this group are sparse. We assessed the impact of the World Health Organization's 2015 policy of "Treat All" on change in population-level VS, and compare VS among older (≥40 years; y) with younger (<40y) PLWH in Lesotho using two nationally-representative cross-sectional household surveys. Data from the Lesotho Demographic Health Survey (DHS) 2014 (pre-"Treat All") and the Lesotho Population-based HIV Impact Assessment (PHIA) 2016 (post-"Treat All") were used to assess VS amongst older adults before and after "Treat All" recommendations. From both surveys, we included available viral load results from consenting PLWH aged 15-59y (DHS enrolled women aged 15-49y) who provided dried blood spots (DHS) or plasma (PHIA), with survey-specific corrections for values <2000 cp/mL or not detectable, and survey-specific weights to achieve population-level estimates. Crude and adjusted prevalence ratios compared VS among older versus younger PLWH. VS was defined as HIV-1 RNA<1000 cp/mL. A total of 1,019 PLWH from DHS (21% ≥40 y and 70% women) and 3,056 PLWH from PHIA (41% ≥40y and 50% women) were assessed. Prevalence of VS among all PLWH in pre- and post-"Treat All" was 6% and 68%, respectively. Among PLWH aged ≥40y, prevalence of VS in pre -and post-"Treat All" was 6% and 49%, respectively. When compared to PLWH aged <40y, and after adjusting for gender, household wealth and urbanicity, older PLWH were 71% less likely to be VS during pre-"Treat All" (95%CI:10%-90%) and 22% less likely during post-"Treat All" (95%CI:10%-30). Our findings quantify the swift impact of "Treat All" on population-level viral suppression among older PLWH in Lesotho with an observed 43% change in prevalence; however, these results may reflect differences in measurement methods, survey inclusion criteria, changes in drug recommendations, and timing of scale-up.

Racial-ethnic majority status modifies the relationship between race-ethnicity and influenza vaccination among New York City adults Johnny Croft* Johnny Croft Elizabeth A. Kelvin Chloe Teasdale

Background: Flu vaccination uptake exhibits racial/ethnic disparities despite vaccine availability. In the US, nativity modifies the association between race/ethnicity and vaccination, which may be explained by racial/ethnic majority status in country of birth. We assessed the association between racial/ethnic identity and uptake of flu vaccination in adults in NYC and examined whether racial/ethnic majority status in birth country (participant born in country where they were in the racial/ethnic majority) led to increased vaccination uptake.

Methods: We used 2015-19 NYC Community Health Surveys with self-reported data from 49,056 participants (47% foreign-born). Logistic regression models, adjusted for demographic confounders, and survey weights were used to assess the relationship between racial/ethnic identity and flu vaccination. We then tested for multiplicative effect modification by majority racial/ethnic status in birth country using an interaction term and ran separate models stratified on racial/ethnic majority status.

Results: We found significant multiplicative effect measure modification of the relationship between racial/ethnic identity and flu vaccination by racial/ethnic majority status in birth country. Among those who were racial/ethnic majorities in their birth country, Blacks (adjusted OR [AOR] 1.6, 95%CI: 1.4-1.9), Hispanics (AOR 2.1, 95%CI: 1.8-2.3), and Asian/Pacific Islanders (PIs) (AOR 2.0, 95%CI: 1.7-2.3) had higher odds of flu vaccination compared to Whites, whereas among those who were racial/ethnic minorities in birth country, Blacks (AOR 0.6, 95%CI: 0.3-1.0), Hispanics (AOR 0.7, 95%CI: 0.4-1.2), and Asian/PIs (AOR 0.9, 95%CI: 0.5-1.6) had lower odds of flu vaccination compared to Whites.

Conclusion: Racial/ethnic majority status in birth country appears to modify and increase the odds of flu vaccination among Black, Hispanic, and Asian/PI adults in NYC.

Infectious Disease

Correction of Diagnostic Coding-based RSV Incidence using NREVSS Data Sabina Nduaguba* Sabina Nduaguba Sabina Nduaguba Phuong Tran Almut Winterstein

Background: Respiratory syncytial virus (RSV) is a common pathogen causing lower respiratory tract infection (LRTI) among young children. Not all LRTI infections are tested or pathogens are not coded in claims data. Previous work used RSV positivity rates from the National Respiratory and Enteric Virus Surveillance System (NREVSS) to correct claims-based inpatient LRTI incidence estimates, which we expanded to examine setting-specific strata.

Methods: Using 2011-2019 commercial insurance claims of children aged 0-4 years, we estimated the weekly incidence of inpatient, outpatient, and total LRTI stratified by US region and matched these data to the corresponding regional weekly NREVSS RSV and influenza positivity data. LRTI incidence from claims was modelled against RSV (antigen and PCR weighted by weekly number of tests) and influenza positivity rates and functions of time using negative binomial models. LRTI events attributable to RSV were estimated as predicted events from the full model minus predicted events with RSV=0.

Results: Models suggested that ~42% of predicted RSV cases were coded in claims data. Depending on region, the corrected RSV estimates yielded 15%-43%, 10%-31%, and 10%-31% of inpatient, outpatient, and overall LRTI episodes attributable to RSV, respectively. Corrections of inpatient LRTI resulted in improbable estimates in 9/10 regions (diagnosed RSV/predicted RSV ratio>1). Sensitivity analysis with separate models for PCR and antigen-based positivity showed similar improbable inpatient estimates.

Conclusion: NREVSS-based adjustment of claims-based RSV incidence may address underestimation based on coding in claims data. However, In absence of setting-specific positivity rates, we recommend modeling across settings, mirroring NREVSS's positivity rates which are similarly aggregated, to avoid inaccurate adjustments.

Impact of patient characteristics and cyst-burden on the longitudinal evolution of neurocysticercosis cysts Meghana G. Shamsunder* Meghana Shamsunder Hongbin Zhang Arturo Carpio Allen Hauser Alex Jaramillo Elizabeth Kelvin

Background:

Neurocysticercosis (NCC) is infection of the CNS with the larval stage of the pork tapeworm, *Taenia solium*. In the human brain, the parasite evolves over time through the active (viable parasite), transitional (degenerating parasite), calcified residual and complete resolution stages. The disease is diagnosed and followed via brain imaging.

Methods:

We used data from an RCT evaluating albendazole treatment for NCC (conducted in Ecuador), disaggregated from the patient to the cyst level to evaluate the association of patient and cyst factors on cyst evolution (months 0, 1, 3, 6, 12, and 24). Albendazole treatment, patient age (dichotomized at the mean [<=42.5 years]), sex, having cysts in multiple brain locations, total cysts at baseline, and total calcified cysts were used in forward stepwise (alpha=0.2) multivariable multistate modeling with confidence intervals estimated by bootstrapping (iterations=100, alpha=0.05). Albendazole treatment, patient age, and having cysts in multiple brain locations were included in the final model.

Results:

A total of 220 NCC cysts located in 116 patients were included in the analysis. in the multivariable model, albendazole (HR: 3.53; 95% CI: 1.49, 13.54) and the presence of cysts in multiple locations (HR: 3.06; 95% CI: 1.37, 8.27) were significantly associated with transition from the active to transitional phase.

Discussion:

Understanding factors that impact the evolution of NCC cysts over time is key to developing treatment to target the parasite at different points in the evolutionary process and improve patient outcomes. Albendazole treatment is known to have an impact on parasite mortality. Having multiple cysts in different locations may increase the rate of parasite mortality by creating a more rapid or stronger host immune response. No factors were found to influence cyst evolution in later stages, after the parasite was already degenerating or deceased.

Infectious Disease

3D Printers in Hospitals: Assessing Bacterial Contamination and Disinfection of 3D Printed Material Katelin Jackson* Katelin Jackson Eric Lofgren Douglas Call

Background: COVID-19 has presented hospitals with unique challenges. A survey of hospitals showed that 40% reported "limited" or worse levels of personal protective equipment (PPE), and 13% were self-producing PPE to address those deficits, including 3D printed items. However, we do not know how efficiently, if at all, 3D printed materials can be disinfected. We assess how these materials may be contaminated and how readily they may be disinfected.

Methods: We used methicillin-resistant *Staphylococcus aureus*, *S. aureus, E. coli, Acinetobacter baumannii*, and *Klebsiella pneumoniae*, commonly found in hospital environments. We conducted bacterial survival assays to determine if bacteria grow on 3D printed material with and without disinfectant. We performed a time series with 3- and 24-hour dry times followed by serial dilutions to attain colony-forming unit (CFU) averages for each strain per disk. To determine if 3D printed material can be cleaned, we used 70% EtOH and Bleach. We conducted the same time series followed by a disinfectant time series with varying dry times. Again, serial dilutions were performed to attain the CFU averages with disinfectant. The CFU averages from the control group (without disinfectant) and testing group (with disinfectant) were compared to see how well each disinfectant decreased bacterial load.

Results: 3D printed material is readily contaminated with bacteria common in hospitals and can sustain that contamination. Disinfected disks had lower CFU averages than those that were not, but the level of disinfection is relatively intensive.

Conclusion: Proper disinfection is essential to halting the spread of HAIs. 3D printers and their products can be invaluable for hospitals, especially when supplies are low and healthcare worker safety is paramount. Environmental services should be made aware of the presence of 3D printed materials and patients should be discouraged from printing their own items for use in hospital environments.

The effect of gun-free school zones on gun related crime in St. Louis, MO (2019) Paul Reeping* Paul Reeping

Objective: To conduct a cross-sectional ecological analysis in St. Louis, Missouri in 2019 comparing the proportion of gun related crimes that occur in gun-free school zones compared to "gun-allowing" zones immediately surrounding the gun-free school zone.

Background: Some argue that gun-free zones are targeted for gun related crime because of the lower chance that a law-abiding citizen will be able to engage defensively with the assailant with a firearm; however, no studies have analytically evaluated the association between gun-free zones and gun crime.

Methods: The outcome in this study was geo-located gun related crimes obtained from the St. Louis Metropolitan and County Police Departments in 2019. Exposed units in this study were gun-free school zones, which are defined as a radius of 1000 feet surrounding all public and private schools. Unexposed units were defined as "gun-allowing" zones of similar area immediately surrounding the gun-free school zones. If zones overlapped, they were combined to a single unit (Figure 1). The data were analyzed using a mixed model with quasi-Poisson distribution accounting for the pairing between the exposed and unexposed units and an offset of area to account for any variation due to the combining of units.

Results: After combining overlapping zones, there were 282 gun-free school zones and 282 corresponding "gun-allowing" zones in the analysis. Gun-free school zones have an insignificant 7% fewer gun crimes than the gun-allowing zones surrounding them. The confidence interval ranges from 17% fewer to 3% more gun related crimes (p-value: 0.17).

Conclusion: There is no statistical evidence that gun-free school zones attract gun crimes in St. Louis, MO. Studies across more cities and a larger geographical area are needed to more reliably evaluate the effect of gun-free school zones on gun related crime.

Injuries/Violence
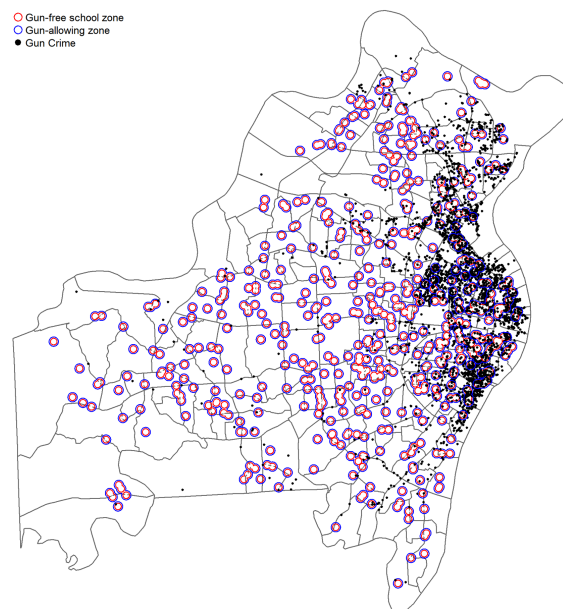
Bike crashes in Philadelphia: is a likely-biased denominator better than no denominator?

Steve Mooney* Stephen Mooney Fred Van Dyk Ghassan Hamra

Estimating hot spots for bicyclist injury risk is hindered by the lack of reliable data on the number of bicycle riders in a given location ('the denominator'). Recently, bicycle-ride tracking applications such as Strava have been proposed as a potential source of location-specific ridership estimates for bike injury research. We merged available bicycle crash data from the Pennsylvania Department of Transportation with bicycle ridership data from Strava to explore the spatial distribution of collisions involving cyclists in Philadelphia, PA from 2016-2018. We assigned each collision to the census tract and year in which it occurred and explored the spatial distribution of crashes descriptively. Both crashes and crashes per rider showed consistent yearly trends (Figure 1), and evidence of spatial autocorrelation (Moran's I for crashes = 0.08, Moran's I for crash per rider = 0.08, $p < 0.001$ for hypothesis test vs. no spatial autocorrelation). Overall, crashes occurred most frequently in the urban core where ridership is high, whereas crashes per Strava rider were clustered in North Philadelphia, a disinvested area where Strava use is unlikely to capture variation in population ridership with high fidelity. Future work, to be completed before June 2022, will develop Besag-York-Mollié spatio-temporal Poisson models to further explore determinants of injury risk and the variation in those estimates conditional on the inclusion of a crowdsourced ridership estimate. Crowdsourced data may partially account for incomplete denominators in bike injury research but also raise concerns that populations contributing to crowdsourcing may be highly selected in ways that bias risk estimates.

Early Medicaid expansion in California and behavioral health: assessing the role of affordable healthcare in drug overdose and self-harm rates Veronica Pear* Veronica Pear Julia Schleimer Christopher McCort Aaron Shev Rose Kagawa Daniel Tancredi Garen Wintemute Aimee Moulin

Under the Low Income Health Plan (LIHP), a provision of the Affordable Care Act, California counties could voluntarily expand health insurance coverage to low-income adults between 2011 and 2013. Increased health insurance coverage may lower healthcare costs, reduce financial instability, and improve access to medical and mental health care. Prior research has linked Medicaid expansion to better health outcomes, including reductions in opioid overdoses; however, few studies have evaluated the association with self-harm or examined within-state variation in adoption and implementation. This study will use variation in the timing of county Medicaid expansion to estimate associations between county-level drug overdose and self-harm rates among those aged 19-64 years (the population eligible for LIHP). Additionally, we will evaluate whether the association with self-harm is modified by county prevalence of firearm ownership, estimated with survey data.

Using statewide mortality, hospitalization, and emergency department data, we will conduct a generalized difference-in-differences analysis, comparing the difference in outcomes over time between counties that adopted LIHP and counties that had not yet or never adopted LIHP. Briefly, this involves estimating the group-time average treatment effect on the treated (ATT) for each group of units sharing a unique intervention start time, and then combining these into an overall ATT estimate. Confidence intervals will be obtained with county-level clustered bootstraps.

Findings from this project will provide a valuable addition to the limited literature on Medicaid's role in violence and injury prevention. Twelve states still have not adopted Medicaid expansion; many of them have above-average rates of drug overdose and/or suicide deaths. Study results may inform policymakers as they consider population-wide prevention strategies as well as researchers interested in the moderating role of firearms.

Symptoms across common posttraumatic neuropsychiatric diagnoses cluster in stable multidimensional phenotypes: results from a large trauma cohort Rachel Gaither* Rachel Gaither Francesca L. Beaudoin Archana Basu Xinming An Ronald C. Kessler Donglin Zeng Kenneth A. Bollen Karestan C. Koenen Kerry J. Ressler Samuel A. McLean

Background

Adverse posttraumatic neuropsychiatric sequelae (APNS) are common after experiencing trauma. Traditional diagnoses (posttraumatic stress disorder, depression, pain) have considerable overlap and diagnostic heterogeneity, and emerging evidence suggests they share common neurobiological processes, highlighting the need for transdiagnostic approaches to classify complex posttraumatic symptoms. Here, we present an approach to identify subgroups of individuals with APNS.
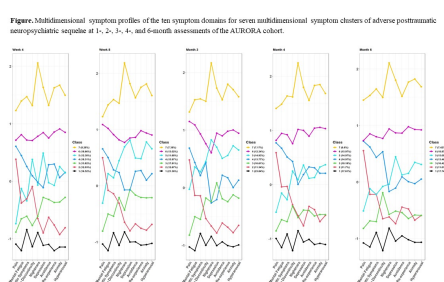
Methods

The Advancing Understanding of RecOvery afteR traumA (AURORA) study is a national cohort of trauma survivors recruited from US emergency departments. Participants completed ≥3 surveys across five timepoints (1-6 months post-trauma). Ten *a priori* APNS symptom domains were used to establish clusters using data-driven . Results were compared using statistical methods (GAP statistics, adjusted Rand index) and assessment of clinical meaningfulness. Descriptive and graphical analyses were used to track cluster features over time.

Results

Among 2069 participants (62% female, 45% Black), a 7-cluster solution fit the data best: a low symptom severity cluster (17-24% of sample over time); two high severity clusters (7-19%); and moderate severity clusters with unique profiles (high pain/moderate sleep disruption/low mental symptoms (14-18%), clusters of low pain/high mental symptoms (11-18%)). Cluster severity was stable over time, and 6-month daily functioning was lower among participants in high severity clusters.

Conclusion

We used a theoretical and data driven approach to identify seven phenotypic subgroups in trauma survivors that show stability over time, clinically meaningful differences, and overlap with traditional posttraumatic diagnoses. Findings highlight the need for comprehensive transdiagnostic approaches to assessing APNS and further research on whether identified subgroups respond differently to interventions.

Figure. Multidimensional symptom profiles of the ten symptom domains for seven multidimensional symptom clusters of adverse posttraumatic neuropsychiatric sequelae at 1-, 2-, 3-, 4-, and 6-month assessments of the AURORA cohort.

LATEBREAKER

Injuries/Violence

Childhood maltreatment and health in the UK Biobank: an outcome-wide analysis Ana Lucia Espinosa Dice* Ana Lucia Espinosa Dice Rebecca Lawn Andrew Ratanatharathorn Andrea Roberts Yiwen Zhu Pedro Antonio de la Rosa Fernández Pacheco Christy Denckla Rebecca Basaldua Caitlin Carey Elise Robinson Karestan Koenen

Childhood maltreatment is associated with adverse mental and physical health outcomes later in life. However, no prior study has employed outcome-wide analysis (OWA), a framework developed to assess associations of an exposure with many outcomes simultaneously, to examine the effect of maltreatment on a full range of social, economic, and health indicators. Using data from 37,990-157,331 middle-aged adults in the UK Biobank, our OWA examined associations of childhood maltreatment with 500 adult health and well-being outcomes. Maltreatment was assessed via the five-item Childhood Trauma Screener and summarized as number of maltreatment types experienced. Outcomes drew from a mix of self-report, hospital record, physical measure, and biological sampling data and covered domains of health including social status, risk behaviors, and mental well-being. In total, 8,701 (22.9%) participants experienced at least one type of maltreatment, 2,797 (7.4%) reported more than one, and 292 (0.8%) experienced four or more. Comparing those who reported 4+ maltreatment types versus none, maltreatment was consistently associated with heightened mental illness (e.g., self-harm: OR = 11.9; 95% CI = 9.1, 15.6) and types of bodily pain (e.g., headache: RR = 1.7; 95% CI = 1.4, 2.0), after correction for multiple testing. Maltreatment in childhood also elevated risk of self-reported respiratory illness symptoms, health risk behaviors, higher socioeconomic deprivation, higher body mass index, and lower general satisfaction and happiness. Maltreatment exposure was not associated with physical measures of cardiovascular and respiratory health such as blood pressure (diastolic: beta = 0.03; 95% CI = -0.08, 0.14) or forced expiratory volume in one second (beta = -0.02; 95% CI = -0.11, 0.05). Our findings underscore the wide-ranging impact of maltreatment on later life and the utility of OWA for improving causal inference in psychosocial research.
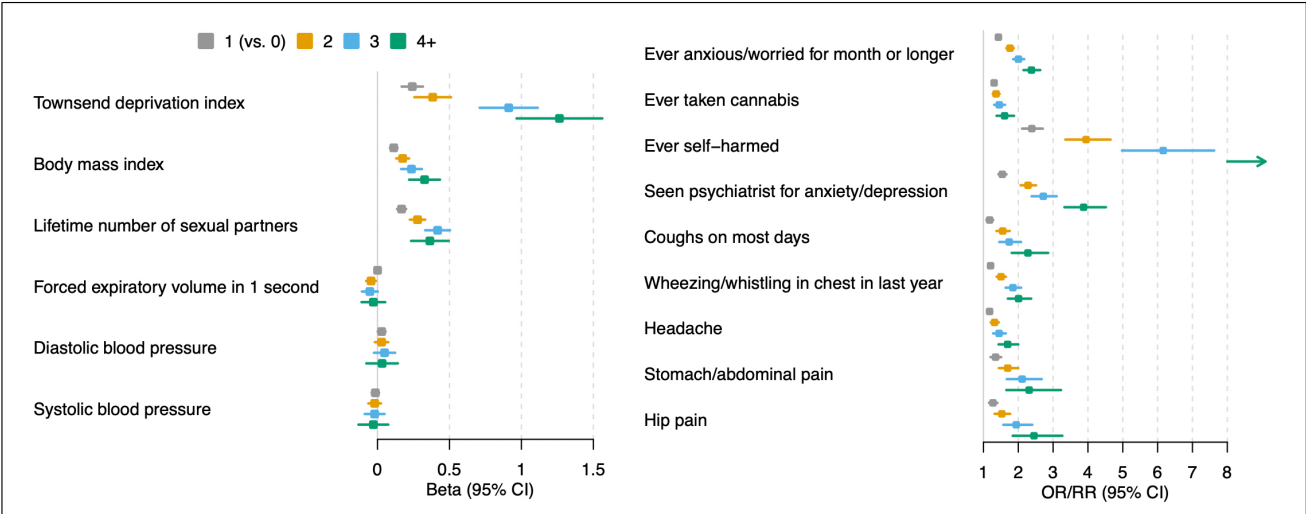

Figure 1 Forest Plot regressing a subset of continuous (left, standardized) and binary (right) adult health outcomes on number of childhood maltreatment types.

Differential indirect effects of deprivation and threat on adolescent psychopathology through objectively measured emotional, cognitive, and developmental mediators Ekaterina Sadikova* Ekaterina Sadikova David G. Weissman Maya L. Rosen Henning Tiemeier Katie A. McLaughlin

Background: High-dimensional mediation analysis is needed to empirically discern mechanisms by which dimensions of early-life adversity—deprivation and threat (D&T)—differentially influence adolescent psychopathology.

Methods: At baseline (age 10.8-13.0), 227 children and their mothers provided data on history of D&T and objectively measured candidate mediators: threat detection(TD), attention bias to threat(ABT), cognitive and affective theory of mind(cToM/aToM), fear conditioning(FC), pubertal development(PD), language ability(LA), inhibitory control(IC), working memory(WM), reasoning ability(RA), automatic emotion regulation(AER), and reward reactivity(RR). Composite psychopathology outcomes were assessed 2 years later. A minimax concave penalty and joint significance testing procedure identified the most salient mediators of D&T.

Results: IC, WM, PD, and RR were selected, with IC and PD differentially mediating effects of D&T. The most consistently identified indirect effects of D&T on general (p=0.04 D, p=0.02 T), externalizing (p=0.02 D&T), and internalizing (p=0.22 D, p=0.12 T) psychopathology were through IC. Protective against psychopathology, IC is improved by threat but reduced by deprivation, resulting in divergent indirect effects. Earlier PD explained 3% of the association between threat and psychopathology. In contrast, deprivation slows PD, and the indirect effect of deprivation through PD was protective. RR was reduced by both D&T, resulting in congruent indirect effects.

Conclusions: Empirical selection confirms discrepant mediation of the effects of D&T by IC and PD, marking these phenotypes as the most salient from a set of correlated mediators. Interventions targeted at improving IC and preventing downstream consequences of early PD will likely ameliorate psychiatric sequelae attributable to early-life adversity in the adolescent population.

Mental Health

Mental health treatment reported by U.S. workers before and during the COVID-19 pandemic: NHIS (2019-2020) Ja Gu* Ja Gu Luenda Charles Penelope Allison John Violanti Michael Andrew

Objectives: We compared the prevalence of mental health treatment before and during the COVID-19 pandemic among U.S. workers.

Methods: Self-reported mental health treatment data were obtained from the Longitudinal Adult Sample data of the National Health Interview Survey (NHIS) (2019 and 2020). Our final sample included 6,117 eligible workers (aged ≥18 years) from the 10,415 original participants. Mental health treatment was defined as having taken medication or received counseling from a mental health professional in the past 12 months. We calculated prevalence estimates and employed t-tests to compare mental health treatment in 2019 and 2020. Analyses were conducted in SAS callable SUDAAN 11.0 with survey sampling weight.

Results: The prevalence of mental health treatment significantly increased from 17.2% in 2019 to 19.1% in 2020 (difference=1.9%, p=0.001). The prevalence of taking medication for mental health significantly increased in 2020 compared to 2019 (14.5% vs. 12.7%, difference=1.8%, p<0.001) while the prevalence of receiving counseling or therapy did not change significantly (9.8% vs. 10.1%, difference=0.3%, p=0.530). In 2020, mental health treatment was highest among workers in the healthcare-related and protective services (26.4%), female workers (26.3%), and non-Hispanic whites (23.6%). The largest change in the prevalence of taking medication was among workers with household incomes ≤$35,000, from 12.8% in 2019 to 16.5% in 2020 (difference=3.7%, p=0.019).

Conclusion: U.S. workers, especially low-income and certain essential workers, experienced higher mental distress during the pandemic period compared to the pre-pandemic period. These findings highlight the need for targeted interventions to address mental health issues in these workers.

Alcohol Consumption and Mental Health during COVID-19 Pandemic Yihua Yue* Yihua Yue
Siyi Wang Ella Smith Divya Goyal Kexin Zhu Joanne Zhang Jo L. Freudenheim Lijian Lei Dwight A.
Hennessy Shauna C. Zorich Zuo-Feng Zhang Lina Mu

Alcohol Consumption and Mental Health during COVID-19 Pandemic

Yihua Yue[1], Siyi Wang[2], Ella Smith[3], Divya Goyal[4], Kexin Zhu[1], Joanne Zhang[5],

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Objectives: To investigate the associations between alcohol use and mental health during the
COVID-19 pandemic and if social determinants modify such associations.

Methods: An anonymous online survey was distributed among U.S. adults during May-August 2020.
We asked individuals' alcohol use during the pandemic and assessed their anxiety, depression,
stress, and post-traumatic stress disorder (PTSD) using Generalized Anxiety Disorder 7-item scale,
Patient Health Questionnaire-9, Perceived Stress Scale 4, and Primary Care PTSD Screen,
respectively. Multivariable logistic regression models were used to examine the association between
alcohol use and mental health symptoms. Stratified analyses were performed by age, gender, race,
social support, financial insecurity, and quarantine status.

Results: 3623 adults were included in the analytical sample. Compared to non-drinkers, individuals
who kept their drinking habits had lower odds of anxiety (OR=0.77, 95% CI: 0.63-0.95), depression
(OR=0.72, 95% CI: 0.59-0.88), stress (OR=0.78, 95% CI: 0.66-0.93), and PTSD (OR=0.73, 95% CI:
0.59-0.90), while those who increased alcohol use had higher odds of PTSD (OR=1.28, 95% CI:
1.02-1.61). Those who drank at least once a week or drank at least 10 drinks per month had lower
odds of depression than non-drinkers during the pandemic with ORs of 0.74 (95%CI: 0.61-0.91) and
0.75 (95%CI: 0.62-0.92), respectively. Individuals who reported any binge drinking had higher odds
of depression (OR=1.3, 95%CI: 1.06-1.59) and stress (OR=1.28, 95%CI: 1.06-1.54). Associations
between binge drinking and mental health symptoms are stronger among females, racial minorities,
those with financial or social insecurities, and those with restricted quarantine status.

Conclusions: More attention should be paid to those who increased their alcohol use or engaged in
binge drinking since the COVID-19 pandemic, especially for females, racial minorities, and those
with financial or social insecurities.

The influence of the Great Recession on adolescent major depressive episodes in the United States: An interrupted time series analysis Melanie S. Askari* Melanie S. Askari Katherine M. Keyes
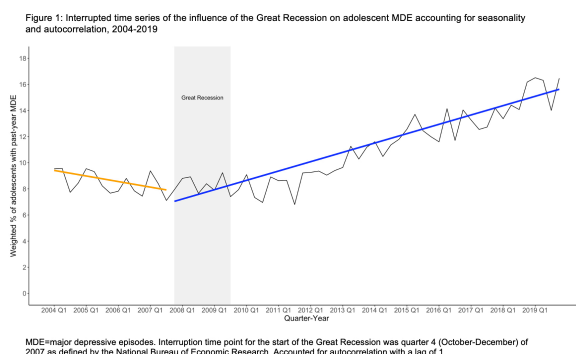
Background: Increases in adolescent depression beginning around 2008-2010 coincided with the timing of the Great Recession and there are many plausible mechanisms through which economic recessions can influence adolescent depression (e.g., caregiver job loss, household economic hardship). We aimed to assess interruptions in adolescent depression occurring at the beginning of the Great Recession.

Methods: We included adolescents ages 12-17 in the 2004-2019 National Survey on Drug Use and Health (N = 256,572). Past-year adolescent DSM-5 major depressive episodes (MDE) were assessed via self-report. Interrupted time-series (ITS) segmented regression models were used to estimate intercept-changes and slope-changes in adolescent MDE from pre-Great Recession (2004 to Fall 2007) to post-Great Recession (Winter 2007 to 2019), accounting for seasonality based on quarter-years (January-March, April-June, July-September, October-December) and autocorrelation with a lag of one quarter-year.

Results: Adolescent MDE increased by 80% from 8.80% in 2004 to 15.84% in 2019. Before accounting for seasonality, the Great Recession coincided with a change in slope of MDE (beta: 0.30, p-value < 0.01) but not a change in intercept of MDE (beta: -0.64, p-value: 0.40). After accounting for seasonality, the slope effects remained stable (beta: 0.29, p-value < 0.01) and intercept effects decreased by 20% (beta: -0.77, p-value: 0.30). MDE was significantly lower during Summer compared with Winter months (beta: -1.06, p-value < 0.01).

Conclusion: After adjusting for seasonality effects, the Great Recession still appeared to alter adolescent depression trends. Interventions should focus on supporting adolescents to mitigate negative consequences of recessions, particularly during Winter months. These ITS methods can inform future research on the implications of recessions (e.g., the COVID-19-related recession) for adolescent depression and the interplay with seasonality effects.
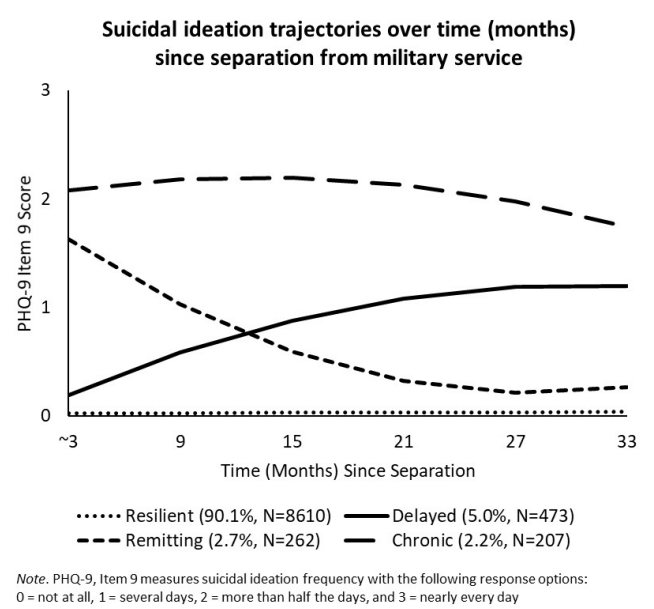
Figure 1: Interrupted time series of the influence of the Great Recession on adolescent MDE accounting for seasonality and autocorrelation, 2004-2019

MDE=major depressive episodes. Interruption time point for the start of the Great Recession was quarter 4 (October-December) of 2007 as defined by the National Bureau of Economic Research. Accounted for autocorrelation with a lag of 1.

Veteran well-being at the time of military separation uniquely predicts trajectories of suicidal ideation following separation from military service Claire Hoffmire* Claire Hoffmire Shelby Borowski Dawne Vogt

Background: The transition to civilian life after separation from military service presents both unique stressors (e.g., need to redefine occupational and social roles) which may increase suicide risk and opportunities to address these stressors via programs designed to support reintegrating veterans. This study examined the unique contribution of veterans' initial post-military vocational, financial, and social well-being to their trajectory of suicidal ideation (SI) during the three years following military separation.

Methods: The Veterans Metrics Initiative population-based, longitudinal cohort study of post-9/11 Veterans' reintegration experiences (n = 9552) examined Veterans' well-being using the Well-Being Inventory and assessed SI using item-9 of the Patient Health Questionnaire-9. Latent Growth Models were used to identify discrete classes characterized by trajectories of change over time in SI frequency. Multinominal logistic regression models were used to evaluate the association between each well-being domain and SI trajectory class membership, adjusting for demographic, military history, and mental health (depression, alcohol misuse, posttraumatic stress disorder) covariates.

Results: Higher levels of vocational, financial, and social well-being at the time of military separation were associated with significantly lower likelihood of experiencing high-risk SI trajectories (delayed onset, remitting, chronic; Figure 1). All associations remained significant after accounting for covariates. Social well-being was most strongly associated with a reduced likelihood of experiencing delayed (OR=0.68; 95% CI = 0.60, 0.78), remitting (OR=0.60; 95% CI = 0.48, 0.76), and chronic (OR=0.68; 95% CI = 0.54, 0.85) SI.

Conclusion: Knowledge of veterans' well-being at the time of separation from military service can be used to identify those who are more likely to experience high-risk SI trajectories and reduce veteran suicide risk.

Suicidal ideation trajectories over time (months) since separation from military service

Note. PHQ-9, Item 9 measures suicidal ideation frequency with the following response options: 0 = not at all, 1 = several days, 2 = more than half the days, and 3 = nearly every day

Mental and Physical Health Before During and After the COVID-19 Pandemic Michaela George* Michaela George Samantha Brown Kelly McDermott

Background: Physical, emotional and social changes, and exposure to certain behaviors can increase an adolescents vulnerability to mental and physical health problems. There is limited research into whether the COVID-19 pandemic has led to a change in mental and physical health and in that relationship has led to an increase in risky behaviors among adolescents. This study aims to examine the change in self reported mental and physical health among adolescents pre, during, and post the COVID-19 pandemic.

Methods: A multi-year stratified study was conducted with data that was obtained each year from 2018-2022. Participants were college aged young adults between the ages of 18- 29 years old. Multivariate regression analysis and ANOVA will examine the relationship between self reported mental and physical health and risky behaviors.

Results: This research will aim to see how the COVID-19 pandemic has impacted self reported physical and mental health controlling for behavioral patterns and risky behaviors in young adults between the ages of 18 and 29 years old. The results of this study are hypothesized to show a decrease in self-reported mental health during the pandemic and post pandemic.

Discussion: With the results from this study, public health interventions can be directed towards our study population. Connecting with community partners who work with young adults will allow the researchers to better understand how these individuals have been impacted by COVID-19 and which programs can be created to help.

Social media intensity, loneliness, and anxiety among Peruvian adolescents during the COVID-19 pandemic Elizabeth Sherwin* Elizabeth Sherwin Marjolein Bardense Ronald Dahl Lucia Magis-Weinberg

Introduction: The impact of social media on adolescent mental health is debated. Current evidence, relying mostly on cross-sectional studies in the Global North, is mixed. We examine the longitudinal, bidirectional associations between social media intensity (SMI) and loneliness and anxiety across 15 months of COVID-19 quarantine for Peruvian adolescents.

Methods: A total of 455 adolescents (grades 6-8) in Perú completed surveys on symptoms of anxiety, loneliness and SMI (Ellison et al., 2007) in May 2020, November 2020, and July 2021. We ran multigroup bivariate latent change score models by gender to assess the cross-sectional and longitudinal relationships between SMI-loneliness and SMI-anxiety.

Results: At baseline, SMI was positively associated with loneliness for females, and SMI was positively associated with anxiety for both genders. SMI was not associated with change in loneliness from May to Nov 20 ($p_{female} = 0.11$; $p_{male} = 0.70$) or Nov 20 to Jul 21 ($p_f = 0.14$; $p_m = 0.93$). Loneliness was not associated with change in SMI from May to Nov 20 ($p_f = 0.40$; $p_m = 0.36$) but loneliness in Nov 20 was positively associated with change in SMI from Nov 20 to Jul 21 for females ($p_f < 0.01$; $p_m = 0.62$). For females, SMI was positively associated with change in anxiety from May to Nov 20 ($p_f = 0.04$; $p_m = 0.76$) and Nov 20 to Jul 21 ($p_f = 0.02$; $p_m = 0.15$). Anxiety was not associated with change in SMI from May to Nov 20 ($p_f = 0.72$; $p_m = 0.73$) or Nov 20 to Jul 21 ($p_f = 0.25$; $p_m = 0.56$).

Conclusions: Female adolescents were more susceptible to increases in feelings of loneliness and anxiety across 15 months of COVID-19 in Perú. Among females, higher feelings of loneliness were associated with an increase in SMI, and higher SMI was associated with an increase in feelings of anxiety. The reverse relationships were not found. Our findings capture the experiences of early adolescents in low-and middle-income urban settings in Perú, an underrepresented sample in the literature.

Mental Health
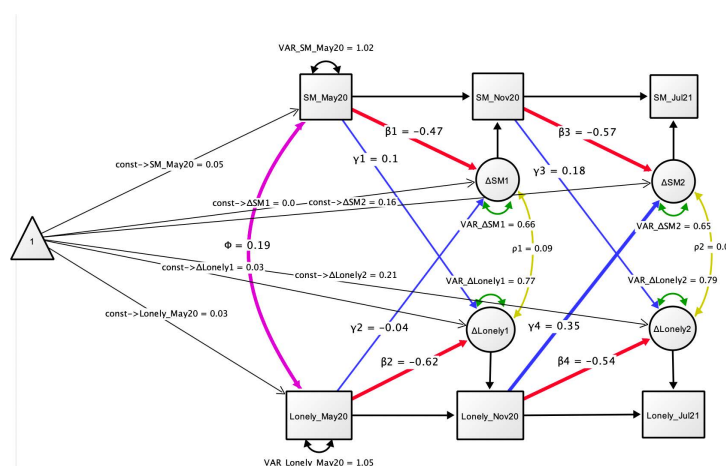
Relationship of brain volumes with behavioral inhibition and anxiety disorders in children: Results from the ABCD study Rawan Hammoud* Rawan Hammoud Lara Abou Ammar Stephen McCall Martine ElBejjani

Anxiety disorders (AD) are common, have an early onset, and severe impact. A key early predictor of AD is behavioral inhibition (BI), a childhood tendency for high caution, avoidance, and fearfulness in novel and unfamiliar situations. In parallel, MRI studies have been identifying brain changes associated with AD, although results remain mixed, even for main candidate regions such as the amygdala. Moreover, the links between behavioral and neurobiological risk of AD remain unclear, particularly at a younger age. This study evaluates the relationship of candidate brain volumes of AD and mental health outcomes with BI and AD among children. Using data from the Adolescent Brain Cognition Development (ABCD) study, we analyzed total and regional brain volumes of 9,645 children (9-10 years old) in relation to BI (Behavioral Inhibition/Behavioral Approach System scale) and AD (Kiddie Schedule for Affective Disorders and Schizophrenia), using linear mixed models adjusting for family clustering and important demographic and socioeconomic covariates. Amygdala volume was not related to BI; larger total white matter (Beta=-0.003; 95%CI: -0.005, -0.0001) and thalamus (Beta =-0.103; 95%CI: -0.190, -0.016) volumes were related to lower BI scores, and larger total hippocampal volume (Beta =0.121; 95%CI: -0.001, 0.244) was associated with higher BI. None of the brain regions studied was associated with AD. Interestingly, past but not current anxiety was associated with smaller total gray and white matter volumes. Results show associations between childhood BI and brain volumes in children. Compared to other reported findings, our results also highlight the importance of accounting for socioeconomic factors in studies of brain volumes and mental health. Finally, results suggest that earlier occurrences of AD may influence brain structures at this young age, motivating longitudinal studies on the links between brain and mental health and the earlier development of AD risk.

LATEBREAKER

Mental Health

Widening Racial and Ethnic Disparities in Mental Health Treatment Following Medicaid Expansion: A State-level Analysis from 2002-2019 Stephen Uong* Stephen Uong Navdep Kaur Riley M. Nesheim-Case Pia M. Mauro

Introduction

We evaluated if state-level Affordable Care Act (ACA) Medicaid expansion could be driving persistent racial/ethnic disparities in mental health treatment. We estimated mental health treatment prevalence differences in states that expanded Medicaid access, comparing pre- and post-ACA implementation (starting in 2014) and across race/ethnicity.

Methods

We obtained state-level biennial mental health treatment prevalence overall and by racial/ethnic group (Hispanic, Non-Hispanic Black [Black], Non-Hispanic White [White]) from the 2002-2019 National Surveys on Drug Use and Health, Medicaid expansion data from the Kaiser Family Foundation, and state covariates from the U.S. Census (population density, median income, poverty, unemployment, proportion age > 26). Linear mixed models tested state-level mental health treatment prevalence differences by Medicaid expansion (no expansion, pre-ACA, post-ACA), overall and by race/ethnicity, using state random intercepts and adjusting for year and state-level covariates.

Results

Across all years and states, mental health treatment prevalence was 11.1% among Hispanic, 10.4% among Black, and 17.0% among White people (15% overall). Compared to the pre-ACA implementation period, mental health treatment overall adjusted prevalence in states post-ACA implementation increased by 0.6% (95% CI: 0.1%, 1.1%). Mental health treatment prevalence among White people increased 2.3% (95% CI: 0.8%, 3.8%) post- vs. pre-ACA implementation. However, mental health treatment prevalence among Black and Hispanic people living in states post-ACA did not change, resulting in significantly lower prevalence changes than among White people post-ACA (-2.5% [95% CI: -0.7%, -4.4%] and -2.0% [-0.2%, -3.7%], respectively) (p-interaction < 0.05).

Discussion

Medicaid expansion may have exacerbated racial/ethnic disparities in state-level mental health treatment. The persistence of inequitable public insurance access remains a barrier to care after the ACA.
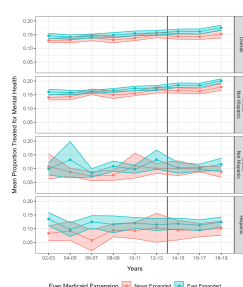
**Investigating the association between inflammation and depression using prospective cohort and genetic approaches** Daisy Crick* Daisy Crick Gemma Clayton Neil Goulding Alice Carter Deborah Lawlor Sarah Halligan Golam Khandaker Carolina Borges Abigail Fraser

Background: Major Depressive Disorder (MDD) is one of the most prevalent psychiatric disorders worldwide, yet its pathogenesis is not fully understood. Studies have identified a link with inflammation, but causality and directionality are unclear. Glycoprotein Acetyls (GlycA) is a novel composite inflammatory biomarker that may help clarify this relationship. We investigated the bidirectional relationship between GlycA and depression, observationally and using Mendelian Randomization (MR).

Methods: We used the Avon Longitudinal Study of Parents and Children (ALSPAC) to investigate the observational association between GlycA and depressive score (measured by the Short Mood and Feelings Questionnaire) (N=1741) and vice versa (N=2244) measured at ages 18y and 24y. For the MR approach we used the UK Biobank (UKBB) GWAS for GlycA (N=115,078), Psychiatric Genomics Consortium and UAS for Major Depressive Disorder (MDD) (N=500,199) and Social Science Genetic Association Consortium GWAS for depressive symptoms (N=161,460). We used the Inverse Variance Weighted (IVW) method and MR-Egger, Weighted Median, Weighted mode, MR-PRESSO, MR-Lap and Multivariable MR (MVMR; adjusting for Body Mass Index (BMI)) were conducted as sensitivity analyses.

Results: After adjusting for confounders (maternal education qualification, participant age, smoking status, drinking status, BMI and ethnicity) we found no associations between GlycA and depression (or vice versa). The MR results are presented in figure 1, where we only found a positive effect of MDD on GlycA (mean difference = 0.09; 95% CI: 0.03, 0.16). The effect was strengthened (0.24; 0.19, 0.29), in MVMR when adjusting for BMI, while the effect of GlycA on MDD attenuated further to the null.

Conclusion: We found no consistent effect of GlycA on depression, whilst MR analyses suggest that a greater genetic propensity for depression causes higher GlycA. Further research is needed to identify potential mechanisms.
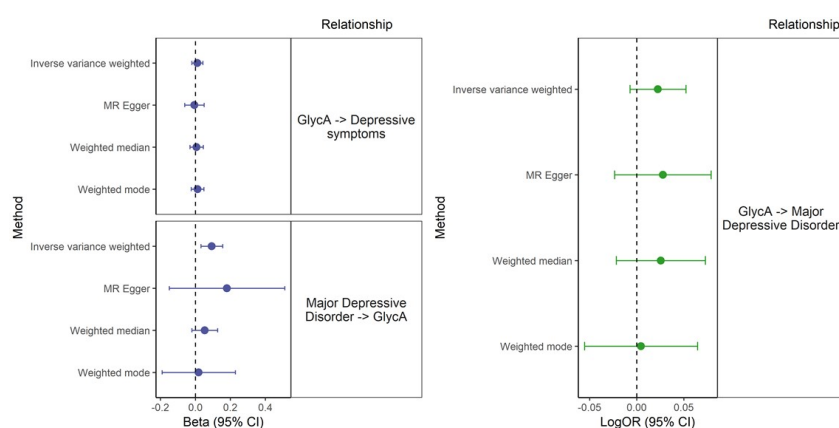
LATEBREAKER

Mental Health

Perceived Stress of Parents and Child Mental Health During the Covid-19 Pandemic

Fareedat Bello* Fareedat Bello Elizabeth Vasquez Melissa Tracy David Nicholas

Abstract

Background: The COVID-19 pandemic led to changes in children's routines, including altered school routines, social isolation, and limited peer and play activities. Parental stress is a significant risk factor for child mental health issues including anxiety and stress. In addition, children's mental health may be affected differently depending on the developmental age of the child. This study aimed to examine the relationship between parental stress and stress/anxiety of children during the pandemic while considering moderating role of a child's age.

Methods: Data from the COACH-NY Study was used for this study. Primary caregivers living in New York state were recruited through social media and other personal and professional networks, resulting in a convenience sample of 641 households. The Perceived Stress Scale was used to assess the stress levels of primary caregivers. Stress/anxiety of children was examined using primary caregiver's reports. Univariate analyses, bivariate analyses, and multivariable Poisson regression were used to assess the relationship between parental stress and child stress/anxiety while controlling for confounders.

Results: The prevalence of increased stress/anxiety since the pandemic began among children was 33% in our study. In the adjusted model, we found that among children with primary caregivers experiencing high perceived stress, the prevalence of increased stress/anxiety was 1.49 times [95% CI: 0.98 – 1.53] that of children with primary caregivers not experiencing high perceived stress. We also found that among older children, the prevalence of increased stress/anxiety comparing children with primary caregivers reporting high perceived stress to children with primary caregivers not reporting high perceived stress was significantly higher than among younger children [PR: 1.68; 95% CI: 1.20 – 2.37 vs. PR: 1.04; 95% CI: 0.77 – 1.38].

Discussion: Primary caregivers are facing increased stress since the pandemic began and this reflects upon the mental health of their children. Among older children, home confinement and lack of peer interaction may further increase the impact of primary caregiver stress on child stress/anxiety. Primary caregivers and children need mental health support in the post-pandemic phase. Longitudinal studies are also needed to examine the long-term consequences of the impact of the pandemic on both primary caregivers and children**.**

Test-retest reliability of self-reported medical history, family history, and common risk factors in the Environmental Health Study for Western New York Cohort (EHSWNY)

Samantha Smith* Samantha Smith Denise Feda Lina Mu James Olson Laurene Tumiel-Berhalter Matthew Bonner

Background/Purpose: Self-reported questionnaires allow for timely and affordable collection of data in large epidemiologic studies. We examined the reliability of questions used to assess medical and family history and selected characteristics in a general population cohort. Methods: EHSWNY is a prospective cohort study designed to investigate industrial pollution and health. We enrolled adults who resided in several western NY communities (N=13,306), using a self-administered mailed questionnaire or an identical online version. Multiple participants submitted duplicate baseline questionnaires (N=295); the median time between the two iterations was 16 days (IQR=1-32). We compared these two iterations to determine reliability, using Cohen's kappa (K), weighted kappa (Kw), percent agreement, and intraclass correlation coefficient (ICC). Results: Common medical conditions like high blood pressure and cholesterol yielded excellent reliability (K=0.80; 95% CI: 0.71, 0.89; K=0.76; 95% CI: 0.66, 0.86). Medical history of cancers ranged from K=0.67 (95% CI: 0.05, 1.0) for colorectal to K=1.00 (95% CI: 1.0, 1.0) for leukemia/lymphoma. Family history of breast cancer had the highest reliability (K=0.81; 95% CI: 0.72, 0.91) and non-melanoma skin cancers had the lowest (K=0.47; 95% CI: 0.28, 0.65). All selected characteristic questions had a reliability ≥ 0.64. Self-reported smoking status and vaping use had excellent reliability with Kw=0.92 (95% CI: 0.86, 0.98) and K=0.75 (95% CI: 0.59, 0.91), respectively. Ability to recall height and weight at age 18 showed excellent reliability (ICC=0.98; 95% CI: 0.97, 0.98; ICC=0.96; 95% CI: 0.94, 0.97). Conclusion: Our questionnaire demonstrated fair-to-excellent test-retest reliability of self-reported medical and family history and selected factors. Although we did not assess validity, self-reported information collected via questionnaire can be used to generate reliable data in epidemiological studies of the general population.

Mendelian randomization selection bias investigation: effect of testosterone on breast cancer Kezhen Fei* Kezhen Fei C. Mary Schooling

Background: The effect of testosterone supplements on breast cancer is not well established, although both observational and mendelian randomization (MR) studies (i.e., instrumental variable analysis with genetic instruments) suggest testosterone increases risk of breast cancer. However, women who die of breast cancer before recruitment into a study are typically not included although the exposure lasts throughout adult life, which could generate selection bias on survival. This study evaluated the influence of selection bias for testosterone on breast cancer in the UK BioBank by comparing estimates for groups more or less open to selection bias, i.e., participants' self-report, compared to proxy reports for participants' mothers and siblings as control outcomes.

Methods: MR estimates were obtained using inverse variance weighting with the weighted median and MR-Egger as sensitivity analysis.

Results: Using the female testosterone instruments derived from the UK BioBank, no significant association was observed with self-reported breast cancer among UK BioBank participants (odds ratio (OR)=1.05; 95% confidence interval (CI): 0.96, 1.14, cases=10,303, controls=452,630). But testosterone increased the risk of breast cancer among UK BioBank participants' siblings OR=1.11 (95% CI: 1.05, 1.17, cases=16,586, controls=345,223) and their mothers OR=1.12 (95% CI: 1.08, 1.16, cases=35,102, controls=388,356).

Conclusion: These different estimates for self and proxy -reported outcomes provide evidence that the observed null effect in self-reports is possibly due to selection bias. Given, MR estimates are particularly vulnerable to selection bias because of the time lag between allocation to genetic instrument (at conception) and recruitment, here in late middle-age, other strategies to assess this concern should also be identified and evaluated.

Application Of Machine Learning Algorithms To Develop A Sampling Strategy For Estimating Ward-Level Malaria Prevalence and Related Risks In A Nigerian City Eniola Bamgboye* Eniola Bamgboye Ifeoma Ozodiegwu

Environmental conditions due to unplanned urbanization have been implicated in the creation of favorable habitats for mosquito breeding and thus result in city-level heterogeneities in malaria transmission. Unplanned urbanization may have accounted for the recent increases in malaria burden in Nigerian cities. Representative estimates of malaria prevalence and related risk factors within city localities are needed to inform intervention planning. Wards are small scale administrative units in Nigeria, which can be easily identified for intervention targeting by malaria programs in cities. However, cities comprise of numerous wards and taking samples from each of them is infeasible in settings with limited resources. Factors relating to malaria transmission could be used to group geographic areas with similar potential for transmission. We apply a clustering algorithm based on Gaussian finite mixture models, an unsupervised machine learning classification technique, to categorize 75 wards in Ibadan metropolis area and identify representative wards for sampling. Clusters were categorized using population size and density, settlement type, a measure of settlement informality based on road accessibility, housing type, enhanced vegetation index and distance to water bodies. Optimal number of clusters was determined using an elbow plot. Results were validated through consultation with local experts. Majority of city inhabitants reside at the boundaries while a higher level of settlement informality and population density existed at the city center. Wards at the city outskirts had a farther distance to water bodies. Four archetype ward clusters were identified. Additional validation will be undertaken from a field study by comparing malaria prevalence estimates from wards in the same cluster. Our study presents a cost-effective technique for generating estimates of disease burden in unsampled locations.

Inverse probability weighting to estimate exposure effects on the burden of recurrent outcomes in the presence of competing events Charles Gaber* Charles Gaber Jessie Edwards Jennifer Lund Anne Peery David Richardson Alan Kinlaw

Background: Recurrent events are common in epidemiologic research. Studies involving recurrent events often focus on time to first occurrence or on event rates which assume constant hazards over time. The Dong-Yasui estimator of the mean cumulative count is a powerful alternative for recurrent event analysis, but its use is limited to settings with expected balance in baseline confounders (as in a randomized trial).

Methods: We contextualized recurrent event parameters of interest using counterfactual theory in a causal inference framework and described an approach for estimating a target parameter referred to as the mean cumulative count. We introduced an inverse-probability of treatment weighted adaptation of the Dong-Yasui estimator that allows one to use this estimator in observational studies with imbalance in measured confounders. We performed simulations to demonstrate the unbiased estimation of the mean cumulative count using the weighted Dong-Yasui estimator under various effect sizes and with known confounding.

Results: Simulation results under a null exposure effect are displayed in Figure 1. The true mean cumulative count by exposure group is shown in panel A. The unweighted Dong-Yasui estimator yielded biased estimates of the mean cumulative count due to the confounding we introduced (grey lines of panel B). When our inverse-probability weighted adaptation of the Dong-Yasui estimator was used to control for these confounders, our weighted estimates (black lines of panel B) recovered the true mean cumulative counts and provided unbiased estimates contrasting the mean cumulative count between exposure groups. Similar results were found in simulations testing small and large effect sizes.

Conclusion: The weighted Dong-Yasui estimator for the mean cumulative count allows researchers to use observational data to estimate and contrast the expected number of cumulative events experienced per individual by a given time point across exposure groups.

Figure 1. Graphical results of a simulation displaying recovery of the true population parameters under a null effect with known confounding
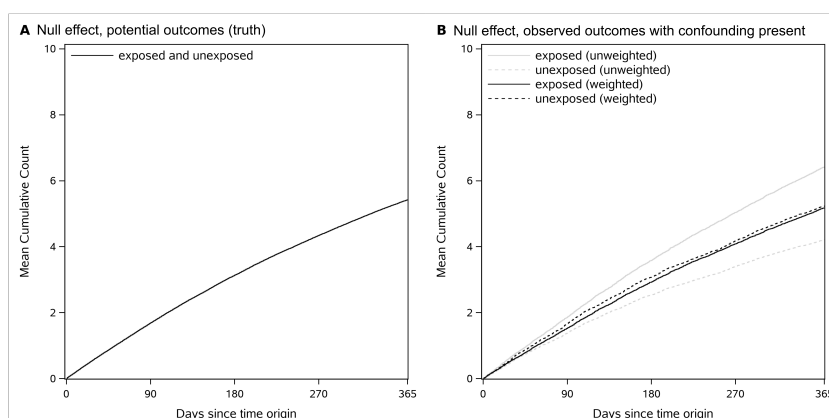
Connecting the DAGs: How to Use a Directed Acyclic Graph to Inform Data Analysis Ruby Barnard-Mayers* Ruby Barnard-Mayers Eleanor Murray

Background: Directed Acyclic Graphs (DAGs) are becoming a more commonly used research tool in epidemiology and health research. However, reviews of published DAGs demonstrate flaws in the application of this tool, including incorrectly designed DAGs that do not comply to the underlying rules, as well as references to DAGs without showing the graph or describing how it informed the analysis. Qualitative research suggests that an important barrier to the widespread adoption and improved use of DAGs in epidemiologic and health research is the lack of training materials. In particular, there are few existing examples describing how to translate a given DAG into a valid data analysis plan.

Methods: In this project, we work through a series of published DAGs describing how to translate these into analytic plans for the estimation of causal effects. Steps in this process include DAG factorization, and differentiation between DAG-implied non-parametric modeling choices and parametric modeling decisions that must be added to the information contained in the DAG.

Results: Using DAGs from infectious disease epidemiology, reproductive epidemiology, cardiovascular disease, musculoskeletal disorders, and social epidemiology, we show how the DAG factorization corresponds to the main data analysis, and how a DAG can used to guide sensitivity analyses and quantitative bias analyses to assess uncertainty related to causal assumptions.

Conclusions: DAGs are critical for data analysis, and incorrect usage of the DAG or the incorrect DAG can lead to inaccurate effect estimates.
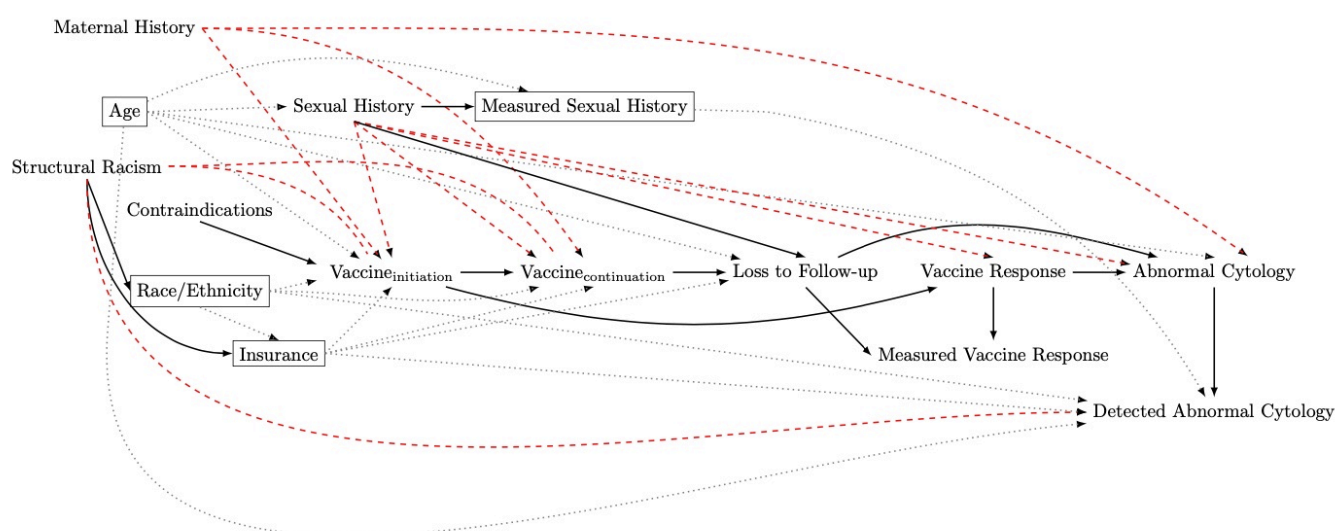
Use of Nested Imputation in a Study with Different Patterns of Missing Exposure and Covariate Data Michelle S. Mellers* Michelle S. Mellers Jennifer A. Rusiecki Shuangge Ma Celia Byrne

Introduction: In epidemiology studies laboratory measurements are often missing at lower levels below the limit of detection (LOD), while other variables are missing across the spectrum of values. Nested multiple imputation (NMI) is one approach not often used in epidemiologic studies, to deal with two types of missing data when the distribution of those missing differs for each variable.

Methods: We compared results from generalized additive models using NMI, complete case (CC), and substitution (S) methods to evaluate associations between persistent chemicals (PC) and thyroid hormone levels from serum from US military service members. For the 21 chemicals, from 1% to 46% of subjects had values below the LOD. 43% of subjects had missing BMI. Step 1 of the NMI imputed BMI, and in step 2 each PC is imputed, nested within each imputation of BMI. With SAS 9.4 and R 4.1.0, we applied Lubin's approach for chemical imputation and predictive mean matching for BMI imputation. For S techniques the lipid adjusted LOD divided by $\sqrt{2}$ and mean value replaced missing chemical and BMI values, respectively.

Results: The analyses of PCB 183 (46% missing) and total thyroxine (TT4) illustrated differences in results. The CC analysis included only 148 individuals compared to 721 in the NMI and S analyses. In the CC analysis PCB 183 had no effect on TT4 level (p=0.62), while both NMI (p=0.014) and S (p=0.011) procedures suggested lower TT4 levels among those with higher PCB 183 levels. Unlike the NMI results the S approach suggested an increase of TT4 below the LOD.

Conclusion: Interpretation of the impact of chemicals on thyroid hormones using the NMI approach differed from the CC technique and in the shape for the area imputed by the S technique. NMI allowed for different distributions of the missing variables using all available data, while acknowledging a degree of uncertainty.
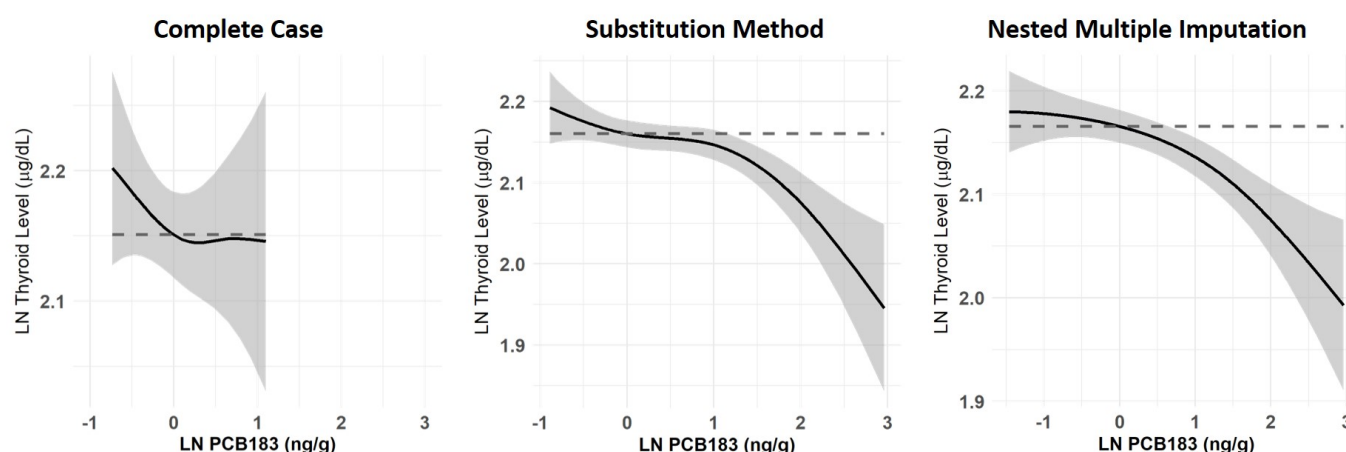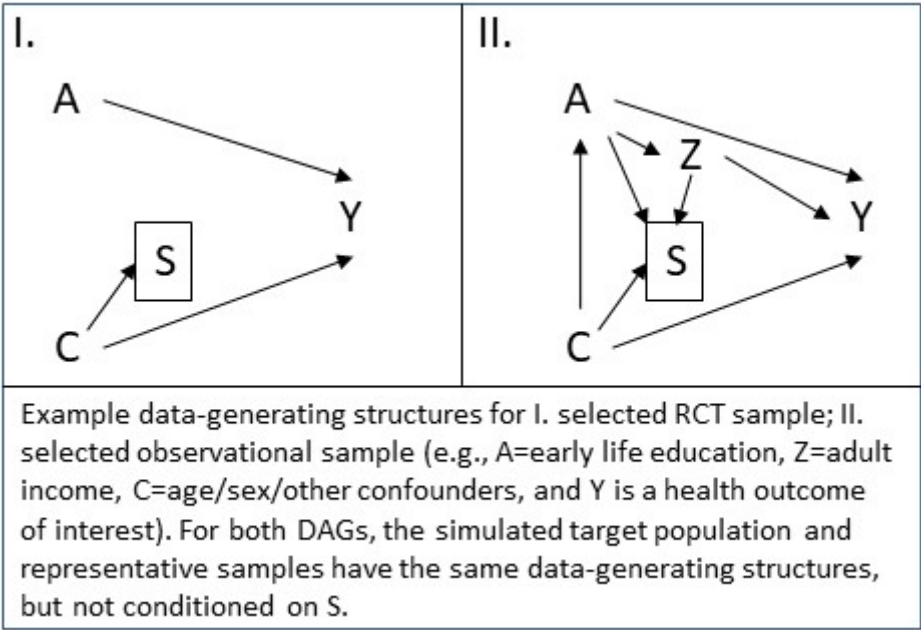
Figure 1: Polychlorinated biphenyl 183 and total thyroxine (TT4). Results of the GAM model indicated by black line, grey area represents the 95% CI, and dotted line shows model without the effect of the chemical measurements.

Average treatment effects in synthetic samples with equitable representation Kenneth Nieser* Kenneth Nieser Amy Cochran

Clinicians rely on population-based inferences to inform care decisions for individuals. If treatment effects vary across population subgroups, inferences blind to this variation will tend to generalize worse for subgroups underrepresented in the study sample. Our goal was to investigate how the disparity in generalizability could be reduced during data analysis. We propose a definition of equity in representation which requires separate data samples for each subgroup. We derived a reweighting estimator, like those developed for generalizability and transportability, that adheres to our definition and can be implemented multiple times to generate various synthetic samples. Non-zero weights are assigned to all individuals, not just those in the subgroup of interest, with the intention of borrowing information across subgroups to improve estimation. To evaluate this approach, we conducted simulations of randomized controlled trials (n=400) with 10,000 replications in which the effect of a binary treatment varied across two subgroups. Treatment assignment indicators were simulated with probability 0.5; group indicator variables were simulated with probabilities 0.9 and 0.1. Continuous outcomes were simulated such that the expected values of subgroup treatment effects were 2 and -2. We compared the subgroup-specific mean-squared errors of the proposed estimator using three different choices of weights with those from subgroup stratification and from a random effects model. We found that our estimator was able to slightly reduce the mean-squared error of the minority group without greatly increasing the mean-squared error of the majority group, relative to the stratified estimator. When baseline outcomes were the same across subgroups, a random slope estimator yielded the lowest mean-squared errors of subgroup-specific effects. In the future, we plan to explore alternate weighting schemes and their impact on estimates in different scenarios.

Transportability methods for observational data: the importance of estimators that can handle selection on mediators Eleanor Hayes-Larson* Eleanor Hayes-Larson Daniel Westreich Marissa J Seamans M Maria Glymour Elizabeth Rose Mayeda

Transportability methods like g-computation and inverse odds of selection weighting (IOSW) were developed to extend inferences from randomized controlled trials to target populations. are also critically needed for observational data, but confounding, selection on the exposure yielding collider bias, and selection on post-treatment covariates (particularly mediators of exposure-outcome effect) are additional challenges. For example, many studies have selection on adult income, often considered a mediator of the effect of early life education, which should therefore not be controlled in studies on the total effect of education on later-life health outcomes. As a result, causal identification conditions for target population effects can be difficult to meet (e.g. if there is no sufficient set that accounts for non-exchangeability between study and target and does not include post-treatment covariates). We conducted simulations to clarify when unbiased estimates for the target effect can be obtained from observational data and evaluate estimator performance. We simulated a target population of all California adults age 65+, and from this, drew both a representative sample (analogous to the American Community Survey or other dataset typically used to represent the target in transportability analyses) and a selected sample (analogous to cohorts with detailed measures of health outcomes). We examined multiple scenarios with varied data-generating rules (examples in Figure), and conducted transportability analyses from the selected sample to the representative sample with seven estimators, including both g-computation and IOSW approaches. We showed that to yield unbiased estimates of the target causal effect, estimators must: 1) account for all selection variables, including mediators, to overcome non-exchangeability between study sample and target, but 2) adjust only for confounding variables when addressing non-exchangeability between exposed and unexposed.

Example data-generating structures for I. selected RCT sample; II. selected observational sample (e.g., A=early life education, Z=adult income, C=age/sex/other confounders, and Y is a health outcome of interest). For both DAGs, the simulated target population and representative samples have the same data-generating structures, but not conditioned on S.

Quantitative bias analysis of the oral-systemic connection in the context of fecundability
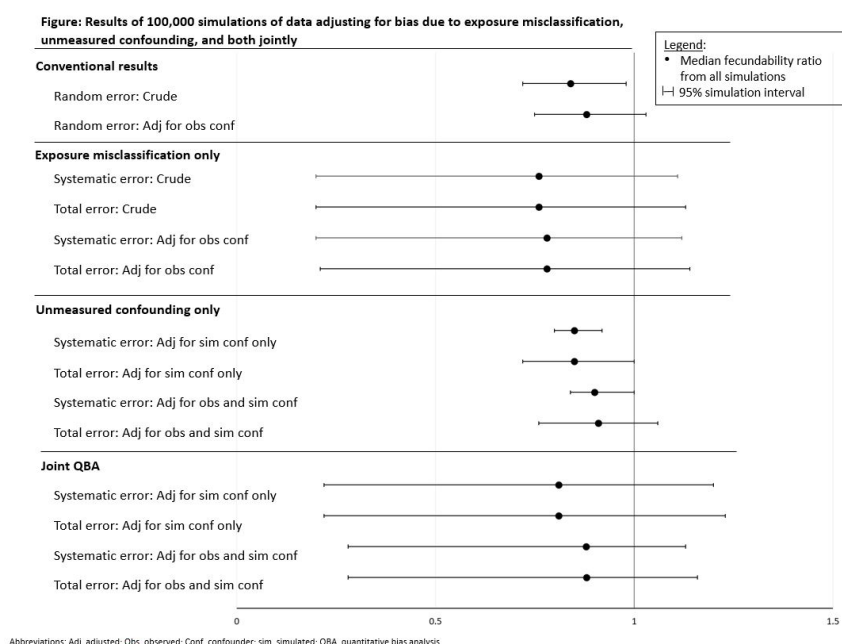
Julia Bond* Julia Bond Brenda Heaton Lauren A Wise Matthew P Fox

Background: Quantitative bias analysis (QBA) enables researchers to estimate the influence of biases on the magnitude, direction, and uncertainty of observed associations using estimates of relevant bias parameters and a model relating these parameters to the observed data. We used QBA to estimate the potential influence of exposure misclassification and unmeasured confounding, separately and jointly, on findings evaluating periodontitis and time-to-conception among 2,764 participants from Pregnancy Study Online (PRESTO), a North American preconception cohort study.

Methods: We used published literature to identify estimates for bias parameters, specifically: confounder prevalence in the exposed (~beta(220.87,226.13), median=0.49) and unexposed (~beta(508.34,831.66), median=0.38), effect of the confounder on the outcome (triangular distribution, min 0.32, mode 0.53, max 0.87), exposure sensitivity (~beta(9,19), median=0.32) and specificity among those with (~beta(68,4), median=0.94) and without the outcome (~beta(69,3), median=0.96). We ran 100,000 Monte Carlo simulations, randomly sampling from the distributions and using standard formulas to adjust the observed fecundability ratio (FR) using sampled values. We summarized simulations accounting for systematic and random error using the median as the point estimate and 2.5^{th}-97.5^{th} percentiles as a 95% simulation interval.

Results: The conventional adjusted FR was 0.89 (95% CI 0.75-1.06) comparing those with periodontitis to those without. After adjusting for exposure misclassification only, the FR was 0.78 (95% simulation interval [SI] 0.21-1.14). After adjusting for unmeasured confounding only, the FR was 0.91 (95% SI 0.78-1.06). Joint adjustment resulted in an FR of 0.88 (95% SI 0.28-1.16).

Discussion: Our results provide insights about the potential influence of these biases on our previous findings and suggest that accounting for these biases may change the interpretation of our observed estimates.

Figure: Results of 100,000 simulations of data adjusting for bias due to exposure misclassification, unmeasured confounding, and both jointly

Abbreviations: Adj, adjusted; Obs, observed; Conf, confounder; sim, simulated; QBA, quantitative bias analysis

Impact of coarsened exposures on falsification approaches for Mendelian randomization

Elizabeth Diemer* Elizabeth Diemer Sonja Swanson Joy Shi Miguel Hernan

Mendelian randomization (MR) is an increasingly popular method that, like all methods, requires strong unverifiable assumptions to estimate causal effects. Importantly, the MR assumptions can be falsified using a method known as the instrumental inequalities. Because these constraints only arise when exposures are categorical, the only option for applying the instrumental inequalities in settings with continuous exposures is to somehow categorize or coarsen the exposure. However, coarsening a truly continuous exposure can itself lead to MR assumption violations. Violations of the instrumental inequalities for an MR model with a coarsened exposure might therefore reflect the effect of coarsening rather than other sources of bias. We aim to explore the ability of the instrumental inequalities to detect bias resulting from coarsened exposure variables in MR models with multiple proposed instruments under various causal structures. We simulated data under a variety of exposure-outcome relationships in which the MR assumptions were met for a continuous exposure. We then categorized the exposure into different numbers of quantiles, and applied the instrumental inequalities to MR models for the effects of exposure quantiles. We discuss how the performance of the inequalities in realistic scenarios is affected by the number of proposed instruments, coarsening strategy, and the nature of the true exposure-outcome relationship, as well as the implications of these findings for the use of the instrumental inequalities in MR.

Lord's 'paradox' explained: The 50-year warning on the analyses of 'change scores' Peter
WG Tennant* Peter WG Tennant Georgia D Tomova Kellyn F Arnold Mark S Gilthorpe

In 1967, Frederick Lord posed a conundrum that has confused scientists for over half a century.
Since termed Lord's 'paradox', the puzzle centers on the observation that the two most common
approaches to analyses of change between two time-points – either (1) analyzing the 'change score'
(i.e. follow-up minus baseline variable) or (2) analyzing the follow-up conditional on baseline – can
produce radically different, even sign-discordant, results. By revisiting the philosophy of change and
using contemporary causal inference methods, this study explains the 'paradox' and highlights the
wider lessons for data science.

The solution to Lord's 'paradox' begins with distinguishing between the three reasons for a variable
changing value. 'Endogenous change' represents scale changes due to the realization of past events,
'random change' represents changes due to random or enigmatic processes and 'exogenous change'
represents all non-endogenous, non-random change.

In most situations, exogenous change is the only component with any real-world meaning or utility.
Alas, in observational data, neither analytical approach can robustly estimate the causes of
exogenous change. Approach (2) is susceptible to mediator-outcome confounding, and there is
generally insufficient data to distinguish exogenous change from random change. Approach (1)
evaluates obscure estimands with little, if any, real-world interpretation. Accurate and precise
estimates instead require the use of appropriate causal inference methods (such as g-methods) and
more than two measures of the outcome variable.

Despite several eccentricities, Lord's original puzzle provides several key lessons for contemporary
data science, including the importance of considering causal questions within a causal framework,
the importance of clearly identifying an estimand, and the dangers of analyzing change scores in
observational data.

Identifying Underlying Patterns in Neighborhood Disorder Data Via Multiple Correspondence Analysis Christopher Pierson* Christopher Pierson Edward Peters Andrew Lawson Steve Mooney Joellen Schildkraut

Ovarian cancer (OC) is the fifth-leading cause of cancer deaths in women in the US. While the incidence of ovarian cancer is 25% lower in Black women compared to White women, the 5-year survival for Black women is 10% lower than White women. Recent evidence suggests that health disparities can be partly explained by neighborhood social and environmental factors such as disadvantage or disorder. To test whether objective neighborhood disorder is associated with OC incidence and survival we developed a novel approach using Google Street View (GSV) to estimate neighborhood disorder (ND) at the block group level within a large multi-center study of women diagnosed with OC (AACES).

AACES participants resided in 544 unique block groups at diagnosis. We sampled 5 points on the underlying street network in each block group and audited GSV images at these points, ultimately completing audits at 2,720 locations. Audit questions assessed the presence of different types of land use, quality of the built structures, and presence of other markers of ND.

To understand underlying patterns in the ND data, multiple correspondence analysis (MCA) was completed. Analysis focused on 17 audit questions with variance in responses and no missing values. Using a 2-dimension model, we observed 1 dimension associated with an absence of residential units (coordinate estimate: .411), specifically detached single-family homes (.351), and the absence of sidewalks (.234), and another was positively associated with a presence of recreational facilities (.703), land uses such as schools and municipal buildings (.488), multi-family residential (.435), and the absence of agricultural land use (.290).

These findings suggest that a naïve application of an MCA model to ND items results in a dimension associated with forms of development and another related to markers of urbanicity, rather than aspects of ND. Future scale building work will explore the specific contributions of audit items in more detail.

LATEBREAKER

Methods/Statistics

A Bayesian Framework for Incorporating ExposureUncertainty into Health Outcome Analyses Saskia Comess* Saskia Comess Joshua Warren

Studies of the relationships between environmental exposures and adverse health outcomes often rely on a two-stage statistical modeling approach, where exposure is modeled/predicted in the first stage and used as input to a separately fit health outcome analysis in the second. Uncertainty in these predictions is frequently ignored, or accounted for in an overly simplistic manner, when estimating the primary associations of interest. Working in the Bayesian setting, we propose a flexible kernel density estimation (KDE) approach for fully utilizing posterior output from the first stage modeling/prediction to make accurate inference on the association between exposure and health in the second stage, derive the full conditional distributions needed for model fitting, detail its connections with existing approaches, and compare its performance through simulation. Our KDE approach is shown to generally have improved performance across several settings and model comparison metrics. Using competing approaches, we investigate the association between lagged daily ambient fine particulate matter levels and stillbirth counts in New Jersey (2011-2015), observing an increase in risk with elevated exposure three days prior to delivery. The newly developed methods are available in the R package KDExp.

Body Mass Index and Atrophy of the Rotator Cuff Muscles in Chronic Cuff Tears Simone Herzberg* Simone Herzberg Ayush Giri Nitin Jain

Rotator cuff tears (RCT) are among the most common causes of pain and disability among adults. Muscle atrophy of the rotator cuff is associated with failed surgical repair and worse clinical outcomes, but reasons for atrophy remain unclear. The primary goal of this study is to evaluate the relationship between body mass index (BMI) and muscle atrophy in adults with rotator cuff tears. This analysis included participants recruited from 10 sites across the US for whom MRI images permitted assessment of muscle atrophy. Information regarding participant characteristics were collected using structured questionnaires at the time of recruitment. Trained medical professionals recorded degree of muscle atrophy of the four rotator cuff muscles. We used multivariable logistic regression to evaluate the relationship between BMI and presence of muscle atrophy while adjusting for age at MRI and participant's sex. A total of 145 patients (33.5%) patients in the cohort (N = 433) had MRI data available on muscle atrophy. Among these patients, 29 (20%) had atrophy of at least one muscle of the rotator cuff. When adjusting for age and sex those that are overweight or obese has 1.71 fold (95% CI =1.09, 2.68) and 2.45 fold (95% CI = 1.46, 4.12) increased odds of muscle atrophy, respectively, compared to those of normal BMI. Each unit of increase BMI was associated with 1.10 fold (95% CI = 1.02, 1.18) increased odds of muscle atrophy. Efforts to modify BMI in patients with rotator cuff pathology may help improve clinical outcomes and candidacy for surgery.

The Perfect Storm: COVID-19 Isolation and Eating Disordered Behaviors in College Students Heather McGrane Minton* Heather McGrane Minton Lydia Bennett

Background: While the incidence of depression, anxiety, and suicidal ideation have increased during the COVID-19 pandemic among college students little research has been conducted on the implications for eating disorders (ED). Given concerns about health and fitness during isolation such as avoiding the "quarantine 15," it is plausible that college students are experiencing distressful thoughts and behaviors around their body.

Objectives: To determine if social isolation is associated with ED behaviors and body image dissatisfaction among college students.

Methods: Undergraduate students (N=337) at a liberal arts college in western New York participated in an online cross-sectional study. Linear regression models were analyzed to determine the associations between isolation, body image, and ED behaviors.

Results: The majority of the sample reported feeling lonely during the pandemic (73%) and 65% were unhappy with their current body image. Forty percent met criteria for Drive for Thinness (DT) referral and 31% for Bulimia referral, with 65% of the sample reporting moderate/high body dissatisfaction scores (BD). Days spent in quarantine/isolation were positively correlated with current weight but not correlated with body image or ED behaviors. Being lonely significantly increased DT (β=2.745, 95% CI: 1.50, 3.99, R=0.26, $p<0.001$), Bulimia, β=2.08, 95% CI: 1.19, 2.97, R=0.27, $p<0.001$) and BD (β = 3.57, 95% CI: 2.18, 4.97, R=0.29, $p<0.001$).

Conclusion: This study provides evidence that social isolation predicts body image dissatisfaction and ED behaviors in undergraduate students. Public health professionals must focus efforts on preventing and mitigating the harmful effects of the COVID-19 pandemic on college students.

Measurement-dependent association between folate and diabetes mortality among US hypertensive adults, an 18-year follow-up of a national cohort Felix Twum* Felix Twum Logan Cowan Lili Yu Evans Afriyie-Gyawu Jian Zhang

Background: The relationship between folate and diabetes remains inconclusive, possibly due to large variations between and within the measurement of folate. With folate measured in diet and blood, we assessed the relationship between folate and diabetes mortality.

Methods: We analyzed the data of 3,133 adults aged > 19 with hypertension who participated in the Third National Health and Nutrition Examination Survey (1991-1994) as the baseline examination and were followed up through December 31, 2010. Cox regression was used to estimate hazard ratios (HRs) of diabetes death for participants with high (4th quartile) dietary, serum, and red blood cell (RBC) folate, and moderate level (2nd and 3rd quartiles) compared with those with low level (1st quartile).

Results: After 33,811 person-years of follow-up, 165 diabetes deaths were recorded. The adjusted HRs of diabetes death were 1.00 (reference), 0.94 (95% CI = 0.79 – 1.13) and 1.43 (95% CI = 1.18 – 1.73) respectively for hypertensive adults with low, moderate, and high serum folate. The corresponding HRs for RBC folate were 1.00 (Reference), 2.02 (1.84 – 2.21) and 3.12 (2.67 – 3.66) respectively. No association was detected for the overall association between dietary folate intake and diabetes death for men and women combined. Women with high folate intake, however, had a significantly lower risk of dying from diabetes compared to women with low intake, HR = 0.70 (0.52 – 0.93).

Conclusion: A measurement-dependent association was found; elevated serum and RBC folate but not dietary folate intake were associated with high diabetes mortality among hypertensive participants.

Nutrition/Obesity

Association between food-related parenting practices and change in child weight status among parents and children living in low-income and racially and ethnically diverse households: A positive deviance approach Junia Nogueira de Brito* Junia Nogueira de Brito Katie A Loth Mark A Pereira Susan M Mason Angela Fertig Allan Tate Amanda Trofholz Jerica M Berge

Background: There is limited prospective evidence on parenting practices that can help prevent obesity in children from low-income and racially and ethnically diverse households. Using the positive deviance approach to childhood obesity, we examined the association between food-related parenting practices and change in child weight status.

Methods: In a longitudinal study of 739 parents with children (aged 7±1.5 yrs), we measured at baseline food-related parenting practices (parent feeding practices [e.g., pressure to eat, emotional control] and parent-led weight-related talks with their child [e.g., eat differently to lose weight]). Children's BMI percentile at baseline and 18-month were retrieved from electronic medical records. A dichotomous outcome variable reflecting change in child weight status over 18 months was created to identify children who were 'positive deviant' (PD) (reduced weight or maintained normal weight status [BMI $\geq 5^{th}$– $<85^{th}$ percentile]) or with 'higher weight status' (gained weight or maintained overweight [BMI $\geq 85^{th}$ and $<95^{th}$] or obese [BMI $\geq 95^{th}$] weight status). Adjusted RRs and 95% CIs were calculated using modified Poisson regressions.

Results: Parents who reported using pressure to eat (RR=1.2, [95% CI 1.1, 1.2]) and food for emotional control (1.1 [1.0, 1.1]) were more likely to have children identified as PD, while parents who reported having conversations with their child about weight (0.9 [0.9, 1.0]) or the need for their child to lose or keep from gaining weight (0.7 [0.6, 0.8]) were less likely to have children identified as PD.

Conclusions: Findings suggest that parents are more likely to use controlling feeding practices among children with lower weight status and to have weight-related conversations among children with higher weight status. Results related to controlling feeding practices were unexpected. More research on parenting practices to reduce weight-related health disparities among children at-risk for obesity is needed.

Nutrition/Obesity

The association between established diet quality indices and peak bone mass in young adult women Sofija Zagarins* Sofija Zagarins Alayne Ronnenberg Elizabeth Bertone-Johnson

Maximizing peak bone mass in young adulthood is important for reducing risk of osteoporosis and fracture later in life. Specific nutrients and foods (e.g., vitamin D, calcium, dairy) have been identified as important for bone health, but given the complex and interconnected nature of diet, it is important to understand how overall diet affects bone mass outcomes. However, few studies have examined the association between overall diet quality and peak bone mass, and no studies have simultaneously examined multiple established diet quality indices to determine whether these are associated with peak bone mass in young women.

To address this gap, we assessed diet using a modified version of the Harvard food frequency questionnaire in a cross-sectional study of 288 women aged 18-30. Overall diet measures included 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). We measured areal bone mineral density (aBMD) and aBMD Z-score using dual-energy x-ray absorptiometry (DXA), and derived bone mineral apparent density (BMAD) from DXA data.

Mean diet scores were 67.7±9.2 (HEI-2015), 52.1±10.4 (AHEI-2010), 27.9±6.0 (aMED), and 52.4±9.7 (HPDI). aBMD Z-scores ranged from -1.9 to 2.6, with a mean of 0.51±0.83; 75% of participants had a positive Z-score, indicating above-average bone density relative to age- and gender-matched peers. Diet quality indices were not associated with any bone measures in multiple linear regression adjusting for age, height, activity level, caloric intake, and age at menarche, with standardized regression coefficients ranging from -0.10 to 0.03, and P values ranging from 0.11 to 0.89. These null findings could indicate that established diet quality indices are not associated with peak bone mass in young adult women, but further research assessing these relations in larger populations is needed.

Nutrition/Obesity

Association between dietary total antioxidant capacity and risk of NAFLD-related fibrosis in the United State: results from the National Health and Nutrition Examination Survey (NHANES) 2011–2018 Rui Li* Rui Li Zhongxue Chen

Background: Nonalcoholic fatty liver disease (NAFLD) is characterized by the presence of hepatic steatosis. Some studies have found the importance of dietary antioxidants in reducing the incidence of NAFLD. However, there is few research in epidemiological studies evaluating the role of antioxidants in patients with NAFLD. Since. dietary total antioxidant capacity (TAC) is a useful indicator for assessing total antioxidant power, we aimed to investigate the association between TAC and severity of liver fibrosis in patients with NAFLD.

Methods: Cross-sectional data from 39,156 participants in the National Health and Nutrition Examination Survey (NHANES) from 2012 to 2018 were identified. TAC was calculated using a 1-day 24 hours dietary recall. The severity of advanced fibrosis was determined by the NAFLD fibrosis score and FIB-4 score in patients with NAFLD.

Results: The prevalence of low, intermediate, and high fibrosis was 68.6%, 29.1%, and 2.3%, respectively. The multinomial logistic regression analysis showed that NAFLD patients in the highest quartile of TAC had higher risks of advanced fibrosis in comparison to subjects in lowest quartile (OR=3.24, 95% CI=1.00-10.05) after adjusting energy intake, age, sex, some lifestyle factors, obesity, diabetes, and important liver enzymes. OR of high probabilities of fibrosis associated with second quartile of TAC (OR=2.78, 95% CI=1.05-7.38) significantly differed (p=0.037) from those of intermediate probabilities of fibrosis (OR=0.99, 95% CI=0.58-1.67). Subgroup analyses revealed that the likelihood of advanced fibrosis would increase among non-obese people (OR quartile 4 vs 1=10.78, 95% CI=1.74-67.00, p=0.021) and non-hypertensive people (OR quartile 3 vs 1=13.32, 95% CI=3.87-45.82, p<.001).

Conclusions: An antioxidant-rich diet is not beneficial to reduce advanced fibrosis risk among patients with NAFLD, the risk may even become higher when consuming more anti-inflammatory diet compared to more pro-inflammatory diet.

Patterns in mother's recollection of healthcare provider's infant feeding recommendations in the United States

Andrea McGowan* Andrea McGowan Heather Hamner Ellen O. Boundy Jennifer M. Nelson

Background: The American Academy of Pediatrics recommends fourteen preventive health visits from birth through 5 years, allowing for comprehensive health supervision. During these visits, healthcare providers (HCP) discuss a variety of topics, including guidance on feeding. This analysis examines feeding guidance mothers recall receiving from their child's HCP.

Methods: Using data from the National Survey of Family Growth (2017-2019), our sample includes 1,298 U.S. mothers reporting information about their youngest child between 6 months and 5 years old, living with the mother at the time of survey completion (weighted n=13,176,280). The weighted percentages of children whose mothers recalled their HCP discussing feeding guidance are described by demographic characteristics.

Results: In our sample, 91.4% of mothers (CI 89.0, 93.8) recalled HCPs discussing when to start solid foods; of these, 63.1% (CI 58.5, 67.7) recalled HCPs recommending introduction at 6 months of age or older. Recall of HCP discussion on when to start solid foods (p=0.043), offering different tastes and textures (p=0.013), and a variety of fruits and vegetables (p<0.0001) differed significantly by education; for these, the lowest percentage of recall was among mothers with high school education or below. Recall of HCP discussion on offering different tastes and textures (p=0.014) and a variety of fruits and vegetables (p=0.049) differed significantly by income; for both, the lowest percentage of recall was among mothers with income ≤75% of the federal poverty level. The least recalled guidance was limiting meals in front of electronic devices (42.8%, CI 38.3, 47.4).

Conclusion: While most mothers recalled HCPs discussing when to start solid foods, recall of other feeding guidance was lower. It is important to understand reasons for variability in recall of feeding guidance for young children and to identify and address any barriers in receipt, retention and use of guidance.

Weighted Percentage of Mothers Reporting Early Feeding Guidance Discussed at Healthcare Visits by Select Demographics Characteristics, National Survey of Family Growth, 2017-2019, United States

	n	Offering foods with many different tastes and textures	Not forcing child to finish food or bottles, even if not interested or didn't have much	Offering a variety of fruits and vegetables	Limiting foods and drinks with added sugar (such as candy, cookies, soda, juice)	Limiting eating meals in front of tv or other electronic devices	None of these topics
		Weighted % (95% Confidence Interval)					
Total Sample	1298	76.7 (73.5, 79.8)	59.5 (55.6, 63.4)	84.7 (81.6, 87.9)	76.5 (72.7, 80.3)	42.8 (38.3, 47.4)	7.1 (5.4, 8.9)
Maternal Education							
≤High School	608	70.9 (64.8, 77.0)	58.4 (53.2, 63.5)	79.5 (74.6, 84.4)	74.3 (69.0, 79.6)	41.6 (35.5, 47.7)	9.2 (6.6, 11.8)
Some College or Above	690	80.3 (76.3, 84.3)	60.2 (54.6, 65.8)	88.1 (85.2, 91.0)	77.9 (73.4, 82.5)	43.6 (38.2, 49.0)	5.8 (3.7, 8.0)
p-value[1]		0.013	0.635	<0.0001	0.248	0.556	0.037
Household Income							
≤75% of Federal Poverty Level	313	65.6 (57.4, 73.9)	52.3 (44.3, 60.3)	79.7 (71.7, 87.8)	75.2 (68.8, 81.7)	38.7 (32.2, 45.2)	8.9 (4.4, 13.4)
76%-185% of Federal Poverty Level	436	77.0 (70.5, 83.4)	62.1 (55.2, 69.1)	82.7 (77.3, 88.1)	74.6 (68.3, 80.9)	47.2 (40.3, 54.1)	7.7 (4.4, 10.9)
>185% of Federal Poverty Level	549	80.3 (75.5, 85.2)	60.3 (53.8, 66.9)	87.8 (84.7, 91.0)	78.2 (73.2, 83.2)	41.5 (34.9, 48.1)	6.2 (3.9, 8.5)
p-value[1]		0.014	0.245	0.0495	0.531	0.186	0.498
Child's Age							
6-11 Months	138	66.4 (55.9, 76.9)	53.5 (42.7, 64.3)	76.8 (68.8, 84.9)	56.0 (41.5, 70.5)	38.4 (25.5, 51.3)	15.5 (7.9, 23.0)
12-23 Months	344	76.9 (70.2, 83.5)	61.1 (54.4, 67.7)	85.1 (80.1, 90.2)	75.9 (69.5, 82.2)	42.5 (34.8, 50.2)	5.9 (3.3, 8.5)
24-35 Months	288	78.3 (72.6, 84.0)	58.6 (52.1, 65.2)	85.9 (80.3, 91.6)	80.3 (73.5, 87.2)	41.6 (32.5, 50.7)	6.2 (2.6, 9.9)
36-47 Months	282	82.4 (76.3, 88.5)	58.9 (50.3, 67.6)	85.6 (80.0, 91.2)	79.3 (72.6, 86.0)	42.5 (34.6, 50.4)	3.9 (1.3, 6.5)
48-71 Months	246	73.8 (65.7, 82.0)	62.2 (53.8, 70.5)	86.4 (80.5, 92.3)	81.7 (73.8, 89.7)	47.2 (37.7, 56.6)	8.9 (3.4, 14.4)
p-value[1]		0.085	0.726	0.266	0.001	0.804	0.008

[1]P-value calculated through Chi-Square test comparing proportions of mothers recalling each early feeding guidance topic by each demographic characteristic(α=.05)

All-cause and cause-specific mortality in a cohort of WTC-exposed and non-WTC-exposed firefighters Ankura Singh* Ankura Singh Rachel Zeig-Owens Madeline Cannon Mayris P. Webber David J. Prezant Paolo Boffetta Charles B. Hall

Background

Studies show that rescue/recovery workers who responded to the World Trade Center (WTC) disaster had reduced mortality compared with general populations, but findings may be influenced by the healthy worker effect or access to care. No study has compared mortality in WTC-exposed workers to that in a comparable occupational cohort.

Objective

To compare mortality rates in WTC-exposed Fire Department of the City of New York (FDNY) firefighters vs in a comparison cohort of similarly healthy non-WTC-exposed firefighters from other cities.
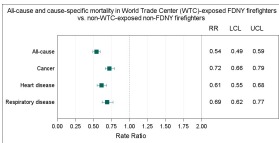
Methods

10,786 male WTC-exposed FDNY firefighters and 8,813 male non-WTC-exposed firefighters from the Chicago, Philadelphia and San Francisco fire departments who were employed on 9/11/01 (9/11) were included in the analyses. WTC-exposed firefighters receive routine health monitoring, even after retirement, via the WTC Health Program (WTCHP). Follow-up began on 9/11 and ended at the earliest of the following: death date or 12/31/16. Death dates and causes of death were obtained from the National Death Index, and demographic data from the fire departments. Poisson regression models estimated RRs of all-cause and cause-specific mortality in WTC-exposed vs non-WTC-exposed firefighters, controlling for age and race.

Results

WTC-exposed firefighters were younger on 9/11 than the non-WTC-exposed (mean±SD=40.4±7.4 vs 43.9±9.2 yrs). Between 9/11/01-12/31/16, there were 261 deaths among WTC-exposed firefighters and 605 deaths among non-WTC-exposed. After controlling for age and race, WTC-exposed firefighters had lower rates of mortality from all causes, cancer, heart disease and respiratory diseases (figure).

Conclusion

In the first 15 years post 9/11, we observed significantly lower mortality rates in WTC-exposed firefighters compared with non-WTC-exposed firefighters. Better mortality outcomes in the WTC-exposed cohort may be a result of the free routine health monitoring, including cancer screenings, that they receive as part of the WTCHP.

All-cause and cause-specific mortality in World Trade Center (WTC)-exposed FDNY firefighters vs. non-WTC-exposed non-FDNY firefighters

	RR	LCL	UCL
All-cause	0.54	0.49	0.59
Cancer	0.72	0.66	0.79
Heart disease	0.61	0.55	0.68
Respiratory disease	0.69	0.62	0.77

Occupational

Occupational exposures and lung cancer risk: a population-based case-control study in France (the WELCA study) Lisa Leung* Lisa Leung Anita Koushik Pascal Guénel

Context: Apart from the major role of smoking, genetic, lifestyle, environmental and occupational factors may also contribute to lung cancer risk. Although past studies on lung cancer have addressed the occupational environment, few have been based on female workers. This exploratory analysis examines associations between occupation, specific workplace exposures, and lung cancer risk in women.

Methods: In a population-based study conducted in the greater Paris area (2014-2017), lifetime occupational history was collected for 735 cases and 751 controls. An industrial hygienist coded the occupation of each job held by a participant. Specific workplace exposures were identified by linking job codes to the Canadian job-exposure matrix. Thirty-six agents with ≥10 exposed cases were identified. Occupations were examined by comparing participants employed in an occupation for ≥10 years vs. never employed in that occupation. For the 36 specific exposures, ever exposure, duration of exposure, and cumulative exposure were assessed. Odds ratios (OR) and 95% confidence intervals (CI) were estimated using logistic regression, adjusting for smoking and other covariates.

Results: Occupations with elevated ORs of at least 2 included Special Education Teachers, Stock Clerks, Material and Production Planning Clerks, Working Proprietors (Wholesale and Retail Trade), Working Proprietors (Catering and Lodging Services), and Building Caretakers (ORs of 2.15 – 4.02); CIs were wide. For specific exposures, elevated ORs of 1.62 to 5.74 were observed for high cumulative exposure to abrasives dust, metallic dust, hair dust, cooking fumes, engine emissions, iron, tin, and aromatic amines, which was significant for cooking fumes (OR=1.90, 95% CI: 1.01-3.56). A decreased risk was observed for high cumulative exposure to biocides (OR=0.40, 95% CI: 0.22-0.72).

Conclusion: Certain workplace exposures may contribute to lung cancer risk among women.

Associations of maternal ACEs and lifetime EOD with child nutritional status and weight trajectory Zachary Fusfeld, MPH* Zachary Fusfeld Kelly Courts, MPH Ana Poblacion, PhD, MS Stephanie Ettinger De Cuba, PhD, MPH Lindsey Rateau, MPH Margaret Shea Tim Heeren, PhD Deborah Frank, MD Felice Le-Scherban, PhD, MPH

Background: Adverse childhood experiences (ACEs) and experiences of racial discrimination (EOD) are consistently related to worse adult health. Less is known about potential intergenerational effects of maternal adversity on child growth. We assessed associations of maternal ACEs and lifetime EOD with underweight, overweight, and obesity, and weight trajectory.

Methods: Mothers were surveyed 2011-2020 in healthcare settings in 4 US urban sites (Baltimore, Boston, Little Rock, Philadelphia). Weight was abstracted from children's electronic health records. Maternal ACEs was categorized as 0, 1-3, and 4+ ACEs; maternal EOD as 0, 1-2, and 3+ EOD settings. Child nutritional status was calculated using CDC weight-for-age indicator (WFA), expressed in percentiles, categorized as underweight (<5% WFA), overweight (>85% and ≤95% WFA), or obese (>95% WFA) vs. normal weight. Weight trajectory was calculated by subtracting weight between two visits, categorized as slow (WFA z-score change < -0.67), expected (WFA Z-score change ≥ -0.67 and ≤ +0.67), and rapid (WFA Z-score change ≥ +0.67). Multivariable analyses (Poisson and Multinomial Logistic Regressions) adjust for site, maternal age, race/ethnicity, and nativity.

Results: Among these samples (ACEs: n=5235; EOD: n=3405) of primarily non-white (ACEs: 84%; EOD: 82%) US-born (ACEs: 88%; EOD: 85%) mothers, 53% had 1+ ACEs and 37% experienced discrimination in 1+ settings. Children whose mothers had EOD in 3+ settings (vs. 0 settings) were more likely to be underweight vs. normal weight (PR 1.23, 95% CI 0.90-1.67), though CIs spanned the null. Maternal EOD were unrelated to weight trajectories; maternal ACEs were not associated with any outcome.

Conclusion: Results suggest maternal lifetime EOD may be related to their young children's nutritional status. Research with a more robust sample size is needed to elucidate potential mechanisms and other child health outcomes.

Unadjusted and adjusted prevalence ratios from modified Poisson regression models of maternal ACEs and EOD with child weight status								
Maternal ACEs (Ref. 0 ACEs) n=5235				Maternal EOD (Ref. 0 EOD) n=3405				
Underweight (4120)				Underweight (n=2688)				
	Unadjusted		Adjusted		Exposure	Unadjusted		Adjusted	
Exposure	PR	95% CI	PR	95% CI		PR	95% CI	PR	95% CI
1-3 ACEs	1.10	0.90-1.35	1.12	0.91-1.37	**1-2 EOD**	0.87	0.65-1.17	0.98	0.73-1.32
4+ ACEs	1.12	0.85-1.47	1.15	0.87-1.53	**3+ EOD**	1.11	0.83-1.49	1.23	0.90-1.67
Overweight (n=4366)				Overweight (n=2787)				
	Unadjusted		Adjusted			Unadjusted		Adjusted	
	PR	95% CI	PR	95% CI		PR	95% CI	PR	95% CI
1-3 ACEs	1.04	0.89-1.21	1.07	0.91-1.25	**1-2 EOD**	1.18	0.94-1.47	1.17	0.93-1.47
4+ ACEs	1.14	0.93-1.40	1.17	0.95-1.43	**3+ EOD**	1.06	0.81-1.37	1.09	0.83-1.42
Obesity (n=4201)				Obesity (n=2740)				
	Unadjusted		Adjusted			Unadjusted		Adjusted	
	PR	95% CI	PR	95% CI		PR	95% CI	PR	95% CI
1-3 ACEs	0.95	0.79-1.15	0.97	0.80-1.16	**1-2 EOD**	0.94	0.73-1.22	0.87	0.67-1.12
4+ ACEs	0.96	0.75-1.24	0.97	0.75-1.25	**3+ EOD**	0.99	9.75-1.31	0.91	0.68-1.20
Models are adjusted for maternal age, race/ethnicity, nativity, and site location, italicized results are statistically significant at the p<.05 level; Zero ACEs is the referent group for maternal ACEs exposure, and Zero EOD is the referent group for maternal lifetime EOD exposure; PR = Prevalence Ratio, 95% CI = 95% confidence interval. Regressions looking at ACEs exposure and EOD exposure were run independently of each other								

Perinatal & Pediatric

Investigating the impact of patient-centered medical homes on racial disparities in severe maternal morbidity using medical expenditure panel survey data Curisa Tucker* Curisa Tucker Nathaniel Bell Cynthia L. Corbett Audrey Lyndon Tisha Felder

Context/Purpose: Severe maternal morbidity (SMM) is disproportionately experienced among racial and ethnic groups. Patient-centered medical homes (PCMH), as defined by the Agency for Healthcare Research and Quality, is a patient-centered, comprehensive, coordinated, and accessible primary care model designed to improve care quality and safety. The PCMH may reduce racial/ethnic disparities in SMM. The primary purpose of this study was to examine the association of the PCMH on SMM outcomes and the association between PCMH enrollment between racial groups on the prevalence of SMM among women who gave birth.

Methods: We conducted a longitudinal analysis of pooled Medical Expenditures Panel Survey data from respondents for the years 2007-2016 merging self-reported primary care experiences with clinical care outcomes. We estimated odds ratios of SMM, adjusting for factors informed by the adapted Anderson-Howell Model of Pathways to Reduce Disparities in SMM using Generalized Estimation Equation models.
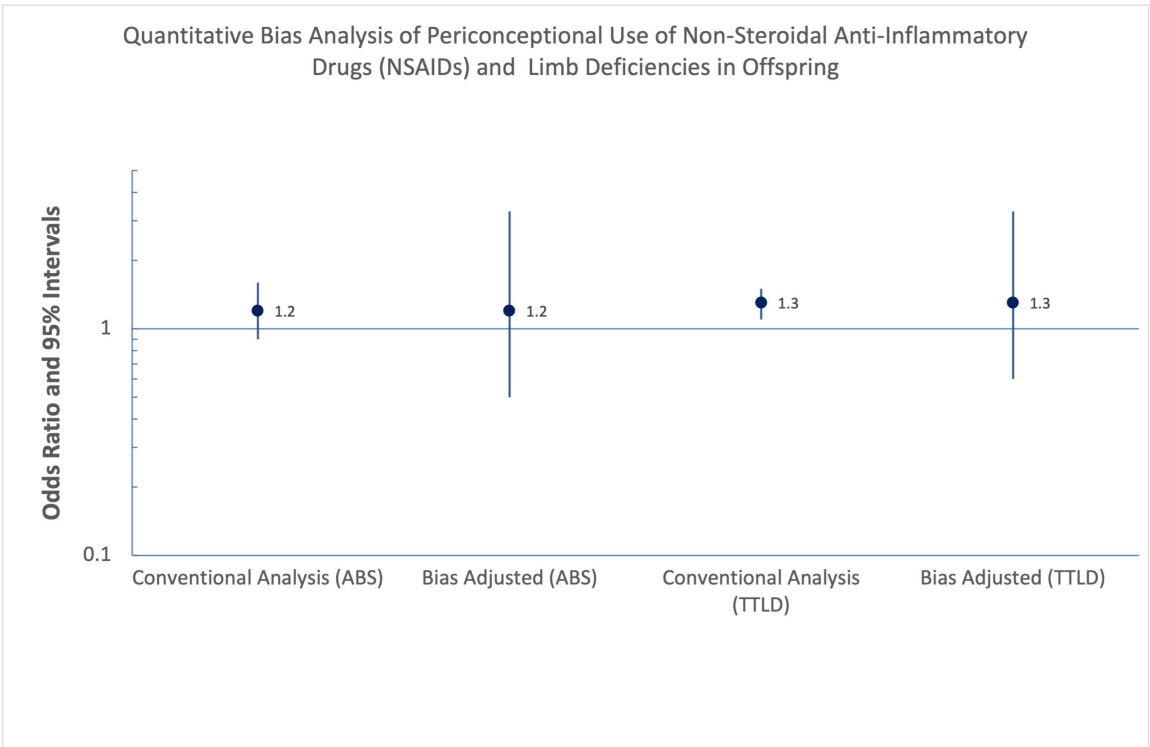
Results: A total of N=2801 respondents who gave birth during the study period were identified, representing 5,362,782 U.S. lives. Among all respondents, 76% were never in a PCMH, 18% were sometimes in a PCMH, and 7% were always in a PCMH. An SMM was experienced by 2% of respondents which did not differ significantly (p=0.11) by PCMH status. We found marginal statistical significance between respondents who were always in a PCMH versus never (p=0.05). There was no overall interaction effect between race and PCMH status on the SMM outcome (p = 0.89).

Interpretation: Few respondents were enrolled in a PCMH. The rate of SMM is similar to national U.S. trends. There is an indication that the PCMH model may produce fewer SMM outcomes.

Conclusion: The trend of decreased SMM outcomes for respondents in a PCMH indicates that more research is needed to investigate this model and the role of race as an effect modifier on SMM outcomes.

Reported Periconceptional Use of Analgesics and Limb Deficiencies in Offspring: Addressing Potential Recall Bias Nedghie Adrien* Nedghie Adrien Julie Petersen Samantha Parker Martha Werler Matthew Fox

Case-control studies have noted associations between non-steroidal anti-inflammatory drugs (NSAIDs) used in the periconceptional period and increased risk of limb defects in offspring. However, exposure information was collected retrospectively after birth- up to 24 months after delivery- which can result in misclassification due to reporting inaccuracies. We conducted a probabilistic bias analysis to explore the potential effects of differential exposure misclassification (i.e., recall bias) of reported periconceptional NSAIDs use. We compared cases (189 amniotic band syndrome (ABS) and 613 terminal transverse limb defects (TTLD)) to 11,829 controls without congenital anomalies from the US National Birth Defects Prevention Study (1997–2011). We simulated 10,000 datasets to adjust for exposure misclassification, using bias parameters identified from external validation studies of medication use among pregnancies with and without birth defects. We conducted our analyses using symmetric triangular distributions to model the probability density functions for the specificity and sensitivity. Specificity lower and upper limits ranged from 0.81 to 0.94 for controls, and 0.96 to 0.99 for cases. Sensitivity ranged from 0.28 to 0.36 for controls and 0.40 to 0.56 for cases. Correcting for differential misclassification of NSAIDs resulted in similar but less precise ORs than the conventional analysis: ABS bias adjusted OR 1.2 (95% SI 0.5, 3.3) vs conventional unadjusted OR 1.2 (95% CI 0.9, 1.6); and TTLD bias adjusted OR 1.3 (95% SI 0.6, 3.3) vs conventional unadjusted OR 1.3 (95% CI 1.1, 1.5). Even under the assumption of low (<0.5) sensitivity, with cases reporting more accurately than controls, and case-control differences in specificity, findings suggested that differences in the accuracy of recall did not result in evidence of biased ORs. These results provide some reassurance that retrospective data collection to study common medications may not lead to biased results.

Quantitative Bias Analysis of Periconceptional Use of Non-Steroidal Anti-Inflammatory Drugs (NSAIDs) and Limb Deficiencies in Offspring

Trends in adult survival, reproductive and educational outcomes for Norwegians born preterm from 1967 – 1990 Sage Wyatt* Sage Wyatt Truls Østbye Liv Grimstvedt-Kvalvik Kari Klungsøyr Rolv Skjærven

Introduction

While many effective interventions were developed during the 1980's to reduce short term risk of mortality for preterm infants, it is less clear how these interventions have impacted long term health and social wellbeing into adulthood. The purpose of this study is to compare adult educational, reproductive, and survival outcomes of people born preterm over time.

Methods

We used data from 586832 singleton female births from the medical Registry of Norway born from January 1967 to December 1990, divided into 5 cohorts of 5 years. Gestational age was divided into extremely preterm (22 – 32 weeks), moderately preterm (33 – 36 weeks) and term (>36 weeks). The cohort was followed through June 2020 for survival and reproduction (any birth). The highest educational attainment of the individual by June 2020 was collected from the Norwegian Statistics Bureau.

Results

The total incidence of preterm birth (extremely preterm 1%, moderately preterm 4%) has remained stable over time, but percent who survive to age 18 has increased (extremely preterm 14% increase, moderately preterm 2% increase). In adulthood, there is lacking evidence for change in mortality (extremely preterm OR 1.91 CI95% 0.59 – 6.13, moderately preterm OR 1.02 CI95% 0.58;1.79). There is a significant increase in reproduction for extremely preterm people (OR 1.28 CI95% 1.04;1.57) but not for moderately preterm (OR 1.01 CI95% 0.93;1.11). High school graduation rates increased for both extremely preterm and moderately preterm people, approximately matching trends in education for people born at term (Figure 1).

Conclusions

Changes in clinical handling that drastically improved survival for preterm infants and children are not reflected in survival of the adult population. However, increasing early survival does not indicate an increase in greater adult disability, as indicators for quality of life show similar or higher levels to the initial period.

Figure 1. Odds of highschool graduation compared to the 1967-1970 birth cohort by gestational age
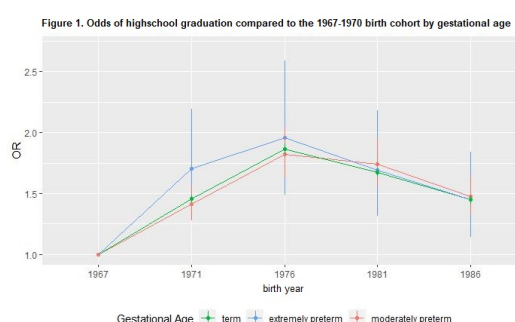
Body composition patterns of infants exposed to gestational diabetes through one year of age Rachel Rickman* Rachel Rickman Patrick Catalano Charlotte Lane Amy Nichols Saralyn Foster Elizabeth Widen

Background: Reliance on weight and length to estimate adiposity may misclassify infants. Body composition measurements provide insight into developmental programming and drivers of excess adipose tissue. Infants exposed to gestational diabetes mellitus (GDM) may experience increased adiposity up to 6 months of age. Beyond this period, trajectories of lean and fat mass accrual are unknown. We sought to examine the role of GDM exposure in body composition changes from birth to 1 year.

Methods: Repeated measures were obtained from infants at the MetroHealth system in Cleveland, Ohio (n=198, 51%male, 51%GDM exposed). Total body electrical conductivity was used to measure adiposity at birth, 4, 8, and 12 months. Latent Class Mixed Modeling (LCMM) was used to identify fat mass (FM), fat free mass (FFM), and % body fat (BF%) trajectory classes. Multinomial logistic regression was used to assess how GDM exposure and covariates related to body composition trajectories.

Results: At birth, unadjusted FM was higher in GDM exposed infants (0.43 kilograms) compared to those unexposed (0.33 kilograms) (95%CI:0.05,0.15); but there was no difference in weight or FFM at birth by exposure. LCMM identified 3 trajectory classes for FM, FFM, and BF%. GDM exposure was associated with certain FM and BF% trajectory groups using chi-square analyses and adjusted models, while there were no differences for FFM trajectories. For example, for BF%, GDM exposed infants were less likely to be in the two trajectory groups with accelerated adipose tissue accrual during the first 100 days, compared to the group with lower adipose tissue accrual rates [RRR:0.22 (95%CI:0.09,0.58) & 0.18 (95%CI:0.07,0.46)].

Conclusions: Infants body composition patterns for FM and BF% varied by GDM exposure while no differences were seen for FFM from birth to 1 year. These findings indicate that GDM exposure may influence distinct patterns of changes in infant adiposity during the first year of life.
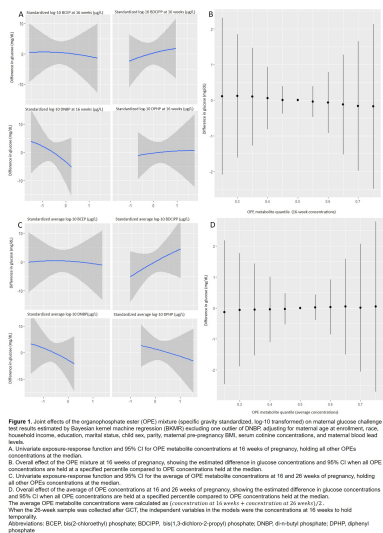
Urinary OPE metabolite concentrations and glucose levels during pregnancy: The HOME Study Weili Yang* Weili Yang Joseph M. Braun Ann M. Vuong Zana Percy Yingying Xu Changchun Xie Ranjan Deka Antonia M. Calafat Maria Ospina Kimberly Yolton Kim M. Cecil Bruce P. Lanphear Aimin Chen

Background: Organophosphate esters (OPEs), replacement flame retardants, altered glucose metabolism in experimental studies. Few studies have examined whether OPE exposure is associated with glucose levels in pregnant women.

Methods: We used data from 301 women with live-born singletons in the Health Outcomes and Measures of the Environment (HOME) Study, a prospective pregnancy and birth cohort in Cincinnati, Ohio, USA. Four OPE metabolites were quantified in maternal spot urine samples at 16 and 26 weeks of pregnancy and standardized by specific gravity before the log-10 transformation. We extracted the results of the glucose challenge test (GCT) and the oral glucose tolerance test (OGTT) from medical charts. We defined elevated glucose as GCT results ≥140mg/dL or any abnormal values in OGTT (≥95 mg/dL fasting glucose, ≥180 mg/dL1-hour glucose, ≥155 mg/dL 2-hour glucose, and ≥140 mg/dL 3-hour glucose). We fitted general linear models to estimate associations of OPEs with continuous glucose levels and modified Poisson regression models for having elevated glucose. We examined effect measure modification by age, race/ethnicity, and pre-pregnancy BMI. Bayesian kernel machine regression (BKMR) was used to assess associations of the OPE mixture.

Results: Diphenyl phosphate (DPHP) had the highest geometric mean urinary concentrations (1.83 µg/L at 16 weeks, 1.24 µg/L at 26 weeks). Thirty (10.0%) women had elevated glucose. OPE metabolite concentrations were not significantly associated with continuous GCT results. We did not observe effect measure modification by maternal characteristics. BKMR results of OPE mixture were similar (Figure1). Compared to women in the 1st tertile of average pregnancy DPHP concentrations, women in the 3rd had a suggestively negative association with elevated glucose levels (RR = 0.41, 95 % CI 0.16-1.06, p for trend = 0.06).

Conclusion: Maternal urinary OPE metabolites were not associated with glucose levels during pregnancy.

Figure 1. Joint effects of the organophosphate ester (OPE) mixture (specific gravity standardized, log 10 transformed) on maternal glucose challenge test results estimated by Bayesian kernel machine regression (BKMR) excluding one outlier of DNBP, adjusting for maternal age at enrollment, race, household income, education, marital status, child sex, parity, maternal pre-pregnancy BMI, serum cotinine concentrations, and maternal blood lead levels.
A. Univariate exposure-response function and 95% CI for OPE metabolite concentrations at 16 weeks of pregnancy, holding all other OPEs concentrations at the median.
B. Overall effect of the OPE mixture at 16 weeks of pregnancy, showing the estimated difference in glucose concentrations and 95% CI when all OPE concentrations are held at a specified percentile compared to OPE concentrations held at the median.
C. Univariate exposure-response function and 95% CI for the average of OPE metabolite concentrations at 16 and 26 weeks of pregnancy, holding all other OPEs concentrations at the median.
D. Overall effect of the average of OPE concentrations at 16 and 26 weeks of pregnancy, showing the estimated difference in glucose concentrations and 95% CI when all OPE concentrations are held at a specified percentile compared to OPE concentrations held at the median.
The average OPE metabolite concentrations were calculated as (concentration at 16 weeks + concentration at 26 weeks)/2.
When the 26-week sample was collected after GCT, the independent variables in the models were the concentrations at 16 weeks to hold temporality.
Abbreviations: BCEP, bis(2-chloroethyl) phosphate; BDCIPP, bis(1,3-dichloro-2-propyl) phosphate; DNBP, di-n-butyl phosphate; DPHP, diphenyl phosphate

Influence of maternal age on birth, growth, and mortality outcomes Elisabeth Gebreegziabher* Elisabeth Gebreegziabher Mamadou Bountogo Ali Sié Alphonse Zakane Guillaume Compaoré Thierry Ouedraogo Elodie Lebas Fanice Nyatigo Maria Glymour Benjamin F. Arnold Thomas M. Lietman Catherine E. Oldenburg

Objective

Maternal age is increasingly recognized as a predictor of birth outcomes. Using data from randomized controlled trial of 21,555 neonates in Burkina Faso (NAITRE trial), this study aimed to examine the effect of maternal age on infant birth and growth outcomes at 6 months and mortality.

Methods

Newborns of mothers aged 13 to 40, dichotomized as adolescent (13-19) and adult (20-40), were included in this analysis. Measurements of child's birthweight (in grams), weight (in kg), length (in cm), mid-upper arm circumference (MUAC), Height-for-Age Z Score (HAZ), Weight-for-Age Z Score (WAZ), and Weight-for-Height Z score (WHZ) were made at baseline and six months. Maternal information was collected via questionnaire. We used multivariable linear regression adjusting for maternal education and residence in urban or rural settings to compare child anthropometric measures at birth and 6 months, and log binomial models to obtain the relative risk of all-cause mortality by 6 months.

Results

We found that babies born to adolescent mothers on average weighed 163 grams less at birth (95% CI 146.7, 178.8) and 0.18kg less at enrollment (95% CI 0.16, 0.20). They were also 0.56cm shorter (95% CI 0.48, 0.64) and had 0.29cm narrower MUAC at enrollment (95% CI 0.25, 0.33). At baseline, HAZ, WAZ, and WHZ were 0.30 (0.26, 0.34), 0.38 (0.34, 0.41) and 0.23 (0.18, 0.28) standard deviations lower for babies born to adolescent mothers compared to adult mothers. Babies born to adolescent mothers also had higher risk of all-cause mortality by six months (RR=2.16, 95% CI (1.35, 3.44)) but similar growth outcomes from enrollment to six months compared to those born to adult mothers.

Conclusion

Our findings suggest that delaying the first birth from adolescence to adulthood may improve birth outcomes and reduce mortality of neonates. Babies born to younger mothers, who are smaller at birth, may experience catch-up growth, reducing some of the anthropometric disparities by 6 months of age.

Early-life Developmental Milestones and Childhood Neurodevelopment in The Adolescent Brain Cognitive Development (ABCD) study

Haoran Zhuo* Haoran Zhuo Jingyuan Xiao Wan-ling Tseng Zeyan Liew

Background and Objectives: Infancy developmental milestones may be early markers for long-term neurodevelopment and mental health, but evidence from large and diverse samples is lacking. We investigated whether developmental milestones are associated with childhood neurocognition, behaviors, and mental health in the Adolescent Brain Cognitive Development (ABCD) study.

Methods: We analyzed data of 8,218 singleton-born children enrolled in the ABCD study in 2016-2020. The ABCD includes a geographically and socio-demographically diverse sample of children aged 9-10 from 17 states around the US. Children's ages (month) attaining four developmental milestones (first rollover, unaided sit, unaided walk, and speak first words) were reported by their biological mothers. Linear mixed-effects models estimated associations of these milestones with clinically evaluated neurocognitive function, children-reported behavioral problems and psychotic-like experiences (PLEs), adjusting for maternal social-demographic variables. We additionally compared models with and without adjusting for perinatal risk factors including maternal pre-pregnancy BMI, prenatal care, substance use, pregnancy disorders and birth outcomes that could affect early brain development.

Results: Later attainment of all milestones was associated with poorer neurocognitive abilities in childhood, with first rollover and unaided walk showing the strongest associations. Early or later attainment of unaided sit and speak first words was associated with externalizing problems and PLEs. Effect estimates were moderately attenuated (~5-20%) after adjusting for perinatal risk factors.

Conclusions: Results suggest that specific motor and language milestones during infancy are predictive of childhood neurodevelopment and mental health, and that perinatal risk factors of brain development have contributed to these links. Longitudinal data are needed to rule out influence of potential recall bias of milestones in this dataset.

Table. Linear mixed-effects model evaluated associations between infancy developmental milestones and mid-childhood neurocognition, behaviors, and PLEs

	Neurocognitive function (Total Score from NIH-TB)					PLEs (Total score from PQ-BC)				
	N	Adjusted[1] estimate (β1)	95% CI	Adjusted[2] estimate (β2)	95% CI	N	Adjusted[1] estimate (β1)	95% CI	Adjusted[2] estimate (β2)	95% CI
Early-life developmental milestones										
Age of first roll over (in months)										
<4	2098	0.57	(0.15, 0.98)	0.63	(0.21, 1.05)	2147	0.02	(-0.15, 0.19)	-0.02	(-0.19, 0.15)
4-6	5145	Ref		Ref		5240	Ref		ref	
>6	83	-2.30	(-4.10, -0.59)	-2.11	(-3.90, -0.31)	85	0.51	(-0.23, 1.25)	0.48	(-0.26, 1.21)
Age of first unaided sitting (in months)										
<7	2287	0.08	(-0.33, 0.49)	0.15	(-0.26, 0.56)	2345	0.13	(-0.04, 0.30)	0.12	(-0.05, 0.29)
7-9	4722	Ref		Ref		4809	Ref		Ref	
>9	272	-1.25	(-2.26, -0.24)	-1.11	(-2.12, -0.10)	275	0.58	(0.16, 1.00)	0.55	(0.13, 0.97)
Age of first unaided walking (in months)										
<12	2203	0.70	(0.29, 1.11)	0.67	(0.26, 1.08)	2264	-0.01	(-0.18, 0.16)	0.00	(-0.17, 0.17)
12-18	5207	Ref		Ref		5298	Ref		Ref	
>18	225	-1.97	(-3.06, -0.88)	-1.93	(-3.02, -0.85)	233	0.11	(-0.34, 0.56)	0.08	(-0.37, 0.53)
Age of speak first words (in months)										
<10	1641	0.03	(-0.43, 0.49)	0.13	(-0.33, 0.59)	1688	0.24	(0.05, 0.43)	0.21	(0.02, 0.40)
10-14	5090	Ref		Ref		5186	Ref		Ref	
>14	358	-1.66	(-2.54, -0.79)	-1.49	(-2.37, -0.62)	362	0.41	(0.05, 0.77)	0.37	(0.01, 0.73)

	Behaviors (Internalizing Problems from BPM-C)					Behaviors (Externalizing problems from BPM-C)				
	N	Adjusted[1] estimate (β1)	95% CI	Adjusted[2] estimate (β2)	95% CI	N	Adjusted[1] estimate (β1)	95% CI	Adjusted[2] estimate (β2)	95% CI
Early-life developmental milestones										
Age of first roll over (in months)										
<4	1914	0.03	(-0.09, 0.14)	0.00	(-0.11, 0.11)	1906	0.20	(0.09, 0.31)	0.18	(0.06, 0.28)
4-6	4667	Ref		Ref		4617	Ref		Ref	
>6	75	-0.23	(-0.73, 0.27)	-0.23	(-0.73, 0.27)	76	-0.09	(-0.56, 0.38)	-0.09	(-0.55, 0.38)
Age of first unaided sitting (in months)										
<7	2083	0.02	(-0.10, 0.13)	0.00	(-0.11, 0.12)	2060	0.14	(0.03, 0.25)	0.13	(0.02, 0.23)
7-9	4277	Ref		Ref		4240	Ref		Ref	
>9	246	0.09	(-0.19, 0.37)	0.06	(-0.22, 0.34)	240	0.33	(0.06, 0.59)	0.29	(0.02, 0.55)
Age of first unaided walking (in months)										
<12	1994	-0.01	(-0.12, 0.10)	-0.01	(-0.12, 0.10)	1975	0.06	(-0.05, 0.16)	0.05	(-0.05, 0.16)
12-18	4753	Ref		ref		4701	Ref		Ref	
>18	200	-0.08	(-0.39, 0.22)	-0.11	(-0.42, 0.18)	197	-0.15	(-0.43, 0.14)	-0.19	(-0.48, 0.09)
Age of speak first words (in months)										
<10	1467	0.12	(-0.01, 0.24)	0.09	(-0.04, 0.22)	1435	0.12	(0.00, 0.24)	0.09	(-0.03, 0.21)
10-14	4654	Ref		Ref		4623	Ref		Ref	
>14	311	0.35	(0.10, 0.60)	0.32	(0.08, 0.57)	306	0.42	(0.18, 0.65)	0.38	(0.15, 0.61)

[1] Adjusted for maternal socio-demographic characteristics and child's sex at birth: maternal age at delivery, race/ethnicity, marrital status, education, family income, maternal psychopathology

[2] Adjusted for maternal socio-demographic characteristics and perinatal risk factors of brain develop: maternal age at delivery, race/ethnicity, marrital status, education, family income, children's sex at birth, maternal psychopathology, maternal pre-pregnancy BMI, prenatal care use, substance use including cannabis, tabacco, alcohol, caffeine use), breastfeeding status, maternal pregnancy disorders and birth outcomes

NIH-TB: The National Institutes of Health Toolbox (NIH-TB) Cognitive Function Battery (ages 7-17 version)

BPM-C: Brief Problem Monitor by Children, a 18-items based self-assessment instrument to measure behaviors

PQ-BC: Prodromal Questionnaire-Brief Child (PQ-BC) version, a 21-item based self-assessment instrument to measure childhood PLEs

Naloxone co-prescribing to youth in the US from 2015-2019 Victoria Jent* Victoria Jent
Magdalena Cerdá Madeline Renny Scott Hadland

Naloxone is a safe, effective opioid overdose reversal agent that can prevent fatalities from opioid overdose; the FDA and CDC recommend that providers consider prescribing naloxone to those at risk of overdose. The extent to which naloxone is co-prescribed with opioids and medications for opioid use disorder (MOUD) to youth is unclear.

In our descriptive analyses, naloxone co-prescribing was definedas patient that was dispensed a naloxone prescription within +/-6 days of an opioid or MOUD prescription (excluding methadone). All-payer retail pharmacy dispensing data were extracted from IQVIA LRx database for the years 2015-2019. Among youth dispensed an opioid and youth dispensed MOUD, proportions of naloxone co-prescribing were calculated for age groups (<10y, 10-14y, 15-19y, 20-24y for opioids; 15-19y and 20-24y for MOUD).

In 2015, youth were dispensed 7,315,657 opioid prescriptions and 1,667 naloxone prescriptions compared to 3,544,051 opioid prescriptions and 24,674 naloxone prescriptions in 2019. MOUD prescriptions were dispensed to 94,996 youth 15-24y in 2015 and 78,437 youth in 2019. In 2015, 0.001% of all youth were co-prescribed naloxone with an opioid prescription; naloxone co-prescribing increased to 0.18% by 2019. From 2015-2019, naloxone co-prescribing with opioids increased annually for all age groups. The proportion of youth 15-24y co-prescribed naloxone and MOUD increased from 0.19% in 2015 to 5.07% in 2019, with annual increases for both 15-19y and 20-24y from 2015-2019 (figure 1).

Naloxone co-prescribing to youth dispensed opioid prescriptions and those dispensed MOUD increased from 2015-2019. Despite its life-saving benefits and availability, naloxone remains markedly under-prescribed to youth. Further investigation of naloxone co-prescribing practices in youth is necessary to develop targeted interventions to ensure appropriate access.
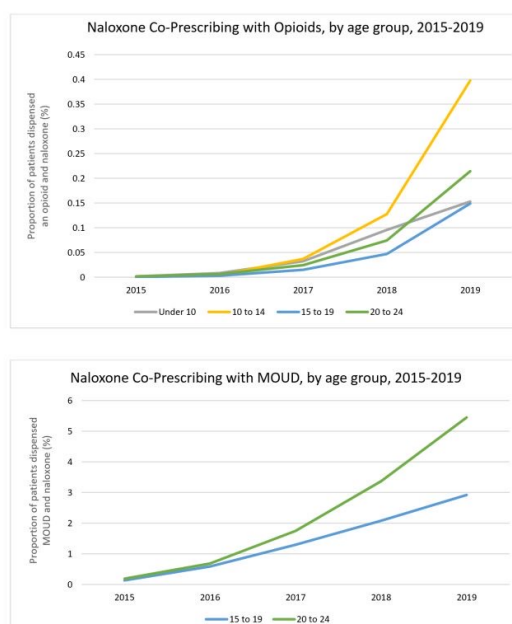
Associations between weekly gestational exposure of nitrogen dioxide and preterm birth in a North Carolina birth cohort, 2003-2015 Alison K. Krajewski* Alison K Krajewski Thomas J. Luben Joshua L. Warren Kristen M. Rappazzo

Preterm birth (PTB) is associated with exposure to criteria air pollutants, though variability in the magnitude and consistency of associations exists. We evaluated the associations between weekly gestational exposure to nitrogen dioxide (NO_2) with PTB (less than 37 weeks completed gestation) in a North Carolina (NC) birth cohort from 2003-2015 (N=1,367,757). Daily NO_2 concentrations from a hybrid model with a spatial resolution of 1 km x 1 km were aggregated to census tract level estimates and linked to residential address at delivery, and then averaged to obtain exposure estimates for each week of pregnancy. Modified Poisson regression with robust errors was used to estimate risk differences (RD) and 95% confidence intervals (CIs) per 10 ppb increase in NO_2, adjusted for gestational parent marital status, race/ethnicity, age at delivery, Medicaid status, and month of conception. The associations between NO_2 exposure and PTB were generally null throughout pregnancy. RDs for weekly exposure during gestation ranged from -7 (95% CI: -14, 1) to 0 (-6, 5) per 10,000 births. However, when adjusting for estimated $PM_{2.5}$ (from hybrid model) and ozone (from EPA's Community Multiscale Air Quality (CMAQ) model) concentrations to account for potential copollutant confounding, there was a consistent pattern of decreased risk of PTB per 10 ppb increase in NO_2 exposure in each week of gestation. RDs in the copollutant model ranged from -29 (-36, -22) to -10 (-15, -5) per 10,000 births for NO_2, 5 (4,6) to 12 (10, 14) per 10,000 births for $PM_{2.5}$, and -17 (-24, -10) to 4 (-3, 11) per 10,000 births for ozone. While NO_2 exposure was not associated with PTB in the single pollutant model, there was decreased risk with PTB when adjusting for other criteria air pollutants.

Endocrine disruption during pregnancy in relation to autism spectrum disorder diagnosis and autistic traits in third generation Gyeyoon Yim* Gyeyoon Yim Andrea Roberts Marianthi-Anna Kioumourtzoglou Marc Weisskopf

Background: Evidence from animal studies suggests that the effect of prenatal exposure to endocrine disrupting chemicals may induce autistic phenotypes in the following generations. However, the multigenerational association of exposure to endocrine disruptors with risk of autism spectrum disorder (ASD) and autistic traits in humans have not been explored.

Objective: To investigate the association of maternal grandmothers' use of diethylstilbestrol (DES), a synthetic form of estrogen, with risk of ASD and autistic traits among the grandchildren.

Methods: The study population was drawn from the Nurses' Health Study II (NHS II), an ongoing prospective cohort study of female registered nurses in the US (N=116,429). The 3 generations in this study refer to the nurses' mothers (Generation 0, G0), the nurses (Generation 1, G1), and the nurses' children (Generation 2, G2). The NHS II participants (G1) and their mothers (G0) independently reported the G0 exposure to DES during pregnancy with G1 and key G0-level covariates. The information on the G2 physician-diagnosis of ASD was collected by the nurses (G1). The quantitative autistic traits were assessed by the Social Responsiveness Scale (SRS) in a nested case-control study.

Results: Of 55,696 grandmother/mother pairs, 1,027 (1.8%) grandmothers (G0) used DES while pregnant with the nurses (G1). Among the 125,177 grandchildren (G2), 528 (0.4%) were ascertained as ASD cases. We observed no association between grandmother use of DES and grandchild risk of ASD. However, grandmother exposure to DES was marginally associated with impaired social cognition traits measured by SRS among the non-affected grandchildren, with an elevated subscale score estimate of 18.87 (95% CI: -2.17, 39.92) at the 90th percentile, using quantile regression.

Conclusions: Maternal grandmothers' use of DES was not associated with increased risk of ASD, but impairments in social cognition traits among the non-affected grandchildren.

Sociodemographic factors and adverse birth outcomes in rural Mysore, India: Examining the Mediating Role of Anemia Sandra Kiplagat* Sandra Kiplagat Karl Krupp Diana M. Sheehan Poornima Jayakrishna Kavitha Chandrappa Mary Jo Trepka Zoran Bursac Dionne Stephens Purnima Madhivanan

Background

India consistently has the highest number of preterm and low birth weight births (3.5 and 7.5 million respectively) in the world. Anemia has been cited as a contributing factor for these adverse birth outcomes. Approximately 60% of pregnant women in India are anemic. However, few studies have examined the mediating role of anemia on adverse birth outcomes. Therefore, the objective of this study was to examine the mediating role of anemia in the relationship between socioeconomic status (SES) and preterm birth (PTB) and low birth weight (LBW).

Methods

We conducted secondary analysis of data from a prospective cohort study of 1540 pregnant women between 2011-2014,. Latent class analysis was performed to identify distinct socioeconomic classes followed by logistic regression to examine the relationship between SES latent classes and birth outcomes. In addition, we conducted causal mediation to examine the mediating role of anemia on the relationship between SES latent classes and PTB/LBW. We estimated the total effects, direct effects and indirect effects.

Results

Two latent classes were identified "low SES and early marriage" and "high SES and later marriage." Women in Class 1 "low SES and early marriage" had higher odds of low birth weight (adjusted odds ratio [aOR]: 2.12, 95% Confidence Interval [CI]: 1.36-3.31) compared to women in Class 2. The analysis indicated that the association between Class 1 and low birth weight was statistically significant for the direct effects (aOR: 2.08, 95%CI: 1.41-3.14). We observed no significant mediation of anemia in the relationship between Class 1 and adverse birth outcomes.

Conclusion

Our findings demonstrate that socioeconomic disadvantage was associated with LBW but this relationship was not mediated by anemia. Targeted interventions such as conditional cash transfers and government subsidies are critical in reducing socioeconomic inequities ultimately improving birth outcomes among rural populations in India.

A prospective cohort study evaluating periconceptional exposure to seasonal inactivated influenza vaccines and risk of miscarriage Annette K Regan* Annette Regan Amelia K Wesselink Tanran Wang Elizabeth Hatch Kenneth Rothman Olivia Orta David Savitz Jennifer Yland Lauren A Wise

Background: Although pregnant individuals are a priority group for inactivated influenza vaccination (IIV), <40% of individuals receive vaccination during pregnancy. Safety concerns are a major contributor to vaccine refusal. While clinical trial and observational data have provided reassurance about the safety of IIV during second and third trimesters, effects of periconceptional IIV exposure on early pregnancy outcomes, such as miscarriage, have not been well studied.

Methods: We analyzed data from PRESTO (2013-2021), a preconception cohort study of female pregnancy planners in the US and Canada. Participants completed a baseline questionnaire, bimonthly follow-up questionnaires until pregnancy, and pregnancy questionnaires at ~8 weeks and ~32 weeks of gestation. In a subset of couples, male partners provided vaccine data. We used Cox proportional hazard models to estimate the hazard ratio (HR) for the association between IIV and miscarriage, with gestational weeks as the time scale. Models included IIV as a time-varying exposure, with fine-stratification weights inversely proportional to the probability of vaccination to control confounding by seasonality and maternal factors.

Results: Of the 7159 pregnancies, 58.2% of female partners reported IIV: 6.2% during early pregnancy, 12.3% <3 months before pregnancy, and 39.8% ≥3 months before pregnancy. Risk of miscarriage was not appreciably associated with IIV before conception (HR 0.96; 95% CI 0.78, 1.16) or during pregnancy (HR 1.09, 95% CI 0.88, 1.34). Among the 2002 couples with male partner data, 9.3% reported IIV <3 months before pregnancy. We observed little association between male partner vaccination and miscarriage (HR 0.90; 95% CI 0.58, 1.39).

Discussion: Neither female partner vaccination before or during pregnancy nor male partner vaccination before pregnancy was materially associated with miscarriage risk. These findings provide additional reassurance about vaccine safety for pregnant individuals.

Interpregnancy intervals and adverse birth outcomes in Australia: Effect modification by maternal age Gizachew Tessema* Gizachew Tessema Jennifer Dune Amanuel Gebremedhin

Maternal age at first birth has been increasing in high income countries in recent decades. Delaying childbirth is associated with increased parental socio-economic resources; however, any such benefits are mitigated by reduced fecundability and an increased risk of adverse maternal and perinatal outcomes. There has been increasing interest in recent years on the association between interpregnancy interval (IPI) and birth outcomes when modified by maternal age. We aimed to investigate the effect modifying role of maternal age for the observed associations between IPI and adverse birth outcomes in Australia. We conducted a retrospective cohort study among 1,331,236 births in Australia (Western Australia and New South Wales) between 1980 and 2016. We estimated the risk of preterm birth (PTB), spontaneous PTB (sPTB), and small for gestational age (SGA) births for 3 to 60 months of IPI according to maternal age at birth prior to IPI (20-24, 25-29, 30-34 and ≥35 years). We modelled IPI using restricted cubic splines and estimated adjusted odds ratios (ORs) with 95% CI at 3, 6, 12, 24, 36, 48 and 60 months, comparing with 18 months as reference. Relative to 18 months of IPI, there was increased odds PTB for births at 6 months of IPI but no significant differences in the odds ratios across maternal age groups ranging between 1.33 (OR =1.33, 95% CI: 1.23-1.45 for women >35 years 1.46 (OR =1.46, 95% CI: 1.38, 1.54 for women 30-34 years). Similarly, we found no evidence of differences in the odds sPTB and SGA at 6 months of IPI compared to 18 months of IPI. The association between IPI and adverse birth outcomes did not vary substantially by maternal age.

LATEBREAKER

Perinatal & Pediatric

Association of adverse childhood experiences and gendered racial stress among pregnant Black women Lasha Clarke* Lasha Clarke Carol Hogue Anne Dunlop Tene Lewis Michael Kramer

Introduction: Exposure to adverse childhood experiences (ACEs) is a risk factor for adverse birth outcomes, although the mechanisms by which they act have not been fully explored. As Black women and their infants are known to be at disproportionate perinatal health risk, it is imperative to understand the role of ACEs in proliferating types of stress specific to American Black women's sociohistorical context. One such type of stress is gendered racism, which suggests that, by virtue of being both Black *and* women, Black women uniquely experience psychosocial stressors that go beyond reports of racism. It is unknown whether ACEs confer risk for gendered racial stress among pregnant Black women. We examined associations between maternal ACEs, the intersectional construct of gendered racial stress, and coping responses among socioeconomically diverse Black women.

Methods: In this cross-sectional study of 405 pregnant Black women, we assessed gendered racial stress, ACEs, and response to unfair treatment via self-report. Women were enrolled if they were receiving prenatal care at one of two Atlanta-area hospitals.

Results: 82% experiences at least one ACE; 21% experienced 4 or more ACEs. Increased ACEs were associated with increased gendered racial stress scores (b=4.3, SE_b=.49, CI_b=3.3-5.3, p<.0001), particularly among those who reported passive versus active responses to unfair treatment (likelihood ratio test, p=.009). Model adjustment did not attenuate the magnitude of the associations of ACEs with gendered racial stress.

Conclusion: This study demonstrates novel associations between childhood adversity and gendered racial stress among pregnant Black women, which are moderated by learned coping responses. Thus, we enhance the call for inequities in Black maternal health to be targeted intersectionally, at multiple levels (inclusive of medical, political, social, and institutional factors), and at multiple points over the lifecourse when coping tools are developed.
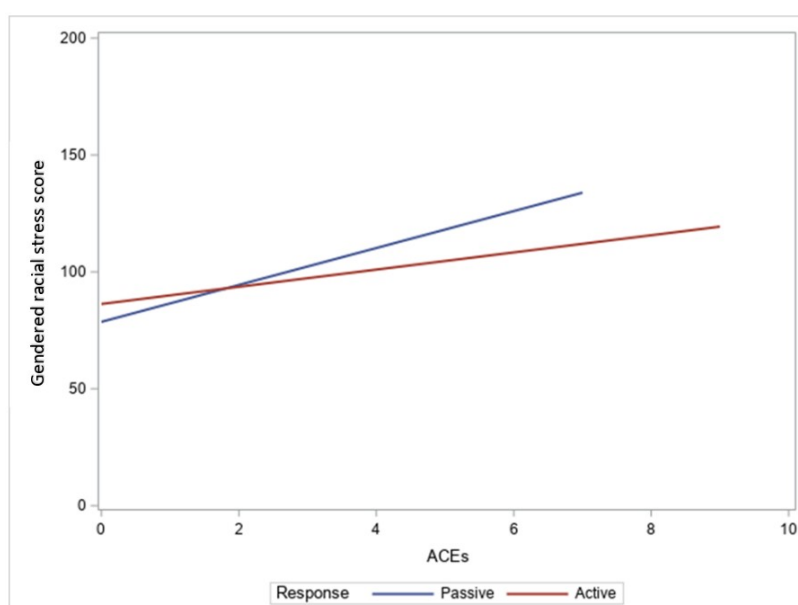
Surveillance of COVID-19 outbreaks in prisons in the US South: The role of economic distress in the communities surrounding prison facilities Mofan Gu* George Pro Nickolas Zaller

Introduction

The US South is the epicenter of the epidemic of mass incarceration. Prisons have experienced substantial challenges in preventing COVID-19. Incarcerated individuals and prison staff are at a high risk for infection due to minimal available preventive measures. Prisons are not closed systems and many staff come from communities in close proximity to the facility. Characteristics of the communities immediately surrounding prisons are an overlooked but critical factor to better understand the role prisons play in pandemics.

Methods

We used facility-level COVID-19 data from the COVID Prison Project to identify the number of unique outbreaks between May 2019 and May 2020. We used a county-level composite indicator of economic distress (0-100) to identify the environment surrounding each prison (2015-2019). Our sample included 570 prisons in 368 counties across 13 Southern states. We modeled the number of outbreaks with negative binomial regression, offset by total county population and adjusted for the percentage of the African American population. We created a bivariate choropleth map to visualize prison outbreak locations and county economic distress.

Results

The mean number of prison outbreaks was 2.5, and reached as high as 30 in Livingston County, MO (distress score = 71). Community economic distress was positively associated with prison outbreaks (B=0.02, 95% CL=0.01-0.03, p<0.0001). Figure 1 illustrates the geographic distribution of the primary study variables. There were 46 prisons in 33 counties that had both high numbers of outbreaks and high distress scores (dark purple).

Discussion

Economic health is a key precursor to physical health. Poorer communities have been disproportionately impacted by the pandemic, and we found that prisons located in these communities were more susceptible to recurring outbreaks. Prison-based disease prevention interventions should consider the impact that the outside world has on the health of incarcerated individuals.
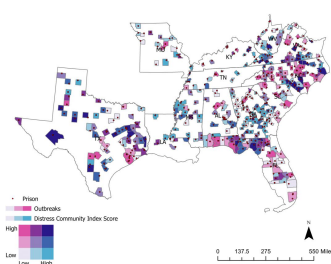
Figure 1: Prison locations and distribution of COVID-19 prison outbreaks and community economic distress in the US South, May 2019 – May 2020

LATEBREAKER

Recruitment strategy

Novel recruitment approaches for a state-wide population cohort for research on cancer early detection during the COVID-19 pandemic- the Healthy Oregon Project Zhenzhen Zhang* Zhenzhen Zhang Katie Johnson-Camacho Paul Spellman Jackilen Shannon Autumn Shafer

Public health research often relies on large-scale cohorts to derive generalizable results. Traditional recruitment methods, such as mass invitation mailings, can be expensive and time-consuming with low response and follow-up rates. While probability sampling reduces recruitment costs of materials/mailings, the sampling procedure can also increase costs through labor and time. During the COVID-19 pandemic, where person-to-person contact is highly restricted, commonly used recruitment alternatives to mass mailings, such as community events, were not efficient or feasible. Thus, developing novel recruitment strategies for the new era that allow us to adapt to changing situations quickly is critical. We aim to report diverse recruitment methods used to establish a cost-effective state-wide sample of people for genetic screening for cancer—the Healthy Oregon Project (HOP).

Prior to the onset of COVID-19, our primary recruitment methods were in-person community events and the installation of vending machines for genetic screening kits pick-up/drop-off. While successful, this in-person approach was labor-intensive and had limited reach. With the onset of COVID-19, we shifted our recruitment model to a remote approach by marketing the study across the state through multiple social media campaigns, both reaching the broad general population and also with more specific targeted efforts at hard-to-reach under-recruited populations. Individuals may enroll from their homes by downloading the HOP app, including eligibility, consent, surveys, and resources information. We have implemented a mail-in option, where the participant can request a DNA collection kit within the app to be sent to their home address and return the self-collected kit via a pre-paid mailing envelope to the designated lab. During the initial 1-year in-person recruitment, we enrolled 4,800 individuals. Enrollment was paused due to COVID-19 and restarted in October 2020 utilizing the fully remote approach. In the ensuing 18 months, we have consented >22,000 adult participants aged 18-80 years old (just over 1% of Oregon's adult population). The data completion rate is >90%. The study provides a novel remote-based, inexpensive recruitment approach to establish a large-scale cohort for population-based studies during the pandemic.

1. Open the "Healthy Oregon Project" app (available from Google Play or Apple iOS app store).

2. Complete the eligibility and consent; then create account to join.
If you are already part of HOP, simply log-in.

3. Follow the detailed instructions in the box to provide a sample.

4. Place the completed kit in the plastic bag. Place the bagged kit into the box.

5. Return the sample according to instructions in the box (via mail or drop slot).

Questions? Email HealthyOregonProject@ohsu.edu. We are here to help!

Reproductive

Association of Gestational Hypertension (GH) and Eclampsia to Maternal Smoking (MS) by pre-pregnancy BMI (pBMI) status Among Mothers Under the Age of 30 Years in the United States Holly Bihun* Holly Bihun Jian Liu

Objective: To investigate whether GH and/or eclampsia was associated with timing of MS when stratified by pBMI status.

Study design and methods: 1,376,271 US-born mothers aged 20 – 29 from the 2019 infant natality data who had a singleton birth (20+ weeks of gestation) were analyzed in this study. MS status was defined into five groups, i.e., G1: non-smokers, G2: quitted smoking before pregnancy, G3: quitted smoking before the 2nd trimester, G4: quitted smoking before the 3rd trimester, and G5: smoked whole-time. Odds ratios (ORs) of GH or eclampsia were estimated using multiple logistic regression for MS by pBMI status (kg/m²): underweight (<18.5), normal (18.5–<25.0), overweight (25.0–<30.0), and obese (≥30.0).

Results: Compared to G1, the adjusted ORs (95% CIs) of GH for mothers in G2 with pBMI underweight, normal, overweight, and obese were 1.17 (0.92-1.49), 1.11 (1.03-1.19), 1.13 (1.05-1.22), 1.13 (1.08-1.19), respectively. While the ORs (95% CIs) of GH for mothers in G5 were 0.71 (0.60-0.84), 0.80 (0.75-0.84), 0.79 (0.74-0.84), and 0.82 (0.78-0.85), respectively. The adjusted ORs for eclampsia showed a different pattern, only that for mothers in G5 with normal and obese showed significantly (0.69 [0.53-0.91] for normal weight, 0.73 [0.58-0.92] for obese).

Conclusion: In comparison to non-smokers, an increase in the odds of GH were observed amongst normal, overweight, and obese mothers quitting before pregnancy meanwhile a decreased odds were observed amongst mothers smoking throughout pregnancy in all pBMI classes.

Self-reported menstrual cycle length during reproductive years in relation to onset of menopause and menopausal symptoms at midlife in Project Viva. Lidia Minguez Alarcon*
Lidia Minguez Alarcon Sheryl Rifas-Shiman Diana C. Soria-Contreras Marie-France Hivert Jan Shifren Emily Oken Jorge E. Chavarro

Background: We investigated whether menstrual cycle length during reproductive years was associated with onset of natural menopause and midlife menopausal symptoms.

Methods: This prospective analysis includes 628 women recruited during pregnancy at obstetric practices in eastern Massachusetts (USA) (1999-2002). Women self-reported menstrual cycle length at baseline (median age 33 years). Approximately 17 years later (median age 52 years), we collected information on menopausal status and the presence of menopausal symptoms using the Menopause Rating Scale [MRS, median IQR=7 (4, 11)]. We used linear and logistic regression models to examine associations of menstrual cycle length with total MRS (continuous) and specific menstrual symptoms (any vs. none). We also used Cox proportional hazard regression, with age as the time scale, to investigate the relation of menstrual cycle length with onset of natural menopause. We adjusted models for age at midlife visit, pre-pregnancy BMI, race/ethnicity, education and parity.

Results: Compared to women whose menstrual cycle length was 26-34 days, women whose cycles were short (<26 days, 14%) had a higher total MRS at midlife [adjusted β (95% CI)= 1.84 (0.50, 3.17)]. Women with short menstrual cycles during their reproductive years had higher odds of midlife depressive mood symptoms, compared to women with a normal menstrual cycle length [adjusted OR (95% CI)= 1.86 (1.15, 3.00)]. Results were similar after further adjustment for history of depression during the reproductive years. In addition, compared to women whose cycle length was 26-34 days, women reporting short cycles had an earlier onset of natural menopause [adjusted HR (95% CI)= 1.64 (1.08, 2.49)].

Conclusions: Women with short menstrual cycles during their reproductive years had a higher frequency of total menopausal and depressive mood symptoms and reached menopause earlier then to women with normal menstrual cycle length.

Reproductive

Factors associated with low birth weight and level of access to maternity care Rexford
Anson-Dwamena* Priyadarshini Pattath Rexford Anson-Dwamena

Background: Access to maternity care has been linked to high risk pregnancies and low birth weight.
Maternity care deserts are counties in which access to maternal health care services is limited or
absent, through lack of services or barriers to access care. In Virginia, 32.3% of counties are
maternity care deserts and 14.6% of counties have low or moderate access affecting 373,686
women. We explored low birth weight rate in Virginia using disaggregated data by level of access to
maternity care, including drive time and sociodemographic factors.

Methods: In this study maternity care deserts were defined as areas where obstetrics and
gynecology services access was over 30 minutes' drive time from the population weighted census
tract centroid, with over 20% population in particular census tracts living below the 200% federal
poverty level, and located in the Health Professional Shortage Areas (HPSA) in the census tract.
Independent variables included the Health Opportunity Index, using social determinants of health
indicators, poverty level, and level of access to maternity care.

Results: Low birth weight was higher in areas with lower level of access to maternity care and
maternity deserts (8.6%), compared to areas with access (8.1%). There is disparity in low birth
weight between areas with very low health opportunity index (10%) and very high health
opportunity index (6.9%). Mother's education, affordability and Townsend index have significant
association with low birth weight ($p < .05$).

Conclusion: Findings indicate that low birth weight was significantly higher in areas of maternal
deserts, low poverty level and areas with low education, affordability index. Targeting high priority
areas include incentivizing providers to work in undeserved areas, and future research on infant
mortality rate.

Plasma Persistent Organic Pollutants in Early Pregnancy and Fetal Growth among Pregnant Women with Obesity Sifang Kathy Zhao* Sifang Kathy Zhao Edwina H. Yeung Yan Qiao Marion Ouidir Katherine L. Grantz Daniel He Roger Newman William A. Grobman Michael S. Bloom Kurunthachalam Kannan Germaine M. Buck Louis John E. Vena Kelly J. Hunt Rajeshwari Sundaram Cuilin Zhang

Background: Maternal persistent organic pollutants (POPs) has been related to fetal growth and may alter adipogenesis and fat storage. However, it remains unclear as to associations of POPs with longitudinal fetal growth specifically for pregnant women with obesity.

Methods: Among 452 women with obesity in the NICHD Fetal Growth Studies, non-fasting blood samples collected at 10-14 weeks' gestation were analyzed for lipids and 76 POPs: 11 poly-and-perfluorinated alkyl substances, 1 polybrominated biphenyl, 9 polybrominated diphenyl ethers (PBDE), 44 polychlorinated biphenyl congeners (PCBs), some detected infrequently, and 11 organochlorine pesticides (OCPs). Fetal biometrics were obtained from 5 ultrasound visits in pregnancy by certified sonographers. Relations of each of the 76 POPs to longitudinal fetal growth were examined using generalized linear mixed models, adjusting for confounders. Using group lasso variable selection, we identified important chemicals associated with fetal growth from the mixture and estimated the mixture effect on fetal growth at each visit.

Results: Higher plasma concentrations of 3 PCBs (PCB167, PCB172/192, PCB196/203) and 1 OCP (trans-Nonachlor) were associated with larger fetal size. For example, β (95% confidence interval) comparing 3rd tertile (median 1.12 ng/g lipid) with 1st tertile (median 0.29 ng/g lipid) of PCB-196/203 was 0.17 g (0.02, 0.32) for estimated fetal weight. Of note, PCB167 and PCB172/192 were detected infrequently (<10% above limits of detection). When we examined the mixture effect in multi-pollutant models, the 3rd compared to 1st tertile of mixture concentrations was associated with larger abdominal circumference at 24-29 (0.08 mm [0.02,0.15]) and 30-33 weeks' gestation (0.07 mm [0.03,0.12]), mainly related to PCB-199 and PBDE-100 (**Figure**).

Conclusion: Among pregnant women with obesity, higher levels of several individual and mixtures of POPs in early pregnancy were associated with accelerated fetal growth.
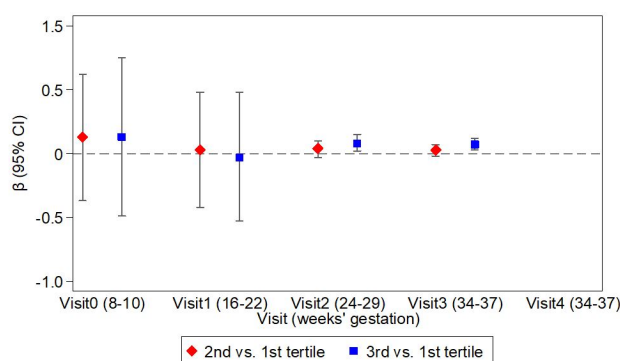
Figure. Association between chemical mixtures (tertiles) in early pregnancy and fetal abdominal circumference by study visit (weeks' gestation)[1]

Abbreviation: AC, abdominal circumference.

[1] Adjusting for maternal age, race/ethnicity, education, total plasma lipids (except for PFASs), plasma cotinine level, infant sex, gestational age at time of ultrasound, and maternal pre-pregnancy BMI. Red compares 2nd vs. 1st tertile, blue compares 3rd vs. 1st tertile.

Sexual practices among NYC adults, and National comparisons, 2013-2014 Ariadne E Rivera Aguirre* Ariadne E Rivera Aguirre Priscilla Lopez Alexa Riggs Rania Kanchi Lorna Thorpe Heidi E. Jones

Introduction: Unconscious biases in sexual risk characterization based on demographic and physical characteristics, like gender, race/ethnicity, age, and obesity may influence sexual history taking and screening practices of obstetric/gynecological and primary care providers in the United States.

Aim: Our objective was to examine variability in sexual behaviors across demographic characteristics and between New York City and the country.

Methods: We present age-standardized reports on lifetime prevalence and past-year partners of vaginal, oral, same-sex, and anal sex by race/ethnicity, sex and BMI for adults 20 years and older in NYC and nationally. We used data from the 2013-2014 NYC Health and Nutrition Examination Survey (n=1,155), and 2011-2014 National Health and Nutrition Examination Survey (n=7,697).

Results: Data from these two population-level surveys show slight differences in sexual behaviors by sex and age, and between NYC adults and the national average. As an example, Figure 1 shows the number of sex partners by age group and geography among those who reported past-year vaginal sex. As age increases the percent of adults reporting 2 or more partners declines. Compared to national average, among adults aged 50-49 a higher proportion of people report at least one vaginal sex partner in the past year. We observed no differences in sexual patterns by race/ethnicity and BMI in NYC or nationally.

Conclusions: Contrary to possible unconscious beliefs, results suggest that sexual behaviors are relatively consistent across sociodemographic or BMI groups among NYC and US adults. In reproductive health care, standard recommendations and preventive measures should be tailored to the patient, not based on assumptions from their sociodemographic profile.

Figure 1: Number of vaginal sex partners in NYC (2013-2014) and National (2011-2014) by age group

Reproductive
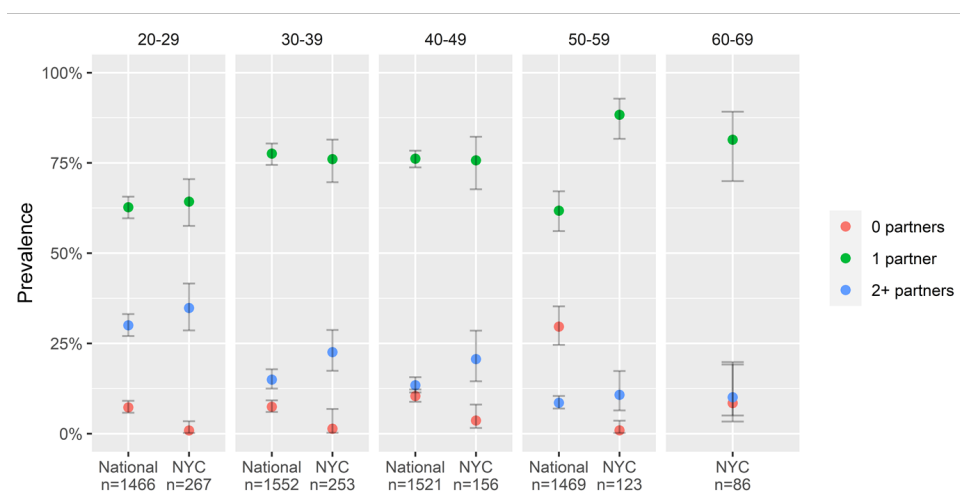
Ambient air pollution and risk of spontaneous abortion among couples trying to conceive

Ellen Margrethe Mikkelsen* Anne Sofie Dam Laursen Katrine Eriksen Sinna Pilgaard Ulrichsen Matthias Ketzel Amelia K Wesselink Lauren A Wise Elizabeth E Hatch Jibran Khan Jørgen Brandt Kenneth J Rothman Henrik Toft Sørensen Ellen Margrethe Mikkelsen

Evidence from cohort studies on air pollution and spontaneous abortion (SAB) remains inconsistent across specific pollutants. We estimated associations between ambient residential air pollution concentrations and the risk of SAB (loss before 22 completed weeks' gestation) in a Danish preconception cohort. From 2007-2019 we recruited couples who were trying to conceive. We ascertained pregnancies through bimonthly follow-up questionnaires completed up to 12 months after enrollment. We identified SABs by self-report on follow-up questionnaires and through the Danish National Patient Registry. We geocoded time-updated residential addresses and used the DEHM/UBM/AirGIS dispersion modelling system to estimate mean daily concentrations of nitrogen dioxide (NO_2), nitrogen oxides (NOx), carbon monoxide (CO), ozone (O_3), particulate matter <2.5 µg ($PM_{2.5}$) and <10 µg (PM_{10}), and sulfur dioxide (SO_2), modeled as weekly updated time-varying cumulative average exposures during the four weeks before conception through pregnancy. We used Cox proportional hazard regression models with gestational weeks as time scale to compute hazard ratios (HRs) and 95% CIs for associations for an interquartile range (IQR) difference in air pollutants with SAB. We analyzed data from 6,195 women who became pregnant within 12 months of enrollment of whom, 17% had an SAB. Adjusted HRs for one IQR higher residential air pollution concentration were 1.00 (95% CI: 0.77-1.28) for NOx, 0.91 (95% CI: 0.60-1.37) for NO_2, 1.19 (95% CI: 0.74-1.93) for O_3, 0.97 (95% CI: 0.70-1.36) for CO, 0.97 (95% CI: 0.66-1.41) for PM_{10}, 1.13 (95% CI: 0.77-1.66) for $PM_{2.5}$ and 1.16 (95% CI: 1.03-1.29) for SO_2. Overall, we observed little association between risk of SAB and higher cumulative concentrations of air pollutants through gestation. For O_3, $PM_{2.5}$ and SO_2, HRs suggested an elevated risk of SAB, although for O_3 and $PM_{2.5}$, the lower CIs were also consistent with a lower risk of SAB.
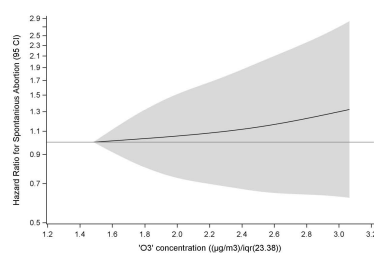
Figure 1. Association between residential concentration of ozone (O_3) and SAB fitted by restricted cubic splines. O_3 is modeled as weekly updated time-varying cumulative average during the 4 weeks before conception through pregnancy. Adjusted for age, month and year of conception, ambient temperature during the month of conception, education, household income, parity conditional on gravidity and co-pollutants. The unit corresponds to the interquartile range among all enrolled participants.

Reproductive

Handedness and fecundability in a North American preconception cohort study Olga Basso*
Lauren Wise Olga Basso Lauren Wise

Background: Studies have reported an association between left-handedness or mixed handedness and delayed conception, but study designs have been retrospective or restricted to pregnant participants. We evaluated the association between handedness and fecundability in Pregnancy Study Online (PRESTO), a prospective cohort of North American couples. **Methods:** Participants completed baseline questionnaires on which they reported sociodemographic, behavioral factors, and handedness (5 categories) for themselves and each of their parents. Females completed follow-up questionnaires every 8 weeks for 12 months or until pregnancy. The analysis was restricted to 12,125 females (and 3,010 male partners) with ≤6 cycles of pregnancy attempt time at enrollment. We used proportional probabilities models to estimate fecundability ratios (FRs) and 95% CIs, adjusting for age, education, income, geographic region of residence, parental education (females only), and maternal smoking (females only). **Results:** Among females, 70.0%, 20.2%, 4.4%, 4.3%, and 1.1% reported being exclusively right-handed, mostly right-handed, exclusively left-handed, mostly left-handed, or mixed handed ("use both hands equally"), respectively. Among males, these respective percentages were: 65.1%, 21.6%, 5.9%, 5.2%, 2.2%. Among females, compared with exclusive right-handedness, FRs (95% CIs) were 0.94 (0.89-0.99), 1.03 (0.93-1.15), 0.89 (0.80-0.99), and 0.90 (0.71-1.15) for mostly right-handedness, exclusive left-handedness, mostly left-handedness, and mixed handedness, respectively. Among males, these respective FRs (95% CIs) were 0.94 (0.85-1.04), 1.02 (0.85-1.22), 0.95 (0.79-1.14), and 1.03 (0.78-1.36). Associations were similar among participants whose parents were exclusively right-handed, and among participants with pregnancy attempt times of 0 or 1 at enrollment. **Conclusions:** Neither left-handedness nor mixed handedness in either partner was appreciably associated with fecundability.

Respiratory

Accelerated lung function decline and mortality among World Trade Center exposed rescue and recovery workers David Goldfarb* David Goldfarb Rachel Zeig-Owens Madeline Cannon Theresa Schwartz Charles Hall David Prezant Michael Weiden

Background: World Trade Center (WTC) exposure caused lung injury with an immediate decline in forced expiratory volume at 1 second (FEV_1) in Fire Department of the City of New York rescue/recovery workers. Lung function stabilized for most, but continued to decline for 11.4% of the cohort, which were found to have FEV_1 loss >64 mL/year (accelerated-FEV1-decline) or double the age-related decline of 32 mL/year (expected-FEV_1-decline). Other population-based studies evaluating non-WTC exposed cohorts have reported an increased risk of all-cause mortality among those with accelerated lung function decline.

Objective: To evaluate the association of accelerated-FEV_1-decline and mortality in the 20-years post 9/11/01 (9/11).

Methods: Individual rates of post-9/11 FEV_1 decline were used to categorize participants as having either accelerated-FEV_1-decline or expected-FEV_1-decline by fitting a linear regression model using years of follow-up time for each repeated FEV_1 measurement in each study participant. Unadjusted Kaplan-Meier estimates were plotted, and adjusted Cox regression models were used to estimate hazard ratios (HR) with 95% CIs controlling for potential confounders.

Results: 129 of 1,281 participants with accelerated-FEV_1-decline (10.1%) died within 20 years after 9/11 vs. 299/9,921 (3.0%) participants with expected decline. Accelerated-FEV_1-decline is associated with a 2.5-fold increased risk of mortality when compared with age-related expected-FEV_1-decline (HR=2.5; 95% CI=2.0-3.1), after controlling for age on 9/11, body mass index (BMI) on 9/11, sex, race/ethnicity, work assignment (firefighter vs. emergency medical service providers), and smoking (ever vs. never).

Conclusions: Participants with accelerated lung function decline had increased all-cause mortality. Future work will compare causes of death in accelerated and expected decline participants and will assess whether persistent inflammation is an underlying mechanism for the observed association.

Figure: Kaplan Meier estimates for accelerated-FEV1-decline (red line) is associated with increased mortality vs. expected-FEV1-decline (blue line)

Screening
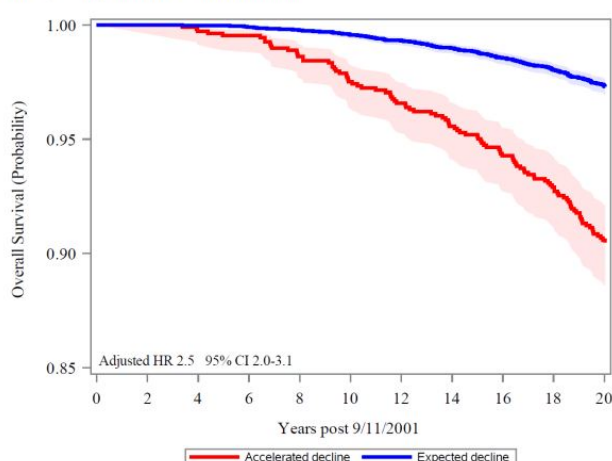
The acceptability of HPV self-sampling for cervical cancer in the US: a systematic literature review Geetanjali D Datta* Geetanjali Datta Patrycja Sleboda Defne Yilmaz Emmeline Lin Bobbie J Rimel Anna R Giuliano

Background: Cervical cancer screening rates are less than optimal in many contexts. HPV self-sampling is being used in some jurisdictions to help increase uptake. HPV self-sampling devices have not yet been approved in the United States (U.S.), but trials are being planned to this end. Therefore, it is important to develop a knowledge base in the U.S. on acceptability and best practices for implementation, especially among vulnerable populations.

Objective: Our objective was to summarize the existing literature and identify knowledge gaps on the acceptability of human papillomavirus (HPV) self-sampling for cervical cancer in the United States.

Method: A systematic search on PubMed and EMBASE was conducted using terms related to vaginal, cervical screening, self- collection, HPV, and acceptability. Studies published in English between 1990 – 2021 among participants living in the U.S. were included.

Results: A total of 49 papers from 46 independent samples were included in the review. Acceptability was assessed via several methods including: percentage who selected self-sampling or were willing to test (theoretically), percentage of kits returned, and assessment of acceptability after self-sampling. Twenty-seven studies focused on racial/ethnic minorities or immigrants, 6 focused on women with low-income, 4 papers included participants who identified as sexual minorities, and 6 studies focused on healthcare providers. Participants were generally positive about collecting their own samples, perceived it as easy and comfortable, although some physical (e.g. discomfort), psychological (e.g. embarrassment), and operational (e.g. distance or time) barriers were noted. Only 1 study investigated barriers for returning to the clinic after receiving a positive test result.

Conclusions: Current literature from the U.S. reports HPV self-sampling for cervical cancer screening is acceptable. Urgent research is needed to address clinical follow-up after self-sampling.

Screening

Effect of National Breast Cancer Screening Program on Long-term Survival of Breast Cancer Patients: A population-based Cohort Study Xuan Quy Luu* Xuan Quy Luu Kyeongmin Lee Jae Kwan Jun Mina Suh Kyu-Won Jun Kui Son Choi

In Korea, breast cancer (BC) is also the most common cancer type diagnosed in women excepting thyroid cancer. The Korean National Cancer Screening Program (KNCSP) provides biannual mammography screening for women aged ≥40. There is no study investigating the association between the long-term survival of BC patients and BC screening. We conducted this study to provide evidence of the effect of BC screening on the long-term survival of BC patients.

The study cohort was constructed from three nationwide databases of KNCSP, the Korean Central Cancer Registry, and the death certificates. From 12,732,772 women who were invited to KNCSP between 2002 and 2009, we included 24,387 women diagnosed with invasive cancer or ductal carcinoma in situ (DCIS), then follow-up until 31/12/2019. The Kaplan–Meier analysis and the log-rank test were recruited to estimate and compare the survival between subgroups. The Cox proportional-hazards regression was used for investigating the effect of BC screening on mortality.

20,916/24,387 patients (85.8%) were alive at the end of the follow-up period (median of 10.5 years), the survival rate was significantly lower among never-screened group (80.3%) compared with screened group (88.9%) (p-value <0.001). The survival rate ranged from only 22.4% in patients with the distant stage to 96.4% in DCIS patients. A 35% BC mortality reduction (Hazard ratio (HR)=0.65, 95% confident interval (CI)= 0.60-0.70) from screening was reported after adjusting for all covariates. In subgroup analysis, this figure was 62%, 36%, and 24% in the subgroup of localized stage, regional stage, and distant stage, respectively. Additionally, women aged 40-49 received the least benefit from BC screening (HR=0.71, 95%CI=0.62-0.81).

Our study highlights the significant reduction of long-term BC mortality by BC screening even within each cancer stage. Also, there was a reduced effect of mammography among women at the age of 40s, which requires a specific screening strategy.
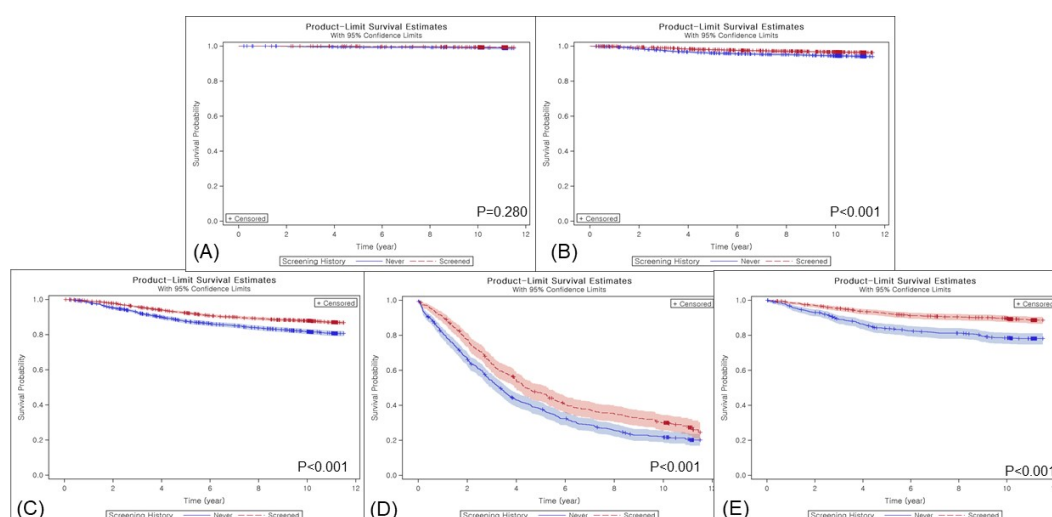
Figure 1: Product-Limit breast cancer-specific survival estimates according to screening history by SEER stages

(A) DCIS; (B) Localized; (C) Regional; (D) Distant; (E) Unknown

Social

Acculturation proxies and progression to type 2 diabetes after gestational diabetes in a multiethnic population-based retrospective cohort Teresa Janevic* Teresa Janevic Katherine Shelley Liu Luciana Vieira Victoria Mayer

Gestational diabetes (GDM) is a common complication of pregnancy for which immigrant women are at increased risk relative to US-born women. Over half of women with GDM will be diagnosed with type 2 diabetes (T2DM) in their lifetime, but it is unknown if region of origin or proxies for acculturation are associated with longitudinal T2DM risk. Our objective was to measure associations between region of origin, years in the US, and paternal nativity with 8-year cumulative risk of T2DM. We used data from the NYC APPLE Cohort, a retrospective cohort of linked 2009-2011 birth certificate and hospital discharge data, and 2009-2018 HbA1C test data. We ascertained GDM with no history of elevated HbA1c to comprise the baseline cohort (n=21,695). We classified women with 2 or more HbA1c tests >6.5% from 12 weeks to 8 years postpartum with T2DM. We used Cox proportional hazards models to estimate associations between acculturation proxies and 8–year cumulative incidence of T2DM. Covariates included sociodemographic and clinical factors at baseline. Models were generalized to accommodate non-proportional hazards by allowing interaction with time. Covariate-adjusted hazard ratios (aHR) for T2DM comparing region of origin to all US-born women were elevated for South Asian women (aHR=1.7, 95% Confidence Interval(CI)=(1.7, 1.4,2.1), Sub-Saharan African women (aHR=1.6, 95%CI=1.6, 1.2, 2.1), and Latin American women (1.4, 95%CI=1.2, 1.6). Compared to women living in the US for 10 or more years, 0-4 years was associated with a borderline increased incidence of T2DM (aHR=1.2, 95%CI=1.0, 1.5); 5-9 years was not (aHR=1.0, 95%CI=0.8, 1.2). Immigrant women whose husband was also foreign born had an increased hazard of T2DM relative to US–born women of 1.3(95%CI=1.1, 1.5). T2DM risk after GDM varies by region of origin. Paternal nativity is associated with T2DM after GDM, but longer time in the US is not, suggesting structural inequities as an explanation for observed findings.

Neighborhood disadvantage and epigenetic aging in the Gulf Long-term Follow-up Study

Kaitlyn Lawrence* Kaitlyn Lawrence Lawrence Engel Jacob Kresovich Katie O'Brien Zongli Xu Jack Taylor Dale Sandler

Background. Neighborhood disadvantage has been associated with poor health. The biological pathways underlying these associations are not well understood. Disadvantaged neighborhoods are often characterized by higher levels of environmental toxicant exposures and crime, lack of social cohesion, and barriers to medical care, healthy food, and physical activity. At the individual-level this is associated with chronic stress, inflammation, and endocrine changes. Epigenetic clocks use DNA methylation patterns as putative markers of biologic aging. To date, few studies have evaluated whether living in disadvantaged neighborhoods influences biologic age measured by epigenetic clocks. **Methods**. We evaluated the relationship between neighborhood disadvantage and epigenetic age acceleration, or the difference between a person's epigenetic and chronological age, in a diverse population of men aged 21-65 who participated in the Gulf Long-term Follow-up Study, a prospective study of health effects associated with the *Deepwater Horizon* disaster. We selected 1,544 participants for assessment of genome-wide blood DNA methylation and computed epigenetic age using several phenotype-based methods including the mortality predictor "GrimAge". We used the Area Deprivation Index (ADI) at the Census block group level to characterize neighborhood deprivation at participants' enrollment address and tested associations between US-based ADI quartiles and epigenetic age acceleration using linear regression. **Results**. Compared living in neighborhoods at the lowest US-based quartile of neighborhood disadvantage, participants living in neighborhoods at the highest quartile had higher epigenetic age acceleration as characterized by the GrimAge epigenetic clock (β: 1.59, 95% CI: 0.79, 2.37) but not other epigenetic age measures. **Conclusions.** We find evidence that living in disadvantaged neighborhoods is associated with a DNA methylation-based marker of mortality risk.

A machine-learning approach to estimate intersectional differences in binge drinking

Jonathan Platt* Jonathan Platt Justin Jager Megan Patrick John Schulenberg Katherine Keyes
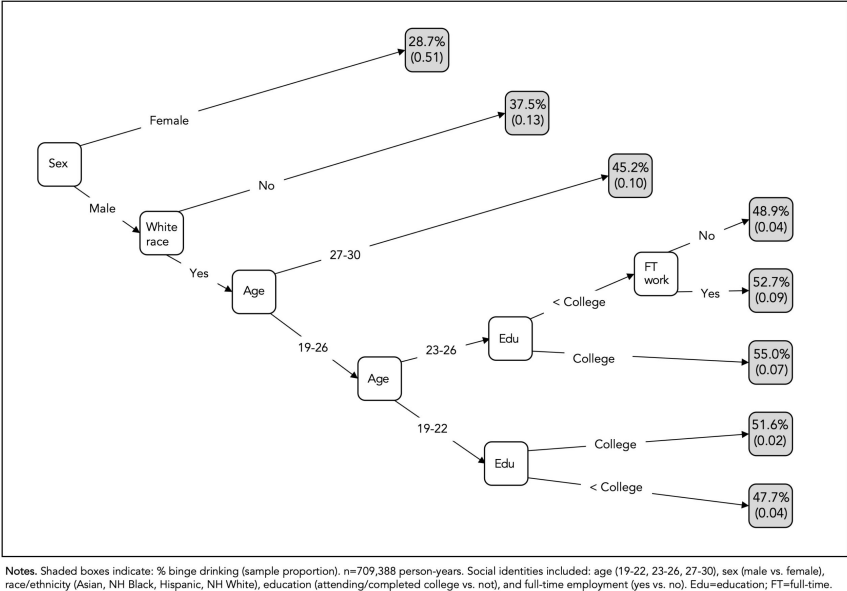
Binge drinking (rapid consumption of 4/5+ drinks) contributes to half of alcohol-related deaths in the US. Rates of binge drinking vary across socio-demographic groups, and generally increase with social and economic status. For example, binge drinking is more prevalent among men vs. women, non-Hispanic whites vs. NH Blacks and Hispanics, and those with vs. without a college degree. However, little is known about how risk varies at the intersections of these and other social axes, where distinct and potentially conflicting statuses may emerge. This study applied machine learning methods to estimate intersectional binge drinking prevalence.

The analytic sample comprised Monitoring the Future Study participants, enrolled from 1991-2018. Age groups 19-22, 23-26, and 27-30 were selected to capture relevant education and employment status acquisition. Social identities were measured as: sex (male, female), race/ethnicity (Asian, NH Black, Hispanic, NH White), education (attending/completed college vs. < college), and full-time employment (yes, no). Differences in binge drinking prevalence were estimated using evolutionary tree algorithms, used to identify the complex and nonlinear effects of multiple social identities. Ten-fold cross-validation and a priori pruning criteria were used to prevent overfitting.

Model accuracy was fair (AUC=0.74) and identified 8 distinct groups (out of 64 possible groups). Binge differences emerged across simple and complex social intersections. Large groups with relatively low prevalence included women (28.7%) and Asian, Hispanic, and NH Black men (37.5%). Small groups with high prevalence included NH white men ages 23-26 with a college degree (55%) (see figure).

Decision trees are promising methods to identify intersectional risk groups in high-dimensional data and advance quantitative intersectionality research. Models offer intuitive decision rules with relevance for clinical and public health policies to mitigate dangerous alcohol use.

Figure. Evolutionary tree-based diagrams of binge drinking prevalence by intersecting social identities, 1991-2018.
Platt, J.M., et al.

Notes. Shaded boxes indicate: % binge drinking (sample proportion). n=709,388 person-years. Social identities included: age (19-22, 23-26, 27-30), sex (male vs. female), race/ethnicity (Asian, NH Black, Hispanic, NH White), education (attending/completed college vs. not), and full-time employment (yes vs. no). Edu=education; FT=full-time.

Ethnic enclave neighborhoods and inflammatory markers: The Multi-Ethnic Study of Atherosclerosis Gabriela Bustamante* Gabriela Bustamante Jinhee Cha Felice Lê-Scherban James Pankow Daniel Duprez Theresa Osypuk

Neighborhood ethnic density and markers of chronic inflammation may be upstream and downstream factors of cancer development, respectively, but a link between them has not been explored. We examined associations between ethnic enclaves and inflammatory markers in a large multiethnic cohort. Using the Multi-Ethnic Study of Atherosclerosis baseline 2000 exam, we included participants who identified as Hispanic (n=1492) or Chinese (n=804). Ethnic enclaves were operationalized as tertiles of the percent of residents in each participant's baseline census tract of the same ethnicity (%Hispanic or % Chinese) from the 2000 Census. Outcomes included baseline levels of six inflammatory markers (IL-6, fibrinogen, hsCRP, D-dimer, GlycA, and sICAM -1). We assessed differences in marker levels using linear regression adjusted for age, gender, marital status, neighborhood poverty, nativity, language, BMI, cholesterol, blood pressure, smoking and alcohol use. We detected an interaction between ethnicity and enclave for all biomarkers, so analyses were stratified by ethnicity. Compared to residents of the bottom tertile of ethnic neighborhood density, Hispanic participants from the top tertile had higher levels of IL-6, fibrinogen, D-dimer and GlycA, and lower levels of hsCRP and sICAM-1 but only sICAM-1 was statistically significant after adjustment (mean 283.2 in highest vs. 312.2ng/mL in lowest Hispanic enclave tertile, p=0.006). Chinese residents of the top ethnic enclave tertile had higher levels of IL-6, fibrinogen, D-dimer, sICAM-1 and GlycA, and lower levels of hsCRP compared to residents of the bottom tertile, but only the difference in IL-6 was statistically significant (mean 1.18 in highest vs. 1.03pg/mL in lowest Chinese enclave tertile, p=0.03). Ethnic enclave neighborhoods are associated with certain markers of chronic inflammation, with variation by ethnicity. Combining social and biological predictors of disease may help better elucidate the cancer pathway.

Physical activity and obesity: examining dimensions of racial residential segregation Hiwot Y. Zewdie* Hiwot Y. Zewdie Carolyn A. Fahey Mary Jewell Claire L. Leiser Elizabeth W. Spalt Joel D. Kaufman Anjum Hajat

Introduction: Physical activity (PA) is a well-established determinant to obesity; however, little is known about how its association with obesity may vary across socio-environmental factors, such as racial residential segregation (RRS).

Methods: We leveraged harmonized data from three observational cohorts ($n_{participants}$ = 27,703), Cardiovascular Health Study (CHS), Reasons for Geographic and Racial Differences in Stroke (REGARDS), and Multi-Ethnic Study of Atherosclerosis (MESA), to assess the cross-sectional association between PA and body mass index (BMI), and the potential modifying roles of four RRS indicators. We evaluated self-reported PA and continuous BMI from the collection time nearest to 2000 (1991-2007). Data from the 2000 Decennial Census was used to derive tract-level RRS measures of evenness (i.e., White-Black dissimilarity and multi-race divergence) and isolation (i.e., Black isolation and White isolation). Linear regression was used to assess the mean difference in BMI across quartiles of PA (4th quantile = highest PA). Models were adjusted for individual sex, age, and employment status. Four additional models were fit to include an interaction term between PA and each indicator of RRS to explore potential effect modification.

Results: The mean BMI among our study sample was 28.45 kg/m^2 (SD = 5.71). A one-quartile difference in PA was associated with an adjusted difference of -0.54 kg/m^2 (95% CI -0.60, -0.47) in BMI. Among the four RRS indicators, only divergence demonstrated evidence of effect modification (β_{PA}= -0.46, 95% CI: -0.54, -0.37, $p_{PA*divergence}$ = 0.02); PA was associated with smaller decreases in BMI in more segregated areas.

Conclusion: Future studies should further explore the role of RRS in PA-obesity associations as the social environment may be important to take into account when designing obesity prevention programs.

Comparison of Predictive Performance of Polysocial Risk Score Models for Mexican Americans in the Health and Retirement Study Neal Jawadekar* Neal Jawadekar Scott Zimmerman Alicia Riley Katrina Kezios Sebastian Calonico M. Maria Glymour Adina Zeki Al Hazzouri

Background: Prior literature suggests social factors such as education and financial status are associated with cognitive decline. However, little is known to what extent social factors can jointly predict cognitive trajectories, particularly in potentially marginalized minority populations such as Mexican Americans. We (1) identified social risk factors most predictive of cognition, (2) evaluated the predictive accuracy of the selected social factors for cognition over time, and (3) compared the performance of polysocial risk score models on Mexican Americans, comparing models trained on different ethnic groups. **Methods:** We used data from 8,942 Health and Retirement Study (HRS) participants ages 50+ years at baseline. Baseline predictors consisted of numerous social risk factors available in the HRS. Cognition was assessed repeatedly over time (2008 to 2016) and domain-specific measures (e.g., attention, memory, executive function, language, and visuospatial function) were harmonized to yield a comprehensive cognitive score. We utilized LASSO regression to identify the variables most predictive of cognitive trajectories. We then fit a generalized linear mixed model using the selected variables as covariates on three training datasets (entire HRS sample, Non-Hispanic-Whites only, Hispanics only), and finally evaluated the model predictive performance on a test set of Mexican Americans. **Results:** Using the LASSO-selected variables for the polysocial risk score models, the model trained on the entire sample had an R-squared of 0.286, the model trained on Whites had an R-squared of 0.277, and the model trained on Hispanics had an R-squared of 0.288. **Conclusion:** The model trained on Hispanic Americans had minutely better performance for predicting cognition among Mexican Americans than a model trained on non-Hispanic White respondents. Even with LASSO applied to a long list of social covariates, most variance was not explained by the model.

Examining the Relationship Between Perceived Care and Positive Health Behaviors in US Young Adults Koya Ferrell* Koya Ferrell Sharon Jackson

Studies support a connection between social support and positive health behaviors, especially among those requiring specific care regimens. Our study examined the effect of perceived care on health behavior during the transition from adolescence to young adulthood.

This study used data from Waves 1 and 4 of the National Longitudinal Study of Adolescent to Adult Health, which surveyed middle and high school students over 23 years. Self-reported chronic disease status included hypertension, diabetes, and heart and respiratory disease. Multivariable logistic regression, adjusted for sex, race/ethnicity, education, and health insurance status, was used to assess the relative influence of perceived care from parents, teachers, and peers during adolescence on the likelihood of engaging in positive healthcare utilization later in life. Results showed that individuals reporting high amounts of perceived care were no more likely to have had a routine checkup in the past year than those who did not report high amounts of perceived care [OR = 1.24, 95% CI (0.87, 1.77)]. Additionally, those same individuals were as likely to neglect seeking medical care when needed as those not reporting high amounts of perceived care [OR = 0.94, 95% CI (0.65, 1.37)].

Despite the lack of statistical significance supporting a positive association between perceived care during adolescence and health behaviors in adulthood, the findings of this study still help provide insight into what social support means for the development of positive health behaviors. It is widely accepted that social dynamics impact both disease progression and management. The findings of this study suggest, however, that the absence of feeling cared for during adolescence has no direct impact on later health behavior. As we move forward, we aim to capture a more complete picture of social support by including additional types of support, including emotional and tangible support, in our analysis of positive health behaviors.

Predictors of Self-Rated Health and Satisfaction with Health. A Machine Learning Analysis
Afshin Vafaei* Afshin Vafaei Jocelyn Stewart Susan Phillips

Background: Self-rated health (SRH) is a valid indicator of general health. However, some who rate their health as 'good' also report dissatisfaction with their health. Our aims were to explore the relationships between SRH and satisfaction with health and to identify factors that predict each of these constructs.

Methods: Data were from the Canadian General Social Survey 2016 which includes participants 15 years of age and older. We used a machine learning approach by performing classification and regression tree (CRT) analyses to identify the best combination of socioeconomic, behavioural, and mental health predictors of good SRH and health satisfaction.

Results: Almost 85% of the population rated their health as good; however, 19% of them were not satisfied with their health. Conversely, about 20% of participants with poor SRH were satisfied with their health. CRT models identified healthy eating, absence of a psychological disability, absence of inability to work due to long-term illnesses, and high resilience as the main predictors of good SRH and health satisfaction. Being younger than 65 years, of high perceived social class and having high family income also aligned with high scores in both self-perception of health measures.

Conclusion: We have identified subpopulations defined by specific characteristics, that could be targeted to promote health and improve well-being.

Figure 1
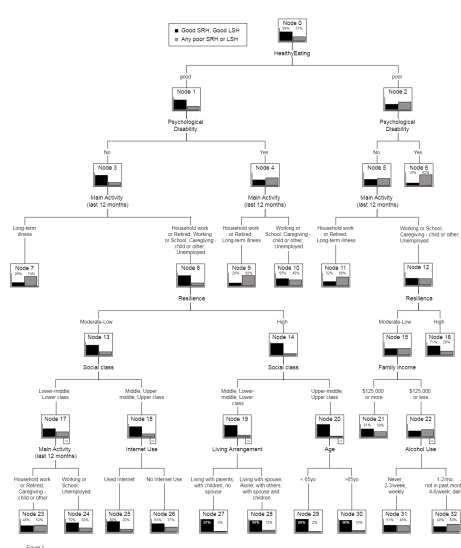
Development and Validation of a County-level Housing Insecurity Scale Ronel Ghidey* Ronel Ghidey Kate Leifheit Qian-Li Xue Aruna Chandran

Background:

Access to stable, secure housing is an established social determinant of health. Housing insecurity has been linked to numerous negative health outcomes, including birth outcomes and child development. Housing insecurity is highly influenced by systematic factors beyond the individual/household level, such as neighborhoods, regional housing markets, local and federal policy. Traditionally, individual-level single-indicator proxies, usually measuring residential instability, have been used to measure this complex construct. Our study aimed to create a multi-indicator scale measuring housing insecurity and validate it against a core birth outcome at the county-level.

Methods:

Twenty-seven literature-supported indicators of housing insecurity were selected for potential inclusion in the scale. Exploratory factor analysis was used to construct a scale containing 11 indicators. The optimal model was selected using standard fit statistics. A composite scale was created by multiplying individual scores with respective factor loading scores and summing the products together. To validate the scale, a linear regression model measured the scale's associated with county-level proportion of low birthweight (LBW) births, adjusting for teen birth rate, number of available primary care physicians, and proportion with health insurance.

Results:

Fit statistics concluded that a four-factor scale fits the data best (RMSEA = 0.074, RMSR = 0.01), and a scale score was calculated for 3093 of 3143 US counties; the score had a mean -0.0016 (SD: 0.5004). The composite score was significantly associated with LBW births (OR = 1.18 (1.05, 1.33)).

Discussion:

Our study shows that a novel county-level composite indicator of residential instability is significantly associated with the proportion of infants born LBW. This study illustrates the importance of considering structural-level housing insecurity as a core determinant of health outcomes.

Longitudinal associations between neighborhood child opportunity and cardiovascular fitness for New York City public school youth Amy Y. Zhao* Hiwot Zewdie Amy Y. Zhao Hiwot Y. Zewdie S. 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: Neighborhood environments can support fitness-promoting behavior; yet, little is known about their influence on youth physical fitness trajectories. We examined longitudinal associations between neighborhood opportunity and youth physical fitness among NYC public school youth.

Methods: The Child Opportunity Index (COI), a composite index of 29 indicators, measured neighborhood opportunity at the census tract-level. Overall COI scores from 2010, along with scores on four built-environment indicators (greenspace, walkability, access to healthy foods, and commute duration), were linked to youth at baseline. Fitness performance was measured annually from 2011 – 2019. Outcomes included body mass index (BMI), curl-up and push-up scores (muscular strength/endurance), and PACER laps (aerobic capacity). Adjusted three-level generalized liner mixed models, nested by census tract and time, estimated the association between COI and fitness outcomes. Effect modification by age was also explored. Coefficients are interpreted as the average linear change in continuous fitness outcome per year for every one-point increase in COI score.

Results: The analytic sample (n=204,939) was 40% Hispanic, 28% Black and most lived in very low (41%) or low (30%) opportunity neighborhoods. Unstratified models indicate overall COI is modestly associated with youth physical fitness over time, with the greatest magnitude observed for PACER (β: 0.06, 95% CI 0.06, 0.07). The strongest associations for individual indicators were also observed for PACER ($\beta_{greenspace}$: 0.72, 95% CI 0.49, 0.95; $\beta_{commute\ duration}$: 0.92, 95% CI 0.82, 1.01). Stratified models show differences in associations across younger vs. older youth.

Conclusion: We find that neighborhood factors are associated with youth fitness trajectories, with the strength of the associations dependent on age. Future implications include better informed place-based interventions tailored to specific life stages to promote youth health.

Study Design

Receiver operating characteristic curve and precision-recall curve analyses using survey data with complex sampling designs Alok Kumar Dwivedi* Alok Dwivedi Luis Alvarado

Receiver operating characteristic curve (ROC) analysis is often conducted to evaluate the prediction and diagnostic accuracy of a binary outcome. For imbalanced datasets, a precision-recall curve (PRC) is more useful than the ROC analysis. Population-based surveys are useful sources for developing predictive and diagnostic models requiring ROC or PRC analyses. However, these surveys involve sampling weights due to complex sampling designs. The sampling weights need to be included in developing predictive models using complex survey datasets. ROC or PRC analysis not properly accounting weights could lead to biased estimates. We developed STATA modules for performing ROC and PRC analyses with area under the curve (AUC) computations for complex survey studies. We further developed adjusted ROC and PRC methods for evaluating quantitative classifiers after adjusting for predictors. For illustration, we used the National Health and Nutrition Examination Survey data for evaluating the performance of sex hormone-binding globulin (SHBG) for predicting metabolically healthy status in adult females. The AUC was estimated as 67% using ROC and 49% using PRC analyses without survey weights. With survey weight parameters, the AUC was estimated to be 70% using ROC and 54% using PRC analyses. The age-adjusted AUC of SHBG was estimated as 72% using ROC and 66% with PRC analyses. Our proposed methods have potential applications in predictive and diagnostic studies using complex survey design methods.

Pre-specified secondary analyses of randomized trials: pre-specified sources of bias Isaac Núñez* Isaac Núñez Pablo F. Belaunzarán-Zamudio

Randomized controlled trials (RCTs), the gold standard for generating evidence, should pre-specify any planned secondary analyses, and post-hoc analyses should be labelled as "hypothesis-generating" in accordance to reporting guidelines. This is due to concerns with data dredging introducing bias. However, pre-specified secondary analyses can still bias results. In RCTs, the interest is to find the size of a causal effect between a treatment and an outcome. Yet, RCTs are often designed and performed with only the main outcome in mind. Thus, other outcomes/subgroups may not have an unbiased causal pathway in the RCT due to its design or analysis. Let us use the START study, a two-arm trial that evaluated immediate antiretroviral therapy (ART) versus deferred ART start in people living with HIV, as an example. The main outcome was a composite of serious AIDS and non-AIDS events (which by themselves were included as secondary outcomes). Randomization was not conditional on any variable. In Figure 1 we show a directed acyclic graph to represent the trial's causal model. While reasonable to consider ART the only cause of AIDS-events, it´s not so for non-AIDS events. A path from ART to non-AIDS outcomes is only shown given the trial evaluated that causal relationship. Certain variables that can cause non-AIDS events (*eg.* diabetes, long-term heart disease, obesity) are not shown, impeding evaluation of random variation. Additionally, 8 pre-specified subgroup analyses were performed, none of which were assessed for random variation of possible confounding variables, impeding a valid assessment of even the main outcome in these subgroups. Thus, the study was designed with a causal model in mind but performed several secondary analyses as if, by default, they were unbiased. Pre-specifying secondary analyses does not by itself eliminate bias, and causal diagrams should be built and evaluated (pre and post data collection) for each to ensure the validity of their assessment.
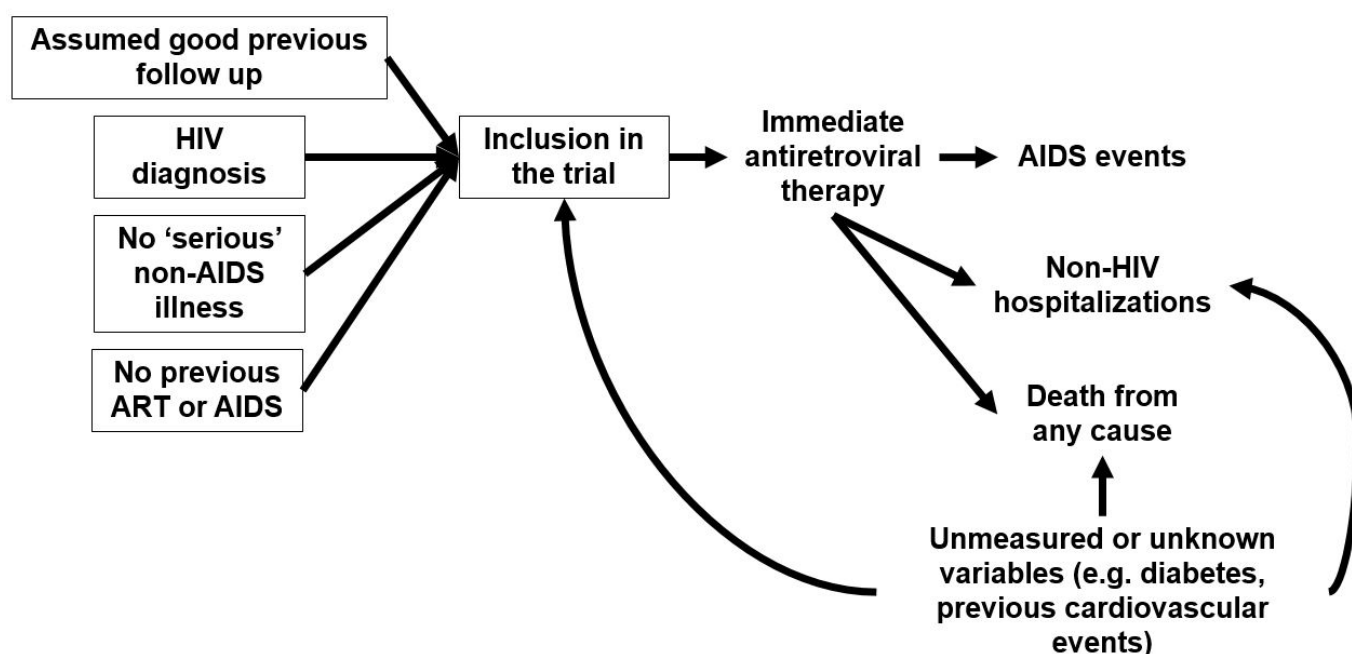
Figure 1. Directed acyclic graph showing a simplified version of the causal model evaluated in the START trial for primary and secondary outcomes.

Tobacco use among blue collar workers in Nigeria: A survey of Artisans in Ekiti state, Nigeria.

Charles Olomofe* Charles Olomofe Hadii Mamudu Caryl Benyon Kabir Durowade Oluwafunmike Olomofe

ABSTRACT

Background: The prevalence of tobacco use among blue-collar workers such as construction artisans is disproportionately higher than in the general population yet very limited studies have been conducted about such workers in Nigeria, the most populous country in Sub-Sahara African (SSA).

Objectives: This study aims to assess the prevalence and the associated risk factors of tobacco use among construction artisans in Ekiti State, Nigeria.

Methods: This cross-sectional study employed a multi-stage stratified sampling technique to select participants (carpenters and bricklayers) artisans, journeymen, and their apprentices who were working in Ekiti State. Chi-square and logistic regression were conducted to delineate factors that are associated with tobacco use in this population.

Results: The prevalence of ever-smoke amongst respondents was 19.3%. Multivariate analysis showed that artisans who were within the age range 31-40 years were four times more likely to use tobacco (aOR=3.410; CI=1.476-7.878). Additionally, being in school and divorced/separated were associated with tobacco use.

Conclusion: The increased prevalence of tobacco use among construction artisans is noteworthy, and few self-reported cases of addiction amongst users demand action from communities and government at all levels.

Keywords

Blue collar workers, construction artisans, tobacco use, Nigeria

Substance Use

Alcohol-attributable mortality in the US from 1999 to 2019: a comparison of age-period-cohort methods Katherine Keyes* Katherine Keyes Carolie Rutherford

Background. Alcohol-related acute mortality has been increasing in the US for over a decade, but whether patterns are specific to particular birth cohorts remains inadequately understood, in part because estimating age-period-cohort (APC) models is methodologically controversial. The present study compares five different age-period-cohort models for acute alcohol death in the US from 1999 to 2019.

Methods. We utilized US vital statistics data from 1999 to 2019; acute alcohol deaths included those due to intoxication, injury and intended and unintended poisoning. Age-period-cohort models included first derivatives, intrinsic estimator, hierarchical APC, and Bayesian.

Results. APC models were convergent in demonstrating that acute alcohol-related deaths peak between age 45-50 in the US, and that those individuals born in the 1960s, thus at the peak age of acute alcohol-related death in approximately 2010 and beyond, have higher risks of death across the lifecourse compared with other cohorts. Methods also converged in factoring out a large period effect in death data due to the change coding. There was divergence, however, in the extent to which methods suggested a period effect after coding change. Two of the four methods indicated that acute alcohol-related deaths are increasing since 2007 across age (i.e. a period effect). Methods also diverged in cohort effect presentation for other cohorts aside from the 1960s cohort effect; some methods suggested an additional cohort effect for those cohorts born in the early 1980s.

Conclusion. Age-period-cohort models can provide useful quantitative framing in unpacking and understanding trends in acute alcohol-related deaths, yet there were differences across methods in assumptions and modeling strategies, and thus differences in results. Moving forward, comparison across method and model when presenting age-period-cohort effects is a critical strategy for triangulating evidence.

Bias in prevalence of alcohol use severity related to selective screening of people with hepatitis C virus infection Mirsada Serdarevic* Brooke MacDonald Matthew Cvitanovich Rohit Ojha

Background: Universal screening for alcohol use is recommended for people diagnosed with hepatitis C virus (HCV) infection, but screening is often selective, which may bias estimates of alcohol use severity and misguide resource allocation. We aimed to explore potential bias in prevalence of alcohol use severity related to selective screening among people with HCV infection.

Methods: We used an institutional registry to identify individuals aged $\geq$18 years with a positive HCV-RNA test between January 2014 and June 2020 and no history of cirrhosis or hepatocellular carcinoma. Only a subset of these eligible individuals was screened using the Alcohol Use Disorder Identification Test (AUDIT) at HCV diagnosis. Alcohol use severity was defined as excess use (AUDIT=8 – 15), hazardous use (AUDIT=16 – 19), and dependence (AUDIT$\geq$20). We used entropy balancing weights to standardize the distribution of age, sex, race/ethnicity, insurance type, and history of substance use of the screened population to the eligible population. We estimated the unweighted and weighted (bias-adjusted) prevalence of alcohol use severity.

Results: Our screened population comprised 491 individuals (of 3,338 eligible), for whom the distribution notably differed from the eligible population by sex (screened: 50% male, eligible: 60% male), race/ethnicity (screened: 61% non-Hispanic White, eligible: 52% non-Hispanic White), and history of substance use (screened: 73%, eligible: 66%). The weighted and unweighted prevalence of excess use, hazardous use, and dependence had overlapping 95% confidence limits (*Figure 1*).

Conclusions: Based on the standardized covariates, our results suggest modest bias in estimates of alcohol use severity despite notable differences in the distribution of certain characteristics. Our estimates provide insight about prevalence in the eligible population and may inform resource allocation if AUDIT screening were universally implemented in our population.

Substance Use
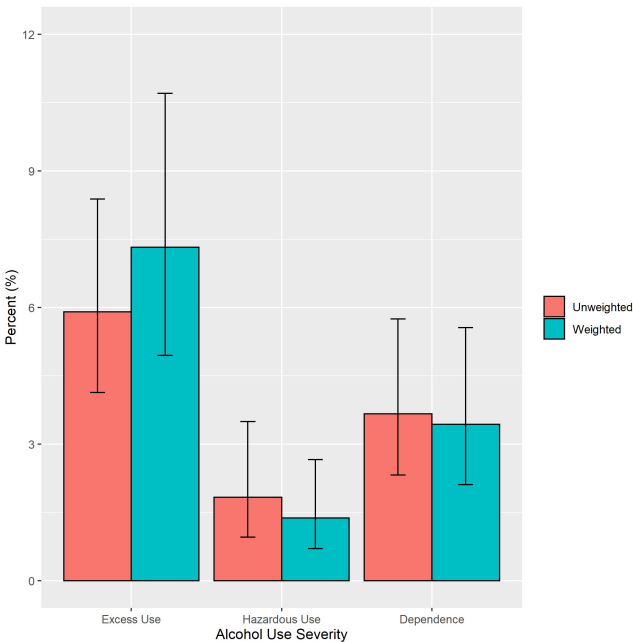
Investigating alcohol use disorder, cannabis use disorder, and opioid use disorder among women with endometriosis Megan E. Marziali* Megan E. Marziali Deborah Hasin Sarah Gutkind Silvia S. Martins

Aim: Endometriosis (ectopic endometrium) causes chronic pain among women. Formal diagnosis can take 4-10 years post-symptom onset, resulting in a gap between symptom development and pain management. Little is known whether chronic pain from endometriosis is associated with increased substance use among women.

Methods: The All of Us data includes electronic health records (EHR) and survey data, with recruitment ongoing (2018-present). We quantified the relationship between endometriosis and lifetime alcohol use disorder (AUD), cannabis use disorder (CUD), and opioid use disorder (OUD) as defined by ICD-9-CM (AUD: 305.0X, 303.X; CUD: 305.2X, 304.3X; OUD: 305.5X, 304.0X) and ICD-10-CM (AUD: F10.1X, F10.2X; CUD: F12.1X, F12.2X; OUD: F11.1X, F11.2X). Analysis was restricted to women ages 18-50. Endometriosis was operationalized through both self-report survey and EHR data (ICD-9/10-CM). Impact of endometriosis on odds of AUD, CUD, and OUD was modeled using logistic regression, adjusting for confounders (age, race/ethnicity, education, health insurance, and other types of chronic pain).

Results: Of the 16,690 women included in analysis, 14% (N=2336) were diagnosed with endometriosis; 9.8% (N=229) of diagnoses were only available via self-reported data. Overall, 13.3% (N=2216), 9.4% (N=1569), and 11.4% (N=1904) were diagnosed with AUD, CUD and OUD, respectively. Among women with endometriosis, odds of AUD were 69.8% (aOR:0.30; 95%CI:0.25-0.36) lower in comparison to those with no endometriosis, adjusting for appropriate confounders. Similar results were observed for CUD (aOR:0.42; 95%CI:0.34-0.52) and OUD (aOR:0.42; 95%CI:0.35-0.52).

Conclusions: These findings demonstrate that endometriosis is negatively associated with AUD, CUD, and OUD. Future research will explore social support as an effect modifier. Our research adds to the literature on chronic pain among women and has important implications related to pain management and substance use.

Substance Use

How maternal and paternal health behaviours change during and after pregnancy: A multi-cohort study Kayleigh Easey* Kayleigh Easey Gemma Sharp

Introduction: Changes in parental health behaviours are advised in pregnancy, with more advice given to expectant mothers than partners. Patterns of health behaviour change from preconception, through pregnancy to postnatally may vary between mothers and partners, and populations. Multicohort studies of parental effects on child health have varied confounding structures influencing behaviour.

Methods: We measured patterns of health behaviour (tobacco, alcohol, caffeine, physical activity) change in pregnancy for mothers and partners, in four birth cohorts (Avon Longitudinal Study of Parents and Children (ALSPAC), Born in Bradford (BiB), Millennium Cohort Study (MCS), the Norwegian Mother, Father and Child Cohort Study (MoBa), and how socioeconomic position and cohabitation impacts each.

Results: Partner health behaviours were measured less often and in less detail than mothers. In all cohorts, maternal and partner health behaviours were generally positively correlated. Compared to pre-pregnancy, maternal teratogenic substances were reduced in first trimester but increased by third trimester and postnatally. Partners alcohol use remained stable across pregnancy. Parental socioeconomic position was negatively correlated with smoking (r -0.25), caffeine (r -1.45), physical activity (r -0.12), and positively correlated with alcohol use (r 0.22). Parents were more likely to reduce substances during pregnancy if they cohabited except for in BiB. Within each cohort increased parental occupation and education level was correlated with increased alcohol use.

Conclusion: Patterns of parental health behaviours vary across pregnancy and between cohorts, having implications for multicohort studies. Not all health behaviours were measured in each cohort, future birth cohorts should include maternal and partner measures. Cohabiting during pregnancy could impact own reduction in health behaviours, dependent on partners behaviour.

Exploring the Dynamic Transitions of Polysubstance Use Patterns Among Canadian Youth: Application of Latent Markov Models on COMPASS Data Yang (Rena) Yang* Yang (Rena) Yang Zahid A. Butt Scott T. Leatherdale Plinio P. Morita Alexander Wong Helen H. Chen

Background: Limited research about the dynamics of youth polysubstance use (PSU) patterns. We addressed the gap in exploring the dynamics of PSU patterns and factors from a large sample of Canadian secondary school students. **Methods:** This retrospective cohort study employed a multivariate latent Markov model (LMM) on a population-based longitudinal health survey, with a linked sample (N=8824) of three annual waves of COMPASS data from 2016. Substance use indicators, i.e., cigarette, e-cigarette, alcohol and cannabis, were self-reported and were categorized into never/occasional/current use. We applied the least absolute shrinkage and selection operator method to select the covariates. **Results:** Four distinct use patterns were: no use (S1), single-use of alcohol (S2), dual-use of e-cigarette+alcohol (S3), and multi-use (S4). Most students remained in the same subgroup over time, particularly those in S4 who had the highest transition probability (0.8668) across the three waves, followed by S3 (0.7092), S1 (0.5740), and S2 (0.5210). With time, those who transitioned typically moved towards a more severe use pattern, with the most likely transition occurring S2→S3 (0.4447), followed by S3→S4 (0.2804) and S1→S2 (0.2510). Students in S3 were least likely to move to S2 (0.0007), followed by S4→S2 (0.0051) and S2→S1 (0.0061). Over time, factors impacting the dynamics were multifaceted and complex across the four patterns. E.g., having more smoking friends ($OR_{S1 \to S4}$=2.98, p<.0001), being male ($OR_{S1 \to S4}$=2.53, p<.0001), or attending a school unsupportive ($OR_{S1 \to S4}$=1.97, p=.0007) affected the dynamics in low→high use. Being male, having more weekly allowance, or more smoking friends significantly affected the transition of high→low use. **Conclusion:** This is the first study to ascertain the dynamics of use patterns and factors in youth PSU utilizing LMM with high-dimensional population-level longitudinal health surveys, providing evidence in developing programs to prevent youth PSU.
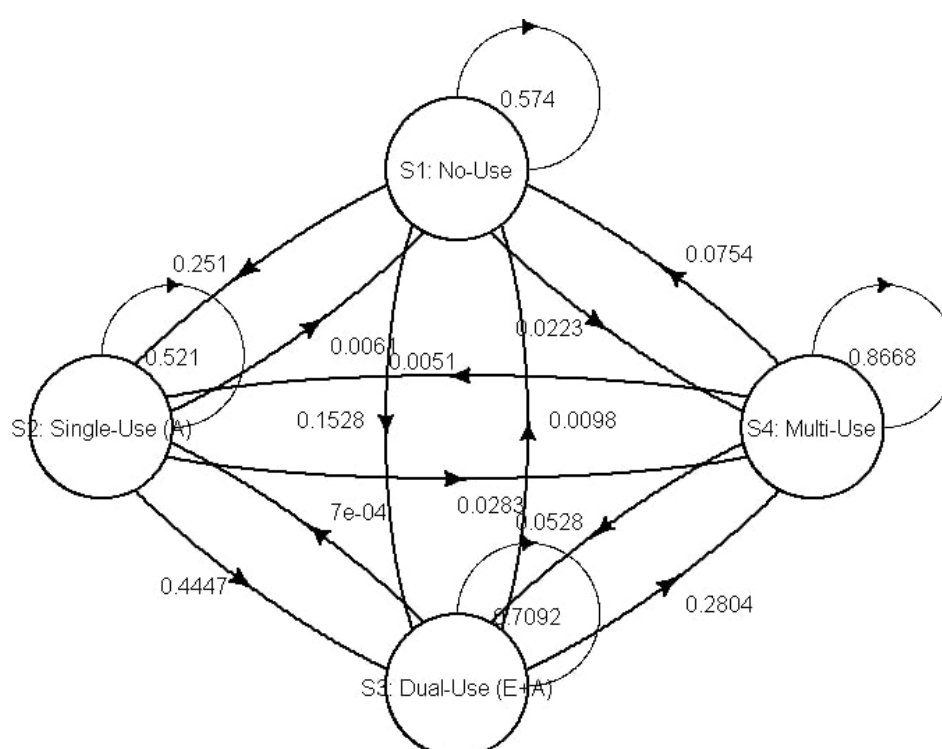
Social, educational, and psychological health correlates of e-cigarette and combustible cigarette use among adolescents in the US from 2015 to 2018 Nabeel Janjua* Nabeel Janjua Noah Kreski Katherine Keyes

Background: The prevalence of e-cigarette and vaping products has increased in the past decade, especially among adolescents. To provide data that will inform identification of youth at high risk, the goals of this study are to determine the social, educational, and psychological health correlates associated with e-cigarette use as distinct from combustible cigarettes.

Methods: Annual nationally representative samples of 12th grade adolescents between 2015-2018 (N=2,565) were analyzed from Monitoring the Future. Students were categorized based on vaping and smoking patterns (no use, vape only, combustible smoking only, or both). Survey-weighted prevalence and logistic regression were used to assess associations.

Results: Between 2015-2018, 80% of students used neither e-cigarettes nor combustible cigarettes, 11.3% used e-cigarettes only (vape-only), 4.2% used combustible cigarettes only (smoke-only), 4.6% used both. Students who vaped-only (OR 1.68 CI 1.10-2.54), smoked-only (OR 3.67 CI 2.11-6.35), or both (OR 2.22 CI 1.32-3.73) had worse academic performance than non-smoking, non-vaping peers. There was no significant difference in self-esteem between neither group and the vape-only group (OR 1.35 CI 0.65-2.77), while the smoke-only (OR 2.18 CI 0.78-6.05) and both (OR 1.51 CI 0.63-3.59) groups were more likely to report low self-esteem. Few differences emerged regarding personal & family beliefs.

Conclusions: Generally, adolescents who report e-cigarette-only use had better outcomes than their peers who smoke cigarettes. However, students who vape-only report poorer academic performance compared to those who do not vape or smoke. Vaping was not significantly related to self-esteem or happiness, unlike smoking. In sum, currently vaping does not follow the same trends as smoking, despite frequent comparisons in the literature.

Eviction moratoria expiration and overdoses in the United States in the context of the Covid-19 pandemic Ariadne E Rivera Aguirre* Ariadne E Rivera Aguirre Giselle Routhier Kelly M Doran Magdalena Cerda

In 2020, 91,799 people died from drug overdoses: a 31% increase in the rate compared to 2019. Prior evidence suggests that eviction is associated with a higher risk of overdose. Amidst the economic fallout from the COVID-19 pandemic and the associated increased risk for evictions and mass displacement, many U.S. states began implementing temporary eviction moratoria in March–April 2020. Between April and September 2020, many of these eviction moratoria expired, putting many households again at risk of eviction. Using the variation in lifting eviction moratoria as a natural experiment, we evaluate whether lifting eviction moratoria during the COVID-19 pandemic are associated with higher overdose rates in the US.

We used monthly state-level counts on drug overdoses in the US from the Vital Statistics rapid release database, and information on timing of state eviction moratoria from the COVID-19 US State Policy Database. To reduce confounding bias, we restricted the analysis to states that implemented any eviction moratoria (n=38) and to the period between April 1st and August 31st 2020, prior to implementation of a national eviction moratorium that went into effect September 4th 2020. We adjusted models for time-varying confounders including unemployment rate, COVID-19 cases and deaths, business closures, school closures, and emergency orders. The average treatment effect was estimated using population weighted OLS regression of the log of state-level overdoses, and negative binomial regression using a population offset. Preliminary results show no significant differences in the incidence rate of overdose deaths in the states that lifted eviction moratoria, versus states that maintained eviction moratoria during the whole study period (IRR 0.019 95%CI -0.17, 0.18 at month 4 of lifting eviction moratoria). This study is limited to monthly level data; we will test whether these results are sensitive to weekly level overdose data

Substance Use

Validity of DSM-5 cannabis use disorder severity levels in adults with problematic substance use David S. Fink* David Fink Malka Zachery L. Mannes Dvora Shmulewitz Melanie Wall Deborah Hasin

The DSM-5 definition of cannabis use disorder (CUD) differs from DSM-IV cannabis dependence by including abuse criteria, withdrawal, and craving, but information on the validity of the DSM-5 CUD diagnosis and severity levels is lacking. This study explores the validity of the DSM-5 CUD in a convenience sample of adult problem substance users, ≥18 years, recruited from two settings: a clinical research setting in an urban medical center and a suburban inpatient addiction treatment program. Participants who reported past-year cannabis use (n=396) consituted the sub-sample for this study. A semi-structured, clinician-administered assessment collected information on DSM-5 CUD criteria, cannabis use related variables, and psychopathology. For each validator (variable predicted to be related to CUD), regression models estimated whether the association with the validator differed by a binary diagnosis of DSM-5 CUD and with its severity levels. Binary DSM-5 CUD and CUD severity levels were associated with greater odds of cannabis use validators, including number of cannabis use days, self-reporting cannabis use as a problem, and cannabis craving scales. In addition, binary CUD and severe CUD were associated with co-occuring psychiatric disorders and social disfunction. DSM-5 CUD and its dimensional measures were shown to have moderate validity, with severe CUD receiving the most support from its association with multiple validators across all domains, compared to the mild and moderate CUD measures associated with cannabis-specific validators alone. Further research is needed to determine the clinical utility of a mild DSM-5 CUD diagnosis among persons with problem substance use.

The impact of implementation strategies on PrEP persistence among female sex workers in South Africa: an interrupted time-series study Amrita Rao* Amrita Rao Hlengiwe Mhlophe Anje Pretorius Mfezi Mcingana Jennifer Mcloughlin Stefan Baral Harry Hausler Sheree Schwartz Catherine Lesko

Background

Female sex workers (FSW) make up a disproportionate share of HIV diagnoses in South Africa. Pre-Exposure Prophylaxis for HIV prevention (PrEP) is freely available to FSW in South Africa through implementing partners/NGOs, including TB HIV Care, however PrEP persistence is low. TB HIV Care has implemented strategies to improve PrEP persistence, but their impact has not been evaluated.

Methods

We used an interrupted time series design to estimate a level change in 1-month PrEP persistence associated with rollout of PrEP delivery strategies: clinical mentoring for providers, SMS PrEP refill reminders, SMS support texts, case management, and loyalty rewards program. We used routinely collected data from all nine TB HIV Care sites distributing PrEP to FSW between 2016-2021. We adjusted for the monthly count of COVID-19 cases; HIV prevention services were considered essential during the pandemic and not subject to lockdown restrictions. In sensitivity analyses, we tested the association between each of the strategies and 4-month persistence.
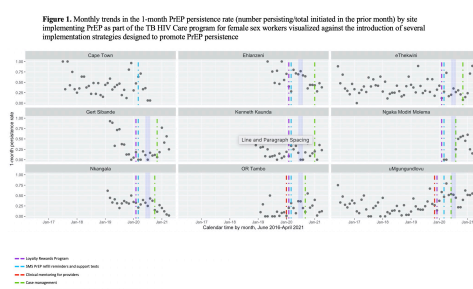
Results

Persistence prior to roll-out of any PrEP delivery strategies was 36% (95% CI: 31.3%-41.8%). We found that SMS support/refill reminders (IRR: 1.35 (95% CI: 1.20-1.53)) and mentoring for providers (IRR: 1.15 (95% CI: 1.05-1.26)) were positively associated with 1-month persistence among FSW. The loyalty rewards program was negatively associated with 1-month persistence (IRR: 0.75, 95% CI (0.67, 0.83)). The strategies that were shown to be useful at promoting persistence at 1-month had no impact on persistence at 4-months.

Conclusions

We harnessed routinely collected data and a quasi-experimental approach to identify key strategies (SMS support and clinical mentoring for providers) that may improve immediate PrEP persistence, and therefore improve the utility of PrEP overall to prevent new HIV infections among FSW.
 Persistence remains a critical issue, however, and strategies to build on these gains longer term are needed.

Figure 1. Monthly trends in the 1-month PrEP persistence rate (number persisting/total initiated in the prior month) by site implementing PrEP as part of the TB HIV Care program for female sex workers visualized against the introduction of several implementation strategies designed to promote PrEP persistence

Women's Health

Variation in menstrual cycle length across age, race, season, and region in a US-based digital longitudinal cohort Huichu Li* Huichu Li Gowtham Asokan Nicola Gallagher Anne Marie Jukic Jukka-Pekka Onnela Michelle A. Willams Russ Hauser Brent Coull Shruthi Mahalingaiah

Objective

Historic studies evaluated variation in menstrual cycle length (MCL) by age, but data on MCL variation by race, season, and region, which may indicate biological, environmental, and socioeconomic factors of MCL, were limited. We explored these associations in the Apple Women's Health Study (AWHS).

Methods

The AWHS is an ongoing mobile-application-based cohort in the US. Participants log their menstrual cycles and complete surveys on health-related factors using their iPhone. Cycles logged from November 2017 – November 2021, when participants were not pregnant, lactating, or using hormones, were included. Age, race, season, region of the country, and other covariates (PCOS, smoking, age at menarche, time to regular cycles, BMI, and socioeconomic status) were obtained from surveys or computed by the first day of the cycle. Differences of MCL associated with these factors were estimated in multivariate linear mixed effect models with random intercepts. Logistic regression models with generalized equation estimates were used to explore associations of these factors with long (MCL>38) and short (MCL<24) day cycles.

Results

A total of 260,707 cycles from 22,626 women were included (mean age=33). After adjusting for all covariates, the mean MCL among women aged 25-30, 30-35, 35-40, 40-45, and 45-50 was shorter by 0.38 (95%CIs: 0.20, 0.56), 0.92 (95%CIs: 0.71, 1.12), 1.57 (95%CIs: 1.36, 1.78), 2.05 (95%CIs: 1.83, 2.27), and 1.63 (95%CIs: 1.38, 1.89) days compared to women at age 20-25. As compared to White women, mean MCL was 1.42 (95%CIs: 1.07, 1.77) days longer in Asian women and 0.58 (95%CIs: 0.32, 0.85) days longer in Hispanic women. Menstrual cycle length varied very little by season and by region across the US. Analyses on long and short cycles supported our findings in mean MCL.

Conclusions

We found MCL differed by age and race but varied little by season and region. Future studies should explore factors explaining these patterns and the health implications.
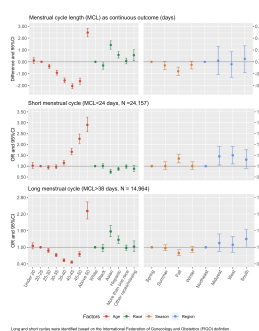
A prospective study of migraine and spontaneous abortion, stillbirth, and ectopic pregnancy Alexandra Purdue-Smithe* Alexandra Purdue-Smithe Leslie V. Farland Jennifer J. Stuart Jae H. Kang Andrea M. Harriott Kathryn M. Rexrode Janet W. Rich-Edwards

Migraine is a neurovascular disorder most prevalent among women 18-45 years of age (~25%). Among those with migraine, 30% experience aura, transient neurological symptoms that precede headache onset. Women with migraine, particularly those with aura phenotype, have elevated inflammatory cytokines, endothelial dysfunction, and platelet activation, which may confer greater risks of adverse pregnancy outcomes. However, prospective studies of migraine and spontaneous abortion, stillbirth, and ectopic pregnancy are lacking. We therefore estimated associations of self-reported physician-diagnosed migraine occurring before pregnancy (14%) and aura phenotype with spontaneous abortion (losses <20 weeks' gestation), stillbirth (losses ≥20 weeks' gestation), and ectopic pregnancy among incident pregnancies in the prospective Nurses' Health Study 2 (1989-2009; n=40,339). Relative risks (RR) and 95% confidence intervals (CI) were estimated using log-binomial regression that accounted for multiple pregnancies per participant. In models adjusted for age, adiposity, chronic hypertension, and other health and behavioral factors, pre-pregnancy migraine was modestly associated with overall risk of spontaneous abortion (RR=1.08; 95% CI=1.02-1.15). This association was more prominent for losses occurring during 12-19 weeks' gestation (RR=1.15; 95% CI=1.01-1.32) than earlier losses (<8 weeks RR=1.04; 95% CI=0.92-1.17; 8-11 weeks RR=1.06; 95% CI=0.95-1.18). The overall risk of spontaneous abortion appeared slightly stronger for migraine with aura (RR=1.12; 95%CI=1.03-1.22) than without aura (RR=1.04; 95% CI=0.96-1.13), compared to no migraine. Migraine was not statistically significantly associated with stillbirth (RR=1.14; 95% CI=0.86-1.52) or ectopic pregnancy (RR=1.31; 95% CI=0.97-1.76), though power for these analyses was limited. Overall, our findings suggest that migraine history is associated with a modestly higher risk of spontaneous abortion, especially later in gestation.

Does adhering to sleep hygiene guidelines impact weight and body composition in post-menopausal women? Results from hypothetical interventions from observational data from the Women's Health Initiative Valeria Elahy* Valeria Elahy Andrew Odegaard

Background: Sleep habits and related sleep disorders are hypothesized to be critical contributors to weight and body composition dynamics, and thus a health-related behavior that may be intervened on to prevent chronic diseases. However, there is little evidence on the potential weight-related impact of aligning sleep hygiene with suggested optimal levels from guidelines. This analysis aimed to answer the question
"what is the average effect of augmenting short sleep duration into the recommended age-appropriate range for good sleep hygiene, and mitigation of insomnia symptoms on visceral (VAT) and subcutaneous (SAT) abdominal adipose tissue, body weight and lean body mass in post-menopausal women."

Methods: We emulated a target trial using observational data from 5,045 post-menopausal women of the of the Women's Health Initiative Observational Study cohort. We estimated body weight and composition change under several hypothetical interventions (short vs guideline sleep duration, and no insomnia vs insomnia symptoms) during the 3 years follow-up. We adjusted for pre-baseline and time-varying confounders using inverse probability weighting with marginal structural models.

Results: If all participants had normal sleep duration they would have gained 0.2 kg of weight (95% CI: -0.2, 0.6) and 7.5 cm^2 of VAT (95% CI: 5.9, 8.8) over 3 years; whereas if all participants had short sleep duration they would have gained 0.6 kg of weight (95% CI: -0.2, 1.2) and 8.3 cm^2 of VAT (95% CI: 6.7, 10.7). If all participants had been insomnia free they would have gained 0.3 kg of weight (95% CI: -0.1, 0.7) and 7.4 cm^2 of VAT (95% CI: 6.1, 8.7) over 3 years, whereas if all participants had insomnia they would have gained 0.6 kg of weight (95% CI: 0.1, 1.0) and 8.2 cm^2 of VAT (95% CI: 5.7, 10.2) over 3 years.

Conclusions: Adherence to sleep hygiene guidelines in post-menopausal women may have a modest, but clinically immaterial impact on weight and accumulation of VAT over 3 years.

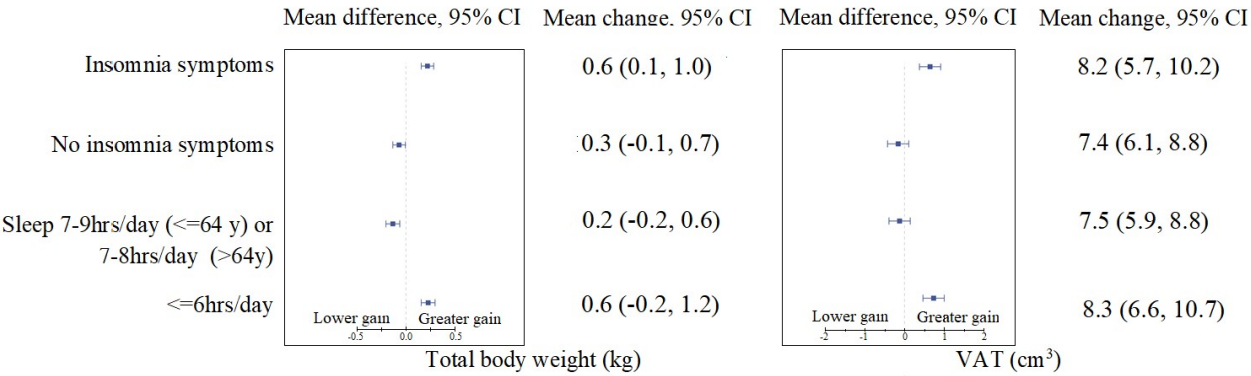|	Mean difference, 95% CI	Mean change. 95% CI	Mean difference, 95% CI	Mean change, 95% CI
Insomnia symptoms		0.6 (0.1, 1.0)		8.2 (5.7, 10.2)
No insomnia symptoms		0.3 (-0.1, 0.7)		7.4 (6.1, 8.8)
Sleep 7-9hrs/day (<=64 y) or 7-8hrs/day (>64y)		0.2 (-0.2, 0.6)		7.5 (5.9, 8.8)
<=6hrs/day		0.6 (-0.2, 1.2)		8.3 (6.6, 10.7)

Figure 1. Estimated mean difference and absolute change of total body weight (kg) and VAT during 3 years of the follow-up compared with no intervention "natural course" in the Women's Health Initiative (WHI) study. If all participants followed no treatment strategy they would have gained 0.4 kg of body weight (95% CI: 0.1, 1.0) and 7.7 cm3 of visceral adipose tissue (95% CI: 5.3, 9.8) over 3 years. Estimates are based on MSMs with IPW accounting for selection bias due to censoring and treatment selection. Abbreviations: MSM, marginal structural model; IPW, inverse probability weighing; IPCW, inverse probability censoring weights.

Women's Health

Vulvodynia and immune related health events across the life course Chad Coleman* Bernard Harlow Chad M Coleman Hanna Muhlrad Donghao Lu Jacinth Yan Matt Fox Nina Bohm_Starke

Vulvodynia is a debilitating chronic vulvar pain condition, estimated to affect 8% of American women by the age of 40, that leads to significant sexual dysfunction, psychological distress, and relationship difficulties. Although the cause of vulvodynia is largely unknown, factors that are associated with immune dysregulation have been more commonly observed in women with, compared to women without, vulvodynia. However, no studies have been large enough or had the ability to assess the wide spectrum of immune related conditions prospectively across the life course. Using data from the Swedish National Patient Register (NPR), we identified all women born between 1981 and 1996 who were diagnosed with vulvodynia between 2012 and 2016 (an age range of 16-35 years representing the most prevalent period for vulvar pain onset) using the International Classification of Diseases (ICD-10 edition) code for vulvodynia (N76.3). Using the same birth cohort, we matched 4 controls with no history of vulvodynia to each case within the same birthyear. For each of the 4,647 cases and 16,358 controls, we used the NPR to identify all clinical diagnoses of immunodeficiencies, inflammatory autoimmune conditions, and allergy/atopy using ICD-9 (1987-1996) and ICD-10 codes (1997-2016). After adjustment for birth year, parity, education, and birth place of residency, women with vulvodynia were more likely to be diagnosed with immunodeficiencies (AOR=2.1, 95%CI 1.4-3.3), inflammatory autoimmune disorders (AOR=1.6, 95%CI 1.5-1.7), and allergy/atopy conditions (AOR=1.8, 95%CI 1.7-1.9) across the life course compared to controls. Although we do not believe these immune-related conditions directly cause the onset of vulvar pain, we speculate they are associated with vulvodynia as a consequence of antecedent immune dysregulation.

Assessing stress-responsive biomarkers as indicators of psychosocial stress among young women in rural South Africa: a secondary analysis of HPTN 068 Nicole K. Kelly* Nicole K Kelly Marie Stoner F. Xavier Gomez-Olive L. Danielle Wagner Kathleen Kahn Allison E. Aiello Audrey Pettifor

Introduction: Psychosocial stressors, like violence and poverty, have been associated with stress-responsive biomarkers, including C-reactive protein (CRP), cytomegalovirus (CMV), and herpes simplex virus type-1 (HSV-1), among older women in high-income settings. However, it remains unknown whether these biomarkers are associated with psychosocial stress among adolescent girls and young women (AGYW) in sub-Saharan Africa, a group at high risk of encountering multiple lifetime stressors.

Methods: We used data from 1,279 AGYW who completed two follow-up visits for the HIV Prevention Trials Network 068 study in rural South Africa. Biomarkers were measured at the second visit using enzyme-linked immunosorbent assays from dried blood spots. Poisson regression with robust standard errors was used to estimate prevalence ratios (PRs) and 95% CIs for the association between stressors (intimate partner violence (IPV), food insecurity (FI), depression, HIV status) and biomarkers (CRP among those within typical range: 1-10mg/L; reactivated CMV/HSV-1 optical density (OD) values among those who were seropositive). We estimated the impact of stressors cross-sectionally (median age=23, in 2018-2019) and during earlier age (median age=20, 2015-2017) on biomarkers sampled during 2018-2019.

Results: Having an HIV diagnosis was associated with elevated CMV (PR: 1.47, 95% CI: 1.08,2.00) and HSV-1 OD levels (PR: 2.21, 95% CI: 1.67,2.92); the magnitude was stronger in the cross-sectional analysis (CMV PR: 1.51, 95% CI: 1.12,2.04; HSV-1 PR: 2.34, 95% CI: 1.78,3.07). IPV was associated with a 2.2 times higher prevalence of elevated CMV cross-sectionally (PR: 2.20, 95% CI: 1.42,3.43), but was not associated with elevated CMV during younger ages.

Conclusion: IPV and HIV were associated with elevated CMV or HSV-1, but associations were stronger when measured closer in time. CRP was not associated with psychosocial stressors and may be harder to accurately measure in rural, low-resource settings**.**

Women's Health

Birthweight in second singleton babies following a first twin versus singleton pregnancy

Prativa Basnet* Prativa Basnet Liv Grimstvedt Kvalvik Rolv Arnold Skjærven Nils-Halvdan Morken Linn Marie Sørbye Janne

Introduction: Birthweight is an important indicator of short and long-term outcome of pregnancy for both the infant and the mother. Previous studies have found that second born babies are on average heavier than first born babies, indicating an independent effect of parity on birthweight. Existing data is mostly based on singleton pregnancies and does not consider higher order pregnancies.

Aims: To determine the parity effect of plurality on birthweight in second born singleton babies after first twin versus singleton birth.

Methods: This was a population-based cohort study with data from the Medical Birth Registry of Norway (1967-2020). The study population included 862 729 first singleton and 5 017 first twin pregnancies followed by a second singleton pregnancy. Birthweight (grams) for second singletons were evaluated by means and ANOVA using STATA. The values were adjusted for maternal age at first pregnancy, year of first pregnancy and maternal education.

Results: Second singleton babies were heavier after a first twin than after a first singleton. This was evident across all gestational ages (GA) in first pregnancy (Fig 1). For GA 34-36 and 37-39 weeks in first twin and singleton, mean birthweight of second babies were 3613 vs 3358 and 3712 vs 3528 grams, respectively. Birthweight in the second singleton declined when the interpregnancy interval was > three years in women with first singleton pregnancy. A similar decline was not observed after a first twin pregnancy. Women with a first twin pregnancy had a lower peak in interpregnancy interval around three years compared to women with first singleton.

Conclusion: Women with first born twins have higher birthweight in a second singleton birth than women with a first-born singleton. Interpregnancy interval differs between women with twins and singletons. Birthweight in a second singleton did not decline after long intervals following a twin pregnancy.
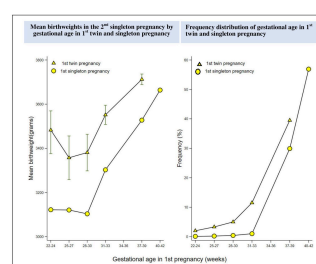
Fig 1: Birthweight in the 2nd singleton pregnancy by gestational age categories in the first pregnancy, twins or singletons
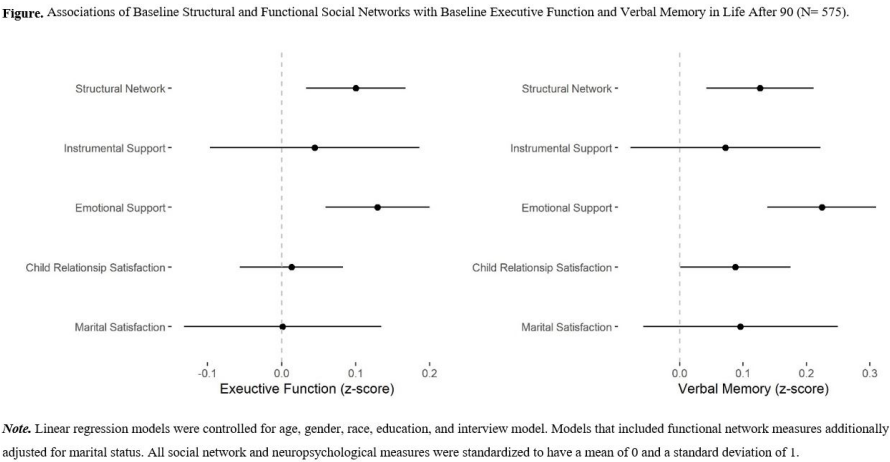
Aging

Associations between Social Networks and Cognitive Decline in a Racially/Ethnically Diverse Cohort of Adults Aged 90 Years and Older
Ruijia Chen* Ruijia Chen Camilla Calmasini Sebastien Haneuse Rachel Peterson Paola Gilsanz Elizabeth Rose Mayeda Rachel A. Whitmer, Maria M Corrada-Bravo M. Maria Glymour

Social isolation is common among the oldest old, but little is known about how social ties influence cognitive function in this population.

LifeAfter90 is an ethnically diverse cohort of Kaiser Permanente Northern California health care members age 90+ who were dementia-free at enrollment. Baseline structural network score was a sum of responses to questions on marital status and number of children, friends, and relatives. Functional social network measures included child relationship satisfaction, spouse relationship satisfaction, emotional support, and instrumental support. Executive function (EF) and verbal memory (VM) were assessed every six months with the Spanish and English Neuropsychological Assessment Scale. Social network and neuropsychological measures were z-scored to the baseline sample. We fit linear regression models to assess the associations between social networks and baseline cognition. To evaluate associations with cognitive decline, we fit random intercepts linear mixed models accounting for practice effects. All models adjusted for age, gender, race/ethnicity, education, and interview mode (phone vs in person). Models that included functional network measures additionally adjusted for marital status. We included interactions between time and social network and time and each covariate to determine whether rate of cognitive decline differed by baseline social networks.

Among 575 older adults (mean age 93.1 years), structural network (β_{EF}=0.10 (95% CI: 0.03,0.17), β_{VM}=0.13 (0.04,0.21)) and emotional support (β_{EF}=0.13 (0.06,0.20), β_{VM}=0.22 (0.14,0.31)) were associated with higher baseline EF and VM (Figure). Child relationship satisfaction (β=0.09 (0.001,0.18) was associated with higher baseline VM. Neither structural nor functional social networks were associated with decline in EF or VM.

Social networks were associated with better baseline cognitive function but not cognitive decline in this oldest-old cohort.

Figure. Associations of Baseline Structural and Functional Social Networks with Baseline Executive Function and Verbal Memory in Life After 90 (N= 575).

Note. Linear regression models were controlled for age, gender, race, education, and interview model. Models that included functional network measures additionally adjusted for marital status. All social network and neuropsychological measures were standardized to have a mean of 0 and a standard deviation of 1.

Effect of Cessation of Metformin Oral Hypoglycemic Therapy on Dementia Incidence among Adults with Type 2 Diabetes: Results from a Treatment-Cessation Design Study in the Kaiser Permanente Northern California Research Program on Genes, Environment and Health Cohort Scott C Zimmerman* Scott Zimmerman Sarah F Ackley Akinyemi Oni-Orisan Vidhu Choudhary Eleanor Hayes-Larson Aline D Folle Kaitlin Swinnerton Elizabeth Rose Mayeda Catherine Schaefer M Maria Glymour

Metformin is the first-line treatment for type 2 diabetes. Prior work suggests metformin use is associated with lower risk of dementia, but this may be confounded by severity and prescribing trends. Most patients who terminate metformin use do so due to kidney dysfunction, but some stop treatment early due to gastrointestinal symptoms. Evaluating the effect of terminating metformin without diabetes progression provides a stronger study design to estimate the effect of metformin use on dementia.

In a cohort of Kaiser Permanente Northern California members taking metformin, we categorized 8994 individuals who stopped metformin use with normal kidney function and continued other antihyperglycemic treatment (e.g. insulin) as "early terminators". We age and gender matched early terminators to eligible participants with similar diabetes duration and treatment histories. These participants, denoted "routine terminators", were eligible to be matched at ages where they were using metformin or had terminated use with abnormal kidney function, avoiding immortal person-time bias: for each matched pair, followup began at the early terminator's age of termination. We used survival models adjusted for demographics, education, cardiovascular disease and cancer. We also determined whether effects were mediated by HbA1c 1 year after metformin termination.

Early terminators had 1.35 (95% CI: 1.21, 1.51) times the hazard of dementia diagnosis of routine terminators and the effect of staying on metformin was 4.6 (95% CI: 1.1, 7.9) years later dementia diagnosis. Terminating metformin was associated with 0.2% (95% CI: 0.14%, .28%) lower HbA1c one year later. This glucose decrease delayed dementia diagnosis by 0.5 (95% CI: 0.1, 0.8) years. This mediated effect was offset by a larger direct effect of a 5.1 (95% CI: 1.4, 8.6) years earlier dementia diagnosis associated with early termination.

Metformin use may decrease the risk of dementia via mechanisms unrelated to glucose control.
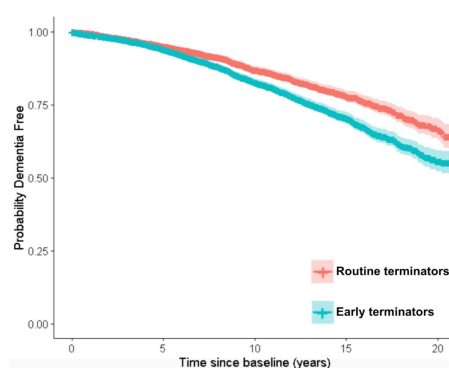

Figure 1: Kaplan-Meier curve showing probability that study participants were not diagnosed with dementia over time for early terminators (participants who stopped using metformin without abnormal kidney function measures) and their matched routine terminators (participants who stopped using metformin with abnormal kidney function measures, or who did not stop taking metformin), matched on baseline age, gender, diabetes duration, diabetes treatment history and glycated hemoglobin (HbA1c).

Aging

**Association of serum antioxidant vitamins and carotenoids with incident Alzheimer's Disease and all-cause dementia among US adults** May A. Beydoun* MAY BEYDOUN Hind A. Beydoun Marie T. Fanelli-Kuczmarski Jordan Weiss Sharmin Hossain Jose A. Canas Michele K. Evans Alan B. Zonderman

Objectives. Serum antioxidant vitamins and carotenoids may protect against neurodegeneration with age. We examined associations of these nutritional biomarkers with incident all-cause and AD dementia among U.S. middle-aged and older adults.

Methods. Using data from the third National health and Nutrition Examination Surveys (1988-1994), linked with Centers for Medicare and Medicaid-Medicare follow-up data, we tested associations and interactions of serum vitamins A, C and E, and total and individual serum carotenoids and interactions with incident Alzheimer's Disease (AD) and all-cause dementia. Cox proportional hazards regression models were conducted.

Results. After ≤26y follow-up (mean:16-17y, n=7,283 participants aged 45-90y at baseline), serum lutein+zeaxanthin was associated with reduced risk of all-cause dementia (65+ age group), even in the lifestyle-adjusted model (per SD, HR=0.93, 95%CI: 0.87-0.99, p=0.037), though attenuated in comparison to a socio-economic status (SES)-adjusted model (HR=0.92, 95% CI: 0.86-0.93, p=0.013). An inverse relationship was detected between serum β-cryptoxanthin (per SD increase) and all-cause dementia (45+ and 65+), for age and sex-adjusted models (HR=0.86, 95% CI:0.80-0.93, p<0.001 for 45+; HR=0.86, 95% CI:0.80-0.93, p=0.001 for 65+), a relationship remaining strong in SES-adjusted models (HR=0.89, 95%CI: 0.82-0.96, p=0.006 for 45+; HR=0.88, 95%CI:0.81-0.96, p=0.007 for 65+), but attenuated in subsequent models. Antagonistic interactions indicate putative protective effects of one carotenoid may be observed at lower levels other carotenoids or antioxidant vitamin.
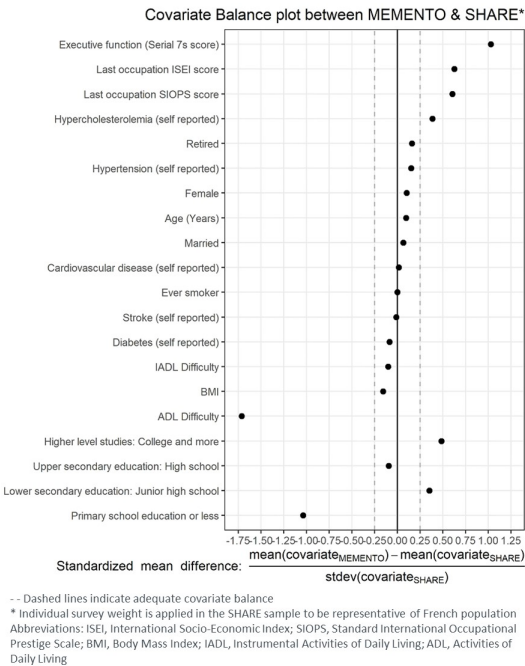
Conclusions. Incident all-cause dementia was inversely associated with serum lutein+zeaxanthin and β-cryptoxanthin levels. Further studies with time-dependent exposures and randomized trials are needed to test neuroprotective effects of supplementing the diet with select carotenoids.
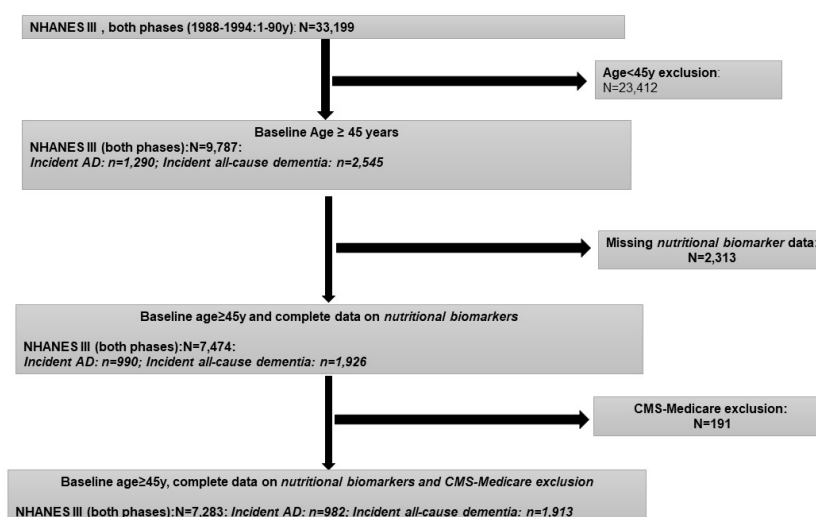
Comparing differences in characteristics of an Alzheimer's disease biomarker in a clinical sample to a population-representative sample: findings from MEMENTO and SHARE-France Yingyan Wu* Yingyan Wu Eleanor Hayes-Larson Taylor M Mobley Marissa J Seamans Vincent Bouteloup Jérémie Lespinasse Carole Dufouil Laura E Gibbons M Maria Glymour Elizabeth Rose Mayeda

Characterizing the biological mechanisms of Alzheimer's disease is crucial for identifying effective strategies for prevention and treatment. It is not feasible to measure Alzheimer's neuroimaging and cerebrospinal fluid biomarkers in population-representative samples; instead, they are measured in clinical samples. It is useful to take sample selection into account to extend findings from clinical samples to broader populations. We aimed to assess the generalizability of an Alzheimer's biomarker study sample of adults without dementia aged 60+ drawn from French memory clinics (MEMENTO, n=2065) to a nationally-representative sample of French adults aged 60+ (French subsample of the Survey of Health, Ageing and Retirement in Europe (SHARE), unweighted n=3,736, survey-weighted n=14,878,406) by comparing standardized mean differences (the differences between the mean of the covariate distribution in MEMENTO and in SHARE divided by the standard deviation of the covariate distribution in SHARE) of sociodemographic and health characteristics measured in both samples. Overall, compared to the French population represented by SHARE, MEMENTO participants had better executive functioning (higher serial 7s test scores), had higher prestige and socioeconomic scores for their last occupation, were more likely to report having hypercholesterolemia, had fewer limitations in activities of daily living (e.g. bathing, dressing), and had higher educational attainment (Figure). Generalizability methods, such as stabilized inverse odds of selection weights and g-computation, can be used to account for the differences in sociodemographic and health characteristics of MEMENTO and other clinical samples vs. population-representative samples to yield estimates of the predictive accuracy of Alzheimer's biomarkers for cognitive outcomes or effects of risk factors on Alzheimer's biomarkers in general populations.

Covariate Balance plot between MEMENTO & SHARE*

$$\text{Standardized mean difference:} \frac{\text{mean(covariate}_{MEMENTO}) - \text{mean(covariate}_{SHARE})}{\text{stdev(covariate}_{SHARE})}$$

- - Dashed lines indicate adequate covariate balance
* Individual survey weight is applied in the SHARE sample to be representative of French population
Abbreviations: ISEI, International Socio-Economic Index; SIOPS, Standard International Occupational Prestige Scale; BMI, Body Mass Index; IADL, Instrumental Activities of Daily Living; ADL, Activities of Daily Living

Aging

Differences in the performance of items on cognition or functional limitations for the measurement of prevalent and incident dementia: Implications for cross-sectional and longitudinal studies Emma Nichols* Emma Nichols Bryan James Derek Ng Jennifer Deal Alden Gross

Epidemiologic studies of dementia use survey items on cognition and functional limitations to assess dementia status. Incident cases are on average milder than prevalent cases, which affects performance of survey items. Longitudinal studies seek to assess incident cases while cross-sectional studies seek to assess prevalent cases, but differences are not typically considered when researchers select items to include in studies. We sought to quantify differences in the performance of items for measurement of incident and prevalent dementia to inform item selection in future studies. We used longitudinal data from the Religious Orders Study and Memory and Aging Project (ROSMAP) (N=3,446) to characterize differences in associations between items and either incident or prevalent dementia, as ascertained through clinical adjudication. We compared associations with incident and prevalent dementia across items (35 items on cognition; 14 items on functional limitations) using multinomial regression models with generalized estimating equations, controlling for cohort (ROS/MAP), age, sex, race, and education. The association between a given item and incident dementia was significantly weaker than the association between the same item and prevalent dementia for 46 of 49 items. However, there was variability, with larger differences in associations for incident versus prevalent dementia for items such as naming a pencil (prevalence OR=0.02 [95% CI 0.02-0.03]; incidence OR=0.10 [95% CI 0.06-0.17]; p for difference <0.001) and difficulty using the telephone (prevalence OR=12.82 [95% CI 10.33-15.92]; incidence OR=5.90 [95% CI 4.73-7.34]; p for difference <0.001). Important differences exist in performance of items for measurement of incident vs prevalent dementia. Such differences can inform choice of items for use in cross-sectional studies of prevalent cases or longitudinal studies of incident cases, leading to reduced misclassification of dementia status and increased power.

Association of PTSD history with confusion or memory loss among World Trade Center Health Registry enrollees Kacie Seil* Kacie Seil Howard Alper Robert Brackbill Shengchao Yu Lucie Millien

The World Trade Center Health Registry includes survivors of the 9/11/01 terrorist attacks who have been surveyed about their health conditions over time. Nearly 20 years after the attacks, enrollees continue to report high levels of posttraumatic stress disorder (PTSD), which is a risk factor for cognitive impairment. We investigated whether PTSD history was associated with self-reported confusion or memory loss among enrollees. The study sample included enrollees who completed all five wave surveys (W1 in 2003-2004 through W5 in 2020-2021), were between the ages of 35-64 during W3-W5, and had no history of stroke or dementia (N=11,432). We categorized PTSD history during W1-W3 as sustained (probable PTSD at all three waves), intermediate (PTSD at least one but not all waves), and never (no probable PTSD during W1-W3). Generalized estimating equations modeling was used for the repeated measures analysis of the outcome, confusion or memory loss (CML), with covariates of interest including but not limited to level of social support (e.g., how often someone is available to hug you or take you to the doctor if you need to go), educational attainment, and history of mental health conditions. Compared to those in the never PTSD group, those in the intermediate PTSD group were at 1.84 times greater risk of reporting CML (95% confidence interval (CI): 1.73, 1.95); those in the sustained PTSD group had 2.16 times greater risk of CML than the never PTSD group (95% CI: 1.99, 2.33). Enrollees with higher levels of social support were at lower risk of reporting CML than those with lower levels of social support (relative risk: 0.74, 95% CI: 0.70, 0.78). Lower educational attainment and having been diagnosed with depression, anxiety, or an alcohol or drug use problem were also associated with higher risk of CML. PTSD is a driver of comorbidity in numerous conditions; those with PTSD should be monitored for outcomes including CML.

Aging

Higher testosterone in men is beneficial according to epigenetic estimators of mortality risk Cynthia D Kusters* Cynthia Kusters Kimberly Paul Ake Lu Beate Ritz Alexander Binder Steve Horvath

Introduction: Sex steroid hormones are hypothesized to cause differences in mortality and morbidity risks. Here, we study the association between sex steroid hormones and epigenetic aging and DNAm biomarkers, specifically Pheno Age Acceleration (AA), Grim AA, DNAm-based Plasminogen Activator Inhibitor 1 (PAI1), and DNAm-based Leptin.

Methods: We used data from 3 population-based cohorts, the Framingham Heart Study (FHS), the Baltimore Longitudinal Study of Aging (BLSA), and the InChianti Study, including 1,075 postmenopausal women without hormone therapy and 1,624 men of European descent. Sex-stratified analyses using linear mixed regression were performed, with a Benjamini-Hochberg (BH) adjustment for multiple testing.

Results: In men, total testosterone was associated with a decrease in Grim AA (-0.11 years; 95%CI: -0.19 to -0.03;BH-P: 0.03), Pheno AA (-0.18 years; 95%CI: -0.32 to -0.05;BH-P: 0.03), and DNAm PAI1 (-239 pg/ml; 95%CI: -303 to -176;BH-P: 1.5e-11). The Testosterone/Estradiol ratio was associated with a decrease in Pheno AA (-0.04 years; 95%CI: -0.07 to -0.01;BH-P: 0.03), and DNAm PAI1 (-31 pg/ml; 95%CI: -44 to -17;BH-P: 6.3e-5). Sex Hormone Binding Globulin (SHBG) is associated with a decrease in DNAm PAI1 among men (-167 pg/ml; 95%CI: -223 to -112;BH-P: 6.6e-8), women (-133 pg/ml; 95%CI: -179 to -87;BH-P: 1.0e-6), and in the meta-analysis of men and women (-147 pg/ml; 95%CI: -182 to -112;BH-P: 9.4e-15).

Conclusion: In men only higher testosterone and increased testosterone/estradiol ratio are associated with a decreased epigenetic AA, suggesting a protective effect of testosterone in men. In addition, we found a strong effect of total testosterone on the DNAm PAI1 concentration among men. Only SHBG was negatively associated with DNAm PAI1 concentration among men and women, indicating a general protective effect on cardiovascular health.

Aging

Dehydroepiandrosterone sulfate and lifespan in men and women: a Mendelian randomization study using the UK Biobank CM Schooling* CM Schooling Jie V Zhao

Background: The prohormone dehydroepiandrosterone sulfate (DHEA-s) falls with age and is implicated in aging. Whether DHEA-s is a biomarker of aging or a modifiable target of intervention is unclear. Previous observational studies suggest DHEA-s could be protective in older men but are open to confounding and selection bias, particularly from inevitably only recruiting survivors.

Methods: To provide a less biased assessment we used a two-sample Mendelian randomization study to assess the association of DHEA-s (n=7667) sex-specifically and overall with parental lifespan based on attained age (current age or age at death) in the UK Biobank (n=415311 for fathers and 412937 for mothers). We used sensitivity analysis, validation using related hormones as positive control exposures and testosterone as a positive control outcome.

Results: Using 4 independent genome wide significant genetic variants to predict DHEA-s, DHEA-s was unrelated to maternal lifespan using inverse variance weighting, 0.64 years lost per log transformed normalized mmol/L DHEA-s, 95% confidence interval (CI) -0.75 to 2.02, and inversely associated with paternal lifespan 1.41 years lost, 95% CI 0.82 to 2.00, giving an overall estimate of 1.30 years lost, 95% CI 0.76 to 1.84. Estimates were similar using sensitivity analysis and for the positive control exposures (epiandrosterone sulfate and androsterone sulfate). DHEA-s was also strongly positively with testosterone.

Conclusions: This study is coherent with a growing body of empirical evidence, suggesting, consistent with evolutionary biology, that drivers of reproduction trade-off against longevity. This study also illustrates the importance of using lifespan as an outcome when assessing effects of likely lifetime exposures at older ages to avoid bias from selective survival to recruitment. Availability of DHEA as an unregulated supplement might bear consideration.

Food insecurity among older adults predicts elevated dementia risk Anusha Vable* Haobing Qian Aayush Khadka Suzanna M. Martinez

Background: Food insecurity is common among older adults, and a potential predictor of dementia risk, however, there are no published studies of this relationship. This study fills this critical gap in the literature using data from the U.S. Health and Retirement Study (HRS) cohort.

Methods: Data come from a subsample of HRS respondents who participated in the 2013 Health Care and Nutrition Study (N=8071) where food security status in the last 12 months was assessed using the validated 6-item U.S.D.A. Food Security Module. Per USDA coding, food security was categorized into three levels: high or marginal food security (reference group), low food security and very low food security. The outcome was a previously validated algorithmically defined dementia probability score (ranging from 0 to 1), estimated biennially from 2014 – 2018. To evaluate the relationship between food insecurity and dementia risk, we fit Generalized Estimation Equations with a logit link, and age as the time scale. All models assumed an autoregressive 1 correlations structure, and were adjusted for the following potential confounders: age at interview, baseline age, gender, race/ethnicity, marital status, birthplace, and several measures of socioeconomic status: years of education, income and wealth, mother and father's years of education, labor force status, home ownership, veteran status, amount social security income, welfare benefits, veteran benefits, food stamps, and total government transfers received. Models were weighted so results are nationally representative.

Results: Those who experienced low (OR=1.52,95%CI:1.11,2.08) or very low food security (OR=1.42,95% CI:0.98,2.03) had higher dementia risk compared to those who experienced high or marginal food security. There was no evidence of a dose-response relationship.

Conclusion: Food insecurity among older adults predicted elevated dementia risk. Future work should determine whether this relationship is causal.

Food Insecurity on Dementia Risk

OR (95%CI) of Dementia Risk
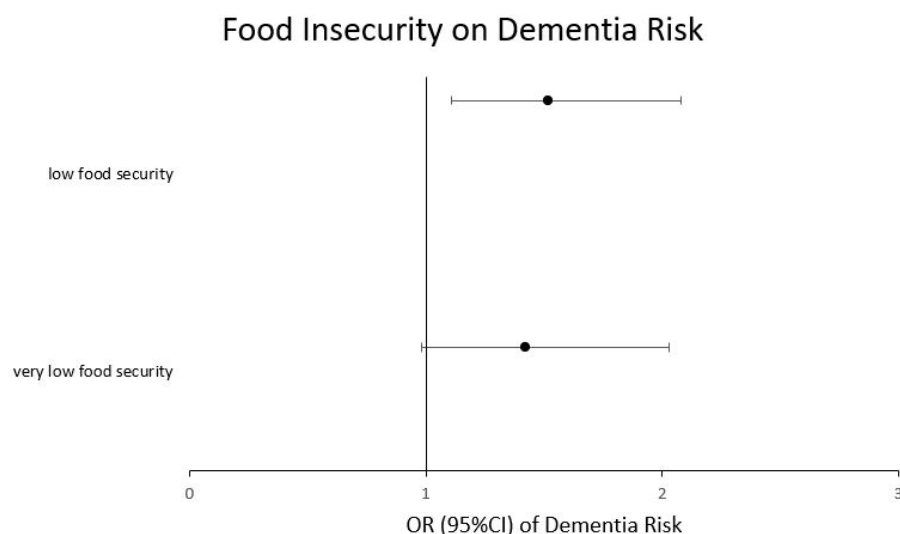
Note: Compared to the high or marginal food secure reference group, those who reported low or very low food security had higher dementia risk. Please note that the confidence interval for the very low food security group crossed the null value of 1.

Behavior

The prevalence and relationships of health behaviors aimed to prevent chronic and infectious diseases Arunas Emeljanovas* Brigita Mieziene Arunas Emeljanovas Ichiro Kawachi

Background. It is well known that physical activity, healthy nutrition, moderate or non-drinking alcohol, non-smoking lower the risks of chronic diseases. Meanwhile, the recent COVID-19 pandemic also highlighted the importance of infection prevention by adopting personal hygiene and avoiding social contact. The study aims to examine the relationships between prevention behaviors of chronic disease and respiratory infection and to explore their sociodemographic correlates.
Methods. The study included 1214 participants. Among them, 61 percent were women. The mean age was 23 years. Physical activity was measured by the IPAQ questionnaire, eating habits by MEDAS scale. Smoking/non-smoking, zero/moderate/heavy alcohol drinking were identified. Sociodemographic characteristics were also collected. Measurement of COVID-19-related personal hygiene and avoiding contacts was performed following the iCARE study.
Results revealed that 47 percent of young adults lack adequate physical activity, 50 percent have a poor diet, 23 percent smoke cigarettes, 10 percent are heavy drinkers. Non-smokers, moderate or non-drinkers, physically active at the recommended level, and those who have at least an average diet are more adherent to COVID-19 related personal hygiene and avoiding contacts than those who are adherent at two or three out of four, or one or none chronic disease preventive behaviors. Education, socio-economic status, place of living were related to personal hygiene and/or avoiding contacts behaviors. Education, socio-economic situation, and gender were related to chronic disease preventive behaviors.
Conclusion. Behaviors aimed to prevent chronic disease and behaviors of respiratory infection prevention are interrelated. Young adults who follow health behaviors are also adherent to respiratory infection prevention. Higher education and higher socioeconomic status of young adults determine both the chronic and respiratory infection preventive behaviors.

Big Data/Machine Learning/AI

Use of genetic programming to explore function spaces Hayden Smith* Hayden Smith

Background: Symbolic regression (SR) is a machine learning method that searches the functional form space using evolutionary algorithms to derive mathematical expressions for variable relationships. The method can recover physical laws using empiric data and has been merged with recurrent neural networks. In six top epidemiology journals, a PubMed search revealed 0.006% (2/33,747) of articles mentioned the process since 1993. Objective: to describe symbolic regression and provide varied applications.

Methods: SR uses inputted data, target and feature variables, to search functional form spaces via stochastic optimization (i.e., genetic programming). Users define a candidate list of mathematical operators (e.g., +, -, *, /, sqrt, log, sine), evolutionary parameters (initial population size, reproduction [replication], crossover [breeding], random mutations [point and branch], fitness parameter, and regularization (tree shrinkage). The fittest functions are propagated across generations. Presented will be examples of deterministic simulated biological, epidemiological, and astrophysical data contrasting SR with linear regression [LR], random forest [RF], and neural networks [NN]) based on default settings and holdout data.

Results: Out-of-sample fitness estimates are presented in Table. SR had similar performance to other algorithms but may require greater processing time. In non-linear spaces, SR may have utility when independent variables are known. An example of an outputted SR mathematical expression is presented in bottom pane of Table.

Conclusions: SR is a transparent, explainable, and interpretable method that may have applications in epidemiology regarding identification of data generating functions and equation reduction. Presented examples were based on deterministic functions, future efforts should examine applications in the presence of epistemic uncertainty and measurement error as well as consider the role of probabilistic interpretations.

Table. Performance of symbolic regression on simulated data generating functions (DGF)

	n-value	R-square values		
Expression	Training Set	SR	LR	RF	NN
Body Mass Index (wt / (ht^2)	75	0.98	0.54	0.90	0.96
Plasma Osmolality*	75	0.90	1.00	0.95	~1.00
Eq. ($X_1^2 - X_2^2 + X_2 - 1$)	150	0.99	0.54	0.88	0.94
Temperature Conversion: (5 / 9) (X - 32)	75	0.35	1.00	~1.00	0.65
Kepler's 3rd law (sqrt(D^3)	6	~1.00	0.44	Error	0.46
Kang & Schafer (2007) eq.	150	0.88	~1.00	0.93	Error
Mystery (g and h distribution formula)	750	0.91	0.70	0.98	0.97

Below: Expression tree for plasma osmolality formula. Right-side is the DGF and left-side is the SR generated tree which had two less nodes, when allowed to run 2000 generations – r-square: ~1.00.
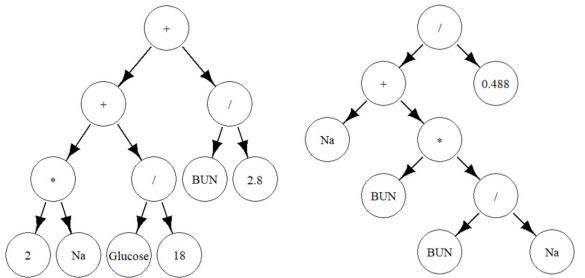
Definitions: Eq = equation; wt = weight; ht = height; d = distance; SR = symbolic regression; LR = linear regression; RF = random forest; NN = neural network; Na = sodium ion; BUN = blood urea nitrogen.
Symbolic regression was executed using gplearn (version: 0.4.1) in Python 3.8.
Mystery expression, a third party was solicited to propose a constructed or general function, see following: a+(b*((exp(g*Z) - 1) /g)*(exp((h*(Z**2))/2))); a=0, b=0.5, g=0.25, h=0.05, Z~N(0,1).
Kang J. & Schafer (2007). Demystifying double robustness; DOI 10.1214/07-STS227.
Eq: X4 = (Z2 + Z4 + 20)**2, though used the following variables as inputs: Z1, Z2, Z3, Z4.
*(2*Na$^+$) + (Glucose / 18) + (BUN / 2.8)

Exploratory Factor Analysis to Identify Multimorbidity Pattern Using Big Data Bomi Park*
Yeonjae Kim Bomi Park

Objectives

As the population ages rapidly, people with multiple chronic disease at the same time, multimorbidity has also been increasing. Multimorbidity is a public health concern because it has negative effects such as increased medical expenses and medical use. In this study, we aimed to explore multimorbidity patterns in Korean adults using big data.

Methods

We used National Health Insurance Service-National Sample Cohort (NHIS-NSC) data in Korea through 2002 to 2013, which included about 1 million people. People aged more than 20 and with a minimum 5-years-follow-up period are considered (total 718,596, women 365,960, men 352,636). 148 chronic diseases were identified using International Classification of Diseases 10th edition code. We defined disease prevalence using the number of hospitalization and outpatient visits. Disease with a prevalence over 1% in each sex are included (women 29, men 18) in the analysis. We used Exploratory Factor Analysis (EFA) to find a chronic disease multimorbidity patterns. The correlation matrix was tested using tetrachoric correlation. The analysis was stratified by age and sex.

Results

The number of people who had multimorbidity were 139,777 (39.6%) for women and 106,576 (33.9%) for men. We identified 4 patters of multimorbidity in women ((1) digestive disease (ds)-mental ds, (2) digestive ds-musculoskeletal ds, (3) stroke-dementia-diabetes, (4) chronic respiratory ds), and 4 patterns in men ((1) chronic respiratory ds-digestive ds-mental ds-musculoskeletal ds, (2) stroke-diabetes, (3) mental ds, (4) diabetes). Each sex and age group showed different disease patterns.

Conclusions

We have found that certain diseases tend to co-occur with a pattern. Understanding multimorbidity pattern is expected to provide important insights to prevent or treat chronic disease more effectively. The results of this study indicate that multimorbidity should be considered when developing clinical guideline for chronic disease.

COVID-19 Mortality Prediction with Machine Leaning: a Multicentric Study of All Brazilian Regions Alexandre Chiavegatto Filho* Roberta Wichmann Fernando Timoteo Fernandes Alexandre Chiavegatto Filho On behalf of the Artificial Intelligence for COVID-19 in Brazil (AICOV-BR) group

The COVID-19 pandemic and its scenario of high medical and managerial complexity, and marked heterogeneities at the hospital level highlights the potential for applying predictive models to improve decisions. Mortality prediction in different regions of a large country like Brazil is a challenge given the large sociodemographic differences between each region. This study aims to identify the strategy that maximizes the predictive performance of identifying the risk of death by COVID-19. This is a multicenter cohort study using data from patients with a positive RT-PCR test for COVID-19 in 18 different hospitals, covering all five Brazilian regions, using data collected between March and August 2020 (n=5,718). Of all hospital patients with a positive RT-PCR test during the period, 1216 (21%) died. Eight different strategies were used for training and evaluating the performance of three popular machine learning algorithms (eXtreme Gradient Boosting, Light GBM, and CatBoost). The strategies ranged from using training data only from a single hospital, up to using groupings by geographic regions. The predictive performance of the algorithms was evaluated by the area under the ROC curve (AUROC) on the test set. The study shows that the best predictive performances were obtained when using training data from the same hospital, which was the winning strategy in 11 (61%) of the 18 participating hospitals. The algorithm with the best overall performance was XGBoost, winning in 67 (46.5%) of the 144 tests performed, followed by LightGBM with 61 (42.4%) and CatBoost with 16 (11.1%). In this study, the use of more data with patients from different regions slightly decreased predictive performance. However, training predictive models with aggregated by region can serve as benchmark until data are available for training the algorithms in a new hospital.


BEST AUCS – DIFFERENCE IN PERFORMANCE ACCORDING TO SAMPLE SIZE

Hospital	Strat 1	Strat 2	Strat 3	Strat 4	Strat 5	Strat 6	Strat 7	Strat 8
SP - Santa (n=1776)	0.71	0.68	0.68	0.61	0.69	0.69	0.69	0.66
SP - HC (n=1500)	0.79	0.74	0.77	0.73	0.77	0.72	0.69	0.64
BA - Salvador (n=1359)	0.89	0.86	0.88	0.87	0.86	0.82	0.81	0.85
CE - UNIMED (n=845)	0.92	0.88	0.8	0.85	0.84	0.79	0.75	0.76
GO - HRL (n=539)	0.69	0.73	0.68	0.71	0.71	0.58	0.71	0.68
RS - HMV (n=456)	0.9	0.78	0.84	0.77	0.81	0.7	0.74	0.83
RJ - UNIMED (n=449)	0.81	0.77	0.7	0.78	0.79	0.73	0.58	0.61
RJ - HU (n=296)	0.78	0.69	0.69	0.64	0.67	0.58	0.67	0.51
DF - SANTA (n=281)	0.81	0.8	0.9	0.76	0.78	0.88	0.66	0.78
AM - ST JULIA (n=247)	0.83	0.78	0.63	0.81	0.78	0.78	0.85	0.75
SC - Blumenau (n=148)	0.98	0.94	0.96	0.87	0.91	0.57	0.91	0.62
SP - Mogi (n=124)	0.98	0.78	0.8	0.84	0.8	0.82	0.87	0.79
PE - HC (n=112)	0.91	0.76	0.77	0.66	0.73	0.71	0.68	0.81
RS - Pelotas (n=91)	0.75	0.81	0.85	0.83	0.84	0.76	0.78	0.55
GO - HUTRIN (n=78)	0.71	0.7	0.83	0.64	0.68	0.68	0.55	0.77
CE - HU (n=73)	0.48	0.55	0.56	0.7	0.42	0.55	0.58	0.55
ES - Evang (n= 56)	0.79	0.46	0.46	0.42	0.56	0.56	0.64	0.29
AM - HU (n=47)	0.88	0.88	0.86	0.84	0.9	0.82	0.86	0.78

BugSigDB: A Comprehensive Database of Published Microbial Signatures for Epidemiological Analysis of Microbiome Data Chloe* Chloe Mirzayi Ludwig Geistlinger Heidi Jones Levi Waldron

Most microbiome studies report "signatures" of differentially abundant microbial taxa for a disease or exposure of interest, but heterogeneity in how complex methods and results are reported make comparisons between studies difficult. A signature represents statistically different bacterial taxa identified in a given study and represents a summary of a study's findings. These signatures can be assessed across studies for consistency and agreement. BugSigDB is a manually curated database of microbial signatures collected from published microbiome differential abundance studies. Key information for each study is curated including study design, sample size, participant information, laboratory methods, and statistical methods in a structured, standardized format. BugSigDB is open source and available for researchers to use and contribute to. As of January 11th, 2022 it contains 2,107 microbial signatures curated from 522 published microbiome research articles. We present an applied example of use of BugSigDB gut microbiome signatures for COVID-19. Analysis of 132 signatures from 32 studies of COVID-19 and the gut microbiome reveal significant co-occurrence of several bacterial taxa within the phylum Firmicutes along with Actinobacteria, Bacteriodetes, and Proteobacteria (Figure 1). Across these studies, the genera Bacteroides and Alistipes were statistically found to be in decreased abundance among COVID-19 patients. bugsigdbr, an accompanying open source R/Bioconductor package, provides signatures and accompanying data downloads in a tidy data format. Data can also be accessed via a semantic wiki web interface at https://bugsigdb.org. Together, they allow for efficient systematic analysis of findings from microbiome studies across a variety of diseases and conditions of interest.

Figure 1. Heatmap of co-occurrence of bacterial taxa for gut microbiome signatures for COVID-19 harmonized to genus level.
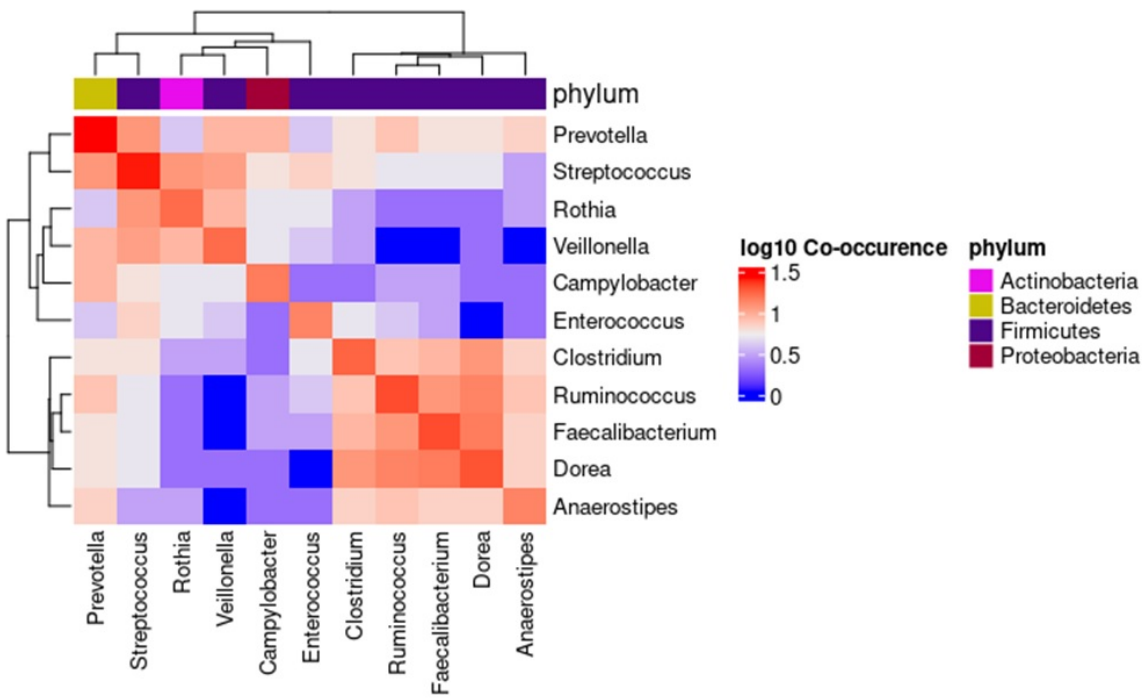
LATEBREAKER

Big Data/Machine Learning/AI

Development of a model to predict antidepressant treatment response for depression among veterans Victor Puac-Polanco* Victor Puac-Polanco Hannah N. Ziobrowski Eric L. Ross Howard Liu Brett Turner Ruifeng Cui Lucinda B. Leung Robert M. Bossarte Corey Bryant Jutta Joormann Andrew A. Nierenberg David W. Oslin Wilfred R. Pigeon Edward P. Post Nur Hani Zainal Alan M. Zaslavsky Jose R. Zubizarreta Alex Luedtke Chris J. Kennedy Andrea Cipriani Toshiaki A. Furukawa Ronald C. Kessler

Background: Antidepressants (ADM) are often the initial treatment for patients with major depressive disorder (MDD). However, only a limited number of patients with MDD respond to the first course of ADMs. A reliable prediction model for ADM nonresponse could be helpful in treatment planning. We investigated the feasibility of creating such a model among patients using services from the US Veterans Health Administration (VHA).

Methods: A 2018-2020 national sample of VHA patients beginning ADM treatment for MDD completed extensive self-report baseline and 3-month follow-up survey assessments (n=660). Using baseline survey, administrative, and geospatial data, an ensemble machine learning model was developed to predict 3-month treatment response defined by the Quick Inventory of Depression Symptomatology Self-Report and a modified Sheehan Disability Scale. The model was developed in a 70% training sample and tested in the remaining 30% test sample. Predictors' importance was examined using the model-agnostic kernel SHapley Additive exPlanations (SHAP) method.

Results: 35.7% of patients responded to treatment. The prediction model had an area under the curve of 0.66 (SE=0.04) in the test sample. A strong gradient in prevalence of treatment response was found across three subsamples of the test sample using thresholds established in the training sample for high [45.6% (5.5)], intermediate [34.5% (7.6)], and low [11.1% (4.9)] probabilities of response. We identified 53 predictors of treatment response. According to SHAP values (Figure), the most important predictors were baseline depression symptom severity, psychiatric comorbidity, treatment characteristics (expectations, history, and aspects of current treatment), and protective/resilience factors.

Conclusions: This tool could meaningfully help patients and providers make MDD treatment decisions, although parallel information about alternative treatments would be needed to inform the selection of optimal treatments.

Figure. Bee swarm plot of individual-level predictor-specific SHAP values for the most important predictors in the Super Learner model
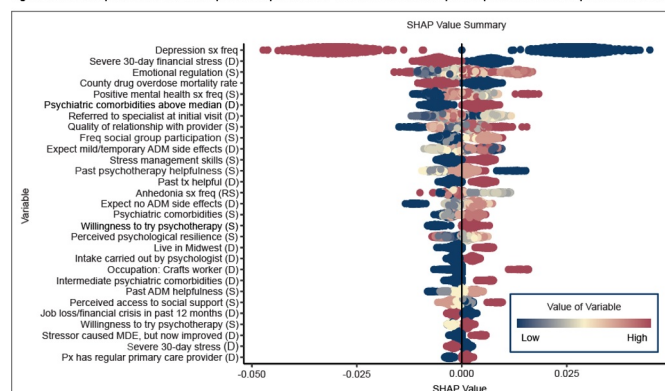
Abbreviations: sx, symptoms; freq, frequency; (D), dummy variable; (S), stabilized variable; ADM, antidepressant medication; tx, treatment; (RS), reverse stabilized; MDE, major depressive episode; px, patient; PCP, primary care provider; PTSD, post-traumatic stress disorder; BMI, body mass index; HRSD, Hamilton Rating Scale of Depression.

LATEBREAKER

Big Data/Machine Learning/AI

Racial Disparities in the Pharmacological Treatment of Insomnia: A Time-to-Event Analysis Using Electronic Health Record Data Emma Holler* Emma Holler Malaz Boustani Zina Ben Miled Paul Dexter Noll Campbell Arthur Owora

Current evidence suggests lower treatment rates among racial minorities compared to White patients for many medical conditions. However, inequities in the pharmacological treatment of insomnia remain unknown. This study aimed to examine racial disparities in time to receipt of an FDA-approved medication among patients diagnosed with insomnia using retrospective electronic health record (EHR) data. The Indiana Network for Patient Care (INPC) was used to identify incident cases of insomnia (≥18 years) between 2011 and 2019 based on ICD diagnostic codes. Patients were required to have at least one encounter per year during the study period and no prior insomnia diagnoses/medications. Demographics, diagnosis, medication, and data were extracted for 8,124 eligible patients with an incident diagnosis. National area deprivation index (ADI) percentile was obtained from the Neighborhood Atlas and used to adjust for socioeconomic status. Follow up time was accrued from the date eligibility was determined until the receipt of FDA-approved medication, or end of the study, whichever came first. A conditional inference tree (CIT) was used to identify potential joint and non-linear covariate effects on survival time that needed to be accounted for. A Cox Proportional Hazards model was used to examine the association between race and time to receipt of an FDA-approved insomnia medication. Compared to White patients, the probability of Black patients receiving an FDA-approved medication declined with a longer duration of follow-up (race*time interaction, $p=0.0031$); the hazard ratios were 0.70 (99% CI 0.50-0.99), 0.57 (99% CI 0.30-0.69), and 0.46 (99% CI 0.31-0.69) at 1, 2, and 3 years, respectively. The disproportionately lower probability of receiving an FDA-approved medication among Black vs White patients, even after adjusting for key sociodemographic factors, highlights disparities in clinical care that may need to be intervened upon to promote equitable care.

The role of breast cancer-related lymphedema in physical functioning and exercise participation among long-term African American Breast Cancer Survivors Sarah Nechuta*

Sarah Nechuta Deepika Boopathy Maureen Sanderson

Background: Breast cancer-related lymphedema (BCRL) is a common chronic condition in survivors that involves accumulation of lymphatic fluid in the arm or hand and can persist many years after completion of primary cancer treatment. Lack of physical activity (PA) and poor physical functioning (PF) are both associated with increased morbidity and mortality among breast cancer survivors. We examined the association of BCRL with PA and PF among African American breast cancer survivors, who have lower PA prevalence and high risk of adverse breast cancer outcomes.

Methods: Women who previously participated in a case-only study in three states (TN, GA, SC) completed a comprehensive survivorship-focused questionnaire on average 4.2 years post-diagnosis (n=323) in 2015-2016. Validated measures were used to determine BCRL, physical health (SF-36), and recreational PA. Adjusted binary logistic regression models estimated ORs and 95% CIs for the association of BCRL (current, never) and meeting PA guidelines ($\geq$150 minutes/week), while multinomial logistic regression was used for PF categorized based on tertiles.

Results: Women were aged 25-75 years (mean: 54.8) at diagnosis. Close to 95% received surgery (38% mastectomy; 57% lumpectomy). Approximately 32% reported BCRL since diagnosis and 25.4% reported BCRL in the last 12 months. In adjusted models, BCRL was associated with lack of meeting PA guidelines (OR=1.98; 95% CI:1.05-3.71). The mean (SD) PF among those with BCRL was 52.5 (28.8) vs. 68.4 (30.0) among those without BCRL. BCRL was associated with lower PF (adjusted-OR for tertile 2: 3.54 (95% CI:1.51, 8.3) and adjusted-OR for tertile 1: 3.82 (95% CI:1.68-8.68)).

Conclusions: BCRL was associated with reduced odds of meeting PA guidelines and lower PF among long-term African American breast cancer survivors. Continued monitoring by health care professionals and increased education and behavioral interventions to improve PA and PF among women living with BCRL are needed.

Cancer

Sarcopenia in relation to all-cause and cardiovascular disease-specific mortality in cancer survivors and counterparts without cancer history Dongyu Zhang* Dongyu Zhang Kori A. Spiropoulos Shama D. Karanth Meghann Wheeler Danting Yang Stephen Anton Dejana Braithwaite

Purpose: To determine how risk of all-cause and cardiovascular disease (CVD)-specific mortality differ by status of sarcopenia in cancer survivors and a matched cohort without cancer history.

Methods: We used cohort data from the 1999-2006 and 2011-2014 National Health and Nutrition Examination Survey. Study participants included 946 adults surviving for at least 1 year since cancer diagnosis and a matched cohort without cancer history based on age, sex, and race (N=1,857). Sarcopenia was defined by appendicular lean mass and body height (males<7.26 kg/m^2, females<5.45 kg/m^2). Death was ascertained via the National Death Index and cause of death was assessed via ICD-10. Multivariable Cox proportional hazards models were used to estimate aHR and 95% CI of sarcopenia in cancer survivors and the matched cohort, followed by restricted cubic splines depicting dose-response curves.

Results: The mean age of cancer survivors and matched cohort was 60.6 (SD=15.0) and 60.2 (SD=14.9) years, respectively. The median follow-up was 10.5 years for survivors and 10.9 years for matched cohort. A total of 321 (33.9%) survivors and 495 (26.7%) participants in matched cohort died during follow-up. CVD-specific deaths were identified in 58 (6.1%) survivors and 122 (6.6%) participants in matched cohort. The multivariable Cox model suggested that sarcopenia was positively associated with all-cause (aHR=1.79, 95% CI=1.36, 2.36) and CVD-specific (aHR=2.17, 95% CI=1.16, 4.05) mortality in cancer survivors. Although the associations between sarcopenia and risk of all-cause (aHR=1.25, 95% CI=0.99, 1.59) and CVD-specific (aHR=1.27, 95% CI=0.80, 2.03) mortality were positive in the matched cohort, the magnitude was less substantial than cancer survivors. Dose-response analysis yielded similar pattern.

Conclusion: Cancer survivors have a higher risk of all-cause and CVD-specific mortality if they have sarcopenia. Such relative increase is larger than increase in counterparts without cancer history.

Evaluation of disparities in esophageal carcinoma risk by age, sex, nativity and period in Kuwait: 1980-2019 Saeed Akhtar* Saeed Akhtar Ahmad M. AlShammari Mohammad Al-Huraiti Fouzan Al-Anjery Iqbal Siddique

Objective: This cross-sectional cohort study assessed the disparities in esophageal carcinoma (EC) risk by age, sex, nativity and period from 1980-2019 in Kuwait.

Methods: The EC incident data were obtained either from Kuwait National Cancer Registry (1980-2016) or projected (2017 to 2019). Relevant Kuwait population data were obtained from Public Authority for Civil Information, Ministry of Interior, Kuwait. EC age-standardized incidence rates (ASIR) (per 100,000 person-years) overall and by subcohorts defined by cross-classification of period (5-year groups) of diagnosis, age (10-year age groups) at diagnosis, sex (male or female) and nativity (Kuwait or non-Kuwaiti) were computed using the direct method and the World Standard Population as a reference. Incident EC cases count as an outcome variable was overdispersed with excessive zeros, therefore, was analyzed using zero-inflated negative binomial (ZINB) model to evaluate the impact of age, sex, nativity and period.

Results: Overall EC ASIR (per 100,000 person-years) was 10.5 (95% CI: 6.4, 10.4). The higher ASIRs were recorded among the older adults ($\geq$ 60 years), males, Kuwaiti nationals and for 1980-84 period (Figure 1). The multivariable ZINB model revealed that compared with 1980-84 period, EC ASIRs consistently and significantly ($p < 0.005$) declined till 2015-19. Regardless of the sex, Kuwaiti nationals were nearly twice as likely to develop the EC as were non-Kuwaiti (IRR = 1.9; 95% CI: 1.6, 2.4; $p < 0.001$) during the study period.

Conclusions: An overall high EC ASIR (per 100,000 person-years) was recorded, which substantially and consistently declined from 1980 to 2019. Kuwaiti nationals and older adults (($\geq$ 60 years) constituted EC high-risk groups. A focused educational intervention in the identified high-risk groups based on the known risk factors for EC may alleviate EC risk in this and similar settings in the region. Future studies may contemplate to evaluate such an intervention.

Smoking trajectories among cancer survivors and the association with cancer survival: a population-based cohort study
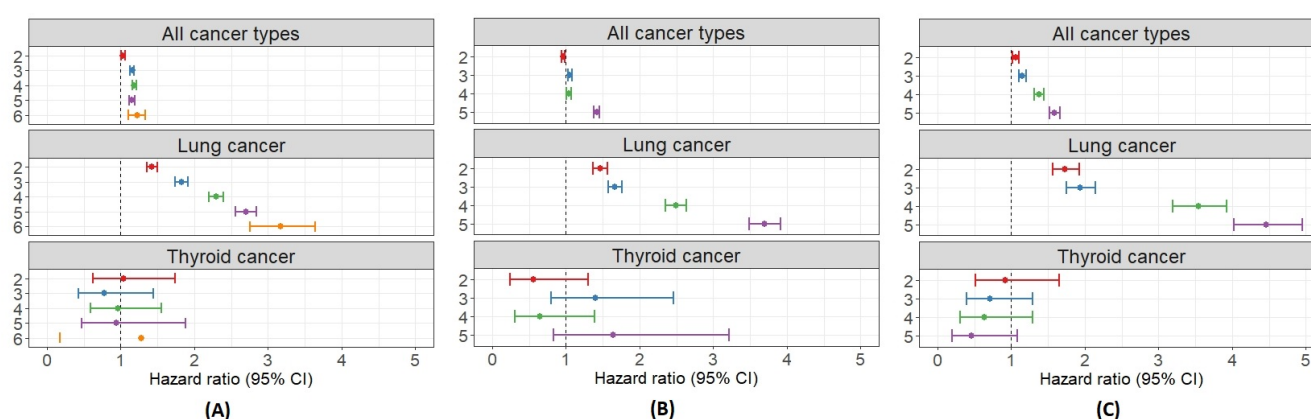Thi Tra Bui* Thi Tra Bui Minji Han Ngoc Minh Luu Thi Phuong Thao Tran Jin-Kyoung Oh

Background: Cancer survivors are advised to adopt healthy behaviors. However, a certain percent of patients continues to smoke. This study aimed to determine smoking trajectories among cancer survivors and assess their associations with cancer survival in Korean men.

Methods: The study included 343,701 men attending the general health examination provided by the Korean National Health Insurance Service in 2002-2003 and diagnosed with cancer during 2004-2015, and followed up to 2018. Trajectory analysis was conducted on smoking measured in ≥2 waves, including one time before diagnosis. The Cox proportional hazards model was used to assess associations of smoking trajectories and survival for all cancers and two cancer sites (lung and thyroid), adjusting for age, income, body mass index, alcohol drinking, physical activity, and comorbidity, and by survival time. Associations of smoking levels before diagnosis were also assessed among patients with smoking measured once only.

Results: Five trajectory groups were defined: (1) non-smoker, (2) newly former smoker, (3) former smoker, (4) decreasing-heavy smoker, and (5) consistent-heavy smoker. In analysis of three waves, compared to non-smoking patients, smokers were less likely to survive, aHRs (95% CI) = 1.06 (1.02-1.11), 1.15 (1.1-1.20), 1.38 (1.32-1.44), 1.59 (1.52-1.66), respectively. For lung cancer, aHRs = 1.73 (1.56-1.93), 1.93 (1.75-2.14), 3.54 (3.19-3.93), 4.46 (4.02-4.95), respectively. No significant difference was found for thyroid cancer. Similar findings were observed in analysis of one and two waves with smaller magnitudes. In subgroup analysis, smoking was related to shorter survival time among five-year survivors, aHRs = 1.1 (1.04-1.16), 1.19 (1.13-1.25), 1.47 (1.39-1.56), 1.67 (1.57-1.77), respectively, and present consistently for lung cancer.

Conclusions: Continuing to smoke was linked to a lower chance of survival. It was recommended to quit smoking, the sooner the better, even after cancer diagnosis.

Figure. Associations of smoking and cancer survival
(A) Smoking levels measured one time before cancer diagnosis,
6 groups: (1) non-smoker (reference), (2) former smoker, (3) 1-10 cigarettes/day, (4) 11-20 cigarettes/day, (5) 21-40 cigarettes/day, (6) > 40 cigarettes/day.
(B) Smoking trajectories with two observed and one imputed measurements,
5 groups: (1) non-smoker (reference), (2) newly former smoker, (3) former smoker, (4) decreasing-heavy smoker, and (5) consistent-heavy smoker.
(C) Smoking trajectories with three observed measurements,
5 groups: (1) non-smoker (reference), (2) former smoker, (3) former smoker, (4) decreasing-heavy smoker, and (5) consistent-heavy smoker.

Cancer

Circulating biomarkers of past infection and endometrial cancer risk Kara Michels* Kara Michels Jolanta Lissowska Beata Peplonska Nicolas Wentzensen Tim Waterboer Britton Trabert

Endometrial cancer is the fourth most commonly diagnosed cancer among women and the sixth leading cause of cancer-related death. Biomarkers that will help us identify women at-risk for this disease, as well as shed light on its etiology, are greatly needed. We assessed whether biomarkers of past reproductive tract infections may be useful. We used data and serum from 443 women with invasive endometrial cancer who were matched on age and study site to 443 women without cancer (The Polish Endometrial Cancer Study, 2001-2003). Using a multiplex fluorescent bead-based assay, we measured circulating antibodies against a range of antigens from microbes known to infect the reproductive tract, including: *Chlamydia trachomatis*, *Herpes simplex virus 2* (HSV-2), and members of the *Human papillomavirus* family. Using logistic regression adjusted for parity and exogenous hormone use, we estimated odds ratios (OR) and 95% confidence intervals (CI) comparing women with positive versus negative serology. We identified a modest association between positive serology to *HSV-2* and endometrial cancer (OR 1.42, CI 1.04, 1.94), which was driven by underlying associations with low-grade (OR 1.50, CI 1.09, 2.08; n=291) and endometrioid tumors (OR 1.39, CI 1.00, 1.94; n=364). Associations with *C. trachomatis* varied by antigen and across analyses stratified by tumor characteristics. Increased risks were consistently identified with seropositivity against three antigens (Tarp-D F2, CT_418, CT_576), but associations with Pgp3 seropositivity were only suggested for serous and clear cell tumors (OR 3.37, CI 0.82, 13.87; n=12). Increased risks for serous and clear cell tumors were indicated for about a third of the ~30 *C. trachomatis* antigens assessed (ORs between 3 and 9), but estimates were often imprecise. Reproductive tract infections likely increase risk for endometrial cancer, but the mechanisms may be microbe, serovar, and histology-specific.

Characterizing the Coexistence of Proteobacteria Species and Cyanobacteria in Cyanobacteria Positive Lung Cancer Samples Christina Joshua* Christina Joshua Heather Robeson Austin Porter Mohammed Orloff

Background: Smoking and genetic factors cannot completely explain the risk of developing lung cancer. Inhalation of aerosol microbial insults can play a role in lung disease development. A recent lung microbiome cross-sectional study revealed an association between cyanobacteria and lung cancer. Further analysis of these patients showed a frequent coexistence between phylum cyanobacteria and proteobacteria in the lung tissues. Based on our findings and literature, we hypothesize that cyanobacteria and a proteobacteria species (*Acidovorax temperans*) are linked to the development of lung cancer. **Methods:** Nucleotide primers specific to *Acidovorax temperans* were used to screen *Acidovorax temperans* on lung cancer individuals positive for cyanobacteria. As a pilot analysis, the resulting amplicons were sequenced and the sequence analyzed. **Results:** A majority (66%) of the cyanobacteria positive samples were also positive for *Burkholderia cepacia* that shares the same lineage with *Acidovorax temperans*. **Conclusions:** Based on our analysis, we were able to identify the presence of Proteobacteria in lung cancer individual samples with positive cyanobacteria presence. Further verification for the exact species will be done using 16S rRNA sequencing.

Lung cancer spatial analysis- cluster characteristics Rexford Anson-Dwamena* Priyadarshini Pattath Rexford Anson-Dwamena

Background: Understanding the spatial patterns of lung cancer in a population provides insight to their causes and controls. Lung cancer incidence rate and mortality rate between years 2009-2018 were explored in association with sociodemographic data in Virginia.

Methods: Lung cancer population data from 2009-2018 from Virginia Cancer Registry for 35 years and above adults were used. We explored lung cancer clusters near hazardous waste sites, using spatial-scan statistical software (SaTScan) to spatially and temporally detect the geographical location of clusters near U.S. Environmental Protection Agency (U.S. EPA) National Priority List (NPL) sites in Virginia. Mortality rates were modeled with Health Opportunity Index indicators using regression analysis.

Results: Incidence rate of lung cancer for clusters with proximity from superfund sites less than 1.5 miles was higher (133.44) compared to that of more than 2 mile (118.77), while mortality rate (for areas less than 1.5 miles) was 91.08 and for areas more than 2 miles distance (80.84). Current median household income is $44,333 in the cluster, compared to $58,100 for all U.S. households. Income inequality index, job participation index, affordability and education index ($p < 0.000$) emerged as significant predictors.

Conclusions: This study presents suggestive evidence of an association between proximity to superfund sites and lung cancer. Living in low-socioeconomic status (SES) areas was associated with higher total lung cancer incidence, and higher total cancer mortality. After accounting for individual age and race living in lower-SES areas remained associated with higher lung cancer incidence, and higher total cancer mortality. Increasing access to screening and healthcare in high priority areas will reduce mortality.

Characterizing the association between BMI and breast cancer risk by menopause status and age-time Ann Von Holle* Ann Von Holle Katie M. O'Brien Dale P. Sandler Minouk Schoemaker Anthony Swerdlow Hazel B. Nichols Michael E. Jones The Premenopausal Breast Cancer Collaborative Group Clarice R. Weinberg

High body mass index (BMI, kg/m^2) is associated with increased risk of breast cancer after menopause and decreased risk prior to menopause. How risk changes near the menopausal transition (typically around age 50 years) is unclear and further investigation can help to understand the role of adiposity in breast cancer risk.

We examined the association between BMI and breast cancer risk in the Premenopausal Breast Cancer Collaborative Group, considering person-time from age 40 years up to breast cancer diagnosis, loss to follow-up, death, or age 55, whichever came first. We used data from 479,132 women in 15 prospective studies, including 11,358 who developed breast cancer before age 55. We used piecewise exponential additive mixed models with age as the primary time scale to estimate three BMI hazard ratios (HRs): constant, linear over age-time, or nonlinear (via splines). Person-time was divided into three menopausal groups: premenopause, natural menopause, or menopause due to interventional loss of ovarian function (surgery or chemotherapy). Sensitivity analyses included adjusting for BMI in young adulthood, excluding those using hormone replacement therapy, and using time since menopause as the age-time scale.

The constant BMI HR model provided the best fit (Akaike's criterion) for all three menopausal status groups. Under this model, the estimated association between a one unit increment in BMI and breast cancer was HR=0.96 (95% CI: 0.96, 0.97) before menopause, HR=0.99 (95% CI: 0.98, 1.00) after natural menopause, and HR=0.99 (95% CI: 0.98, 1.00) after interventional menopause. The sensitivity analyses largely confirmed these results.

The BMI breast cancer HRs remain less than one during the 40-55 year age range typically associated with the transition to menopause, suggesting that the expected positive association between higher BMI and breast cancer among postmenopausal women develops after this time period.

Relationship between quantitative measures of mammographic density and terminal ductal lobular unit involution in Chinese breast cancer patients Waruiru Mburu* Waruiru Mburu Changyuan Guo Yuan Tian Ning Lu Erni Li Jing Li Ariane Chan Hela Koka Gretchen Gierach Kai Yu Xiaohong R. Yang

Background:

Higher mammographic density (MD) and lower terminal duct lobular unit (TDLU) involution are breast cancer risk factors. Previous studies, among predominantly White women and using subjective measures, have shown inconsistent relationship between MD and TDLU involution that differed by menopausal status.

Aim:

We examined the relationship between MD and TDLU involution using objective measures of MD and TDLU involution in a cohort of 652 breast cancer patients diagnosed 2016-2017 at a tertiary hospital in Beijing, China.

Methods:

TDLU involution was assessed in adjacent normal tissue sections using three standardized measures which are inversely associated with TDLU involution: (count/100 mm^2, median span[μm], and median acini count/TDLU). MD was assessed using percent dense volume (PDV) and absolute dense volume (DV) in the contralateral breast, obtained from VolparaDensity software. Associations between TDLU and MD measures were examined using generalized linear models with PDV/DV as outcome variables (log-transformed) and TDLU measures as explanatory variables (categorized into quartiles, adjusted for age, body mass index, parity, and age at menarche. P values were obtained by testing 4-level TDLU variables as ordinal trends.

Results:

Overall, the only TDLU measure associated with MD was TDLU count, which was positively associated with PDV (P_{trend}=0.04). Among women <50 years, greater TDLU count and median TDLU span were associated with higher DV (P_{trend}=0.02 and 0.004, respectively). Among women ≥ 50 years, TDLU count was positively associated with both PDV (P_{trend}=0.02) and DV (P_{trend}=0.02).

Conclusion:

Our findings suggest a complex relationship between MD and TDLU involution which depends on the MD/TDLU measures and age. Further evaluations of the MD-TDLU relationship by intrinsic breast cancer subtypes are currently ongoing.

Cancer

Sleep characteristics among cancer survivors Rina Yarosh* Rina Yarosh Chelsea Anderson Dale P. Sandler Hazel B. Nichols

We investigated sleep characteristics among cancer survivors compared to cancer-free counterparts overall and evaluated if the association varied by cancer type or time since diagnosis.
Data were from the Sister Study, a cohort of 50,884 U.S. and Puerto Rican women without a history of breast cancer. Women with a non-breast cancer history at enrollment were matched to five cancer-free women on age at enrollment. Outcomes included sleep duration, long sleep-latency onset (≥30 minutes to fall asleep), and frequent night awakenings (waking ≥3/night, ≥ 3 times/week). Multivariable linear regression was used for continuous outcomes (regression parameter, 95% CI) and multivariable logistic regression (OR, 95% CI) for categorical outcomes. The sample included 12,750 women: 2,135 with a history of non-breast cancers, and 10,615 cancer-free. After adjustment for age and BMI at enrollment, and depression, diabetes, hypertension, and menopausal status at cancer diagnosis/index age, no difference in mean sleep duration was observed for cancer survivors vs. cancer-free counterparts (parameter = 0.03, 95% CI -0.02, 0.08), but an increased odds of long sleep duration (>9 hours; OR=1.34, 95% CI 0.89-2.03) and frequent night awakenings (waking ≥3 times/night, ≥ 3 times/week; OR=1.12, 95% CI 0.98-1.28) were observed among those with a cancer history vs. without. In cancer type specific analyses, women with head and neck cancer (N=30) had increased odds of long sleep duration (OR=6.10, 95% CI 1.37-27.08) and frequent night awakenings (OR=2.56, 95% CI 1.15-6.67) vs. cancer-free counterparts. Long-term survivors (>20 years) had greater odds of short sleep duration (<7 hours vs. 7-9 hours; OR=1.55, 95% CI 1.03-2.33), and long sleep onset latency (≥30 minutes to fall asleep vs. <30, OR=1.66, 95% CI 1.03-2.67) vs. those with <2 years since diagnosis.
Disturbed sleep is associated with adverse health outcomes and may be a modifiable characteristic to improve well-being for cancer survivors.

Colorectal Cancer Risk Perceptions in Black Men Meng-Han Tsai* Meng-Han Tsai Daramola N. Cabral Jemal Gishe Getachew A. Dagne

Background: Black Americans have the greatest colorectal cancer (CRC) incidence and mortality rates in the United States. Suboptimal CRC screening rates may be mediated by health literacy, a lack of knowledge about the screening benefits and influenced by health services factors. We examined the relationship between CRC risk perceptions and socio-demographic characteristics, disease prevention activities, and personal/family history of CRC among Black men.

Methods: The cross-sectional survey used a self-administered questionnaire and was conducted in five cities in the State of Florida between April 2008 and October 2009. Of the total 425 participants, 331 responses were valid for analysis. Descriptive statistics and logistic regression were performed.

Results: Of 331 participants, higher CRC risk perceptions were exhibited among those aged ≥60 years (70.5%) and American nativity (59.1%). Multivariate analyses found men aged ≥60 had three times greater odds of having higher CRC risk perceptions compared to those ≤ 49 years. Obese participants had more than four times the odds and over-weight subjects had more than twice the odds as compared to healthy weight/underweight participants, to have higher CRC risk perceptions (OR = 4.07; 95% CI = 1.66 -10.00 for obesity and OR = 2.55; 95% CI = 1.03-6.31 for overweight). Men with a personal/family history of CRC also had greater odds of having higher CRC risk perceptions (OR = 9.18; 95% CI = 2.02-41.79). Although, not statistically significant, participants with greater social and emotional support were less likely to have higher CRC risk perceptions.

Conclusion: Given early-onset of CRC in Black men, community educational programs tailored to Black men are needed to improve CRC screening uptake. This information will inform culturally resonate health promotion interventions to elevate CRC risk perceptions and increase screening in Black men.

Figure 1. Intentions and subjective norms: Conceptual framework of factors influencing CRC risk perceptions among Black men
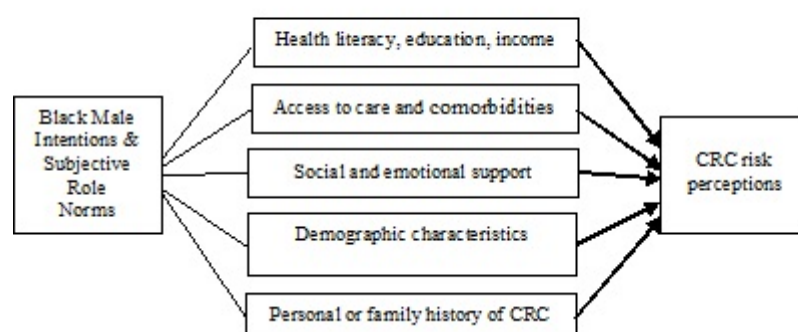
Racial Differences in Survival among Head and Neck Cancer Patients in the United States

Shama Karanth* Shama Karanth Tomi Akinyemiju Dongyu Zhang Cesar Migliorati Meghann Wheeler Danting Yang

Background Head and Neck cancers (HNC) encompass cancers of the oral cavity, pharynx, larynx, paranasal sinuses, and nasal cavity. The competing causes of death due to tobacco use, such as chronic obstructive pulmonary disease (COPD), lung cancer, and cardiovascular disease (CVD) are common in HNC survivors but rarely assessed. The objective of the study was to estimate disparities in overall, HNC-specific, and competing causes of mortality by racial groups.

Methods Data were analyzed from patients with primary HNC (2000–2016) identified from the Surveillance, Epidemiology and End Result (SEER) database. Kaplan-Meier estimation and multivariable Cox proportional hazards models were used to estimate mortality rates per person-years (pys) and adjusted HR and 95% CI by race/ethnicity. A multivariable competing risk survival analysis yielded cause-specific HRs for mortality due to HNC, CVD, COPD, and lung cancer.

Results A total of 165,159 patients were included with mean age 61.7 (SD=13.1) years: 79,460 (48%) were deceased including 27,516 deaths (35%) from competing causes, 12% due to CVD, 3% due to COPD and 2% lung cancer. Compared with NH-Whites, NH-Blacks had a higher overall (154.6 vs 100.7/1000 pys) HNC-specific (114.2 vs 62.9/1000 pys) and CVD-specific (22.5 vs 12.9/1000 pys) mortality rates. However, NH-Blacks had lower COPD-specific (2.7 vs 3.9/1000 pys) and lung cancer (2.6 vs 2.8/1000 pys) mortality rates. In adjusted models, relative to NH-White patients, NH-Blacks had a higher risk of all-cause mortality (HR1.32 95%CI 0.1.29, 1.35), HNC-specific (HR1.38 95%CI (1.35,1.42) and CVDs-specific (HR1.32 95%CI (1.22 1.40)). Hispanics had a higher risk of HNC-specific mortality, but not all-cause mortality.

Conclusion Even after accounting for tobacco-related competing causes of death, NH-Blacks are still at a higher overall and HNC-specific mortality rate compared with NH-Whites. In addition to smoking, other drivers of mortality disparities should be elucidated

Reproductive factors in relation to incidence of lung and colorectal cancers in a Norwegian women cohort: the HUNT Study Marion Denos* Marion Denos Xiao-Mei Mai Yi-Qian Sun Ben Michael Brumpton Arnulf Langhammer Yue Chen
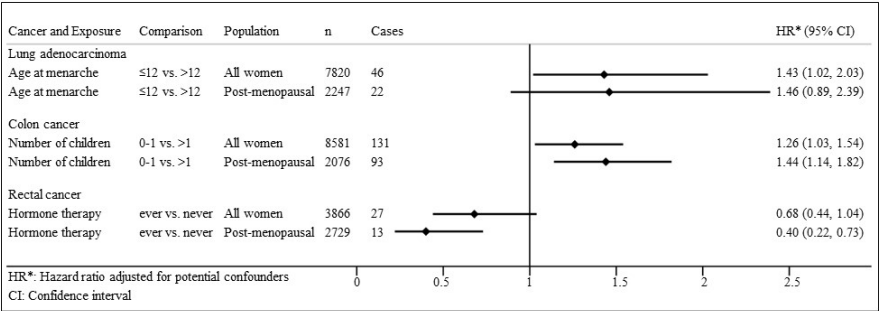
Introduction: Breast cancer is the most common cancer in women. Reproductive factors such as early menarche, late age at first live birth, and low number of children have been identified as risk factors for developing breast cancer. However, the roles of reproductive factors in the aetiology of lung and colorectal cancers, among the most common cancers in women, are still unclear.

Methods: We followed up 33,314 cancer-free women who participated in the HUNT Study in Norway from 1995-1997 to 2018. A large panel of reproductive factors were self-reported at baseline: age at menarche, age at menopause, menopause status (natural/non-natural), reproductive period, number of children, age at first birth, oral contraceptive use, as well as hormone therapy. Incident lung and colorectal cancer cases were ascertained from the Cancer Registry of Norway. Cox regression models were used to estimate hazard ratios (HRs) with 95% confidence intervals (CIs) after adjustment for important confounders.

Results: During a median follow-up of 22.2 years, 467 women developed lung cancer including 169 lung adenocarcinoma, 660 developed colon cancer and 211 had rectal cancer. Early menarche (≤12 years) was associated with an increased incidence of lung adenocarcinoma (HR 1.43, 95% CI 1.02–2.03). Women with one or no child had an increased colon cancer incidence (HR 1.26, 95% CI 1.03–1.54). Hormone therapy appeared to be associated with a decreased incidence of rectal cancer (HR 0.68, 95% CI 0.44–1.04). Results in the subgroup of post-menopausal women were similar or strengthened. Other reproductive factors were not related to the risks of lung, colon, and rectal cancers.

Conclusion: Certain reproductive factors might play a role in the aetiology of lung and colorectal cancers. The causal relationships warrant further investigation.

Figure 1. Illustration of our main findings between age at menarche and lung adenocarcinoma, number of children and colon cancer as well as hormone therapy and rectal cancer in all women (n=33,314) and post-menopausal women (n=12,210) in HUNT2

Cancer and Exposure	Comparison	Population	n	Cases	HR* (95% CI)
Lung adenocarcinoma					
Age at menarche	≤12 vs. >12	All women	7820	46	1.43 (1.02, 2.03)
Age at menarche	≤12 vs. >12	Post-menopausal	2247	22	1.46 (0.89, 2.39)
Colon cancer					
Number of children	0-1 vs. >1	All women	8581	131	1.26 (1.03, 1.54)
Number of children	0-1 vs. >1	Post-menopausal	2076	93	1.44 (1.14, 1.82)
Rectal cancer					
Hormone therapy	ever vs. never	All women	3866	27	0.68 (0.44, 1.04)
Hormone therapy	ever vs. never	Post-menopausal	2729	13	0.40 (0.22, 0.73)

HR*: Hazard ratio adjusted for potential confounders
CI: Confidence interval

Cardiovascular

Evaluating the role of liver function in cardiovascular diseases and type 2 diabetes: A Mendelian randomization study in Europeans and East Asians Shiu Lun Au Yeung* Shiu Lun Au Yeung MC Borges THT Wong DA Lawlor C Mary Schooling

Introduction: Whether poor liver function causes cardiovascular disease (CVD) and type 2 diabetes (T2D) is not clear and possible differences in effect between ethnicities has rarely been explored. We conducted a Mendelian randomization study using large genome wide association study (GWAS) summary statistics from Europeans and East Asians.

Methods: We used summary statistics from GWAS of associations of single nucleotide polymorphisms (SNPs) with four proxies of liver function: alanine aminotransferase (ALT) (n=188 SNPs), liability to non-alcoholic fatty liver diseases (n=44), aspartate transaminase (AST) (n=215), and liver magnetic resonance imaging corrected T1 (n=5). We obtained associations of the same SNPs with our outcomes from GWAS summary statistics of cardiovascular diseases, T2D and glycemic traits. Inverse variance weighted analyses were used as the main analyses, with replication analyses in FinnGen. We conducted analyses in East Asian populations using Asian specific ALT, AST instruments and respective East Asian outcome GWAS summary statistics. Multiple sensitivity analyses were used to explore possible bias due to horizontal pleiotropy.

Results: In Europeans, higher ALT (SD) was potentially causally related to T2D (OR: 1.77 95% confidence interval (CI) 1.5 to 2.08), with similar results for liability to NAFLD, AST, and cT1, across sensitivity analyses, and in FinnGen. Although higher ALT, liability to NAFLD, and AST were potentially causally related to higher risk of CAD, overall stroke, MR-Egger results suggested the associations could be biased by horizontal pleiotropy. In East Asians, higher ALT potentially caused a higher risk of T2D (OR: 1.19 per SD of log, 95%CI 0.92 to 1.53) and a possible inverse effect of ALT (OR: 0.63 per SD of log, 95%CI 0.39 to 1.00) and AST (OR: 0.61 per SD of log, 95%CI 0.35 to 1.06) on CAD.

Conclusion: Poorer liver function likely increases the risk of T2D in Europeans and East Asians. The potential differential effects on CAD between Europeans and East Asians, and effects in other ethnic groups, require further investigation.

Potential Missed Opportunities for Prescription of Cholesterol-Lowering Medications for Eligible Adults Ifedioranma Anikpo* Ifedioranma Anikpo Hannah Cranford Amrit Baral WayWay M. Hlaing

Background: Socioeconomic vulnerabilities are known to affect the quality of preventive cardiovascular care. Nevertheless, little is known about how patients' health insurance coverage affects prescriptions for cholesterol-lowering medications (CLMs). We aimed to estimate the proportion of eligible adults who received prescriptions for CLMs and evaluate the association between health insurance coverage and prescriptions for CLMs.

Methods: We used data from the 2017 – 2018 cycle of the National Health and Nutrition Examination Survey (NHANES). We computed descriptive statistics and used a multivariable logistic regression model to estimate the association between having health insurance and receiving a prescription for CLMs, adjusting for age, gender, race/ethnicity, and household income. Eligibility was determined based on the American Heart Association/American College of Cardiology guidelines, focusing on individuals with definitive indications for CLMs.

Results: The median age of eligible participants (n=1,272; weighted n=40,725,489) was 63 years. The sample consisted of 53% males, 66% non-Hispanic white, and 11.5% non-Hispanic black. Seven percent of the sample did not have health insurance coverage. The proportion of eligible adults who received prescriptions for CLMs was 71% (95%CI: 67% – 74%), but among eligible adults, 27% (95% CI: 23% – 31%) did not received a CLM prescription and had health insurance coverage. The association between health insurance coverage and receipt of CLM prescriptions was modest but not significant based on our data (adjusted odds ratio: 1.19, 95%CI: 0.48 – 2.95).

Discussion: Our study highlights that CLMs are underused in the nationally representative sample of eligible US adults, despite the limitations. Although physician and patient-attributed factors or contraindications may account for the observed underuse of CLMs, our findings may also indicate suboptimal care. Thus, barriers to prescribing CLMs should be further explored.

Prescriptions for cholesterol-lowering medication by insurance status in eligible individuals, NHANES 2017 - 2018
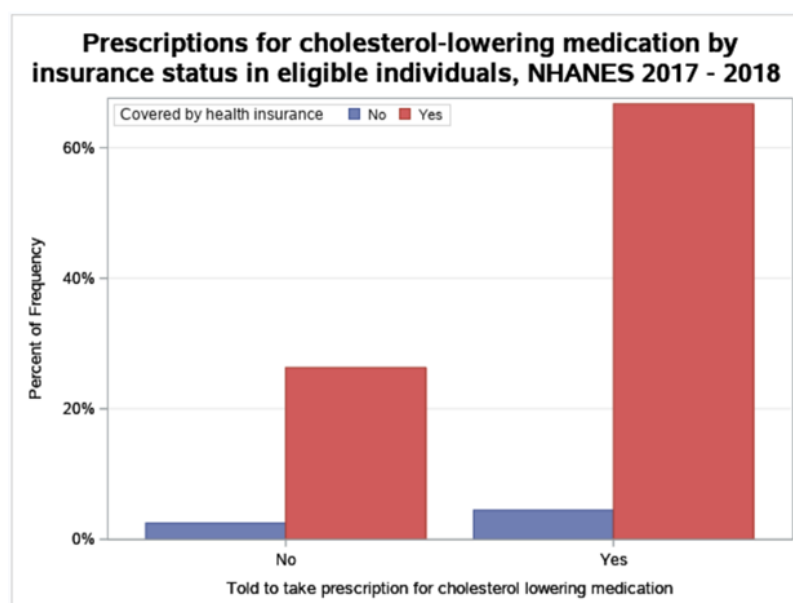
Improved re-estimation of perioperative cardiac risk using the Surgical Apgar Score Julian
Daza* Julian Daza Justyna Bartoszko Wilton Van Klei Karim Ladha Stuart McCluskey Duminda
Wijeysundera

Background: The Surgical Apgar Score is a novel risk index that integrates three easily measurable
intraoperative parameters (blood loss, heart rate, mean arterial pressure) to predict outcomes. We
conducted a retrospective cohort study to assess whether the Surgical Apgar Score improves re-
estimation of perioperative cardiac risk when used in combination with a standard preoperative risk
index.

Methods: The cohort included adults (≥18 y) who underwent elective non-cardiac surgery at a
quaternary care hospital in Canada (2009 to 2014). The primary outcome was postoperative
myocardial injury. The Surgical Apgar Score (range 0 to 10) was calculated based on intraoperative
estimated blood loss, lowest mean arterial pressure, and lowest heart rate documented in electronic
medical records. Incremental prognostic value of the Surgical Apgar Score when combined with the
Revised Cardiac Risk Index was assessed based on discrimination (c-statistic), reclassification
(integrated discrimination improvement, net reclassification index), and clinical utility (decision
curve analysis).

Results: The cohort included 16,835 patients, of whom 607 (3.6%) had postoperative myocardial
injury. Addition of the Surgical Apgar Score to the Revised Cardiac Risk Index improved risk
estimation based on the integrated discrimination improvement (2.0%; 95% CI 1.5% to 2.4%),
continuous net reclassification index (54%; 95% CI 46% to 62%), and c-index, which increased from
0.68 (95% CI 0.65 to 0.70) to 0.75 (95% CI 0.73 to 0.77). Based on decision curve analysis, addition
of the Surgical Apgar Score to the Revised Cardiac Risk Index resulted in a higher net benefit at all
decision thresholds (Figure 1).

Conclusions: When combined with a preoperative risk index, the Surgical Apgar Score improved the
accuracy of cardiac risk assessment for non-cardiac surgery. Further research should delineate how
intraoperative data can better guide postoperative decision-making.
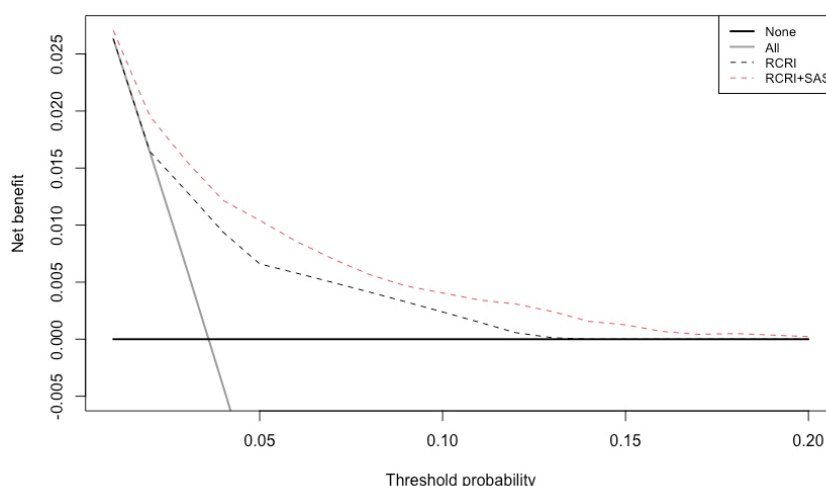
Trends in Cardiovascular Risk Factors by Income Levels among Adults Aged 30-49 Years in Japan between 2017 and 2020

Kosuke Inoue* Kosuke Inoue Naoki Kondo Koryu Sato Shingo Fukuma

Background: Income is one of the major social determinants of cardiovascular health. However, individual-level evidence about the trends in cardiovascular risk factors by income levels among young working-age adults is limited.

Objective: To examine trends in cardiovascular risk factors among men and women aged 30-49 years by their income levels.

Methods: This is a longitudinal study using a nationwide database of Japanese adults aged 30 to 49 years (in 2017) who participated in the national health screening program from April 2017 to March 2021 (i.e., from 2017 to 2020 fiscal year). Modified Poisson regression models were used to investigate the trends in the prevalence of cardiovascular risk factors (obesity, hypertension, diabetes, and dyslipidemia) according to tertiles of individuals' yearly income levels, adjusting for potential confounders.

Results: Of 58,814 adults, 50,024 (85%) were men; the mean (SD) age was 42.1 (5.4) years in the 2017 fiscal year. Across all three income groups, the prevalence of each cardiovascular risk factor gradually increased every year between 2017 and 2020. Over the study periods, the low-income group consistently showed a higher prevalence of obesity, hypertension, diabetes, and dyslipidemia than the high-income group. The difference in the prevalence of hypertension between the low-income group and the high-income group increased from 2017 to 2020 among both men (low-income vs. high-income: +5.69% [95%CI, 4.67-6.70] in 2017 and +8.18% [95%CI, 7.06-9.30] in 2020) and women (low-income vs. high-income: +2.53% [95%CI, 0.99-4.06] in 2017 and +3.69% [95%CI, 1.90-5.49] in 2020) (**Figure**).

Conclusions: Among adults aged 30-49 years in Japan, we found an increase in the gap of cardiovascular risk factors between the low-income group and high-income group over the last four years. Further studies are warranted to establish an effective policy to avoid increasing social disparities in cardiovascular health among young working-age adults.

A) Prevalence of hypertension according to income levels among men

B) Prevalence of hypertension according to income levels among women

C) Differences in the prevalence of hypertension according to income levels (vs. high-income group) among men

D) Differences in the prevalence of hypertension according to income levels (vs. high-income group) among women
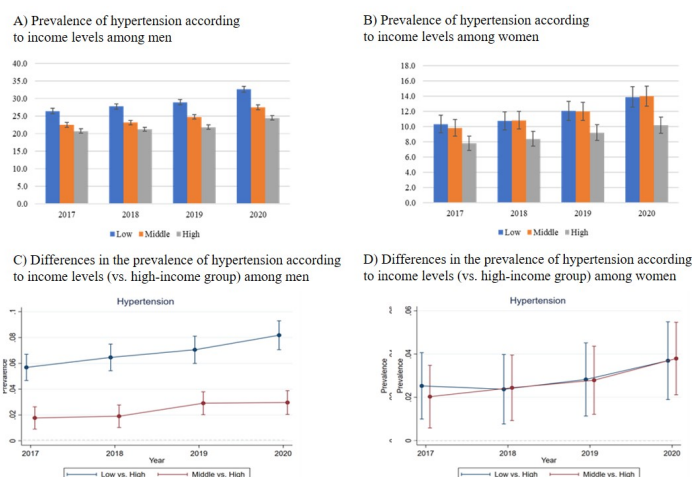
The association of Gastro-esophageal reflux symptoms and disease (GERS/GERD) with myocardial infarction, stroke, and angina among World Trade Center disaster exposed persons

Robert Brackbill* Robert Brackbill Howard Alper Ayda Ahmadi Jiehui Li Shengchao Yu

Background. It has been reported that GERS/GERD is co-morbid with several cardio/cerebrovascular diseases (CCVD) including myocardial infarction (MI), stroke, and angina. GERS/GERD is highly prevalent among 9/11 exposed persons (especially those with 9/11-related PTSD and exposure to building debris and dust) and thus there is a potential risk for these other conditions among persons with reflux disease. This study evaluated the association between GERS/GERD and MI, angina, and stroke. Methods and Results. A 9/11 exposure observational longitudinal cohort (World Trade Center Health Registry or Registry) provided data encompassing five waves over 17 years (n=22,978 have completed all five waves, see figure). Self-report of ever diagnosis of GERD, frequency of reflux symptoms, and use of medication were used to define GERS/GERD reported between 2012 and 2020 (Waves 3, 4, and 5). Extended Cox regression methods were used to investigate the association between GERS/GERD that met the definition at each wave that preceded or were concurrent with self-reported MI (n=316 cases), stroke (n=284) and angina (n=162), diagnosed between 2011 and 2020. After appropriately adjusting for age, sex, race/ethnicity, hypertension, cholesterol, BMI, diabetes, and smoking history, having GERS/GERD significantly increased the hazard of stroke (HR=1.5,95%CI,1.13,2.0) but not angina (HR=1.2,95%CI,0.8,1.8) or MI (HR=0.9,95%CI,0.7,1.3). Conclusion. The fact that stroke is associated with GERS/GERD and not MI or angina is congruent with evidence that GERS may cause atrial fibrillation (AF) and AF is a significant risk factor for stroke. Given that 30% of Registry enrollees report GERS and that this condition is a significant health burden among those in the WTC treatment program, it is important that this population be closely monitored for stroke.

World Trade Center Health Registry Study

WTC attacks 9/11/2001	Wave 1 2003-2004	Wave 2 2006-2007	Wave 3 2011-2012	Wave 4 2015-2016	Wave 5 2019-2020
	9/11 exposures		GERD, frequency of reflux, use of meds	GERD, frequency of reflux, use of meds	GERD, frequency of reflux, use of meds

Diagnosed MI, angina, stroke

Using Change Scores as Independent Variables in Causal Models: A Simulation Study Josée
Dussault* Josée Dussault Brian Pence Alexander Keil

Background: Change scores, or the difference between observed values of a variable at two
different timepoints, are often used in regression analyses of longitudinal data. Prior research
demonstrates that change scores as dependent variables allow valid inference only under strong
constraints. However, little research has investigated settings in which regression with independent
variable change scores are valid, although such analyses are common.

Methods: We analyzed simulated data under 3 scenarios. All scenarios included time-varying
exposure (X_t) and outcome (Y_t) variables at times $t = 0,1$, with the following variations: 1) a static
confounder (Z) as a direct cause of the exposure and outcome at all timepoints; 2) a static
confounder (Z) as a direct cause of X and Y at $t = 1$ only; 3) time-varying confounder Z_t, where Z_t is a
direct cause of X_t, Y_t, and Z_{t+1}. To estimate the causal effect of X_1 on Y_1, we ran 4 regression analyses
per scenario: 1) crude linear model with a change score ($X_{change} = X_1 – X_0$) independent variable and Y_t
dependent variable; 2) additionally adjusted for Z; 3) adding X_0 as a confounder; and 4) adding Y_0.

Results: Independent variable change scores induced bias in all scenarios, except when using
models 3 (adjusted for Z and X_0) and 4 (adjusted for Z, X_0, and Y_0.). In these 2 models, the coefficient
for X_{change} produced an unbiased estimate of the effect of X_1 on Y_1. Models 3 and 4 produced equal
power estimates (100%) to a correctly specified model with X_1 as the exposure variable (i.e., without
X_{change}).

Conclusion: Analyses with change score exposures do not answer substantively different questions
than standard analysis methods for continuous exposure variables and they can even induce bias.
Before choosing a change score approach, researchers should weigh the utility that the change
score provides and whether the processes they believe to have generated the data fall into a
scenario where a change score analysis would not induce bias.

Figure 1. Simulated data scenarios using
directed acyclic graphs (DAGs)
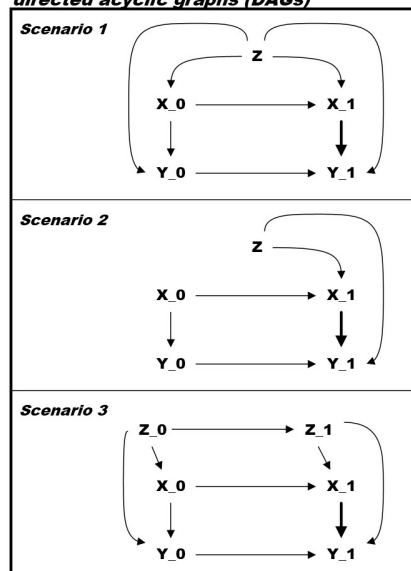
Should cognitive screening tests be corrected for age and education? Insights from a causal perspective Marco Piccininni* Marco Piccininni Jessica L. Rohmann Maximilian Wechsung Giancarlo Logroscino Tobias Kurth

Cognitive screening tests like the Mini-Mental State Examination are widely used in clinical routine to predict cognitive impairment. The raw test scores are often corrected for age and education, although documented poorer discrimination performance of corrected scores has challenged this practice. Nonetheless, test correction persists perhaps due to the seemingly counterintuitive nature of the underlying problem. We use a causal framework to inform the longstanding debate from a more intuitive angle. We illustrate and quantify the consequences of applying the age-education correction of cognitive tests on discrimination performance. In an effort to bridge theory and practical implementation, we computed differences in discrimination performance under plausible causal scenarios using OASIS-1 data. Since age and education are nearly ubiquitously considered causal risk factors for cognitive impairment, we show that correcting test scores for age and education removes meaningful information, thereby diminishing discrimination performance in conceivable real-world scenarios.

Causal Inference

Application-friendly tool to evaluate suitability of machine learning-based effect estimation for user-specified data: the Realistic Evaluations of Finite sample INference using Efficient Estimators (REFINE2) app. Jonathan Huang* Jonathan Huang Xiang Meng

Background: Practical challenges to using newer estimators (e.g. targeted maximum likelihood estimation; TMLE) are well known to methodologists, but opaque for most applied epidemiologists. In particular, whether practical positivity violations or finite samples undermine the use of flexible "machine learning" algorithms (e.g. random forests) for any given dataset is not always apparent. Moreover, the degree to which slightly mis-specified models (e.g. residual confounding) obviate the use of computationally-intensive estimators is also contextual.

Method: We conduct plasmode simulations from high dimensional (331 covariates, 1178 subjects) birth cohort data to generate known treatment effect sizes while retaining original covariate structure. We compare bias and confidence interval coverage of inverse probability weighted, augmented inverse probability weighting (AIPW), and TMLE-based approaches. We evaluate crossfit vs. non-crossfit and regression vs. flexible algorithm-based SuperLearners, as well as various degrees of model misspecification.

Results: When simulating from real data, we found estimators fit with flexible algorithms were often suboptimal. For example, in a scenario where covariate interactions were omitted, crossfit AIPW using a SuperLearner of linear regression, LASSO, & polynomial splines achieved 92% coverage, but only 76% when ensembling xgboost and random forest. Importantly, we found no obvious positivity violations and manual tuning did not improve performance. We develop an offline Shiny application (REFINE2) to allow users to test various estimators, model specifications, & fitting algorithms on simulations from their own data. Importantly, cautious interpretations are generated.

Discussion: Threats to the application of machine learning-based efficient estimators are not easily detectable in applied settings. A tool to quickly evaluate the relative performance of estimators for data-at-hand could enhance uptake and prevent misapplications.

The impact of the COVID-19 pandemic on system expenditures related to health services delivered for persons living with dementia María Alejandra Rodríguez Duarte* María Alejandra Rodríguez Duarte Isabelle Vedel Claire Godard-Sebillote Geneviève Arsenault-Lapierre Mary Henein Lise Gauvin Nadia Sourial

Background: Expenditures related to the care of persons living with dementia are five times higher than those of the population of the same age but without the disease. The COVID-19 pandemic acts as a natural experiment and requires a strong quasi experimental design to evaluate its effect on health care expenditures. The pandemic disrupted daily activities and access to health and social services, may have had a impact the persons living with dementia.
Objective: This study aims to estimate the impact of the pandemic on health care expenditures of services delivered to persons living with dementia.
Methods: A cohort of 127 508 persons aged 65+ with a diagnosis of dementia will be extracted from health administrative data in Quebec. Pre intervention period will consist of 18 monthly data points from March 2018 to December 2019 and post intervention period will consist of 9 data points from March to December 2020. An interrupted time series design using segmented regression will be estimated to compare the expenditures of health services before and after the COVID-19 outbreak.Expenditures for each service will be calculated as a function utilization per month and cost per service based on government service fee codes. Total expenditure will be a calculated as the sum across separate service expenditures.
Results: Descriptive statistics of the mean and total expenditure will be presented. The expected results will provide estimates of the change in level and slope due to the pandemic. Results will be presented in the form of risk ratios with corresponding 95% confidence intervals.
Conlusions: This study demonstrates the application of a strong quasi-experimental design to estimate the causal effect of a natural experiment like COVID-19. Results will help inform priorities to reduce morbidity, increase the efficient use of resources and ensure access and continuity of health services.
Key words: Dementia, interrupted time series, expenditure, healthcare, COVID-19

Evolution of the healthcare expenditures of services delivered for persons living with dementia
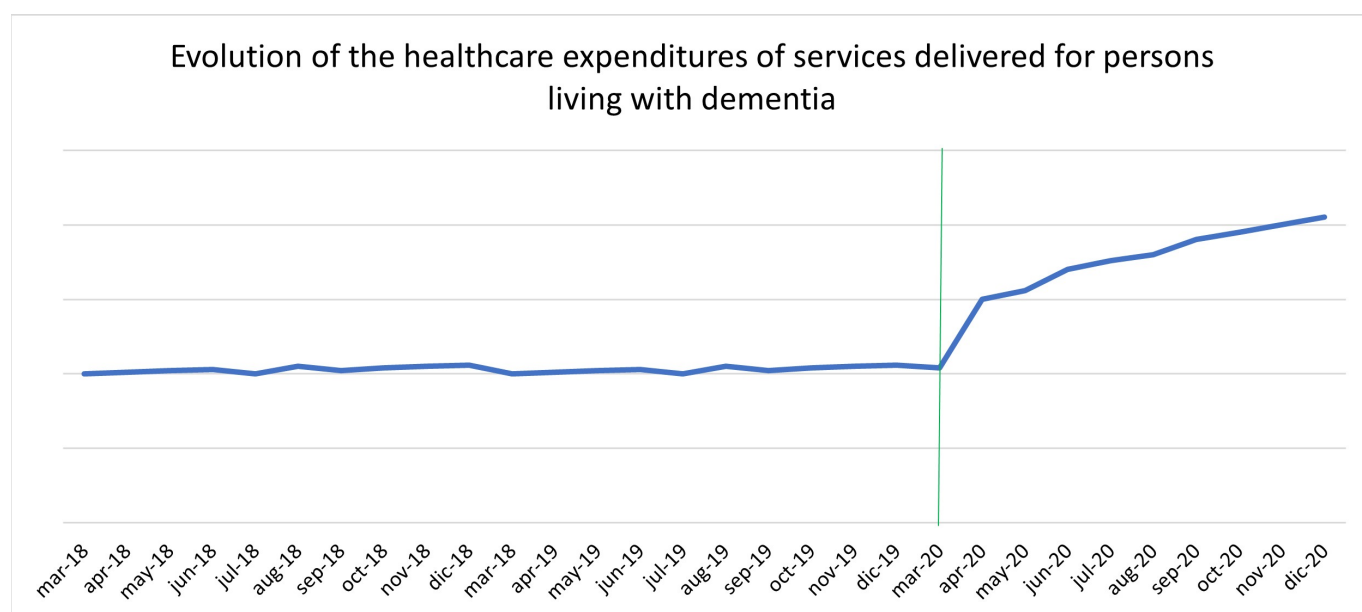
A protocol to examine the direct and indirect effect of interprofessional primary care teams on quality of care and health service use in older adults (OPTIMISE) Maria Alejandra Rodriguez Duarte* Pamela Fernainy Nadia Sourial Anaïs Lacasse Catherine Hudon Claire Godard-Sebillotte Cristina Longo Janusz Kaczorowski Joe-Guillaume Pelletier Marie-Thérèse Lussier Mylaine Breton Roxane Borges Da Silva Svetlana Puzhko Yves Couturier Maria Alejandra Rodriguez

Background: Interprofessional primary care (IPC) teams, have been promoted as part of health system reforms to improve access to high quality primary care for chronic disease management in older adults. IPC teams appear to have a positive impact on quality of care, but data is still lacking for their effect on health services use. Current evaluations do not provide a deconstruction of the causal relationship between IPC teams, quality of care, and health services.

Objective: This study aims to understand the causal effects of IPC teams on quality and health service use in older adults by examining the direct and indirect effect of IPC teams on quality and health service use. This study will identify the role of quality of care as a possible mediator of the effect of IPC on health service use.

Methodology: Target population will be older adults 65+ living in Quebec, Canada between 2007 and 2016. Data from the TorSaDE (The Care Trajectories-Enriched Data) cohort, containing health-administrative data linked to the Canadian Community Health Survey (CCHS), a cross-sectional survey, will be used. A quantitative analysis will help clarify the direct and indirect effect of IPC teams (exposure), on health service utilization (outcome), and any possible mediation by quality of health care. Thus, the overall effect of IPC teams on health services use, in the presence of quality of care with which the IPC teams may interact, will be decomposed into four components based on the propositions of VanderWeele (2014). The effect on the direct causal relationship of IPC team types and health service use will also be considered.

Results: The relative risks and 95% confidence intervals will be presented for the direct and indirect effects assessed.

Impact: This study will generate evidence comparing the relative influence of IPC teams on the quality of care and the health services use that will help guide changes in primary health care policy for the well-being of older adults.

Causal Inference
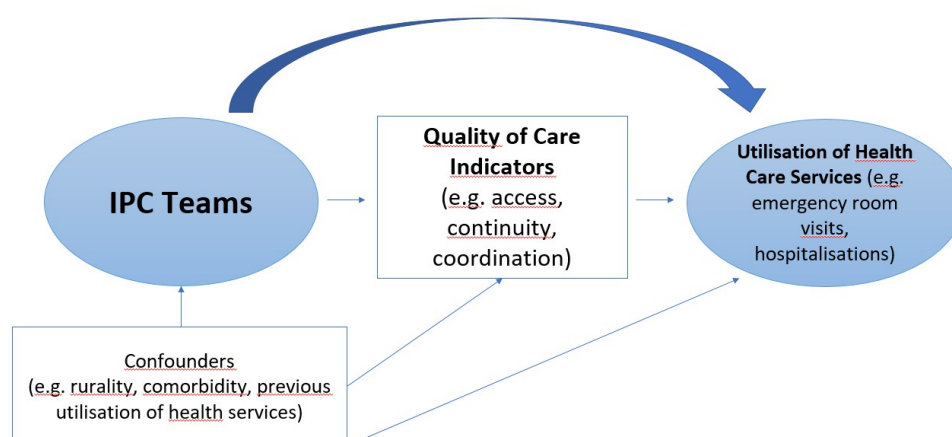
Extending treatment effects from a randomized trial using observational data Anthony Matthews* Anthony Matthews Issa Dahabreh Ole Fröbert Bertil Lindahl Stefan James Maria Feychting Tomas Jernberg Anita Berglund Miguel Hernan

To increase confidence in the use of observational data for extending inferences from randomized trials, one can first benchmark. That is, demonstrate the observational analysis can replicate an index trial's findings, before using the observational data to estimate what the trial could not. We use Swedish registry data to emulate a target trial similar to the TASTE randomized trial, which found no difference in the risk of death or myocardial infarction by 1 year with or without thrombus aspiration among individuals with ST-elevation myocardial infarction (STEMI). We benchmark the emulation against the trial at 1 year, then extend the emulation's follow up to 3 years and estimate effects in subpopulations underrepresented in the trial. Like TASTE, the observational analysis found no differences in risk of outcomes by 1 year between groups (risk difference 0.7 (-0.7, 2.0) and -0.2 (-1.3, 1.0) for death and myocardial infarction respectively), so benchmarking was considered successful. We additionally show no difference in risk of death or myocardial infarction by 3 years, or within subpopulations by 1 year. Benchmarking before using observational data to extend treatment effects from a randomized trial allows us to understand if the observational data can be trusted to deliver valid estimates of treatment effects.

Causal inference-informed re-analyses of factors associated with dropout from weight-loss programmes for adults Ridda Ali* Ridda Ali Andrew Prestwich Jiaqi Ge Georgia D Tomova Claire Griffiths Mark S Gilthorpe

Background: Understanding which factors predict or cause individuals' dropout from weight-loss programmes can provide insight into possible adaptations that minimise dropout. Prior research indicating 'predictors' of dropout does not allow causal interpretation, which limits its utility to inform possible adaptations.

Objective: Re-analysis of secondary datasets to: (1) explore if, and by how much, insights differ between prediction and causal inference approaches; and (2) identify associated methodological issues in both prediction and causal inference.

Methods: The primary analyses attempted to identify variables that *predict* or are *correlated* with whether a participant dropped out of a weight-loss intervention, without recognising that this might conflate the two distinct data science tasks of *prediction* and *causal inference*. The same datasets were re-analysed for prediction and causal inference, using approaches appropriate for each task. To identify predictors, a single model containing a full set of variables was developed for each dataset. To estimate causal effects, a directed acyclic graph (DAG) was coproduced with authors from each original study, and multiple models were generated depending on the exposures of interest.

Results: Age and body mass index (BMI) were frequently identified as predictors of dropout in primary analyses, whereas in the secondary analyses, factors causally associated with dropout were older age, women, higher baseline weight, and more challenging weight-loss targets. The primary studies could not inform causal interpretation due to methodological issues such as Table 2 Fallacy.

Conclusion: Weight-loss programme design cannot be improved by knowing which factors predict dropout; in fact, this may cause more harm than good. There were some differences in the coefficients generated by the prediction and causal inference models (even sign reversal), indicating that the potential for misinterpreting causal relationships could be severe.

Mental Well-being and Associated Factors during COVID-19 pandemic among medical students in Vietnam

Thi Huyen Trang Nguyen* Thi Huyen Trang Nguyen Jin-Kyoung Oh Thi Huyen Trang Nguyen

Background: The COVID-19 pandemic is a global health emergency that endangering the mental well-being of human lives. In Vietnam, there are few studies that investigated the mental health among medical students who play an important role to support health care workers to fight the spread of the COVID-19 pandemic in Vietnam. This study aimed to investigate the mental well-being and associated factor during the COVID-19 pandemic among Vietnamese medical students.

Methods: We conducted a cross-sectional study using an online questionnaire to do the rapid assessment during the fourth wave of the pandemic from October to December 2021 among medical students in Vietnam. General Anxiety Disorder (GAD-7), Perceived Stress Scale (PSS-4), and The Patient Health Questionnaire (PHQ)-9 were utilized to assess the mental well-being of the medical students.

Results: Among 1664 medical students, the mean score of anxiety, depression, and stress was 5.1 (SD =5.0), 6.2 (SD=4.1), and 10.0 (SD=2.9), respectively. 85.9% of students were willing to give psychological counseling to friends and 8% sought consults from doctors or psychologists during the pandemic. The mean value of the EQ-5D index is 0.9 (SD = 0.2), and sleep quality score is 7.7 (SD=1.7). Being female, over 20 years old and 20% increase in working time compared to before the COVID-19 were positively associated with higher depression score (Coef.=1.16, 95%CI=0.70; 1.6; Coef.=0.57; 95%CI=0.18; 0.97; Coef.=0.78; 95%CI=0.21; 1.36). Students who exposing to confirmed cases were more likely to report higher scores of stress (Coef. = 0.94, 95%CI=0.06; 1.82).

Conclusion: There was a relatively high score of anxiety, depression, and stress among medical students during the fourth wave of COVID-19 in Vietnam. We suggest implementing digital interventions and interactive programs such as telehealth or online storytelling to tackle the restriction of in-person mental health services of medical students throughout the pandemic.

Table 4: Factors associated with anxiety, depression, and stress status of medical students (n = 1,664)

Characteristic	Anxiety Coef.	Anxiety 95%CI	Depression Coef.	Depression 95%CI	Stress Coef.	Stress 95%CI
General information						
Gender (Ref: Male)						
Female			1.16***	0.70; 1.61	0.25	-0.09; 0.60
Age groups (Ref: 18 - 20 years old)						
Over 20 years old			0.57***	0.18; 0.97		
Living areas (Ref: City)						
Countryside	0.68*	-0.03; 1.39	0.54**	0.03; 1.04		
Others	-0.19	-0.95; 0.57	0.01	-0.52; 0.55		
Job information						
Time to participate in the prevention of COVID-19 (Ref: Not on duty)						
< 1 month	0.22	-0.54; 0.98	-0.05	-0.59; 0.49	0.24	-0.18; 0.66
1 to <3 months	-0.88**	-1.58; -0.17	-0.82***	-1.32; -0.32	-0.18	-0.57; 0.21
From 3 months or more	-0.76	-2.16; 0.64	-0.18	-1.16; 0.80	-0.82**	-1.59; -0.06
Number of sessions per week (Ref: Not on duty)						
1 session	-0.75	-1.68; 0.18				
From 2 sessions or more	-0.50	-1.41; 0.42				
Average working time per day (Ref: Less than 8 hours/day)						
8 hours/day			-0.53**	-1.01; -0.05		
Over 8 hours/day			-0.31	-1.00; 0.37		
Workload changes (Ref: No increase)						
Increase 20% or more	0.59	-0.11; 1.29			-0.50	-1.14; 0.13
Working time changes (Ref: No increase)						
Increase less than 20			0.78***	0.21; 1.36	0.76**	0.13; 1.38
Increase 20% or more			0.29	-0.39; 0.98	0.90**	0.18; 1.63
Exposure to people infected with COVID-19 (Ref: No)						
F0 person (Yes)			-0.88	-2.21; 0.45	0.94**	0.06; 1.82
F1 person (Yes)			1.51**	0.19; 2.83		
Nothing (Yes)			0.57**	0.07; 1.07		
EQ - VAS score (range: 0 -100)	-0.05***	-0.07; -0.03	-0.03***	-0.05; -0.02	-0.02***	-0.04; -0.01
EQ - 5D index	-8.07***	-9.80; -6.35	-5.56***	-6.80; -4.32	-0.85*	-1.82; 0.12
Sleep quality score (range: 0 -10)	-0.95***	-1.13; -0.77	-0.83***	-0.96; -0.70	-0.30***	-0.40; -0.20
Methods to help improve mental health (Ref: No)						
No support needed (Yes)	-0.95*	-2.04; 0.15			-0.58**	-1.15; -0.01
Doctor/psychologist (Yes)			-0.57	-1.28; 0.14	0.38*	-0.05; 0.81
Read psychological support material (Yes)						
Talk to family (Yes)	-0.68**	-1.26; -0.11	-0.55**	-0.98; -0.12	0.43**	0.09; 0.77
Talking with friends (Yes)			0.44*	-0.03; 0.90	0.69***	0.32; 1.05
Talk to colleagues (Yes)					0.48*	-0.04; 0.99
Play game (Yes)			0.50**	0.04; 0.96		
Using social media/internet (Yes)	0.51	-0.11; 1.13	0.70***	0.27; 1.14	0.29*	-0.04; 0.62
Exercise/yoga (Yes)	-0.78***	-1.35; -0.20	-0.60***	-1.00; -0.20		

*** p<0.01, ** p<0.05, * p<0.1

Differential care-seeking behaviors during the beginning of the COVID-19 pandemic in Michigan Catherine A. Vander Woude* Catherine Vander Woude Elizabeth King Jana L. Hirschtick Andrea R. Titus Laura E. Power Michael R. Elliott Patricia McKane Nancy L. Fleischer

At the beginning of the COVID-19 pandemic in the US in the spring of 2020, many Americans avoided the healthcare system, while those with COVID-19 symptoms were faced with decisions about seeking healthcare services for this novel virus. Using a probability sample (n = 1094) from the Michigan adult population of PCR-confirmed COVID-19 cases who were diagnosed prior to July 31, 2020, we used logistic regression to examine sociodemographic and symptom severity predictors of care-seeking behaviors. The analyses examined three different outcomes: (1) whether respondents sought care and, among those who sought care, whether they sought care from (2) a primary care provider or (3) an emergency room. Final models were adjusted for sex, age, race/ethnicity, income, education, marital status, living arrangement, health insurance, and self-reported symptom severity. We found that participants ages 65 and older had 4.1 times higher odds of seeking care than 18-34-year-olds (95% CI = 2.4, 7.0), while adults reporting very severe symptoms had roughly 15 times higher odds of seeking care than those with mild symptoms (95% CI: 8.3, 29.0). Adults who were non-Hispanic Black or were uninsured had lower odds of seeking care from a primary care physician versus seeking care from other locations in comparison to adults who were non-Hispanic White or were privately insured, respectively (non-Hispanic Black: OR = 0.29, 95% CI = 0.18, 0.48; Uninsured: OR = 0.21, 95% CI = 0.10, 0.46). Conversely, adults who were older or reported more severe symptoms had higher odds of seeking care from an emergency room versus other locations in comparison to adults who were younger or reported less severe symptoms (Age 65+: OR = 3.3, 95% CI = 1.6, 6.5; Very Severe Symptoms: OR = 6.4, 95% CI = 3.3., 12.7). Our results suggest that healthcare services were not accessed equitably at the beginning of the COVID-19 pandemic. Further analyses are needed to examine the reasons for these differences.

Persisting gastrointestinal symptoms and post-infectious irritable bowel syndrome following SARS-CoV-2 infection: results from the Arizona CoVHORT Erika Austhof* Erika Austhof Melanie L Bell Mark S. Riddle Colin Catalfamo Caitlyn McFadden Kerry Cooper Elaine Scallan Walter Elizabeth Jacobs Kristen Pogreba-Brown

Background and Aims: Persisting gastrointestinal (GI) symptoms and post-infectious irritable bowel syndrome (PI-IBS) can follow acute viral infection, but less is known about these conditions following SARS-CoV-2 infection. The aim of this study is to examine the association between GI symptom presence during acute SARS-CoV-2 infection and the prevalence of GI symptoms ≥45 days post-acute infection. We also seek to identify the incidence of PI-IBS in those with acute GI symptoms.

Methods: We used a sample of data from a prospective cohort of adult participants with a positive polymerase chain reaction or antigen SARS-CoV-2 test in the Arizona CoVHORT study. We used logistic regression to examine the association between GI symptom status during acute infection and prevalence of persistent gastrointestinal symptoms at ≥45 days, reporting unadjusted and adjusted odds ratios and 95% confidence intervals. We also report the incidence of PI-IBS following acute infection with GI symptoms.

Results: Of the 1,475 participants enrolled from May 2, 2020 to October 1, 2021, 33.8% (n=499) had GI symptoms during acute infection. Cases with acute GI symptoms had an odds of persisting GI symptoms 4 times higher than cases without acute GI symptoms (OR=4.04, 95% CI: 2.42, 6.77); symptoms lasted on average 8 months following infection. After adjusting for age, sex, and perceived stress during acute infection, the results remain similar (OR=4.29, 95% CI: 2.45, 7.53). The health experience of persisting GI symptoms was considerable, and 42 of the 68 participants with persisting GI symptoms (67%) sought care for their symptoms. Incident PI-IBS occurred in 3.0% (n=15) of participants on average 6 months following acute infection.

Conclusions: Those with acute GI symptoms after SARS-CoV-2 infection are likely to have similar persistent symptoms on average 8 months from acute infection. These data indicate that attention to a potential increase in related healthcare needs is warranted.

The role of COVID-19 in young adults' depressive symptoms: data from Monitoring the Future. Noah Kreski* Noah Kreski Megan Patrick Katherine Keyes

Introduction: The coronavirus pandemic has fundamentally harmed young adults' mental health, but minimal research has quantified the prevalence of specific depressive symptoms and the extent to which these symptoms are attributable to COVID-19.

Methods: Using data from Monitoring the Future (N = 1,244 young adults) collected in a 2020 supplement, we examined depressive symptoms using the Patient Health Questionnaire (PHQ) (e.g., "little interest or pleasure in doing things") dividing the sample into those without clinically significant scores, those who had significant scores (significance threshold: score ≥ 10), but minimal self-reported attribution of symptoms to COVID-19, and those who had high scores with substantial attribution to COVID-19. We then conducted logistic regression analyses linking COVID-related experiences (e.g., lacking a place to sleep or money for rent, gas, or food due to COVID-19) to these depressive symptom groups.

Results: Depressive symptoms were highly prevalent among young adults, with most symptoms occurring among more than half of young adults at least several days over the past two weeks (Figure 1). Among those with each symptom, over one fifth attributed their symptom more than somewhat to COVID-19 for all but one symptom. Major changes in education, employment, and resource availability were linked to elevated risk of high depressive symptoms (e.g., those who lacked a place to sleep or money for rent, gas, or food due to COVID-19 had 3.45 [95% CI: 2.22, 5.35] times the risk of high depressive symptoms).

Discussion: The harmful impact of COVID-19 on depressive symptoms among young adults warrants urgent attention in the form of improved mental health treatment infrastructure as well as stronger structural support in the event of shifts in employment, education, and resource availability.
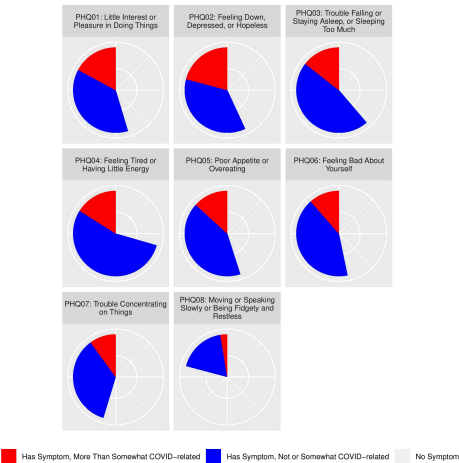
Disparities in COVID-19 hospitalization at the intersection of race/ethnicity and income

Blair Whittington* Blair Whittington Giovanna Buttazzoni Akash Patel Laura E. Power Patricia McKane Nancy L. Fleischer Jana L. Hirschtick

Significance: COVID-19 hospitalizations are an important indicator of illness severity and metric of pandemic surveillance. While existing studies have elucidated racial/ethnic disparities in COVID-19 hospitalizations, few have examined disparities at the intersection of race/ethnicity and income.

Methods: We used data from the Michigan COVID-19 Recovery Surveillance Study (MI-CReSS), a population-based survey of non-institutionalized adults in Michigan with a positive SARS-CoV-2 test before November 16, 2020. We categorized respondents by race/ethnicity and annual household income: Low-income (<$50,000) Non-Hispanic (NH) White, high-income (≥$50,000) NH White, low-income NH Black, high-income NH Black, low-income Hispanic, and high-income Hispanic. We used modified Poisson regression, adjusted for sex, age group, survey mode, and sample wave, to estimate COVID-19 hospitalization prevalence by race/ethnicity and income.

Results: Over half of the analytic sample (n=1593) was female (54.9%) and age 45 or older (52.5%), with 16.5% hospitalized for COVID-19. Hospitalization was most prevalent among low-income (32.9%) and high-income (31.2%) NH Black adults, followed by low-income NH White (15.3%), low-income Hispanic (12.9%), high-income NH White (9.7%) and high-income Hispanic adults (8.8%). In adjusted models, NH Black adults, regardless of income (low-income PR: 1.86, 95% CI: 1.36-2.54; high-income PR: 1.57, 95% CI: 1.07-2.31), and low-income NH White adults (PR: 1.52, 95% CI: 1.12-2.07) had significantly higher prevalence of hospitalization compared to high-income NH White adults. The prevalence of hospitalization for low- or high-income Hispanic adults did not significantly differ from high-income NH White adults.

Conclusions: We observed disparities in COVID-19 hospitalization at the intersection of race/ethnicity and income for NH Black and NH White adults, but not Hispanic adults.

Vaccine Hesitancy Among Adults During COVID-19 Michaela F George* Michaela George Braelyn Wakefield Angelica Gonzalex Almanza Jennifer Borromeo Madison Huckabay Benjamin Rosenberg

Background

Vaccine hesitancy became a term spiraling throughout the media and social networks, growing the public response tremendously. This study assesses the motivations, beliefs, and perceptions of individuals who have decided to remain unvaccinated against COVID-19.

Methods

We conducted a mixed-methods analysis with unvaccinated adults throughout 2021-2022. The analysis was composed of an interview with open-ended and closed-ended questions and a short survey about individuals perceptions on the COVID-19 vaccine and their intentions to get vaccinated.

Results

The results illuminated which characteristics and patterns accounted for vaccine hesitancy during COVID-19. It is hypothesized that the use of in depth interviews and a detailed survey will greatly contribute to understanding vaccine hesitancy.

Discussion

These findings can identify specific characteristics of individuals and provide connections for their reasoning to remain unvaccinated. Therefore, we can tailor public health programs and interventions to encourage vaccine acceptance across all infectious diseases. Interventions should target reasons for hesitancy, address concerns about safety and side effects, and underscore the importance of vaccinations for all populations and ethnic groups.

Heterogeneous impact of COVID-19 on multiple domains of mental health in Nurses' Health Study II

Yiwen Zhu* Yiwen Zhu Laura Sampson Shaili C. Jha Archana Basu Laura D. Kubzansky Karestan C. Koenen

The growing literature on COVID-19 related stressful experiences and mental health has yielded many insights, emphasizing the importance of addressing mental health needs in addition to mitigating threats to physical health. However, most existing studies are cross-sectional and do not account for prior psychological and physical health. Moreover, very few studies examined multiple domains of stress and mental health simultaneously, making it challenging to understand the overall impact of COVID.

Using data from non-active healthcare workers in the COVID substudy of the Nurses' Health Study II (n=26,440), we characterized the heterogeneity of individual experiences during COVID and assessed associations between stressors that emerged in the beginning of the pandemic and mental health outcomes over one year (May 2020–May 2021). In addition to psychological distress, we considered several well-being outcomes, which extend beyond the absence of symptoms and focus on broader aspects of life such as purpose and belongingness. An exploratory factor analysis of common individual stressors measured at the beginning of the pandemic revealed two distinct domains of stress exposures: infection risks and caregiving & living arrangement. Accounting for pre-pandemic physical and mental health, longitudinal analyses using generalized estimating equations revealed that caregiving & living arrangement related stress had stronger associations with anxiety, posttraumatic stress symptoms, and perceived stress over the course of the pandemic, compared to infection risks. However, it was linked to decreased loneliness and did not associate with psychological well-being, gratitude, or social well-being. Our findings suggest at the initial stage of the pandemic, COVID did not have one uniform effect on all psychosocial health outcomes. It remains a research priority to examine the ongoing mental health impact of the pandemic across domains and individuals to inform policy interventions.
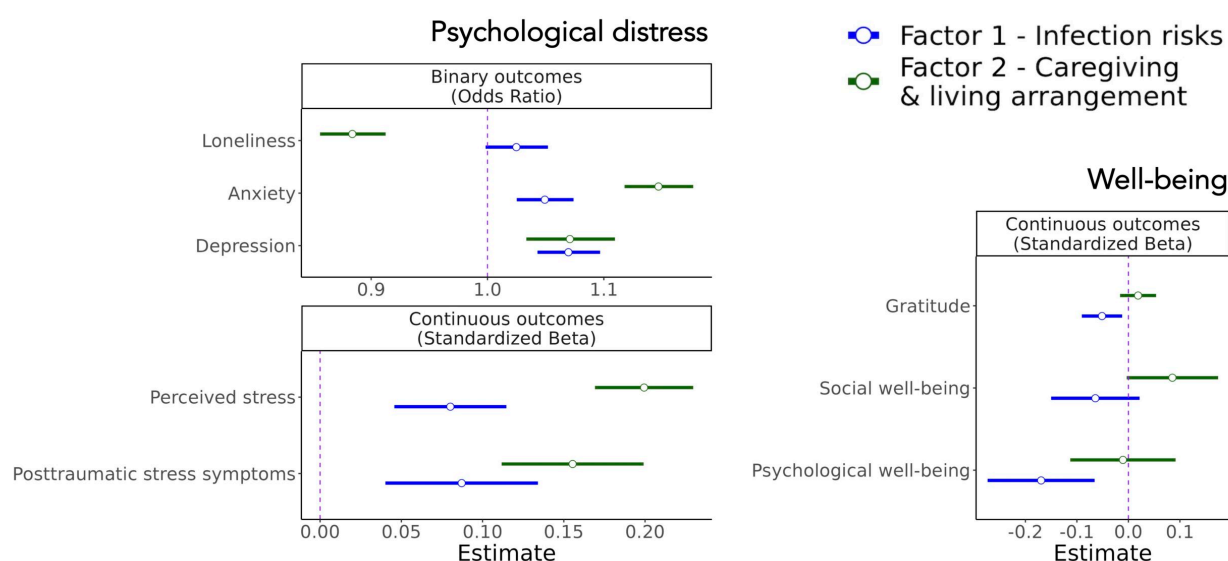

Figure 1. Associations between latent factors of stressors and mental health outcomes during COVID-19, adjusting for sociodemographic information and pre-pandemic health, estimated using generalized estimating equations.

Methods for Using the Census Bureau's Household Pulse Survey for Analyzing Publicly Available Data on the Social and Economic Impacts of COVID-19 Leah Chapman* Leah Chapman Jean Hu Sarah Seidel

The United States Census Bureau's Household Pulse Survey (HPS) contains 39 weeks of repeated cross-sectional data on the social and economic impacts of COVID-19 on American households. Key measures include demographics, education, employment, food sufficiency, household spending, housing security, and physical and mental health during the pandemic. The survey began on April 23, 2020 and currently contains data through October 11, 2021. HPS is extremely unique in that it provides near real-time data on the COVID-19 pandemic; new data are continuously released, and the newest phase of data collection began on December 1, 2021. All data files are publicly available and can be downloaded by week as Excel or SAS files. However, there are many important steps needed to accurately analyze the HPS data. After introducing the HPS dataset and its key measures, this presentation will describe the methods for downloading, cleaning, and analyzing the HPS data for researchers. Topics will include sub-setting the data, proper statistical methods for weighting the HPS survey data, merging multiple weeks of data, and additional analytic steps needed if analyzing multiple weeks of combined HPS data. Of note, while the Census Bureau provides this information in its HPS technical documentation, this presentation distills and summarizes this detailed information (as the technical documentation contains numerous, highly detailed files for the different phases of the study). Lastly, the presentation will provide and review the SAS and Stata code needed for merging and analyzing HPS data. Overall, this presentation will 1) increase awareness of the HPS data, and 2) assist researchers in analyzing the HPS data, potentially increasing COVID-19 research that informs federal and state response and recovery planning for the pandemic.

Factors Associated with COVID-19 Vaccine Hesitancy Among Texas Households Leah Chapman* Leah Chapman Jean Hu Sarah Seidel

Many Americans, including many Texans, are hesitant to receive a COVID-19 vaccine. Using cross-sectional data from the Census Bureau's Household Pulse Survey, this presentation: 1) describes who, among Texans, is most likely to experience COVID-19 vaccine hesitancy and 2) examines the reasons behind COVID-19 vaccine hesitancy among Texans. We present this information for two time periods: the beginning of vaccine rollout (January 6-March 29, 2021) and during widespread vaccine availability in Texas (April 24-May 24, 2021). To measure intention to vaccinate, Pulse asks: Once a vaccine to prevent COVID-19 is available to you, would you: 1) Definitely get a vaccine, 2) Probably get a vaccine, 3) Probably not get a vaccine, or 4) Definitely not get a vaccine. Multinomial logistic regression models were estimated and incorporated sampling weights. Being female and Black were associated with the highest odds of vaccine hesitancy, while being Asian, being of Hispanic/Latino ethnicity, having a college degree, and older age (40 years or older) were associated with a lower odds of vaccine hesitancy. During the beginning of vaccine rollout, the top 3 reasons for COVID-19 vaccine hesitancy included: I plan to wait and see if it is safe and may get it later (weighted n=4,050,641); I am concerned about possible side effects of a COVID-19 vaccine (weighted n=4,033,238); and I think other people need it more than I do right now (weighted n= 2,290,190). During the later stage of vaccine rollout, the top 2 reasons remained the same, but the 3rd changed from "I think other people need it more than I do right now" to "I don't trust COVID-19 vaccines." Efforts to promote COVID-19 vaccination in Texas may benefit from a focus on black, female, and younger Texans and crafting public health messaging to address Texans' top reasons for vaccine hesitancy. Additionally, other states may benefit from performing this analysis using their own Census Pulse Survey data.

Demographic factors associated with COVID-19 vaccine hesitancy among Census Bureau Household Pulse Survey participants in Texas.

	Probably Will Receive a COVID-19 Vaccine			Probably Will Not Receive a COVID-19 Vaccine			Definitely Will Not Receive a COVID-19 Vaccine		
	OR[a]	95% CI	p-value	OR[a]	95% CI	p-value	OR[a]	95% CI	p-value
Age[b]									
30-39 years	0.87	0.65 - 1.16	0.33	1.00	0.75 - 1.34	0.99	1.00	0.70 - 1.43	0.99
40-49 years	0.72	0.54 - 0.95	0.02	0.69	0.49 - 0.97	0.03	0.62	0.42 - 0.92	0.02
50-59 years	0.50	0.40 - 0.63	<0.0001	0.57	0.42 - 0.79	0.001	0.44	0.30 - 0.64	<0.0001
60+ years	0.36	0.29 - 0.45	<0.0001	0.31	0.24 - 0.40	<0.0001	0.29	0.19 - 0.44	<0.0001
Female[c]	1.34	1.21 - 1.58	<0.0001	1.48	1.26 - 1.74	<0.0001	1.25	1.00 - 1.56	0.05
Race[d]									
Black alone	1.75	1.44 - 2.13	<0.0001	1.56	1.24 - 1.96	<0.0001	1.38	1.05 - 1.81	0.02
Asian alone	0.67	0.51 - 0.88	0.005	0.21	0.14 - 0.30	<0.0001	0.23	0.12 - 0.44	<0.0001
Any other race alone or in combination	1.07	0.75 - 1.52	0.72	1.49	0.92 - 2.43	0.11	1.56	0.95 - 2.58	0.08
Hispanic, Latino, or Spanish origin[e]	1.00	0.84 - 1.19	0.99	0.53	0.41 - 0.67	<0.0001	0.41	0.31 - 0.54	<0.0001
College degree[f]	0.54	0.48 - 0.60	<0.0001	0.50	0.42 - 0.60	<0.0001	0.32	0.25 - 0.40	<0.0001

[a]Odds ratios estimated from a multinomial logistic regression model. The reference category is "definitely will receive a COVID-19 vaccine."
[b]The reference category is "18-29 years."
[c]The reference category is "male."
[d]The reference category is "white alone."
[e]The reference category is "not of Hispanic, Latino, or Spanish origin."
[f]The reference category is "less than a college degree."

Creating Novel Surveillance Data Products for Briefing Health Department Leadership and Elected Officials During the COVID-19 Pandemic in Texas Leah Chapman* Leah Chapman Emily Hall Sarah Seidel

Beginning in March 2020, the Texas Department of State Health Services (DSHS) developed several internal surveillance tools for briefing state health department leadership and elected officials on the status of the COVID-19 pandemic in Texas. This presentation will describe the initial conceptualization and methods for daily production of three of these internal surveillance tools, which include: 1) a COVID-19 data book displaying case, fatality, hospitalization, and testing data by county and statewide by day, 2) graphs and data files displaying new daily COVID-19 fatalities among residents of long-term care facilities in Texas, and 3) graphs and data files comparing COVID-19 cases and hospitalizations between the three COVID-19 waves in Texas. We also provide details on methods, challenges, and lessons learned around creating and maintaining these tools for leadership. These surveillance products are easily replicable, and our methods and lessons learned may be helpful for researchers or health department officials in states experiencing rapid increases in cases and hospitalizations due to the Delta or Omicron variants, or for any future outbreaks of COVID-19 or new highly transmissible respiratory illness. Additionally, while these surveillance methods were used for continuous surveillance by Texas DSHS, they may also be useful for researchers or health department officials who wish to better understand the story of COVID-19 in their states or communities and gain additional insights from their data.
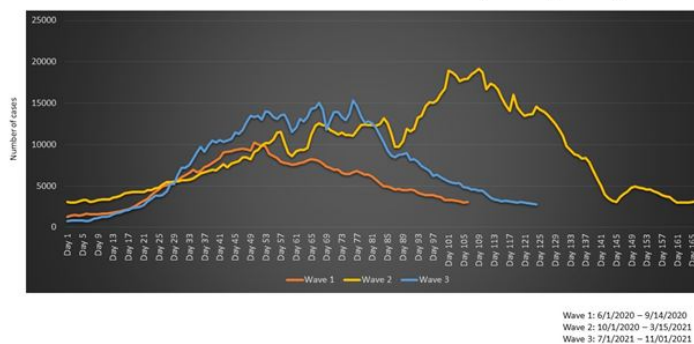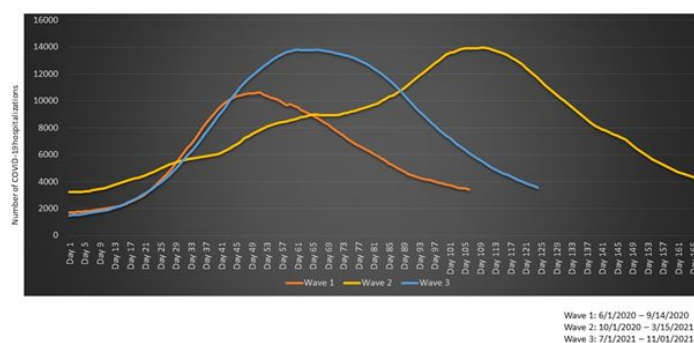
Sample graphs from the third surveillance product, which compares daily COVID-19 cases and hospitalizations between the three COVID-19 waves in Texas.

**Dear Pandemic: A topic modeling analysis of themes and longitudinal trends in COVID-19 information needs** Aleksandra Golos* Aleksandra Golos Sharath Chandra Guntuku Rachael Piltch-Loeb Lindsey J Leininger Amanda M Simanek Aparna Kumar Sandra S Albrecht Jennifer Beam Dowd Malia Jones Alison M Buttenheim

Background: The COVID-19 pandemic has been accompanied by an "infodemic"—an excess of accurate and inaccurate information. The social media-based health communication campaign *Dear Pandemic* was established to address this infodemic, in part by soliciting reader submissions to an online question box. We characterized the information needs of *Dear Pandemic's* readers by identifying themes and trends among a year's worth of submissions.

Methods: We retrospectively analyzed questions submitted from August 24, 2020, to August 24, 2021. We used Latent Dirichlet Allocation topic modeling to identify 25 topics among the submissions, then qualitatively interpreted the topics based on their most highly-associated words and submissions. We used t-Distributed Stochastic Neighbor Embedding to visualize the relationship between topics, and used generalized additive models to describe trends in topic prevalence over time.

Results: We analyzed 3839 submissions, 90% from United States-based readers. We classified the 25 topics into 6 overarching themes: "Scientific and Medical Basis of COVID-19," "COVID-19 Vaccine," "COVID-19 Mitigation Strategies," "Society and Institutions," "Family and Personal Relationships," and "Navigating the COVID-19 Infodemic." Trends in topics about viral variants, vaccination, COVID-19 mitigation strategies, and children aligned with the news cycle and reflected the anticipation of future events. Over time, vaccine-related submissions became increasingly related to those surrounding social interaction.

Conclusions: Question box submissions displayed distinct themes that evolved over time. *Dear Pandemic's* readers sought information that would not only clarify scientific and epidemiological concepts, but also be timely and practical in their personal lives. Our question box format and topic modeling approach offers other infodemiologists and health communicators a robust methodology for tracking, understanding, and responding to online information needs.
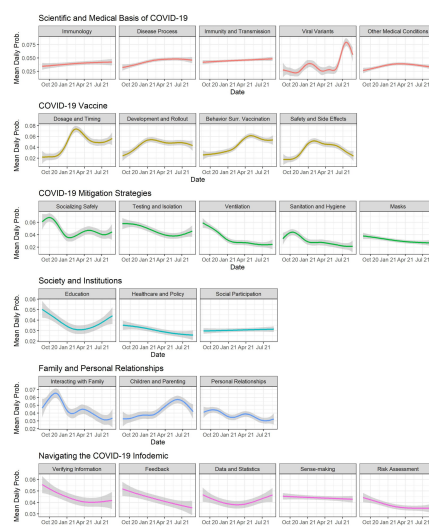
Extent and predictors of preventive practices in the first months of the COVID-19 pandemic in Lebanon Martine Elbejjani* Martine Elbejjani Rawan Hammoud Catrina Ziade Batoul Assi Ahmad Assi Samya El Sayed Hala Kerbage

As countries worldwide struggle to adapt to the COVID-19 pandemic, lessons from earlier phases of the outbreak can help guide global and local public health strategies. We assessed the extent and predictors of preventive practices as well as worries related to the pandemic and mental health (depression (Patient Health Questionnaire PHQ-9) and anxiety (Generalized Anxiety Disorder GAD-7), during the first country-wide lockdown in Lebanon (March-May 2020), using an online survey distributed on social media platforms.

Among 510 participants with complete data (mean age=36.1 (SD=11.3)), adherence to preventive measures was high (adhering to the lockdown (82.6%), social distancing (86.4%), wearing face masks (75.6%), canceling social gatherings (84.2%), and hand washing (82.9%)). Participants reported having high pandemic-related worries (most prevalent were fear of spreading the virus to others (80.2%), not getting proper healthcare (35%), isolation (32.7%), contracting the virus (29.5%), and having health complications (29.2%)); 32.3% had elevated depression and 27.3% had elevated anxiety symptoms. Factors related to higher preventive practices were older age, gender (women), believing that preventive measures were necessary, and higher depression scores, knowledge about the pandemic, pandemic-related worries, satisfaction and trust in the government response, and trust in information provided by health institutions, the government, and media. Multivariable analysis will be presented. Results are limited by the potentially selective sample. Results show that although infection rate was still low (0.6% of participants had contracted the virus and average national case count was ~0.1/100,000), worries and mental health burden were elevated. Results also highlight the importance of contextual factors and of information and trust in government response – which are particularly relevant in Lebanon where the pandemic is occurring amid ongoing political and economic crises.

Differences in Pandemic Fatigue by Type of Contact and Sociodemographic Factors Gillian A.M. Tarr* Gillian Tarr Damon Leach Keeley J. Morris Mark Fiecas

The impact of pandemic fatigue on willingness to adopt protective behaviors emerged early in the course of the COVID-19 pandemic, yet little is known about how pandemic fatigue manifests in different groups. We sought to determine whether pandemic fatigue demotivated physical distancing behavior and whether the effect differed by sociodemographic factors.

In April-May 2020, we recruited: adults living with children (n=1001); and adults ≥50 years (n=340). Participants completed detailed online surveys at baseline; 2, 4, 8, and 12 weeks after enrollment; and in fall 2020. Surveys asked about frequency of various non-work outings (e.g. retail) in the past 7 days, and on the most recent outing of each type, how many individuals they came into contact with at <6 feet. We estimated the weekly average number of contacts for each outing type by multiplying the 7-day outing count by the most-recent outing contact count. For each type of contact, we used a Poisson generalized estimating equation model to estimate the adjusted effect of calendar week on contact rate; interactions were examined for week and sociodemographic factors.

Both linear and quadratic terms for week were significant predictors of contact rate for each contact type, indicating initial increases in contact rates followed by decreases in late summer and early fall 2020 (Figure). Modeled peaks in contact rates ranged from week 27 (July 29) for retail contacts among adults ≥50 years to week 32 (August 3) for all but residential contacts in the family cohort. The effects of week on contact rate differed by age, gender, income, and education level; however, relevant factors differed by contact type.

Pandemic fatigue is a complex behavior, which we have shown can potentially increase risk though increased non-household contacts during essential and non-essential activities. Pandemic fatigue differed by sociodemographic characteristics, identifying opportunities for targeted public health messaging and support.
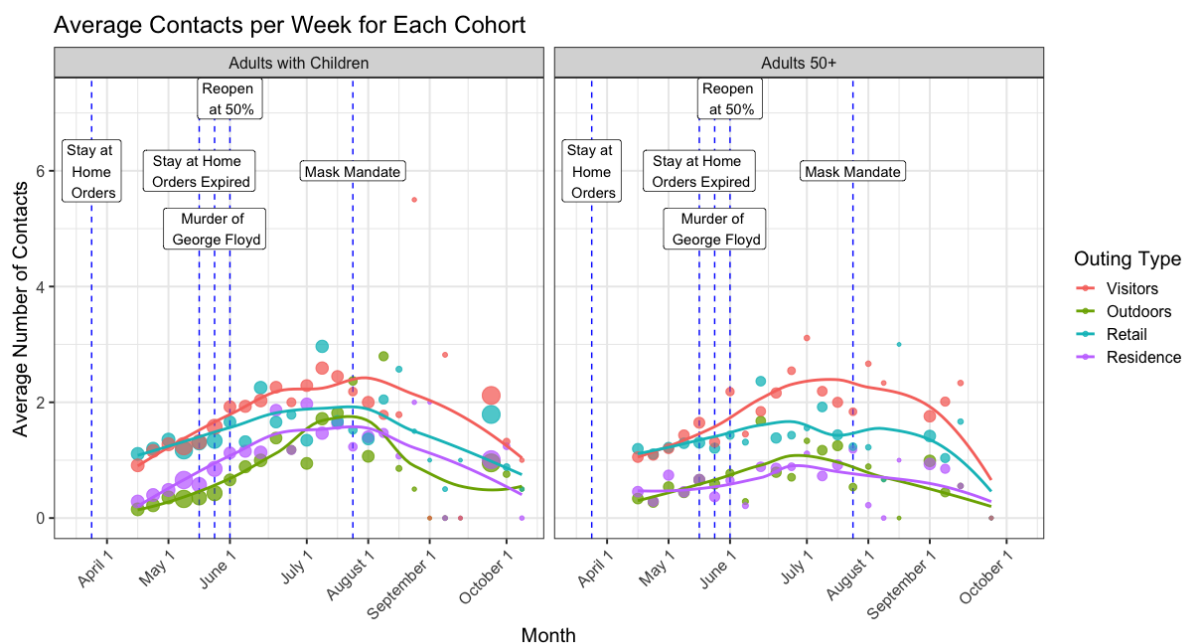
Affects of COVID-19 on hospital staffing levels and benefits, March 2020-June 2021

Stephanie Sikavitsas Johnson* Stephanie Johnson Katelin C Jackson Eric T Lofgren

The COVID-19 pandemic has taken over 5.5 million lives, and hundreds of thousands more are hospitalized every day. The drain on the healthcare system has been immense, both in supplies and personnel, but it has not been even across all hospitals and times. We wanted to obtain an accurate picture of what challenges COVID brought to health care workers. We asked hospitals in a multi-country research network to participate in an online survey asking about staffing levels.

Fourteen hospitals completed the survey from April-June 2021. They had a mean of 596 total beds, 100 ICU beds and 39 ER beds. They were asked to answer staffing questions about the peak of the pandemic as well as prior to the pandemic. At the peak of their pandemic, more than 50% of patients were being treated for COVID in 68% of hospital's ICUs and 40% of the ERs. These 15 hospitals had 77 different ICUs, and 30 of them were turned COVID patient-only. Overall, ICU and ER staffing ratios increased slightly but not significantly from before the pandemic. Traveling ICU/critical care staff increased from 6% to 32%, and 80% of hospitals reassigned staff to help with the ICU surge. Three hospitals reported furloughing staff. Two hospitals had all staff members take a pay cut and three cut retirement benefits, for a median of 8 months. Thirteen hospitals restricted the number of students trained in person, for a mean of 8 months. Seven offered remote training, and five allowed students to work with known or suspected COVID patients.

This data offers insight to what hospitals were suffering before COVID variants hit. We see a very sharp demand of ICUs and a smaller one for ERs. Staffing levels were steady overall, but some hospitals did have to sharply increase the ratio. This small pilot data showed that hospitals all over the world were affected by COVID in different ways, but small patterns could still be found that could be used for future use.

Comparison Of SARS-Cov-2 Blood Nucleocapsid Antigen To Nasal PCR RNA Positivity And Infectious Viral Shedding Sujata Mathur* Sujata Mathur Michelle C. Davidson Khamal Anglin Scott Lu Sarah Goldberg Miguel Garcia-Knight Michel Tassetto Amethyst Zhang Mariela Romero Jesus Pineda-Ramirez Ruth Diaz Sanchez Paulina Rugart Kevin Donohue Joshua R. Shak John Winslow Christos Petropoulos Chenna Ahmed David Glidden George W. Rutherford Steven G. Deeks Michael J. Peluso Raul Andino Jeffrey N. Martin J. Daniel Kelly

Background: Limited data are available about the performance of the N-antigen test on blood samples in outpatient settings and people living in the community. Therefore, we assessed the clinical performance of the SARS-CoV-2 nucleocapsid antigen (N-antigen) blood test using Single-Molecule Array (Simoa) technology in a non-hospitalized household cohort.

Methods: We enrolled a household cohort of individuals within the first 5 days of symptom onset and longitudinally sampled them for evidence of SARS-CoV-2 by collecting weekly blood and daily nasal samples during the infectious period. We used RT-PCR and anti-spike serological testing to classify participants as true positives and true negatives (gold standard measurements). We then estimated the sensitivity, specificity, positive predictive value, and negative predictive value of the N-antigen test from blood plasma samples against true positives and true negatives. We also used viral culture data to measure infectious viral shedding and re-estimated test performance against SARS-CoV-2 N-antigen. Longitudinal measurements of SARS-CoV-2 N-antigen were correlated to infectious viral shedding as potential biomarkers. Analyses were stratified over 7-day periods.

Results: Applying our gold standard against 80 participants, 58 individuals were true positives (had infection) while 22 individuals were true negatives (did not have infection). Sensitivity, specificity, positive predictive value, and negative predictive value of the blood N-antigen test against the gold standard were 86.2% (95%CI: 74.6-93.9), 100% (95%CI: 84.6-100), 100% (95%CI: 84.6-100) and 73.3% (95%CI: 59.1–83.9), respectively. Sensitivity (76%) and negative predictive value (65%) were highest during the earliest assessed period (0-7 days) and subsequently decreased over time. Specificity and positive predictive values were outstanding (100%) and remained stable over time. Levels of N-antigen correlated to infectious viral shedding. Within 7 days of symptoms onset among truly infected individuals evaluated for infectious viral shedding, the sensitivity, specificity, positive predictive value, and negative predictive value of N-antigen testing were as follows: 96.7% (95%CI: 82.8-99.9), 61.1% (95%CI: 35.7–82.7), 80.6% (95%CI: 35.7–82.7) and 91.7% (95%CI: 60.7-98.7), respectively.

Conclusion: We found that the blood-based antigen testing could identify truly infected individuals in a highly sensitive manner, and the test correlated with infectious viral shedding within the first 7 days of infection. Early in acute illness, blood-based N-antigen testing may be a viable option for screening or diagnosis and inform isolation practices among community-dwelling individuals.

Prevalence of major depressive disorder among Hispanics/Latinos during the COVID-19 pandemic
Kevin Villalobos* Kevin Villalobos Francisco Montiel Ishino Faustine Williams

The COVID-19 pandemic has affected communities across the United States (US) in multiple ways exacerbating existing health disparities among underserved and underrepresented groups. One factor that is absent from current epidemiological and disparities studies concerning the pandemic is mental health. As the pandemic has exacerbated mental health crises precipitated by various socioeconomic factors and health access issues, there is a need to understand current mental health status among Hispanics/Latinos. The purpose of our study was to assess the prevalence of major depressive disorder (MDD) among Hispanics/Latinos during the pandemic. We conducted a nationally representative COVID-19 survey of US adults aged ≥18 (N=5,938) from May 2021 to January 2022 about the effect of COVID-19 on physical and mental health. Our sub-sample consisted of 1,202 Hispanic/Latino (Mexican, Puerto Rican, Cuban, Dominican, Central American, South American, and Other) adults that identified as male (36%); female (62%); or other (2%). When asked about general mental health, the majority responded with good, very good, or excellent mental health [74% (n=879/1,191)]. The Patient Health Questionnaire-2 was used to determine the likelihood of having MDD; where 32% (n=374/1,187) were likely to have MDD. When asked about treatment for mental health conditions, 12% (n=46/369) responded to have received treatment for depressive disorder, but 39% (n=144/369) said COVID-19 interfered with their treatment. See Table 1 for detail. The next steps will examine how health behaviors, socioeconomic, and sociodemographic factors impact Hispanic/Latino community's mental health. Also, future directions will examine the role of MDD on vaccine hesitancy and acceptance of misinformation among Hispanics/Latinos during the COVID-19 pandemic; as 33% (n=397/1,198) of our participants had not taken the vaccine as of January 2022.

Table 1. US Hispanic/Latino adults aged ≥18 descriptive statistics (N=1,202)

	Mexican/Mexican American	Puerto Rican	Cuban/Cuban American	Dominican	Central American	South American	Other	Total
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	N (%)
Sample	543 (45.17)	191 (15.89)	86 (7.15)	71 (5.91)	61 (5.07)	144 (11.98)	106 (8.82)	1,202
Gender								
Male	214 (39.48)	58 (30.37)	24 (28.24)	23 (32.39)	22 (36.07)	55 (38.19)	31 (29.25)	427 (35.58)
Female	313 (57.75)	132 (69.11)	60 (70.59)	44 (61.97)	38 (62.30)	86 (59.72)	68 (64.15)	741 (61.75)
Other	15 (2.77)	1 (0.52)	1 (1.18)	4 (5.63)	1 (1.64)	3 (2.08)	7 (6.60)	32 (2.67)
General mental health								
Poor	44 (8.16)	14 (7.41)	2 (2.35)	3 (4.29)	3 (4.92)	7 (4.93)	7 (6.67)	80 (6.72)
Fair	106 (19.67)	41 (21.69)	19 (22.35)	12 (17.14)	13 (21.31)	17 (11.97)	24 (22.86)	232 19.48)
Good	186 (34.51)	63 (33.33)	23 (27.06)	31 (44.29)	15 (24.59)	47 (33.10)	32 (30.48)	397 (33.33)
Very good	127 (23.56)	40 (21.16)	21 (24.71)	13 (18.57)	23 (37.70)	38 (26.76)	22 (20.95)	284 (23.85)
Excellent	76 (14.10)	31 (16.40)	20 (23.53)	11 (15.71)	7 (11.48)	33 (23.24)	20 (19.05)	198 (16.62)
PHQ-2 major depressive disorder (MDD)								
No MDD	368 (68.02)	123 (65.43)	60 (70.59)	47 (70.15)	44 (72.13)	110 (76.92)	61 (59.80)	813 (68.49)
Likely MDD	173 (31.98)	65 (34.57)	25 (29.41)	20 (29.85)	17 (27.87)	33 (23.08)	41 (40.20)	374 (31.51)
Mental Health condition received treatment								
Depressive disorder	19 (11.66)	6 (8.00)	5 (16.67)	2 (10.53)	4 (28.57)	5 (14.29)	5 (15.15)	46 (12.47)
Anxiety disorder	62 (38.04)	31 (41.33)	11 (36.67)	7 (36.84)	3 (21.43)	13 (37.14)	13 (39.39)	140 (37.94)
Bipolar disorder	12 (7.36)	6 (8.00)	2 (6.67)	2 (10.53)	0 (0)	0 (0)	1 (3.03)	23 (6.23)
Post-traumatic stress disorder	19 (11.66)	14 (18.67)	3 (10.0)	0 (0)	0 (0)	4 (11.43)	2 (6.06)	42 (11.38)
Obsessive-compulsive disorder	15 (9.20)	7 (9.33)	4 (13.33)	2 (10.53)	1 (7.14)	3 (8.57)	3 (9.09)	35 (9.49)
Eating disorder	15 (9.20)	5 (6.67)	3 (10.0)	2 (10.53)	0 (0)	7 (20.0)	4 (12.12)	36 (9.76)
Substance dependence/Abuse	13 (7.98)	4 (5.33)	1 (3.33)	3 (15.79)	5 (35.71)	0 (0)	3 (9.09)	29 (7.86)
Other	8 (4.91)	2 (2.67)	1 (3.33)	1 (5.26)	1 (7.14)	3 (8.57)	2 (6.06)	18 (4.88)
COVID-19 interfered with treatment								
No	96 (58.90)	46 (61.33)	21 (70.0)	13 (68.42)	7 (50.0)	20 (57.14)	22 (66.67)	225 (60.98)
Yes	67 (41.10)	29 (38.67)	9 (30.0)	6 (31.58)	7 (50.0)	15 (42.86)	11 (33.33)	144 (39.02)
Taken the vaccine								
No	184 (34.01)	70 (36.84)	28 (32.94)	33 (46.48)	19 (31.15)	27 (18.75)	36 (33.96)	397 (33.14)
Yes	357 (65.99)	120 (63.16)	57 (67.06)	38 (53.52)	42 (68.85)	117 (81.25)	70 (66.04)	801 (66.86)

Disaggregating race and ethnicity data to advance health and racial equity: COVID-19 vaccination data among pregnant people as a case-study Hanna Shephard* Hanna Shephard Susan Manning Eirini Nestoridi Anne Marie Darling Darien Mather Sharon Pagnano Mahsa Yazdy

Background: With recent efforts to increase COVID-19 vaccination among pregnant people, Hispanic and non-Hispanic Black pregnant people still have the lowest rates of vaccine uptake during pregnancy despite disproportionately higher rates of COVID-19. However, these large race/ethnicity categories limit actionability. Data disaggregation efforts are needed to understand disparities within groups that require further research and tailored outreach.

Methods: We estimated COVID-19 vaccine uptake (receipt of $\geq$1 vaccine doses) during pregnancy retrospectively among pregnancies resulting in live birth during May 2021—October 2021 by linking COVID-19 vaccination data from the Massachusetts (MA) Immunization Information System to data from MA birth certificates. Birthing people could select from a list and/or write-in all races and ethnicities with which they identified on the birth certificate. We disaggregated broad race/ethnicity categories into more detailed racial/ethnic subgroups to make within group comparisons.

Results: Among 30,711 pregnancies, vaccine uptake during pregnancy was highest among those who reportedly identified as Asian (45.9%), but within this group ranged from as low as 25.8% among those who also identified as Cambodian to 67.8% among those who identified as Japanese. And while vaccination was lowest among Black pregnant people (16.0%), it was even lower among those who identified as Cape Verdean (10.5%) and highest among those who identified as European (30.0%).

Conclusions: COVID-19 vaccine uptake among pregnant people in MA was lowest among racially and ethnically minoritized pregnant people; however, there is wide heterogeneity within groups that is masked when aggregating data into large race/ethnicity categories. Disaggregating data provides more meaningful information about subgroup populations in diverse and marginalized communities. Investment in adequate reporting on race and ethnicity is a necessary first step to advance health and racial equity.

Late Breaker Justification: The data for this analysis were not made available until after the regular abstract submission deadline. Moreover, there is a high urgency for dissemination of this information as pregnant people infected with SARS-CoV-2 are at elevated risk for severe illness, hospitalization, and death when compared to nonpregnant people and vaccination uptake among pregnant people is lower than the general population. Vaccination access and outreach strategies are developed at the state level, yet state-level estimates on vaccination uptake among pregnant people are not widely available. Moreover, data are often aggregated into large race/ethnicity groupings that conceal the diversity of the subpopulations within these groupings that we often fail to make visible. Given the disparate impact of COVID-19 on communities of color, there is an urgent need for public health agencies to invest in adequate reporting on race and ethnicity to inform tailored outreach, resource allocation, and policy making.
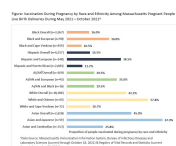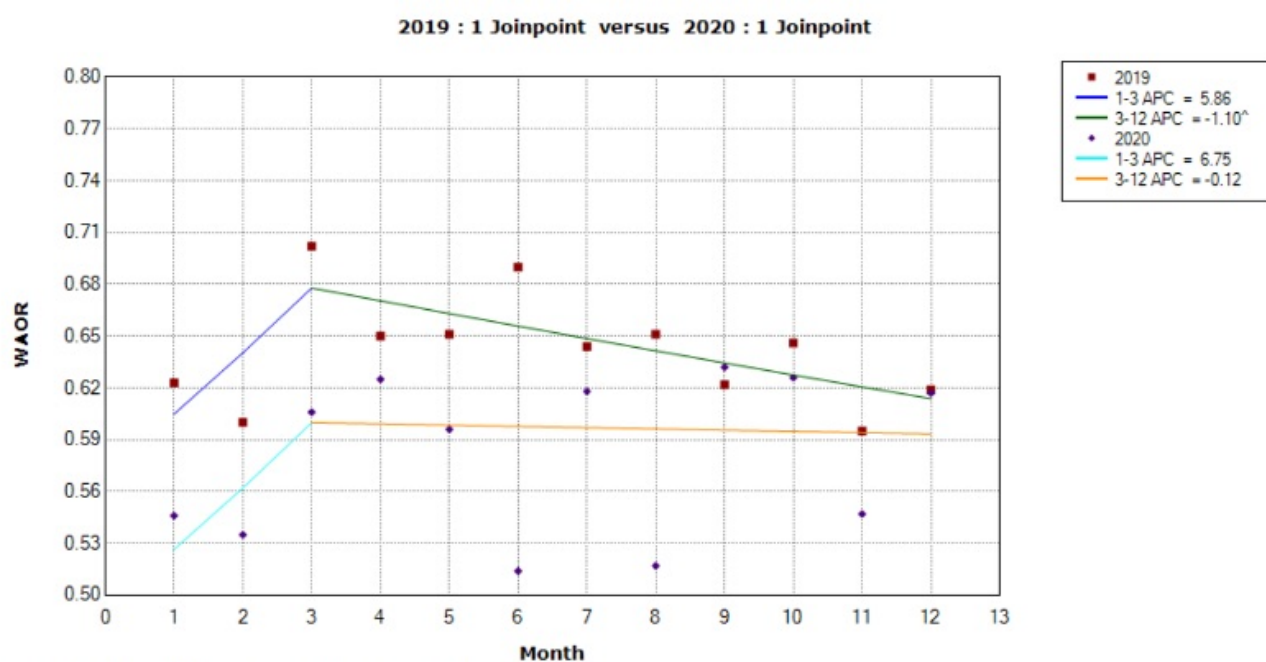
LATEBREAKER

COVID-19 Pandemic

Trend analysis of the association between physical activity for leisure and obesity before and after the start of the Covid-19 pandemic Chia-Lin Chang* Chia-Lin Chang Cristina Oancea

After COVID-19 has been declared a US national emergency on March 13th, 2020, US state governments have deployed Stay-at-home orders to try to stop the spread of the disease. However, studies have shown that the Stay-at-home order may change people's lifestyle and health-related behavior due to the closure of fitness facilities and other public places during the pandemic as well as decreased passive movement for work from home. The aim of this study is to investigate how the COVID-19 pandemic Stay-at-home orders and facility closures may have affected the association between physical activity for leisure (PAL) and obesity, by using the 2019-2020 BRFSS national level data. Weighted and adjusted logistic regression was used to obtain weighted and adjusted odds ratios (WAORs) and 95% CIs of PAL associated with obesity month by month from Jan 2019 to Dec 2020, and WAOR trend analyses were performed thereof. Findings suggest that the WAOR of obesity trend for 2019 compared to 2020 is very similar for the first 3 months of the year. However, for the months 4 through 12, for the year 2019 we see a significant decrease in the WAOR's (significant decrease in the annual percent change (APC)), and no significant/almost no decrease in the WAOR in 2020. In other words, in 2019, months 4-12, the WAO of obesity significantly decreased for those who performed PAL compared to those who didn't perform PAL. In 2020 there was no significant decrease in these odds. This parallels with the COVID-19 stay-at-home order and facilities closure that occurred in March 2020 and continued throughout the year. Future longitudinal studies are needed to evaluate obesity in people who had been impacted by the COVID-19 pandemic related restrictions.

2019 : 1 Joinpoint versus 2020 : 1 Joinpoint

Legend:
- 2019
- 1-3 APC = 5.86
- 3-12 APC = -1.10^
- 2020
- 1-3 APC = 6.75
- 3-12 APC = -0.12

^ The Annual Percent Change (APC) is significantly different from zero at alpha = 0.05

LATEBREAKER

COVID-19 Pandemic

End-of-life Outcomes Among Chinese and Non-Chinese in Chinese Ethnic and Non-Chinese Ethnic Long-Term Care Homes: Comparison Between Before and During COVID-19 Pandemic Prabasha Rasaputra* Prabasha Rasaputra Annie Sun Anna Clarke Amy Hsu

Background: Ethnic minority populations have been demonstrated to experience great disparities in quality of care and health outcomes. However, little is known about the health outcomes of minority residents residing in long-term care (LTC) homes, which have been the epicenter of the COVID-19 pandemic in Canada.

Objective: To examine the outcomes of Chinese residents in a Chinese ethnic LTC home (language-concordant care) vs. a non-ethnic LTC home (possible language discordant care) during pre-pandemic and pandemic periods.

Methods:

Design: A population-based retrospective cohort study capturing deceased individuals aged above 65 years old. The study timeframe included pre-pandemic (between March 2019 and December 2019) and pandemic (between March 2020 and December 2020) periods.

Setting: Chinese ethnic LTC homes(defined as having a proportion of 20% or more residents being Chinese), and all other LTC homes in Ontario
Main outcome(s): burdensome transitions to acute care, location of death, and pain management

Results: During the pre-pandemic period, Chinese in Chinese LTC homes had a much higher rate of having hospital admissions in the last 3 days (14.9%,) than non-Chinese residents (8.3%). During the pandemic period, the proportions of Chinese in Chinese homes and non-Chinese in all other homes for having hospital admission in the last 3 days both decreased to 8.4% and 5.7% respectively. In the adjusted model, Chinese were also more likely to have any hospital admission in Chinese LTC homes (OR 1.77, 95%CI 1.22- 2.57, p=0.003)and die in hospital (OR 1.51, 95%CI 1.12- 2.04, p=0.007) compared to non-Chinese residents. Chinese residents in Chinese homes reported less pain (OR 0.32, 95%CI 0.15-0.70, p=0.004) than non-Chinese residents.

Conclusion: The results suggest that Chinese residents were more likely to be hospitalized and die in acute care settings compared to non-Chinese residents. Both groups were less likely to be hospitalized during the pandemic.

Circadian eating behaviours and risk of type 2 diabetes: The Observational Prospective NutriNet-Santé study, France Anna Palomar-Cros* Anna Palomar-Cros Bernard Srour Valentina Andreeva Serge Hercberg Dora Romaguera Manolis Kogevinas Mathilde Touvier

The time we eat might have an impact on glucose tolerance and insulin sensitivity and on the risk of developing type 2 diabetes. The objective of the present study is to investigate the prospective associations between circadian eating behaviours defined by meal timing and frequency and risk of type 2 diabetes.

The NutriNet-Santé cohort (2009-2021) enrolled 103,312 volunteers aged at least 18 years across France (79% females). Participants' usual food consumption was assessed using repeated 24 h dietary records. Timings and frequency were calculated as an average of the available records for each subject during the first two years of follow-up. Associations of time of first and last meal, meal frequency and of time restricted eating with risk of type 2 diabetes were assessed by multivariable Cox proportional hazard models adjusted for known risk factors.

During a median follow-up time of 7.1 years, 963 new cases of type 2 diabetes were identified. Compared with subjects reporting a first meal (breakfast) before 8AM, those having breakfast after 9AM were at higher risk of developing diabetes (HR = 1.58, 95% CI 1.30 – 1.94, P for trend<0.001). Results remained stable after considering night shift work, sleep duration, job or weight gain during follow-up. Time of last meal was not significantly associated with risk of diabetes. Time restricted eating with a nightly fasting of 13 hours or more was associated with a lower risk of diabetes when breakfast was consumed before 8AM (HR = 0.42, 95% CI 0.24-0.73, p-value 0.002). Each additional eating episode was associated with a reduction of the risk of developing diabetes by a 5% (HR = 0.95, 95% CI 0.90 – 0.99, p-value 0.01).

In this large prospective study, a late time of breakfast was associated with an increased risk of type 2 diabetes. A circadian eating behaviour defined by an early breakfast and dinner and a shorten eating window was associated with a reduced risk of this metabolic disease.

Associations between thyroid hormones and incident diabetes among postmenopausal women in the Hispanic Community Health Study/ Study of Latinos (HCHS/SOL) Konstantina Tsintsifas* Konstantina Tsintsifas Mary E. Turyk Robert M. Sargis Chibuzor Abasilim Tessa Day Arielle Grieco Sally Freels Martha Daviglus Gregory A Talavera Amber Pirzada Robert Kaplan Carmen R Isasi Michelle L Meyer Noel Chavez Jianwen Cai Bharat Thyagarajan Shivani Aggarwal Victoria Persky

Background: Both hypo- and hyperthyroidism are associated with diabetes, but most studies have been cross-sectional leaving open the possibility that existing diabetes alters thyroid homeostasis. The stages of diabetes development and levels of hormones at which thyroid hormones might be operative have not been delineated. We explored associations of thyroid-stimulating hormone (TSH), triiodothyronine (TT3), and free thyroxine (FT4) with incident prediabetes and diabetes in women from a Hispanic population with high risk for diabetes.

Methods: HCHS/SOL is the largest multiethnic cohort of Hispanics/Latinos in the US. Our sample included 305 normoglycemic and 388 prediabetic post-menopausal women with on average 6 years of follow up. Women on medications that affect endogenous thyroid hormones or diabetes were excluded. The effect of baseline hormone levels on progression of 1) normoglycemia at baseline to prediabetes or diabetes at follow-up and 2) prediabetes at baseline to diabetes at follow-up were evaluated with multivariable Poisson regression with robust variance analysis, adjusting for sampling design.

Results: TT3 was positively and FT4 was inversely associated with development of diabetes from prediabetes (Figure). In 329 prediabetic euthyroid women, with all thyroid hormones within clinical reference ranges, progression from prediabetes to diabetes remained significantly associated with FT4 and TT3. TSH was significantly and positively associated with transition from prediabetes to diabetes in euthyroid women, but not the full study sample (Figure). No statistically significant associations were found for any hormone with progression to prediabetes or diabetes from normoglycemia.
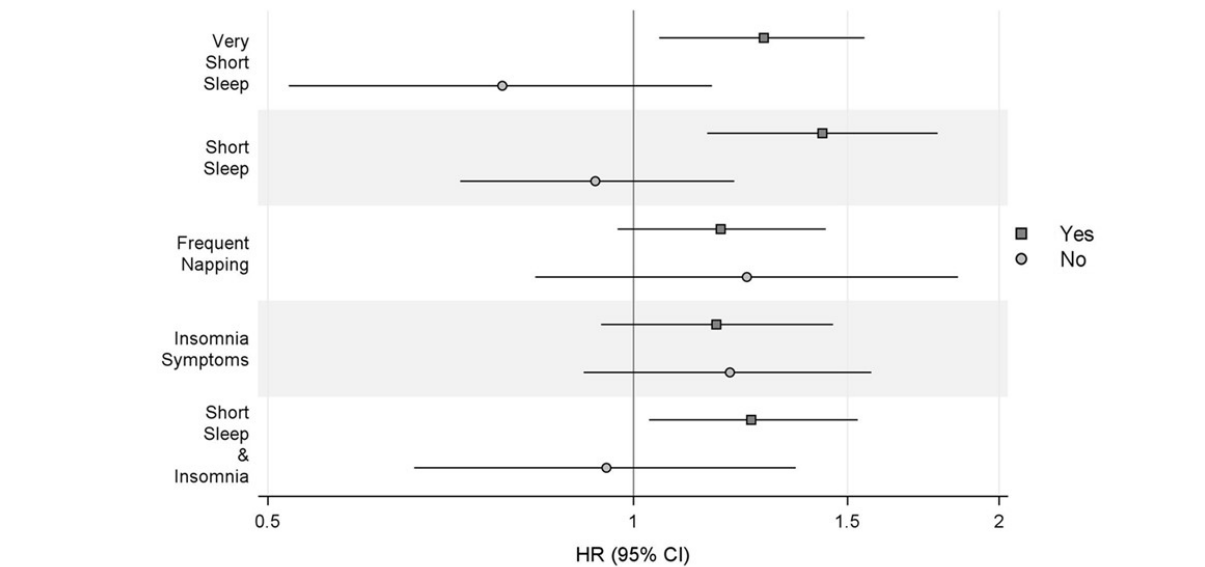
Conclusion: The positive associations of TT3 and TSH and inverse association of FT4 with conversion from prediabetes to diabetes, but not with conversion from normoglycemic to prediabetes or diabetes, suggests effects of thyroid hormones later in the development of the disease.
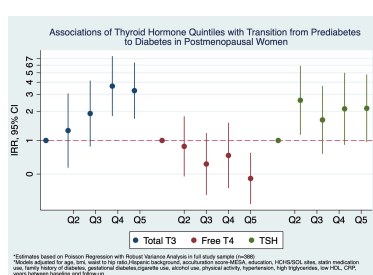
Sleep Health: A Modifier of the Association between Racial/Ethnic Discrimination and Type 2 Diabetes Risk among Women Symielle A. Gaston* Symielle Gaston Erline Martinez-Miller Dale P. Sandler Chandra L. Jackson

Background: Racism has been associated with both poor sleep – a risk factor for type 2 diabetes mellitus (T2D) – and incident T2D, likely at least partially through psychosocial stress response pathways. Although improving sleep health may be a target for T2D reduction, research is sparse. **Methods**: To investigate sleep dimensions as modifiers of the association between racial/ethnic discrimination and T2D risk among Hispanic/Latina (Latina), non-Hispanic Black (NHB), and non-Hispanic White (NHW) women, we used data from 39,078 Sister Study participants with no prior T2D diagnosis who were enrolled from 2003-2009 and followed through 2019. Participants reported whether they ever experienced major racial/ethnic discrimination (MRD: being stopped, searched, or threatened by the police; unfair treatment at work or in home renting, buying, or mortgage lending). Sleep dimensions included very short (≤5 hours) and short (<7 hours) duration, frequent napping (≥3 times/week), and insomnia symptoms (difficulty falling or staying asleep). Adjusting for sociodemographic characteristics, cause-specific Cox Proportional Hazards regression estimated T2D HRs and 95% CIs. Models with interaction terms were tested and then stratified by race/ethnicity and sleep dimensions. **Results**: Mean±SD age at report of MRD was 58±8.9 years, 4% identified as Latina, 7% NHB, and 87% NHW. MRD prevalence was 6% overall and highest among NHBs (52% vs. 13% Latina and 2% NHW). Over 9±2.0 follow-up years, there were 1,769 incident T2D cases. Sleep duration modified associations across all races/ethnicities: MRD was associated with a higher T2D risk among participants with very short or short sleep duration (HR=1.28 [1.05-1.55] and 1.43 [1.15-1.78]; $p_{interactions} < 0.05$). **Conclusion**: Sleep duration modified associations between MRD and T2D risk and may serve as an intervention target to mitigate T2D disparities until structural racism is eradicated, particularly among minoritized women who have higher MRD.

Figure 1. Overall Associations between Major Racial/Ethnic Discrimination and Type 2 Diabetes Mellitus Risk, Stratified by Sleep Health Dimensions

Note: Results were comparable across racial/ethnic groups; therefore, overall estimates are presented. Age (in years) is the time scale. Models are adjusted for race/ethnicity (Hispanic/Latina, non-Hispanic Black, non-Hispanic White), region of residence lived in longest (Northeast, Midwest, South, West, Puerto Rico/Other), and educational attainment (≤high school, some college, ≥college).

Walkable neighborhood environment is associated with lower diabetes risk over 25 years

Simin Hua* Simin Hua Sandra India-Aldana Byoungjun Kim Tess V. Clendenen James W. Quinn Yelena Afanasyeva Karen L. Koenig Mengling Liu Kathryn M. Neckerman Anne Zeleniuch-Jacquotte Andrew G. Rundle Yu Chen

Background: Prospective studies of long-term neighborhood walkability (NW) and diabetes incidence are scarce.

Methods: We examined the associations of baseline and long-term average NW with the risk of incident diabetes among 11,037 women in the New York University Women's Health Study, a prospective cohort study that enrolled women between the ages of 35-65 from 1985-91 at a mammographic screening center in NYC. Women in the cohort have been followed-up every 2-5 years to update residential address history, lifestyle factors, chronic diseases including information on physician diagnosis of diabetes, antidiabetic medication use, and their dates. We geocoded residential addresses of participants and constructed 1) baseline NW scores with population density, destination accessibility, intersection density, and density of public transit, and 2) average annual NW with population density and destination accessibility across all years of follow-up. We used multivariable Cox PH regression models with robust variance to estimate the hazard ratios (HRs) of diabetes by NW quartiles.

Results: A total of 1,107 women (10 %) developed diabetes during a median follow-up of 25 years. Compared with women in the bottom quartile of baseline NW, the adjusted HRs of incident diabetes for women in baseline NW quartiles 2-4 were 0.93 [0.85-1.02], 0.86 [0.77-0.98], and 0.67 [0.61-0.74] (P-trend=0.0001), respectively. When average annual NW was considered with three years of lagging, the HRs of diabetes comparing average annual NW Q2-4 with Q1 were 1.05 [0.91 – 1.20], 1.07 [0.94 – 1.21], and 0.79 [0.73 – 0.85], respectively. The associations remained similar with additional adjustment for baseline body mass index, or when inverse probability of attrition weights were included in the model to account for the effect of censoring due to death or non-response.

Conclusion: Long-term residence in more walkable neighborhoods is protective against diabetes in women.

education, anti-racism

Disrupting White Supremacy In Classrooms: A Case Study Of Racial Affinity Caucusing as An Anti-Racist Teaching Approach In An Epidemiology Course Ramya Kumar* Ramya Kumar Wendy Barrington Jennifer Balkus Anjum Hajat

In response to demands to address racism in curricula, the University of Washington Department of Epidemiology offered a virtual anti-racism journal club in the academic year 2020-2021. Although the focus was on anti-racism frameworks in research, students still noted that discussions were dominated by white voices. In an effort to support inclusivity in class discussions, Black, Indigenous, and People of Color (BIPOC) students worked with instructors to implement racial affinity caucuses (RACs) as an anti-racist teaching and learning strategy. We present a case study of innovation within an epidemiologic classroom.

Instructors worked with all students to select a RAC (i.e., BIPOC or White) that best represented their self-identified race and/or ethnicity. Each class began with students discussing readings in their RAC. Instructors then convened all RACs and opened class discussions by inviting the BIPOC RAC to report their key themes. Instructors then opened the discussion to all students. As the discussion progressed, instructors would read aloud chatted responses from students, prioritizing BIPOC student responses. Instructors closed discussions by re-reading BIPOC students' chatted responses or instructors yielded the floor to BIPOC students to amplify, reinforce, and recenter BIPOC perspectives and ideas.

Overall, students reported that RAC implementation and accompanying facilitation strategies supported inclusion of BIPOC perspectives in discussions. Successful implementation of RACs in our classroom required communicating the supporting pedagogy as well as humility in facilitation, a willingness to make mistakes, and the ability to problem-solve and co-create solutions. This case study highlights students going beyond a journal club to read and discuss anti-racist frameworks, but actually using the frameworks to restructure the very space in which they were discussing them. In this way, they modeled strategies for increasing inclusion in research.

Air pollution, neighborhood deprivation, and dementia incidence in a diverse US cohort

Aisha S. Dickerson* Aisha Dickerson Zhengyi Deng Roland J. Thorpe, Jr. Cavin Ward-Caviness

Air pollution has been proposed as a biologically plausible risk factor for dementia and cognitive decline, but findings regarding the association between ambient air pollutant concentrations and dementia are conflicting. However, co-occurring social and environmental factors – at the individual, community, and area-based level – may concurrently contribute to cognitive health risk. Using data from 9204 older adults enrolled in the National Health and Aging Trends Study (NHATS), we examined differences in associations between residential air pollutants and dementia by historically marginalizing characteristics and neighborhood measures of disadvantage using Cox regression analysis with clustering for state and geographic region. Although interquartile range increase in annual PM(2.5) concentrations was initially associated with incidence of dementia in our unadjusted analysis (Hazard ratio (HR) = 1.14; 95% confidence interval (CI): 1.02, 1.27), this association was no longer significant once adjusted for individual and area-based sociodemographic factors, including sex, income, < high school graduation, non-Hispanic Black race/ethnicity, and neighborhood deprivation (HR = 1.05; 95% CI: 0.96, 1.09). Notably, in mutually adjusted models, incidence of dementia was significantly higher for study participants with < high school graduation (HR = 1.33; 95% CI: 1.14, 1.54), who identified as non-Hispanic Black (HR = 1.24; 95% CI 1.05, 1.47), and who were from disadvantaged neighborhoods (HR = 1.29; 95% CI: 1.11, 1.49). Although incidence was higher in females with higher PM(2.5) exposures than males in stratified analyses (HR=1.09 and 0.99, respectively), there were no notable differences with stratification by race/ethnicity or neighborhood disadvantage. Although our findings do not support an association between air pollutant exposures and increased incidence of dementia, these finding highlight the importance of access to services in disadvantaged communities.

Heterogeneity of changes in PM2.5 -related premature deaths for 2001-2010 across different socioeconomic subpopulations in South Korean aging population Cham Thi Nguyen* Cham Thi Nguyen Sun-Young Kim

Background: There is a growing interest in the change of health burden due to $PM_{2.5}$ over time. However, a few studies focused on the difference in changes of health burden depending on the susceptibility.

Purpose: We aimed to assess the difference in the changes of $PM_{2.5}$ -related premature deaths in elderly people between different subgroups defined by socioeconomic characteristics.

Methods: We used the annual-average $PM_{2.5}$ concentration, and age-stratified population and mortality for older adults aged 65 years and above in each of 180 districts in South Korea for 2001-2010. District-specific annual $PM_{2.5}$ concentrations were estimated from a previously-developed exposure prediction model. For socioeconomic subgroups, we divided all districts into two groups using the medians of gross regional domestic product (GRDP), proportion of high school graduates attainment or above, and urbanization. Finally, we estimated the number of premature deaths related to $PM_{2.5}$ for all districts using the three types of data and the exposure-response function obtained from a previous study in South Korea and aggregated to the entire country by each of three subgroups.

Results: The annual $PM_{2.5}$ concentration decreased from 30.47μg/m^3 to 25.74 μg/m^3 from 2001 to 2010. Districts with higher education attainment, GRDP, and urbanicity experienced the reduction in numbers of premature deaths due to $PM_{2.5}$ over time. In contrast, there was an opposite trend with counterpart groups.

Conclusions: This study indicates that populations with higher living standard are more likely to get benefits from reduction of $PM_{2.5}$ concentration.

Taking a "landscape epidemiology" approach to investigate the burden of multiple carcinogenic air pollutants on invasive breast cancer incidence in Metro Chicago Garth H Rauscher* Garth Rauscher Alpana Kaushiva Serap Erdal

Introduction: The US EPA's National Air Toxic Assessment (NATA) creates annualized, modeled estimates of outdoor inhalation exposures for approximately 190 chemicals at the census tract. Estimates, however, are fraught with exposure misclassification, and individual associations of hazardous air pollutants (HAPs) with disease are likely to be severely attenuated. We took a "landscape epidemiology" approach to examine the distribution of associations for 60 carcinogenic HAPs with breast cancer incidence in order to determine if we could detect a shift in central tendency in the hypothesized direction of increased risk.

Methods: Census tract-level measures of identified carcinogenic HAP's were obtained from NATA cycles conducted in 2002 (n=54 HAPs) and 2005 (n=53 HAPs) and linked to patient residential tracts. For each HAP, we estimated the log hazard ratio (HR) with BC incidence while adjusting for patient and clinical risk factors and other HAPs at least marginally associated (p<0.20) with incidence. Kernel density plots of log HRs were generated and p-values from t-tests were conducted to detect a shift in the distribution away from the null. Analyses were repeated separately by estrogen receptor (ER) subtype and for patient subgroups.

Results: The distribution of log HRs for HAP associations with ER-negative BC were shifted above the null in both the 2002 and 2005 NATA cycles, for all women combined (mean log HR=0.05, p-value <0.001) and specifically for postmenopausal (mean log HR=0.07, p-value <0.001), obese (mean log HR=0.08, p-value <0.001), and African-American women (mean log HR=0.04, p-value=0.08). Shifts in distributions for ER-positive BC were inconsistent. Results from 2011 and 2014 NATA cycles will also be presented.

Conclusion: We observed a shift in the distributions of log HRs for more aggressive, ER-negative BC that were consistent with an etiologic role for carcinogenic air pollutants in the etiology of ER-negative BC.

HAP log hazad ratios with ER negative breast cancer (2005)

p-value: <0.0001
mean: 0.05
median: 0.05
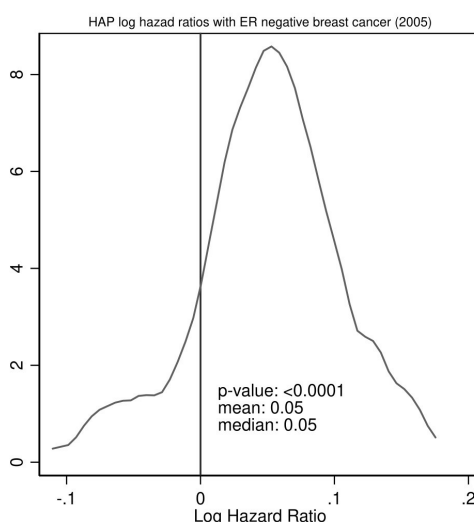
Outdoor air pollution and tissue composition of the normal breast Jennfier Ish* Jennifer Ish
Mustapha Abubakar Nicole Niehoff Sharon Fan Gretchen L Gierach

Background: Biologic pathways underlying the association between outdoor air pollution and increased breast cancer risk are poorly understood. Breast tissue histologic characteristics, including increased percent epithelium and epithelium-to-stroma proportion, may reflect cumulative exposure to breast cancer risk factors and have been associated with elevated breast cancer risk. We evaluated whether exposure to particulate matter <2.5 μm in diameter ($PM_{2.5}$) was associated with tissue composition metrics in normal breast tissue.

Method: Machine-learning algorithms were applied to hematoxylin and eosin-stained biopsies of normal breast tissue to quantify the epithelium, stroma, adipose and total tissue area from 4,146 United States-based women aged 18-75 years who donated tissue samples to the Susan G. Komen Tissue Bank (2009-2019). The 2009 annual levels of $PM_{2.5}$, estimated using the Environmental Protection Agency's Downscaler Model, were assigned to each woman's residential address at the time of tissue donation. We examined the association between quartile-based categories of $PM_{2.5}$ and the square root-transformed proportion of epithelium, stroma, and adipose tissue, as well as epithelium-to-stroma proportion, using adjusted linear regression models stratified by menopausal status (n=2,661 premenopausal; n=1,477 postmenopausal).

Results: Among premenopausal women, outdoor residential $PM_{2.5}$ was positively associated with proportion of epithelium tissue (β_{Q2vsQ1} = 0.17, 95% CI: 0.07-0.26; β_{Q3vsQ1} = 0.09, 95% CI: 0.00-0.19; β_{Q4vsQ1} = 0.12, 95% CI: 0.02-0.23). We observed limited evidence for associations among postmenopausal women or when considering other tissue composition metrics.

Conclusions: Our study supports the possible role of $PM_{2.5}$ in breast cancer etiology and suggests that premenopausal breast tissue composition may be a potential pathway by which outdoor air pollution impacts breast cancer risk.

Traffic-related air pollution and fetal growth in Eastern Massachusetts, USA Michael Leung*

Michael Leung Anna M Modest Michele R Hacker Blair J Wylie Yaguang Wei Joel Schwartz Brent A Coull Francine Laden Marc G Weisskopf Stefania Papatheodorou

Background: Previous studies have examined the association between prenatal NO_2 —a traffic emissions tracer— and fetal growth based on ultrasound measures during pregnancy. Yet, most studies have used exposure assessment methods with low temporal resolution, which limits the identification of critical exposure windows given that pregnancy occurs over a relatively short period. Here, we used NO_2 data estimated from a high-resolution spatiotemporal ensemble model to examine the association between prenatal NO_2 exposure and fetal growth measures (ultrasound parameters and birth weight [BW]) and identify critical exposure windows in a Massachusetts-based pregnancy cohort. **Methods:** We used ultrasound and obstetric data from 9,446 singleton births at Beth Israel Deaconess Medical Center in 2011-2016. Fetal characteristics included biparietal diameter (BPD), head circumference, femur length, abdominal circumference, and BW. We fitted linear mixed-effects models to examine the associations between NO_2 and measures of fetal growth in three windows: 1) first 16 weeks of gestation, 2) cumulative exposure from conception to fetal growth measure, and 3) one-month prior to fetal growth measure. Fetal growth was assessed by anatomic scans (ultrasounds <24 weeks), growth scans (ultrasounds ≥24 weeks), and BW. All models were adjusted for sociodemographic characteristics, time trends, and temperature. **Results:** We found that higher NO_2 in all three exposure windows was associated with smaller fetal growth measures, with associations particularly strong for BPD and BW. For example, a 10-ppb increase in NO_2 in the first 16 weeks was associated with lower mean z-score of -0.06 (95% CI: -0.11, -0.02) for anatomic BPD scans, -0.07 (95% CI: -0.11, -0.03) for growth BPD scans, and -0.06 (95% CI: -0.09, -0.02) for BW. **Conclusion:** Higher NO_2 —a gaseous pollutant derived from traffic combustion— in three exposure windows during pregnancy was associated with smaller fetal growth measures.
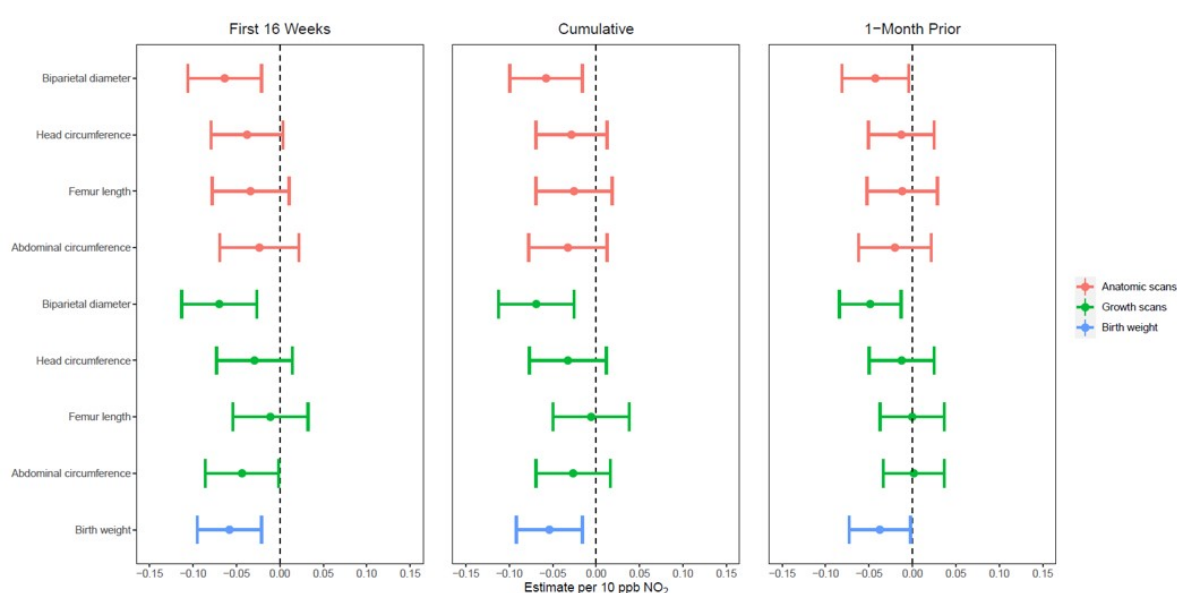
Figure 1. Estimates and 95% CIs for the association of nitrogen dioxide (NO_2) in three exposure windows (first 16 weeks of gestation, cumulative exposure from conception to fetal growth measure, and one month prior to fetal growth measure) with anatomic scans (ultrasounds <24 weeks), growth scans (ultrasounds ≥24 weeks) and birth weight from singleton births at Beth Israel Deaconess Medical Center, Massachusetts in 2011-2016 (N=9,446). All models were adjusted for maternal age, race, education, insurance type, parity, fetal sex, conception year, day of the year of conception, temperature, and Area Deprivation Index.

Association between long-term and short-term PM2.5 exposure and respiratory-related hospitalizations among a cohort of COPD patients, North Carolina, 2002-2015 Kristen N Cowan* Kristen Cowan Lauren H Wyatt Thomas J Luben Kristen M Rappazzo

Approximately nine million adults in the United States are living with Chronic Obstructive Pulmonary Disorder (COPD). Previous research has found that short-term air pollution is associated with increased risk of hospitalization for COPD in older adults. The objectives of this study were to measure if there is an association between short-term ambient $PM_{2.5}$ exposure and respiratory hospitalizations, to measure if there is an association between long-term ambient $PM_{2.5}$ exposure and respiratory hospitalizations and to measure if the association between short-term exposure is modified by long-term exposure in a cohort of individuals with COPD. The study population consists of a cohort of randomly selected individuals with electronic health records from the University of North Carolina Healthcare System, then restricted to patients with a COPD diagnosis from 2002-2015 (n=22,733). Estimated ambient $PM_{2.5}$ concentrations are from a previously validated ensemble model. Binomial regression was used to estimate the Relative Risk (RR) (95%CI) of respiratory-related hospitalizations with 0 and 1-day lags of $PM_{2.5}$, annual average of $PM_{2.5}$, and their interactions; models were adjusted for individual race, and area level urbanicity, education, unemployment, and proportion on public assistance. We observed no evidence of an association with short-term exposures (RR for 1 µg/m3 increase in 1-day lag $PM_{2.5}$: 0.99 (0.99, 1.00)), while the same increase in annual average $PM_{2.5}$ was associated with increased risk of respiratory hospitalizations (1.06 (1.05, 1.08)). There was no evidence of interaction between long and short-term $PM_{2.5}$ exposures. Long-term PM2.5 exposure, but not recent short-term exposure, was associated with respiratory related hospitalizations in COPD patients. Differences in associations may be related to behavioral differences in short-term periods (e.g., avoiding the outdoors on low air quality days) that are not possible for long-term exposures. This abstract does not reflect EPA policy.

The Association between Environmental Noise and Prevalence of Mental Ill-Health was Modified by Neighborhood Income and Race in Jefferson County, Kentucky Lindsey A. Wood*

Lindsey Wood Jeremy Gaskins Kira C. Taylor Brian Guinn Ray Yeager Natalie C. DuPre

Few studies have examined environmental noise exposure on adult mental ill-health. Most epidemiologic studies define noise by specific sources and utilize a 24-hour average, which may not capture relevant time windows to adult mental ill-health. We estimated the association of 5PM – 9AM cumulative environmental winter and spring noise with prevalence of mental ill-health at the census-tract level in Louisville, KY. Average census tract noise was estimated via land use regressions using noise data collected from 15 sites during Jan/Feb and Apr/May 2021 and multiple geographic variables. Prevalence of mental ill-health data for Louisville census tracts were obtained from CDC PLACES. We used multivariable linear regression models to estimate the relationship between noise and mental ill-health prevalence adjusted for neighborhood confounders. Effect modification was tested with likelihood ratio tests (LRT). Louder noise in the winter (β for 1 dB increase=0.09, 95% CI: 0.01, 0.16) and spring (β for 1 dB increase=0.07, 95% CI:0.02, 0.13) were associated with higher prevalence of adult mental ill-health after adjusting for census-tract median age, income, race, education, unmarried population, prevalence of physical ill-health, and income inequality. The positive association was observed among lower income neighborhoods (LRT p<0.01; winter noise β for 1 dB increase=0.14, 95% CI: 0.07, 0.22; spring noise β for 1 dB increase=0.12, 95% CI: 0.06, 0.17) and among neighborhoods with less white population (LRT p<0.01; winter noise β for 1 dB increase=0.23, 95% CI: 0.14, 0.32). In conclusion, the relationship between environmental noise and mental health outcomes may be modified by economic and sociodemographic factors. To inform policymakers on disparities of environmental noise exposure in urban environments, individual-level analyses should examine potential effect modifications.

Association of Blood Total Mercury with Dyslipidemia in a Sample of U.S. Adolescents
Chibuzor Abasilim* Chibuzor Abasilim Victoria Persky Mary Turyk

Background: Abnormal lipid profiles in adolescents predict metabolic and cardiovascular diseases in adulthood. Prior analyses indicate that blood total mercury (TBHg) has endocrine disrupting effects and may be associated with abnormal lipid profiles in adolescents. However, findings are inconclusive on 1) the relationship of TBHg with high-density lipoprotein cholesterol (HDL-C) and low-density lipoprotein cholesterol (LDL-C) levels and 2) sex differences for these relationships. We investigated the relationship of TBHg with lipid profiles.

Methods: We examined 1,390 National Health and Nutrition Examination Survey participants 12-19 years of age from the 2011-2018 cycles. Using linear regression adjusted for survey design variables, we estimated the associations of TBHg with total cholesterol (TC), HDL-C and LDL-C levels. Our analysis was stratified by sex *a priori* to assess sex specific associations of TBHg with lipid profiles.

Results: After adjusting for sociodemographic covariates, body mass index, serum selenium, and age at menarche (females only); a 50% increase in TBHg (μg/L) was significantly associated with an increase of TC levels by 2.17 mg/dL (95% CI: 0.43, 3.91) and HDL-C levels by 0.85 mg/dL (95% CI: 0.09, 1.62) in females. Further adjustment for number of fish meals with moderate or high omega-3-fatty acid levels produced slightly attenuated and marginally significant estimates in females. There were no significant associations in males for TC or HDL-C levels, nor for LDL-C levels in either male or female adolescents.

Conclusion: TBHg was associated with increased TC and HDL-C levels in female but not male adolescents. Further research is necessary to evaluate the underlying mechanisms driving these sex differences.

Exposure to indoor along with outdoor light at night in relation to multiple dimensions of sleep health: Findings from the Sister Study Marina R. Sweeney* Marina R. Sweeney Hazel B. Nichols Rena R. Jones Andrew F. Olshan Alexander P. Keil Lawrence S. Engel Peter James Dale P. Sandler Alexandra J. White Chandra L. Jackson

Background: Light at night (LAN) has been shown to disrupt circadian rhythms and suppress melatonin production. Population studies of LAN and sleep, which is driven partly by circadian rhythms and is disrupted by melatonin suppression, are limited. We examined the impact of LAN exposure on multiple dimensions of sleep health in a large cohort of US women.

Methods: Among 44,929 Sister Study participants, indoor LAN (light/TV on, light from outside room, nightlight, no light) and sleep dimensions were self-reported at baseline; outdoor LAN was determined from satellite data at baseline residence. We defined combined LAN using dichotomous indoor (high vs. low) and outdoor (< vs. ≥median) LAN. We used Poisson regression with robust variance to estimate adjusted PRs and 95% CIs for the cross-sectional associations of LAN with short sleep (<7 hours/night), insomnia symptoms (difficulty falling/staying asleep), frequent napping (≥3 naps/week), inconsistent sleep/wake time (differed day-to-day and week-to-week), sleep debt (≥2 hours between longest and shortest duration), sleep aid use, and cumulative poor sleep score (≥3 poor sleep characteristics). Indoor and outdoor LAN models were mutually adjusted for each other.

Results: Sleeping with a light/TV on vs. no light on in the bedroom was associated with a higher prevalence of most sleep outcomes (e.g., short sleep: PR=1.33, 95% CI: 1.27-1.40; insomnia symptoms: PR=1.41, 95% CI: 1.34-1.49; inconsistent sleep/wake time: PR=1.45, 95% CI: 1.35-1.56; sleep debt: PR=1.32, 95% CI: 1.25-1.39). Higher outdoor LAN was associated with more sleep aid use (Quintile 5 vs. 1: PR=1.13, 95% CI: 1.04-1.23), but no other outcomes. Combined LAN was not associated with any sleep outcomes.

Discussion: Sleeping with a light or TV on for most of the night was associated with worse sleep health among women. Prospective studies are needed to determine whether objectively measured indoor LAN is associated with poor sleep incidence.

Light at Night and Multiple Sleep Dimensions in the Sister Study
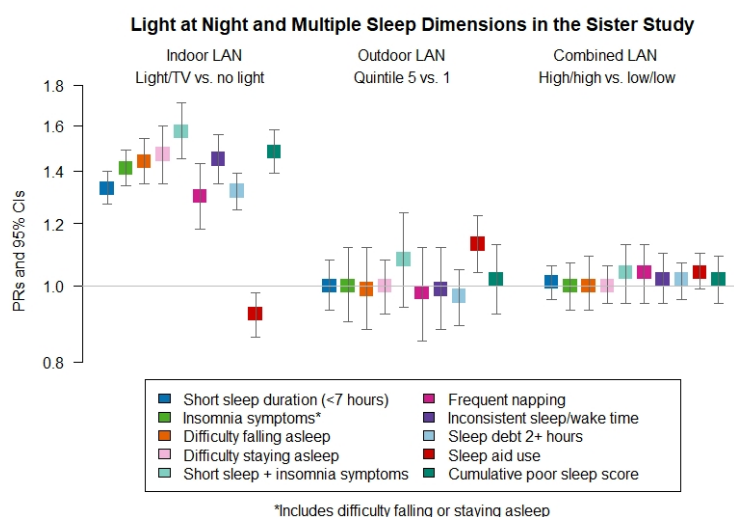
Joint exposures to metals and nutrients in early pregnancy in association with offspring neurocognition Ruwan Thilakaratne* Ruwan Thilakaratne Pi-I D. Lin Sheryl L. Rifas-Shiman Robert O. Wright Marie-France Hivert David Bellinger Emily Oken Andres Cardenas

The brain develops rapidly during pregnancy, but little is known about the associations of prenatal metal and nutrient mixtures with child neurocognition. Within the Project Viva cohort in Boston, MA, concentrations of five essential metals (Cu, Mg, Mn, Se, Zn) and two nutrients (vitamin B12 and folate), together comprising the "nutrient mixture", as well as six non-essential metals (As, Ba, Cd, Cs, Hg, Pb), together comprising the "neurotoxic mixture", were measured in first trimester (~12 weeks) maternal blood. Neurocognition in offspring was assessed in early childhood (~3 years) using the Peabody Picture Vocabulary Test (PPVT), and in mid-childhood (~8 years) using the non-verbal component of the Kaufman Brief Intelligence Test (KBIT). We used adjusted linear regression and quantile g-computation to estimate the independent and joint effects of the mixture components in the full study sample and stratified by sex. We adjusted for child sex and maternal factors including KBIT score, pre-pregnancy body mass index, fish consumption, education, race/ethnicity, age, smoking, and household income. In the full study sample (954 mother-child pairs, 52% male), each doubling of Mg (4.12 points, 95% confidence interval: 0.88, 7.36) and Se (3.71 points; 0.66, 6.76) was associated with a higher early childhood PPVT score. Among females, each quartile increase in the nutrient mixture was associated with 2.41 points (0.21, 4.61) higher PPVT score, versus 1.02 (-1.11, 3.15) in males. In the full study sample, each doubling of Mn was associated with 2.22 points (0.37, 4.08) higher mid-childhood KBIT score. Among females, each quartile increase in the nutrient mixture was associated with 3.45 points (0.08, 6.81) higher KBIT score, versus -0.77 (-3.84, 2.29) in males. The neurotoxic mixture was not associated with the outcomes. In this cohort, increased exposure to essential nutrients in early pregnancy was associated with improved neurocognitive development in female offspring.

LATEBREAKER

Environment/Climate Change

Associations between In-Utero Air Pollution Exposure and Body Mass Index (BMI) z-score trajectories in the Extremely Low Gestational Age Newborns (ELGAN) cohort Eric Brown Jr.*
Eric Brown Rebecca Fry T. Michael O'Shea Thomas Luben

More specifically, ambient air pollution exposure during the gestational period has been associated; these associations are understudied in the extremely preterm children. In a sample of extremely preterm children, we analyzed the hypothesis that increased gestational exposure to fine particulate matter < 2.5 µm ($PM_{2.5}$) and ozone (O_3) would lead to higher BMI z-scores. We analyzed data from 173 children within the Extremely Low Gestational Age Newborn (ELGAN) cohort, which was recruited in five states between the years 2002-2004. Gestational exposure $PM_{2.5}$ and O_3 was estimated based upon the maternal address from the Environmental Protection Agency's Downscaler Model combining Community Multiscale Air Quality (CMAQ) System modeling with air quality monitoring data. BMI scores and gestational ambient air pollution were analyzed in relation to BMI at ages 10 and 15 using multiple linear regression adjusting for key covariates. For $PM_{2.5,}$ the average gestational exposure was 12.71 (interquartile range (IQR) 11.57 – 13.95). For O_3, the mean gestational exposure was 40.31 (IQR : 33.98 – 46.31). BMI at age 2 was statistically associated with mean PM2.5 gestational exposure (β = 0.226, p = **0.0144**). Senstivity analyses that included both exposures showed that the mean PM2.5 exposure and BMI at age 2 (β = 0.25822, p = **0.00802**) was statistically significant. Mean O3 and BMI at age 10 was also significantly associated (β = -0.0434, p = **0.0241**) . This study highlights the relationship between gestational ambient air pollution and BMI z-scores later in life and support for the developmental origins of health and disease hypothesis.

Genetics

Associations between plasma proteome and polygenic risk scores for mitochondrial DNA copy number: the Atherosclerosis Risk in Communities Study (ARIC) Ethan Moser* Ethan Moser Brian Steffen Jiaqi Xie Nathan Pankratz Dan Arking Thomas Mosley Weihua Guan Sanaz Sedaghat James S. Pankow Pamela Lutsey Weihong Tang

Introduction: The number of copies of the mitochondrial (MT) genome, termed MT DNA copy number (MTCN), varies by cell. The maintenance of MTCN is essential for normal MT function. Critically, lower MTCN has been associated with aging and chronic diseases such as dementia and cancer. MTCN can be predicted using a polygenic risk score (PRS). We conducted a large-scale proteomics analysis of a PRS for leukocyte MTCN (L-MTCN) in the ARIC study to identify proteomic signatures for genetically determined MTCN.

Methods: Previous genome-wide association study have identified 133 statistically significant and independent SNPs for L-MTCN. We calculated a PRS based on published summary statistics for 117 autosomal SNPs measured in the ARIC Study (n= 7241 White and 1674 Black participants). We then analyzed the associations of the L-MTCN PRS with plasma levels of 4,870 proteins measured in ARIC using SOMAscan v4. Race-specific generalized linear models were used to evaluate association between levels of each protein and L-MTCN PRS, adjusting for age, gender, field center, principal components for genetic ancestry, and a measure of kidney function. A Bonferroni correction was used to account for the number of proteins tested in White participants ($p \leq 1 \times 10^{-5}$). Significant associations were tested for replication in Black participants.

Results: Five proteins were significantly associated with the L-MTCN PRS in White participants: VPS29, MLP3B, MLP3A, GBRL2, and ING4 ($p \leq 1 \times 10^{-5}$). Of these, MLP3A was significantly replicated in Black participants ($p = 0.01$). The direction of associations for all five proteins was consistent between the two groups.

Conclusion: This large proteomics analysis for L-MTCN PRS identified associations with 5 plasma proteins, some of which have previously been implicated in studies of Alzheimer's disease and cancers. Our findings may provide further insight into the biological pathways affected by MTCN.

Genetics

Associations Between Preconception Maternal Sleep Characteristics and Neonatal Cord Blood DNA Methylation Sunni Mumford* Joshua Freeman Kristen Polinski Edwina Yeung Louise O'Brien Galit Dunietz Charles Matthews Robert Silver Enrique Schisterman Sunni Mumford

Maternal sleep has been associated with infant growth and animal studies suggest maternal sleep may influence fetal circadian rhythms. Epigenetic modification may link maternal sleep to fetal growth and circadian rhythms programming. However, whether maternal sleep influences DNA methylation (DNAm) in fetal tissue is understudied. In a secondary analysis of the EAGeR study, we evaluated maternal sleep and newborn DNAm profiles (n=358). Women aged 18-40 years with a history of 1-2 pregnancy losses were followed from preconception to delivery. Maternal sleep patterns were assessed via a preconception questionnaire from which we calculated sleep duration, sleep midpoint, social jetlag, and differences in weekend-weekday sleep duration. DNAm was profiled from the cord blood buffy coat of singletons using the MethylationEPIC 850K BeadChip. To estimate associations between continuous sleep measures and DNAm, we used multivariable robust linear regression with a false discovery rate correction (FDR). Among women, median sleep duration was 7.92 (Interquartile Range (IQR): 1.00) hours and median sleep midpoint was 3:35AM (IQR: 76 minutes). Maternal sleep duration and midpoint were not associated with cord blood DNAm (FDR p-values <0.05). However, per hour increases in social jetlag were associated with lower DNAm at cg05754361 near *FAM192A* (β=-0.0096, SE=0.0018, FDR P=0.02) and at cg10363203 near *MED13L* (β=-0.0271, SE=0.0040, FDR P=1.24 x 10^{-5}). Moreover, per hour increases in the difference in maternal weekend-weekday sleep duration was associated with lower DNAm at cg05622663 near *RN5S143* (β=-0.0048, SE=0.0009, FDR P=0.049). In summary, sleep duration and midpoint were not associated with cord blood DNAm, though greater social jetlag and differences in weekend-weekday sleep duration were associated with cord blood DNAm. Thus, sleep patterns that may lead to maternal circadian disruption may be related to neonatal growth and programming.

Global Health

Impact evaluation of healthcare and community worker trainings on maternal health in Tanzania Erin Hetherington* Erin Hetherington Sam Harper Rebecca Davidson Charles Festo Nadia Lampkin Sally Mtenga Clarissa Teixeira Ilona Vincent Arijit Nandi

Background: From 2018 to 2019, a multi-component intervention to improve maternal and newborn health was delivered in the Tabora region of Tanzania, by Tanzanian and Canadian collaborators. Intervention components included training healthcare and community workers, infrastructure upgrades to health facilities and improvements to regional planning and management. The study aim was to examine the impact of trainings on three key outcomes: skilled birth attendance, antenatal care and respectful maternity care.

Methods: Trainings were delivered sequentially in 8 districts (2 districts at a time), resulting in 4 treatment groups. A series of cross-sectional surveys were administered to a random sample of households in all districts at baseline and after each wave of training. Risk differences were estimated using a difference in difference approach comparing outcomes in treated districts to not yet treated districts. The overall Average Treatment Effect on the Treated (ATT), and group/time dynamic effects were aggregated using estimators for multiple groups in multiple time periods.

Results: Respondents reported 3,895 deliveries and 3,492 pregnancies over the course of the intervention and up to 2 years prior. The overall ATT for women receiving 4 or more antenatal care visits was -0.02 (95%CI -0.22, 0.18); for delivery with a skilled birth attendant 0.13 (95%CI 0.00, 0.25); and for disrespectful treatment at delivery 0.03 (95%CI -0.06, 0.13). Results of the dynamic treatment estimates suggest that skilled birth attendance began to increase 4 months after the end of training in each district.

Discussion: We found stronger evidence of impact on skilled birth attendance than other outcomes, though all estimates were imprecise. Practical considerations, including the non-sequential delivery of other parts of the intervention (facility upgrades, ambulance purchase and community meetings), made estimating the overall impact of the intervention challenging.

Global Health

The Community Health Worker Effect: A Multilevel Model Approach To Explore Improvements In Child Development
Caitlin Hemlock* Caitlin Hemlock Maria Dieci Ann Weber Emanuela Galasso Lia C.H. Fernald

Background: Interventions to improve child development are often delivered through home visits but many have not exhibited substantial gains in low-resource settings. A previously conducted trial hypothesized that constraints on delivery agents, community health workers (CHW), may have contributed to null results. The objective of this observational analysis was to determine if any CHW characteristics improved child development during the intervention.

Methods: We analyzed data from one treatment arm in a cluster-randomized trial, a stimulation intervention delivered through biweekly home visiting in children 6-30 months, conducted in rural Madagascar from 2014-2016. Children and CHWs (1 per cluster) were surveyed at baseline, one, and two years later. Child scores from the Ages and Stages Questionnaire-Inventory (ASQ) were collected via caregiver report and internally age-standardized. We used LASSO to determine importance of CHW variables at baseline (including demographics, motivation, skills and environment) against subsequent ASQ scores. We performed multivariable regression using random intercept models adjusting for child level variables and a village wealth proxy.

Results: We analyzed 1,178 ASQ scores after intervention delivery from 669 children in 25 clusters. CHWs were on average 30 years old and 40% had at least secondary education. Having another income-generating activity was the most important variable; children in clusters where CHWs had another activity had subsequent ASQ scores 0.95 SD higher than children in clusters where CHWs had no other activity (95% CI: 0.16, 1.7). Among types of activities, agricultural worker, trader, and government employee were associated with higher ASQ scores.

Conclusions: While time constraints are thought to reduce effective intervention delivery, our research suggests participation in another activity by CHWs may be capturing a dimension beneficial to behavior change message delivery (e.g. grit, status in community).

LATEBREAKER

Global Health

A 2020 global update on folic acid-preventable spina bifida and anencephaly – 30- year anniversary of gaining knowledge about folic acid's prevention potential for neural tube defects Godfrey P. Oakley, Jr.* Vijaya Kancherla Kaustubh Wagh Pretty Priyadarshini Helena Pachón

Mandatory folic acid fortification of staple foods is an effective public health intervention to prevent spina bifida and anencephaly. We estimated the global proportion of folic acid-preventable spina bifida and anencephaly (FAP SBA) prevented through mandatory folic acid fortification of wheat and/or maize flour and rice during the year 2020, marking 30 years of knowledge on folic acid's FAP SBA prevention potential. We used the Food Fortification Initiative database to identify countries with mandatory fortification policies with folic acid added to cereal grains (wheat flour, maize flour, and/or rice). We built FAP SBA prevention model assuming mandatory folic acid fortification at 200 mcg/day of folic acid fully protects against FAP SBA and reduces their prevalence to a minimum achievable 0.5 / 1,000 live births for live births in 2020. Overall, our prevention model showed that 63,340 FAP SBA cases were prevented in the year 2020 through folic acid fortification of wheat flour, maize flour, and/or rice in 58 countries. The global prevention percent of FAP SBA was 23%. An additional 216,600 FAP SBA could have been averted globally through mandatory folic acid fortification in many countries in Asia, Africa, and Europe, where cereal grain food fortification with folic acid is not implemented. In conclusion, global prevention efforts for FAP SBA are inadequate 30 years after gaining knowledge on folic acid's FAP SBA prevention potential. Mandatory fortification should be urgently implemented in all countries to limit preventable FAP SBA and associated elective terminations, stillbirths, and child mortality.

Legend
- No Prevention
- Moderate Prevention
- High Prevention
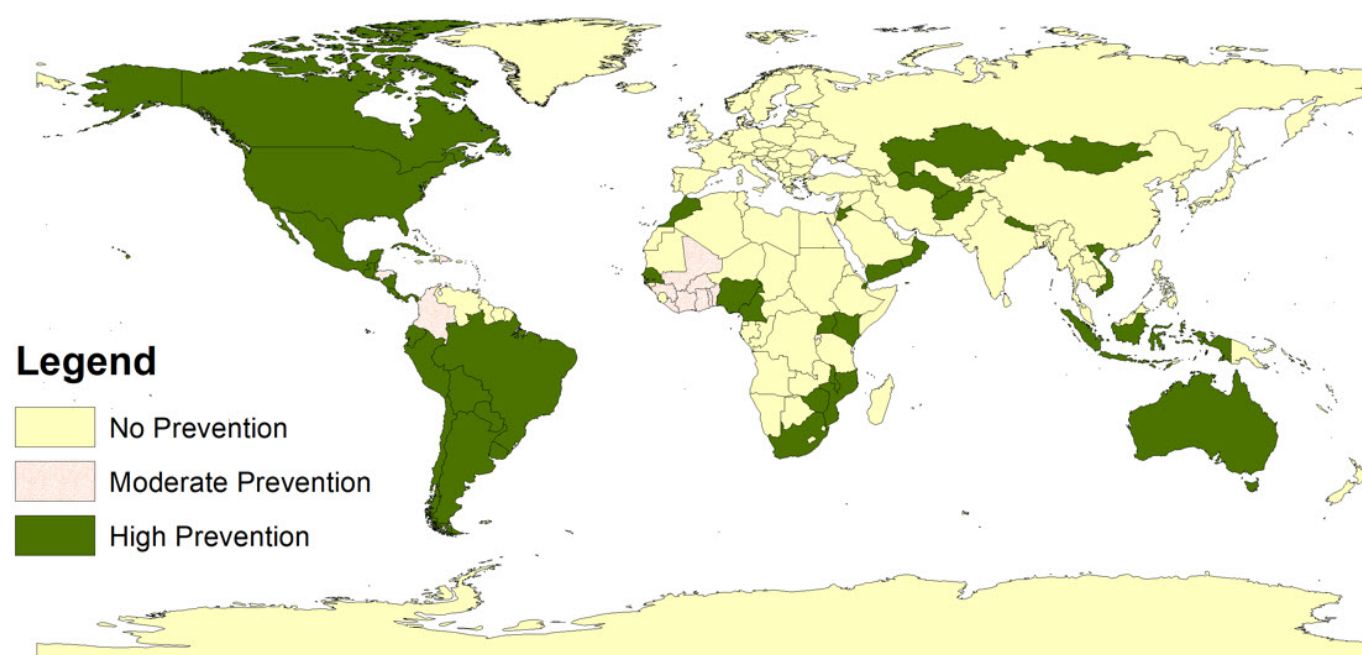
Income inequality and mental health among Canadian secondary school students, findings from the COMPASS Study 2016-2020: a longitudinal analysis. Claire Benny* Claire Benny Karen A. Patte Paul J. Veugelers Ambikaipakan Senthilselvan Scott T. Leatherdale Roman Pabayo

Background. Depression and anxiety among teens are major public health concerns. Previous research has shown an association between income inequality and increased depression among adolescents, specifically among girls; however, the role of income inequality in adolescent mental health has not yet been tested longitudinally. The aim of this current study is to quantify the association between income inequality and mental health among Canadian secondary school students over time.

Methods. Longitudinal data come from four waves (2016/17 to 2019/20) of the Cannabis, Obesity, Mental health, Physical activity, Alcohol, Smoking, and Sedentary behaviour (COMPASS) school-based study. The cohort included 51,823 students attending 75 Canadian secondary schools that were nested in 43 Census divisions (CDs). Multilevel modeling was used to assess the relationship between CD-level income inequality and depressive and anxiety symptoms and the odds for depression and anxiety over time, based on accepted scale cut-off values indicating clinically relevant symptoms.

Results. The sample was primarily female (52.6%), white (79.7%), had weekly spending money over $100 (21.3%), and the median CD-level after tax household income was $62,148.31 (SD= $8,596.33). Living in areas with higher levels of income inequality was associated with higher depressive scores (B= 0.04; 95% CI= 0.01, 0.07) and an increased odds for depression (OR= 1.08, 95% CI= 1.01, 1.16) over time. Income inequality was not significantly associated with anxiety symptoms or the odds for experiencing anxiety over time.

Discussion. The findings from this study indicate that income inequality is associated with depression over time among Canadian adolescents, but do not support a prospective association with anxiety. Given that most students majorly spend their waking hours in schools, this study highlights potential points of intervention to alleviate the potential harmful effects of income inequality on mental health.

Increased years of schooling predicts lower risk for diabetes at the higher quantiles of the HbA1c distribution: An unconditional quantile regression analysis Jillian Hebert* Jillian Hebert Amanda Irish Aayush Khadka Anusha Vable

Prior work notes a robust relationship between higher educational attainment and diabetes; however, it is unknown if the relationship is constant across the diabetes distribution. If more education especially benefits those at the low end of the diabetes distribution, programs and policies to increase education could result in the expansion of inequalities. Alternatively, if more education especially benefits those at the high end of the diabetes distribution, inequalities could reduce. We empirically evaluate the relationship between education and hemoglobin A1c (HbA1c) across the A1c distribution using unconditional quantile regressions among Health and Retirement Study (HRS) participants.

Our exposure, educational attainment, was defined as number of years in school (0-17+). Our outcome was first recorded HbA1c value (measured 2006-2016); lower HbA1c levels indicate a reduced risk of diabetes. We used unconditional quantile regressions (UQR) to assess the relationship between education attainment and HbA1c across different quantiles of the marginal HbA1c distribution. To account for confounding, we adjusted UQR models for demographics, parent's education, and childhood characteristics.

The mean HbA1c level was 5.9% with 15.5% of participants meeting diabetic criteria (HbA1c >= 6.5%). Each additional year of education consistently predicted lower HbA1c levels across the HbA1c distribution (e.g., 50th quantile, β = -0.013, 95% CI: -0.006, -0.020). The relationship was especially strong at the high tail of the HbA1c distribution. At the 75th quantile, each additional year of education predicted a reduction of 0.016% in HbA1c (95% CI: -0.003, -0.029), compared to the 90th quantile that predicted a reduction of 0.062% in HbA1c (95% CI: -0.019, -0.105). We found each additional year of education especially benefited those at the high end of the HbA1c distribution, suggesting programs and policies to increase educational attainment may reduce diabetes disparities.

Relationship between Years of Schooling and HbA1c Levels
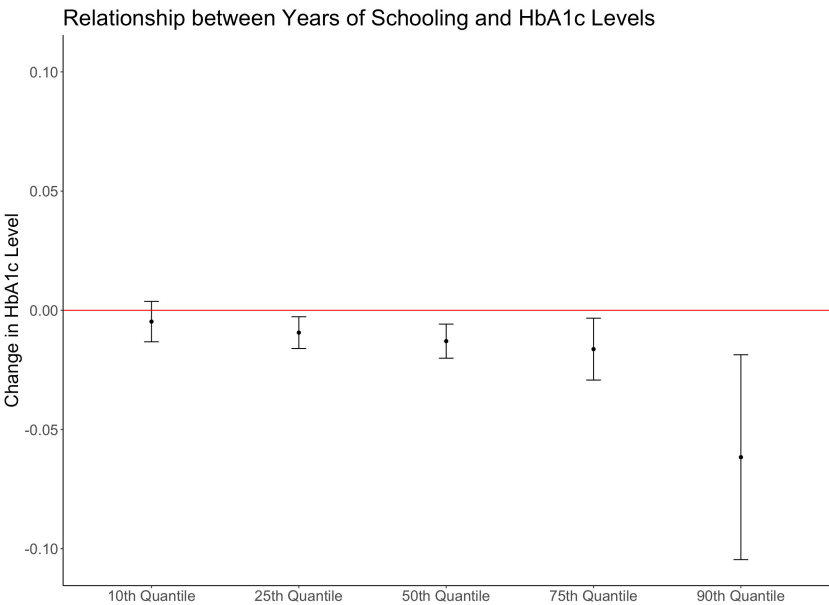
Pre-disaster income inequality and mental health after a natural disaster: A natural experiment from the 2011 Great East Japan Earthquake and Tsunami Sakurako Okuzono*

Sakurako Okuzono Koichiro Shiba Kawachi Ichiro

Income inequality is associated with worse health outcomes. However, little is known about whether living in areas with higher income inequality modifies health outcomes in the aftermath of disasters. We used a prospective cohort study of older adults (≥65 years) who survived the 2011 Great East Japan Earthquake to examine whether income inequality potentiates the association between disaster-related trauma and mental health outcomes. The baseline survey in 2010 predated the disaster by seven months. Participants completed the post-disaster survey in 2013, 2016, and 2019. Participants retrospectively reported on disaster-related home loss. To assess the level of income inequality, the Gini index was calculated using individual income data in 2010 aggregated to 94 communities (range 0.05-0.50: median=0.32, interquartile range=0.06) and categorized into tertiles (low, middle, high). Depressive symptoms and post-traumatic stress symptoms (PTSS) were assessed in the three post-disaster surveys using validated instruments. Multilevel analysis was conducted adjusting for pre-disaster characteristics and stratified by pre-disaster income inequality. Among those living in areas with middle-to-high income inequality before the earthquake, home loss was associated with greater depressive symptoms in 2013 compared to those living in the most egalitarian areas. The association disappeared in the subsequent two follow-up surveys. Home loss was associated with higher PTSS scores from 2013 to 2019 among individuals living in middle-to-high income inequality, but not among those who lived in low Gini index communities. Our findings suggest that pre-disaster income inequality may have a persistent impact on aggravating survivors' PTSS symptoms and a short-term impact on making people more susceptible to experiencing greater depressive symptoms in the aftermath of the disaster.
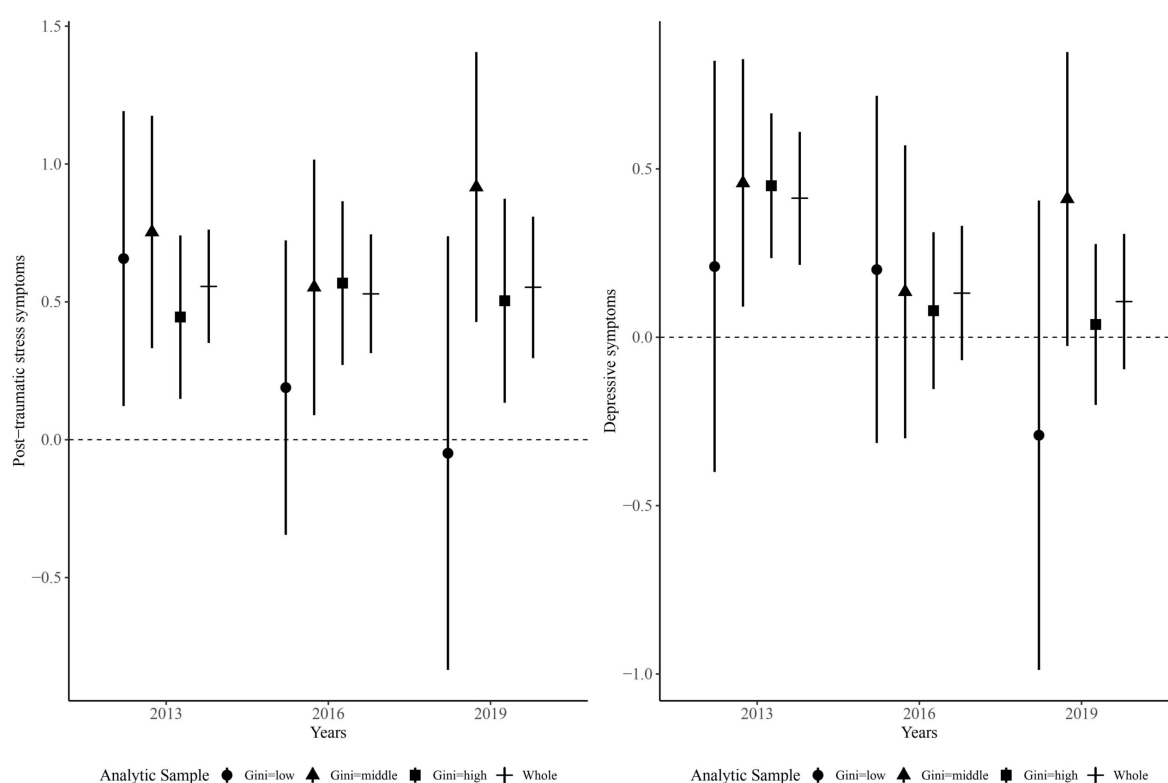
Heterogeneous treatment effects in social policy studies: A quantitative review Dakota Cintron* Dakota Cintron Maria Glymour Ellicott Matthay

Purpose. Understanding heterogeneous treatment effects (HTEs) is critical to assessing whether social policies alleviate or exacerbate health inequities. However, little is known about how often HTEs happen, for what types of social policies, or for what population subgroups.

Methods. We used an existing systematic sample of 55 contemporary studies of the health effects of social policies. For each study, we recorded the social policy that was evaluated, whether HTEs were assessed, for what subgroups HTEs were reported, and the effect estimates and sample size for each subgroup. We converted effect estimates to uniform measures of association on both the additive (standardized mean differences, SMDs) and multiplicative scales (ORs). For each study-subgroup, we fit a random-effects meta-analysis model. We quantified heterogeneity in social policy effects, overall and by population subgroup and policy category, using tau (the standard deviation of the effect estimates across study subgroups after accounting for sampling variability).

Results. 24 studies (44%) evaluated treatment effect heterogeneity. The degree of heterogeneity in policy effect estimates (tau) ranged from 0 to 0.45 SMDs. Heterogeneity in estimated policy effects was evident for all population subgroups and most types of social policies (at least one SMD>0.3), including employment, family benefit, and alcohol and substance use policies. Results on the multiplicative scale (OR) were similar.

Conclusions. The health effects of social policies are generally small in magnitude (<0.2 SMDs), but we find substantial evidence of heterogeneity in the effects of social policies across diverse types of social policies and population subgroups. Findings should be interpreted cautiously because some subgroupings were small, but results indicate the potential impact of policies on disparities and the importance of evaluating HTEs.

Figure 1
Distribution of heterogeneity in social policy effect estimates (tau), overall and by social policy and population subgrouping
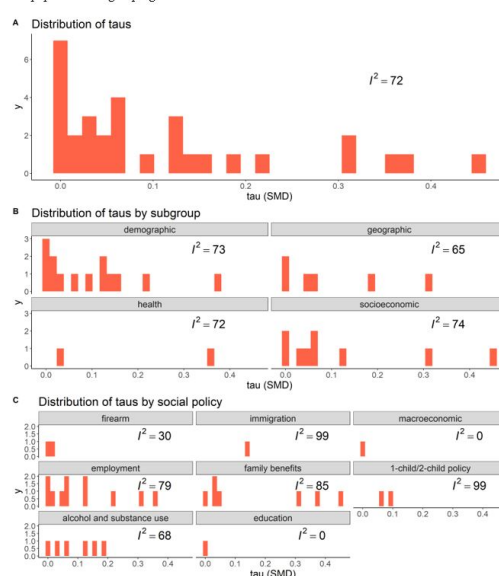
Note. Tau is the standard deviation of the effect estimates across study subgroups after accounting for sampling variability. I^2 is the percent of the variation in effect estimates reflecting real variation rather than sampling error. The number of policy effect estimates (study-subgroups) contributing to each estimated tau ranged from 1 to 108.

Relationship Between Pain and LGBT Status among Veterans Kirsha Gordon* Kirsha Gordon Eugenia Buta Ralitza Gueorguieva Allison R. Warren T. Elizabeth Workman Mandi L. Pratt-Chapman Qing Zeng Joseph L. Goulet

Background

Pain assessment is performed in many healthcare systems, such as the Veterans Affairs, but prior studies have not assessed whether pain screening varies in sexual and gender minority populations that include individuals who identify as lesbian, gay, bisexual, and transgender (LGBT). An understanding of the epidemiology of pain and pain screening in the growing population of LGBT Veterans will be essential for planning pain treatment services. We evaluate pain screening and overall pain by LGBT status in Veterans.

Methods

Data from the Corporate Data Warehouse, a national repository with clinical/administrative data on Veterans, was analyzed. Veterans were classified as LGBT using Python natural language processing. We used a robust Poisson model to examine the association between LGBT status (yes/no) and binary outcomes of pain screening and any pain within 1 year of enrollment, and a truncated negative binomial for the non-zero pain values. All models were adjusted for demographics, mental health, substance use, musculoskeletal disorder, and number of clinic visits.

Results

There were 1,187,785 Veterans whose LGBT status could be determined (mean age 52), of which 235,847 (20%) were classified as LGBT. LGBT were more likely to be female, have musculoskeletal disorder, mental health, substance use, and more clinic visits (Figure 1). Among LGBT, 94% were screened for pain within 1 year of enrollment vs. 89% among non-LGBT. LGBT were slightly more likely to report any pain (50% vs. 48%). In adjusted models, the LGBT risk of pain screening, vs. non-LGBT, was 2.4% higher (95% CI 2.3%, 2.5%); risk of any pain was 1.9% lower (95% CI 1.5%, 2.4%); and among those with any pain, the mean pain score was 0.8% lower (95% CI 0.5%, 1.1%).

Conclusions

In a nationwide sample, LGBT veterans were more likely to be screened for pain but had lower pain scores, though adjusted differences were small. Studies are needed to examine whether LGBT are more likely to request screening.

Figure 1. Characteristic of LGBT and non-LGBT
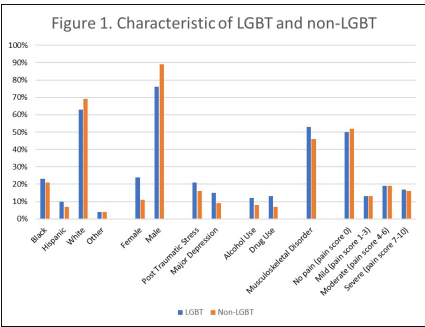
Temporal trends in phthalate exposure of adolescent girls in the United States: National Health and Nutrition Examination Survey 1999-2016 Jasmine McDonald* Jasmine McDonald Sabine Oskar Julia Mook Jasmine McDonald

Importance: Exposure to phthalates during the pubertal window impacts chronic disease risk and temporal trends in exposure can inform public health initiatives.

Objective: Characterize temporal trends in phthalate exposure for girls overall and by sociodemographic characteristics.

Methods: We used cross-sectional data from the 1999-2016 cycles of the National Health and Nutrition Examination Survey. Participants were females between the ages of 8-14 with at least one urinary measurement of the selected 12 phthalate metabolites within the study period (n=2,148). We used multivariable linear regression to assess temporal trends for individual phthalate concentrations (ng/ml) and source groupings (low and high molecular weight phthalates) overall and by sociodemographic characteristics (race/ethnicity, nativity, socioeconomic status (SES), intersection of race/ethnicity-income).

Results: Overall ∑HMW and ∑LMW concentrations declined between 2001 and 2016; however, only ∑LMW consistently differed by sociodemographic characteristics. ∑LMW concentrations were higher for Mexican-Americans (ß =0.3, 95% CI:0.2-0.4), Other Hispanics (ß=0.3, 95% CI:0.1-0.6), and Non-Hispanic Blacks (ß =0.5, 95% CI:0.4-0.6) compared to Non-Hispanic Whites. Foreign-born participants had higher ∑LMW concentrations than those born in the US (ß =0.2, 95% CI: 0.0-0.4, p=0.03). Individuals with low SES had significantly lower ∑LMW concentrations than those of high SES (p<0.0001). Compared to Non-Hispanic Whites, all racial/ethnic groups had statistically significant higher ∑LMW concentrations independent of SES status.

Conclusions: Personal care products are the primary source of LMWs and ∑LMW exposure burden is higher among girls in the most vulnerable social strata. Girls identifying within a socially disadvantaged racial/ethnic group have elevated ∑LMW concentrations even if jointly high SES. Interventions in girls should mitigate ∑LMW phthalate exposure among the most socially disadvantaged strata.

Spatial analysis of high need and low access census tracts within the service area of a Southwestern Pennsylvania Food Bank Lynne Pavlic Marshall* Lynne Pavlic Marshall Gwendolyn Parker Natalie Suder Egnot Olivia Messina Leleck Marnie Schilken

This study aimed to identify communities of high need and low access (i.e., service gaps) within the Greater Pittsburgh Community Food Bank's ("Food Bank") 11-county Southwestern Pennsylvania service area. All Food Bank programs available to the general public (i.e., no age, ability, or residency restrictions) were geocoded. All analyses were stratified by urban vs. non-urban status using Rural-Urban Commuting Area (RUCA) codes. Need was assessed using the Centers for Disease Control and Prevention's Social Vulnerability Index (SVI). Specifically, the SVI was normalized to the service area; census tracts with an SVI above the median were classified as "higher need" and tracts with an SVI below the median were classified as "lower need". Access was assessed based on distance to the nearest Food Bank program. Census tracts with a population-weighted centroid greater than 0.5 miles (urban tracts) or greater than five miles (non-urban tracts) from the nearest Food Bank program were classified as "low access". Our spatial analysis revealed that non-urban census tracts are more likely to experience higher need compared to urban tracts (64.4% vs. 44.9%). Additionally, Food Bank programs are located closer to higher need centroids compared to lower need centroids regardless of urban vs. non-urban classification (distance to closest program for higher need vs. lower need: 0.70 vs. 1.45 miles in urban tracts; 2.24 vs. 3.15 miles in non-urban tracts). However, our analysis found 125 service gaps (Figure 1), and non-urban tracts were less likely to experience a service gap (i.e., higher need + low access) compared to urban tracts (11.6% vs. 46.3%, respectively). This identification of service gaps can inform targeted resource allocation efforts for future Food Bank programming.
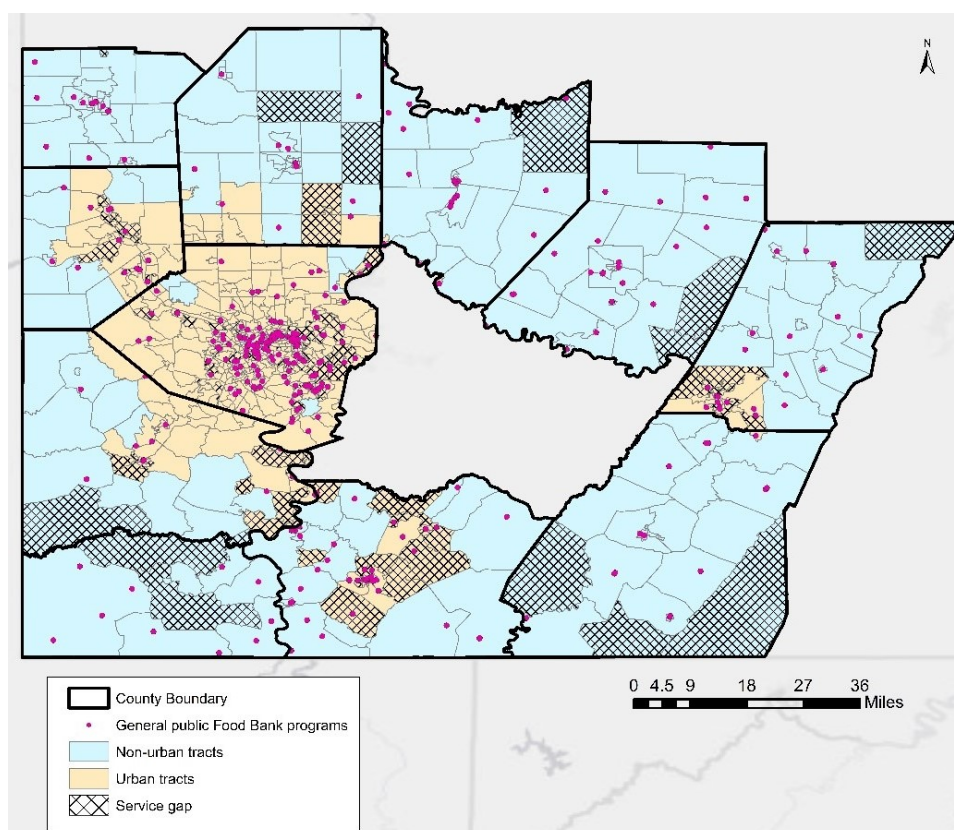
Do racial inequities in cognitive function persist when SES is taken out of the equation?
Rebecca Stebbins* Rebecca Stebbins Grace Noppert Y. Claire Yang

There is a great deal of existing research regarding the interaction between socioeconomic status (SES) and racial/ethnic disparities in relation to cognitive health outcomes. However, many of the existing studies focus only on the relationship of SES and outcome within particular racial or ethnic groups. Furthermore, these studies are of cohorts in a single life stage due to the natural limitations of existing cohort studies. This leaves key questions unanswered: will racial/ethnic disparities remain as strong if SES were equal, and do associations differ by lifecourse period? Integrating longitudinal data from two or more waves of four US population-based surveys (Add Health, ACL, MIDUS, and HRS), covering the full lifecourse from young adulthood to later life, we will investigate associations between racial and ethnic categories and cognitive change within strata of three measures of SES: poverty-to-income ratio, wealth, and education. This method will use harmonized measures of global cognitive function and SES across studies. We will adapt Ward et al.'s framework for disparities investigations by applying it to the populations within each SES strata: we will describe the (1) outcome distributions and (2) the size of the association between race/ethnicity and cognition, allowing us to go beyond the existing literature demonstrating stronger relationships between race/ethnicity and cognition within certain SES levels. We will also test for lifecourse variations in the SES and race differences across studies in the IDA. We will use inverse probability weights to account for informative loss-to-follow-up and confounding (adjustment set determined via DAG analysis). Results of this analysis are forthcoming, but we expect our results to be representative and valuable for understanding how SES and racism interact across a wider age range than any existing study of a single dataset.

The Influence of Multiple Sources of Selection Bias on Racial Differences in Cardio-Metabolic Disease Onset in a Cohort of Midlife Aging

Alexis Reeves* Alexis Reeves Michael Elliott Tené Lewis Carrie Karvonen-Gutierrez William Herman Sioban Harlow

Cohort studies of aging recruit participants at an age before most of the population experiences the study outcome, to document its natural history and related risk factors. The age of study commencement is usually based on "normative" aging among Whites. However, "weathering" can cause accelerated health declines in minoritized populations compared to Whites due to cumulative experience of multiple forms of marginalization. Thus, considering if weathering among minoritized individuals could affect selection into cohort studies is necessary to effectively estimate and understand racial/ethnic disparities in aging and disease. Using the Study of Women's Health Across the Nation (SWAN), a multi-ethnic longitudinal cohort, and its cross-sectional screening survey, we examine the effects of left truncation, left censoring and right censoring on the racial/ethnic differences in the age of onset of 4 cardio-metabolic outcomes (hypertension, isolated systolic hypertension, insulin resistance and diabetes). Left truncation was adjusted for using inverse probability weighting, left censoring via interval censored accelerated failure time models and right censoring via multiple imputation. Left truncation and left censoring had greater effects on outcomes with earlier age at onset (hypertension) and right censoring had greater effects on outcomes with later onsets (metabolic). Full adjustment for selection bias led to an average 20-year decrease in predicted median age of onset for all groups across the 4 outcomes and tended to decrease the predicted difference in age at onset for Black and Hispanic women compared to White women. However, earlier onset of each outcome for Black and Hispanic women remained. Not considering the full extent of selection bias in cohort studies can misinform our understanding of aging and disease for all groups, especially for minoritized populations who have higher prevalence of these leading causes of morbidity and mortality earlier in life.

Percent Difference in Survival Time and Predicted Median Age at Onset of 2 (of 4) Cardio-Metabolic Outcomes by Racial/Ethnic Group

	Isolated Systolic Hypertension						Insulin Resistance					
	%	LCI	UCI	Median	LCI	UCI	%	LCI	UCI	Median	LCI	UCI
Unadjusted[a]												
Overall				92.0	77.9	106.1				100.2	90.5	109.8
Racial/Ethnic Group												
White				96.0	81.6	110.4				104.4	94.0	114.8
Black	-19.5	-27.6	-10.5	77.3	66.3	88.2	-9.1	-14.6	-3.3	94.9	85.6	104.1
Chinese[b]	-7.8	-21.7	8.7	88.6	70.2	106.9	5.7	-8.6	22.1	110.3	91.9	128.8
Hispanic	-2.7	-27.1	29.9	93.4	64.2	122.7	-18.0	-27.0	-8.0	85.6	74.5	96.6
Japanese[b]	-7.9	-20.8	7.1	88.4	71.7	105.1	-2.4	-13.3	9.8	101.8	87.4	116.3
Incorporating Left Censored												
Overall				45.2	41.9	48.5				101.1	90.5	111.7
Racial/Ethnic Group												
White				48.5	44.9	52.1				106.9	95.3	118.5
Black	-18.4	-23.1	-13.5	39.6	36.4	42.7	-10.1	-16.4	-3.3	96.1	85.7	106.5
Chinese[b]	8.9	-1.7	20.5	52.8	46.7	59.0	9.1	-7.7	28.9	116.6	94.7	138.6
Hispanic	-12.6	-23.2	-0.5	42.4	36.6	48.2	-27.2	-35.7	-17.6	77.8	66.9	88.7
Japanese[b]	-4.4	-12.8	4.7	46.4	41.4	51.3	4.9	-10.2	22.6	112.2	92.1	132.2
+ Accounting for Right Censoring												
Overall				50.3	48.3	52.2				78.0	73.3	82.7
Racial/Ethnic Group												
White				53.0	50.8	55.2				83.7	77.8	89.6
Black	-16.0	-19.4	-12.6	44.5	42.5	46.5	-11.2	-15.2	-7.2	74.3	69.9	78.7
Chinese[b]	5.9	0.1	11.6	56.1	52.4	59.8	-5.2	-17.2	6.7	79.4	37.9	120.9
Hispanic	-0.6	-5.9	4.6	52.6	49.5	55.8	-25.8	-32.2	-19.4	62.1	56.2	68.0
Japanese[b]	-2.2	-7.4	3.0	51.8	48.7	54.9	-4.2	-12.7	4.3	80.2	68.4	92.0
+ Adjusted for Left Truncation												
Overall				49.3	47.0	51.6				75.2	67.5	82.9
Racial/Ethnic Group												
White				51.8	49.2	54.5				80.1	70.5	89.8
Black	-14.9	-18.9	-10.9	44.1	41.9	46.4	-6.2	-12.2	-0.2	75.2	67.1	83.3
Chinese[b]	7.3	0.3	14.2	55.6	51.2	60.0	-4.2	-17.9	9.5	76.8	26.5	127.2
Hispanic	1.1	-4.1	6.4	52.4	49.2	55.7	-25.1	-34.2	-16.0	60.0	52.7	67.4
Japanese[b]	0.5	-5.1	6.2	52.1	48.7	55.6	-10.1	-27.4	7.1	72.0	55.7	88.3

Note: Percent difference calculated as (exp(β)-1)*100.
All models adjusted for covariates including educational level, self-reported health, waist circumference, smoking status, alcohol use and physical activity score.
Covariates for predicted median age were set to: educational level (some college), self-reported health (very good), waist circumference (86.34 cm), smoking status (never), alcohol use (moderate) and physical activity score (7.65).
[a]Data in model is left censored, right censored and unadjusted for left truncation.
[b]Small number of cases for Chinese (n with insulin resistance ~ 46) and Japanese (n with insulin resistance ~ 51) women.

Estimating recent changes in educational inequality in cancer mortality among adults in Canada: a study of four consecutive CanCHEC cohorts Diego Capurro* Diego Capurro Sam Harper
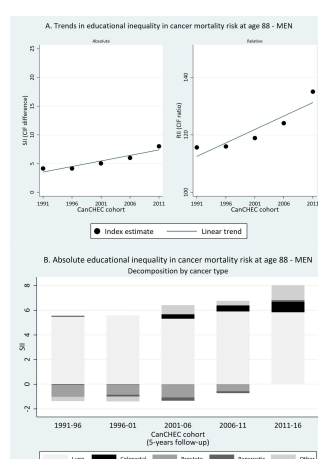
Background. Monitoring socioeconomic inequalities in cancer mortality is important to assess efforts and inform decisions towards health equity. The present study describes trends in absolute and relative educational gradients in cancer mortality in Canada from 1991-2016 and estimates the contribution of major cancer types to the absolute gradients.

Methods. We used a series of four retrospective population-based cohorts, which consist of census samples from 1991, 1996, 2001, 2006, and 2011, linked to 5-year subsequent mortality data. For each of the five periods, we estimated absolute and relative educational inequalities in cancer mortality in terms of the Cumulative Incidence Function (risk) and Years of Life Lost (YLL) at ages 88 for men and 92 for women. Risk and YLL estimations are based on a recently proposed pseudovalue approach. Absolute and relative inequalities are expressed by the Slope Index of Inequality (SII) and the Relative Index of Inequality (RII). We further estimated inequalities for selected cancer types and assess their contribution to the absolute educational gradient in cancer mortality.

Preliminary Results: Inequalities affecting those with lower education were present in all periods assessed, in terms of cancer mortality risk and YLL. Absolute and relative inequalities were greater for men than for women (average SII for the risk was 5.5 percent points for men and 2.5 percent points for women; average SII for YLL was 1.6 years for men and 1.1 years for women). Absolute and relative inequalities in the risk increased over time in a close-to-linear fashion. For YLL, inequalities did not change for men and slightly increased for women, while relative inequality increased for both. On average, the contribution of cancer to absolute inequality in total mortality was 34% (men) and 19% (women) for the risk, and 35% (men) and 30% (women) for YLL. These contributions slightly decreased for men and increased for women over time. The major single contributor to absolute inequality in cancer mortality was lung cancer, with average contributions of 108% (men) and 143% (women) for the risk, and 71% (both) for YLL.

General conclusions are robust to the use of an alternative summary measure of inequality, the use of cause-specific hazard models in risk and YLL estimations, and the use of other reference ages.

A. Trends in educational inequality in cancer mortality risk at age 88 - MEN

B. Absolute educational inequality in cancer mortality risk at age 88 - MEN
Decomposition by cancer type

Health Disparities

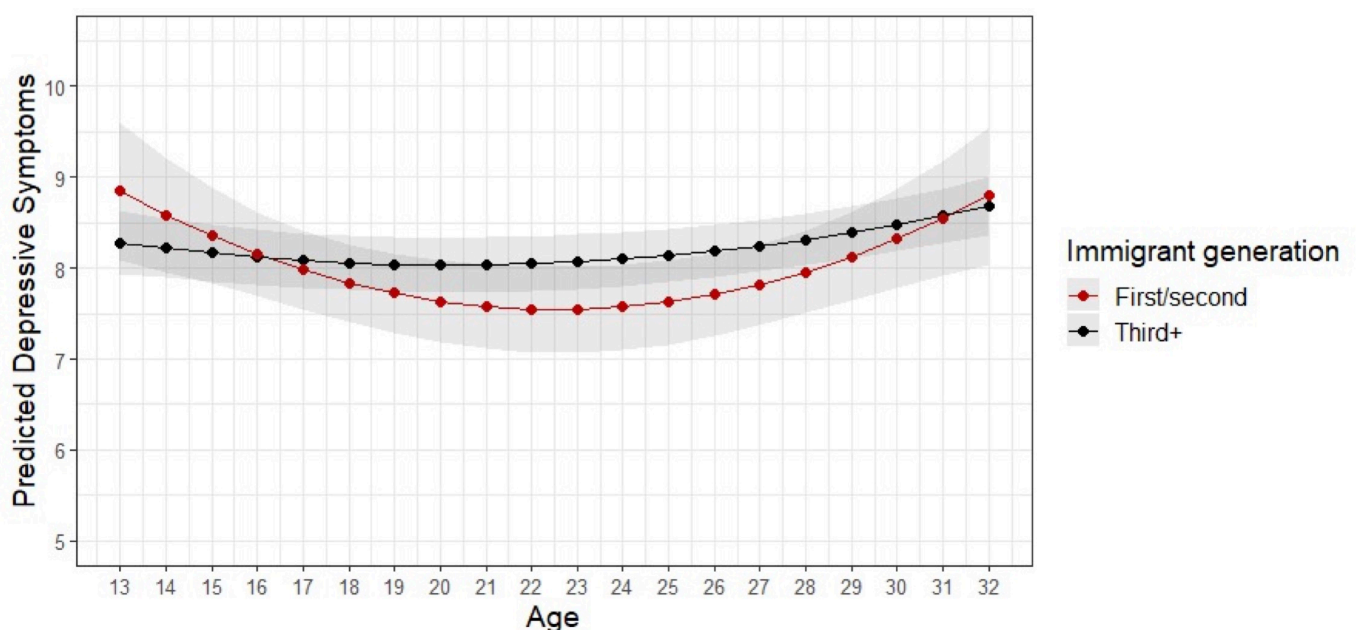**Trajectories of depressive symptoms from adolescence to adulthood — exploring variation by immigrant generation among Black Americans** Precious Esie* Precious Esie Lisa Bates

There is evidence of a transition in depressive symptoms within the US Black population across the life course, suggesting those with recent immigrant origins, compared to African Americans, have elevated levels in adulthood that are not present during adolescence. Racial socialization is a process that largely occurs during adolescence where youth of color develop protective coping strategies against poor mental health outcomes. Ethnographic research among Black youth finds variation in this process between those with immigrant parents (first- and second-generation immigrants) vs. those with US-born parents (third+ generation), providing a rationale for why late adolescence may be a period marked by a trajectory of heightened depressive symptoms levels for the first/second-generation. However, longitudinal data are needed to assess whether this transition occurs. We tested whether trajectories of depressive symptoms varied between first/second-generation and third+ generation Black youth using nationally representative, longitudinal data.

Data were drawn from Waves I-IV of the National Longitudinal Study of Adolescent to Adult Health, covering ages 13-32. We used growth curve models (GCMs) to estimate depressive symptoms across age separately for first/second-generation and third+ generation Black respondents.

GCMs indicated varying trajectories of depressive symptoms between each subgroup. Symptoms followed a U-shape for both groups. For first/second-generation immigrants, symptoms appeared higher at age 13, then decreased faster from adolescence to the early 20s, followed by a faster increase into adulthood, relative to the third+ generation. By age 31, models indicated higher levels of symptoms for first/second-generation immigrants.

Findings from longitudinal data offer additional insight into depressive symptoms variation within Black Americans. As the US immigrant population continues to rapidly increase, future work is needed to better understand the causes of varying trajectories of depressive symptoms.

The Mediating Role of Systemic Inflammation on Racial Disparities in Dementia Incidence

Cesar Higgins* Cesar Higgins Erin B Ware Margaret Hicken Matthew Zawistowski Lindsay C Kobayashi Bhramar Mukherjee Kelly M Bakulski

Background: Disparities in dementia incidence between minoritized racial/ethnic groups and their White counterparts are well documented. The construction of racial memberships captures unequal exposure to socio-economic resources maintained through structural racism. Identifying physiologic mechanisms linking exposure to racism with dementia is important because these pathways could be intervention targets. We tested the mediating role of systemic inflammation, measured as high sensitivity C-reactive protein (hsCRP) concentrations, on racial/ethnic disparities in incident dementia.

Methods: In the Health and Retirement Study (n=6,361), we used baseline serum hsCRP from 2006 and 2008 to explore the mediating role of hsCRP on 2-year incidence of dementia. We used race/ethnicity as proxy for exposure to structural racism. We employed mediation-interaction analysis to decompose the racial/ethnic disparities into: 1) the mediated pure indirect effect of hsCRP on the racial/ethnic disparity, 2) the portion attributable to the interaction between race/ethnicity and hsCRP, and 3) the controlled direct effect (pathways through which racism operates besides hsCRP).

Results: The 2-year incidence of dementia was 3.5% among non-Hispanic White, 13.4% among non-Hispanic Black, and 8.4% among Hispanic participants. Higher hsCRP levels were observed among participants with incident dementia (4.6 mg/mL) versus normal cognition (4.2 mg/mL). Among non-Hispanic Black relative to non-Hispanic White participants, the pure indirect effect of hsCRP was 1% (95% CI: 0%, 2%), the portion attributable to interaction was 4% (95% CI: -8%, 28%), and the controlled direct effect of racism was 95% (95% CI: 71%, 100%). Analysis for Hispanic relative non-White participants did not show mediation by hsCRP.

Conclusions: In Black versus White participants, the mediating effect of hsCRP in incident dementia was minor. Structural factors driving racial disparities may be mediated through other pathways.

Health Promotion

Fractionalized model of the primary prevention in preventive medicine from a light of health promotion activities Hideo Yamazaki* Hideo Yamazaki Soichi Sakabe Xiao Qing Minako Danbara Hikaru Yamazaki Noriko Miyake

Introduction: The model of phased preventive measures in preventive medicine has been classified into three steps at present. However, health promotion proposed by WHO has advocated a five-phased model. Then non-communicable diseases (NCDs) are responsible for 60% of the causes of death in many developed countries. Furthermore, NCDs will be to have cumulative exposure to some disorder or illness. The present study proposed a modernized model of health status which indicated people's poor health state in a transitional stage from wellness to illness. A fundamental scheme of the concept was based on theoretical relation between the theory of natural history of diseases and preventive medicine.

Methods: The authors surveyed time-series on main disease from the past to present in order to extract a fundamental scheme of the present concept using the secondary survey. The survey regarding primary diseases which have been attacked human beings should be covered a period of time from the Dark Ages to the present. Then we examined the relationship between the theory of natural history of diseases and preventive medicine for classifying the primary prevention.

Results: The time-series on main diseases should have four stages. The first stage was shown as an epidemic of acute and infectious digestive diseases. The second was shown as an epidemic of respiratory diseases and the third was shown as an epidemic of chronic and non-infectious diseases. Next, we analyzed the relationship between the theory of natural history of diseases and preventive medicine. Then tree patterns were extracted based on each the corresponding phase. The phases were the correspondence of the susceptibility with primary prevention, of the preclinical with secondary prevention, and of the clinical with tertiary prevention.

Conclusions: It is likely that the first phase of the primary prevention is necessary for dividing into two sub-phases from a light of health promotion activities.

Federal legislation to reduce racial/ethnic inequities in access to worker policies that promote maternal and child health Candice Johnson* Candice Johnson Penelope Howards Helen Chin

Background. Three bills currently under consideration by Congress—the Build Back Better Act, the Healthy Families Act, and the Pregnant Workers' Fairness Act—would provide workers nationwide with access to paid parental leave, paid sick time, and reasonable accommodations during pregnancy. These policies promote maternal and child health, particularly among low-wage workers whose jobs are unlikely to offer these benefits in the absence of a mandate. Without federal legislation, some states have enacted their own version of these policies. We quantified current racial/ethnic inequities in workers' access to these state-level benefits that are caused by this patchwork of policies and that could be reduced by federal legislation.

Methods. Using demographic data from 96,468 participants in the 2016–2019 American Community Survey, we estimated the proportion of recently pregnant workers in each racial/ethnic group who lived in a state with these policies. We used six broad racial/ethnic groups (Latina; non-Latina American Indian/Alaska Native [AIAN], Asian or Pacific Islander, Black, Multiracial, White) and further disaggregated groups when sample sizes allowed.

Results. Among the six broad racial/ethnic groups, Asian or Pacific Islander (50%) workers were the most likely to live in a state that offered all three of paid parental leave, paid sick time, and reasonable accommodations during pregnancy, followed by Latina (41%), Multiracial (31%), White (23%), Black (16%), and AIAN (13%) workers. After disaggregating racial/ethnic groups, Chinese and Dominican workers were the most likely to live in a state with all three policies (65% each) and Cuban workers were the least likely (9%).

Conclusions. Federal legislation granting nationwide access to paid parental leave, paid sick leave, and reasonable accommodations during pregnancy could reduce existing racial/ethnic inequities in coverage.

Do patients receive care from their family physician near the end of life after referral to home care? A retrospective cohort study Mary Scott* Mary Scott Colleen Webber Anna E Clarke Abe Hafid Sarina Isenberg Aaron Jones Amy T Hsu Katrin Cohen James Downar Douglas G Manuel Peter Tanuseputro Michelle Howard

Introduction

Physician home visits at the end of life are associated with better health outcomes including better quality of life, reduced acute care use and costs, and more out-of-hospital deaths. However, the majority of dying patients never receive a physician home visit. Previous literature has shown physicians who perform home visits may be more likely to have previous provided healthcare for their patient. The objectives of this study are to describe the receipt of home visits and community-based care from physicians in Ontario, Canada, and to measure associations between patient characteristics and the receipt of a home visit from a physician during the last year of life.

Methods

We conducted a retrospective cohort study using linked population-based health administrative databases housed at ICES. The study population included all community-dwelling decedents in Ontario between April 1, 2013-March 31, 2018 who were referred to publicly funded homecare services and who had a rostered primary care physician for at least six months before referral. We performed a descriptive analysis to examine the provision of rostered and non-rostered physician home visits and community-based care and fitted a multivariable logistic regression model on the odds ratio (OR) of receiving a home visit from a rostered primary care physician in patients' last year of life after referral to homecare services.

Results

Of the 58,753 decedents with a family physician who received home care in the last year of their life, only 5.3% received a home visit from their family physician. Patient characteristics with higher odds of receiving home visits from their physician were being female (OR: 1.28 [95% CI: 1.21-1.35 p<.0001]), being 85 years of age or older, living in rural areas (OR: 1.09 [95% CI: 1.00-1.18, p 0.047]), and being frail before death (OR: 1.10 [95% CI: 1.02-1.19, p 0.010]). Furthermore, increased odds of receiving a home visit from a physician was observed in those with referrals from a physician (OR: 1.49 [95% CI: 1.39-1.58, p<.0001]) and those with referrals occurring during a hospital admission (OR: 1.20 [95% CI: 1.13-1.28, p<.0001]).

Conclusions

These findings contribute to evidence on community-based care provided to dying patients and how involved rostered primary care providers remain as patients' illness progresses. Building a strong evidence base can contribute to providing appropriate interventions that support patients' desire to receive care at home during the end-of-life period.

Health Services/Policy

Efficacy of a nursing home-based transitional care program for increasing the potential for independent living in the community among hospitalized older adults Maya Murmann* Maya Murmann Annie Sun Amy Hsu Danielle Sinden Benoît Robert Anan Bader Eddeen Kednapa Thavorn Annie H. Sun

Background: Transitional care units offer a potential opportunity to address the capacity pressures and health risks associated with prolonged hospital stays. However, within a publicly-funded system, there are few opportunities for infrastructure development to augment current capacity for sub-acute or post- discharge care and rehabilitation. The aim of this study was to assess the cost and effectiveness of a nursing home (NH)-based transitional care program, which leverages existing infrastructure, to support a hospitalized older adult's transition to independent living at home.

Methods: Using a population-based cohort of older adults, we calculated the total direct cost of care for 190 patients in a NH-based transitional care program (cases) compared to 190 hospitalized older adults who did not receive the intervention (controls). The primary outcome was days without requiring institutional care 6- months following discharge, defined as institutionally-free days. This was calculated by excluding any and all days in hospitals, rehabilitation facilities and NHs within 180 days post-discharge. The incremental cost- effectiveness ratio (ICER) was calculated for cases who received transitional care compared to propensity score–matched control patients.

Results: Transitional care patients had shorter hospital stays, by 9.2 (mean [SD] of 15.7 [12.5] for cases and 24.9 [30.3] for controls) days. Recipients of transitional care had a higher total cost of care by CAN\$957.43 (95% CI: -\$4254.5—\$5552.6) but had 26.9 (95% CI:13.9-39.4) more institutionally-free days compared to control patients. The corresponding ICER was CAN\$35.66 (95% CI: -\$151—\$272) per institutionally-free day.

Conclusions: Through rehabilitative and restorative care, transitional care units have the potential to reduce length of stay in hospital, increase potential for independent living, and reduce risk for subsequent institutionalization.

Documenting insurance discontinuity: improving measurement of a social driver of perinatal health Anna Booman* Anna Booman Kalera Stratton Teresa Schmidt Janne Boone-Heinonen Jonathan M Snowden

Insurance discontinuity occurs when a person experiences changes in health insurance, including uninsurance, and is common perinatally due to relaxed Medicaid eligibility during pregnancy. Self-reported, cross-sectional data document widespread perinatal insurance discontinuity in the US, but detailed longitudinal data are lacking. Our objectives were to (a) define insurance discontinuity frequency and patterns using newly available, provider-recorded longitudinal data from a national safety net population and (b) describe the frequency of insurance discontinuity among sociodemographic groups, relevant to health equity.

Data were taken from the ADVANCE Research Network as part of the PROMISE Study on gestational weight gain. 52,543 OCHIN patients from 47 US states/territories met inclusion criteria, had a pregnancy in 2004-2020, and received care at OCHIN community health centers: clinics that provide care regardless of insurance or ability to pay. Visit-specific insurance type was categorized as Public (e.g., Medicaid, Medicare), Private, or Uninsured. Insurance discontinuity was defined as two types of insurance (e.g., uninsured/public) or all three compared to continuous insurance during a pregnancy.

Of 61,688 pregnancies, 22% showed insurance discontinuity. The median number of prenatal visits was 12 (IQR=5). Pregnancies were more likely to have had uninsured/public discontinuity (16%) than continuous private insurance or continuous uninsurance combined (14%). Of pregnancies with uninsured/public discontinuity, 66% were Hispanic, compared to 56% of the entire population. Additionally, 52% of those who were continuously uninsured and 51% of those who experienced uninsured/public discontinuity were Spanish speaking (vs. 39% overall).

We measured longitudinal insurance patterns throughout pregnancy and stratified them by race/ethnicity and language. Improving measurement of insurance patterns surrounding pregnancy is vital for understanding health and equity outcomes.

Hypothetical interventions on anemia to reduce HIV disparities in adverse birth outcomes

Ellen Caniglia* Ellen Caniglia Rebecca Zash Modiegi Diseko Gloria Mayondi Mompati Mmalane
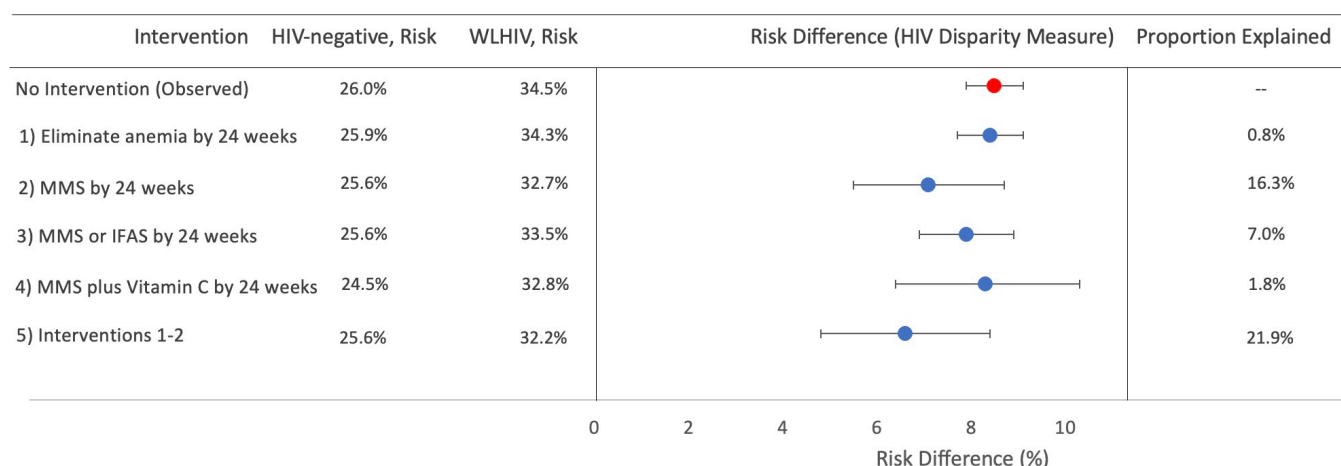Joseph Makhema Angela Bengtson Shahin Lockman Roger Shapiro Sonja A. Swanson

Background: Women living with HIV (WLHIV) have a higher risk of adverse birth outcomes than
HIV-negative women, even in the modern era of antiretroviral therapy. A higher risk of anemia in
WLHIV could partially explain this persistent disparity. We evaluated whether hypothetical
interventions on anemia could reduce these disparities.

Methods: The Tsepamo Study measured birth outcomes at up to 18 delivery sites in Botswana from
2014-2021. We evaluated 5 hypothetical interventions on anemia among women presenting to
antenatal care <24 weeks gestation: 1) eliminate all maternal anemia by 24 weeks; 2) initiate all
women on multiple micronutrient supplementation (MMS) by 24 weeks; 3) initiate all women on iron
and folic acid supplementation (IFAS) or MMS by 24 weeks; 4) initiate all women on MMS plus
Vitamin C by 24 weeks; and 5) a joint intervention including 1 and 2. Any adverse birth outcome
comprised stillbirth, preterm delivery, small-for-gestational-age, or neonatal death. We estimated the
counterfactual disparity measure (CDM) under each intervention using inverse probability weighted
marginal structural models. We compared the CDM with the observed disparity measure (ODM)
under no intervention by calculating the proportion explained (PE).

Results: Of 137,499 eligible women (22% WLHIV), risk of anemia was 13.9% in HIV-negative
women and 25.4% in WLHIV. The observed risk of any adverse birth outcome was 26.0% in HIV-
negative women and 34.5% in WLHIV (ODM, 8.5% [95% CI, 7.9%-9.1%]). The risk of any adverse
birth outcome was smaller under each intervention in both groups. CDMs (95% CIs) ranged from
6.6% (4.8%-8.4%) for the joint intervention eliminate anemia and initiate all women on MMS to 8.4%
(7.7%-9.1%) for eliminate anemia only, corresponding to modest PEs (0.8% to 21.9%) (Figure).

Conclusions: Preventing maternal anemia and expanding MMS access may decrease the risk of
adverse birth outcomes overall and modestly reduce HIV disparities in adverse birth outcomes.

Figure. Observed (Red) and Counterfactual (Blue) Disparity Measures for Any Adverse Birth Outcome
Under Different Hypothetical Interventions on Anemia

Intervention	HIV-negative, Risk	WLHIV, Risk	Risk Difference (HIV Disparity Measure)	Proportion Explained
No Intervention (Observed)	26.0%	34.5%		--
1) Eliminate anemia by 24 weeks	25.9%	34.3%		0.8%
2) MMS by 24 weeks	25.6%	32.7%		16.3%
3) MMS or IFAS by 24 weeks	25.6%	33.5%		7.0%
4) MMS plus Vitamin C by 24 weeks	24.5%	32.8%		1.8%
5) Interventions 1-2	25.6%	32.2%		21.9%

Risk Difference (%)

Systematic Review of Factors Influencing PrEP Use Among Pregnant and Postpartum Women in Sub-Saharan Africa Yangxi An* Yangxi An Anqi Wang

Background: Women across sub-Saharan Africa (SSA) are at an increased risk of HIV acquisition during pregnancy and the postpartum period. Pre-exposure prophylaxis (PrEP) is a safe and effective HIV prevention strategy, but little is known about key influences on maternal PrEP use in high-burden settings. We conducted a systematic review of factors related to PrEP use among pregnant and postpartum women (PPW) in SSA.

Methods: Using PRISMA guidelines, we searched PubMed, Embase, CINAHL, Web of Science, and Cochrane Library for quantitative and qualitative studies published in English between January 2004 and November 2021. Records were screened independently by two reviewers using Covidence. Studies reporting factors that influence PrEP use (initiation, adherence, persistence) among HIV-uninfected PPW in SSA were eligible. Facilitators and barriers to PrEP use were extracted and organized thematically within a socio-ecological framework.

Results: Of 3170 records screened, 14 studies from six countries (South Africa, Kenya, Uganda, Zimbabwe, Malawi, Eswatini) met our inclusion criteria. Individual-level barriers included fears of side effects and lower perceived HIV risk. A desire to protect one's child and higher perceived PrEP effectiveness were associated with improved initiation and persistence. At the interpersonal level, male partners' positive HIV status and risky behaviors motivated women to take PrEP. Anticipated or experienced partner opposition was the most commonly reported barrier. Healthcare providers' approval of PrEP and PrEP counseling were institutional-level facilitators. Anticipated stigma at the community level was a major barrier.

Conclusions: Multi-level barriers can impede oral PrEP use among PPW in SSA despite their interest in HIV prevention. To maximize initiation, adherence, and persistence in this vulnerable population, PrEP should be delivered within complex interventions that target these barriers.
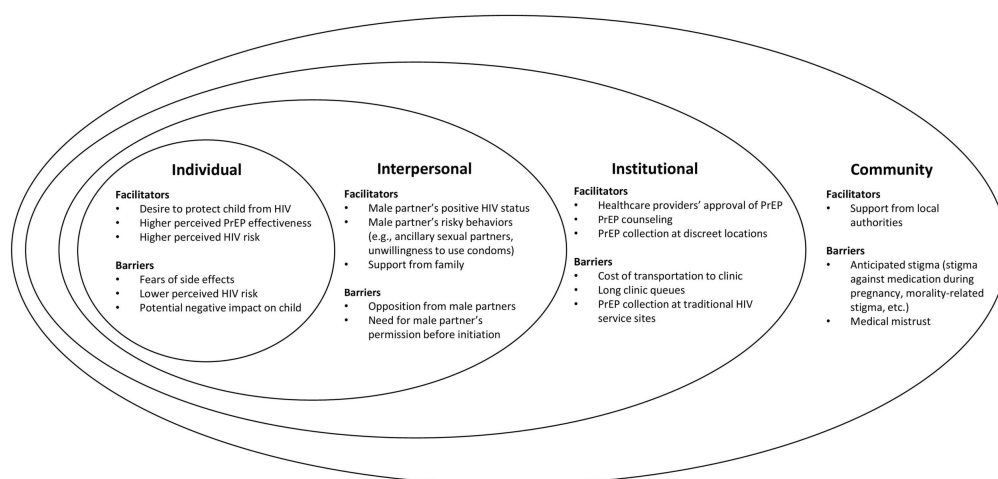
The safety of seasonal influenza vaccination among patients prescribed immune checkpoint inhibitors: a self-controlled case series study using administrative data Alicia Grima* Alicia Grima Jeff Kwong Lucie Richard Jacques Raphael Nicole Basta Alex Carignan Karina Top Nicholas Brousseau Phillip Blanchette Maria Sundaram

Background: Immune checkpoint inhibitor (ICI) therapy for cancer patients carries a risk of severe immune-related adverse events (IRAEs). Since vaccines are immunomodulatory, administering seasonal influenza vaccinations to individuals on ICI therapy may exacerbate this risk. However, these vaccines provide substantial benefit to this at-risk population. As severe IRAEs are rare, previous vaccine safety studies in this population have been underpowered and have shown conflicting results.

Methods: We used health administration data on adult Ontarians who initiated ICI therapy and received an influenza vaccine between January 1, 2012, and December 31, 2019. We conducted a self-controlled case series study, with a pre-vaccine control period (12-weeks post-ICI initiation to 14 days before vaccine), risk period (42 days post-vaccine), and a post-vaccine control period (until observation end). Each individual contributed a maximum of 2 years of person-time. Emergency department (ED) visit(s) and/or hospitalization for any cause was used as a surrogate measure of severe IRAE event frequency. We fitted a fixed effect Poisson regression model incorporating seasonality and time to estimate incidence.

Results: We identified 1133 patients who received an influenza vaccine on ICI therapy. The majority were aged ≥66 years (72.7%), male (62.8%), and had lung cancer (53.9%). A quarter (25.9%) experienced an ED visit and/or hospitalization during the observation period. The rate of ED visits and/or hospitalization per person-days in the risk and control periods were similar, with an incidence rate ratio of 1.04 (95% CI: 0.75, 1.45). Subgroup and sensitivity analyses revealed similar findings.

Conclusion: Receipt of a seasonal influenza vaccine was not associated with an increased incidence of ED visit or hospitalization among adults on ICI therapy. The results from this analysis suggest no significant safety concern with administering influenza vaccines to this patient population.

Impact of Ear Infection History and Hearing Impairment on Children's Academic Achievement in Primary School: The U.S. Early Childhood Longitudinal Study–Kindergarten Class of 2010-11 (ECLS-K:2011) Chuan-Ming Li* Chuan-Ming Li Howard J. Hoffman Le Chen Christa L. Themann Gregory A. Flamme Mabel L. Rice

Background: Ear infections (EIs) are a common cause of hearing loss in children. The link between these conditions and academic performance is inconclusive in the literature.

Objective: To estimate prevalence of medically-diagnosed EIs, hearing loss, and associations with academic performance.

Methods: ECLS–K:2011 drew a national sample of 18,170 children and followed them from kindergarten to 5th grade. Parent-reported health/demographic information was obtained, including history of medically-diagnosed EIs and perceived hearing trouble (HT). Reading, math, and science achievement were assessed annually. Pure-tone thresholds were obtained on a subsample of ~3,500 in 2nd, 3rd, and 5th grades. Statistical analysis included logistic mixed models, generalized estimating equations, and PATH modeling.

Results: EI prevalence was 58% before age 2, 50% from age 2 to kindergarten entry, 31% in kindergarten, 20% in 1st, 17% in 2nd, 15% in 3rd, and 13% in 4th and 5th grades. By 5th grade, 82% of children had at least one EI and 30% had one or more time periods with 3 or more EIs. Prevalence of reported HT ranged from 2.6% to 3.2% in each time period. Prevalence of measured hearing impairment (HI) was 11.7% in 2nd grade, 7.7% in 3rd, and 6.5% in 5th. After controlling for other risk factors, EIs were significantly associated with increased HT [OR (95% CI): 3.4 (2.7-4.0)] and measured HI [2.2 (1.2-3.1)]. EI history was significantly associated with decreased reading (p=0.0001), math (p=0.002), and science scores (p=0.06). Measured HI was also associated with decreased reading (p=0.001), math (p=0.0003), and science scores (p=0.03). EIs were associated with reading (p=0.007) and math scores (p=0.006) only in the current year, not in subsequent years.

Conclusion: Prevalence of EIs and hearing loss is high in children. EIs and HT/HI are associated with decreased academic achievement. EIs only impacted school performance in the current year. Prior history of frequent EIs is associated with occurrence of subsequent EIs.

Hepatitis C virus and lung cancer: a population-based 14-year long-term descriptive study
Cheng-Chih,Teng* Cheng-Chih Teng Yu-Ching Chou Chien-An Sun

Hepatitis C virus and lung cancer: a population-based 14-year long-term descriptive study

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Background: Lung cancer (LC) is third leading cancer in Taiwan. Hepatitis C virus (HCV) has been recognized as potential risk factor in developing disease. However, secular trend studies of lung cancer with HCV are limited. This descriptive study examined the incidence of lung cancer with HCV in a large-scale, population-based Taiwanese cohort.

Methods: From 2000 to 2008, 5182 new cases with HCV were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating incidence rates in different sex, age groups and periods. For long term trends, we followed up until December 31, 2013.

Results: The incidence of lung cancer was 18.50 among HCV patients per 10,000 person-years. The incidence rate was 20.50 among men and 16.48 among women per 10,000 person-years. The incidence rate of lung cancer was higher in men. After stratifying age into 5 groups, we found that the incidence rate of lung cancer per 10,000 person-years was 3.18 in 30-39 years old, 18.75 in 50-59 years old and 34.81 in ≥60 years old(there is no cases in 20-29 and 40-49 years old). Patients have higher incidence rate of lung cancer when age is increasing. Also, incidence rate of lung cancer was 13.79, 19.52, 14.42, and 14.47 by visiting 0 time, 1-2 times, 3-8 times, and >9 times in HCV clinical visits respectively.

Conclusion: In the past 14 years, the incidence of lung cancer had a profound impact on our life. By means of the big data, our finding suggested incidence rate of lung cancer with HCV is steadily rising. Thus, the study indicated a positive correlation between HCV and lung cancer. Future research on lung cancer might extend the explanations of HCV.

Keywords: Lung cancer (LC), National Health Insurance Research Database (NHIRD), Hepatitis C virus (HCV).

Weight gain during tuberculosis treatment is associated with increases in post-tuberculosis blood glucose levels Argita Salindri* Argita Salindri Maia Kipiani Teona Avaliani Leila Goginashvili Sergo Vashakidze Zaza Avaliani Sara Auld Hardy Kornfeld Russell Kempker Matthew Magee

Background: Weight loss is characteristic of tuberculosis (TB) disease, and weight gain during TB treatment is associated with successful outcomes. Yet little is known about weight gain during TB treatment and post-TB metabolic health. We assessed the association between change in body mass index (BMI) during TB treatment and post-TB markers of metabolic health.

Methods: During 2018-2022, we conducted a cohort study of patients successfully treated for TB in the country of Georgia. Eligible participants were HIV-negative adults with newly diagnosed laboratory-confirmed pulmonary TB. The study exposure was relative BMI change between treatment initiation to end of TB treatment (dichotomized using ≥5% increase cut-off). Study outcomes were changes in glycated hemoglobin (HbA1c) and visceral adipose index (VAI), both measured at the end of TB treatment and 6-months post-TB treatment. We estimated the association between change in BMI and study outcomes using multilevel linear models.

Results: Among 124 participants enrolled at the end of TB treatment, 93 (75%) had 6-month follow-up and BMI change information available and were included in analyses. Median relative BMI change was +4.3% (interquartile range 0–9%). There were 39 individuals (42%) with ≥5% increase of BMI, 53 (57%) had similar BMI, and 1 (1%) had ≤5% decrease. Among those with an increase of BMI during TB treatment, the adjusted post-TB change in mean HbA1c was 0.43 (95%CI 0.06, 0.80) percentage points higher than those with no BMI change, accounting for repeated measures. Similarly, among those with an increase of BMI during TB treatment, the adjusted post-TB change in mean VAI was 0.11 (95%CI -0.26, 0.48) points higher than those with no BMI change.

Conclusions: Our findings indicate that weight gain during TB treatment may influence blood glucose levels after TB treatment completion and could be a potential marker of metabolic health post-TB treatment.

Nosocomial Amplification: Identifying Important Parameters in a Community-Hospital Model Katelin Jackson* Katelin Jackson Eric Lofgren

Background: The phenomena of emerging infectious diseases accelerating once they reach healthcare facilities has been well documented. Outbreaks of MERS-CoV, SARS-CoV, and COVID-19 have led to in-hospital transmission where the initial patient infects healthcare workers, patients, and visitors, with infection control policies unable to curtail the spread early on. Nosocomial amplification, the phenomenon, causes an undue burden on a hospital that's already strained from the pandemic. We aimed to understand which hospital-level parameters have the greatest impact on the community and vice versa.

Methods: We adapted an SEIR compartmental model to have three interconnected units: a community, an ER, and an ICU to determine the number of COVID-19 acquisitions in each of them over a hypothetical year. The model was stochastically simulated using Gillespie's Direct Method for 1000 iterations. A parameter sensitivity analysis assessed each parameter's effects on the model, with original parameter values allowed to vary +/- 50%.

Results: Our analysis found that parameters impacting the shorter stay ER had a disproportionate impact as compared to the ICU, as did parameters governing the level of asymptomatic transmission. Transmission between healthcare workers facilitated within-hospital transmission even when strict patient-based cohorting and testing was in place. Extensive community-level transmission was also found to readily overwhelm hospital-level infection control at realistic levels of effectiveness and compliance.

Conclusion: These findings illustrate that hospitals and the community are tightly linked systems. Hospitals may reintroduce infection into the community that might have contained or mitigated ongoing outbreaks or introduce the disease into a disease-free population; community transmission puts tremendous pressure on infection control. We can model policies in the future to curb COVID-19 outbreaks to minimize nosocomial amplification.

Trends in self-harm rates among adolescents, by rural/urban location, United States, 2013-2019 Jing Wang* Jing Wang Trinh Eva Welder Laura Yard Ellen Brown M Melissa Stone Deborah

Adolescents experience the highest rate of self-harm among all ages. Rural adolescents are disproportionally affected by higher self-harm rates compared to urban peers. However, trends in self-harm rates by rural/urban setting have not been studied to inform rural-urban disparities overtime. We examined 2013-2019 Nationwide Emergency Department Sample to identify emergency department (ED) visits for self-harm among adolescents aged 10-19 years in rural and urban settings. Annual population estimates for rural and urban residents were obtained from Census data. We calculated the rates of ED visits for self-harm among adolescents at rural and urban settings respectively. Then we derived rate ratios (RR) between rural and urban residents and estimated the confidence intervals for RRs using delta methods. Significant changes in ED visit rates or RRs overtime were determined by non-overlapping confidence intervals. Among adolescents in both rural and urban settings, ED visit rates for self-harm increased from 2013-2015 and 2016-2017, then leveled off from 2017-2019 (Figure). The rural-urban gap in self-harm remained unchanged (RR: 1.3[95% CI: 1.1, 1.4] in both 2013 and 2015; 1.3[1.2, 1.5) in both 2016 and 2019). In 2019, the ED visit rate for self-harm was 437.6 per 100,000 for rural adolescents, 33% greater than the rate for urban adolescents (327.8 per 100,000 residents). For subgroups, rates of self-harm increased between 2016 and 2017 and plateaued thereafter for both age groups (10-14 years and 15-19 years) and boys and girls at both rural and urban settings. RRs remained stable for all subgroups. In conclusion, despite increasing and leveling off trends in the rates of self-harm for adolescents during 2013-2019, no improvement in rural-urban disparity was observed. Rural adolescents continued to experience one-third higher rates for self-harm than urban peers. These findings call for effective prevention strategies to address rural-urban disparities in self-harm.

Rates And Rate Ratios for Emergency Department Visits for Self-harm Between Adolescents Aged 10-19 Years at Rural and Urban Settings, United States, 2013-2019
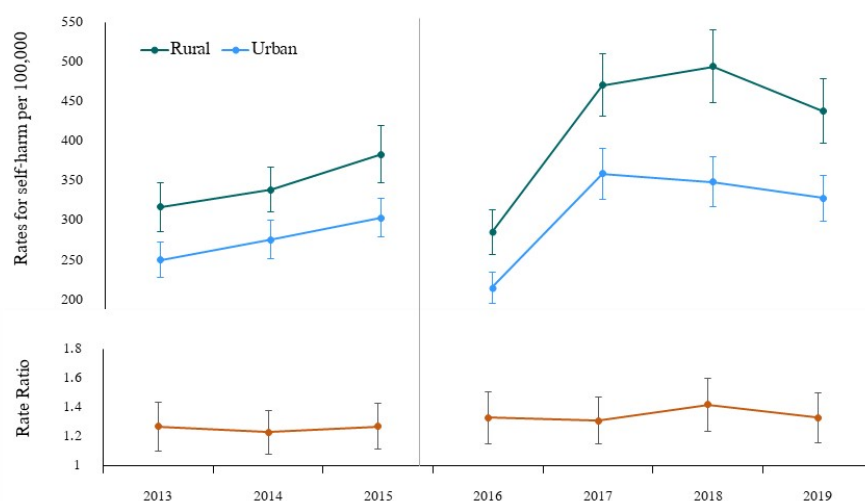
Data sources: National Emergency Department Sample (NEDS) and Annual County Resident Population Estimates from Census

The grey vertical line indicates the switching in diagnosis coding to ICD-10-CM system in 2015. The error bars indicate 95% confidence intervals

Injuries/Violence

Reporting of intimate partner violence among male couples: cross-sectional and serial interpartner agreement of reported IPV experiences and perpetration Alison Walsh* Alison Walsh Rob Stephenson

Intimate partner violence (IPV) in male couples is a public health concern, but measurement error in self-reported IPV data from gay, bisexual, and other men who have sex with men (GBMSM) is understudied. Research in heterosexual couples has found that IPV-underreporting can be differential between victims/perpetrators, and by gender; it is unknown if data from GBMSM has similar limitations. This study analyzed dyadic concordance in IPV data from a sample of 404 male couples in the US (2016-2017); IPV data was collected from individual male partners at 3 time-points (baseline (past-year IPV), 3- and 6-months (past 3-months IPV)). Interpartner agreement between self-reported IPV experiences and partner-reported IPV perpetration was calculated at each time-point (observed agreement; kappa statistics), for emotional, physical/sexual, controlling, monitoring, and/or any IPV. Serial dyadic concordance over the 3 surveys was analyzed to determine if couples had reliable data over time. Past-year experienced-IPV prevalence was 66.41% and perpetration, 64.42%; past 3-month experienced-IPV at 3- and 6-months were 47.30% and 52.57%, respectively, and perpetration, 46.30% and 46.30%. Emotional IPV was the most commonly reported IPV type. Interpartner agreement was consistently low across surveys, any IPV, and 4 IPV types. Observed agreement was higher for those who did not report IPV, compared to those who reported experiencing IPV. At an individual-level, interpartner agreement on one survey was not significantly associated with agreement on subsequent survey(s). Researchers should be cognizant of the potential for discordant reports of IPV experiences and perpetration among GBMSM couples and that measurement error in this data may vary across IPV types; perpetration and victimization; and longitudinally. Further research on IPV data quality in male couples is needed.

Youth Violence and Mental Health Outcomes: A Sex-Disaggregated, Cross-Sectional Analysis for Colombia Luissa Vahedi* Luissa Vahedi Ilana Seff Melissa Meinhart Arturo Harker Roa Lindsay Stark

The mental health burden of violence among Latin American youth is a substantive public health issue. We explored sex-stratified relationships between violence exposures and mental health among Colombian youth.

The analysis uses the 2018 Colombian Violence Against Children and Youth Survey: a nationally representative sample of 13-24-year-old girls (N=1406) and boys (N=1299). Exposure variables were, (1) binary lifetime sexual, emotional and physical violence victimization and (2) poly-victimization. Six binary mental health-related outcomes were considered: Lifetime suicidal thoughts, lifetime self-harm, past month psychological distress, past month binge drinking, current smoking and past moth drug use. Sex-stratified logistic regressions estimated the odds of each outcome given violence exposure, while adjusting for covariates.

Female youth exposed to *emotional violence* had higher odds of suicidal thoughts (aOR: 4.229; 95%; CI: 2.087,8.57), self-harm (aOR: 2.524; CI: 1.197,5.325), and psychological distress (aOR: 2.505; CI: 1.246,5.035), compared to unexposed females; exposure to *sexual violence* was associated with suicidal thoughts (aOR: 3.926; CI: 1.871,8.236) and self-harm (aOR: 3.959; CI: 1.615,9.707). *Physical violence* was generally not associated with internalized mental health sequelae for females or males. For males, exposure to *emotional violence* was significantly associated with suicidal thoughts (aOR: 4.592; CI: 1.324, 15.928) and psychological distress (aOR: 3.514; CI: 1.738, 7.104), but not self-harm. *Sexual violence* was associated only with suicidal thoughts (OR: 4.805; CI: 1.836,12.576) for males.

Poly-victimization was consistently and positively associated with internalized mental health sequela among females, and to a lesser degree for males. *Substance use outcomes* for males or females were not associated with violence. Findings highlight the mental health burden of emotional violence and the need to elucidate gender and sex specific mechanisms.

Assessing the importance of past physical activity in predicting current injury risk using weighted cumulative exposure methods Chinchin Wang* Chinchin Wang Michal Abrahamowicz Marie-Eve Beauchamp Russell Steele Jay Kaufman Ian Shrier

Background: While physical activity is important for health, it can also lead to injury. Injury risk is affected by current and past activity. Past activity may predispose to injury through tissue damage and insufficient recovery or protect against injury by strengthening tissue with sufficient recovery. It is unclear what the relevant time window and relative importance of past activity are in predicting time to injury. Flexible weighted cumulative exposure (WCE) methods may be applicable to this problem.

Objective: Determine the relative importance of activity done in past weeks in predicting current injury risk conditional on activity in the current week.

Methods: We applied WCE methods to weekly data from 1670 schoolchildren collected over 5.5 years. We estimated weight functions for the association between the number of activity sessions in past weeks and time to first injury, conditioning on the number of activity sessions in the current week. We estimated functions using different time windows and used the Akaike Information Criterion to determine the best fitting function. We generated 95% confidence bands by bootstrap resampling.

Results: Higher levels of activity recorded in the previous 2 to 9 weeks were predictive of increased risk of injury, as reflected by positive weights (Figure 1). Given the same recent activity history, activity more than 9 weeks previous appeared protective. There was limited evidence of a protective association for activity recorded in the previous week, with great uncertainty. This may be expected even if previous week activity is not causally protective. Those with many activities in the previous week have smaller increases in activity in the current week relative to those with few activities in the previous week. This smaller proportional increase in activity is expected to lead to fewer injuries.

Conclusion: WCE methods provide insight into the time-specific associations between past physical activity history and injury.
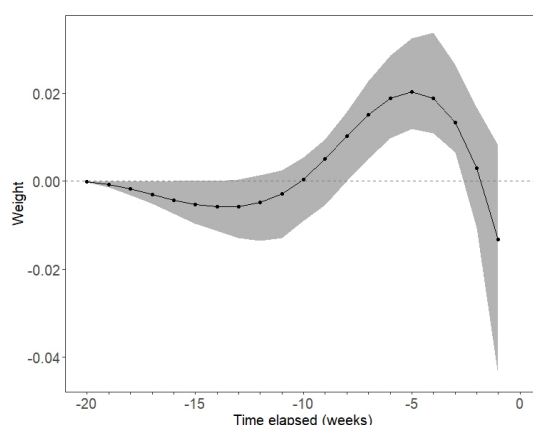

Figure 1. Weighted cumulative exposure function for the association between the number of physical activity sessions in the past week and injury risk in the current week (time 0), conditional on the number of physical activity sessions in the current week. Dots represent weights; shaded area represents 95% bootstrap confidence interval. Positive weights imply a harmful association while negative weights imply a protective association.

Association of downgraded felony convictions and subsequent violent and firearm-related crime perpetration in Washington State Julia Schleimer* Julia Schleimer Miriam Haviland Andrew Bowen Amy Gallagher Deirdre Bowen Ali Rowhani-Rahbar

Background: Individuals convicted of a felony are generally prohibited from purchasing firearms under US federal law. However, those charged with a felony but convicted of a misdemeanor ("downgraded conviction") are in many states, including Washington, legally able to acquire firearms. The risk of subsequent violent and firearm-related crime among these individuals is unknown. Methods: In this retrospective cohort study, we obtained data on all individuals 18 and older convicted of a misdemeanor in Washington superior courts from 1/1/2015-12/31/2019. We used a propensity score and nearest-neighbor algorithm to match individuals with a downgraded conviction to individuals without a downgraded conviction (i.e., only misdemeanor charges) on age and gender in a 4:1 ratio. We examined the first subsequent charge for violent crime and, separately, firearm-related crime, following individuals until the outcome of interest, incarceration, death, or the end of the study (12/31/2020), which ever occurred first. The Fine-Gray method was used to estimate subdistribution Hazard Ratios (sdHR), considering death and incarceration as competing events. Results: The cohort comprised 4,797 individuals, 80% of whom had a downgraded index conviction. The rate of subsequent violent crime per 1,000 person-years was lower among individuals with downgraded (40.5) vs. non-downgraded convictions (43.7), while the rate of subsequent firearm-related crime was higher among those with downgraded (8.4) vs. non-downgraded convictions (5.2). The sdHR for violent and firearm-involved crime comparing those with vs. without a downgraded conviction was 0.92 (95% CI 0.73, 1.17) and 1.56 (95% CI 0.77, 3.17) respectively, controlling for whether the index crime was violent or firearm-related. Conclusion: Those convicted of a misdemeanor in superior court, regardless of the level at which they were charged, experience high risk of subsequent firearm-related and, particularly, violent crime perpetration.

A 28-Year Prospective Analysis of Serum Vitamin E, Vitamin E-Related Genetic Variation and Risk of Prostate Cancer Wayne R. Lawrence* Wayne Lawrence Jung-eun Lim Jiaqi Huang Stephanie J. Weinstein Satu Mannistö Demetrius Albanes

Objective: Investigate the relationship between serum α-tocopherol concentration and long-term risk of prostate cancer, and evaluate the interaction with vitamin E–related genetic variants and their polygenic risk score (PRS).

Methods: We conducted a biochemical analysis of 29,102 male Finnish smokers in the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Serum α-tocopherol was measured at baseline using high-performance liquid chromatography, and 2,724 prostate cancer cases were identified during 28 years of follow-up. Cox proportional hazards models examined whether serum α-tocopherol concentrations were associated with prostate cancer risk. Among 8,383 participants, three SNPs related to vitamin E status (rs964184, rs2108622, and rs11057830) were examined to determine whether they modified the relationship between serum α-tocopherol concentrations and prostate cancer risk, both individually and as a PRS using logistic regression models.

Results: No association was observed between serum α-tocopherol and prostate cancer risk (fifth quintile (Q5) versus Q1 hazard ratio (HR)=0.87, 95% confidence interval (95% CI) 0.75, 1.02; p-trend=0.57). Though no interactions were seen by population characteristics, high α-tocopherol concentration was associated with reduced prostate cancer risk among the trial α-tocopherol supplementation group (Q5 quintile versus Q1 HR=0.79, 95% CI 0.64, 0.99). Finally, no associated interaction between the three SNPs or their PRS and prostate cancer risk was observed.

Conclusion: Although there was a weak inverse association between α-tocopherol concentration and prostate cancer risk over nearly three decades, our findings suggest that men receiving the trial α-tocopherol supplementation who had higher baseline serum α-tocopherol concentration experienced reduced prostate cancer risk. Vitamin E–related genotypes did not modify the serum α-tocopherol-prostate cancer risk association.

Mental Health

A network approach on PTSD symptoms with comorbid depressive symptoms in Korean general population after the outbreak of the COVID-19 pandemic Yu Jin, Lee* Yu Jin Lee Hyeon Chang, Kim Sun Jae, Jung

Background

The prolonged COVID-19 pandemic has a significant impact on mental health in the general population. These stressful events can result in high rates of comorbidity such as post-traumatic stress disorder (PTSD) and depression. However, the post-traumatic implication of this symptom topology with depressive symptoms has not been adequately studied yet. In the current study, we used network analysis approach to explain the interplay between PTSD and depressive symptoms after the outbreak of the COVID-19, stratified by age.

Methods

Participants (N=1,970) completed an online mental health survey from a community-based prospective cohort study known as the Cardiovascular and Metabolic Etiology Research Center. The PTSD and depressive symptoms were estimated by online survey versions of the PTSD Checklist for the DSM-5 (PCL-5) and Patient Health Questionnaires (PHQ-9), respectively. Partial correlation network was utilized to plot the comorbid network structure incorporating both the PCL-5 and the PHQ-9 items, and then identify centrality and bridge centrality after the goldbricker test for a redundancy test.

Results

The PCL-5 and PHQ-9 items formed two separate clusters within the comorbid network. Flashbacks of the PCL-5 and depressed mood of the PHQ-9 had a high centrality, and the same result was suggested after stratifying by age group. Additionally, the most bridge central symptoms were sleeping disturbance of the PCL-5 and sleeping problems of the PHQ-9, and the same results were suggested in the 30-40s.

Conclusion

Flashbacks and sleep problems were the most central and bridge central symptoms, respectively, in the comorbid network of PTSD and depressive symptoms after the COVID-19 pandemic. Inspection of the comorbid network of interactions between symptoms may have resulted in new understanding of the comorbidity structures of mental disorders and may improve the effectiveness of prevention of comorbidity.

Mental Health

The association between previous social network properties and PTSD symptoms during COVID-19 pandemic Jisu Yang* Jisu Yang Hyeon Chang Kim

Background: This study aimed to investigate the association between social network properties and Posttraumatic Stress Disorder (PTSD) status during the Coronavirus disease (COVID-19) pandemic.

Methods: Among people who participated in the community cohort study from 2013 to 2018, a total of 1144 people who responded to all three online surveys in March 2020(1st), August 2020 (2nd), and March 2021(3rd) were included (381 men and 763 women). As social network variables, social network size and subjective intimacy were measured. The association between the baseline social network indices and the Post Traumatic Stress Disorder Checklist for DSM-5 (PCL-5) score in the 1st, 2nd, and 3rd online surveys were respectively analyzed and the associations were compared with each other. The association between subjective intimacy and PTSD was further stratified by social network size. A generalized linear model was applied after adjusting for confounders. All analyzes were conducted separately for men and women.

Results: In both men and women, subjective intimacy was negatively associated with PCL-5 scores (men: β=-0.49, SE=0.18, p=0.008; women: β=-0.30, SE=0.14, p=0.029). There was no statistically significant association between social network size and the PCL-5 score. Stratified by median social network size, only men with higher social network size showed a statistically significant association between subjective intimacy and PCL-5 scores (β=-0.50, SE=0.21, p=0.018). For women, the lower social network size group showed a marginally significant negative association between subjective intimacy and PCL-5 scores (β=-0.66, SE=0.34, p=0.053). When comparing the first, second, and third online surveys, the negative associations between subjective intimacy and PCL-5 scores gradually increased over time.

Conclusion: Subjective intimacy is associated with the lower PTSD association in the COVID-19 pandemic situation and the magnitude of association tends to increase over time.

Association between social network and cognitive function: a cross-sectional assessment from the Cardiovascular and Metabolic Disease Etiology Research Center cohort (2013–2018) Jimin Kim* Jimin Kim Ji Su Yang Hyeon Chang Kim Sun Jae Jung

Background

This study aimed to investigate how social networks are associated with cognitive function in the middle-aged and elderly Korean community population.

Methods

A total of 7,704 individuals over the age of 50 were included from the baseline recruitment of the Cardiovascular and Metabolic Disease Etiology Research Center cohort from the years 2013 to 2018. Egocentric social network characteristics including network size, intimacy, and frequency of face-to-face meetings were measured as exposures, and Korean version of Mini-Mental State Examination score was measured to reflect general cognitive function as an outcome. We also stratified the analysis by income level to investigate the interaction effect. A generalized linear regression model was used, adjusting for age, gender, socioeconomic status, lifestyle factors, depressive symptoms and study settings.

Results

Social network properties were positively associated with cognitive function in both men and women. However, the specific estimates varied according to gender. In men, frequency was most significantly associated with cognitive function (standardized ß=0.093, p-value=0.0001). In women, the strongest association with cognitive function was found in size (standardized ß=0.055, p-value=0.001). The interaction was only significant between income and frequency on cognitive function in both men and women.

Conclusion

There were positive associations between social network properties (i.e., size, intimacy and frequency of face-to-face meetings) and cognitive function. The degree of association varied according to social network properties, gender, and income level. Overall, among social network properties, social network size was an important factor in cognition of women, whereas frequency was important in cognition of men.

Time-series analyses of suicidality-related Google searches and emergency department visits in California and Arizona, 2007-2015. Hilary Colbeth* Hilary Colbeth Sidra Goldman-Mellor Ellen Eisen Krista Neumann Corinne Riddell

Objective Rates for United States emergency departments (ED) visits for nonfatal self-harm increased by 42% from 2001-2016, reflecting a growing public health challenge. Previous research on the use of suicide-related Internet searches as a proxy for self-harm and suicidal ideation has focused on suicide mortality and provided conflicting evidence. Our analysis focuses upstream and explores the internet as a prediction tool for ED visits related to suicidal ideation with or without self-harm.

Methods Over a 9-year study period (2007-2015), suicidality-related search volume data were queried from the Google Health Application Programming Interface (API) for California and Arizona. These states were chosen for their differing age distributions and rigorous ED injury coding policies. We examined results separately by search category (general, methods, or prevention-related) and for all queries combined. Prewhitened autoregressive integrated moving average (ARIMA) models temporally assessed the correlation between each Google search category and ED visits.

Results Most search categories in both states were not temporally associated with overall ED visits and no associations were observed with methods-related searches. However, in both states, strong negative correlations at negative time lags were associated with prevention-related searches. Higher prevention-related queries were associated with lower ED visits approximately four to six weeks later.

Conclusions Increased Google searches representative of help-seeking terms were consistently associated with lower ED visits in the following four to six weeks. Our results indicate that help-seeking internet-based searches may be predictive of future ED visits and that online suicide prevention resources may present meaningful support opportunities.

Mental Health

Women's Mental Health Status in the First 8 Years after Childbirth: Longitudinal Findings from the All Our Families Cohort in Canada Kamala Adhikari* Kamala Adhikari Nicole Racine Erin Hetherington Sheila McDonald Suzanne Tough

Objective: This study examined the prevalence of elevated maternal anxiety and/or depression up to 8 years after childbirth and the association between work-life balance and relationship dynamic factors and mental health challenges over time.

Methods: This study used data from the All Our Families longitudinal pregnancy cohort. Work-life balance, relationship factors, anxiety, and depression were measured at repeated time points from 4 months to 8 years after the index delivery. The proportion of women with elevated anxiety and/or depression was calculated at each available time period. Generalized estimating equation models were used to examine the association between work-life balance and relationship factors and anxiety and/or depression from 3 to 8-years after childbirth. Absolute probability of having anxiety and/or depression, averaged over time, was estimated across those with and without challenges with work-life balance and relationship dynamics. The models were adjusted for known risk factors such as maternal age, education, income, and perinatal anxiety and/or depression.

Results: The prevalence of elevated anxiety and/or depression within an 8-year period ranged from 18.8% (at 4-months) to 26.2% (at 8-years). The adjusted odds ratio of anxiety and/or depression was 3.2 (95% CI (confidence interval)=2.6, 4.0) for those with the high-level time crunch and 3.5 (95% CI=2.9, 4.3) for those juggling family responsibilities compared to their counterparts. Similarly, experiencing financial crunch and poor partner relationship and support were associated with increased mental health difficulties. Women without risk factors had a 24% lower absolute adjusted prevalence than those with a risk factor.

Conclusions: Findings suggest that monitoring mothers for anxiety/depression and early management of work-life balance and relationship risk factors beyond the postpartum period may be important.

Reported Discrimination and Mental Health: Survey Responses from Upwardly Mobile African Americans Akilah Collins-Anderson* Akilah Collins-Anderson Darrell Hudson

Introduction. Although studies have shown that higher adult socioeconomic status decreases health disparity, the socioeconomic position of upwardly mobile African Americans does not guarantee larger health gains as it often takes extensive social and mental investments to achieve. As a common psychosocial stressor, discrimination is associated with poor mental health in racial minority groups. Understanding exposure of discrimination within a socioeconomically upwardly mobile racial minority group is underexplored.

Objective. Investigate "costs of upward mobility" on the mental health of Black Americans by examining the prevalence and types of discrimination and association between depression and exposure to discrimination.

Method. A cross-sectional online survey (n=507) was collected in early 2021 that included 135 items, including assessment of sociodemographic, health, and psychosocial variables. Eligibility criteria included self-identified as Black/African Americans, 25 years old or older, and completed a 4-years college degree or higher. We used ordinal logistic regression to examine the association between discrimination and depression among the sample.

Results. Overall, 77% of the respondents experienced major discrimination. Based on the Expanded Everyday Discrimination Scale, being treated with less courtesy than others was the most reported experience of discrimination. After controlling for sociodemographic variables (age, gender, income, relationship status, education), respondents who reported being treated with less courtesy were almost four times more likely to report depressive symptoms compared to those who did not report this form of discrimination (OR =3.88, 95%- CI= 1.35-11.16).

Conclusion. The findings drawn from this study indicate the pernicious effect of costs of mobility, including exposure to racial discrimination and high-effort coping. These factors have a deleterious effect on the health and well-being of Black Americans, notwithstanding the effects of greater socioeconomic resources. These findings corroborate results from previous studies that have demonstrated differential returns on human capital investments among Black Americans.

Identifying risk factors for hospitalization with mental illness and/or behavioral disorders and concurrent temperature-related illness in New York State Heather Aydin-Ghormoz*

Heather Aydin-Ghormoz Temilayo Adeyeye Seema Nayak Tabassum Insaf

Background: New York State (NYS) experiences extremely low temperatures in the colder months (October – April). In NYS extreme heat events in the warm months (May – September) are expected to increase over the next 60 years. Extreme temperature events are linked to increased mortality, hospitalizations, and emergency department visits for individuals with mental and behavioral disorders (MBD). **Methods:** Using data from the NYS Statewide Planning and Research Cooperative System between 2005 – 2019, multivariate adjusted log binomial regression models were used to estimate risk ratios (RR) of risk factors for hospitalizations with a diagnosis of MBD and concurrent heat-related illness (HRI) or cold-related illness (CRI). **Results:** Dementia (RR 1.65; 95% CI:1.49, 1.83), schizophrenia (RR 1.24; 95% CI:1.10, 1.39), and non-dependent drug/alcohol use (RR 1.10; 95% CI:1.00, 1.21) were associated with an increased risk for HRI among MBD hospitalizations; while alcohol dependence (RR 2.10; 95% CI:1.99, 2.22), dementia (RR 1.52; 95% CI:1.44, 1.60), schizophrenia (RR 1.22; 95% CI:1.15, 1.30), and non-dependent drug/alcohol use (RR 1.20; 95% CI:1.15, 1.26) were associated with an increased risk of CRI among MBD hospitalizations. Risk factors for hospitalization with MBD and HRI include increasing age, male gender, African American race, uninsured status, and medium hospital size. Risk factors for hospitalization with MBD and CRI include increasing age, male gender, African American race, being on Medicare, Medicaid, or uninsured, presence of respiratory disease, and rural hospital location. **Conclusion:** Our results agree with prior risk factor findings for MBD hospitalization with a concurrent HRI. This study adds to the literature by identifying additional risk factors for MBD hospitalization with a concurrent CRI, such as substance related addictive disorders, alcohol dependence, Medicare status, Medicaid status, and rural hospital location.

**Race and gender differences in the effect of precarious employment on mental health and cognitive functioning in older age** Anita Minh* Anita Minh Sarah Andrea Shanise Owens Jessie Seiler Lindsey Richardon Anjum Hajat

Background: Racialized minorities and women have a disproportionately high burden of mental and neurological disorders in older age. This study examines how race and gender modify the impact of precarious employment conditions (including low wages, employment insecurity, part-time and inconsistent work, the lack of union representation, and inadequate benefits) on mental health and cognitive functioning in older Americans.

Methods: We used data on adults over age 50 in the labor force from the Health and Retirement Study (1992-2018, n=22,383, median observations=3). We created a precarious employment score (PES) from 13 self-reported items capturing respondents' employment relationship using Principal Components Analysis. Depression was measured using 8 items from the Centre for Epidemiological Studies-Depression Scale. Cognitive functioning was measured using a task-based assessment of Episodic Memory (score range:25.3-78.5). We used generalized estimating equations to estimate the joint effects of PES, race, and gender.

Results: On average, participants had 1.3 (+/-1.8 SD) depressive symptoms and a cognition score of 52.4 (+/-9.5 SD). Across the studied period, white men had the lowest PES and women of color had the highest PES. Higher PES was related to 1.2% greater depressive symptoms (95%CI:1.0,1.3) and 0.1% lower (worse) episodic memory (95%CI:-0.1,-0.6), even after accounting for education and other characteristics. Relative to white men, the magnitude of association between PES and depression was larger for both men and women of color. The magnitude of the association between PES and episodic memory was smaller for white women.

Implications: Conditions of precarious employment are detrimental to mental health and cognitive functioning in older age. Race-based marginalization may exacerbate the effect of precarious employment. Policies to improve employment conditions may protect against neurological and mental health declines among racialized minorities.
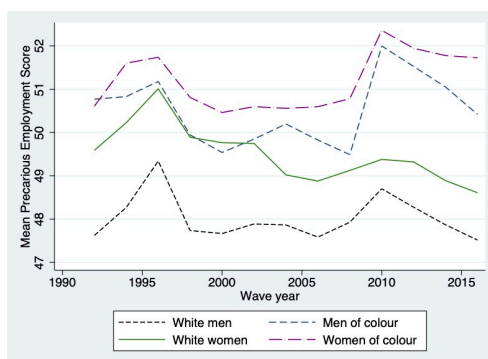
The Association Between Mental Health Outcomes and Social Determinants of Health in Diverse Families Junia Nogueira de Brito* Christopher Prokosch Jerica Berge Ayomide Ojebuoboh Angie Fertig Amanda Trofholz

Introduction

The association between mental health and Social Determinants of Health (SDOH) is an understudied relationship in marginalized communities. This study investigates this association with parents and children from six racial/ethnic communities of the Twin Cities, Minnesota.

Methods

The *Family Matters* Study surveyed families (n=1307) with children from Latino, Native American, Somali/Ethiopian, White, Hmong, and African American families in St. Paul and Minneapolis, Minnesota in 2017-2018. Logistic regression models were used to estimate the adjusted associations between parent and child mental health and SDOH, and false discovery rate q-values were computed to account for multiple comparisons.

Results

While White communities on average experienced 1.7 SDOH, communities of color on average experienced 5.3-7.8 SDOH barriers (p<0.001). Adjusted analyses indicate that low family functioning and high perceived discrimination were adversely associated with multiple measures including severe psychological distress and high anxiety in parents and elevated child internalizing scores (p<0.05). Other SDOH that appeared to be adversely associated with at least one measure of parent or child mental health included lack of social support, recent traumatic events, adverse childhood events among parents, food insecurity, and high neighborhood violence.

Conclusions

Communities of color consistently experienced significant barriers to achieving healthy social determinants when compared to white communities across all social determinant domains. SDOH in the social and community context were the most likely to be associated with mental health problems. Raising awareness of these inequities is the first step to reducing health inequities and must be followed up by community-engaged evidence-based policy and social interventions to improve population health.

Mental Health

Developing a framework for projecting prevalence of anxiety disorder considering potential impacts of COVID-19 pandemic in Germany: a feasibility study Chisato Ito* Chisato Ito Tobias Kurth Bernhard Baune Ralph Brinks

The global burden of mental disorders is vast. 971 million people were estimated to suffer from mental disorders worldwide in 2017. The COVID-19 pandemic has raised concern for this disease burden being exacerbated. Early evidence shows disturbing effects on mental health, particularly in the early phase of the pandemic; however, long-term population-level impacts remain unknown. Further, increasing infectious disease outbreaks globally indicates urgency for future pandemic preparedness planning, inclusive of the mental health aspect. Such an effort would require quantification of mental health care needs of a population.

We aim to provide a prediction framework for the prevalence of mental disorder that allows for simulations under varying incidence over time, accounting for potential impacts of the COVID-19 pandemic. To achieve this, we conducted a feasibility study, building on the illness-death model for chronic diseases which leverages the relationships between incidence, remission, prevalence, and mortality. We model the impact of the first four waves of COVID-19 on the number of women with anxiety disorders in Germany. Different durations of the waves and an additional wash-in- and wash-out-period of 8 and 4 weeks are assumed. During a wave, an increased incidence of 15% is assumed. In the wash-in- and wash-out-periods, this percentage changes linearly from 0 to 15 and back from 15 to 0. The total numbers of women with anxiety disorders in 2019, 2022, 2025, and 2030 are compared with the hypothetical baseline with no pandemic impact.

The simulation resulted in expected additional numbers of cases of anxiety disorders compared to the hypothetical baseline as follows: 0 (+0%) in 2019, 47,019 (+1.2%) in 2022, 34,804 (+0.9%) in 2025, and 22,808 (+0.6%) in 2030. These preliminary results indicate that even if there are no further COVID-19 waves, it is likely that the pandemic impact on anxiety disorders will persist for years.

Mental Health

Identifying Spatial Clusters of Self-Harm Behavior Using California Emergency Department Data from 2009 to 2013 Jordan Jensen* Jordan Jensen Alec Chan-Golston Jennifer Howell Sidra Goldman-Mellor

Every year in California over 500,000 people present to emergency departments with deliberate self-harm injuries. Although suicide fatalities have demonstrated spatial clustering, it remains unclear whether nonfatal self-harm events do the same. Understanding the underlying causes of geographic differences in suicidal and self-harm behavior could support the development of regionally targeted intervention activities. Using statewide emergency department data from 2009 to 2013 in combination with data from the 2010 U.S. census, this study aimed to identify if and where clusters of self-harm-related emergency department visits occurred in California. Kulldorff's spatial scan statistic, via the SaTScan Software, was used to identify non-overlapping clusters of ZIP codes with higher-than-expected reports of self-harm visits through purely spatial analysis. During the study period, 16 distinct clusters of self-harm emergency department visits were identified. Specifically, larger clusters were found in the Central Valley and Northern California in comparison to Southern California. Overall, our findings indicate that self-harm events do cluster in space which suggests possible compositional effects. These findings may be used to develop regionally specific intervention activities located within ZIP codes in which clustering was identified. The next steps include stratifying the data by age, sex, and race to investigate clustering in specific demographic groups. Alternative spatial metrics for clustering will also be considered to assess the robustness of clusters identified by the spatial scan technique. Following this, Bayesian conditional autoregressive models will be fit to determine significant predictors of rates of self-harm visits, accounting for spatial variability.

Association between food security and depression among U.S. adults in the National Health and Nutrition Examination Survey, 2013 – 2018 Sarah E. Laurent* Sarah Laurent Amanda M. Simanek

Background: Understanding the risk factors for depression is critical, as an estimated 1 in 5 U.S. adults will suffer from a depressive disorder throughout their lifetime. Food insecurity has been hypothesized to contribute to depression onset, yet no studies to date have assessed this association in a U.S. representative sample of adults, specifically whether this relationship varies across men and women.

Methods: Data were from 14,082 U.S. adults aged 20 years and older in the National Health and Nutrition Examination Survey (NHANES) (2013-2018). We used logistic regression models to examine the association between household food insecurity (low, marginal, or full) experienced over the past 12 months and elevated depressive symptoms (score ≥ 10 on the nine-item Patient Health Questionnaire [PHQ-9]), adjusting for age, gender, race/ethnicity, marital status, and household poverty ratio. Analyses were repeated stratified by gender.

Results: A total of 1,252 (8.2%) participants reported elevated depressive symptoms experienced within the past 2 weeks. Those reporting low/very low household food security (versus full food security) or marginal food security had 3.13 (95% CI: 2.56, 3.83) and 2.00 (95% CI: 1.52, 2.63) times higher odds of elevated depressive symptoms, respectively. Findings were similar across men and women, though women reported higher odds of depressive symptoms than males for both low/very low food security (OR for women: 3.23, 95% CI: 2.59, 4.03 versus OR for men: 2.95, 95% CI: 2.23, 3.91) and marginal food security (OR for women: 2.20, 95% CI: 1.54, 3.12 versus OR for men: 1.69, 95% CI: 1.12, 2.54).

Discussion: Our findings suggest that household food insecurity experience over the past year is associated with elevated depressive symptoms among U.S. adults. Public health interventions and policies that focus on improving food insecurity may therefore be warranted to decrease the burden of depression among this subset of the population.

Mental Health

The association of back and neck pain with persistent posttraumatic stress disorder symptoms in wounded U.S. military personnel Andrew J. MacGregor* Andrew MacGregor Judy Harbertson Cameron T. McCabe Amber L. Dougherty John J. Fraser

Introduction: Posttraumatic stress disorder (PTSD) is a global health problem and frequently occurs among military personnel with combat injury. Back and neck pain (BNP) is also common in both military and civilian populations. Previous studies have found that musculoskeletal pain can occur with PTSD, but less is known on whether it is linked to persistent PTSD symptoms. This study's aim was to assess the relationship between BNP and persistent PTSD symptoms in combat-injured military personnel.
Methods: The study sample included 3,706 service members wounded in combat from 2004–2013 who screened positive for PTSD within one year after injury. Persistent PTSD symptoms were defined as screening positive for PTSD on a second assessment 90–365 days after the initial screening. Medical outpatient data were abstracted from electronic health records for the period between the two PTSD assessments. Outpatient visits for BNP were defined using diagnostic codes and categorized into none, one, or multiple. Multivariable logistic regression was used to assess the association between BNP and persistent PTSD symptoms, adjusting for age, service branch, sex, injury severity, and time between PTSD assessments.
Results: Overall, 61.5% had persistent PTSD symptoms, and 74.8% had no BNP visits, 9.3% had one, and 15.9% had multiple. Compared with no BNP visits, service members with one (OR: 1.68; 95% CI: 1.32-2.15) or multiple visits (OR: 2.19; 95% CI: 1.78-2.68) had significantly higher odds of persistent PTSD symptoms.
Conclusion: BNP was associated with persistent PTSD symptoms in U.S. military personnel with combat injuries. The higher magnitude association observed with multiple BNP visits may indicate a dose-response relationship. These findings provide further evidence of the relationship between psychological and physical health, and highlight the need for comprehensive clinical management of concomitant BNP and PTSD.

Mental distress and depressive symptoms among Guatemalan health care workers during the COVID-19 Pandemic: findings from the longitudinal HEROES study Victor Puac-Polanco* Alejandra Paniagua-Avila Victor Puac-Polanco Aida Barrera-Perez Erwin Calgua Dorian E. Ramirez

Background: The COVID-19 pandemic has affected the mental health of populations globally. Of particular concern are health care workers (HCW) due to their higher exposure to SARS-CoV-2, heavy workloads and limited mental healthcare, particularly in low- and middle-income countries. Longitudinal data is needed to identify subgroups of HCWs with positive mental health screens over time. We investigated at-risk groups of positivization of mental distress or worsening depressive symptoms during the COVID-19 pandemic using longitudinal data from HCWs.

Methods: A sample of HCWs (n=537) from Guatemalan public and private health care institutions completed a self-reported questionnaire at baseline and 6-months follow-up (July 2020-June 2021). Outcomes were mental distress (General Health Questionnaire-12) and depressive symptoms (Patient Health Questionnaire-9). Exposures included COVID-19 experiences and sociodemographic factors. We graphically evaluated the longitudinal distribution of outcomes (Figure) and identified exposures associated with positivization or worsening symptoms using adjusted Poisson regression models.

Results: From baseline to 6-months, the overall proportion of participants who screened positive for mental distress decreased from 58.7% to 51.1% (p<0.001), while the proportion of those reporting depressive symptoms did not change. Only 12.6% (SE=1.72) of participants reported positivization of mental distress. Almost one-quarter of participants [23.7% (1.80)] reported worsening depressive symptoms. No statistically significant differences for sociodemographic or COVID-19-related exposures were found for those with positivization or worsening symptoms.

Conclusions: Guatemalan HCWs experienced worsening depressive symptoms and decreasing mental distress during the first year of the COVID-19 pandemic. No sociodemographic subgroup was more affected than others by positivization of mental distress or worsening depressive symptoms.

Figure. Mental distress positivization from baseline to 6-month follow-up
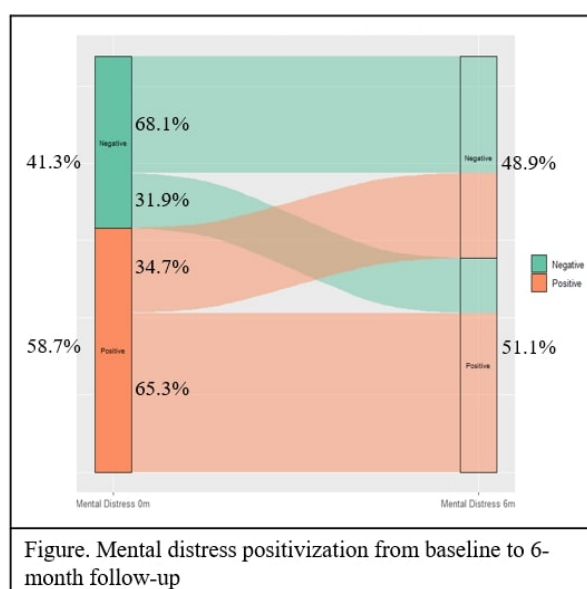
LATEBREAKER

Mental Health

Validation and clinimetric properties of the Danish version of the Flourish Index and Secure Flourish Index Tobias Kvist Stripp* Tobias Kvist Stripp Sonja Wehberg Arndt Büssing Karen Andersen-Ranberg Lars Henrik Jensen Finn Henriksen Christian Laursen Jens Søndergaard Niels Christian Hvidt

Measuring human flourishing proposes a salutogenic approach in epidemiological research to the understanding of the strengths and positive conditions of human life, rather than pathology and deficits. As such flourishing may be a fruitful construct to investigate, perhaps especially in secular culture such as Denmark, as it does not directly draw on religious concepts. To pave the way for human flourishing research in Denmark, we translated and clinimetrically tested the 10-item Flourish Index (FI) and 12-item Secure Flourish Index (SFI) in a convenience sampled test-retest digital survey setup. A total of 325 and 148 respondents participated in the test and retest respectively. Confirmatory factor analysis was used to confirm the structure of the indexes. Cronbach's alphas and McDonald's omegas were computed for the indexes which indicated high internal consistency (alphas and omegas between 0.84-0.89). The FI and SFI may be used to measure human flourishing in secular culture such as Denmark. Studies on the predictors, outcomes, and clinical implications of human flourishing are warranted.

Association between maternal depressive symptoms and offspring epigenetic age at 3-5 weeks of age Alonzo Folger* Alonzo Folger Lili Ding Milan Parikh Kimberly Yolton Robert Ammerman Jennifer Frey Katherine Bowers

Background. Accelerated/Decelerated biological age has gained interest as an epidemiologic measure of developmental health. Epigenetic clocks continue to be developed from models that include DNA methylation (DNAm) across multiple tissue types, CpG sites and ages. Parental psychological distress may impact offspring development, and these effects may be detected using estimates of accelerated or decelerated biological age derived from epigenetic clocks. We hypothesized a significant association between maternal depressive symptoms and offspring predicted age deviation at 3-5 weeks of age. **Methods**. We followed 92 low-income women and their offspring (87 with complete data) from pregnancy to 3-5 weeks postpartum. We collected the Edinburgh Postnatal Depression Scale (EPDS) during pregnancy (7 postnatal) and offspring buccal epithelial DNA at 3-5 weeks. DNAm values were generated using the Illumina MethylationEPIC BeadChip; standard normalization and quality control measures were performed. We used the Pediatric-Buccal-Epigenetic (PedBE) clock to derive predicted age. Age deviation was calculated as the difference between chronological age at sample collection from PedBE predicted age. General linear models were used to examine associations between EPDS scores and age deviation. We also examined a binary cutoff of an EPDS score less than 3 in an effort to combine sub-clinical and clinical depressive symptoms. Age deviation was corrected for gestational age at birth in a sensitivity analysis. **Results**. The relationship between maternal EPDS score and age deviation was non-significant, adjusting for confounding factors including maternal age and race. However, mothers with a 'non-low' EPDS score had significantly lower age deviation than the 'low score' mothers in the cohort (means: -0.09 vs. 0.01; beta: -0.09, 95% CI: -0.18, -0.01). Results were similar when using corrected age. **Conclusion**. Maternal depression may be associated with early infant developmental processes.
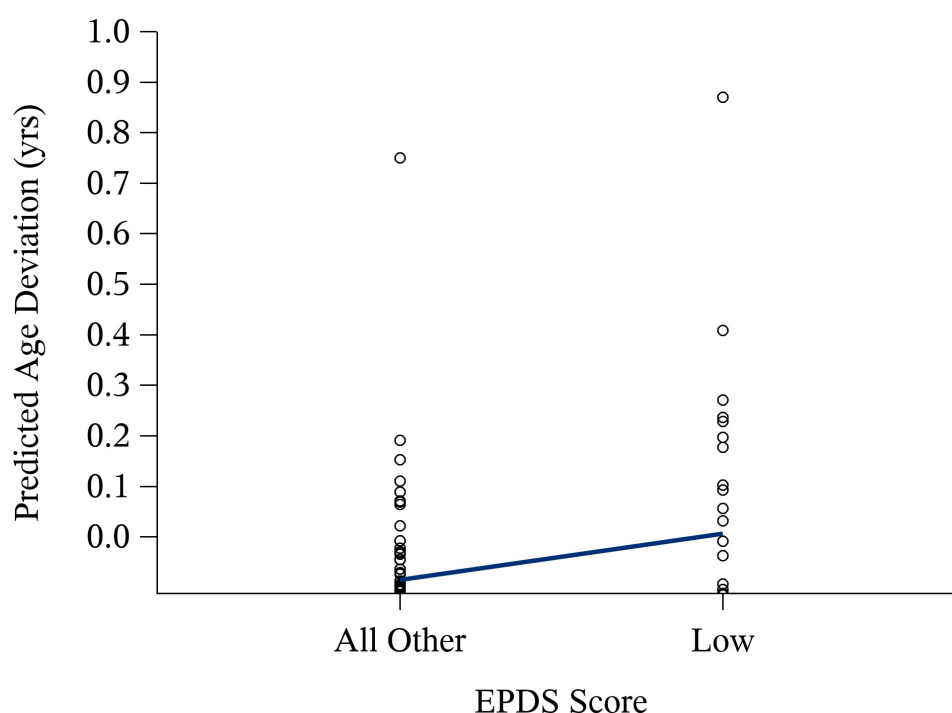
Evaluation of a methicillin-resistant Staphylococcus aureus testing change in the Intensive Care Unit based on Bayesian quantile regression counterfactuals Hayden Smith* Hayden Smith Samuel DuMontier Jonathan Hurdelbrink Steven Craig

Background: Methicillin-resistant *Staphylococcus aureus* (MRSA) infection is a concern in the Intensive Care Unit (ICU) and is commonly treated with vancomycin. This drug is not without risks and its use should be minimized when possible.

Objective: To decrease time between MRSA test ordering and time to results in admitted ICU patients.

Methods: A testing change was implemented at two adult (tertiary 37 bed and community 15 bed) ICUs in a U.S. Midwestern health system. In 2018, laboratories for study hospitals were requested to change the default MRSA testing from culture to polymerase chain reaction (PCR) in admitted ICU patients. Of note, the tertiary hospital used an in-house and the community hospital used an off-site laboratory. Data were collected for 2016-2020. A Bayesian quantile regression model was fit to examine median level change in time to results with counterfactual estimates calculated (additional details to be presented at conference). A Monte Carlo simulation was used to estimate MRSA positive test percentages at tertiary hospital in post-change period.

Results: During the 58-month period, 71% of 19,975 adult ICU patients received MRSA testing. In the pre-change period, 91% and 99% of ICU patients at the tertiary and community hospitals received culture testing, respectively. Culture was used 1% and ~0% of the time at the hospitals in the post-change period. The counterfactual-based estimated change in result time at the mid-point of the post-change period was 36 (95% CrI: 35, 37) and 32 fewer hours (95% CrI: 31, 33) at the tertiary and community hospital (Figure), respectively. Additionally, 16% (95% CI: 14%, 18%) of tertiary patients post-change are estimated to test positive for MRSA.

Conclusions: Study revealed MRSA results were available faster at both facilities. This information can aid anti-microbial stewardship decisions related to delaying drug initiation until results are known or initiating drug discontinuation sooner in negative tests.
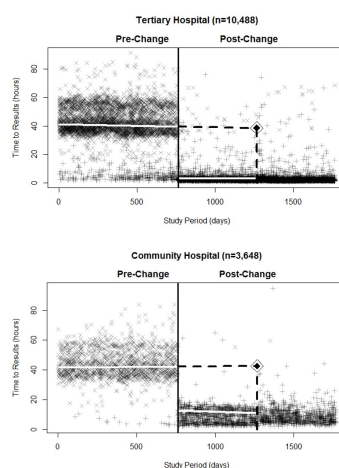

Figure: Plotted time (hours) to receiving methicillin-resistant *Staphylococcus aureus* (MRSA) test results in patients admitted to adult Intensive Care Unit by study period day. Top panel presents tertiary hospital and bottom panel presents community hospital data. Solid black vertical line represents point of testing change; solid white lines are the estimated time to results per period; dashed black horizontal and vertical lines represents the counterfactual estimate at the midpoint of the post-change period marked with a

**Causal and Associational Linking Language From Observational Research and Health Evaluation Literature in Practice: A systematic language evaluation** Noah Haber* Sarah Wieten Julia M. Rohrer Onyebuchi A. Arah Peter W.G. Tennant Elizabeth A. Stuart Eleanor J. Murray Sophie Pilleron Sze Tung Lam Emily Riederer Sarah Jane Howcutt Alison E. Simmons Clémence Leyrat Philipp Schoenegger Anna Booman Mi-Suk Kang Dufour Ashley L. O'Donoghue Rebekah Baglini Stefanie Do Mari De La Rosa Takashima Thomas Rhys Evans Daloha Rodriguez-Molina Taym M. Alsalti Daniel J. Dunleavy Gideon Meyerowitz-Katz Alberto Antonietti Jose A. Calvache Mark J. Kelson Meg G. Salvia Camila Olarte Parra Saman Khalatbari-Soltani Taylor McLinden Arthur Chatton Jessie Seiler Andreea Steriu Talal S. Alshihayb Sarah E. Twardowski Julia Dabravolskaj Eric Au Rachel A. Hoopsick Shashank Suresh Nicholas Judd Sebastián Peña Cathrine Axfors Palwasha Khan Ariadne E. Rivera Aguirre Nnaemeka U. Odo Ian Schmid Matthew P. Fox

Background: Avoiding "causal" language with observational study designs is common practice, often justified as being a more cautious approach to interpretation. We aimed to estimate the degree to which causality was implied by both the language linking exposures to outcomes and by action recommendations in the high-profile health literature and examine disconnects between language and recommendations.

Methods: We identified 18 of the most prominent general medical/public health/epidemiology journals, and searched and screened for articles published from 2010 to 2019 that investigated exposure/outcome pairs until we reached 65 non-RCT articles per journal (n=1,170). Based on written guidance, two independent reviewers and an arbitrating reviewer rated the degree to which they believed causality had been implied by the language in abstracts. Reviewers then rated causal implications of linking words in isolation.

Results: Reviewers rated the causal implication of the sentence and phrase linking the exposure and outcome as None (i.e., makes no causal implication) in 14%, Weak in 34%, Moderate in 33%, and Strong in 19% of abstracts. Among the 34% of abstracts which had action recommendations, reviewers rated the causal implications as None in 5%, Weak in 19%, Moderate in 43% and Strong in 33% of cases. The implied causality of action recommendations was higher than linking sentences in 45%, commensurate in 40%, and weaker in 15% of cases. The most common linking word root identified in abstracts was "associate" (n=535/1,170; 45%). Reviewer ratings for causal implications of word roots were highly heterogeneous.

Discussion: We found substantial disconnects between causal implications used to link exposures and outcomes vs action implications made. We recommend that instead of policing words related to cause, editors, researchers, and communicators should increase efforts at making research questions, as well as the potential of studies to answer them, more transparent.

Panel a) Density plot of observations

Panel b) Distribution within levels of linking sentence strength
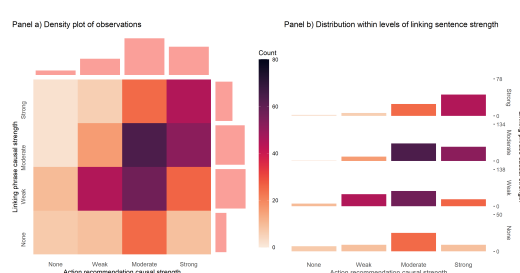
Better Analysis of RCTs Timothy Feeney* Timothy Feeney Stephen

Intro: Randomized controlled trials are the gold standard to learn the effects of medical treatments. Standard Intent to treat (ITT) estimators are unbiased in large randomized trials, but are often imprecise because they ignore covariate information. Augmented inverse probability weighted (AIPW) estimators combine the robustness of standard ITT estimators (the treatment model is known by design as a result of randomization) with the added precision from covariate-adjusted outcome models. Here we leverage AIPW to improve the precision of ITT estimators and allow for better analyses of trials.

Methods: Reanalysis of 795 participants of the AIDS Clinical Trial Group (ACTG) 5202 phase 3 trial evaluating the impact of HIV treatment with abacavir/lamivudine (ABC/3TC) or emtricitabine/tenofovir (TDF/FTC). AIPW analysis combines inverse probability of treatment weighting with an outcome model to evaluate follow-up CD4 count (cells/mm^3). The outcome model included the following baseline covariates: sex, age (categorized as 3 groups, 16-25 years, 26-49 years, and ≥ 50 years), viral load (log10 copies/ml), and CD4 count (cells/mm^3). Inverse probability of treatment weighting used the empirical estimates of treatment to obtain the probability of receiving ABC/3TC versus TDF/FTC.

Results: The standard ITT and AIPW estimates of the difference in follow up CD4 count were -6.9 cells/mm^3 and -6.7 cells/mm^3, respectively. The standard error was 37% smaller in the AIPW estimate (SE:10.33) versus the ITT estimate (SE:16.34) (Figure 1). To obtain a standard error similar to the standard ITT analysis, we would have only needed to enroll 416 (60%) of the 695 patients. Alternatively, to obtain the standard error given by AIPW the standard ITT analysis would require an additional 1030 participants (total n=1725).

Conclusion: AIPW estimation of ITT effects can improve the precision of trial analyses, and facilitate ethical and financially responsible trial design and 'better' analysis.

Figure 1
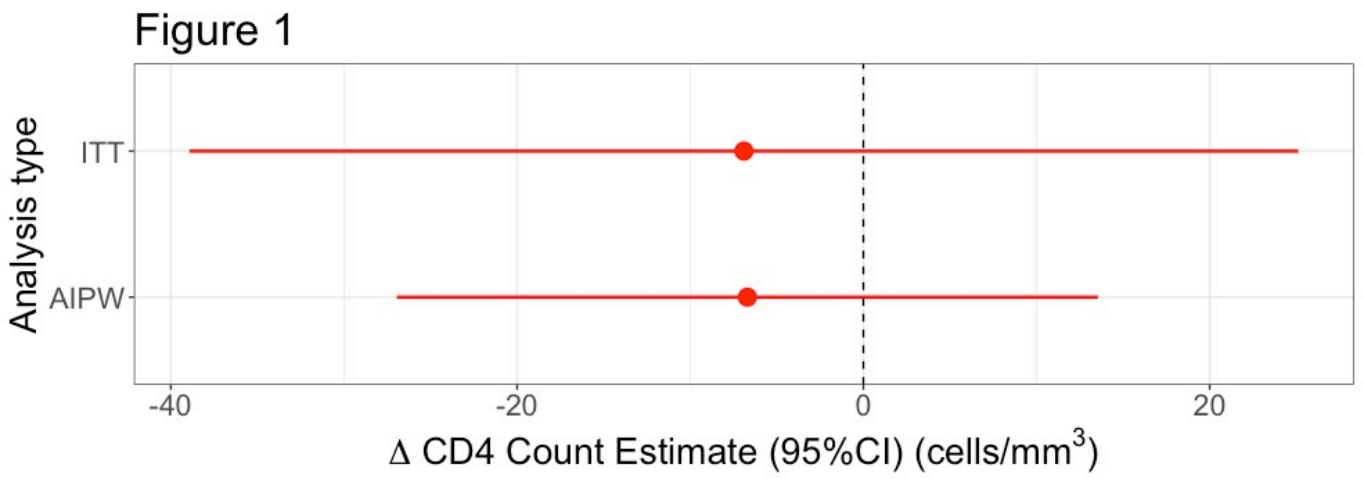
Estimating the extent to which nicotine vaping increases cannabis initiation risk in the presence of positivity violations Alexander* Alexander Perlmutter Kara

Background: Prior studies found evidence that nicotine vaping increases cannabis initiation risk. Were these studies' estimates to be interpreted as causal effects (identifiable), the positivity assumption (the existence of vaping and comparison individuals across all covariate strata) would be required; however, none evaluated evidence of the extent to which this assumption held. We estimated two kinds of effects of nicotine vaping on cannabis initiation among a nationally representative sample of US youth—one that assumes positivity and another that does not. For the former, we examined the extent to which there were practical positivity violations.

Methods: Our sample was 5,324 12-16-years olds who never used cannabis or prohibited substances (cocaine, methamphetamine, etc.) from the baseline Wave (1) of the Population Assessment of Tobacco and Health (PATH). We estimated 1) the four-year average treatment effect (ATE) of vaping in all years versus never vaping on subsequent cannabis initiation, which assumes positivity; and 2) the four-year incremental effect of shifting everyone's odds of vaping in each year by increasing increments on subsequent cannabis initiation, which does not assume positivity.

Results: We found evidence of substantial practical violations of the positivity assumption (Figure 1). Estimating the ATE in the presence of these violations would have led us to conclude that nicotine vaping is associated with 25 excess initiations per 100 youth (95%CI: 0-51) by Wave 5. However, estimating the incremental effect of increasing nicotine vaping odds would have led us to conclude that there is no evidence that nicotine vaping increases cannabis initiation risk by Wave 5. For instance, increasing odds of nicotine vaping by 10 times each year would have resulted in 6 excess initiations per 100 youth (95%CI: -54-66) by Wave 5.

Conclusions: Incremental effects may be useful alternative causal effects in the presence of practical positivity violations.
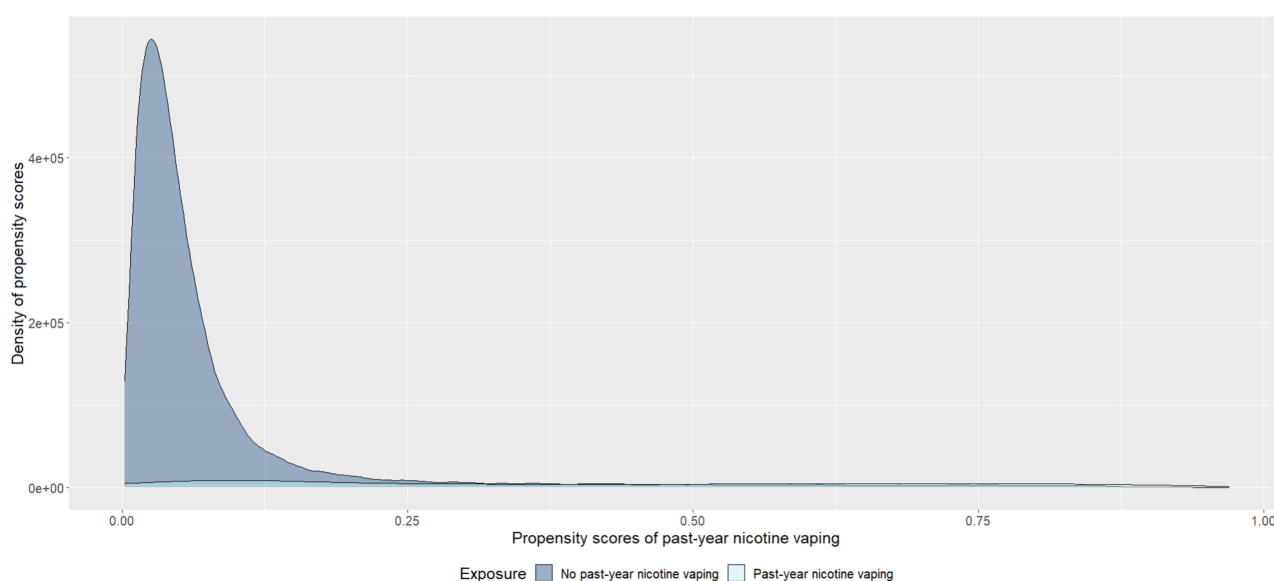

Figure 3.3: Propensity score overlap plot for past-year nicotine vaping in the Population Assessment of Tobacco and Health Waves 1-4 (2013/14–2016/18).

Physical activity & sleep among men 20-64 yrs: an exercise in weighting Alvaro J. Castro Rivadeneira* Alvaro Castro Rivadeneira Lindsey Russo Faith English Laura B. Balzer

Background: While the prevalence of and risk factors for sleep disorders have been well-characterized in women, less is known about factors influencing sleep among men. We aimed to evaluate the effect of regular physical exercise (150+ minutes of moderate intensity or 75+ minutes of vigorous intensity activity) on getting a full night's sleep (7+ hours/night) among men aged 20-64 years in the US.

Methods: Data on potential confounders (e.g., age, race/ethnicity, education, marital status, household size, income, BMI, waist size, smoking, alcohol intake, and depression), physical activity, and sleep were obtained from 2 cycles of NHANES (2015/6, 2017/8). Our target statistical parameter was the adjusted risk difference (RD): the difference in the probability of a full night's sleep associated with exercise, adjusting for measured confounders. For estimation, we compared an unadjusted estimator, G-computation among those with complete data, G-Computation after using multiple imputation by chained equations (MICE), and G-computation after MICE and including survey weights. Inference was obtained with Rubin's rules and the non-parametric bootstrap.

Results: An unadjusted analysis of 3,782 participants suggested men who exercised were 4.2% more likely to sleep 7+hrs/night (RD: 0.042, 95%CI: 0.012,0.069). Among 2,995 participants with complete data, adjusting for potential confounders reduced the estimated association (RD: 0.037, 95%CI: 0.007, 0.072). After imputing missing data, adjusted estimates were further reduced (RD: 0.028, 95%CI: -0.002, 0.058). Adding the weights with masked variance units to account for complex sampling eliminated the estimated association (RD: 0.005, 95%CI: -0.04, 0.05).

Conclusion: Estimated associations between exercise and sleep outcomes among men depended heavily on the statistical approach, which should reflect the target population and plausible assumptions on confounding and missingness.
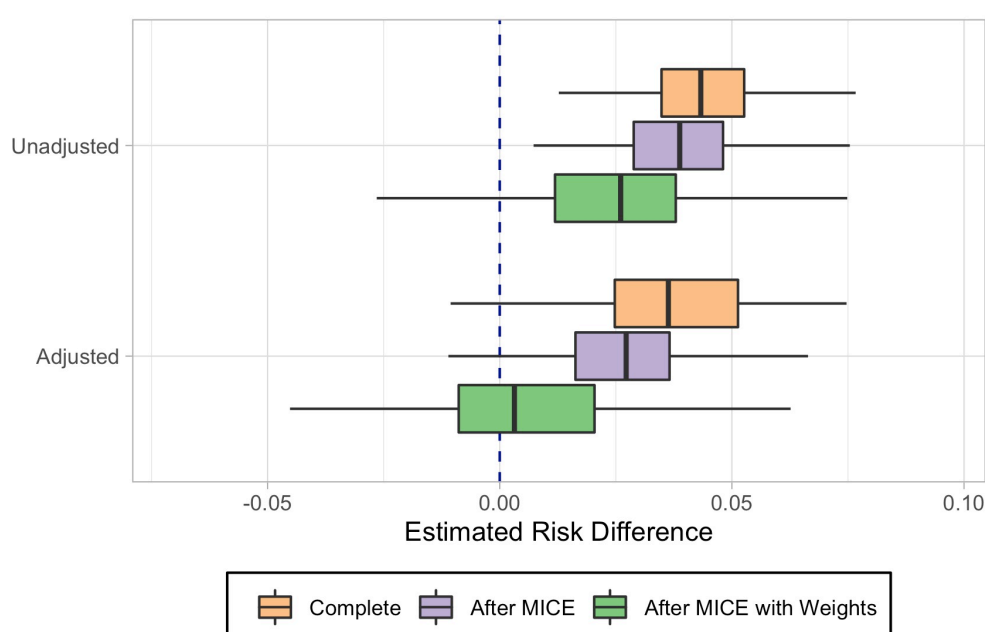
Best practices for incomplete longitudinal data: a comparison of imputation strategies for exposure trajectories Crystal Shaw* Crystal Shaw Yingyan Wu Scott C. Zimmerman Eleanor Hayes-Larson M Maria Glymour Melinda C. Power Thomas R. Belin Elizabeth Rose Mayeda

In lifecourse epidemiology, exposures are often observed at different ages and with different patterns of missingness within cohorts. Multiple imputation (MI) is an appealing general strategy for handling missing data, but its performance can depend on assumptions embedded in its implementation. Starting with a subset of complete data from the Health and Retirement Study (HRS), we imposed varying missing-data mechanisms and percentages of missing data in evaluating three MI strategies: Joint Multivariate Normal Modeling (JMVN), Predictive Mean Matching (PMM), and Fully Conditional Specification (FCS). Specifically, we identified HRS participants with at least 4/6 waves of Center for Epidemiological Studies-Depression (CES-D) scores (1998-2008) and mortality data through 2018. Classifying CES-D scores 4/8 as elevated, we applied Cox proportional hazards models to characterize associations between mortality and four CES-D measures: baseline elevated CES-D, end-of-follow-up elevated CES-D, elevated average CES-D, and proportion of waves with elevated CES-D. Missing Completely at Random (MCAR), Missing at Random (MAR), and Missing Not at Random (MNAR) mechanisms were studied, each with 10%, 20%, and 30% missingness induced. In each scenario, we used JMVN, PMM, and FCS to impute missing values, evaluating bias, 95% interval coverage, root mean squared error (RMSE), and computation time. Alternative MI strategies performed similarly across scenarios, regularly recovering nominal coverage with MCAR and MAR missingness while not surprisingly yielding less than nominal coverage with MNAR missingness. PMM imputation had consistently low RMSE across scenarios, computation times faster than FCS and only slightly greater than JMVN, and few challenges to implementation. This finding was consistent in sensitivity analyses with increased exposure prevalence, suggesting that PMM is apt to be an appealing strategy for imputing lifecourse exposure data.

Average 95% CI of beta across 700 simulation runs by exposure, missing data mechanism, imputation method, and percent missing data. Elevated CES-D defined as CES-D score ≥ 4. Solid black line represents true beta obtained from analyses run original, unmasked sample. Dashed gray line represents the null value. Abbreviations: MCAR = "Missing Completely at Random"; MAR = "Missing at Random"; MNAR = "Missing Not at Random"; CC = "Complete Case Analysis"; JMVN = "Joint Multivariate Normal"; PMM = "Predictive Mean Matching"; FCS = "Fully Conditional Specification."
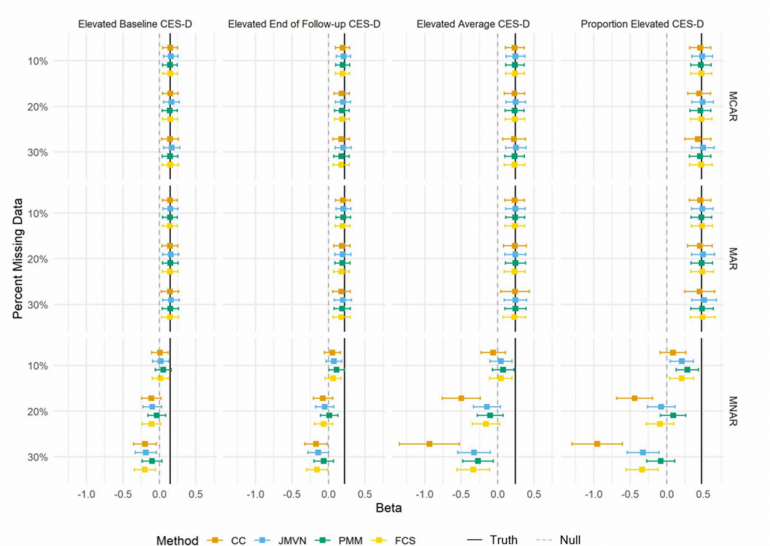
Evaluation of Confidence Interval Methods for the Stratified Matched Net Benefit. Zili Zong* Zili Zong Roland Matsouaka

In the traditional time to first event analysis of composite endpoint, treatments are compared based on the time to first event in patients without considering the severity, priority and clinical relevance. However, more frequent, less fatal events tend to occur earlier, so time to first event could lead to incorrect and misleading results. The alternative net benefit (NB) method which assess treatment effects using prioritized component outcomes based on clinical importance has been proposed to address the problem. Previous research has shown robust statistical inference for the matched net benefit in the unstratified design. It is common that clinical trials require a stratified analysis to reduce the chance covariates imbalances. In this paper, we aim to generate robust inference for net benefit in a stratified paired-sample design. Several stratified confidence intervals method for the difference between two proportions, including novel combinations and extensions from existing methods are evaluated under different scenarios. We use the method of variance estimates recovery (MOVER). Besides, stratified Fisher's z transformation is used as an extension of its unstratified counterparts. We evaluate the methods in terms of coverage probability, confidence width and the balance between the mesial non-coverage probability (MNCP) and the distal non-coverage probability (DNCP). Simulations show that modified stratified Wald method with Agresti adjustment outperforms other methods when comparing the coverage probability and the balance between MNCP and DNCP. Modified stratified MOVER and Fisher's z transformation method with Wilson or Agresti adjustment outperforms other methods when comparing the confidence width. We discuss the use of stratified CI methods for the difference between two proportions in two data examples.

Performance of approaches for confounder control in the presence of missingness in EHR-based comparative effectiveness analyses Daniel T Vader* Daniel Vader Rebecca Hubbard Ronac Mamtani Yun Li Sandra D Griffith Gregory S Calip

Electronic health record (EHR)-derived data represent an enormous research resource covering large and diverse populations. However, missingness in confounder variables is common and may lead to biased treatment comparison estimates if inadequately handled. EHR-based comparative effectiveness research often uses inverse probability of treatment weighting (IPTW) via propensity scores for confounder control. In IPTW, missingness in confounder variables can be handled using multiple imputation (MI) to impute missing values prior to fitting propensity score models. Alternatively, propensity score calibration (PSC) can handle missingness by transforming this missing data problem into a measurement error problem, and PSC may be appealing due to the computational resources required to run MI on large EHR datasets. Motivated by a real-world EHR-based comparative effectiveness analysis on advanced bladder cancer treatment, we used plasmode simulation to characterize the statistical properties of IPTW hazard ratio estimates when accounting for missingness in confounder variables using MI or PSC. Plasmodes maintain some of the complex inter-variable relationships of real EHR data, providing a more realistic testing ground than purely synthetic data. Our simulation sourced the nationwide Flatiron Health EHR-derived de-identified database and included 3,895 patients treated for advanced bladder cancer in 2011-2021. MI and PSC approaches performed similarly , exhibiting minimal bias both when confounder data were missing at random or missing not at random (even when 70% of subjects were missing data). As anticipated, MI required greater computational resources, taking nearly 40 times as long as PSC to complete on identical hardware. We recommend MI and PSC approaches to handling missingness in confounder variables when conducting EHR-based IPTW comparative effectiveness analyses, even when missingness is high and in select situations when confounder data are missing not at random.

The attack of the bots: identifying bot responses from internet-based recruitment for covid-19 study. Veena Billioux* Veena Billioux Yisi Liu Gabriela Calderon Harshini Sampathkumar Jessica Duchen Laura Prichett Erin Hager Lorece Edwards Sara Johnson

Background: Internet-based study recruitment provides an opportunity for faster data collection, provides access to hard-to-reach populations, and is often less expensive than other recruitment approaches. However, with these benefits also come risks, such as bots, also known as automatic survey-takers or fraudsters, as well as professional survey takers, threatening the integrity of academic research conducted online.

Methods: We analyzed data collected from 8:00 PM to 11:30 PM EST on December 23, 2021, when our Facebook ads were active. The aim is to describe and identify factors associated with fraudulent and bot responses.

Results: When our Facebook ads were active, our survey received 2,578 screener attempts and 2,463 completed screeners 98% met the eligibility criteria for our survey. There were 1,027 survey attempts and 953 completed surveys. Only 90% of completed surveys gave matching zip codes in the screener and the survey. The mean time to complete the survey was 21 minutes. However, the distribution was heavily left-skewed – with 59% taking less than 15 min to complete the survey.

Conclusion: The new reality is that survey data bots and professional survey takers are inevitable. Evidence from the data we collected suggests that automated screening techniques (such as CAPTCHAs) are insufficient to filter out bots. Based on the lessons learned from this analysis, we are re-launching the survey with added mechanisms to distinguish bots from genuine survey responses. These include attention capturing questions, speed bump questions, and requiring the same open-ended question at multiple time points to examine the constancy among responses. To maintain and ensure high quality of online research, we must remain vigilant in our fight against bots and professional survey takers.

The use of Cohort Size Shrinkage Index (CSSI) to quantify regional famine intensity during the Chinese famine of 1959-61 Chihua Li* Chunyu Liu Chihua Li Hongwei Xu Zhenwei Zhou L.H. Lumey

There has been a growing interest in studying the impact of the Chinese Famine of 1959-61. The Cohort Size Shrinkage Index (CSSI), $(N_{\text{non-famine}}-N_{\text{famine}})/N_{\text{non-famine}}$, is a common measure of famine intensity and was used in 28 Chinese famine studies to date. We examined the potential impact of violations of three requirements for a valid CSSI measure: reliable information on cohort size by year of birth; a stable trend of cohort size by year of birth; and no significant regional migration. We used data from the 1% China 2000 Census to examine the trend of cohort size over time and examined the time window between 1950-70 to exclude policies and events with a large impact on birth trends other than the famine itself.

Across China we established a significant difference in cohort size trends between pre-famine births and post-famine births, violating one of the main requirements for a valid CSSI measure. This leads to systematic differences in CSSI depending on what non-famine years are selected for comparison. At the province level, CSSIs estimated based on pre- & post-famine births tend to overestimate famine intensity at higher exposure levels and underestimate intensity at lower levels compared to CSSIs based on pre-famine births alone. This is problematic and demonstrates that the CSSI is not as robust an estimator of famine intensity as had been assumed previously. We recommend therefore that all CSSI calculations and estimates should be based on pre-famine birth trends.

Using data from Sichuan province, we demonstrate a less pronounced dose-response relation between famine intensity and tuberculosis outcomes using pre-famine based CSSI as compared to reported patterns based on pre- & post-famine based CSSI. We encourage researchers to re-examine their results of Chinese famine studies as local differences in cohort size of pre-famine and post-famine births may lead to significant discrepancies of CSSI estimation and change the interpretation of their findings.

Pre-famine based cohort size shrinkage indexes (CSSI), pre- & post-famine based CSSI, and their difference at the province level
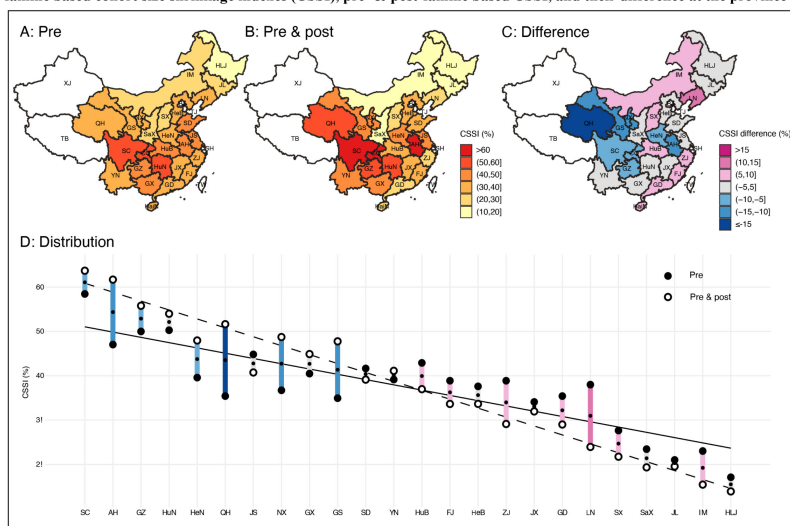
A. Provincial CSSI (%) based on pre-famine births in 1950-57; B. Provincial CSSI (%) based on pre- & post-famine births in 1950-57 & 1963-70; C. Difference of provincial CSSI (%) between panel A and panel B; D. Provinces are ordered by the average of pre-famine based and pre- & post-famine based CSSIs. The solid line represents the linear regression of pre-famine based CSSI (filled circles) over the average of the two CSSIs. The dash line represents the linear regression of pre- & post-famine based CSSI (unfilled circles) over the average of two CSSIs. Each bar represents the difference of pre-famine based and pre- & post-famine based CSSIs for each province, and its color coding follows the panel C. Data: 1% China 2000 Census, place of birth.

LATEBREAKER

Methods/Statistics

Explaining Differences in Outcomes Across Subpopulations: A Unification of Two Decomposition Frameworks in Health Disparities Research Fan Zhao* Fan Zhao Roch Nianogo

Background: The field of health disparities research is an area of growing interest and development in Epidemiology. Of particular interest are two major decomposition frameworks: the Oaxaca-Blinder econometric decomposition (OBD) which disaggregates the differences in outcomes into an explained and an unexplained portion and a counterfactual framework via causal mediation analysis which decomposes effects into an indirect and direct effect. The extent to which these two frameworks converge is seldom studied and a general framework that unifies the two is needed.

Objective: We sought to evaluate the circumstances under which these two frameworks yield similar findings and to propose a general framework unifying the two.

Methods: We simulated four scenarios: 1) no confounder (C), no interaction between exposure and mediator (M); 2) no confounder, but interaction; 3) confounder, but no interaction; 4) confounder, and interaction. We estimated two- and three-way decompositions via OBD and via a mediation analysis using g-computation.

Results: Only when there is no confounder, does the OBD have a similar decomposition as the causal mediation analysis. The total effect (TE) from mediation analysis is equal to the total difference estimated from OBD in the absence of confounding. In the three-way OBD, the total difference can be decomposed in 1) the endowment (this corresponds to the Pure Indirect Effect [PIE]), 2) the coefficient (this corresponds to the Pure Direct Effect [PDE]), and the interaction (this corresponds to the mediated indirect effect [MIE]). In the two-way OBD, the total difference can be decomposed in the 1) the explained (this corresponds to the PIE if weight =0 and Total Indirect Effect [TIE] if weight=1) and 2) the unexplained (this corresponds to the Total Direct Effect [TDE] if weight =0 and PDE if weight=1). In other words, TE = [PIE + (MIE*weight)] + [PDE + (MIE*(1-weight)]. When confounding is present, these equivalencies no longer hold.

Conclusion: The OBD is not a causal model as it does not distinguish between a mediator and a confounder in explaining the differences in outcomes across subpopulations. The two frameworks converge in the absence of confounders. The OBD is a descriptive method, while the counterfactual framework allows one to give a causal interpretation under some assumptions.

LATEBREAKER

Methods/Statistics

Social Determinants Modify the Relationship between Neonatal Inflammation and Brain Volume Later in Life Carmen A. Marable* Carmen Marable Lei Zhang Kyle Roell Karl Kuban Hernan Jara Caitlin K. Rollins David Kennedy Ryan McNaughton T. Michael O'Shea Rebecca C. Fry

While neonatal inflammation is tied to adverse neurodevelopmental outcomes later in life, relationships between inflammation and brain volume in adolescence are understudied. Additionally, the influence of socioeconomic status (SES) on the relationship between neonatal inflammation and reduced brain volumes has not been well characterized. To fill this gap, we used data from the Extremely Low Gestational Age Newborn (ELGAN) cohort, to investigate the relationship between neonatal inflammation measured during the first few weeks of life and brain volume measured at age 15. From the originally enrolled cohort born extremely preterm (23 to 27 weeks' gestation), we examined a sub-cohort of 190 children with paired neonatal inflammatory protein and adolescent MRI data. Elevated blood concentrations of 6 inflammatory proteins (e.g., C-reactive protein) in the first few weeks of life were measured. As an index of SES, we used a composite score based on mother's health insurance, marital status, education, and food stamps. We hypothesized that there would be an association between neonatal inflammation and reduced total brain volumes in adolescents and that this effect will be modified by SES. Neonates who displayed moderate levels of sustained neonatal inflammation (e.g., 2-3 inflammatory proteins) had reduced total brain volume, (δ – 49; p = 0.014). When stratified by SES risk score at birth, in the high SES group (n=128), the inflammation-associated brain volume reduction remained significant (δ -58; p = 0.038), but in the low SES group (n=62), this association was not found (δ -24; p = 0.47). In conclusion, among individuals born extremely preterm, neonatal systemic inflammation was associated with decreased brain volume in adolescence, but this association was not found among individuals with indicators of social disadvantage. This introduces the need to measure childhood adversity as a later life proxy capturing social determinants such as exposure to environmental stressors, abuse (physical, emotional, and sexual), family dysfunction, and neglect that may modify the relationship between neonatal inflammation and brain volumes at age 15.

Implementation of molecular serotype-specific diagnostic identification for Streptococcus pneumoniae Danial A. Malik* Danial Malik Dr. Leslie Wolf Dr. Subathra Marimuthu Holly Aliesky Brigid Connelly

Streptococcus pneumoniae (*S. pneumoniae*) is a commensal human pathogen that is typically present in the upper respiratory tract of the host. The high burden of pneumococcal disease is mainly observed in elderly individuals, especially with underlying comorbidities causing substantially high mortality rates. Since the introduction of pneumococcal conjugate vaccines (PCV7 & PCV13), the incidence of disease caused by *S. pneumoniae* has decreased. Invasive infections caused by PCV13-targeted serotypes are still a major public health concern, however, due to documented antibiotic resistance in certain serotypes. The Quellung reaction remains the gold standard for serotyping, which is dependent on culture, microscopy, and rabbit antisera to visualize capsule swelling. The primary limitations of this assay are that it is not suitable as a high throughput assay, and it lacks specificity for certain serotypes. The University of Louisville Infectious Diseases Laboratory (IDL) implemented the Centers for Disease Control and Prevention (CDC) protocol to develop the real-time PCR for the molecular serotyping-specific characterization of *S. pneumoniae* that proved to be highly sensitive, specific, and reproducible on isolates of *S. pneumoniae.* The overall aim for the development of this molecular serotyping assay for *S. pneumoniae* is to improve the timely diagnosis of pneumococcal disease with serotype identification. This assay will provide a better understanding of geographical distribution and shifts in the prevalence of pneumococcal disease over time. Ultimately, the data will aid in surveillance efforts for vaccine optimization and development, yielding a clearer picture of pneumococcal vaccines on disease burden.

Circulating Resistin Concentrations And Risk Of Colorectal Cancer In The European Prospective Investigation Into Cancer And Nutrition (EPIC) Study Thu Thi Pham* Thu Thi Pham Katharina Nimptsch Krasimira Aleksandrova Mazda Jenab Tobias Pischon on behalf of the EPIC group

Background: Resistin is a polypeptide implicated in inflammatory processes and as such could provide a mechanistic link to colorectal carcinogenesis. Rodent studies suggest that resistin is primarily secreted by adipocytes, whereas in humans it is produced predominantly by mononuclear cells. Higher resistin levels have been found in colorectal cancer (CRC) patients compared to healthy individuals. However, evidence for the association between pre-diagnostic resistin and CRC risk are scarce.

Methods: We investigated pre-diagnostic resistin concentrations and CRC risk within the European Prospective Investigation into Cancer and Nutrition (>520,000 participants, 10 European countries) using a nested case-control study among 1293 first incident CRCs diagnosed over a mean follow-up time of 4.8 years and 1293 incidence-density matched controls. Conditional logistic regression models controlled for matching factors (age, sex, study center, fasting status, menopausal status in women) and potential confounders (education, dietary and lifestyle factors, body mass index (BMI), BMI-adjusted waist circumference residuals) were used to estimate incidence rate ratios (IRRs) and 95% confidence intervals (CIs) for CRC.

Results: Higher circulating resistin concentrations were not associated with CRC (IRR per 2-fold higher resistin, 1.11; 95% CI 0.94, 1.30; p=0.22). There were also no associations by tumor subsite, sex, or in two-year lag analyses. We observed no substantial correlation between baseline circulating resistin concentrations and adiposity measures (BMI, waist circumference), adipokines (adiponectin, leptin), or inflammatory and metabolic biomarkers (C-peptide, C-reactive protein, high-density lipoprotein cholesterol, reactive oxygen metabolites) among controls.

Conclusion: In this large-scale prospective cohort, we found no association between circulating resistin concentrations and CRC risk in European men and women.

Neurology

Understanding the course of migraine with increasing age and differentiating between inactive and active symptom profiles

Jessica L. Rohmann* Jessica L. Rohmann Marco Piccininni Ralph Brinks Tobias Kurth

Aim/Rationale: According to the International Classification of Headache Disorders diagnostic criteria, once a person is classified as having migraine, it is not possible for the individual to leave the "pool" of prevalent disease unless that individual dies, even if all symptoms of active migraine stop ("remission"). In contrast, the Global Burden of Disease (GBD) study and other studies pragmatically operationalize migraine as having recent symptomatic activity. To date, the state of inactive migraine has been largely ignored, though pathophysiological changes in the brain may still be relevant despite reduction of symptoms. Thus, our aim was to construct age-prevalence curves of migraine separately for active and inactive migraine.

Methods and Results: We quantified the remission age-sex specific rates of migraine activity in both Germany and globally using GBD data. We developed a multistate model, which explicitly considers the state of inactive migraine. Implementing this model and relying on published migraine lifetime prevalence estimates, we generated age-sex-prevalence estimates of never having migraine, having active migraine, and having inactive migraine, for both Germany and globally using a theoretical cohort. To complement these findings, we developed and administered an online questionnaire to headache experts in Germany to obtain aggregate estimates of prevalence, incidence, and remission rates of active migraine based on their experiences. The surveyed headache experts generally overestimated remission rates for both men and women, though their aggregated guesses correctly reflected main trends in migraine activity trajectories among women.

Conclusion: Ultimately, this project generated important estimates needed for future population-based research of migraine. Having a better understanding of inactive migraine prevalence across age, and a quantification of remission rates will hopefully allow for more informed clinical decision-making.

Impact assessment of the first gulf war on multiple sclerosis risk in Kuwait: A quasi-experimental study Saeed Akhtar* Saeed Akhtar Jasem Y. Al-Hashel Raed Alroughani

Objective: It has been argued that the unexpected stressful life events tend to alter immune function thereby increasing the susceptibility to autoimmune diseases including multiple sclerosis (MS). Using the database of the national MS registry, this quasi-experimental study assessed the impact of first gulf war on MS risk in Kuwait.

Methods: MS incidence data from 1980 to 2019 were obtained from Kuwait National MS registry. Age-standardized incidence rates (ASIRs) (per 100,000 person-years) by year (1980-2019) were computed using World Standard Population as a reference. Interrupted time series analysis with option of autoregressive order (1) was used to evaluate the impact of first gulf war (Iraqi invasion of Kuwait in 1990) on MS risk by treating 1990 as an intervention year.

Results: Estimated starting level of annual ASIR per year was 0.38. MS ASIR appeared to increase significantly every year preceding to 1990 by 0.45 (ASIR = 0.45; 95% CI: 0.15, 0.76; p = 0.005). In the first year of gulf war (1990), there seemed to be a non-significant increase in ASIRs of MS (ASIR = 0.85; 95% CI: – 5.16, 6.86; p = 0.775). Subsequent to interruption in the time series (gulf war of 1990), an upward trajectory continued until 2019 with a non-significant contribution in the annual increase in MS ASIR by 0.65 (ASIR = 0.65; 95% CI: – 0.22, 1.52; p = 0.138) (Fig 1). Durbin-Watson statistic both original (1.30) and transformed (1.89) showed non-significant autocorrelations across the time series observations on ASIRs.

Conclusions: The results provided the evidence that first gulf war of 1990 did not significantly contribute to the MS risk in Kuwait. Further studies may contemplate to look at this issue using multivariable time series to account for time-dependent covariates while modeling this and other stressful events.

Body Composition as a risk factor for Rotator Cuff Disease: A Systematic Review and Meta-Analysis Simone Herzberg* Simone Herzberg Gustavo Garriga Ayush Giri Nitin Jain

Several studies have investigated the relationship between obesity and rotator cuff disease. However, findings are inconsistent, and no systematic review or meta-analysis exists on this topic. We conducted a systemic review and meta-analysis on the association between obesity and rotator cuff disease. Articles meeting eligibility criteria and reporting on the association of any measure of obesity and rotator cuff disease were considered. Risk of bias was assessed with the ROBBINS-I tool. Meta-analysis was performed to quantitatively summarize associations between the most common measure of obesity, body mass index (BMI), and rotator cuff disease to report odds ratios (OR), and corresponding 95% confidence intervals (CI) for regression-based models and BMI mean differences (MD) between cases and controls. After full-text review of 218 articles, 12 articles assessing measures of obesity were eligible for meta-analysis. Individuals with rotator cuff disease were 1.16 times as likely to be overweight (OR: 1.16; 95% CI: 1.05, 1.29), and 1.29 times as likely to be obese (OR = 1.29; 95% CI: 1.16, 1.44) as compared with individuals without rotator cuff disease. Each unit increase in BMI was associated with 3% higher odds of rotator cuff disease (OR = 1.03; 95% CI: 1.02, 1.04). On average, individuals with rotator cuff disease had 0.48 kg/m^2 higher BMI than individuals without (MD: 0.48 95% CI: 0.11,0.84). We found obesity is associated with higher odds of having rotator cuff disease, however, concerns regarding confounding, inability to establish temporality and publication bias remain in extant literature. Research focused on causality is warranted. Targeting obesity as a risk factor for rotator cuff disease could decrease prevalence and progression of rotator cuff disease and improve patient care.

Adverse childhood experiences and adult weight and waist circumference in Mexican women Jocelyn Jaen* Jocelyn Jaen Dalia Stern Mario Flores-Torres Martín Lajous

Adverse childhood experiences (ACEs) cause severe stress among children and are highly prevalent, particularly in low- and middle-income countries. Experiencing ACEs could influence negative coping mechanisms related to food intake, thus increasing weight, and adiposity. Understanding the potential impact of childhood adversity on adiposity later in life requires analytic choices that consider factors occurring early in life. We evaluated the relation between ACEs and weight and waist circumference in adulthood among Mexican women. We conducted our analysis in 39,539 non-pregnant women with a valid assessment of ACEs by ACE-Questionnaire in 2014-20 from the Mexican Teachers' Cohort. Women were classified according to the number of *ACEs* (0, 1-2, 3,≥4), *ACEs domain* (Abuse, Neglect and, Home disfunction), and *ACE domain* combinations. We used self-reported weight and waist circumference which in this cohort are highly correlated to measured anthropometry. In our main multiple regression analyses, we included age, ethnicity, adult height, and indicators of childhood and adult socioeconomic status. We explored the impact of covariate choice on results and their interpretation. Mean weight was 69.9 Kg (IC95%:69.8-70.0) and waist circumference 89.0 cm (IC95%: 88.8-89.1). In our main analyses, we found that the higher the number of ACEs reported the stronger the association. Among those that reported ≥4 ACEs were 1.3 kg (IC95%0.8-1.8) heavier and had a larger waist circumference (3 cm, IC95%:2.3-3.7) relative to women who did not report ACEs. Women that experienced abuse, either alone or in combination with neglect, also had the highest weight (1.1 Kg, IC95%:0.8-1.5; 2.5 Kg, IC95%:1.4-3.5) and waist circumference (2.6 cm, IC95%:2.1-3.0; 3.3 cm, IC95%: 1.9-4.7) differences. Number and type of ACEs may affect adiposity later in life in women. Adequate covariate choice is essential for the interpretation of analyses that address early life factors and adiposity in adulthood.

Figure 1. Direct acyclic diagram for the association between adverse childhood experiences and weight and waist circumference in adulthood. MTC
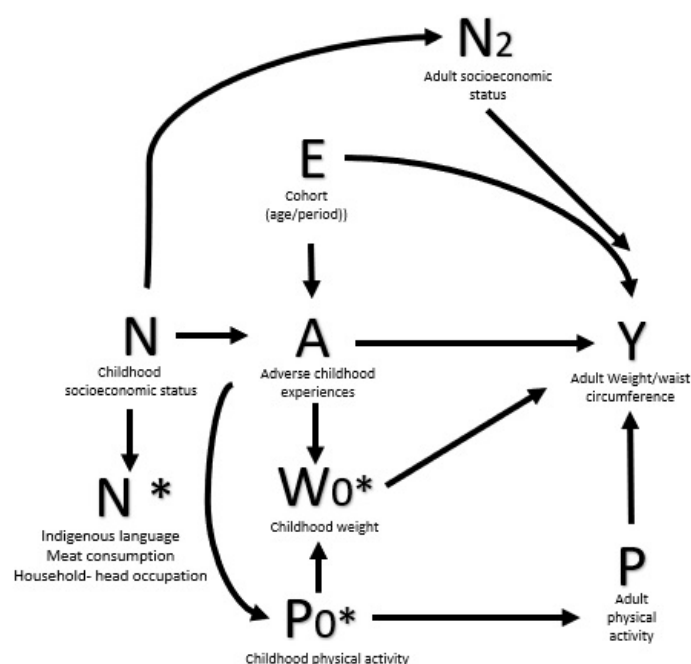
The Association Between Maternal Diet Quality and Perinatal and Subacute Postpartum Outcomes among Latinas
Megan Ward Harvey* Megan Harvey Sofija Zagarins Katherine Tucker Bess Marcus Milagros Rosal JoAnn Manson Lisa Chasan-Taber

Maternal diet quality has been inversely associated with adverse pregnancy and birth outcomes, although findings are inconsistent. Few studies have examined the impact on subacute postpartum outcomes, used a measure of diet quality designed for pregnancy or focus on Latinas, a group with poorer diet quality and higher rates of adverse maternal outcomes, relative to non-Latina White women. Therefore, we evaluated the association between the Alternate Healthy Eating Index for Pregnancy (AHEI-P) and pregnancy, birth and subacute postpartum outcomes among 168 predominantly Puerto Rican participants in Estudio PARTO, a randomized trial of a lifestyle intervention in Western Massachusetts (2013-2017). Diet was measured at a mean of 28.1 (SD=6.6) weeks gestation by trained bicultural/bilingual personnel via three 24-hour recalls. Associations were modeled with multivariable linear and logistic regressions, adjusting for age, pre-pregnancy body mass index, activity level, caloric intake, and intervention group. Higher scores on the AHEI-P (indicating better diet quality) were not associated with total gestational weight gain (β=-0.08, p=0.30), hypertension (OR=0.99 95% CI=0.95-1.03) or fasting glucose during pregnancy (β=0.04, p=0.65). Women with higher scores on the AHEI-P experienced a slightly longer second stage of labor (β=0.23, p=0.048), but AHEI-P scores were not associated with other birth outcomes, including gestational age at delivery, infant birth weight, number of days spent in the hospital, length of first or third stage of labor, or APGAR scores. AHEI-P scores were also not associated with postpartum body mass index (β=-0.17, p=0.08) or fasting glucose tolerance (β=-0.07, p=0.72).Findings suggest that current measures of maternal diet quality may be of limited value among Puerto Ricans in the United States and highlight the need for better tools to identify the nutrient profile among Latinas in the United States to best predict positive birth outcomes.

Nutrition/Obesity

Body mass index and mortality among Hispanic adults in the United States Yingxi Chen*

Yingxi Chen Cari Kitahara Meredith Shiels Neal Freedman Christian Abnet Amy Berrington de González

Background

A high body mass index (BMI) is associated with increased mortality in healthy, non-Hispanic White and Black individuals, though inconsistent results have been reported among Hispanic adults. The aim of this study was to examine the association between BMI and mortality among US Hispanic adults using data from two large well-characterized US prospective studies, the NIH-AARP and the PLCO cohort.

Methods

Baseline was defined as the date of completion of study questionnaire with self-reported information, including height, weight, smoking status, and history of chronic diseases. We excluded participants with a BMI≥50 at baseline. We used Cox regression to estimate hazard ratios (HRs) for the association between BMI and mortality with age as the underlying time scale. Models were adjusted for marital status, education, smoking, and comorbidities. A total of 12,949 self-reported Hispanic adults were included in the study with a median age at baseline of 61 years (range, 50-74 years).

Results

During a median follow-up period of 16 years, 2,604 deaths were identified. We observed a J-shaped relationship between BMI and mortality. Mortality was generally lowest among participants with a BMI of 22.5-24.9. Compared to this reference, mortality risk increased significantly with a BMI of 15.0-18.4, 30.0-34.9, 35.0-39.9, and 40.0-49.9 [HR: 1.3 (95%CI 1.6-3.4), 1.3 (1.2-1.5), 1.6 (1.3-1.9), and 2.1 (1.7-2.7), respectively]. Similar results were observed among healthy participants who reported never smoking at baseline. Additionally, risk of heart disease mortality was 2.2 times higher for a BMI ≥30 (2.2, 1.4-3.6) whereas risk increased for 40% for cancer mortality (1.4, 0.9-2.1). We also observed a strong association between waist circumference and mortality among women (HR: 1.7, 1.1-2.8) for waist circumferences of ≥95 vs <75cm, and men (1.4, 1.1-1.9) for waist circumferences of ≥110 vs <90cm.

Conclusions

Among Hispanic adults, a high BMI was associated with all-cause mortality and mortality from heart disease and cancer. Our results further highlight the need for efforts to reduce the rising population trend for excess weight.

Socioeconomic and acculturation predictors of weight loss during a 10-week intervention among Latino children Michael S. Bloom* Michael Bloom Robyn Mehlenbeck Jenna R. Krall Margaret T. Jones

Child obesity is a public health crisis that disproportionately impacts Latino children. For the purpose of informing culturally-appropriate weight management strategies, we estimated associations of socioeconomic and acculturation factors with weight loss during a 10-week intervention. From 2017-21, n=113, 4-11 years of age, were enrolled into a community-based, culturally-adapted weight-loss intervention delivered in Spanish. Children of Latino descent were eligible if pre-pubertal, BMI-for-age ≥85th %tile, without chronic disease, and not taking medication. Body mass index (BMI), BMI-for-age %tile (BMI-Z), waist circumference (WC), and body fat % (BF%) were measured pre- and post-intervention, and parents completed a survey. Children and parents attended weekly meetings, which included health and nutritional counseling, cooking demonstrations, and group exercise. We used linear regression to estimate predictors of pre-post intervention weight change, adjusting for child's age, sex, year enrolled, and household income. Adjusted mean BMI (-1.19 kg/m^2; 95%CI:-1.86, -0.52), BMI-Z (-0.16; 95%CI:-0.26, -0.05), BF% (-2.77; 95%CI:-4.43, -1.10), and WC (-1.15 cm; 95%CI:-4.32, 2.01) decreased among n=42 study completers without missing data. Receipt of reduced price school breakfast was associated with a decrease in BMI vs. no receipt (β=-0.75 kg/m^2, 95%CI:-1.38, -0.11). Greater Spanish proficiency was associated with a decrease in BMI-Z (β=-0.03; 95%CI:-0.07, 0.01). Summer meal program use (β=-5.81 cm; 95%CI:-11.69, 0.08) and emergency food assistance use (β=-4.78 cm; 95%CI:-10.12, 0.56) were associated with decreases in WC vs. no use. In contrast, recent SNAP-use was associated with an increase in BF% vs. no use (β=2.84; 95%CI:0.88, 4.80). Household income and English proficiency and use were not associated with weight loss. The results suggest that socioeconomic factors were associated with weight loss during a community-based intervention program among Latino children.

Prospective associations of sleep with diet and adiposity among toddlers born preterm
Samrawit F. Yisahak* Samrawit Yisahak Kelly M. Boone Sarah A. Keim

Objective: Associations of sleep with diet and adiposity are understudied during toddlerhood when lifestyle habits and taste preferences establish. Prior studies focused on total sleep duration, though day and nighttime sleep could have different associations due to circadian regulation of appetite/metabolism. Further, studies mostly focused on short sleep, rather than examining the entire range of sleep duration. In a secondary analysis of a randomized controlled trial of toddlers born preterm, we examined prospective associations of sleep duration and timing with dietary and anthropometric measures.

Design/methods: Children born at <35 weeks' gestation were randomized at 10-17 months (age corrected for prematurity) to placebo or fatty acid supplementation for 180 days. Caregivers reported toddlers' sleep habits at baseline using the Brief Infant Sleep Questionnaire. We defined short and long sleep per American Academy of Sleep Medicine recommendations (<12 hrs./day and >16 hrs./day for children <1 year, and <11 hrs./day and >14 hrs./day for children 1-2 years, respectively). After 180 days, caregivers reported the child's past month diet in a food frequency questionnaire, and child's anthropometry was measured using standardized protocols. We used linear and logistic regression to assess associations with outcomes in 284 toddlers with sleep and plausible dietary data.

Results: Nearly 30% of toddlers had long or short sleep. More nighttime sleep (per hour) was associated with higher intake of fiber (beta= 0.87 grams (95% CI: 0.20, 1.54)), and short sleep was associated with lower fiber intake (beta= -3.37 grams (95% CI: -6.11, -0.63)). Sleep duration and timing were not associated with measures of adiposity (**Table**).

Conclusions: Longer nighttime, but not daytime sleep, was associated with higher intake of fiber suggesting that sleep timing maybe important for diet quality. Higher than recommended sleep showed no associations with unfavorable diet or adiposity.

Table: Prospective associations of sleep with diet and adiposity in the Omega Tots trial (2012-2017, n=284, Columbus, Ohio)

Dietary Outcomes	Total sleep	Daytime sleep	Nighttime sleep	Long sleep[1]	Short sleep[2]	Long or short sleep
	Beta (95% CI) per 1 hr. of sleep			Beta (95% CI)		
Total energy intake (kcal/day)	22.32 (-13.24, 57.88)	17.07 (-42.24, 76.37)	26.27 (-19.09, 71.63)	87.98 (-91.39, 267.35)	-104.51 (-289.42,80.39)	-6.13 (-145.06, 132.80)
Carbohydrates (grams/day)	3.48 (-1.21, 8.18)	1.66 (-6.17, 9.50)	4.69 (-1.29, 10.67)	12.29 (-11.39, 35.98)	-15.20 (-39.60, 9.21)	-1.19 (-19.54, 17.16)
Added sugars (grams/day)	0.08 (-1.48,1.64)	0.30 (-2.30, 2.89)	-0.04 (-2.03, 1.95)	-3.23 (-11.07, 4.61)	-1.79 (-9.89, 6.31)	-2.93 (-9.00, 3.13)
Fiber (grams/day)	0.49 (-0.04, 1.02)	-0.13 (-2.14, 1.58)	**0.87 (0.20, 1.54)**	0.69 (-2.00, 3.37)	**-3.37 (-6.11, -0.63)**	1.48 (-3.55, 0.59)
Total fats (grams/day)	0.49 (-1.02, 2.01)	0.97 (-1.55, 3.49)	0.23 (-1.70, 2.17)	3.40 (-4.24, 11.04)	-1.67 (-9.56, 6.21)	1.09 (-4.82, 7.01)
Saturated fats (grams/day)	0.16 (-0.47, 0.78)	0.75 (-0.28, 1.78)	0.18 (-0.98, 0.61)	1.91 (-1.22, 5.05)	-0.02 (-3.27, 3.22)	1.13 (-1.30, 3.56)
MUFAs (grams/day)	0.18 (-0.36, 0.72)	0.18 (-0.72, 1.08)	0.19 (-0.50, 0.87)	0.93 (-1.79, 3.66)	-0.98 (-3.79, 1.83)	0.01 (-2.10, 2.12)
PUFAs (grams/day)	0.07 (-0.25, 0.40)	-0.04 (-0.58, 0.51)	0.14 (-0.28, 0.56)	0.28 (-1.37, 1.93)	-0.10 (-1.80, 1.61)	0.11 (-1.16, 1.38)
EPA + DHA (grams/day)	0.002 (-0.007, 0.01)	-0.01 (-0.02, 0.01)	0.01 (-0.003, 0.02)	0.02 (-0.06, 0.03)	-0.03 (-0.07, 0.01)	-0.03 (-0.06, 0.01)
Protein (grams/day)	1.26 (-0.58, 3.10)	0.52 (-2.55, 3.59)	1.75 (-0.60, 4.09)	3.24 (-6.06, 12.53)	-8.08 (-17.63, 1.46)	-2.61 (-9.79, 4.58)
Anthropometric outcomes	Beta (95% CI) per 1 hr. of sleep			Beta (95% CI)		
Weight-for-height z-score	-0.04 (-0.12, 0.03)	- 0.07 (-0.19, 0.05)	-0.03 (-0.12, 0.07)	0.04 (-0.33, 0.41)	0.17 (-0.21, 0.56)	0.12 (-0.17, 0.41)
Subscapular skinfold z-score	0.00 (-0.09, 0.09)	0.02 (-0.13, .17)	0.01 (-0.13, 0.10)	0.17 (-0.29, 0.63)	0.01 (-0.47, 0.50)	0.11 (-0.25, 0.48)
Triceps skinfold z-score	-0.01 (-0.07, 0.06)	0.05 (-0.05, 0.16)	-0.05 (-0.13, 0.04)	0.24 (-0.08, 0.56)	0.14 (-0.21, 0.48)	0.22 (-0.03, 0.48)
Weight-for-height z-score categories[3]	OR (95% CI) per 1 hr. of sleep			OR (95% CI)		
Wasted (2.14%)	1.18 (0.67, 2.06)	0.91 (0.37, 2.23)	1.38 (0.68, 2.81)	9.21(0.59, 143.03)	Inestimable	1.74 (0.22, 13.76)
Normal (76.16%)	Referent	Referent	Referent	Referent	Referent	Referent
At risk of overweight or above (21.7%)	0.93 (0.78, 1.11)	0.83 (0.61, 1.13)	0.99 (0.79, 1.24)	1.86 (0.79, 4.39)	1.40 (0.57, 3.45)	1.77 (0.90, 3.49)

Abbreviations: MUFA, monounsaturated fatty acids. PUFA, polyunsaturated fatty acids. EPA, eicosapentaenoic acid. DHA, docosahexaenoic acid.
Covariates, measured at baseline, were child's sex, race, ethnicity, pre-maturity corrected age (in months), birthweight, breastfeeding history, as well as maternal education, marital status, annual household income, and treatment arm. Z-scores using World Health Organization growth charts.
1. Long sleep: >16 hours/day for children < 1 year and >14 hours/day for children 1-2 years
2. Short sleep: <12 hours/day for children <1 year and ,<11 hours/day for children 1-2 years
3. Weight-for-height z-score categories: Wasted (<-2.0), Normal (-2.0 – 1.0), At risk of overweight (>1.0 – 2.0), Overweight (>2.0 – 3.0), Obese (>3.0). At risk of overweight, overweight, and obese collapsed due to small sample size

Association between prenatal exposure to per- and polyfluoroalkyl substances mixture and childhood obesity at age of 7 years Shanyu Zhang* shanyu zhang

Background: Perfluoroalkyl substances (PFAS) were consider as obesogens that cross placenta. However, few studies assess the joint effects of prenatal PFAS mixture exposure on childhood adiposity.

Method: Pregnant women enrolled in the Laizhou Wan Birth Cohort (LWBC) of Shandong, China. Ten major PFAS in third trimester serum (n=369) were measured using LC-MS. Body mass index (BMI), waist circumference (WC), waist to height ratio, fat mass, and % body fat were ascertained in 7 year old children as measures of adiposity (n=206). Multivariable linear regression and weighted quantile sum (WQS) regression were used to assess the association between prenatal individual PFAS and PFAS mixture and child obesity. The sex-interaction was also analyzed in our study.

Results: The detection rate of ten PFAS was more than 80%, and the highest PFAS was PFOA (45.14 ng/mL). Among all children, PFHpA was associated with decreased WC (β= -4.97, 95% CI: -9.47, -0.46), and PFOSA (β= -9.05, 95% CI: -17.31, -0.79) was associated with decreased fat mass and % body fat (β= -18.77, 95% CI: -34.84, -2.71). The joint effect of PFAS was also associated with decreased fat mass and % body fat in WQS, and PFOSA was the greatest contributor. The sex-specific was observed in our study: PFHpA, PFOSA and the joint effect of ten PFAS was negatively associated with five obesity measurements in boys, PFHpA and PFOSA were the two greatest contributors; However, only PFHpA was associated with BMI in single PFAS analysis in girls, while the joint effect of ten PFAS was positively associated with fat mass, BMI, WC and waist to height ratio, the PFBS was the greatest contributors for the four.

Conclusion: Our results suggested the effect of prenatal exposure to PFAS on Childhood obesity was in a sex- or PFAS-dependent manners.
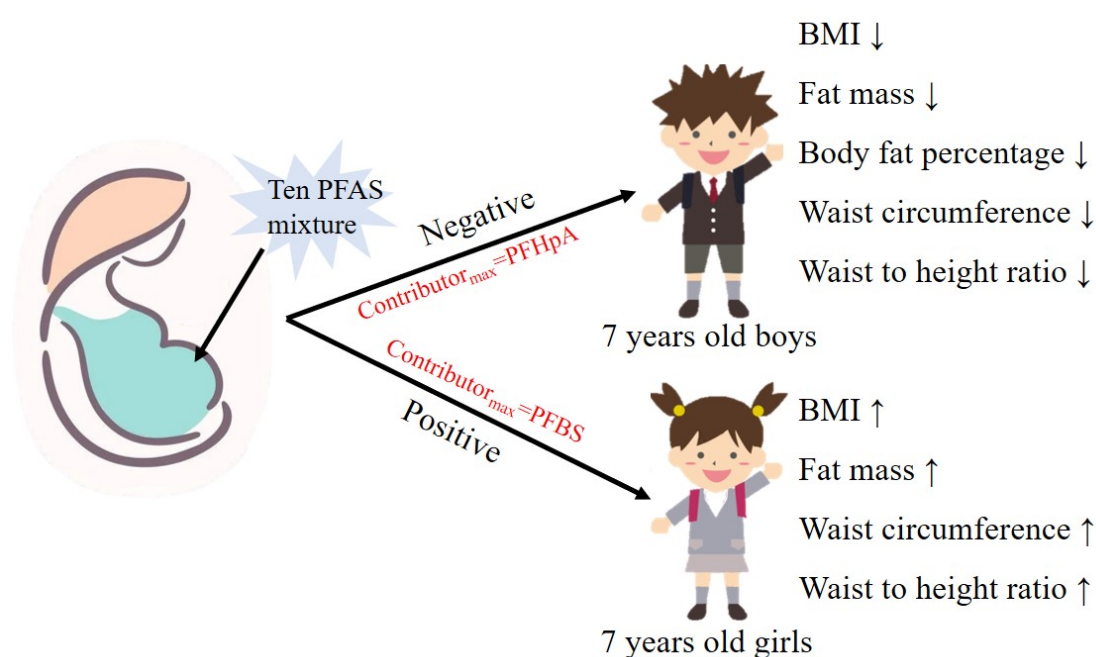
Community food environment in Mexican cities: the role of social environment on healthy food availability. Letícia de Oliveira Cardoso* Letícia Cardoso Dayan Carvalho Ramos Salles de Oliveira Mariana Carvalho de Menezes Joanna Miguez Nery Guimarães Adriana Lúcia Meireles Yenisei Ramirez Toscano Carolina Perez-Ferrer Usama Bilal

Dietary behaviors and the distribution of the community food environment in cities are shaped by its social environment. Using a harmonized dataset from the SALURBAL project, we investigated associations between social environment inequities and the community food environment in 28.628 Mexican neighborhoods within 406 sub-cities in 32 Mexican cities. The Mexican community food environment was composed of 1.711.896 food stores classified into fresh food stores (16.2%), mixed food stores (63.8%), ultra-processed food stores (19.6%), and supermarkets or hypermarkets (0.4%). To characterize distinct social environments, we combined z-scores standardized socioeconomic indicators from national census as factors reflecting living conditions, service provision, and educational attainment based on principal component analysis. Urban features included landscape, street design, and natural environment metrics. The associations between environments were modeled by zero-inflated negative binomial multilevel models with random intercepts for sub-cities nested at the city level. Higher social environment index score levels were associated with higher densities of general food stores across Mexico. When adjusted for urban characteristics, better living conditions were associated with higher densities of fresh food stores, ultra-processed food stores, and supermarkets/hypermarkets. Greater service provision was associated with higher densities of fresh food stores, mixed food stores, and supermarkets/hypermarkets. Better educational attainment was associated with higher densities of general food stores. These results highlight a considerable heterogeneity in food, social, and built environments across Mexico, revealing modifiable factors that could be amenable to policies aimed toward improving healthy food availability, and consequently, healthy diets in Mexico.

Occupational
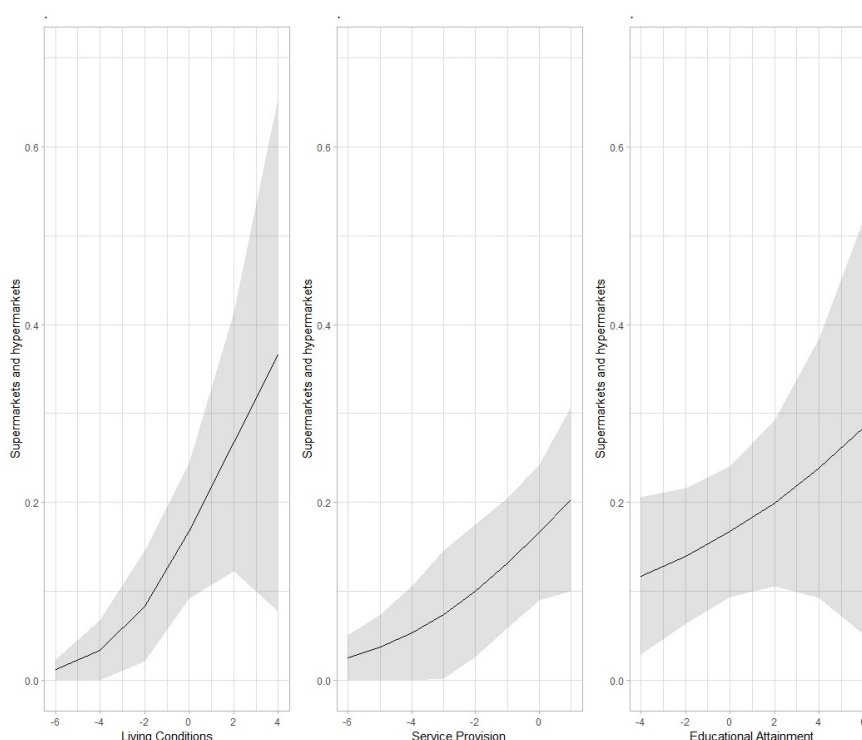
A Bayesian approach to estimating prevalence of hearing loss in post-9/11 Veterans using VA health care Kelly M Reavis* Kelly Reavis Garnett McMillian James A Henry Jonathan M Snowden Brandon Smith Wendy Helt Kathleen F Carlson

Objective: To estimate the prevalence of mild, moderate, and severe hearing loss among post-9/11 Veterans who have recently separated from the military and who use the Veterans Affairs (VA) health care system for their primary or mental health care. This estimate is critical for audiologic service resource allocation and planning. Estimation of the burden of hearing loss requires measurement of hearing thresholds. However, because not all Veterans are tested, such data are not readily available. To overcome this gap, we leveraged VA healthcare data linked to primary data collected from Veterans and employed a novel estimation technique.

Methods: The VA administrative study sample (n=475,305) included Veterans who separated from the military between August 2011 and August 2017 and were classified as either having a hearing test or not. Primary data included Veterans enrolled in the Noise Outcomes in Service members Epidemiology (NOISE) Study (n=476), a prospective cohort study conducted within the VA Portland Health Care System. The analysis used cross-sectional data. Predictors of hearing loss severity included age, sex, and military service branch. We used Bayesian logic within a multilevel regression model with poststratification to estimate the prevalence of hearing loss.

Results: Only 18.2% of the VA sample had hearing tests. Based on model results, we estimated the prevalence of hearing loss among all Veterans in the target population to be 10.6% (90% credible intervals: 7.8%-19.9%). Most hearing loss was mild.

Conclusions: There is a high burden of hearing loss among recently separated post-9/11 Veterans who use VA healthcare. Mild hearing loss can impose difficulties in everyday life, and when present during earlier ages can culminate in reduced functioning and quality of life during older ages. Therefore, it is imperative that we investigate structural interventions and secondary or tertiary prevention strategies to mitigate the consequences of hearing loss.

Safety climate and self-reported injury: Assessing differences by fire department organization type Ashley M. Geczik* Ashley M. Geczik Jin Lee Andrea L. Davis Joseph A. Allen Jennifer A. Taylor

Background Safety climate is an upstream predictor of safety behaviors (e.g. safety compliance), organizational outcomes (e.g. burnout), and safety outcomes (e.g. injuries). The Fire Service Organizational Culture of Safety (FOCUS) survey measures the industry-specific safety climate of the US fire and rescue service. It is expressed by two factors, Management Commitment to Safety and Supervisor Support for Safety.

Methods Using the FOCUS beta test, our analytic population resulted in 8,414 individuals nested within 611 stations in 125 fire departments after exclusionary criteria. We reported on the descriptive statistics of our sample. Multilevel logistic regression was used to examine the relationship between the odds of self-reported injury in the 12 months prior to completing FOCUS and safety climate scores. Specifically, individual-level injury status (yes/no) was regressed on department level Management Commitment or Supervisor Support scores, while random effects were specified at the department and station levels. These models were adjusted for age, years of experience, sex, and rank.

Results Individuals within our sample belonged to three different organization types: career (82.0%), combination (career and volunteer) (13.5%), and volunteer (4.5%) fire departments. 1,406 individuals (16.7%) reported that they had experienced an injury. Among all individuals, we observed that a one-unit increase in Management Commitment decreases the odds of injury by 3% (OR:0.97, 95% CI:0.97-0.98). We observed that a one-unit increase in Supervisor Support decreases the odds of injury by 4% (OR:0.96, 95% CI:0.94-0.98). Similar associations were observed among career departments.

Discussion We observed that individuals had decreased odds of self-reported injury in the past 12 months with increasing Management Commitment and Supervisor Support. This finding suggests that these safety climate elements are important drivers in fire service injury prevention.

Prenatal weight change trajectories among twin gestations Amy R. Nichols* Amy Nichols Sina Haeri Anthony Rudine Natalie Burns Paul J. Rathouz Monique Hedderson Saralyn F. Foster Rachel Rickman Elizabeth M. Widen

Despite an increase in twin pregnancies in recent decades, the Institute of Medicine twin gestational weight gain (GWG) recommendations remain provisional and provide no guidance for timing or pattern of weight change. We sought to characterize GWG trajectory patterns and examine associations with birth outcomes.

Prenatal and delivery records were examined for 320 women who delivered twins at a maternal-fetal medicine practice in Austin, TX 2011-2019. We modeled GWG for those with at least 1 measured weight in the first trimester and a minimum of 3 prenatal weights. Trajectories were modeled to 32wk (mean delivery 33.7±3.3wk) using flexible latent class mixed models with low-rank thin plate splines. Associations between trajectory classes and neonatal outcomes were analyzed using linear or Poisson regression.

GWG at delivery was 15.4±6.3kg for underweight BMI, 15.4±5.8kg for normal weight, 14.7±6.9kg for overweight, and 12.5±6.6kg for obesity. Three GWG trajectory classes were identified: low (1), moderate (2), or high gain (3). Those in Class 1 (24.7%) maintained weight to 15wk, then gained an estimated 6.6kg at delivery. Class 2 (60.9%) exhibited steady gain with 13.5kg predicted gain, and Class 3 (14.4%) showed rapid gain with a predicted 21.4kg gain. Compared to Class 3, Class 1 pregnancies were associated with lower continuous size for gestational age z-score (CSGAZ; b=-0.50, 95%CI -0.81,-0.19), and reduced risk for large for gestational age (LGA) infants (IRR=0.19, 95%CI 0.05,0.65) and preterm birth <32wk (IRR=0.54, 95%CI 0.32,0.93). Class 2 pregnancies were associated with decreased CSGAZ (b=-0.28, 95%CI -0.55, -0.01) and LGA risk (IRR=0.40, 95%CI 0.20,0.80).

GWG followed a low (1), moderate (2), or high (3) weight gain trajectory; both low and moderate patterns were associated with lower CSGAZ and reduced risk for LGA and preterm birth. The optimal pattern of maternal weight change that balances risk for mothers and infants requires further investigation.

Utilizing Causal Survival Curves to Assess the Influence of PM2.5 Exposure on Emergency Department Visits During the First Year of Life in Term and Preterm Births Anaïs Teyton*

Anaïs Teyton Tarik Benmarhnia Gretchen Bandoli

The impact of $PM_{2.5}$ on infant health is critical to study, given the consequences that childhood air pollution exposure can have across the life course. Air pollution exposure is also modifiable through shifts in behavior and policy implementation, making it possible to reduce these health impacts. To date, few studies have evaluated the effects of air pollution on the risk of infant hospitalization or emergency department visits, as birth certificates and hospital admissions data are rarely combined. This study assessed the relationship between $PM_{2.5}$ exposure and all-cause emergency department visits during the first year of life and examined whether preterm infants are more susceptible to $PM_{2.5}$ exposure than term infants. Using data from over 2 million births across 2014-2018 from the Study of Outcomes in Mothers and Infants, a discrete time model with pooled logistic regressions was used to assess $PM_{2.5}$ exposure and time to emergency department visits during each week of the first year of life, and pooled mixed effects models were utilized to aggregate effect estimates across the first year of life. Moreover, since the health impacts of $PM_{2.5}$ can change over time, adjusted causal survival curves using g-computation were utilized, as these do not assume a proportional hazard, they provide the probability of not having the outcome at each given time point had everyone been exposed or unexposed, they allow for relative and absolute scale estimates to be calculated, and confounders can be adjusted for. Adjusted odds ratios were found to be positive for most weeks during the first year of life across the full population, and odds ratios tended to be positive and stronger for preterm infants than term infants, particularly during the first few weeks of life. Overall, adjusted causal survival curves allow for complex time-varying structures to be considered and make it possible to simulate the benefits of interventions at different exposure windows.

Prenatal PM2.5 Exposure is Associated with Third Trimester Fetal Weight and Abdominal Circumference within the MADRES Cohort Alicia Peterson* Alicia Peterson Rima Habre Zhongzheng Niu Monica Amin Shohreh Farzan Sandrah Eckel Nathana Lurvey Deborah Lerner Fred Lurmann Nathan Pavlovic Brendan Grubbs Daphne Walker Edward Grant Theresa Bastain Carrie Breton

Prenatal air pollution exposure has been significantly associated with low birthweight and pre-term birth; however, few studies have assessed the influence on fetal growth measured *in utero*. This study's objective was to examine whether exposure to air pollutants during pregnancy was associated with fetal growth during the third trimester of pregnancy in 281 mothers from the larger Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) cohort. Mean pollutant concentrations were computed for four ambient air pollutants (Particulate Matter $(PM)_{2.5}$ µg/m^3, PM_{10} µg/m^3, Nitrogen Dioxide (NO_2) ppb, and Ozone (O_3) ppb) from daily average concentrations assigned to the participant's residence from conception date until ultrasound scan date (gestational age (GA): 32±2 weeks). Fetal growth outcomes were measured during the third trimester study visit by a certified sonographer and included estimated fetal weight (EFW) in grams, head circumference (HC) in mm, abdominal circumference (AC) in mm, biparietal diameter (BPD) in mm and femur length (FL) in mm. Linear regressions adjusted for maternal age, income, education, race, parity, pre-pregnancy BMI, fetus sex, GA at scan, season of scan, and average temperature were used to investigate associations between each prenatal ambient air pollutant and fetal growth outcome. Participants were 29±6 years old, predominately Hispanic (82%) and had a high school diploma or less of education (58%). Results showed that for every µg/m^3 increase in $PM_{2.5}$ there were significant inverse associations with both AC (β = -1.7; 95% CI -3.1,-0.3) and EFW (β= -24.0; 95% CI -47.3,-0.8). Associations remained significant in multipollutant models adjusted for O_3 (EFW (β=-32.2; 95% CI -61.2,-3.2); AC (β= -1.9; 95% CI -3.7,-0.3)). These results in an environmental health disparities population indicate that exposure to $PM_{2.5}$ during development may have critical implications on fetal growth that are detectable prior to birth.

Late preterm and early term birth and child growth: A retrospective cohort study Yulika Yoshida-Montezuma* Yulika Yoshida-Montezuma Branavan Sivapathasundaram Hilary K. Brown Charles Keown-Stoneman Russell J. de Souza Teresa To Cornelia M. Borkhoff Catherine S. Birken Jonathon L. Maguire Laura N. Anderson

Accelerated postnatal growth is a risk factor for obesity. It is unclear whether children born late preterm (34-36 wks) or early term (37-39 wks), compared to term (>39 wks), have different growth trajectories. To assess the association between gestational age groups and growth trajectories, we conducted a retrospective cohort study of children born between 2006-2014, followed to 2021 in Ontario, Canada. Children from singleton births in TARGet Kids! primary care network with repeated measures of weight and height from birth to 14 yrs were linked to provincial health administrative databases. Piecewise linear mixed models were used to model weight (kg/mo) and height (cm/mo) trajectories for each gestational age group with knots at 3, 12, and 84 mos. A total of 4423 children were included with a mean of 11 weight and height measures per child. The mean difference in rate of weight gain for late preterm compared to term was -0.05 kg/mo (95% confidence interval [95% CI] -0.41, 0.31), 0.08 (95% CI -0.04, 0.20), -0.00 (95% CI -0.01, 0.01), and -0.04 (95% CI -0.06, -0.03) at 0-3, 3-12, 12-84, and >84 mos of age, respectively. There were no differences between early term and term birth for rate of weight gain. The mean difference in rate of height gain for late preterm compared to term was 0.84 cm/mo (95% CI 0.33, 1.35) at 0-3 mos, and 0.06 (95% CI -0.04, 0.17) at 3-12 mos, but no differences afterwards. Differences in rate of height gain between early term compared to term were 0.38 cm/mo (95% CI 0.11, 0.65) at 0-3 mos, and 0.04 (95% CI -0.02, 0.10) at 3-12 mos, but no differences afterwards. Weight trajectories were similar between children born late preterm and term with only small differences beyond 84 mos. Differences in height trajectories were observed with children born late preterm or early term having increased rate of height gain at 0-3 mos compared to term. Extended follow-up is needed to determine if these differences influence obesity risk later in life.

Motor disorders and health-related quality of life at age five in a European multi-country cohort of children born extremely preterm Adrien M. Aubert* Adrien Aubert Raquel Costa Mariane Sentenac Ulrika Ådén Samantha Johnson Marina Cuttini Mairi Männamaa Iemke Sarrechia Arno F. van Heijst Michael Zemlin Véronique Pierrat Jennifer Zeitlin

Background

Motor disorders are a common consequence of extremely preterm birth (EPT; <28 weeks' gestation) and can limit daily activities, schooling and social relationships. Cerebral palsy (CP) affects about 10% of children and non-CP movement difficulties (MD) are highly prevalent, although they have been less studied and tend to be under-diagnosed, especially in the absence of other sensory, cognitive or behavioural difficulties. We investigated the association of CP and non-CP MD with health-related quality of life (HRQoL) among 5-year-old children born EPT.

Methods

We included children followed-up at age 5 from a population-based EPT birth cohort in 2011-2012 in 11 European countries (N=1,021). Children without CP were classified using the Movement Assessment Battery for Children – 2nd edition as having significant MD ($\leq 5^{th}$ percentile of standardised norms) or being at risk of MD (6th-15th percentile). Parents reported on CP diagnoses and HRQoL using the Pediatric Quality of Life Inventory™. We compared HRQoL scores between groups and used linear regression to adjust for social characteristics overall and among children without other developmental difficulties.

Results

The prevalence of children born EPT with CP, significant MD and at risk of MD were 10.5%, 25.8% and 21.0%, respectively. They had lower HRQoL total scores [95% confidence intervals] than those without MD: -26.1 [-29.0; -23.2], -9.7 [-11.9; -7.4] and -5.7 [-7.9; -3.5]. Decreases were greater for physical scores: -37.6 [-42.0; -33.3], -12.8 [-16.1; -9.5] and -6.5 [-9.8; -3.3] than psychosocial scores: -20.0 [-23.1; -16.9], -8.1 [-10.4; -5.7] and -5.3 [-7.7; -3.0]. Lower scores associated with MD persisted after adjustment for social circumstances and exclusion of children with other developmental difficulties.

Conclusion

Motor disorders among 5-year-old children born EPT were associated with lower HRQoL, even among children with less severe motor difficulties and without other developmental difficulties.

Longitudinal growth patterns in twins and singletons in the Upstate KIDS cohort Jessica L Gleason* Jessica Gleason Edwina Yeung Rajeshwari Sundaram Pauline Mendola Erin Bell Kristen Polinski Katherine Grantz

Twins are typically smaller than singletons at birth, but little is known about their growth patterns in childhood and whether they show the same signs of excess growth displayed by singletons born small for gestational age (SGA), which may indicate future risk of cardiometabolic morbidity. The Upstate KIDS study collected longitudinal data on children's growth among twins and singletons. We compared z scores for height, weight, and BMI at 0-3 and 7-9 years of age, as well as risk of rapid weight gain in infancy and overweight/obesity among non-SGA twins (n=1132), non-SGA singletons (n=3129), and two groups of SGA twins: uncertain SGA twins (<10th percentile for birthweight by a singleton reference but >10th% by a twin reference; n=316) and true SGA twins (<10th% by a twin reference; n=144). Using generalized linear mixed models, we found that non-SGA twins were generally smaller than non-SGA singletons at both time points. Compared to non-SGA twins, both SGA twin groups had lower weight and BMI z scores at both time points, though both SGA twin groups caught up in height with non-SGA twins by 7-9 years (Figure). Similarly, compared to non-SGA singletons, differences in z scores decreased between 0-3 and 7-9 years for uncertain SGA and true SGA twins, though true SGA twins had the lowest z scores for all measures. Both twin groups had higher risk of rapid infant weight gain compared to non-SGA singletons (RR=2.31; 95% CI 2.10, 2.54), but excess weight didn't persist into childhood. Compared to non-SGA singletons, no twin group had elevated risk of overweight/obesity at either 2-3 years or 7-9 years with RR at 7-9 being 0.88 (0.67, 1.15), 0.82 (0.52, 1.28), and 0.85 (0.44, 1.62) for non-SGA twins, uncertain SGA twins, and true SGA twins, respectively. Though twins had lower height, weight, and BMI z scores at birth and into toddlerhood, differences were reduced by 7-9 years, even for true SGA twins, and no group of twins showed heightened risk of overweight/obesity.
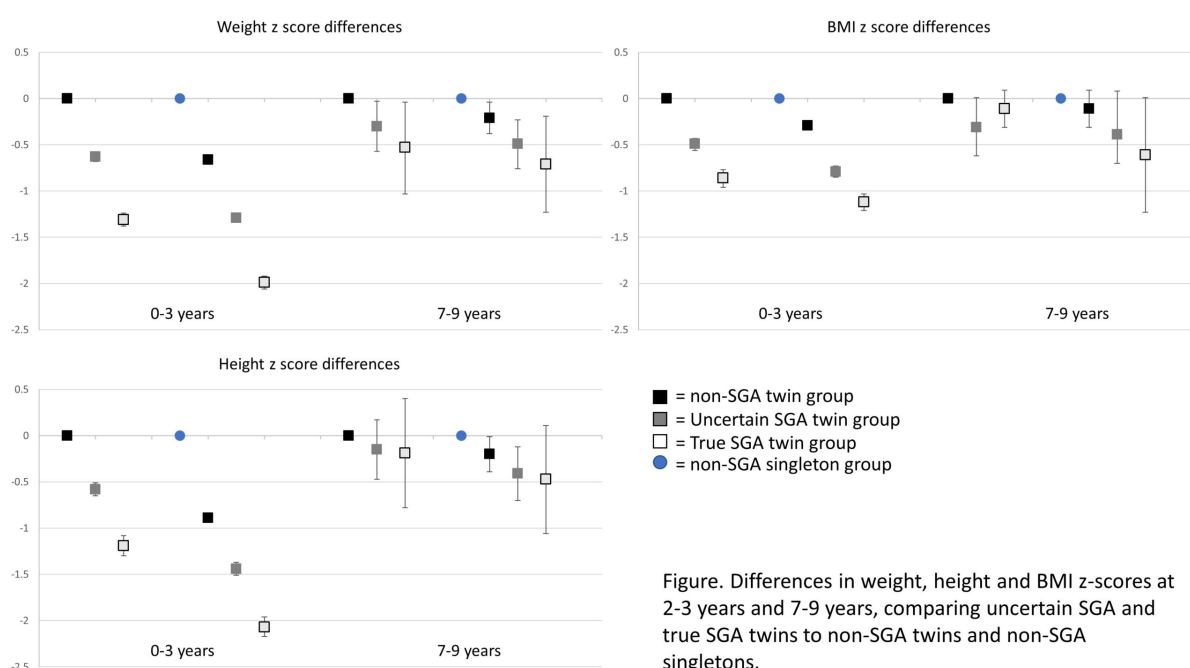

Figure. Differences in weight, height and BMI z-scores at 2-3 years and 7-9 years, comparing uncertain SGA and true SGA twins to non-SGA twins and non-SGA singletons.

Using a neural network to derive neurobehavioral profiles in the New Hampshire Birth Cohort Study Julia Anglen Bauer* Julia Bauer Margaret Karagas Megan E. Romano John Pearce Susan Korrick David Bellinger

Background: Neurobehavioral outcomes are often interdependent across assessments and over time, necessitating statistical approaches to simultaneously model outcomes. Our objective was to characterize childhood neurobehavioral profiles using scores from multiple neurobehavioral assessments and determine their association with known predictors of individual neurobehavioral measures.

Methods: A map-based hierarchical clustering method, the self-organizing map (SOM), was applied to longitudinal neurobehavioral data from New Hampshire children from approximately 3- to 5-years of age (n=235) to identify common neurobehavioral profiles. Profiles derived from measures of maladaptive and adaptive behavior, social responsiveness, cognition and motor performance were examined in relation to maternal-child characteristics using multinomial logistic regression.

Results: We identified six distinct neurobehavioral profiles with 18 to 57 members per profile. As compared to mean scores, profiles included participants with 1) higher maladaptive behavior and social impairment that reduce over time as well as higher cognitive and motor performance, 2) near average scores for all neurobehavioral outcomes, 3) higher maladaptive behavior, motor and cognition but lower social impairment, 4) higher maladaptive behavior and social impairment but lower cognitive, motor and adaptive performance, 5) higher motor, cognitive and adaptive performance and lower maladaptive behavior and social impairment, and 6) higher adaptive skills, cognitive and motor performance. In multinomial logistic regression models, child sex, maternal IQ and child-parent relationships differed by profile in expected directions (e.g., higher maternal IQ associated with higher child cognitive performance).

Conclusions: We used a novel classification and visualization method to derive neurodevelopment profiles. This method could be applied to future studies designed to uncover early drivers of neurodevelopmental profiles.

Figure 1. Self-organizing Map (SOM) of neurobehavioral profiles of the New Hampshire Birth Cohort (n=235). Assessment scores mean centered (mean = 0) and scaled (SD = 1) with higher scores radiating from mean center.
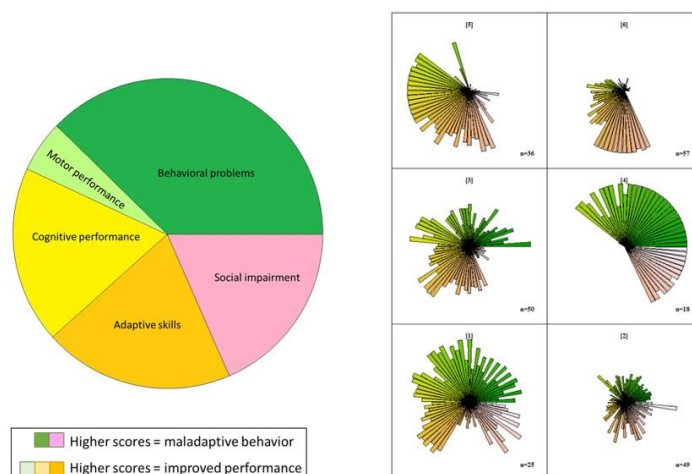
The association between measures of acculturation and established diet quality indices in Hispanic women Sofija Zagarins* Sofija Zagarins Megan Harvey Katherine Tucker Bess Marcus JoAnn Manson Lisa Chasan-Taber

Prior research indicates that maternal diet quality impacts pregnancy and birth outcomes. Puerto Rican populations living in the continental US have lower diet quality as compared to those living in Puerto Rico, although research examining the association between acculturation and diet quality in pregnancy in this population is sparse. Therefore, we evaluated this association using baseline data from 169 Hispanic (predominantly Puerto Rican) participants enrolled in Estudio PARTO, a randomized controlled trial conducted in Western Massachusetts (2013-17). Acculturation was assessed via Psychological Acculturation Scale (PAS), language preference, and birthplace. Trained bicultural/bilingual personnel assessed diet at a mean ± SD of 28.6±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, and Healthy Plant-Based Diet Index, and adjusted for age, pregnancy BMI, activity level, and energy intake in multivariable models. Mean PAS score was 2.46 ± 0.67, and 23.7% of women reported Spanish language preference. Mean diet scores were 54.9 ± 14.6 (HEI-2015), 36.5±11.6 (AHEI-2010), 24.4±5.5 (aMED), and 51.8±7.7 (HPDI). In unadjusted models, each one-unit lower PAS score was associated with a 3.2-unit higher HEI-2015 (SE=4.3; P=0.06) and 2.6-unit higher AHEI-2010 (SE=1.3; P=0.05), although associations were attenuated in multivariable models. Spanish language preference (indicating lower acculturation) was associated with a 5.6-unit higher HEI-2015 (SE=2.7, P=0.04) and 4.2-unit higher AHEI-10 (SE=2.0, P=0.04) in adjusted models. No significant associations were seen with aMED or HPDI. Lower psychological acculturation and Spanish language preference were associated with higher maternal diet quality in Puerto Rican women. Public health interventions aimed at improving pregnancy outcomes in this population should be tailored to acculturation level.

Influence of prenatal and postnatal lead exposure on allostatic load in adolescence: Findings from a Mexican cohort study Olivia M. Halabicky* Olivia Halabicky Mara Maria Tellez-Rojo Jaclyn M. Goodrich Dana C. Dolinoy Alison L. Miller Adriana Mercado García Libni Torres Olascoaga Howard Hu Karen E. Peterson

Background: A potential pathway linking lead exposure with disease is dysregulation of physiological stress systems. This study aims to identify relationships between prenatal and postnatal lead exposure and adolescent allostatic load (AL), a measure of cumulative body burden of chronic stress estimated from biomarkers of physiologic dysregulation.

Methods: 239 mother-child pairs participating in the Early Life Exposures in Mexico to ENvironmental Toxicants cohort were included. Maternal bone lead levels (patella and tibia) were measured one month postpartum. Children's venous blood lead levels were measured at 12 and 24 months. An AL index score was created using high risk cut-points for 14 biomarkers inclusive of cardiovascular, metabolic, immune, and neuroendocrine function in adolescence (11-18 years). AL was regressed on bone and blood lead measures while controlling for age and sex in generalized linear models and in models stratified by sex.

Results: The sample included 122 females (51%). Mean age at AL collection was 14.84 years and mean AL score was 3.44 (range 0-11). We found significant associations between maternal patella lead and AL ($\beta= 0.03$, 95%CI [0.01, 0.06]). In stratified models, male AL was associated positively with maternal patella lead ($\beta= 0.07$, 95%CI [0.04, 0.10]), 12 month blood lead ($\beta= 0.15$, 95%CI [0.02, 0.28]) and negatively with 24 month blood lead ($\beta= -0.33$, 95%CI [-0.52, -0.15]). Female AL was associated positively with 24 month blood lead ($\beta= 0.20$, 95%CI [0.06, 0.34]) and negatively with 12 month blood lead ($\beta= -0.18$, 95%CI [-0.30, -0.06]).

Conclusion: Our findings suggest prenatal and early postnatal lead exposure may influence adolescent physiological stress system functionality and body burden of chronic stress, although directionality was unclear. Future research may consider AL, and other measures of chronic stress, as mediators for relationships between lead exposure and cardiovascular, metabolic, and neurocognitive dysfunction.

Teratogenic effect of first trimester use of augmented metformin therapy versus exclusive insulin therapy: emulating a target trial using real-world data Yu-Han Chiu* Yu-Han Chiu
Miguel A. Hernán Sonia Hernández-Díaz

Pregestational diabetes is one of the most common medical complications in pregnancy.

Outside of pregnancy, metformin for the treatment of type 2 diabetes has gained wide popularity. However, as pregnant women and women planning pregnancies are often excluded from clinical trials, the safety of metformin in pregnancy is uncertain. Using real-world data from a US healthcare claims database (MarketScan, 2011-2019), we emulated a target trial of two antidiabetic strategies in the first trimester to evaluate the relative risk of major birth defects. Eligible women were those with pregestational type 2 diabetes, who were on metformin and had not used insulin in the past 6 months, and who had just recognized their pregnancy. We defined baseline as 4 weeks after the last menstrual period. We compared two treatment strategies: 1) exclusive insulin therapy: stop metformin immediately and initiate insulin within 6 weeks from baseline or 2) augmented metformin therapy: continue metformin and initiate insulin within 6 weeks from baseline. Metformin discontinuation was defined as no metformin dispensing within 6 weeks of baseline. We estimated a modified per-protocol effect: the effect of adhering to the assigned treatment among women who deliver a live birth, the validity of which requires no unmeasured common causes of adherence, live birth, and birth defects. Of 464 women who met eligibility criteria, 151 used exclusive insulin therapy (3.7% with birth defects), and 313 used augmented metformin therapy (8.1% with birth defects). The adjusted odds ratio of birth defects was 0.55 (95% confidence interval 0.16 to 1.55). Our estimates suggest that continuation with metformin in early pregnancy is unlikely to increase the risk of major birth defects.

Development and validation of an algorithm to predict stillbirth gestational age in Medicaid billing records Thuy Thai* Thuy Thai Nicole E. Smolinski Sabina Nduaguba Yanmin Zhu Loreen Straub Brian T. Bateman Sonia Hernandez-Diaz Krista F. Huybrechts Sonja A. Rasmussen Almut G. Winterstein

Introduction

Covering nearly half of US pregnancies, Medicaid Analytic eXtract (MAX) claims provide an important data source for pregnancy research, including for the assessment of stillbirth (SB) due to exposure to drugs or other risk factors. However, claims lack detail on gestational age (GA) at SB, complicating measurement of pregnancy onset and accurate timing of exposure.

Objective

To develop and validate an algorithm to predict GA at SB in MAX.

Method

We linked the SBs identified in MAX 1999-2013 to Florida Fetal Death records to obtain clinical estimates of GA (gold standard). We tested several algorithms with increasing complexity, from assigning a fixed median GA to all SBs to linear regression and random forest (RF) models that considered the median GA at specific prenatal screening tests, risk factors for early or late SB and other GA markers to predict the GA at SB. We estimated proportion of SBs with estimated GA within ± 1 to 4 weeks of the gold standard and the model mean square error (MSE). We validated the selected algorithms in two external cohorts identified in hospital electronic health records (N=123 and 25).

Results

Among 6,197 linked SBs between MAX and Fetal Death (MAX-FD), 825 had mothers met the continuous enrollment requirement in MAX SBs and were included. The RF algorithm had the best performance with the smallest MSE (12.67 weeks^2), and the proportion of SBs with estimated GA within ± 1 to 4 weeks was 49, 58, 78, and 84%, respectively. In contrast, assigning 28 weeks GA to all SBs resulted in an MSE of 60.21 (weeks^2) and the proportion with GA within 1 and 4 weeks were 10, 17, 24, and 32%, respectively. The best RF model in the MAX-FD remained the best algorithm in the external validation cohorts.

Discussion

This is the first algorithm to predict GA for SBs in a publicly insured population, which can facilitate pregnancy research for SB outcomes in the Medicaid population. Results may be transportable to other claims databases.

Racial/Ethnic Differences in the Risk of Preterm Delivery and Small for Gestational Age in Hypertensive Disorders of Pregnancy Angela Malek* Angela Malek Dulaney Wilson Julio Mateus Tanya Turan Daniel Lackland Kelly Hunt

Introduction: Hypertensive disorders of pregnancy (HDP) are associated with adverse infant and maternal outcomes. Less is known about racial/ethnic group differences which have been reported to persist after covariate adjustment. Therefore, we aimed to evaluate the relationship between HDP and pre-pregnancy hypertension with preterm delivery and small for gestational age (SGA), and compare differences by maternal race/ethnicity.

Methods: All live, singleton births in South Carolina between 2004-2016 to mothers aged 12-49 years were included in a retrospective cohort study. Birth certificate and/or hospitalization/emergency department visit data defined maternal HDP (pre-eclampsia, eclampsia, gestational hypertension) and pre-pregnancy hypertension. Birth certificate data were used to define preterm delivery and small for gestational age (SGA).

Results: Of the 667,359 births, 377,007 (56.5%) were in non-Hispanic white (NHW) women, 215,205 (32.2%) were in non-Hispanic black (NHB) women, 60,256 (9.0%) were in Hispanic women, and 14,891 (2.2%) were in women of other races/ethnicities. Diagnoses included pre-pregnancy hypertension without superimposed HDP (pre-pregnancy hypertension: 0.3%), HDP without pre-pregnancy hypertension (HDP; 16.9%), and both conditions (pre-pregnancy hypertension with superimposed HDP; 2.1%). Preterm delivery odds were increased for women with HDP (2.27 to 2.63-fold) and with both conditions (3.61 to 4.23-fold), especially early preterm delivery, compared to neither condition after controlling for sociodemographic, behavioral, and clinical characteristics; SGA odds were also elevated for HDP (1.29 to 1.79-fold) and both conditions (1.47 to 2.51-fold). There was a significant race/ethnicity interaction (p<0.001) with race-specific adjusted odds ratios reported in the Table.

Discussion: In all three racial/ethnic groups, the odds of preterm delivery and SGA were highest for pre-pregnancy hypertension with superimposed HDP followed by HDP.

Table. The association of hypertensive disorders of pregnancy (HDP) with preterm delivery and small for gestational age by racial/ethnic group*

	Non-Hispanic White		Non-Hispanic Black		Hispanic	
	n	OR (95% CI)	n	OR (95% CI)	n	OR (95% CI)
Preterm delivery (<37 weeks)						
Neither pre-pregnancy hypertension nor HDP	20,384	referent	15,178	referent	3,325	referent
Pre-pregnancy hypertension	15,178	1.79 (1.45-2.21)	163	1.73 (1.43-2.08)	18	2.07 (1.23-3.49)
HDP	3,325	2.45 (2.38-2.52)	8,722	2.27 (2.20-2.34)	981	2.63 (2.42-2.86)
Pre-pregnancy hypertension with superimposed HDP	970	3.61 (3.37-3.87)	2,172	3.66 (3.46-3.88)	120	4.23 (3.38-5.31)
Early preterm delivery (28 to <34 weeks)						
Neither pre-pregnancy hypertension nor HDP	3,819	referent	4,392	referent	695	referent
Pre-pregnancy hypertension	4,392	3.11 (2.19-4.42)	55	1.76 (1.29-2.41)	4	2.11 (0.76-5.84)
HDP	695	3.04 (2.87-3.22)	3,079	2.45 (2.33-2.58)	236	2.82 (2.39-3.31)
Pre-pregnancy hypertension with superimposed HDP	193	5.87 (5.23-6.57)	873	4.30 (3.95-4.69)	52	7.72 (5.53-10.8)
Late preterm delivery (34 to <37 weeks)						
Neither pre-pregnancy hypertension nor HDP	16,565	referent	10,786	referent	2,630	referent
Pre-pregnancy hypertension	10,786	1.46 (1.14-1.88)	108	1.67 (1.34-2.08)	14	2.01 (1.12-3.59)
HDP	2,630	2.24 (2.17-2.31)	5,643	2.07 (2.00-2.15)	745	2.49 (2.27-2.73)
Pre-pregnancy hypertension with superimposed HDP	777	2.91 (2.69-3.15)	1,299	3.06 (2.85-3.27)	68	3.05 (2.31-4.02)
Small for gestational age (SGA)						
Neither pre-pregnancy hypertension nor HDP	22,095	referent	25,352	referent	4,013	referent
Pre-pregnancy hypertension	25,352	1.21 (0.95-1.54)	127	0.94 (0.77-1.15)	9	0.63 (0.28-1.43)
HDP	4,013	1.39 (1.35-1.44)	8,442	1.29 (1.25-1.33)	815	1.79 (1.64-1.95)
Pre-pregnancy hypertension with superimposed HDP	1,468	1.59 (1.46-1.73)	1,420	1.47 (1.38-1.56)	74	2.51 (1.93-3.25)

Abbreviations: CI, confidence interval; HDP, Hypertensive disorders of pregnancy; OR, odds ratio; SGA, small for gestational age.
*Adjusted for case group, age group, education, income, insurance, smoking during pregnancy, pre-pregnancy BMI group, change in BMI after delivery, previous pregnancies, previous cesarean section, previous preterm delivery, R-GINDEX group, pre-pregnancy or gestational diabetes, baby sex, mode of delivery, and induced labor. Models for preterm delivery additionally adjusted for size for gestational age, and small for gestational age models additionally adjusted for gestational age (continuous).

Impact of the COVID-19 pandemic on stillbirth rates in the United States: Preliminary findings from 8 states Hannah Mandle* Hannah Mandle Carson Bohl Bereket Getachew Nicole Pozzo Lauren Christiansen-Lindquist

Those who are pregnant are particularly vulnerable to COVID-19: they are at increased risk of severe illness relative to those who are not pregnant and are at an increased risk of having an adverse pregnancy outcome if they are infected at the time of delivery. While the impact of COVID-19 on pregnancy is known, nationwide data are not available to assess the population-level impact of the COVID-19 pandemic on the incidence of stillbirth in the United States. The CDC posts up-to-date data for both stillbirths and live births; although national birth data are already available for 2020, stillbirth data are not. The objectives of this study were to 1) determine whether individual reporting areas had published stillbirth data for 2020, and 2) for those with 2020 data, assess whether there was a change in stillbirth incidence during a pandemic year (2020) relative to pre-pandemic (2019). The health department websites, public health tracking systems, and/or annual reports for all US reporting areas (all 50 states, District of Columbia, New York City, Puerto Rico and Guam) were reviewed by two reviewers to abstract stillbirth and live birth data for 2019 and 2020. As of February 2022, almost 14 months since the very last day of 2020, the number of stillbirths in 2020 was only available for 8 states. Six of the eight states had an increase in stillbirth rates (0.64-13.71%; Figure 1). Two states (GA and MS) had race-specific data available. The increase in rates was greater among Black women in GA, but not in MS. Although most states had an increase in stillbirth rates from 2019 to 2020, the data are too sparse to draw definitive conclusions about the impact of COVID-19 on stillbirth rates. Stillbirth was a public health crisis in the US long before COVID-19; however, as we enter the third year of the pandemic, this study highlights how stillbirth has been left behind. With inadequate data, we remain unable to quantify the pandemic's effects on stillbirth nationwide.
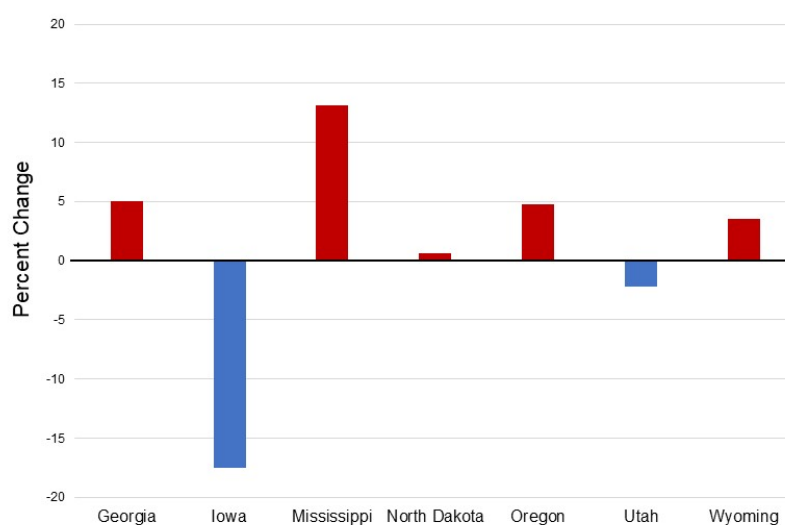
LATEBREAKER

Perinatal & Pediatric

Sensitive Windows of Fine Particulate Matter Exposure and Trajectories of Estimated Fetal Weight in the Spanish INMA (INfancia y Medio Ambiente) Project Wei-Jen Chen* Wei-Jen Chen Alison M. Rector Carmen Iñiguez Elaine Symanski Michael D. Swartz Mònica Guxens Albert Ambros Jesús Ibarluzea Aitana Lertxundi Ana Fernández-Somoano Jennifer Ish Kristina W. Whitworth

To fill a gap in the literature regarding temporally refined sensitive windows of exposure to air pollution on fetal growth, we utilized distributed lag non-linear models (DLNMs) to identify weekly windows of exposure to fine particulate matter ($PM_{2.5}$) on estimated fetal weight (EFW) trajectories.

We included 2,635 women enrolled in the Spanish INMA Project from 2003-2008. Prenatal ultrasound scans were conducted at 12, 20, and 34 gestational weeks and longitudinal growth curves were constructed for each fetus to calculate z-scores describing EFW trajectories during early (0-12 weeks), mid- (12-20 weeks), and late (20-34 weeks) pregnancy. $PM_{2.5}$ exposure was calculated at each woman's residence for 2009 using a random forest model that combined ground-level and satellite-based measures, land-use, and meteorology and were temporally-adjusted to estimate weekly exposures during each woman's gestation. We applied DLNMs within the Bayesian hierarchical model framework to identify sensitive windows of exposure to $PM_{2.5}$ (per 5-$\mu g/m^3$) on EFW z-scores (represented as %change in EFW), adjusted for covariates. Cumulative effects [β_{cum}, 95% credible interval (CrI)] were calculated by aggregating β's across adjacent weeks.

We identified gestational weeks 1-2 as a sensitive window of exposure for increased mid-pregnancy EFW [β_{cum}=0.46%, 95% CrI (0.24%,0.68%)] while weeks 7-19 were associated with reduced mid-pregnancy EFW [β_{cum}=-1.21%, 95%CrI (-1.63%,-0.79%)]. We observed two sensitive windows of exposure for reduced late pregnancy EFW: weeks 1-6 [β_{cum}=-0.80%, 95%CrI (-1.09%,-0.50%)] and 21-22 [β_{cum}=-0.29%, 95%CrI (-0.43%,-0.14%)]. Exposure during weeks 27-33 was associated with increased late pregnancy EFW [β_{cum}=0.73%, 95%CrI (0.42%,1.05%)].

Our results reveal $PM_{2.5}$ exposures during specific weeks may affect EFW during different pregnancy periods, highlighting the importance of refining exposure estimates in studying differential impacts of environmental exposure on fetal growth.
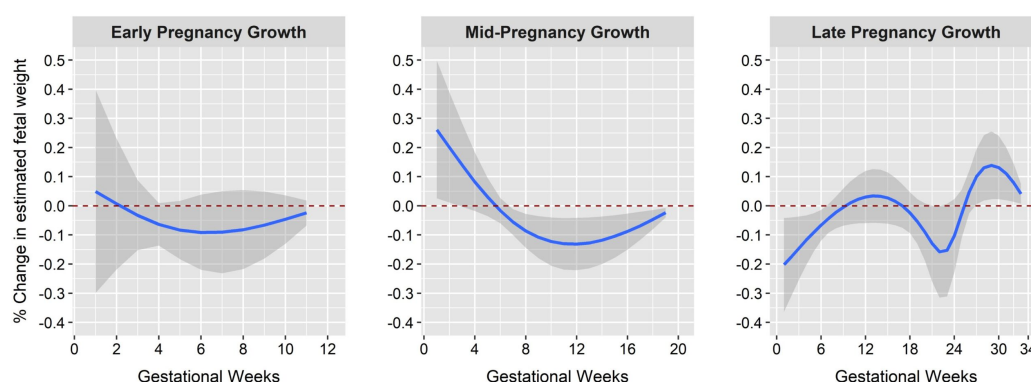
Associations between weekly prenatal $PM_{2.5}$ exposure (per 5 $\mu g/m^3$ increase) and percentage change in fetal growth of estimated fetal weight during early (first 12 weeks of gestation), mid- (12-20 weeks of gestation), and late (20-34 weeks of gestation) pregnancy. Models accounted for heterogeneity between regions while adjusting for maternal age, maternal and paternal education, social class, cohabitation, pre-pregnancy BMI, parity, and smoking and alcohol use during pregnancy. The solid lines represent the estimated values from the fitted distributed lag non-linear models, and the shaded areas represent 95% CrI around the estimate for each gestational week. The gestational weeks where the 95% CrI excludes null value (dotted horizontal line) were identified as sensitive windows.

Associations between air pollution and early life mortality Sandie Ha* Sandie Ha Erika
Ramsey Sandy Rubio Valerie Martinez Sneha Ghimire

Background: Air pollution is linked to multiple adverse pregnancy outcomes such as preterm
births, but few studies have evaluated its acute impact on fetal and infant mortality. We aim to
evaluate short-term impacts of warm-season ozone and cold-season fine particulate matter <2.5
microns ($PM_{2.5}$) exposures on the risk of fetal death (death >20 weeks) and infant mortality (death
from live birth to one year).

Methods: This time-stratified case-crossover analysis includes 1,880 singleton fetal deaths
(2007-2011) and 3,229 singleton infant deaths (2007-2015) from the San Joaquin Valley (SJV),
California. Daily exposures to ozone and $PM_{2.5}$ were estimated by the SJV Air Pollution Control
District and geospatially linked to maternal zip code at birth. Critical exposure windows of interest
included the day of death (lag 0) up to 14 days before (lag 14). We used conditional logistic
regression models to estimate the odds ratio (OR) and 95% confidence intervals (CI) for each 5 units
increase in pollutant.

Results: During the warm season (May-October), a 5-ppb increase in ozone exposure was associated
with a 7% (95% CI: 2%-13%) increased risk of fetal death and 6% (95% CI: 2%-10%) increased risk
of infant death within two weeks. The estimates were generally consistent from lag 0 to lag 14 for
both mortality outcomes, with evidence of slightly stronger estimates for fetal death compared to
infant death during certain lags. For example, during lag 7, a 5-ppb increase in ozone was associated
with a 9% increased risk in fetal death (95% CI: 5%-14%) and a 4% (95% CI: 1%-7%) increased risk
in infant death. No associations were observed between cold season $PM_{2.5}$ and either mortality
outcome.

Conclusions: Ozone exposure is positively associated with short-term risk of fetal and infant
mortality in the warm season. Given the ubiquitous nature of air pollution, these associations merit
further investigation. Meanwhile, efforts to minimize exposures among pregnant women may be
warranted.

Correlates and the confluence of early breastfeeding cessation and expression of breast milk among mothers with and without HIV infection in Uganda: a retrospective cohort study Yu Du* Yu Du Arthur H. Owora Bhavneet Walia

Abstract

Background: Mothers with HIV infection continue to have disproportionately lower rates and shorter duration of exclusive breastfeeding than un-infected mothers in part due to the fear of Mother to Child Transmission of HIV. However, it is not clear how and to what extent breast milk expression may be related duration of breastfeeding among mothers with and without HIV infection. Our study objective is to identify the correlates and characterize the confluence of early breastfeeding cessation and expression of breast milk among mothers in Uganda.

Methods: Between November 2005 and April 2006, mothers who were breastfeeding infants six-months or younger were recruited from ongoing Prevention of Mother to Child Transmission of HIV (PMTCT) programs in Uganda. Mothers who provided study consent were tested for HIV infection at baseline and breastfeeding practices (i.e., early breastfeeding cessation and expression of breast milk) were prospectively determined before a child's first birthday. Univariate and bivariate logistic regression models were used to identify correlates of early breastfeeding cessation and breastmilk expression as independent and related outcomes, respectively.

Results: Of the 477 eligible mothers who consented to study participation, 146 (30%) had early breastfeeding cessation. The odds of early cessation were higher among mothers who received breastfeeding advise from their partners (adjusted Odd Ratio[aOR] 3.15; 95% CI 1.66,6.08) or non-family members (aOR 2.64; 95% CI 1.41, 4.96). Separation from an infant for longer than 24 hours at any point before the child's 1st birthday was also associated with higher odds (aOR 4.07; 95%CI 1.37,13.52) of early breastfeeding cessation. The odds of breastfeeding and expressing breastmilk after the first year of life were 75% (aOR 0.25; 95%CI 0.08, 0.80) lower among mother with HIV-infection than un-infected mothers.

Conclusion: Our findings highlight the confluence of early breastfeeding cessation and lower odds of breastmilk expression among at-risk children who stand to benefit the most from breastmilk. Given the known challenges associated with breastfeeding, promotion of cost-effective breastmilk expression among mothers with HIV-infection could extend substantial health benefits to at-risk children.

Pharmacoepidemiology

One-year opioid use following discharge from post-acute care after hip fracture Meghan A. Cupp* Meghan Cupp Francesca L. Beaudoin Richa Joshi Melissa R. Riester Kaleen N. Hayes Andrew R. Zullo

Background: Hip fracture is a major traumatic event requiring complex pain management. Following hip fracture hospitalization, older adults commonly receive post-acute care (PAC) in Skilled Nursing Facilities (SNFs), Inpatient Rehabilitation Facilities (IRFs) and Long Term Acute Care Hospitals (LTACHs) to rehabilitate. However, little is known about post-PAC opioid use.

Methods: We assessed opioid dispensings among Medicare beneficiaries aged > 66 years with a hip fracture related hospitalization followed by PAC in a SNF, IRF or LTACH between 2012 and 2018. Patients were followed from PAC discharge for up to one year or until censoring due to re-fracture, re-entering PAC, Medicare disenrollment, or death. The cumulative incidence of opioid use was estimated using a Fine-Gray model. Multivariable logistic regression (adjusted for age, sex, race, year, comorbidity score, and days in PAC) was used to estimate the predicted probabilities of long-term opioid use and discharge with an opioid, based on PAC setting.

Results: We included 513,497 patients discharged from PAC (76% SNFs, 24% IRFs, 0.4% LTACHs). SNF patients were older on average, while LTACH patients had more co-morbidities and longer PAC stays. Opioids were dispensed to 89,591 (17%) patients following PAC discharge and the one-year cumulative incidence was notably higher in SNF patients (21.3%) than IRF (18.8%) or LTACH (18.4%). LTACH and SNF patients had a 3.99 [95%CL -5.03, -2.95] and 2.11 [95%CL -2.31, -1.92] percentage point (PP) reduction, respectively, in the probability of discharge with an opioid, compared to IRF. LTACH and SNF patients had a 0.53 [95%CL -1.20, -0.10] PP reduction and 1.04 [95%CL 0.90, 1.20] PP increase, respectively, in the probability of long-term opioid use, compared to IRF.

Conclusions: Opioid use is common upon discharge from PAC after hip fracture. Further research is needed to assess the long-term effects of post-PAC opioid use and how PAC practices can improve pain management.

Table 1 – Demographic profiles of Medicare beneficiaries discharged from post-acute care following a hip fracture hospitalization, by PAC setting

	IRF, N = 121,951[*]	LTACH, N = 2,205[*]	SNF, N = 389,341[*]
Year			
2012	17,825 (15%)	432 (20%)	49,062 (13%)
2013	17,569 (14%)	364 (17%)	52,283 (13%)
2014	19,630 (16%)	349 (16%)	58,171 (15%)
2015	18,160 (15%)	329 (15%)	58,146 (15%)
2016	16,376 (13%)	287 (13%)	55,648 (14%)
2017	16,516 (14%)	223 (10%)	58,063 (15%)
2018	15,875 (13%)	221 (10%)	57,968 (15%)
Biologic Sex			
Male	33,475 (27%)	884 (40%)	93,014 (24%)
Female	88,476 (73%)	1,321 (60%)	296,327 (76%)
Age	82 (75, 87)	80 (72, 86)	85 (78, 90)
Race			
White	110,604 (91%)	1,842 (84%)	357,530 (92%)
Black	4,718 (3.9%)	178 (8.1%)	14,178 (3.6%)
Other/Unknown	1,715 (1.4%)	33 (1.5%)	4,605 (1.2%)
Asian	1,682 (1.4%)	56 (2.5%)	5,322 (1.4%)
Hispanic	2,738 (2.2%)	85 (3.9%)	5,941 (1.5%)
Native American	494 (0.4%)	-	1,765 (0.5%)
Comorbidity Score[‡]	6.0 (3.0, 9.0)	9.0 (7.0, 12.0)	6.0 (3.0, 9.0)
Days in PAC	20 (16, 27)	48 (32, 72)	39 (25, 60)
Discharged with Opioid[§]	13,870 (11%)	127 (5.8%)	29,827 (7.7%)
Opioid Use[§§]			
None	101,820 (83%)	1,932 (88%)	320,154 (82%)
Short-term	15,592 (13%)	184 (8.3%)	50,640 (13%)
Long-term	4,539 (3.7%)	89 (4.0%)	18,547 (4.8%)
Total MME[†]	150 (52, 500)	250 (90, 800)	172 (60, 600)
Maximum daily MME[†]	7.5 (5.0, 7.5)	7.5 (5.0, 10.0)	5.0 (5.0, 7.5)

[*] n (%); Median (IQR)
[‡] Gagne Combined Comorbidity index
[§] Filled a prescription for an opioid within 7 days of discharge from PAC
[§§] Short-term use <90 days, Long-term use >=90 days with a 30 day permissible gap
[†] Among those dispensed an opioid during follow-up (n=89,591)
(PAC) Post-acute care, (IRF) Inpatient Rehabilitation Facilities, (LTACH) Long Term Acute Care Hospitals, (SNF) Skilled Nursing Facilities, (MME) Morphine Milligram Equivalent

Gastroesophageal Reflux Disease and Paraneoplastic Neurological Syndrome Associated with Long-Term Survival in Small-Cell Lung Cancer Ping Yang* Ping Yang Vinicius Ernani Lin Du Helen J. Ross Joanne E. Yi Jason A. Wampfler Hao Xie Karen L. Swanson Henry D. Tazelaar Steven E. Schild

Small-cell lung cancer (SCLC) is the most fatal subtype of lung cancer, with a hallmark of favorable response to standard therapy but quick and invariable recurrence. However, a subset of SCLC patients does achieve long-term survival beyond expectation. We aimed to investigate factors and pattern of long-term survival in patients with limited-stage small cell lung cancer who achieved a complete response after chemoradiotherapy. This was a retrospective cohort study. The analysis of hazard ratios (HR) and 95% confidence intervals (CI) was performed using Cox proportional hazards model. For pattern analysis, the date of recurrence was used as the endpoint. The nominal categorical variables were analyzed by the chi-square test. Survival length was estimated using the Kaplan-Meier model. Results: We identified 162 eligible patients; median age was 64.7 (56.2-70.2) years; and 94 (58%) were females. Eighty-one patients (50%) had recurrence during follow-up. Gastroesophageal reflux disease (GERD) (HR, 0.65; 95% CI, 0.45-0.93; P=0.016) and neurological paraneoplastic neurological syndrome (PNS) (HR, 0.46; 95% CI, 0.29-0.72; P<0.001) were independent factors associated with prolonged overall survival (OS). Patients with GERD had significantly longer recurrence-free survival (RFS) compared to patients without GERD (median, 29.1 [15.0-59.5] months vs. 13.9 [10.1-19.4] months, P<0.001), while patients with neurological PNS had a reduced recurrence rate compared to those patients without neurological PNS (No. [%], 8 [20.5] vs. 73 [59.3], P<0.001). Conclusions: In patients with LS-SCLC achieving a complete response after chemoradiotherapy, GERD and neurological PNS were associated with improved OS. GERD and neurological PNS were associated with longer RFS and lower recurrence rate, respectively. GERD could potentially be a manifestation of a paraneoplastic syndrome in patients with SCLC, calling for further studies to corroborate our results and elucidate the mechanisms.

**Inequities in Life Course Involvement in the Criminal Legal System: Moving Beyond Incarceration** Katherine LeMasters* Katherine LeMasters Audrey Renson Jesse K. Edwards Whitney R. Robinson Lauren Brinkley-Rubinstein Paul Delamater Brian Pence

Background: Life course involvement in the criminal legal system – inclusive of arrests, charges, probation, and incarceration – is poorly understood yet critically important; current involvement precipitates future involvement and contributes to health inequities. The goal of this analysis was to characterize patterns of adult criminal legal involvement across the life course and differences in pathways by juvenile involvement and by demographic characteristics.

Methods: We used the National Longitudinal Survey on Youth 1997, a longitudinal data set of adolescents (baseline age: 12-17 years) followed into midlife (1997-2017) over 18 study visits. We explored patterns of criminal legal involvement over the life course and inequities in these patterns using the mean cumulative count of the most severe criminal legal encounter per study visit (in increasing severity: arrest, charge or conviction without punishment, probation, incarceration). Death was treated as a competing event and individuals were censored at the first missed visit.

Results: 7,427 individuals were followed a median of 16 years and reported 3,370 encounters. Of 1,813 respondents with any criminal legal involvement, 987 experienced one encounter and 826 experienced multiple. By 2017 (33-38 years), there was an average of 13 arrests, 32 charges, 13 probation encounters, and 17 incarceration events per 100 individuals. Those with juvenile encounters, encounters before age 18, (N=1,151) had 2.86 times the number of adult encounters than those without juvenile encounters (**Figure 1**).

Conclusion: The criminal legal system has a pervasive, long-term, and inequitable presence in our society. "Low level" involvement (i.e., not incarceration) is common, as is repeat involvement. Future epidemiologic research on the health effects of criminal legal involvement must consider both life course trajectories and encounters beyond incarceration.

Figure 1. Estimated Mean Cumulative Count curves based on NLSY97, 1997-2017
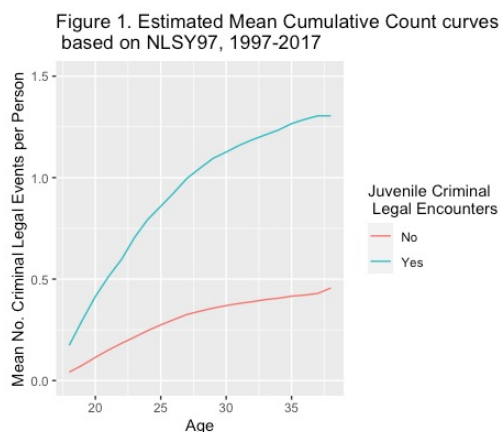
LATEBREAKER

Policing/Incarceration

Historical series of pregnant and lactating women incarcerated in Brazil (2016-2020): comparisons between different data from the Public Power Lisiane Freitas Leal* Natalia Barbieri Paola Stuker Alceu Braga Laís Sette Galinari Tamara Vaz de Moraes Santos Lisiane Leal

Background:

In 2016, the Legal Framework of Early Childhood expanded the possibility of replacing pretrial detention with house arrest for pregnant women and mothers of children under 12 years old. Law No. 13,769 was implemented in 2018 and public data is available for monitoring the law execution. However, these public data have not been yet analyzed. We aimed to assess two public data sources and describe the profile of pregnant and lactating women incarcerated in Brazil.

Methods:

National public data from the Statistical Panel of the National Registry of Inspections in Prison Establishments (CNIEP/CNJ) and the National Penitentiary Department's Information System (SisDepen) were used. We assessed the historical series of pregnant and nursing women incarcerated from 2016 to 2020.

Results:

The data sources CNIEP/CNJ and SisDepen presented divergences over the study period. Despite differences, the percentage of pregnant women decreased from 2016-2018: 1.47%-0.76% in SisDepen and 1.04%-0.92% in CNIEP/CNJ, respectively. In 2014, 350 pregnant women were incarcerated, according to SisDepen, and 397 in CNIEP/CNJ (11.8% difference). Divergences of pregnant women in both systems were also identified from 2016 onwards: 563 (SisDepen) versus 302 (CNIEP/CNJ) in 2016; 252 (SisDepen) versus 265 (CNIEP/CNJ) in 2018. The numbers were also divergent between both systems for nursing mothers, with a decrease observed from 2018 onwards. In 2020, information on the existence of pregnant and lactating women was not declared by approximately 80% of mixed penitentiary units and 40% of female penitentiary units.

Conclusion:

Pregnant and lactating women continued incarcerated in Brazil after the Law execution. However, data is inconsistently recorded, revealing a reality of misinformation in this area. Centrality and improvement in obtaining these data are necessary to establish public policies consistent with the Brazilian reality.

Reproductive

Variability in risk factors and outcomes related to maternal and infant health among Asian, Native Hawaiian, and Pacific Islander Individuals giving birth in California Shalmali Bane*

Shalmali Bane Barbara Abrams Mahasin Mujahid Chen Ma Aileen Xu Latha Palaniappan Suzan Carmichael

Despite Asian, Native Hawaiian, and Pacific Islander (ANHPI) populations being the fastest growing racial/ethnic group in the US, they are understudied, underrepresented, and underfunded in research. Existing research often aggregates these populations, thus obscuring diversity and disparities among ANHPI sub-groups. Our goal was to examine variability in risk factors and outcomes related to maternal and infant health among disaggregated subgroups of ANHPI populations.

We used linked live birth and fetal death certificate and maternal hospital discharge data from California (2007-2017), for the following subgroups: Cambodian, Chinese, Filipino, Guamanian, Hawaiian, Hmong, Indian, Japanese, Korean, Laotian, Samoan, Thai, Vietnamese, Other-Asian, Other-PI.

For assessed risk factors, there was high variability ranging from a 2-fold difference between the lowest and highest groups for English as the principal language spoken (Chinese: 54.2% to Hawaiian: 99.8%) to 54-fold for smoking during pregnancy (Hawaiian: 5.9% to Indian: 0.1%). For perinatal outcomes, variability ranged from 2-fold for severe maternal morbidity (Korean: 1.1% to Samoan:1.9%) to 5-fold for high birthweight (Vietnamese: 3.1% Vietnamese to Samoan: 17.2%). Within sub-groups, the number of variables ranked highest or lowest risk varied considerably (i.e., no single sub-group was consistently high or low risk across all variables).

There is substantial variability in risk factors and perinatal health outcomes across ANHPI subgroups, and for high- or low-risk status across these variables within subgroups. Future work on this topic should consider disaggregated subgroups.

Table. Heat map of risk factors and perinatal outcomes by ANHPI subgroups, among births in California 2007-2017 (N = 758,750)

	Subgroup	Cambodian	Chinese	Filipino	Guamanian	Hawaiian	Hmong	Indian	Japanese	Korean	Laotian	Samoan	Thai	Vietnamese	Asian - Other	PI - Other	Overall	Variability*
	N	18,869	209,296	146,626	2,357	3,302	24,873	117,971	26,656	50,927	8,881	7,455	8,357	77,900	41,655	13,625	758,750	
Indicators of Social Disadvantage	Foreign-born	61.4	86.6	69.3	47.7	1.7	48.1	91.9	61.8	83.0	58.2	30.5	83.0	86.8	50.3	53.1	77.1	55
	Principal language: Not English	5.3	39.8	2.5	0.3	0.2	14.5	6.7	14.7	16.8	6.2	0.6	9.9	20.6	5.1	1.9	17.4	221
	High school education or less	49.5	10.1	13.3	42.1	37.8	48.4	9.1	8.9	5.5	47.7	58.4	22.8	30.3	19.6	45.3	17.0	11
	College education or higher*	17.5	70.9	51.7	18.5	24.4	15.7	79.5	65.7	75.8	16.2	6.3	53.2	42.7	58.7	15.0	59.2	13
	Low-poverty neighborhood^b,*	11.5	25.5	24.8	20.3	20.6	5.2	33.3	29.4	25.7	10.9	10.2	20.2	19.8	24.2	16.1	24.5	6
	High-poverty neighborhood^b	49.4	21.2	22.2	26.9	28.1	65.1	15.4	16.2	24.3	54.2	43.2	31.1	28.9	26.3	36.5	24.7	4
	Public payer	52.5	13.2	21.6	38.0	39.4	63.6	13.3	9.9	16.0	51.8	58.7	34.1	32.6	28.5	49.2	22.3	6
Maternal Risk Factors	Age < 20 years	5.9	0.2	1.9	7.5	5.4	8.4	0.2	0.5	0.2	6.9	7.5	1.4	0.8	2.2	4.8	1.4	52
	Age ≥ 35 years	16.4	35.2	30.6	17.8	18.9	9.1	18.0	48.0	37.5	17.9	13.7	29.9	33.2	25.8	16.5	29.2	5
	Low height (< 61")	21.9	8.0	23.7	19.1	8.4	51.3	9.4	13.7	5.5	30.4	1.7	17.6	26.2	14.2	8.6	15.6	31
	Pregestational diabetes	1.1	0.8	2.0	2.7	1.5	1.0	1.5	0.6	0.8	1.2	3.1	1.0	1.1	1.2	2.7	1.3	5
	Pregestational hypertension	1.1	0.9	4.4	5.0	3.6	1.5	1.3	1.6	1.3	1.7	3.4	1.4	1.0	1.9	3.3	1.9	6
	Smoking before pregnancy	1.9	0.4	2.0	7.5	8.4	1.7	0.2	2.2	1.2	3.0	7.6	1.5	0.5	1.6	4.9	1.2	49
	Underweight pre-preg. BMI^c	7.6	11.6	4.4	2.1	2.4	2.6	5.0	10.8	11.6	5.8	0.5	10.0	13.1	6.1	2.5	8.2	28
	Obese pre-preg. BMI^c	9.8	2.2	11.2	29.5	28.3	18.1	7.5	4.9	2.9	13.4	53.4	7.2	2.6	8.6	37.7	7.5	24
	Early PNC^d	77.3	84.6	85.4	77.2	77.5	70.4	90.2	89.8	88.8	77.4	62.8	83.2	85.3	84.7	68.9	84.9	1
	Late or no PNC^d	3.1	4.6	2.1	3.9	4.2	2.8	1.3	1.2	1.8	3.2	8.0	2.0	1.6	2.1	6.9	2.8	7
	Low GWG^e	23.5	24.3	19.1	12.8	13.2	29.3	23.9	34.0	25.8	23.4	8.8	20.7	27.0	20.9	14.2	23.4	4
	High GWG^e	35.5	29.6	44.1	57.4	57.5	29.9	36.8	25.1	31.9	39.1	67.7	39.1	30.9	39.1	56.8	35.6	3
	Nulliparous	39.8	50.2	42.3	37.0	37.3	27.6	51.1	51.8	50.7	34.1	31.9	49.3	43.4	48.5	36.0	46.4	2
	High parity: 3+	28.0	9.9	22.9	34.0	32.5	48.5	8.4	12.8	13.1	35.0	43.8	19.0	18.5	17.3	35.8	16.9	6
	Plurality: Multiple birth	1.0	1.8	1.4	1.3	1.7	0.8	1.9	2.3	1.6	1.1	1.4	1.8	1.4	1.6	1.5	1.6	3
Pregnancy-related conditions and perinatal outcomes	GDM	10.7	13.1	16.9	13.8	10.4	11.5	17.7	9.3	8.7	12.1	10.4	13.8	16.1	12.9	14.7	14.3	2
	HDP	4.7	3.3	10.0	11.5	9.8	4.7	5.3	4.9	3.6	5.9	10.3	5.2	3.4	6.0	9.7	5.5	3
	Cesarean, overall	25.8	35.9	36.9	34.5	33.0	14.3	39.9	29.7	32.2	23.9	35.1	32.9	34.3	32.8	33.4	34.7	3
	Cesarean, low-risk births	22.9	26.4	32.9	29.7	29.5	13.6	32.8	25.3	26.5	21.3	29.7	28.7	29.3	28.7	30.3	28.8	2
	Severe Maternal Morbidity	1.3	1.4	1.8	1.2	1.6	1.6	1.4	1.2	1.1	1.3	1.9	1.4	1.2	1.5	2.2	1.5	2
	Moderately preterm (32-<37 wks)	8.3	5.1	8.9	9.6	8.0	5.9	6.5	6.5	4.8	8.5	7.2	7.0	6.8	6.8	7.8	6.6	2
	Very preterm (<32 wks)	1.7	0.7	1.6	1.2	1.5	1.3	1.1	1.0	0.8	2.0	1.8	1.3	1.0	1.2	1.7	1.1	3
	SGA	15.5	12.0	13.8	10.3	9.1	14.1	18.8	15.4	11.0	15.9	6.3	13.6	14.3	13.6	9.7	13.9	3
	LGA	4.9	5.5	6.8	11.5	11.4	5.2	4.7	4.7	6.2	5.2	20.4	5.8	4.6	6.6	16.1	6.0	4
	Very low birthweight	1.4	0.6	1.5	0.9	1.2	1.2	1.1	0.8	0.7	1.7	1.3	1.2	0.8	1.1	1.5	1.0	3
	Very high birthweight	3.4	4.4	4.8	8.5	9.2	4.3	3.8	4.0	5.4	3.5	17.2	4.4	3.1	5.4	13.5	4.7	5

Abbreviations: BMI body mass index, GDM gestational diabetes mellitus, GWG gestational weight gain, HDP hypertensive disorders of pregnancy, LGA large for gestational age, NTSV nulliparous transverse singleton vertex, PNC prenatal care, SGA small for gestational age,
Note: Gradient is from green to red, with green corresponding to lower frequency and red to higher frequency. * Indicates gradient is reversed from red (high-risk) to green (low risk) for certain variables where higher frequency represents lower-risk and vice versa.

Shifts in assisted reproduction coverage and trends in Canadian fertility/births: an exploratory analysis Nichole Austin* Nichole Austin

Background: Canadian access to subsidized assisted reproduction (ART) varies by province and has evolved considerably in recent years, with notable policy shifts in 2010 (expanded coverage in Quebec) and 2015 (expanded coverage in Ontario, reduced coverage in Quebec). These shifts matter because the upfront costs of IVF may be prohibitive: coverage may influence the sociodemographic characteristics of the patient pool, which could have an important effect on subsequent fertility and birth outcomes. The relationship between these policy shifts and fertility/birth outcomes remains largely unexplored in the Canadian context.

Methods: We compiled data from Statistics Canada (2000-2020) to assess population-level trends in births, plurality, total fertility rates, age-specific fertility rates, and age-specific birth rates in Quebec, Ontario, and all of Canada, paying particular attention to the timing of shifts in ART coverage. Age-specific rates were relevant because the proportion of ART pregnancies is higher among women of advanced maternal age (35+); policy-related changes may therefore be more apparent in older subgroups at the population level.

Results: Maternal age increased by approximately 2.5 years over the observation period (all locations). Baseline crude birth rates were lowest in Quebec, but trends over time differed by province (Quebec's rates surpassed Ontario's in 2007 and remained higher through 2020). Live births among women 35+ increased in parallel in all locations until 2010, when Quebec's rates began to increase before declining again in 2016. The timing of these shifts coincides with Quebec's expansion and subsequent restriction of ART coverage.

Conclusion: These findings offer preliminary, population-level evidence of shifts in fertility endpoints plausibly influenced by ART coverage. Individual-level data are required to further explore the impact of these policy shifts on patient sociodemographic composition and pregnancy/birth outcomes.
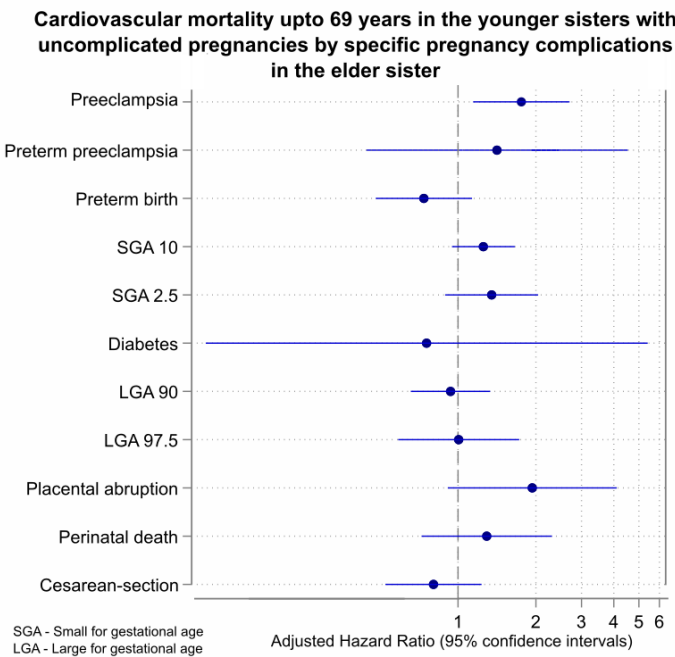

Age-specific fertility rate, 40-45
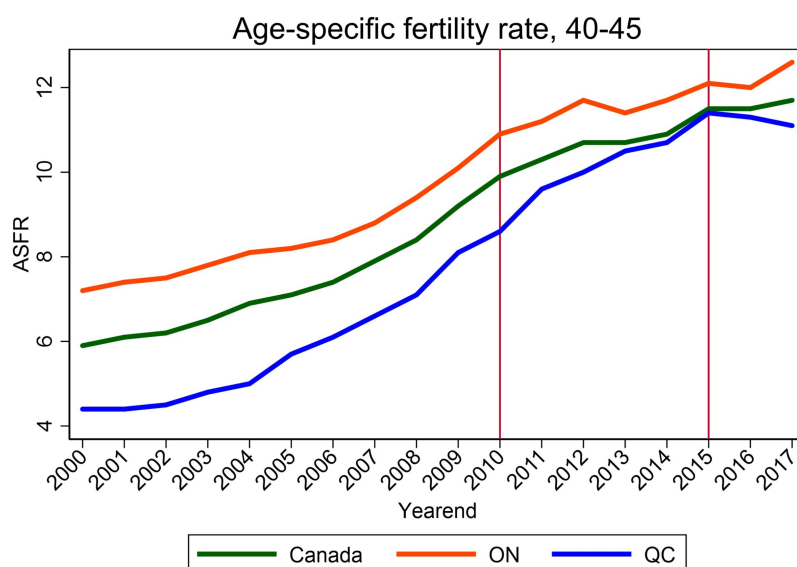
Association between specific pregnancy complications in the elder sister and later cardiovascular death in the younger sister with uncomplicated pregnancies Aditi Singh*

Aditi Singh Liv Grimstvedt Kvalvik Rolv Arnold Skjærven Kari Klungsøyr

Background: Studies have shown an increased risk of later cardiovascular (CVD) death after pregnancy complications, e.g. preeclampsia (PE) and preterm birth. It is also shown that women without PE, but whose sister had PE, transfer an increased risk of PE to their daughters. It is unknown whether women without pregnancy complications have increased CVD mortality if their sister had pregnancy complications.

Method: The Medical Birth Registry of Norway and the Population Registry were used to identify 87,580 sister pairs (82,216 full and 5364 maternal half-sisters) whose first births were between 1967–2013 and where the younger sister had neither preterm birth, PE, placental abruption, small or large for gestational age, diabetes, plural birth, perinatal loss, or caesarean section in her pregnancies. Exposure was any of the mentioned pregnancy complications in the older sister, each analyzed separately. The Cause of Death Registry with follow-up until 2020 identified CVD deaths, up to 69 years, in the younger sister. Cox regression analyses was used to estimate hazard ratios (HR) and 95% confidence intervals (CI), allowing adjustment for maternal age at first birth, year of first delivery and maternal education (three categories) of both sisters.

Results: 255 younger sisters died due to CVD by 2020. Younger sisters (all) had increased risk of CVD death only if the elder sister had PE (HR 1.76; 95% CI 1.14-2.70) in any of her pregnancies. There was heterogeneity in the risk increase, where the HR estimate for younger maternal half-sisters was 5.56; 95% CI 2.05-15.09, while in younger full-sisters HR was 1.47; 95% CI 0.91-2.39.

Conclusion: The increased CVD mortality after an older sister with PE was stronger in half-sisters than full-sisters. This heterogeneity in risk will be further analyzed.

Cardiovascular mortality upto 69 years in the younger sisters with uncomplicated pregnancies by specific pregnancy complications in the elder sister

Reproductive

Preconception vitamin D and miscarriage in a prospective cohort study Anita Subramanian*

Anita Subramanian Anne Z. Steiner Clarice R. Weinberg Ginna L. Doss Anne Marie Z. Jukic

Background: In humans, low vitamin D has been associated with prolonged menstrual cycles, delayed ovulation, and a lower probability of conception. Animal and in vitro data indicate that vitamin D may affect implantation. Our objective was to estimate the association between preconception vitamin D level and risk of miscarriage.

Methods: Participants were trying to conceive naturally for 3 months or less at enrollment and aged 30-44 years. A preconception blood sample was collected and 25-hydroxyvitamin D [25(OH)D] was measured. Women who conceived (n=362) were at risk of a miscarriage from the day of a reported positive pregnancy test until either a participant-reported pregnancy loss or 20 weeks post day of ovulation, whichever came first. Gestational age was defined by ovulation. Time to miscarriage (days) or censoring was modeled using a multivariate Cox proportional hazards model. Multiple imputation was performed for missing covariates and missing day of ovulation.

Results: The mean age was 33 years (standard deviation (SD): 3.0 years). Mean 25(OH)D was lower among those who reported their race as African-American and those with higher BMI. After adjustment for age, race, BMI, education, exercise, alcohol, and caffeine intake, compared to the referent group (30-<40 ng/ml), the hazard ratio (HR) and 95% confidence interval (CI) for those with a 25OHD level of less than 30 ng/ml was 1.10 (CI: 0.63, 1.93). Among participants with a higher 25OHD level (≥ 40 ng/ml), the HR was 1.04 (CI: 0.61, 1.79).

Conclusion: In this population of women conceiving naturally, preconception vitamin D levels do not appear to predict miscarriage. Future research should focus on women at greater risk for miscarriage or in populations at risk for vitamin D deficiency or on supplementation.

Age of menarche in relation to vitamin D level: cross-section and prospective study.

Abdullah Al-Taiar* Abdullah Al-Taiar Reem Al-Sabah Lemia Shaban Praveen K. Durgampudi Hadiza Galadima

Background and objectives: Very few studies have examined the direct link between age of menarche and vitamin D level and controversial results have been reported. This study aimed to investigate the association between vitamin D and age of menarche in a group of adolescent girls in an area with plenty of sunshine.

Methods: At baseline, data were collected on 722 middle schoolgirls that were randomly selected by probability proportional to size sampling method. Of this group, 598 were followed including 173 who had their menarche during the follow-up. Serum 25-hydroxyviatmin D (25OHD) was measured at baseline using liquid chromatography-tandem mass spectrometry (LC-MS/MS). Data on potential confounders were collected at baseline from the parents using self-administered questionnaire and from schoolgirls through face-to-face interview. Multiple linear regression and time-to-event analysis were used to investigate the association between 25OHD concentration and age of menarche.

Results: The prevalence of vitamin D deficiency (<50 nmol/L) among schoolgirls was 91.69%. We found no evidence for association between 25OHD levels and age of menarche before (p=0.808) or after (p=0.765) adjusting for potential confounders. We also found no evidence for association between 25OHD status and age of menarche before (p=0.424) or after (p=0.35) adjusting for potential confounders. However, categorizing 25OHD into quartiles showed significant positive association before (p=0.023) and after (p=0.018) adjusting for potential confounders. Time-to-event analysis showed no association between 25OHD level or status and age of menarche (p=0.850).

Conclusion: In Middle Eastern setting, where vitamin D deficiency is common despite plenty of sunshine, vitamin D is not a major determinant of the age at menarche. Regardless of the link between vitamin D and age of menarche, there are several other health benefits of having adequate vitamin D level during childhood and adolescence.

Reproductive

Risk of cardiovascular disease in women and men with subfertility: the Trøndelag Health Study Karoline H. Skåra* Karoline Skåra Bjørn Olav Åsvold Álvaro Hernáez Abigail Fraser Janet W. Rich-Edwards Leslie V. Farland Øyvind Næss Deborah A. Lawlor Ben Brumpton Maria C. Magnus

Fertility rates are decreasing in many European countries. Subfertility, defined as being unable to conceive after trying for more than twelve month, is estimated to affect between 10 and 15% of couples. However, subfertility remains unexplained in around 25-30% of all cases. Some studies have suggested an association between subfertility and risk various chronic diseases, such as cardiovascular disease (CVD). The aim of the present study was to investigate the association between subfertility and CVD outcomes in both sexes. We studied 31,629 women and 17,630 men participating in The Trøndelag Health Study (HUNT). We assessed the association between self-reported subfertility and CVD outcomes using Cox proportional hazards models adjusted for age, birth year, body-mass index, blood pressure, diabetes mellitus, cholesterol, smoking history, cohabitation, and education. Information on CVD (stroke, coronary heart disease (CHD), myocardial infarction, and angina) was available by linkage to hospital records. A total of 17% of women and 15% of men reported subfertility. In women, subfertility was modestly associated with increased risk of CHD (adjusted hazard ratio [aHR] 1.15; 95% confidence interval [CI]: 1.02, 1.29), angina (aHR 1.22; 95% CI: 1.06, 1.41), stroke (aHR 1.17; 95% CI: 1.01, 1.37) and any CVD (aHR 1.09; 95% CI: 0.99, 1.20) compared to women who were fertile. In men, with the exception of stroke, for which we observed a weak imprecise positive association (aHR 1.11; 95% CI: 0.91, 1.34), associations were weakly inverse (e.g., aHR for CHD: 0.92; 0.81, 1.05), though mostly with no statistical evidence that they differed from equivalent associations in women. We observed modest increased risks of CVD outcomes explored in women and weak inverse associations in men, though with no strong statistical evidence on sex differences. Despite the large sample size, our results indicate the need for larger studies to obtain precise results in both sexes and determine whether there are true sex differences.

Reproductive

Birth Weight and Subsequent Pregnancy Intention in the Context of Disease Outbreaks
David Mallinson* David Mallinson Letícia Marteleto

Pregnancy intentions are associated with low birth weight (LBW) delivery (<2,500 grams). However, it is uncertain whether LBW delivery influences subsequent pregnancy intentions. LBW causes morbidity and developmental delays for children. These stressors may shift a parent's decision to prevent or forgo future childbearing. Further, the experiencing LBW delivery during a disease outbreak may also influence reproductive behaviors. This study's purpose is two-fold: to investigate LBW delivery and subsequent pregnancy intentions; and to investigate LBW delivery during the Zika epidemic and subsequent pregnancy intentions. We use data from the Demographic Consequences of Zika and COVID project, which investigates the impact of the Zika virus and Coronavirus outbreaks on reproductive outcomes among women in the state of Pernambuco, Brazil. Our preliminary sample consists of 547 respondents aged 18-30 years old who had a live delivery at least once during 2014-2020 (data collection is ongoing). We consider two exposures: any prior LBW delivery (no; yes), LBW delivery during the Zika epidemic (2015-2017) in Brazil (no; LBW outside epidemic; LBW during epidemic). Our primary outcome is whether a respondent wants to have (more) children (no; yes). We also consider several other secondary outcomes. For descriptive analyses, we tabulate the distribution of outcomes by both LBW exposures. For logistic regressions, we run models in which we regress dichotomized outcomes on LBW exposures. Of the 547 respondents, 28 (5.1%) had a LBW delivery outside the Zika epidemic and 31 (5.7%) had a LBW delivery during the Zika epidemic. Preliminary results indicate that experiencing a LBW delivery during the epidemic was negatively associated with fertility intentions. Only 38.7% of individuals with a LBW delivery during the Zika epidemic wanted (more) children compared to 41.2% and 57.1% of individuals with no LBW deliveries or LBW deliveries outside the epidemic, respectively.

Respiratory

Acculturation and asthma in non-Hispanic Asian American in a nationwide study of US population Yueh-Ying Han* Yueh-Ying Han Erick Forno Juan C. Celedón

Background: The prevalence of asthma is lower in Asians than in other racial/ethnic groups in the U.S. Whether acculturation increases the risk of asthma in Asian Americans is unknown.

Methods: Cross-sectional study of acculturation and asthma in 636 non-Hispanic Asian American children (aged 6-17 years) and 2,486 non-Hispanic Asian American adults (aged 18-79 years) who participated in the 2012-2018 National Health and Nutrition Examination Survey (NHANES) in the U.S. Current asthma was defined as physician-diagnosed asthma and self-report of still having asthma. Acculturation was categorized as low, medium, and high based on country of birth, time living in the U.S., and language spoken at home. Logistic regression was used for the multivariable analysis, which was adjusted for age, sex, health insurance coverage, family history of asthma, body mass index, serum cotinine, and (in adults) smoking status.

Results: The prevalence of asthma was 7.4% in children and 4.4% in adults. In a multivariable analysis, children with high acculturation had 2.3 times higher odds of current asthma than those with low or medium acculturation (95% CI for OR=1.04 to 5.06). Similarly, adults with high acculturation had 4.3 times higher odds of asthma than those with low or medium acculturation (95% CI for OR=2.37 to 7.71). To reduce potential misclassification of chronic obstructive pulmonary disease (COPD) as asthma in adults, we repeated the analyses after excluding current and former smokers. In this sensitivity analysis, high acculturation remained associated with current asthma (OR=4.85, 95% CI=2.20 to 10.71).

Conclusions: In a nationwide U.S. survey, high acculturation was associated with increased odds of asthma among non-Hispanic Asian Americans. Further studies of acculturation and asthma are needed in well-defined Asian subgroups.

Screening

Mental illness and participation in colorectal cancer screening: a Danish register-based study Ellen M. Mikkelsen* Mette Kielsholm Thomsen Marie Dahl Jørgensen

Introduction

Persons with mental illness have increased mortality from colorectal cancer (CRC), but similar CRC incidence compared with persons with no mental illness. Screening has the potential to alleviate this gap in mortality.

We aimed to evaluate participation in CRC screening for persons with and without a diagnosis of mental disease.

Methods

The Danish CRC screening program is a newly initiated tax-funded population-based using biennial fecal immunochemical testing. The program is offered free of charge to all residents aged 50-74. We retrieved data from national registries on all persons invited in the first two screening rounds of the program (2014-2019). We defined mental illness as an international classification of diseases F diagnosis up to five years prior to the first screening invitation.

We calculated participation proportions for person with and without mental illness, and estimated a crude relative risk. In coming analyses, we will also calculate incidence rate differences and incidence rate ratios and adjust all analyses for socioeconomic and demographic variables. Further, we will repeat all analyses for non-participants who were re-invited in the second screening round.

Results

Of 2,031,303 persons invited to their first screening, 83,559 had a mental illness diagnosis. Participation was 46.2 % for persons with mental illness, and 64.2 % for persons without. The absolute risk difference was 18 percentage points (95% CI: 17.61;18.30) and the relative risk was 0.72 (95% CI: 0.71;0.73).

The remaining analyses are ongoing, and results will be available at the conference.

Conclusion

Crude results suggest that persons with mental illness participated less in the Danish population-based CRC screening program compared with persons without mental illness. Screening program interventions and further insights into reasons for non-participation in this group may be considered.

State-level structural sexism and eating disorder risk: An intersectional, life-course analysis of the Growing Up Today Study Ariel Beccia* Ariel Beccia S. Bryn Austin Jonggyu Baek Madina Agénor William Jesdale Kate L. Lapane

Background: Structural sexism is likely a key driver of social inequities in mental health outcomes such as eating disorders (EDs); however, few studies have considered life-course exposure trajectories and/or intersectional effects. We examined the relationship between cumulative exposure to state-level structural sexism and ED risk at the intersection of gender and sexual orientation.

Methods: Participants came from the Growing Up Today Study, a cohort of 16,875 children aged 9-14 years in 1996 who we followed through 2007. Using an index of relevant state policies/social inequalities from the Institute for Women's Policy Research, we classified states as having high or low levels of structural sexism (Figure) and summed the number of years participants lived in a high structural sexism state to quantify their cumulative exposure. We fit sequential conditional mean models to estimate the effect of cumulative exposure through a given study wave on subsequent ED behaviors (purging, binge eating), controlling for individual- and state-level demographic characteristics via propensity scores. We then tested for intersectional effects by including interaction terms between gender, sexual orientation, and structural sexism and calculating a 3-way relative excess risk due to interaction (RERI).

Results: In the full sample, each additional year of living in a high structural sexism state was associated with a 6% increased risk of purging (95% confidence interval (CI): 4-8%) and a 9% increased risk of binge eating (95% CI: 7-11%). Sexual minority girls/women who lived in a high structural sexism state for ≥ 4 years (the top tertile of the cumulative exposure distribution) had the largest risk increases for both outcomes and excess risk of purging (RERI: 3.98, 95% CI: 1.01-6.96).

Conclusion: Long-term exposure to structural sexism may disproportionately increase ED risk among young people with marginalized gender and sexual identities.
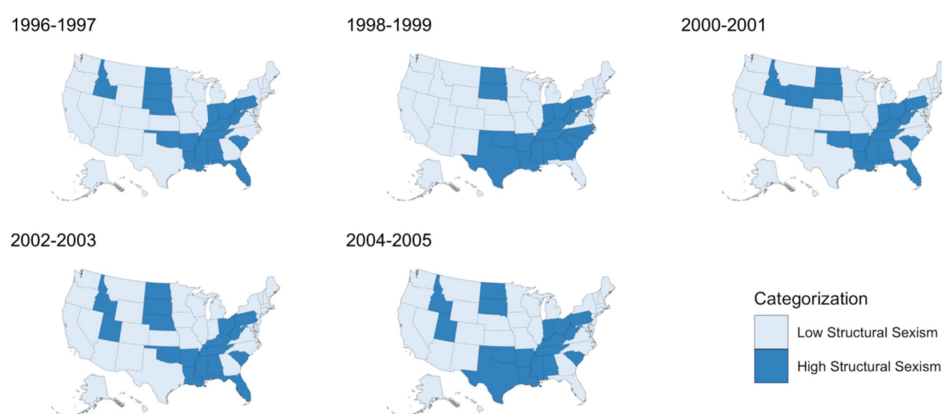
1996-1997   1998-1999   2000-2001

2002-2003   2004-2005

Categorization

Low Structural Sexism

High Structural Sexism

Figure. Time-varying categorization of the 50 U.S. states and the District of Columbia as having high or low levels of structural sexism across the exposure window. Note that structural sexism index values were provided for five "even" years (1996, 1998, 2000, 2002, and 2004); last observation carried forward imputation was used to define such values for all subsequent "odd" years (1997, 1999, 2001, 2003, and 2005).

Suicides and male twin live births in the US, 2003 to 2019: an updated test of collective optimism and in utero selection Parvati Singh, PhD* Parvati Singh Samantha Gailey Abhery Das Tim-Allen Bruckner

Prior research based on Swedish data suggests that higher collective optimism, indicated by a relatively low monthly frequency of suicides among reproductive-aged women, may correspond with lower in utero selection against male twins in a population. It remains unclear whether this finding holds in the US—which reports the greatest suicide rate of all high-income countries. We examine whether and to what extent monthly changes in overall suicides (all age and sex groups) precede changes in the ratio of male twins to male singletons. To maintain comparability with prior work, we also test this relation with
suicides among women aged 15-49 years. We retrieve monthly data on suicides and male twin live births from CDC WONDER, from 2003 to 2019. We apply Box-Jenkins iterative time-series routines to detect and remove autocorrelation from percent monthly change in suicides (exposure) and monthly ratio of male twin to male singleton live births (outcome) series. Results indicate that a one percent increase in monthly change in overall suicides precedes a 0.005 unit decline in male twin live births 6 months later (coefficient = -0.005, p value = 0.004). This relation persists but is attenuated when using suicides among reproductive-aged women as the exposure (coefficient = -0.0012, p value = 0.014). The present study lends external validity to prior research and supports the
notion that collective optimism can affect an understudied aspect of fertility—in utero selection.
Key words: collective optimism, suicides, in utero selection, male twins, time-series analysis

Neighborhood-level racialized economic segregation and SARS-CoV-2 seropositivity among a Chicago adult community-based sample Elijah Watson* Elijah Watson Amy K. Johnson C. Scott Smith Michael Newcomb Rana Saber Joshua M. Schrock Daniel T. Ryan Alexis R. Demonbreun Brian Mustanski Richard D'Aquila Elizabeth M. McNally Thomas W. McDade

Examining racialized economic segregation in relation to SARS-CoV-2 seropositivity can further our understanding of how structural inequities impact COVID-19 exposure.

From June-December 2020, Chicago-area community-based adults were recruited. Those eligible completed an online survey and self-sampled dried-blood spot via mail for seropositivity testing. Our measure of neighborhood racialized economic segregation was an Index of Concentration at Extremes (ICE) for race/ethnicity-income, ranging from a score of -1 (low), reflecting census tracts with 100% low-income people of color residents, to 1 (high), reflecting 100% high-income non-Hispanic white residents. Symptom severity scores were created by weighting 8 symptoms reported since March 1 associated with higher IgG concentrations (range 0-4.4). Modified Poisson regression was used to estimate the crude prevalence ratios (PR) for ICE race/ethnicity-income quintiles and seropositivity.

Unadjusted seroprevalence was 18.08% (95% CI: 16.98%, 19.18%) for the sample, restricted to those with precise geocoded Chicago city addresses (n=4,695). In the lowest (n=915) and highest (n=1,455) ICE quintiles, 21.64% and 16.98% were seropositive, respectively. Comparing the lowest to the highest quintile, the seropositivity PR was 1.27 (95% CI: 1.08, 1.51). In the lowest and highest quintiles, 19.39% and 34.73% were asymptomatic and mean (±SD) symptom severity was 1.63±1.33 and 1.13±1.28, respectively.

In this Chicago adult community-based sample, seroprevalence and symptom severity were higher in predominately lower-income, people of color neighborhoods, while asymptomatic and milder cases were more common in higher-income, non-Hispanic white neighborhoods. Public health monitoring of COVID-19 should consider measures of spatial social polarization to clarify the contexts in which disparities arise.

Health predictors of neighborhood selection: a prospective cohort study of residential mobility in Ontario, Canada
Emmalin Buajitti* Emmalin Buajitti Laura C. Rosella

Background

Health selection into neighborhoods – whereby health status influences movement into areas of low or high neighborhood socioeconomic status (SES), for instance – may bias observed neighborhood effects on health. Studies of health selection have often relied on small populations and subjective measures of health. Residential histories linked to survey and health administrative data in Ontario, Canada offer a unique opportunity to quantify health selection into neighborhoods in a diverse and representative population.

Methods

We identified Canadian Community Health Survey (CCHS) respondents aged 25 to 64, interviewed between 2005 to 2014, who moved within 5 years (n=25,502). We captured updated neighborhood SES from income quintiles in the Canadian census, and health at baseline using both subjective (self-rated health) and objective measures (# of chronic conditions, from health administrative records).

We used multinomial logistic regression to quantify associations between health status and subsequent neighborhood SES. Effects reported are adjusted for baseline SES, year of survey, sex, and age (minimally-adjusted), household income, immigrant status, and residential instability (SES-adjusted), smoking, physical activity, and alcohol use (SES and behavior adjusted).

Results

For both subjective and objective measures, less healthy individuals were more likely to move into low-SES neighborhoods and less likely to move into high-SES neighborhoods (Figure 1). Effects were strongest for the poorest-health group selection into lowest-SES, which persisted after confounding adjustment (Fair/Poor SRH OR=1.32, 95%CI=1.03,1.71; 4+ chronic conditions OR=1.41, 1.06-1.87).

Conclusions

Both objective and subjective measures of health predict future neighborhood SES. Our findings provide important evidence of health selection into neighborhood SES groups, which may bias neighborhood-level studies of SES effects. Future studies must consider strategies to mitigate this bias.
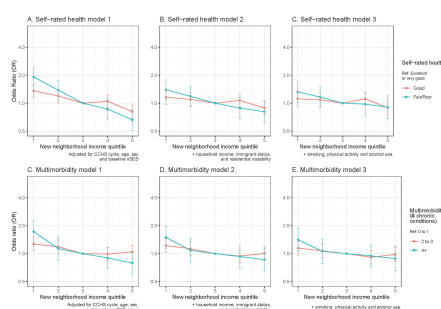

Figure 1. Odds ratios for new neighborhood socioeconomic status after first move, Ontario CCHS respondents ages 25 to 64, 2005 to 2014 (n=25,502).

Social

School suspension and expulsion predicts higher dementia risk in late life through educational pathways: A lifecourse mediation analysis among the National Longitudinal Survey of Youth 1979 Cohort Catherine Duarte* Catherine Duarte Jennifer Ahern Irene Yen Alison Cohen Anusha Vable

Exclusionary school discipline – which removes students from their classrooms via suspension and/or expulsion – may alter educational pathways via interruptions and delays in schooling with implications for later life health. In National Longitudinal Survey of Youth 1979 (NLSY79) data (N=7125), we used linear regression to evaluate if early-life exclusionary discipline (3-levels: no discipline, ever suspended, ever expelled by mean age 14.8 yrs) predicted 20-year cumulative dementia risk. Dementia risk was estimated with a risk score calculator previously developed and validated using cognitive and social factors measured up to mid-life in the *Health and Retirement Study*. Applying this calculator in NLSY79, we estimated participants' cumulative 20-year dementia risk from age 50 to 70. We then used inverse odds weighting to estimate the natural direct and indirect effects of the educational pathways (ascertained annually from age 14-48 for each participant then collapsed into 15 distinct educational trajectories using sequence and cluster analysis) as mediators of the punitive discipline-dementia risk association. Analyses adjusted for exposure-outcome, mediator-outcome, and exposure-mediator confounders (e.g., sociodemographics, childhood socioeconomic status, school-based behavior/performance, substance use, parental death). Compared to no punitive discipline, both suspension (RD:0.021;95%CI:0.013-0.028) and expulsion (RD:0.064;95%CI:0.045-0.084) were associated with increased dementia risk. We also found that this association was mediated by participants' educational trajectories. Specifically, the education sequences accounted for 65.8% (95%CI:38.1%-93.5%) of the total suspension-dementia effect (indirect effect RD:0.014; 95%CI: 0.008, 0.019) and 72.2% (95%CI:39.8%-104.5%) of the total expulsion-dementia effect (indirect effect RD:0.0463;95%CI:0.0457-0.0469). These results suggest punitive discipline increases dementia risk, largely by altering educational paths.

Among working and not working Latinos in the United States, food insufficiency and difficulty with expenses associated with adverse mental health during the COVID-19 pandemic Cara Frankenfeld* Cara Frankenfeld Carol Cleaveland

Identifying key contributors to mental health among vulnerable populations can be used to prioritize and target social services. Latino workers are often in low-paying jobs with little autonomy for personal protections, and may have differing sources of stress. Data from US Census Household Pulse Survey, covering April 14, 2021 to October 11, 2021, were analyzed. Latino individuals with available mental health data were included (n=50,755) to evaluate factors associated with adverse mental health in relation to work. Ordinal logistic regression was used to evaluate categorical frequencies (not at all, several days, more than half of days, and nearly every day) of anxiety, loss of interest, worry, and feeling down over the previous two weeks. Demographic, household, and financial covariates were mutually adjusted, and jackknife replications and population weights were applied. Analyses were stratified by work status in past 7 days: non-essential (n=14,222), non-essential (n=17,424), and no work (n=19,109). More than half of individuals reported several days of adverse mental health symptoms. Individuals not working had higher frequency of adverse mental health symptoms (p<0.001), compared to workers in non-essential settings. Higher frequency of food insufficiency and difficulty with expenses were strongly associated with higher frequency of adverse mental health symptoms in workers in non-essential settings, workers in essential settings, and individuals not working (Figure): often not enough to eat (ORs: 2.60-4.99), sometime not enough to eat (ORs: 1.60-3.22), very difficult with expenses (ORs: 4.46-7.73), and somewhat difficult with expenses (ORs: 2.27-3.34). Lower age and less education seemed to be protective in workers in essential and non-essential settings. However, in Latino workers and non-workers, ensuring food sufficiency and financial resources may be important pathways relevant to improving mental health in all US Latinos.

Figure: Heat map of ORs from mutually adjusted mutual ordinal logistic regression of frequency of anxiety in relation to demographic, financial, and household characteristics in Latinos in the US surveyed from April 2020 to October 2021 in the US Census Household Pulse Survey working in non-essential or essential settings, or not working in the past 7 days. Red indicates OR>1 and blue indicates OR<1, with darker coloration indicating stronger magnitude.

		Work in past 7 days, non-essential				Work in past 7 days, essential				No work in past 7 days			
Group	Characteristic	Anxiety	Worry	Interest	Down	Anxiety	Worry	Interest	Down	Anxiety	Worry	Interest	Down
Age	Age in 10 years	0.81	0.83	0.84	0.84	0.80	0.84	0.82	0.81	0.85	0.87	0.91	0.86
Race	White (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Black	0.88	0.88	0.84	0.87	0.88	0.93	1.01	0.87	0.73	0.97	0.70	0.81
	Asian	0.75	1.03	0.92	0.65	0.88	1.07	0.82	0.83	1.08	1.12	1.21	1.25
	Other	1.00	0.94	1.11	0.97	1.16	1.10	1.05	1.09	0.98	1.01	1.04	1.06
Gender	Male	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Female	1.43	1.37	1.13	1.19	1.46	1.48	1.16	1.17	1.33	1.33	1.22	1.17
Education	Less than HS	0.52	0.47	0.71	0.48	0.82	0.84	0.72	0.89	0.93	0.86	0.94	0.87
	Some HS	0.74	0.73	0.66	0.55	0.86	0.76	0.62	0.88	0.98	0.98	0.98	1.02
	HS grad or equiv (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Some college	1.25	1.33	1.20	1.11	1.54	1.56	1.30	1.43	1.65	1.37	1.33	1.36
	Associate degree	1.41	1.37	1.21	1.09	1.54	1.41	1.13	1.25	1.34	1.16	1.16	1.19
	Bachelor degree	1.92	1.77	1.41	1.36	1.68	1.54	1.21	1.31	1.44	1.18	1.11	1.17
	Graduate degree	2.15	1.80	1.40	1.40	1.83	1.47	1.14	1.20	1.74	1.44	1.26	1.30
Marital status	Married (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Widowed	1.24	1.65	1.41	1.37	1.34	1.46	1.90	1.46	1.45	1.31	1.28	1.69
	Divorced	1.05	1.10	1.10	1.17	1.27	1.30	1.41	1.39	1.47	1.33	1.57	1.63
	Separated	0.91	0.89	0.98	1.20	1.25	1.19	1.46	1.43	1.24	1.14	1.38	1.46
	Never married	1.14	1.14	1.25	1.41	1.14	1.15	1.47	1.40	1.26	1.16	1.39	1.46
Household	Number adults	1.04	1.06	1.08	1.08	0.98	0.99	1.03	1.01	1.02	1.02	1.07	1.08
	Number children	0.96	0.96	0.91	0.91	0.92	0.94	0.91	0.89	0.90	0.89	0.86	0.84
Living quarters	Mobile home	0.58	0.54	0.68	0.83	0.91	0.98	1.06	1.00	0.89	0.98	0.95	0.90
	Single-family, detached (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Single-family, attached	0.87	0.92	0.80	0.78	1.01	1.08	0.96	1.04	0.86	0.93	0.88	0.92
	Building with 2 apts	0.95	0.98	0.94	1.13	1.05	0.96	1.02	1.03	0.82	0.79	0.76	0.77
	Building with 3 or 4 apts	0.86	0.85	0.84	1.04	1.03	0.92	0.90	0.96	0.91	0.91	1.05	1.04
	Building with 5+ apts	1.03	1.03	1.01	1.10	1.08	0.99	1.20	1.04	0.89	0.97	0.99	0.97
	Boat, RV, van, etc	1.88	0.55	1.89	0.68	1.83	3.38	2.66	3.48	1.23	1.19	1.30	1.90
Food sufficiency in past 7 days	Enough of kinds of food wanted (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Enough, but not always kinds of food wanted	1.71	1.68	1.88	1.66	1.51	1.50	1.53	1.32	1.43	1.47	1.46	1.41
	Sometimes not enough to eat	2.46	2.48	2.80	3.22	1.88	2.00	1.94	1.99	1.60	1.84	1.65	1.60
	Often not enough to eat	4.26	4.46	3.82	4.99	3.61	2.72	2.60	2.87	4.27	3.21	3.37	3.18
Difficulty with expenses	Not at all (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	A little	1.75	1.97	1.63	1.54	1.99	2.11	1.92	2.20	2.13	2.19	2.15	2.00
	Somewhat difficult	2.48	2.92	2.38	2.27	3.00	3.34	2.68	2.68	2.95	3.19	2.90	2.63
	Very difficult	5.23	5.77	3.76	3.60	7.41	7.73	4.46	5.00	5.67	6.47	5.00	5.05
Confidence in ability to pay rent or mortgage	Not at all	2.04	2.61	2.13	2.27	1.22	1.34	1.37	1.33	1.27	1.30	1.40	1.63
	Slightly	1.44	1.50	1.39	1.59	1.31	1.44	1.63	1.58	1.27	1.28	1.26	1.35
	Moderately	1.41	1.59	1.50	1.58	1.18	1.25	1.30	1.25	1.43	1.50	1.39	1.57
	Highly (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Payment deferred	0.95	1.45	0.98	1.08	1.07	1.42	1.48	1.83	0.84	0.75	1.03	1.13

Neighborhood disadvantage and immune-related illnesses among residents living in the US Gulf States Opal Patel* Opal Patel Kaitlyn G. Lawrence Christine G. Parks Mark Bodkin Lawrence S. Engel Dale P. Sandler

Background: Neighborhood disadvantage has been associated with increased risk for pneumonia and influenza-associated hospitalizations. Few studies have investigated how neighborhood disadvantage may influence immunologic health.

Objective: The aim of this study was to examine the association between neighborhood disadvantage and multiple health endpoints as general markers for potential immune suppression.

Methods: We used data on 10,543 participants from the Gulf Long-term Follow-up (GuLF) Study. Neighborhood disadvantage was assessed using the 2013 Area Deprivation Index (ADI), which assigns a ranking of 1 to 100 for lowest to highest disadvantage. We linked ADI to participants' geocoded enrollment addresses at the census block group level and. ADI was categorized into quartiles based on the national distribution. Outcomes self-reported at the home visit (May 2011-May 2013) included occurrence of shingles, pneumonia, cold sores, any flu, and any colds since the Deepwater Horizon oil spill (April 2010). Frequent colds and frequent flu were defined as ³4 colds and ³2 flu episodes since the spill. An aggregated outcome (occurrence of any pneumonia, cold sores, flu, and ³4 colds since the spill) was also examined.

Results: We found elevated prevalence ratios (PR) and 95% confidence intervals (CI) for pneumonia associated with ADI in the third (PR: 2.04, 95% CI: 1.04, 4.02) and fourth (PR: 2.00; 95% CI: 1.00, 3.98) quartiles compared to the first quartile. PRs for frequent colds were also elevated for increasing ADI quartiles relative to the first quartile, but with CIs including the null value.

Conclusions: Self-reported outcomes may be subject to misreporting, the number of individuals reporting some outcomes, such as shingles, was small, and there is potential confounding by other factors. The observed associations of frequent colds and pneumonia with increasing neighborhood disadvantage may warrant further research using more robust measures of immune suppression.

A tale of many neighborhoods: latent profile analysis to derive residential neighborhood typologies in the US Hiwot Y. Zewdie* Hiwot Y. Zewdie Jamaica R.M. Robinson Stephen J. Mooney

Introduction: Neighborhoods are critical to shaping health. However, multicollinearity between neighborhood features make them challenging to model effectively and consistently. We used latent profile analysis to derive nationally representative neighborhood typologies from contextual factors relevant to health.

Methods: Estimates for six neighborhood variables were derived for a random national sample of 1,000 Census tracts. We compiled 2011-2015 ACS tract-level estimates for five of six neighborhood variables: % of residents commuting alone by car, % of residents with at least a high school education, % of US-born residents, % of non-Hispanic white residents, and number of housing units. National Landcover Database data from 2011 was used to estimate the proportion of each Census tract covered by impervious surface. One- to six-profile LPA models were fit over derived data for model specification.

Results: Model fit statistics identified a 4-profile LPA model permitting varying variances and covariances as the optimal categorization of neighborhood profiles. Profiles were characterized as "Urban 1" (low drive alone, high racial/ethnic diversity, low education, and high impervious surface), "Urban 2" (moderate drive alone, moderate US-born, moderate racial/ethnic diversity, and moderate impervious surface), "Suburb" (high drive alone, high education, moderate racial/ethnic diversity), and "Rural" (high drive alone, low racial/ethnic diversity, low education, and low impervious surface). These profiles comprised 24%, 32%, 12%, and 32% of selected census tracts, respectively.

Conclusion: Findings suggest distinct neighborhood typologies can be derived using social and environmental correlates of health. Further research should explore the use of derived profiles to better model the complex relationships between various contextual indicators in neighborhood health research.

Using area-level eviction data as a population health exposure: theory, practice, and pitfalls Gabriel L. Schwartz* Gabriel Schwartz
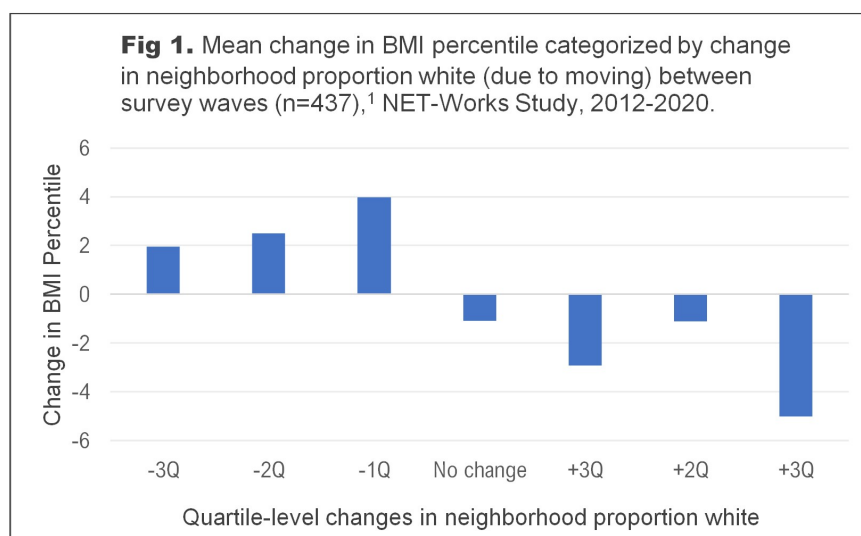
Interest in estimating the health effects of residential eviction is growing, but individual-level cohort data on evictions and health are scarce. Many epidemiologists have turned to area-level eviction rates as a more readily accessible measure of eviction exposure, finding associations with a variety of health outcomes (usually aggregated to the area-level). Other epidemiologists are turning to area-level policy changes as instruments for estimating the causal effects of area-level evictions on health.

However, estimates of the extent to which area-level eviction rates are associated with health suffer important biases that are rarely appreciated. These arise from eviction causing displacement, potentially outside the boundaries of the areas where evictions took place, and by people who move across area boundaries more generally. Here, we define two such biases: Movers' Bias (resulting when health outcomes are measured in different places than where the evictions that caused those health outcomes occurred) and Retention Bias (resulting from evictees' having worse health prior to eviction, meaning people in worse health are disproportionately displaced as eviction rates rise and disproportionately retained as eviction rates fall). These biases can yield coefficient estimates that are positively or negatively biased and remain even if one perfectly eliminates confounding or uses policy instruments for area-level eviction risk. We offer potential solutions for future work.

Neighborhood and school diversity, cortisol, and obesity: a prospective longitudinal study in low-income school-aged children Samantha Gailey* Samantha Gailey Alicia S. Kunin-Batson David Van Riper

The impact of persistent exposure to neighborhood racial segregation on health in early childhood remains unclear. Relatively few studies examine racial segregation in schools, which may strongly influence children's social, economic, and health trajectories. Moreover, epidemiologic research on segregation in both neighborhoods and schools relies predominantly on cross-sectional data. Past studies, therefore, may be biased by residential self-selection, where the selective movement of healthier families into neighborhoods (and school districts) with a higher proportion of white residents confounds associations. Here, we examine associations between racial/ethnic diversity (using a multigroup entropy index and proportion white), in neighborhoods and schools, with children's hair cortisol concentration (HCC) and body mass index (BMI) percentile. Demographic, health, and neighborhood data were collected at baseline, 12-, 24-, 36-, and 60-month follow-up visits as part of the NET-Works Study (n=534, ages 2-4 and household income < $65,000/year at baseline). Cross-sectional analyses estimated relations between neighborhood and school diversity and health factors at the 60-month (wave 5) follow-up visit. Longitudinal analyses using random effects (intercepts) models and data from all 5 waves estimated changes in HCC and BMI percentile as a function of changes in neighborhood diversity due to moving. Children exposed to higher levels of school and (to a lesser extent) neighborhood diversity at wave 5 showed higher HCC and BMI. Moving to a more diverse neighborhood also corresponded with increases in HCC and BMI. Findings suggest that exposure to racial diversity in early childhood may increase stress and elevate obesity risk. Results showing stronger associations between health factors and school, relative to neighborhood, diversity warrant more rigorous (e.g., longitudinal) analysis once school-level data become available.

Fig 1. Mean change in BMI percentile categorized by change in neighborhood proportion white (due to moving) between survey waves (n=437),[1] NET-Works Study, 2012-2020.

Abbreviations: BMI, body mass index; Q, quartile.
[1]Participants who moved more than once are represented more than once.

Study Design

Comparison of the test-negative design and the cohort design with explicit target trial emulation for evaluating COVID-19 vaccine effectiveness Guilin Li* Guilin Li Barbra A. Dickerman Miguel A. Hernán

Observational studies are widely used for estimating vaccine effectiveness under real-world conditions. Two types of study designs are commonly used: cohort design and test-negative design. A cohort design with explicit emulation of a target trial can reduce bias and yield estimates of both absolute risks and relative risk, but these estimates may be affected by residual confounding, especially by health-seeking behaviors. The test-negative design only yields estimates of relative risk, but may reduce confounding because it restricts the study population to those who seek health care and get tested for the infection of interest. However, the test negative design does not explicitly emulate a target trial and thus its estimates may be difficult to interpret. Specifically, conditioning on receiving a test during the follow-up period is a form of post-baseline stratification that may result in selection bias.

Despite the reliance of vaccine policy on these two designs, no quantitative comparison has been carried out for COVID-19 vaccines. We use nationwide data from the Department of Veterans Affairs, the largest integrated healthcare system in the United States, to estimate the effectiveness of the BNT162b2 (Pfizer-BioNTech) vaccine using both designs. First, we explicitly emulate a target trial using follow-up data and evaluate the potential for confounding using appropriate negative controls. Second, we implement the test-negative design and describe the reasons why it deviates from a target trial. We then summarize the relative advantages and disadvantages of these designs and provide recommendations for their implementation in real world data.

Low Uptake of Prediction Intervals in Meta-Analysis Studies
Samuel Governor* Samuel Governor Emmanuel Tetteh Veronica Danquah Gyasi Kodua Frederick Gyabaa Stephan Lanes

Background: Meta-analysis commonly seeks to summarize effect estimates from individual studies. When the individual studies' effect sizes vary widely, the pooled mean effect size in meta-analysis may not be consistent from one population to another. Describing heterogeneity of effect sizes is a crucial element of meta-analysis in order to understand effect sizes likely to be seen in comparable populations. Common methods for assessing heterogeneity include I^2 and Cochran's Q test. The prediction interval measures the range of results that can be expected in future studies and can provide useful information not conveyed by more popular methods of assessing heterogeneity.

Objectives: We conducted a literature review to explore methods used to assess heterogeneity with special attention to the contribution of prediction intervals.

Methods: A total of 10,110 studies published from 2018-01-01 to 2021-12-31 were identified in PubMed using the keywords combination search of ***meta-analysis & (i-square|i-squared|prediction interval|i2).*** We randomly sampled 300 studies and reviewed 206 articles with full-text access for methods used to determine heterogeneity. We examined methods used to assess heterogeneity and reviewed key citations.

Results: Nearly all (95.9%) studies assessed heterogeneity using I2, Cochran's Q test was used by 36.8% of studies, and only 1.0% of studies estimated the prediction interval.

Conclusions: Prediction intervals are rarely estimated in meta-analyses studies. The use of prediction intervals has been encouraged because it informs in absolute terms about the variation in effect sizes estimated in meta-analysis from one population to another and helps us understand how effect sizes are likely to vary in the future in populations comparable to the ones in our analytics.

Table 1. Characteristics of Included Studies, N = 206

Variables	Overall
Pooled Number of Studies	
Mean (SD)	15.27 (14.98)
Median (Min- Max)	10.00 [2.00, 121.00]
I2, N (%)	187 (95.9)
Q test, N (%)	71 (36.8)
Year of Publication, N (%)	
2018	31 (15.0)
2019	38 (18.4)
2020	66 (32.0)
2021	71 (34.5)
No Chi Square Value Reported, N (%)	134 (65.0)
Prediction Interval, N (%)	2 (1.0)
Familiarity with Prediction Interval, N (%)	
Borenstein et al., 2017[1]	2 (1.0)
Chiolero et al., 2012[2]	0 (0.0)
Inthout et al., 2016[3]	0 (0.0)
Familiarity with I2, N (%)	
Higgins et al., 2002[4] & 2003[5]	61 (30.3)

[1] Borenstein, M., et al., *Basics of meta-analysis: I(2) is not an absolute measure of heterogeneity.* Res Synth Methods, 2017. **8**(1): p. 5-18.
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[5] Higgins, J.P., et al., Measuring inconsistency in meta-analyses. Bmj, 2003. 327(7414): p. 557-60.

State-level Prevalence and Factors Associated with Current Marijuana, ENDS, and Cigarettes use among Asthmatic US adults

Mohammad Ebrahimi kalan* Mohammad Ebrahimi kalan Zoran Bursac Rime Jebai Samane Zare Wei Li Prem Gautam Abir Rahman Kenneth D Ward Ziyad Ben Taleb

Background

Use of marijuana (MJ), cigarettes, and electronic nicotine delivery system (ENDS) is widespread among United States (US) adults and is linked to worsening respiratory symptoms, especially among asthmatic patients. This study examined state-specific prevalence and factors associated with MJ, ENDS, and cigarette use among asthmatic adults in the U.S.

Methods

We analyzed data of 41,974 adults aged ≥18 years having self-reported current asthma from the 2018 Behavioral Risk Factor Surveillance System (BRFSS). We reported weighted prevalences to account for complex survey design and performed multivariable logistic regression models to examine factors associated with current use of MJ, ENDS, and cigarettes.

Results

Overall prevalence of current MJ, ENDS, and cigarette use among asthmatic adults was 14.5%, 6.6%, and 27.2%, respectively. Our results showed the US states and teritories with highest and lowest use prevalence for MJ (CA:23.6% vs. Guam: 3.2%), ENDS (Indiana:12.8% vs. North Dakota:4.0%), and cigarettes (West Virginia:42.1% vs. Guam:12.3%). Both MJ and ENDS users were more likely to be male, younger, and live in an urban area, but MJ users were more likely and ENDS users less likely to be NH American Indian/Alaskan Native. Cigarette users were more likely to be older, have at least one health condition, and were less likely to be NH Black or Hispanic, and college-educated.

Conclusion

A large proportion of asthmatic US adults use MJ, ENDS, and cigarettes. Our findings provide insights for physicians––especially pulmonologists––about the urgent need for effective interventions to reduce the use of tobacco products and MJ among asthmatic patients.

Substance Use

Exploring the association between school-level alcohol use prevention programs and adolescent binge drinking in Ontario, Canada Urvi Rai* Urvi Rai Scott T. Leatherdale Elaine Hyshka Roman Pabayo

Background

Alcohol is the most commonly used substance by Canadian adolescents. In 2017, 17% of grade 7-12 students in Ontario reported binge drinking (having 5 or more drinks on one occasion) in the past month. Because characteristics of the school environment, including peer networks and access to athletic participation, can influence alcohol misuse, public health and education officials have implemented school-level prevention programs. Our research objective was to study the association between school-level programs and binge drinking among adolescents.

Methods

In this cross-sectional study, data was obtained from grade 9-12 students participating in the 2018-19 wave of the Cannabis, Obesity, Mental health, Physical activity, Alcohol use, Smoking, and Sedentary behaviour (COMPASS) study. The case complete sample included 27,072 students from 55 secondary schools in Ontario. The exposure was defined as the presence of alcohol prevention programs separate from class curriculum, run by either the school or local public health unit (PHU). Multilevel logistic regression was used to determine the association between presence of school- or PHU-run programs and past month binge drinking.

Results

Overall, 18% of students reported binge drinking at least once per month. Students attending schools with school-run alcohol prevention programs had higher odds of past month binge drinking (OR=1.21; 95% CI=0.70, 2.09) compared to students in schools without such programs. Students in schools with PHU-run programs had lower odds of binge drinking (OR=0.79; 95% CI=0.50,1.24) compared to students in schools without such programs. These estimates were not statistically significant.

Conclusion

We found no conclusive evidence that the presence of school- or PHU-based programs is associated with binge drinking among adolescents. However, further research is required to examine whether different types and intensities of programs have differing associations with adolescent binge drinking.

Substance Use

Validity of DSM-5 cannabis use disorder severity levels in adults with problematic substance use David S. Fink* David Fink Malka Zachery L. Mannes Dvora Shmulewitz Melanie Wall Deborah Hasin

The DSM-5 definition of cannabis use disorder (CUD) differs from DSM-IV cannabis dependence by including abuse criteria, withdrawal, and craving, but information on the validity of the DSM-5 CUD diagnosis and severity levels is lacking. This study explores the validity of the DSM-5 CUD in a convenience sample of adult problem substance users, ≥18 years, recruited from two settings: a clinical research setting in an urban medical center and a suburban inpatient addiction treatment program. Participants who reported past-year cannabis use (n=396) consituted the sub-sample for this study. A semi-structured, clinician-administered assessment collected information on DSM-5 CUD criteria, cannabis use related variables, and psychopathology. For each validator (variable predicted to be related to CUD), regression models estimated whether the association with the validator differed by a binary diagnosis of DSM-5 CUD and with its severity levels. Binary DSM-5 CUD and CUD severity levels were associated with greater odds of cannabis use validators, including number of cannabis use days, self-reporting cannabis use as a problem, and cannabis craving scales. In addition, binary CUD and severe CUD were associated with co-occuring psychiatric disorders and social disfunction. DSM-5 CUD and its dimensional measures were shown to have moderate validity, with severe CUD receiving the most support from its association with multiple validators across all domains, compared to the mild and moderate CUD measures associated with cannabis-specific validators alone. Further research is needed to determine the clinical utility of a mild DSM-5 CUD diagnosis among persons with problem substance use.

Investigating Patterns of Polysubstance Use Among Canadian Youth: A Latent Variable Modelling Approach on COMPASS Data Yang (Rena) Yang* Yang (Rena) Yang Zahid A. Butt Scott T. Leatherdale Plinio P. Morita Alexander Wong Helen H. Chen

Background: Limited evidence about youth polysubstance use (PSU) patterns and factors. We addressed the gap in identifying PSU patterns among Canadian secondary school students. **Methods:** This retrospective cohort study took a multivariate latent Markov modelling (LMM) approach on a population-based longitudinal health survey, with a linked sample (N=8824) of three annual waves of COMPASS data from 2016. Substance use indicators, i.e., cigarette, e-cigarette, alcohol and cannabis, were self-reported and were categorized into never/occasional/current use. We applied the least absolute shrinkage and selection operator method to select the covariates. **Results:** Four distinct use patterns were: no use (S1), single-use of alcohol (S2), dual-use of e-cigarette+alcohol (S3), and multi-use (S4), with the initial probabilities of being 0.5887, 0.2156, 0.1487, and 0.0470. The marginal distribution of S1 decreased, while that of S3 and S4 increased over time, indicating a tendency towards increased substance use as students grew older. Factors impacting the initial membership across the four patterns and three waves were multifaceted and complex. E.g., students who were not gambling online ($OR_{S2}=0.22$, $OR_{S3}=0.14$, $OR_{S4}=0.08$), eating breakfast ($OR_{S2}=0.80$, $OR_{S3}=0.64$, $OR_{S4}=0.56$), living in large urban areas ($OR_{S2}=0.82$, $OR_{S3}=0.77$, $OR_{S4}=0.66$), or having higher school connectedness ($OR_{S2}=0.95$, $OR_{S3}=0.91$, $OR_{S4}=0.82$) had positive effects on the PSU pattern membership in S2 through S4, relative to S1. Students who skipped more classes ($OR_{S4}=2.79$), had more smoking friends ($OR_{S4}=2.75$) or more weekly allowance ($OR_{S4}=1.34$), were older ($OR_{S4}=1.51$), or attended a school unsupportive ($OR_{S4}=1.43$) had negative effects. All *p*-values associated with ORs were significant (*p*<.001). Sex had mixed effects. **Conclusion:** The four distinct PSU patterns among Canadian youth showed good heterogeneity between use patterns, evidencing the diverse associations between PSU and multifaceted health behaviours.
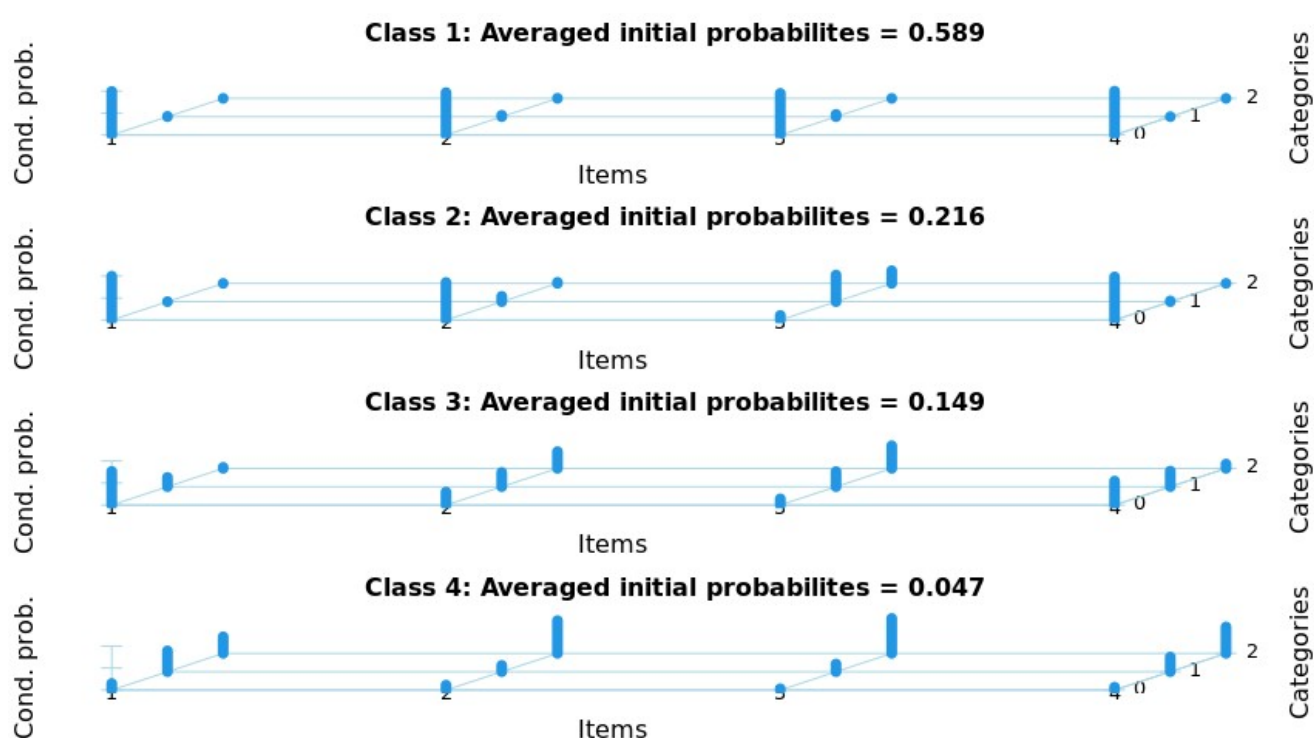
Long-term, bidirectional associations between depressive symptoms and opioid use among patients with HIV: A prospective cohort study Yu (Seashore) Li* Alexandria Macmadu Yu Li Rachel Vickers-Smith Fiona Bhondoekhan Stephen Crystal Robert Kerns Chung-Chou (Joyce) Chang Anees Bahji Jennifer Edelman Brandon Marshall

Background: Scarce prior literature has examined long-term, bidirectional relationships between depressive symptoms and opioid use among patients with HIV (PWH). We evaluated bidirectional associations between depressive symptoms and opioid use in a national sample of PWH.

Methods: We analyzed data from 2002 to 2012 in the Veterans Aging Cohort Study (VACS) survey sample, a prospective cohort of PWH receiving care at 8 Veterans Health Administration sites. We used time-lagged, generalized estimating equation models to estimate the independent association of time-updated depressive symptoms (none [reference], mild, moderate, moderately severe and severe) with subsequent opioid use frequency (never [reference], none in the past year, less than monthly, at least monthly), as well as the independent association of time-updated opioid use frequency with subsequent depressive symptoms, adjusting for sociodemographic and clinical characteristics.

Findings: The analytic sample included 2,033 PWH, contributing a mean of seven approximately annual follow-up visits. We included PWH with sufficient data for key variables during the study period, which represents 55% of PWH who completed baseline assessments. In unadjusted models, at least monthly frequency of opioid use was associated with greater subsequent depression severity ($\beta = 2.6$, 95% confidence interval: 1.6, 3.6), and moderately severe to severe depression was associated with greater subsequent opioid use frequency ($\beta = 1.0$, 95% CI: 0.5, 1.5). In adjusted models, at least monthly frequency of opioid use was associated with greater subsequent depression severity ($\beta = 2.4$, 95% CI: 1.2, 3.5); depression severity was not associated with subsequent opioid use frequency.

Interpretation: Regular use of opioids may exacerbate depression severity among PWH. Future research should more deeply interrogate the causal paths linking depression and opioid use to ascertain common causes and guide responsive interventions.

Substance Use

Transporting the association between supervised consumption site use and syringe sharing from Toronto to Philadelphia Tanner Nassau* Tanner Nassau Alison Evans Seth Welles Alexis M. Roth Kathleen A. Brady Daniel Werb Ayden Scheim

Introduction: Previous studies found a negative association between supervised consumption service (SCS) use and syringe sharing. Less is known about the impact SCS may have among North American people who inject drugs (PWID) during the synthetic opioid era in settings where SCS are not yet sanctioned, and where needle and syringe program (NSP) access varies.

Methods: Using the Ontario Integrated Supervised Injection Services (OiSIS-Toronto) cohort data, we calculated the association between SCS use and syringe sharing using inverse probability of observation weights (IPOW) to control for confounding and selection bias. We combined OiSIS-Toronto and Philadelphia's National HIV Behavioral Surveillance (NHBS) data to transport the association with inverse probability of sampling weights (IPSW), controlling for housing, HIV and HCV status, drugs injected, and NSP use. We trimmed and multiplied IPOW and IPSW together to obtain final weights. We applied weights to generalized linear models to estimate the association between SCS use and syringe sharing in both settings.

Results: SCS use was not associated with syringe sharing in Toronto, where NSP use was near universal. After transporting from Toronto to Philadelphia, frequent and never SCS users had an adjusted PR of 0.80 (CI: 0.54-1.17) and 0.75 (0.43-1.30), respectively, for syringe sharing, compared to infrequent SCS users.

Conclusions: While important for preventing overdose deaths, SCS may not significantly impact syringe sharing if implemented in Philadelphia in the synthetic opioid era. Good access to NSP may attenuate the protective effect of SCS on syringe sharing. The transported association may represent a protective effect for subpopulations that warrants further study. Lower baseline risks may explain the direction of association between never SCS use and syringe sharing. Transportability analysis is helpful for understanding the impact of sanctioning SCS on disease transmission in new contexts.

	Crude PR	IPOW adjusted PR	IPSW adjusted PR	IPOW x IPSW adjusted PR
Infrequent SCS use	Ref	Ref	Ref	Ref
Frequent SCS use	0.92 (0.64-1.32)	0.90 (0.62-1.31)	0.88 (0.62-1.26)	0.80 (0.54-1.17)
Never SCS use	0.63 (0.36-1.10)	0.77 (0.44-1.34)	0.60 (0.36-1.01)	0.75 (0.43-1.30)

Substance Use

Residence in Urban or Rural Counties in Relation to Opioid Overdose Mortality in Kentucky Before and During the COVID-19 Pandemic Lyndsey Blair* Lyndsey Blair Natalie DuPre Liza Creel Nicholas Peiper Bert Little Kira Taylor Richard Baumgartner Jeff Howard

Objectives: At the beginning of the opioid epidemic, opioid overdose death rates were higher in urban than in rural areas; however, the rise of illicitly manufactured opioids reversed this trend. We examined the association between urban residence and subsequent opioid overdose mortality in Kentucky, a state highly impacted by the opioid epidemic, and whether this was modified by the COVID-19 pandemic.

Methods: We used inpatient or outpatient encounters in KY from 2016 to 2020. Each record includes demographic data, vital status, discharge codes, length of stay, and facility type. We captured hospitalizations involving an opioid using *ICD-10-CM* codes T40.0-T40.4 and T40.6. Patient's county was classified as urban (e.g., large metropolitan and suburban areas), or rural (e.g., micropolitan and small population areas). Multivariable logistic regression was used to estimate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of opioid overdose mortality, adjusted for demographics, hospitalization severity, and zip code SES. We assessed effect modification by the COVID-19 pandemic.

Results: Patients living in urban counties had 46% higher odds of opioid overdose death than patients in rural counties (OR=1.46; 95% CI=1.22, 1.74). Before the pandemic, patients in urban counties had 63% increased odds of opioid overdose death (OR=1.63; 95% CI=1.34, 1.97); however, during the COVID-19 pandemic, urban and rural counties became more similar in regard to their association with opioid overdose mortality (OR=0.72; 95% CI=0.45, 1.16; p-value for interaction =0.02).

Discussion: In KY between 2016-2019, living in urban areas was associated with higher opioid overdose mortality among KY hospitalizations; however, the COVID-19 pandemic evened the playing field, despite a continued rise in overdose deaths. COVID-19 posed social, economic, and healthcare challenges that may be contributing to worsening mortality trends affecting both urban and rural patients.

Substance Use

Impact of Cannabis Decriminalization and Legalization on Road Safety Outcomes: A Systematic Review Sarah Windle* Sarah Windle Peter Socha José Ignacio Nazif-Munoz Sam Harper Arijit Nandi

Background: There is substantial debate concerning the impact of cannabis decriminalization and legalization on road safety outcomes, however this literature has not been comprehensively synthesized.

Methods: We systematically searched the Embase, MEDLINE, and PsycINFO databases via Ovid, as well as the Web of Science Core Collection, SafetyLit, Criminal Justice Database (ProQuest), and Transport Research International Documentation databases from inception to June 16, 2021. Eligible studies examined the impact of group-level cannabis decriminalization or legalization on road safety outcomes in any population.

Results: A total of 64 reports of 63 observational studies were eligible, including 38 which applied quasi-experimental designs. Studies examined recreational cannabis legalization (RCL; n=49), medical cannabis legalization (MCL; n=21), and decriminalization (n=4). All studies except one used North American data. Findings were mixed concerning the impact of legalization on attitudes, beliefs, and self-reported driving under the influence. MCL, RCL, and decriminalization were all associated with increases in cannabis-positivity among drivers, and findings were suggestive of a decrease in alcohol-positivity associated with MCL. MCL was associated with reductions in fatal motor vehicle collisions, while RCL was associated with increases.

Conclusions: Increased cannabis-positivity may reflect changes in cannabis use, however does not in itself indicate impaired driving. MCL was associated with reductions, and RCL with increases, in fatal motor vehicle collisions, likely due to the subgroups impacted by MCL and RCL, respectively. Mixed findings for other outcomes may be the result of residual bias due to study methodology and/or heterogeneity in policy, legal, and demographic characteristics. More research is needed concerning decriminalization, as well as the impact of MCL and RCL on non-fatal injuries and road safety outcomes related to alcohol and other drugs.

Substance Use

The Syndemic of Hepatitis C and Substance Use during Pregnancy Amna Umer* Amna Umer
Christa Lilly Candice Lefeber Janine Breyel Collin John

Introduction: The rise in Hepatitis C (HCV) infection has been linked to the intensification of the opioid epidemic. As substance use disorder prevalence among pregnant women increased, a parallel increase of HCV infection has been observed in this vulnerable population. West Virginia (WV) has one of the highest rates of substance use during pregnancy in the United States. The aim of this study was to examine the prevalence of HCV infection by types of substances used during pregnancy in WV.

Method: The study used data of all births between February 2020 to November 2021 at two birthing hospitals in north central region in WV. Maternal HCV diagnosis and substance use data was recorded by the nurses in a statewide surveillance tool called Project WATCH. Sociodemographic characteristics included maternal age, race, education, health insurance status, and maternal smoking during pregnancy. Multiple logistic regression was performed to examine the association between HCV and substance use adjusting for sociodemographic factors.

Results: During the 22-month study period there were 102 (1.76%) reported cases of maternal HCV infection among 5,781 women who gave live birth. The odds of HCV among women with opioid use was 7.40 (95% CI 4.23 – 12.96), cannabinoid use was 3.16 (95% CI: 1.76 – 7.52), stimulant use was 4.31 (95% CI: 1.52 – 12.23), and polysubstance use was 7.04 (95% CI: 2.66 – 18.62) vs. those with no history of substance use after adjusting for maternal age, race, education, health insurance, and smoking during pregnancy.

Conclusion: Women who use substances during pregnancy face concurrent HCV infections. This syndemic puts vulnerable pregnant women at a higher risk of negative health outcomes for themselves and for their newborn. Project WATCH future plans include developing a statewide referral system to ensure these newborns are screened in a timely manner.

Estimating the Cost of Non-Fatal Overdose in Tennessee Allison Dara* Allison Dara

Drug overdoses continue to be a major health crisis. Estimating the cost of overdose is a useful way to quantify its impact, but cost estimates are complex to calculate, particularly for nonfatal overdoses. This analysis uses Tennessee as a case study to evaluate three methods of calculating the cost of a nonfatal overdose for hospitals, to determine whether a resource-intensive method provides significantly different results than faster calculations. Tennessee hospital discharge non-fatal overdose records from 2016-2019, which provide only the charges billed for each overdose, not the amount paid, were linked to three different data sources: a State hospital financial report (readily available but state-specific), the Centers for Medicaid and Medicare (CMS) total cost report (slower but universal), and CMS line-level cost reports (slowest and most complex). Visit cost is calculated using a Cost-to-Charge Ratio (CCR). The first two calculations use State data and the CMS total cost report to calculate one CCR for each hospital for each year and multiplies it by the total visit charges. The third uses CMS line-level data to calculate a CCR for each hospital department, which is then multiplied by department-level charges to calculate costs by type of treatment. This method may yield more accurate estimates of cost but is also the slowest. The median cost of overdose in Tennessee was $1,302.43 using State data, $1,133.70 using CMS totals, and $1,728.37 using departmental CCRs. A linear regression on the log cost of care found that non-white, inpatient, and polydrug overdoses faced significantly higher costs after adjusting for demographics. Covariate effects were smallest using departmental costs, but all three yielded effects in the same direction and with similar significance values. Overall, using readily available State data did not misrepresent the cost of overdose and preserved the most observations, suggesting it may be the best choice for surveillance.

Regulations limiting the number of patients a clinician can treat with buprenorphine may cause early discontinuation of treatment Michelle Nolan* Michelle Nolan Alex Harocopos

Background: Despite research that shows the efficacy of buprenorphine to treat opioid use disorder, regulations prevent clinicians from treating > 30 patients with buprenorphine unless clinicians receive a waiver. We assessed the effect of patient cap regulations on buprenorphine discontinuation during the first six months of treatment.

Methods: Using 2015-2019 New York State Prescription Monitoring Data, we identified incident buprenorphine episodes among New York City residents. We used the parametric g-formula to estimate the hazard of discontinuing buprenorphine during the first six months of treatment under two scenarios: (1) always treated by a prescriber at or near their cap, and (2) never treated by a prescriber at or near their cap, accounting for baseline covariates (age, sex, borough of residence, borough of prescriber). Being treated by a clinician at or near their cap was modeled as a time-varying exposure based on the prescriber's buprenorphine patient panel that month. Prescribers treating 1-24 patients were defined as below their cap; those treating ≥ 25 patients were defined as at or near their cap. Because prescribers can apply for a higher patient cap, prescribers treating ≥ 35 patients in ≥ 2 months were assumed to have a cap waiver and defined as below their cap.

Results: From 2015-2019, 28,160 individuals had an incident buprenorphine episode; 70% discontinued buprenorphine during the first six months of treatment. The hazard of discontinuing buprenorphine during the first six months of treatment under the simulated scenario of always treated by a prescriber at or near their cap was 1.06 (95% CI: 1.02, 1.10) compared with never treated by a prescriber at or near their cap. Excluding prescribers assumed to have a cap waiver did not appreciably change results (HR=1.07; 95% CI: 1.03, 1.11).

Conclusion: Regulations limiting the number of patients a clinician can treat with buprenorphine may contribute to early buprenorphine discontinuation.

Figure: Simulated cumulative incidence of buprenorphine discontinuation over follow-up in the always treated by a prescriber at or near their patient cap (grey), never treated by a prescriber at or near their patient cap (pink), and natural course (blue) g-formula scenarios
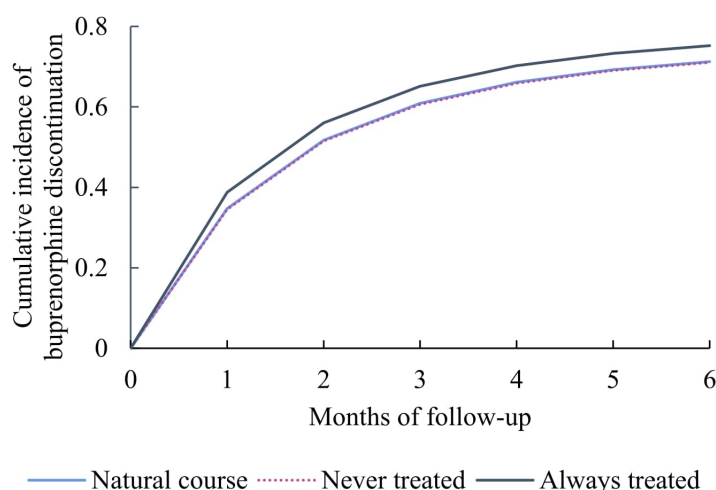
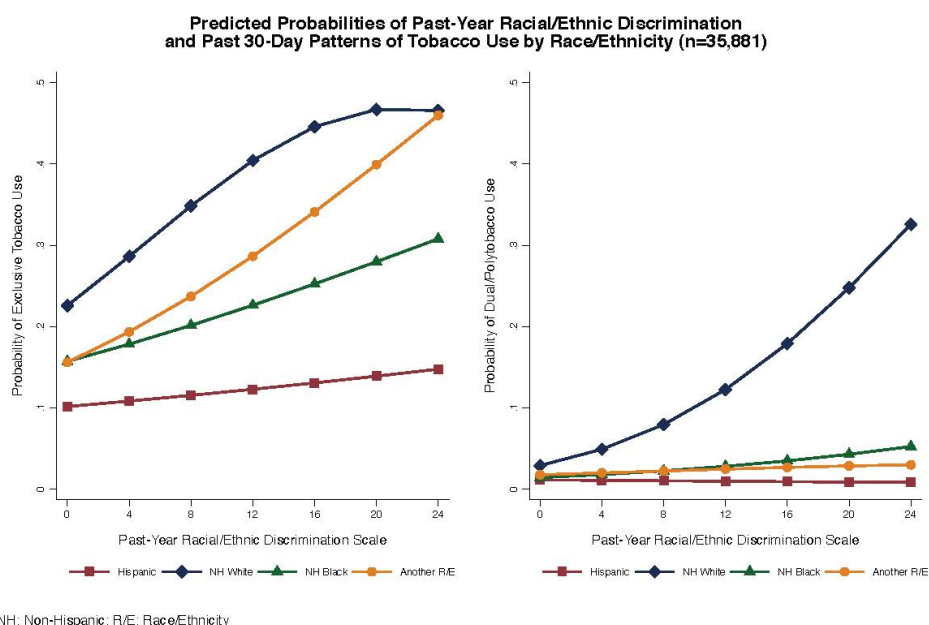**Racial/ethnic discrimination and tobacco use outcomes among US adults** Delvon T. Mattingly* Delvon Mattingly Briana Mezuk Michael R. Elliott Nancy L. Fleischer

Introduction: Racial/ethnic discrimination is a risk factor for individual tobacco products. However, little is known about the relationship between discrimination and dual/polytobacco use, including how these relationships vary by race/ethnicity.

Methods: We used data on adults 18+ from the 2012-2013 National Epidemiologic Survey on Alcohol and Related Conditions-III (n=35,881, mean age: 46.6). The exposure was past-year racial/ethnic discrimination indexed using a summary scale (range: 0-24) based on six scenarios. Outcomes included past-30-day use of four tobacco use groups (cigarettes, e-cigarettes, cigars and pipe, and smokeless tobacco) to create a mutually exclusive use variable (never/former, exclusive, dual, and polytobacco), and past-year tobacco use disorder (TUD) defined by DSM-5 criteria. We estimated adjusted associations between discrimination and exclusive, dual, and polytobacco use and discrimination and TUD using multinomial logistic regression and logistic regression, respectively. Models were stratified by race/ethnicity to assess effect modification; dual and polytobacco use were collapsed for stratified analyses.

Results: About one-fifth of respondents (21.3%) used tobacco exclusively, 2.7% used two products, and 0.2% used 3+ products; 19.9% of respondents had a past-year TUD. More discrimination was associated with higher odds of all tobacco use outcomes. Stratified models indicated that discrimination was associated with dual/polytobacco use among NH Black (OR: 1.05, 95% CI: 1.02-1.06) and NH White (OR: 1.18, 95% CI: 1.13-1.22). While more discrimination was associated with TUD among all racial/ethnic groups, the relationship was strongest for NH White adults.

Conclusions: Discrimination was associated with tobacco use outcomes among multiple racial/ethnic populations, but associations were most pronounced for NH White adults. Further work that aims to unravel factors contributing to racial/ethnic disparities in tobacco use is necessary.

Predicted Probabilities of Past-Year Racial/Ethnic Discrimination and Past 30-Day Patterns of Tobacco Use by Race/Ethnicity (n=35,881)

NH: Non-Hispanic; R/E: Race/Ethnicity

An intersectional approach to examining alcohol use among alternative high school students Cameron Ormiston* Cameron Ormiston Charlotte Talham James Pike Bin Xie Alan Stacy Melanie Sabado-Liwag Faustine Williams

The effects of generational immigration status (GenIm) on substance use among high-risk youth attending alternative high schools (AHS) has not been thoroughly studied. We investigated whether GenIm altered the trajectory of alcohol use (AU) in a longitudinal cohort of AHS students from Southern California (n=1020, mean age 17.5 years, 49.7% female, 76.1% Hispanic). GenIm among youth was defined as foreign-born adolescent with foreign-born parent(s) (FBA-FBP), US-born adolescent with foreign-born parent(s) (UBA-FBP), or US-born adolescent with US-born parent(s) (UBA-UBP). Ethnicity (Hispanic [H], Non-Hispanic [NH]), sex (Male [M], Female [F]) and GenIm were used to define intersectional subgroups. Cross-classified mixed effects models that accounted for similarities among students attending the same school and students belonging to the same intersectional subgroup were used to model the odds of AU over a 3-year period. After adjusting for sociodemographic and psychological risk factors, fixed effects showed FBA-FBP youth had lower odds of AU at baseline (aOR=0.44; 95% CI=0.27-0.71) but increasing odds each subsequent year (aOR=1.51; 95% CI=1.00-2.28). However, random effects and residuals revealed that the rising probability of AU may be less pronounced among H-M-FBA-FBP youth (Fig 1). Overall, FBA-FBP youth may have a lower initial AU that steadily increases to match their UBA-UBP peers, but this effect may not be present among H-M-FBA-FBP youth.
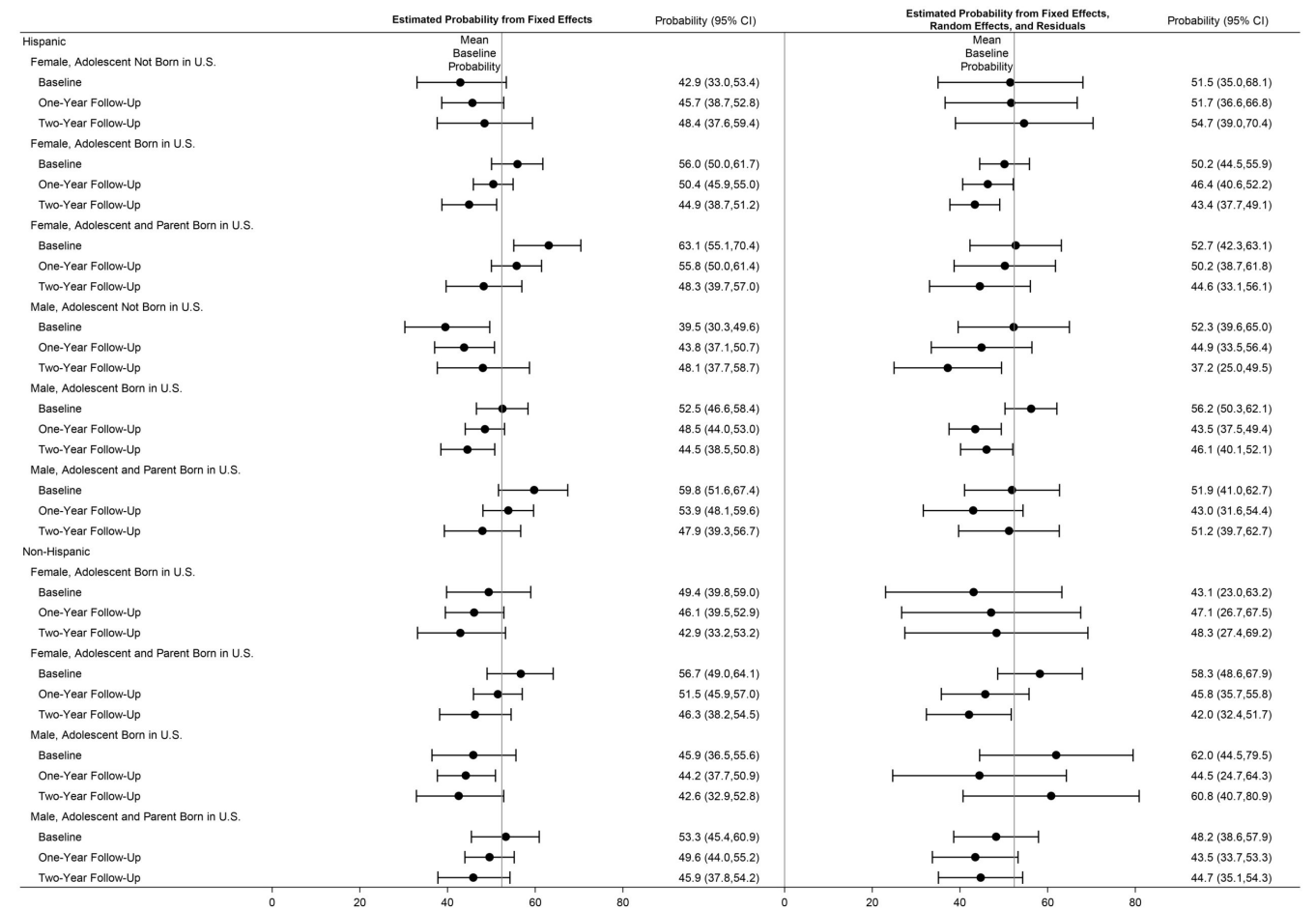
Women's Health

Longitudinal investigation of constipation status and breast cancer: a population-based retrospective cohort study Chia-Yu Tsai* Chia-Yu Tsai Chien-An Sun Yu-Ching Chou

Longitudinal investigation of constipation status and breast cancer: a population-based retrospective cohort study

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Background: Breast cancer (BC) is the first leading cancer in Taiwanese women. Constipation may keep excessive female hormones which have been recognized to cause breast cancer in the body. However, few secular trend studies investigated the association between BC and constipation. This descriptive study examined the incidence of BC with constipation in a large-scale, population-based Taiwanese cohort.

Methods: From 2000 to 2008, 14,2237 new cases with constipation were identified in Taiwan's National Health Insurance Research Database (NHIRD). Chi-square test was used for evaluating incidence rates in different sex, age groups and periods. For long term trends, we followed up until December 31, 2013.

Results: The incidence of breast cancer was 8.10 among constipation patients per 10,000 person-years. The incidence rate was 0.15 among men and 12.29 among women per 10,000 person-years. The incidence rate of BC was higher in women. After stratifying age into 5 groups, we found that the incidence rate of BC per 10,000 person-years was 2.52 in 20-29 years old, 9.30 in 30-39 years old, 15.62 in 40-49 years old, 12.98 in 50-59 years old and 5.58 in ≥60 years old. Patients have highest incidence rate of BC when age is at 40-50. Also, incidence rate of BC was 11.01, 18.24 and 23.10 by visiting 0 time, ≤3 times and >3 times in constipation clinical visits respectively.

Conclusion: In the past 14 years, the incidence of constipation had a profound impact on our life. By means of the big data, our finding suggested incidence rate of BC with constipation is steadily rising. Thus, the study indicated a positive correlation between constipation and BC. The possibility of the results warrants further investigation.

Keywords: Breast cancer (BC), National Health Insurance Research Database (NHIRD), Constipation.

Women's Health

Gestational weight gain patterns among pregnant Black women Suzanne Hyer* Suzanne Hyer Carmen Giurgescu

The Institute of Medicine's (IOM) 2009 guidelines for gestational weight gain (GWG) are aimed at optimizing maternal and infant outcomes. The high variability of methodologies used by researchers to calculate GWG makes direct comparisons across studies challenging, particularly when GWG is not adjusted for length of gestation. The purpose of this study was to explore changes in GWG classification when adjusted for length of gestation.

Using longitudinal data from the Biosocial Impact on Black Births (BIBB) study, a subset of 226 pregnant non-Hispanic Black women were included in this analysis. Body mass index (BMI, kg/m^2) was calculated from weight and height retrieved from the electronic medical record. Maternal weight was measured by prenatal clinic staff, height was self-reported. Total weight gain was calculated 1) as the difference between the final weight in pregnancy minus the initial weight, and 2) weight gain adjusted for length of gestation. BMIs >30 kg/m^2 were stratified into obesity class 1 (30-34.9 kg/m^2), 2 (35-39.9 kg/m^2), or 3 (^{3}40 kg/m^2). Women who delivered before 20 weeks were excluded.

The mean (±SD) gestational age (GA) at the initial visit was 9.9±2.2 weeks, GA at last recorded weight was 37.1±2.6. Mean BMI was 32.5±9.8 kg/m^2(23.9% overweight, 53.5% obese). Across all BMI categories, when GWG was adjusted for length of gestation, the prevalence of women who exceeded the IOM recommendations increased from 40.7% to 47.3%. When BMI >30 was stratified, the prevalence of women with class 1 obesity who exceeded the IOM recommendations increased from 38.3% to 51.1%, class 2 from 59.3 to 63%, and class 3 from 25.5 to 29.8%.

Among this cohort of Black women, there was a change in classification of adherence to IOM guidelines, particularly among women with class 1 obesity. This analysis highlights the benefit of calculating GWG based on length of gestation. It also fills a gap on data reported for stratified pre-pregnancy BMI > 30 kg/m^2.

Women's Health
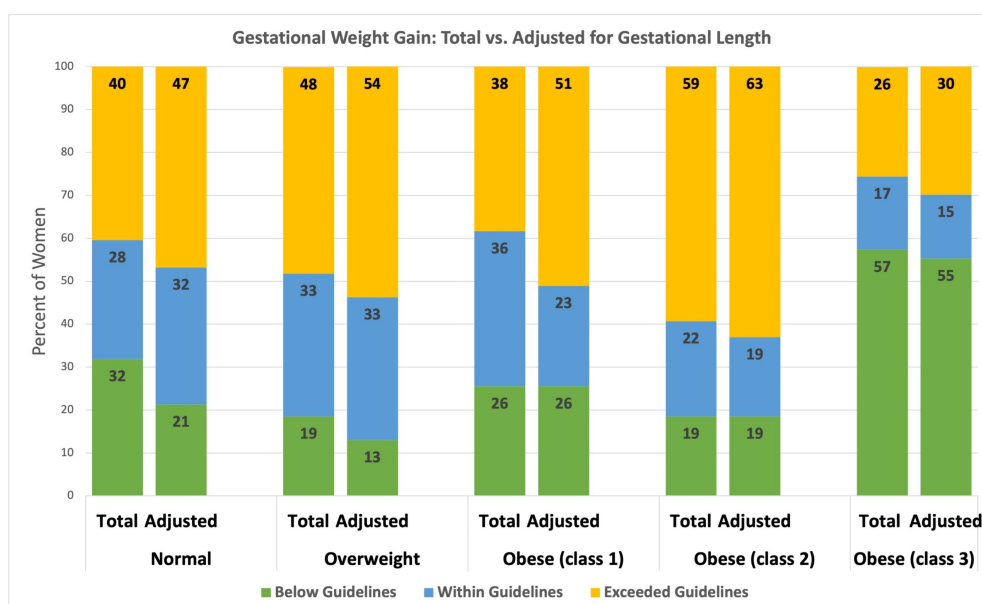
Examining the Association Between Adequacy of Prenatal Care Utilization and Low-Risk, Primary Cesarean Births Among Women in the United States Chelse Spinner* Chelse Spinner Larissa R. Bruner Huber, PhD

Introduction: Within the U.S., cesarean births are one of the most performed surgical procedures, and are often deemed medically necessary. However, cesarean births have been linked to increased risk of delivery complications. Access to prenatal care (PNC) and education are possible strategies to reduce the number of low-risk, primary cesarean births. However, there is scant research that has assessed the impact of these strategies on reducing low-risk, primary cesarean births. This study evaluates the association between adequacy of PNC utilization and low-risk, primary cesarean births.

Methods: The analysis used 2018 birth certificate data, and the sample consisted of nulliparous women, with no reported chronic conditions, pregnancy or delivery complications (N=729,140). Logistic regression was used to model the association between adequacy of PNC utilization, delivery method, as well as to identify other factors associated with delivery method.

Results: Among women with a low-risk, primary cesarean birth, 36.2% had received adequate plus PNC. After adjustment, there was no association between women receiving intermediate PNCand primary cesarean birth (OR, 0.98; 95% CI, 0.96-0.99). However, women who received adequate plus PNC had an increased odds of having a primary cesarean birth compared to woman with adequate PNC, and this finding was statistically significant (OR, 1.18; 95% CI, 1.17-1.20).

Conclusion: Study findings indicate that among a relatively healthy sample of women there was a high utilization of PNC, which was associated with an increased likelihood for a woman to have a primary cesarean birth. The overuse of PNC may result in medically unnecessary procedures, potentially leading to complications. Due to the patient-provider relationship, health care providers have the unique opportunity to provide education and inform patients of the risks and benefits of all delivery options.

Mode of delivery and maternal sexual wellbeing: a longitudinal investigation of the UK ALSPAC cohort

Florence Z Martin* Florence Martin Paul Madley-Dowd Viktor H Ahlqvist Egill Jónsson Bachmann Abigail Fraser Harriet J Forbes

Background The rate of cesarean section is increasing globally. Qualitative evidence suggests that cesarean section is perceived to be protective of sexual function, however, this is evidenced by a few short-term, and almost no long-term, quantitative studies. Emerging evidence suggests that cesarean section may be associated with sex-related pain postpartum, but further longitudinal studies are needed. We investigated the relationship between mode of delivery and subsequent maternal sexual enjoyment, sexual frequency, and sex-related pain.

Methods Using the UK-based Avon Longitudinal Study of Parents And Children (ALSPAC) cohort, eligible women had data available for mode of delivery (from obstetric records) and at least one self-reported sexual outcome (via questionnaire). Sexual enjoyment and frequency were measured repeatedly between 33 months and 18 years postpartum; sex-related pain, both in the vagina during sex and elsewhere after sex, was measured at 11 years postpartum. Missing covariate and outcome data were imputed and associations between mode of delivery and sexual outcomes were investigated using ordinal logistic regression.

Results In our sample of 10,327 women, 1,094 (11%) participants gave birth via cesarean section. Mode of delivery (cesarean section vs vaginal delivery) was not strongly associated with sexual enjoyment at any timepoint (e.g., adjusted odds ratio (aOR) 1.12, 95% confidence interval (CI) 0.98–1.28, P-value=0.10 at 33 months) or sexual frequency (aOR 0.99, 95% CI 0.88–1.11, P=0.84 at 33 months). Cesarean section was, however, associated with an increased odds of both types of sex-related pain at 11 years postpartum as compared with vaginal delivery in the adjusted models (aOR 1.68, 95% CI 1.42–2.01, P<0.001 and aOR 1.42, 95% CI 1.09–1.86, P=0.01, respectively).

Conclusions Cesarean section was not associated with improved sexual enjoyment and frequency up to 18 years postpartum (compared to vaginal delivery), however, it was associated with increased sex-related pain at 11 years postpartum as compared with vaginal delivery. These findings contradict perceptions of sexual wellbeing in the mode of delivery debate, suggesting that women who have delivered via cesarean section can suffer from sex-related pain that is not limited to abdominal scarring.
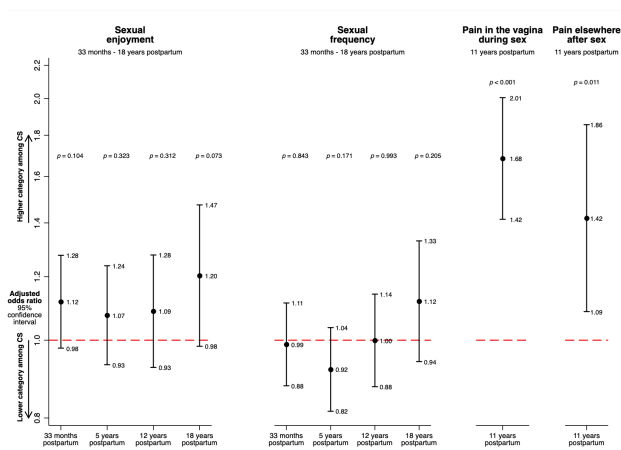
The association between ADHD, pregnancy, and induced abortion in girls and young women

Jacqueline M. Cohen* Jacqueline M. Cohen Maria C. Magnus Kari Furu Øystein Karlstad Chaitra Srinivas Olga Basso Siri E Håberg

Background: Attention-deficit/hyperactivity disorder (ADHD) is defined by symptoms of inattention and hyperactivity-impulsivity that interfere with social, academic, or occupational functioning. The impulsivity associated with ADHD might lead to more unplanned pregnancies and induced abortions.

Objective: To determine if young women with ADHD have higher rates of pregnancy and induced abortion than their peers without ADHD.

Methods: We identified all women ages 15-30 living in Norway from 2010-2020. We defined ADHD as having filled two or more prescriptions for ADHD medication at any time from 2004-2020. Pregnancies, including spontaneous and induced abortions, and births were identified from registers of primary and specialist healthcare, and the Medical Birth Registry. We estimated risk ratios (RRs) and 95% confidence intervals (CIs) for having a pregnancy or induced abortion by Poisson regression comparing people with and without ADHD, separately for ages 15-19, 20-25, and 26-30, adjusted for birth year and country of birth. We also estimated the proportion of pregnancies that resulted in an induced abortion at each age.

Results: Our study population included 937,791 women born 1979-2005 and 3.1% had ADHD. Those with ADHD were more likely to become pregnant at ages 15-19 (RR 2.4, 95% CI 2.2-2.5), and 20-25 (RR 1.4, 95% CI 1.4-1.5), but less at ages 26-30 (RR 0.7, 95% CI 0.7-0.8). However, those with ADHD were more likely to have an induced abortion in all three age groups: RRs 2.2, 1.7, 1.8. Individuals with ADHD were as likely as peers to choose to have an abortion if they became pregnant before age 22, and more likely if they became pregnant at later ages (30% versus 10% at age 30).

Conclusions: Girls and women with ADHD are at increased risk of experiencing an induced abortion. This suggests a need for more public health attention to these individuals to improve contraceptive use and reduce the rates of unplanned pregnancies.

Percent of pregnancies ending in induced abortion, by age
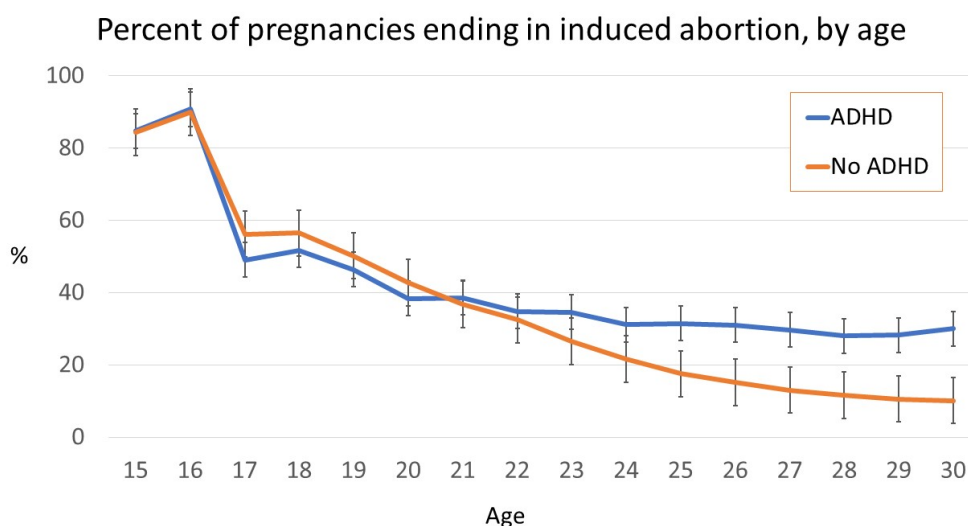
Protection for some, purgatory for others: Evidence from helplines on the evolution of violence against Peruvian women and children during the COVID-19 pandemic Renzo Calderon Anyosa* Renzo Calderon Anyosa Jay Kaufman Felicia Knaul

Background: The COVID-19 pandemic created conditions that aggravated violence against women and children. Several countries expanded helplines and we analyze the process and outcomes in Peru.

Methods: We divided the year into three periods: pre-lockdown, lockdown, and post-lockdown. Based on the mean difference in calls by month per million population between 2020 and 2019 in the pre-lockdown period we calculated the expected calls that we would have observed in the absence of the pandemic in the following periods. We performed stratified analyses by type of violence and perpetrator relationship in women and children.

Findings: We identified 77% more calls per month in 2020 compared to 2019. In women, during the lockdown period, there was an increase in calls when the perpetrator was the partner (45·2, 95%CI:14·2; 76·3) and other relatives (17·5, 95%CI: 3·6; 31·4) and in the post-lockdown period, there was an increase from all types of perpetrators. Regarding sexual violence, in the lockdown period, calls related to a perpetrator from outside the household decreased for both children (-8·6, 95% CI: -14·5; -2·6 calls/month per million) and women (-5·2, 95% CI: -8.1; -2·3).

Interpretation: The lockdown may have had a protective effect against violence by perpetrators from outside the household for both children and women in Peru. However, when the origin of the violence was within the family environment, a decrease in calls is inconclusive, especially in calls related to sexual or physical violence, as the lockdown could affect either the incidence of events or the failure to report.

Women's Health

Weekly processed red meat intake and incidence of diabetes in Mexican women Claudia Martínez* Claudia Martínez Dalia Stern Martín Lajous

Several studies conducted in the US, Europe, and Asia suggest that processed red meat consumption increases diabetes incidence. However, there are no clear biological mechanisms to support this association. Alternative explanations include confounding by unmeasured factors and differences in the causal structure and relative importance of diabetes risk factors across populations. We used data from the Mexican Teachers' Cohort, a prospective study of female Mexican teachers, to evaluate the relation between red processed meat intake and diabetes. We included 74,444 participants at baseline (2006-2008). Diet was assessed using a validated food frequency questionnaire. Participants were classified according to their weekly processed meat consumption as follows: ≤1, >1-≤3, >3-≤ 5, <5-≤ 7, or >7 portions/week (1 portion=30g/week). Incident diabetes was assessed by self-report or cross-linkage with clinical and administrative databases. We used Cox proportional hazards models to calculate HR and 95% confidence intervals. We adjusted for sociodemographic, lifestyle, and diet based on subject-matter knowledge and explored different strategies to adjust for confounding. We identified 3,816 diabetes incident cases from baseline to the first follow-up (2011-2014). In our main multivariable models, compared to women who consume ≤1 portion/week of processed meat, those who eat >7 portions/week had 19% higher rate of diabetes (HR=1.19; 95%CI 1.05, 1.36). We conducted several analyses to evaluate our strategy to address confounding. Our results suggest that daily consumption of processed red meat may increase diabetes incidence in Mexican women. Conducting analyses in populations with distinct dietary patterns may provide additional insights on the potential effects of foods on diabetes risk.

LATEBREAKER

Women's Health

Perspectives on Counseling Women of Reproductive Age About Emergency Preparedness by Primary Healthcare Providers — DocStyles, United States, 2021 Jessica Meeker* Jessica Meeker Regina Simeone Margaret Christine Snead Carrie Shapiro-Mendoza Rebecca Hall Romeo Galang

Pregnant, postpartum, and lactating women (PPLW) face unique challenges during disasters that may be mitigated by emergency preparedness. Healthcare providers have opportunities to counsel this population on emergency preparedness, but the extent of counseling provided has not been reported. Our objective is to report healthcare provider attitudes and practices related to counseling women of reproductive age (WRA), including PPLW, on emergency preparedness. DocStyles, a web-based panel survey of a convenience sample of primary healthcare providers in the United States, was conducted March 17–May 17, 2021. Family-practitioners, internists, obstetricians-gynecologists, nurse practitioners, and physician assistants were asked about the importance of emergency preparedness counseling, level of confidence of counseling, frequency of counseling, barriers to providing counseling, and preferred resources to support counseling among their WRA and PPLW patients. We calculated frequencies of provider attitudes and practices by using R version 4.0.3. Among 1,503 respondents, family practitioners (33%), internists (34%), obstetrician-gynecologists (17%), nurse practitioners (8%), and physician assistants (8%), 88% thought that emergency preparedness for keeping reproductive-aged patients safe, and counseling patients of reproductive age about emergency preparedness were both important. However, 45% of respondents were not confident in WRA emergency preparedness counseling, and most (70%) had never talked to PPLW about this topic. Respondents cited not having time during clinical visits (48%) and lack of preparedness knowledge (34%) as barriers. Most respondents (79%) stated they would use educational materials especially fact sheets or brochures and patient text alerts. Emergency preparedness resources combined with training may improve healthcare provider confidence in counseling WRA and PPLW.

Quantifying the impact of intimate partner violence on mid-life cognitive functioning: a first step towards understanding the long-term impacts of intimate partner violence on women's health Audrey Murchland* Audrey Murchland Jiaxuan Liu Rebecca B. Lawn Jae H. Kang Andrea L. Roberts Laura D. Kubzansky Karestan C. Koenen

Background: Intimate partner violence (IPV) is the most common form of violence against women worldwide. However, few studies have evaluated the impact of IPV on cognitive aging. Therefore, we evaluated the relationship of IPV victimization with mid-life cognitive functioning among women.

Methods: We included 14,782 Nurses' Health Study II participants who completed assessments of adult (age>=18) emotional, physical, and sexual IPV in 2001 and/or 2008 and a cognitive battery in 2014. Any versus no IPV experience was the primary exposure. Associations with specific IPV types (e.g., emotional, physical, sexual) were evaluated secondarily. Cognition was measured with a z-scored 4-component cognitive assessment, the Cogstate Brief Battery. We fit linear regression models adjusted for age, racial identity, parental education, and indicators of childhood physical abuse and sexual abuse at ages17 years.

Results: Mean age at cognitive assessment was 60.6 years (SD=4.6); 46.5% of participants reported any IPV, 42.4% reported emotional IPV, 22.6% physical IPV, and 11.3% sexual IPV. Mean number of years experiencing IPV was 6.4 (7.0 SD). Experiencing IPV was associated with 0.020 SD-unit (95% CI: -0.042, 0.002) lower global cognitive score. The magnitude of the association varied across IPV types, with emotional IPV having the strongest association (b=-0.034; 95% CI: -0.057, -0.012), followed by sexual IPV (b=-0.016; 95% CI: -0.050, 0.018) and physical IPV (b=-0.003; 95% CI: -0.028, 0.023).

Conclusions: IPV experience was associated with lower global cognitive functioning in midlife in US women, with emotional IPV having the strongest association with cognitive functioning. Future work should potential pathways linking emotional IPV and mid-life cognitive functioning such as physiological stress responses and social and material resource deprivation.

Aging

Midlife systolic blood pressure and later-life neuroimaging markers of brain health: findings from the KHANDLE study Joseph Fong* Joseph Fong Taylor Mobley Eleanor Hayes-Larson Charles DeCarli Dan Mungas Paola Gilsanz M. Maria Glymour Rachel Whitmer Kristen M. George Elizabeth Rose Mayeda

Background: Midlife hypertension is robustly associated with later-life dementia incidence. Characterizing effects of midlife blood pressure on neuroimaging markers of late-life brain changes will help elucidate the underlying mechanisms.

Methods: We used data from the Kaiser Health Aging and Diverse Life Experiences (KHANDLE) study. KHANDLE participants were long-term Kaiser Permanente Northern California members aged 65+ years at study recruitment in 2017 and with a clinical exam recording blood pressure between 1964-1985. Our sample included n=253 participants with MRI and amyloid PET brain imaging. We used linear regression models to evaluate associations of continuous midlife systolic blood pressure (SBP, measure assessed closest to age 45 years) with MRI markers of structural brain integrity (total brain, hippocampal, white matter hyperintensity, and lobar cortical gray matter volumes). Volumetric outcomes were adjusted for total cranial volume and Blom-standardized (mean=0, SD=1.0). We used logistic regression to evaluate the association between midlife SBP and amyloid positivity (standardized uptake value ratio cutoff = 1.10). All models were adjusted for KHANDLE baseline age, sex, race/ethnicity, education, and parental education.

Results: Mean age at SBP assessment was 37.2 years (SD=7.1), and mean SBP was 119.2 mm Hg (SD=15.5). Mean age at KHANDLE baseline was 75.0 years (SD=5.6). Midlife SBP was not associated with brain MRI markers, though point estimates indicated a potentially negative association between higher midlife SBP and brain volumes. Higher midlife SBP was associated with higher odds of amyloid positivity (OR = 1.23; 95% CI: 1.02, 1.50 per 10 mm Hg).

Conclusions: Higher midlife SBP was not strongly associated with MRI markers of structural brain integrity in later-life but was associated with amyloid positivity. Further analyses leveraging more midlife data may bring light to the association between midlife SBP and late-life brain health.

Regression Model Output Estimates - Midlife Blood Pressure (per 10 mm Hg) Associations with Late-Life Brain Health Neuroimaging Markers

MRI Indicators	β-coefficient [95% CI]
Total Brain Volume	-0.01 [-0.09,0.06]
Total Hippocampal Volume	-0.01 [-0.10,0.07]
Total Lobar Cortical Gray Matter Volume	-0.05 [-0.13,0.03]
Lobar Cortical Gray Matter Volume	
Frontal	-0.04 [-0.13,0.04]
Occipital	-0.02 [-0.10,0.07]
Parietal	0.00 [-0.08,0.08]
Temporal	-0.08 [-0.16,0.00]
White Matter Hyperintensity Volume	-0.01 [-0.08,0.07]

PET Indicators	OR [95% CI]
Amyloid Positivity	1.23 [1.02,1.50]

Longitudinal Associations Between Vision Impairment and Correction and All-cause Mortality: A Nationally Representative Cohort Study Among Chinese Adults 45 Years or Older Ziyue Wang* Ziyue Wang Xiaochen Ma

Importance: Although vision impairment (VI) is associated with mortality, little is known about how existing and new cases of VI influence future death among the middle-aged and older population.

Objective: Comparing the effects of pre-existing and new cases of VI on all-cause mortality among Chinese populations aged 45 or older.

Design: we used four waves of data from the China Health and Retirement Longitudinal Study (CHARLS, in 2011, 2013, 2015, and 2018), a nationally representative prospective cohort study of people aged 45 or older in China. 15,808 Chinese with self-reported vision status were followed for an average period of 6.4 years in our study.

Exposures: Pre-existing VI (time-independent exposures), new cases of VI, and vision correction (time-dependent exposures).

Main Outcomes and Measures: risk of all-cause death and risk stratification for pre-specified risk factors.

Results: Compared to participants with normal vision, all-cause mortality was higher among participants with pre-existing VI (Crude hazard ratio, cHR= 1.29, 95% CI: 1.17–1.44; adjusted hazard ratio, aHR= 1.22, 95% CI: 1.09–1.37) or new cases of VI (cHR= 1.42, 95% CI: 1.28–1.58; aHR= 1.36, 95% CI: 1.21–1.51). Mortality risk was lower among female, rural patients, and patients who had graduated high school or higher. Participants who were wearing eyeglasses/contact lenses or had cataract surgeries at the baseline did not have a significantly higher all-cause mortality (eyeglasses: aHR= 0.82, 95% CI: 0.65–1.02; cataract surgeries: aHR= 1.12, 95% CI: 0.74–1.69) compared to participants with good vision. A similar pattern was found among newly corrected VI (glasses: aHR= 1.01, 95% CI: 0.78–1.24; cataract surgeries: aHR= 0.95, 95% CI: 0.68–1.31).

Conclusion: Newly developed VI, not just those that are pre-existing, could place Chinese residence aged 45 and older at significantly elevated risks for all-cause mortality.

Genetic Correlates of Biological Aging and the Influence on Prediction of Mortality

Oluwasefunmi Akeju* Oluwasefunmi Akeju Michelle Mens Robert Warmerdam Marjolein Dijkema Anita van den Biggelaar Lude Franke Jaap Goudsmit Julia W. Wu

Background

Biological age (BioAge), a measure of age based on composite biomarkers, may outperform chronological age in predicting health and longevity. Accelerated biological aging (Δ_{age}), defined as the difference between BioAge and chronological age, varies from person to person. Yet, the extent of genetic influence on Δ_{age} and BioAge's predictive value on mortality, is poorly understood. We investigated to what extent BioAge can predict mortality and assessed the relationship between genetics, lifestyle factors, and Δ_{age}.

Methods

Using a validated algorithm, BioAge was estimated for 52,418 participants from the LifeLines' Dutch population-based cohort, who were enrolled from 2006 and followed up till March 2021. Two polygenic risk scores (PRS) for healthspan and DNA methylation-based aging clock were computed for 21,581 participants with available genotyping data. We examined the association between PRS, lifestyle, socioeconomic status (SES), and Δ_{age}, using linear regression. The ability of BioAge to predict all-cause mortality for a given age and sex was further assessed, by using a Cox model, while accounting for PRS.

Results

Participants' mean age was 45 years (SD=12) and they had a mean Δ_{age} of -3.0 years (SD= 3.6). After adjusting for potential confounders, PRS, male sex, smoking, low SES, and aberrant sleep duration, were associated with higher Δ_{age}. For a given age and sex, a year increase in BioAge was associated with increased risk of all-cause mortality ranging from 6% (HR= 1.06; 95% CI= 1.04, 1.08) among participants 65 years and older to 17% (HR=1.17; 95% CI= 1.06, 1.28) among those who were 18 to 34 years. These estimates remained constant after accounting for PRS.

Conclusion

Lifestyle, SES, and genetic variations in a population contribute to the differences in accelerated aging. Across age, sex, and genetic risk strata, we demonstrated that BioAge can predict mortality and is useful for risk stratification in aging interventions.

Aging
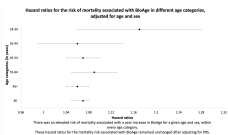
Are practice effects due to repeated cognitive assessments smaller among people with neurodegeneration? Camilla Calmasini* Camilla Calmasini Ruijia Chen Elizabeth Rose Mayeda Rachel Peterson Kristen M. George Yenee Soh Eleanor Hayes-Larson Kaitlin Swinnerton Lisa L. Barnes Paola Gilsanz Charles DeCarli Rachel A. Whitmer Maria M. Corrada M. Maria Glymour

Practice effects (PE) are defined as improvements in cognitive test scores resulting from repeated testing. PEs can bias longitudinal studies by masking differences in rate of cognitive decline. Brain neurodegeneration may influence learning and thus PE, but few studies have evaluated PE and neuroimaging measures.

We examined PE across repeated cognitive assessments in 3 cohorts of Kaiser Permanente members (KHANDLE, n=293; STAR, n=204; LA90, n=87). Executive function [EF] and verbal memory [VM], both z-scored, were assessed via the Spanish and English Neuropsychological Assessment Scales for 2 waves in KHANDLE and STAR, and 3 waves in LA90. Brain MRIs were completed throughout follow-up and assessed total brain volume (TBV), hippocampal volume (HCV) and white matter hyperintensity volume (WMH), all standardized to total intracranial volume. KHANDLE and LA90 also assessed brain amyloid burden using PET scans (classified as Aβ+ or Aβ-). For each cohort, we fit linear mixed-effects models with random intercepts and included assessment wave as a PE indicator. In separate models, we then added each neuroimaging measure and an interaction between each neuroimaging measure and PE. All models were adjusted for age at cognitive assessment, education, gender, and, for KHANDLE and LA90, race/ethnicity.

Mean participant age at wave 1 was 75 (SD=6) in KHANDLE, 67 (SD=8) in STAR and 92 (SD=2) in LA90. Average PE were negligible in STAR, but larger in KHANDLE and LA90. PEs (slope across waves conditional on age at assessment) were modified by amyloid status but not by TBV, HCV or WMH. For example, KHANDLE Aβ- participants had larger PE on VM than Aβ+ [β_{Ab-}=0.22(0.10,0.35), β_{Ab+}=0.00(-0.18,0.18)] and LA90 Aβ- participants had larger PE on EF than Aβ+ [β_{Ab-}=0.43(0.21,0.66), β_{Ab+}=0.11(-0.13,0.36)] (Fig.1).

Participants with amyloid positive PET scans, a marker of AD, had smaller PE. The pathology leading to Alzheimer's disease may reduce improvements in scores from repeated testing.

Figure 1: Predicted cognitive scores at each wave in KHANDLE, STAR and LA90 by MRI measure and amyloid status.
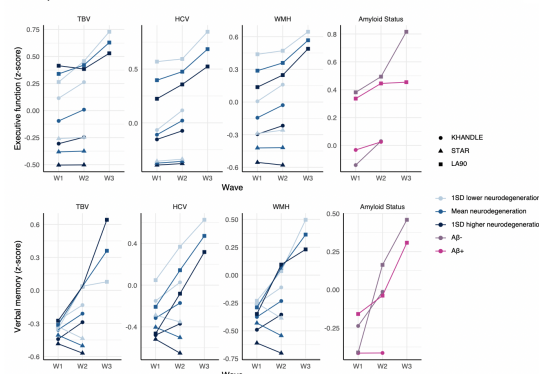
Note: Values are predicted for a reference person who is average age (75 for KHANDLE, 67 for STAR, and 92 for LA90), male, white (KHANDLE and LA90 only, because STAR enrolled only Black participants), and with a high school or lower than high school education. Amyloid PET data were only available for KHANDLE and LA90. Greater values of TBV and HCV indicate less neurodegeneration, whereas greater values of WMH indicate more neurodegeneration.

Aging

A Regression Tree Analysis to Identify Factors Predicting Frailty: The International Mobility in Aging Study (IMIAS) Afshin Vafaei* Afshin Vafaei Yan Yan Wu Carmen-Lucia Curcio Cristiano dos Santos Gomes Mohammad Auais Fernando Gomez

Background: Frailty is a complex geriatric syndrome with a complex etiology. We aimed to identify the best combinations of risk factors that predict the development of frailty using recursive partitioning models.

Methods: We analyzed reports from 1724 community-dwelling men and women aged 65 to 74 years participating in the International Mobility in Aging Study (IMIAS) which is a prospective cohort study. Frailty was measured using Fried scale. Socio-demographic, physical, lifestyle, psycho-social, and life-course factors were included in the analysis. We used recursive partitioning with conditional inference tree (CTree) algorithm to identify high-risk subgroups. Potential predictors included socio-demographic, physical, lifestyle, psycho-social, and life-course factors.

Results: Frailty status of 21% of participants more exacerbated in 2014 compared to 2012. In addition to functioning variables, fear of falling (FOF), income, and research site (Canada vs. Latin America vs. Albania) were significant predictors of the development of frailty. Additional significant predictors after exclusion of functioning factors included education, self-rated health, and BMI.

Conclusion: In addition to obvious risk factors for frailty (such as functioning), socio-economic factors and FOFs are also important predictors. Clinical assessment of frailty should include measurement of these factors to identify high-risk individuals.

**Association of Healthcare Utilization with Incident Dementia Diagnosis: Results from the UK Biobank**

Jingxuan Wang* Jingxuan Wang Sarah F. Ackley Min Hee Kim Scott C. Zimmerman Camilla Calmasini Stephen Asiimwe Lindsay C. Kobayashi M. Maria Glymour

Background: Previous studies suggest that hospitalization due to critical illness is associated with an increased risk of dementia diagnoses. Yet, most studies are based on populations with high rates of preclinical disease. Little is known about how healthcare utilization might increase dementia diagnosis through increased surveillance.

Methods: Using longitudinal UK Biobank data, we examined the association between total healthcare utilization and dementia incidence across 2 years of follow-up among 140,958 dementia-free participants aged 55 years or older. Total healthcare utilization was measured by summing the number of primary care clinical events and inpatient admissions in the year before the baseline visit. Dementia diagnoses were obtained from linked hospital, primary care, and death registry data. We used Cox models and adjusted for demographics, socioeconomic status, body mass index, smoking, alcohol use, APOE-ε4, and comorbidities. In sensitivity analyses, we varied the maximum follow-up time (i.e., when the follow-up was censored) from 1 to 11 years.

Result: The two-year cumulative incidence of all-cause dementia was 0.10% (0.04% for Alzheimer's disease [AD]). In the fully adjusted model, a one standard deviation increase in total healthcare utilization frequency (8.3 encounters) was associated with a 24% increase in the hazard of all-cause dementia diagnosis (HR = 1.24, 95% CI= 1.13-1.35) and 40% increase in the hazard of AD diagnosis (HR = 1.40, 95% CI= 1.16-1.69) in the following 2 years. Smaller hazard ratios, whose CIs also exclude the null, were obtained for censoring times over 3 years for all-cause dementia (Fig.1).

Conclusion: Encounters with the health care system in one year predict higher rates of diagnosis with all-cause dementia and AD diagnoses in the two subsequent years, consistent with surveillance bias. Studies assessing relationships between risk factors and dementia may be susceptible to surveillance bias in dementia diagnosis.
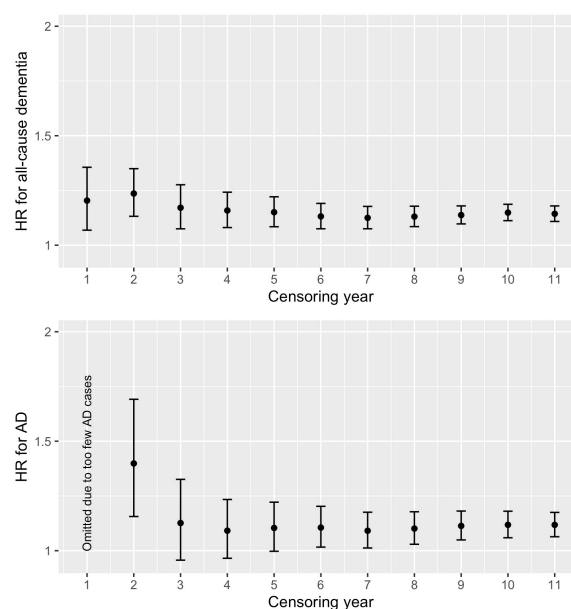
Using mixture models to identify smoking cessation profiles based on self-efficacy, positive expectancy, motivation, and cessation fatigue: an exploratory latent profile and latent transition analysis Yajnaseni Chakraborti* Yajnaseni Chakraborti Donna L. Coffman

Introduction: The addictive nature of tobacco makes smoking cessation a dynamic and challenging process. Smokers who attempt to quit, transition through different phases based on their withdrawal symptoms, motivation, outcome expectancies, and self-efficacy. Relapse risk is determined collectively by these behavioral constructs, and their effect varies over time. Our study aims to identify underlying classes (or profiles) among smokers participating in a pharmacotherapy cessation program based on these constructs. Our interest further lies in examining changes in class membership over 4 weeks since the target quit day (TQD) and its association with long-term abstinence outcomes.

Methods: We apply Latent Profile Analysis to classify 1086 participating smokers into subgroups based on their responses to Ecological Momentary Assessment (EMA) prompts indicating latent quitting behavior at four different time points. We then determine the changes in membership over time using Latent Transition Analysis (LTA).
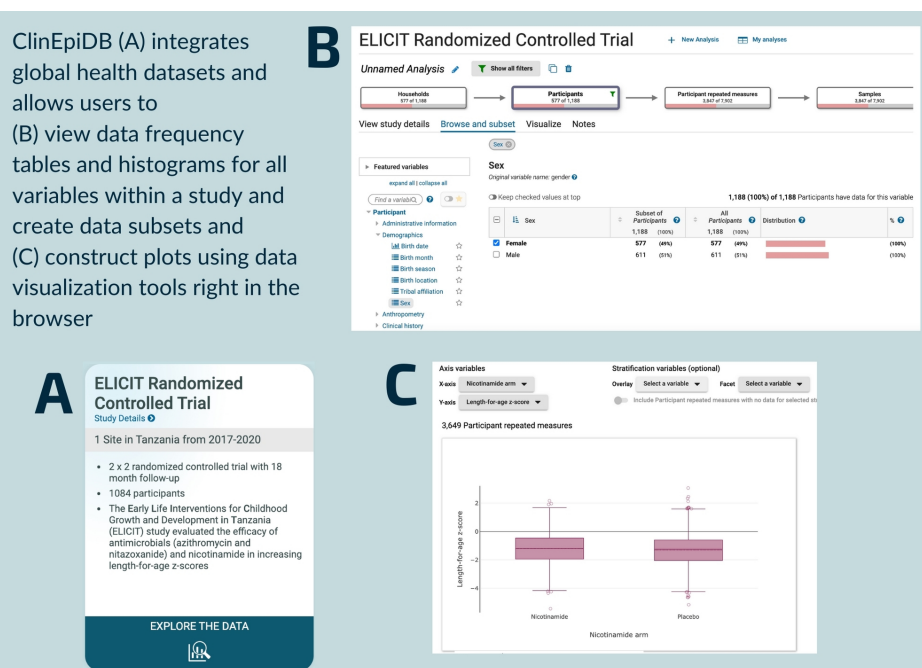
Results: A four latent class model solution is selected through a holistic assessment of model fit-statistics (BIC, VLMR LRT p-value, entropy) and interpretability of profiles. The transition probabilities estimated via the LTA model indicate a moderate to high percentage of neutral/motivated subjects tend to improve on their motivation or stick to the same subgroup, and the demotivated subjects transition to improved subgroups over 4 weeks. In addition, the associations between baseline covariates, smoking profiles, the transition trend, and long-term abstinence outcomes were also examined and identified key predictors of relapse risk.

Conclusions: Change in behavioral patterns due to fluctuating withdrawal tendencies and motivational processes during cessation attempts is useful to identify vulnerable subgroups and target interventions to prevent relapse risk in smoking cessation trials.

Lowering the barrier for exploratory data analysis of global health studies with ClinEpiDB.org Nupur Kittur* Nupur Kittur Cristina Aurrecoechea John Brestelli Brian P. Brunk Danielle Callan Dave Falke Steve Fischer Danica Helb Jay Humphrey John Judkins Sarah Kelly Jessica C. Kissinger Bob MacCallum David S. Roos Steph Wever Schulman Weilu Song Sheena Shah Tomko Christian J. Stoeckert Jie Zheng

Open access to data from epidemiological studies has tremendous potential to preserve data over time, increase secondary data use, and accelerate discovery and translational impact. The clinical epidemiological database, ClinEpiDB.org, first released in 2018, was built to facilitate access to de-identified data from large, high-quality global health studies. ClinEpiDB currently hosts data from >1.1 million participants representing 31 global studies in three major domains – maternal, newborn & child health; malaria; and neglected tropical diseases. Studies vary in design and include both observational studies such as the longitudinal cohort Study of Illness in Preterms (SIP; release expected in 2022) and the case-control Global Enteric Multicenter Study (GEMS) of enteric disease in children under five and experimental studies such as the Early Life Interventions for Childhood Growth and Development in Tanzania (ELICIT) randomized controlled 2×2 factorial trial of antimicrobials and nicotinamide in increasing growth. ClinEpiDB enables investigators to exceed the requirements of journals and funders to make data publicly available by integrating study data with standardized ontologies to make data more machine readable and improve data reusability. Study pages provide context and relevant documentation like consent forms, case report forms, and codebooks. The ClinEpiDB platform lowers barriers to data use with an intuitive point-and-click interface that allows users to view variable frequency tables and histograms and explore associations between variables using built-in data visualization tools. Entire datasets or customized subsets may be downloaded for further analysis. A tiered data access system offers a simple interface for users to submit a download request and for data providers to manage requests. ClinEpiDB will expand in 2022 with integration of new datasets as well as enhanced visualization tools and the ability to derive variables.

ClinEpiDB (A) integrates global health datasets and allows users to (B) view data frequency tables and histograms for all variables within a study and create data subsets and (C) construct plots using data visualization tools right in the browser

HHEAR Data Repository: A Resource for Epidemiologic Research Jeanette A Stingone*
Jeanette Stingone Sofia Bengoa Nancy Mervish James Masters Paulo Pinheiro Liyang Yu Sheersha Kandwal Deborah McGuinness Patricia Kovatch Susan Teitelbaum

The U.S.-based, NIH/NIEHS funded, Human Health Exposure Analysis Resource (HHEAR) provides scientific investigators access to both laboratory and statistical analyses aimed at incorporating and expanding environmental exposures within their research. To benefit the broader research community, the HHEAR Data Center has created a public data repository that houses deidentified epidemiologic and biomarker data from all studies accepted into the HHEAR program. The goal of this repository is to promote the secondary analysis of pooled environmental health data by providing data in a manner that is findable, accessible, interoperable and reusable. The public repository has been constructed by coupling the open-source Human-aware Data Acquisition Framework with precisely-developed semantic annotation templates for epidemiologic metadata. Users of the public repository have the ability to simultaneously view, search and download data from multiple epidemiologic studies that have been harmonized to a common vocabulary (the HHEAR ontology). This facilitates data pooling across studies to conduct novel epidemiologic investigations of environmental contributors to human health. To illustrate the value of this repository, we demonstrate the application of common data standards to harmonize epidemiologic variables across multiple studies. We then provide examples of pooled analyses conducted with these harmonized data. This increased availability of data will encourage secondary data analysis of pooled epidemiologic studies, allowing for investigations that can leverage larger sample sizes and greater exposure variability.

From the machines to clinical practice: preferences of healthcare professionals regarding AI algorithms Alexandre Chiavegatto Filho* Roberta Wichmann Thales Pardini Tiago Oliveira Alexandre Chiavegatto Filho On behalf of the Artificial Intelligence for COVID-19 in Brazil (AICOV-BR) group

Artificial intelligence (AI) algorithms are transforming several areas of the digital world and are increasingly being used in healthcare. Mobile apps based on predictive machine learning models have the potential to be used to help better predict health outcomes, but there is still no consensus on how to inform doctors about its results. The aim of this study was to investigate how healthcare professionals prefer to receive predictions generated by machine learning algorithms. A systematic search in MEDLINE, via PubMed, EMBASE and Web of Science was first performed. A questionnaire called System Usability Scale (SUS) was identified as the most frequent tool to assess the usability of mobile apps. Regarding the available mobile applications that use artificial intelligence, no usability and user experience evaluation was identified. These findings motivated the development of a questionnaire by our research group to collect data on physician preferences for receiving the predictions of machine learning algorithms. Part of the items that make up this questionnaire are from the SUS. These items were incorporated into RandomIA, a mobile app developed by the research group to predict the occurrence of clinical outcomes, initially for COVID-19 and expected to be expanded to other diseases. A total of 45 doctors from the five Brazilian regions tested RandomIA and received three different ways to visualize the prediction output. For predictions of prognostic outcomes (need of mechanical ventilation, admission to an intensive care bed, and death), 18 (40%) preferred a partially complex visualization, characterized by a bar graph with three outcomes (low, medium, and high probability of outcome) expressed in three different colors, green, yellow and red. For the diagnostic prediction of COVID-19, there was also a preference (40%) for the same partially complex option. Our results indicate that doctors may not want very detailed results from predictive machine learning algorithms.
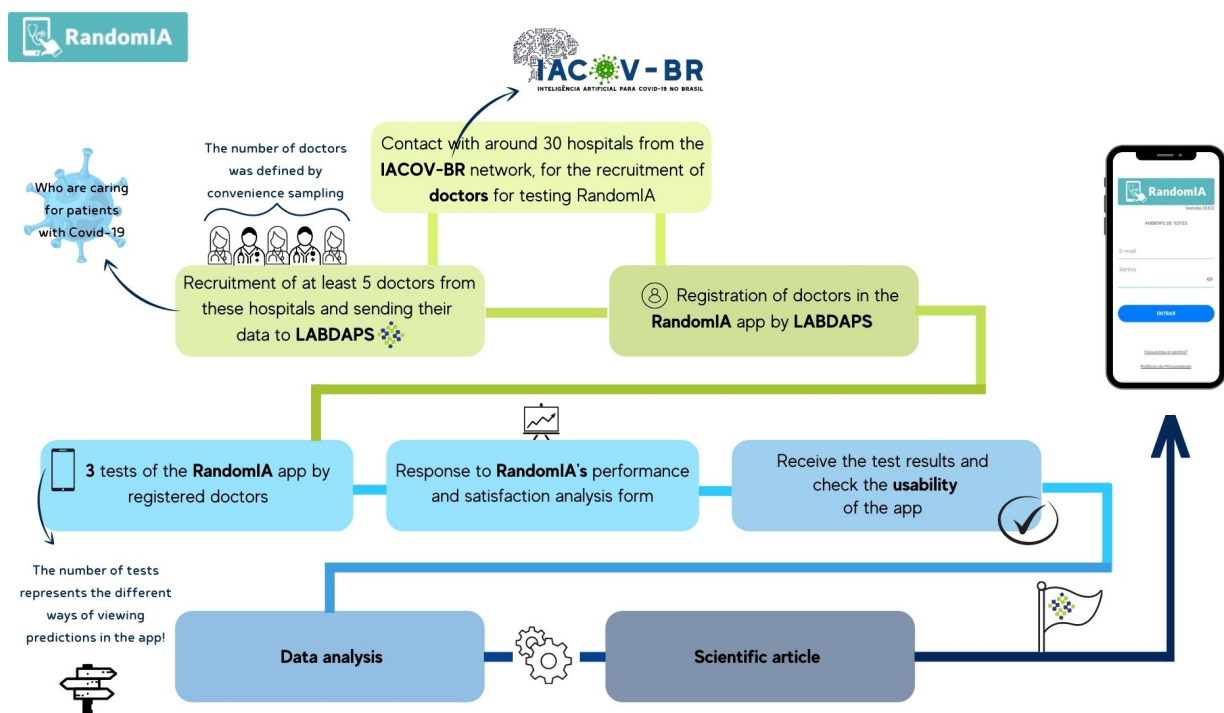
Harnessing Individual and Neighborhood Variables to Predict Low-Levels of Blood Lead in Uruguayan Children: Where Should We Focus Our Prediction Efforts? Seth Frndak* Seth Frndak Elena Queirolo Nelly Mañay Guan Yu Zia Ahmed Gabriel Barg Craig Colder Katarzyna Kordas

Background: Children with blood lead levels (BLLs) below the current actionable threshold (<5 µg/dL) demonstrate lower IQ and problem behaviors. Attempts to predict child BLLs have met with mixed success and the literature provides little guidance on what types of variables (individual- or neighborhood-level) are most important for prediction. We addressed this gap by implementing a machine learning (ML) approach to identify the most relevant predictors of low BLLs in urban children.

Methods: The sample included 788 children (~7 years of age) recruited between 2009-2019 from Montevideo, Uruguay. A total of 84 variables (56 individual- and 27 neighborhood-level) were used to predict low BLLs (≥ 2 µg/dL). Four base learners (generalized linear models, random forest, support vector machine, and K-nearest neighbor) and a stacked ensemble were implemented using 100 randomly sampled training (70%) and test (30%) datasets. The least complex, most accurate model, on average, was selected. The top 10 most important variables were iteratively added to the most accurate model, one by one, until the model with the highest accuracy and lowest number of predictors was identified. Explainable ML was used to create partial dependence plots to clarify the relationships between predictors and probability of low BLL in this final, parsimonious model.

Results: Random forest and stacked ensemble models had similar accuracy (~0.75); random forest was selected to maximize parsimony. After iteratively adding the top 10 most important variables to the random forest model, the top 4 variables were selected to represent the most parsimonious model: year of enrollment, distance to nearest bus route (meters), HOME Inventory (a measure of household enrichment) and average dietary calcium intake. Partial dependence plots revealed that probability of BLL ≥ 2 µg/dL was: greater before 2015, greater among children living closest to bus routes, and lower above 0.5 SD from the sample mean dietary calcium intake (> 791.4 mg/day). HOME Inventory was associated with BLL ≥ 2 µg/dL, but no consistent pattern was noted.

Conclusions: A combination of individual- and neighborhood-level variables, are best used for predicting low BLLs in Montevideo. Our most predictive variable was year of enrollment. Given that child BLLs are decreasing worldwide, deploying ML models to predict child BLLs across time and contexts should proceed with caution.

Shiga Toxin-Producing Escherichia coli Subtype-Specific Sources of Exposure: A Supervised Machine Learning Approach Gillian A.M. Tarr* Gillian Tarr

Shiga toxin-producing *Escherichia coli* (STEC) is one of the most significant reportable zoonotic enteric pathogens in the U.S. The exposures that pose the greatest risk of human disease depend on multiple factors, one of the greatest being pathogen characteristics (e.g. infectivity, environmental survival, resistance to decontamination). Our objective was to identify specific exposures that were associated with STEC's major defining characteristics, its serogroup and Shiga toxin gene (*stx*) genotype.

We obtained routine public health surveillance data on STEC cases reported to the Minnesota Department of Health (MDH) from 2010 to 2019. Random forests were used to determine variable importance in differentiating STEC serogroups and *stx* genotypes. Parameters mtry and ntree were tuned on stability and accuracy from bootstrap sampling (500 repetitions) with out-of-bag evaluation. For each multiply imputed dataset, random forests were generated overall for serogroup and *stx* genotype, separately, and for each major subtype. Variable importance was ranked using conditional permutation importance with a threshold of 0.5. Variable importance rankings were summarized across all multiply imputed datasets to identify the exposures with the greatest influence on differentiating serogroups/genotypes.

Of 3,098 STEC cases reported to MDH during the study period, 3,058 were symptomatic and included in the analysis. Region, age, urbanicity, consuming cabbage, and ruminant meat, were ranked as important exposures for different serogroups and *stx* genogroups (example in Figure).

While the most exposures for some serogroups and *stx* genotypes reflected major outbreaks during the study period, others likely indicate drivers of ongoing exposure. This work can help focus both epidemiological and microbiology research on specific mechanisms driving type-specific routes of exposure, including targeting the most virulent types, and identify opportunities for prevention.

Serogroup O103 1
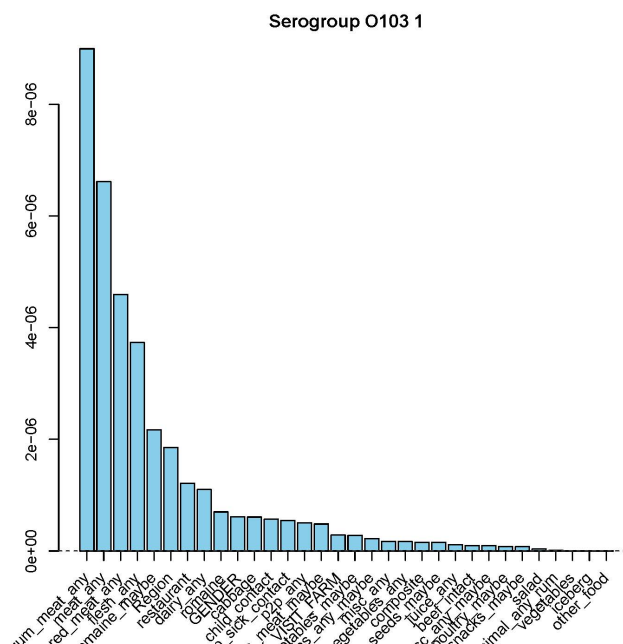
LATEBREAKER

Big Data/Machine Learning/AI

Developing a risk prediction model for gastric adenoma using machine learning Bomi Park*
Bomi Park Hyun Jin Oh Chung Ho Kim

An accurate risk prediction model that detects high risk groups for gastric cancer is very important to facilitate earlier detection of gastric cancer and ultimately contribute to reducing morbidity and mortality of gastric cancer. We aimed to develop machine learning (ML) based prediction model for gastric adenoma, a precancerous lesion of gastric cancer, using different algorithms and compare their performance characteristics.

A total of 19,552 participants older than 40 years of age who underwent gastric cancer screening from the National Cancer Center in Korea were analyzed in this study. We used gastric cancer screening data including pre-screening questionnaire and screening results. We considered risk factors including age, sex, intestinal metaplasia, atrophic gastritis, helicobacter pylori infection, TG, high-density lipoprotein, low-density lipoprotein, BMI, past history, family history, smoking, and drinking. We trained and validated logistic regression, support vector machine (SVM), Naïve Bayes, decision tree, random forest, gradient boosting machines (GBM), and Extreme gradient boosting (XGBoost) to predict gastric adenoma. The synthetic minority oversampling technique was used to solve the problem of imbalance dataset. Data were randomly split into a training set (70%) and a test set (30%). Discrimination was evaluated using the area under the receiver operator characteristic curve (AUC). Calibration was graphically evaluated with the goodness-of-ft test.

A total of 4,147 patients found to have a gastric adenoma. The SVM model achieved the highest AUC (0.713), followed by logistic regression (0.702) and Naïve Bayes (0.702). Sensitivity was the highest for logistic regression (0.741) and specificity was the highest for random forest (0.911).

The ML based prediction model showed a great ability to predict gastric adenoma. ML based prediction model can be used for better identification of patients at risk for gastric adenoma in the clinical settings.
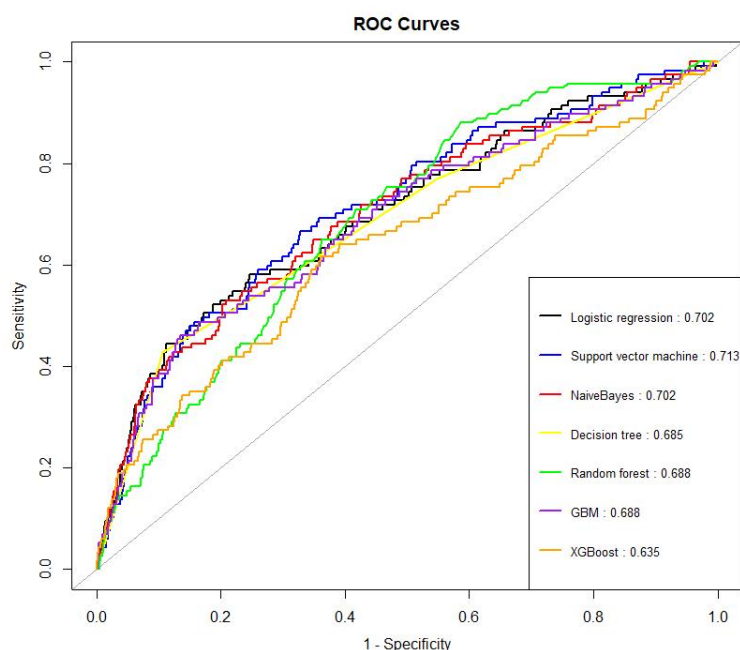
LATEBREAKER

Big Data/Machine Learning/AI

Developing a natural language processing pipeline to characterize female firearm suicides from coroner/medical examiner and law enforcement reports in the National Violent Death Reporting System Evan Goldstein, PhD, MPP* Evan Goldstein Julian Takagi-Stewart, BS Brianna Agnew, BA Miriam Haviland, PhD, MSPH Erin Morgan, PhD Steve Mooney, PhD, MS Laura Prater, PhD, MPH, MHA

Background: Since 2005, female firearm suicide rates have increased by 34%, outpacing the rise in male firearm suicide rates over the same period. It remains unclear why these changes have occurred.

Objective: To develop a natural language processing (NLP) pipeline to code circumstantial details efficiently and better contextualize female firearm suicides in the NVDRS.

Methods: We used data from the NVDRS Restricted Access Database. Our study sample was a random selection of 1,462 female firearm decedents, representative of all female firearm suicides in NVDRS from 2014-2018. We manually coded free-text medical examiner/law enforcement reports for all 1,462 female firearm suicide reports for 13 binary circumstance labels, systematically defined and agreed upon by 3 researchers. Our NLP preprocessing procedure included tokenization, stemming and weighting of tokens using Term Frequency Inverse Document Frequency, and other steps. We split-tested Naïve Bayes, Random Forest, and Support Vector Machine (SVM) classifier models using K-fold cross-validation (CV) with 5 folds to identify each preceding circumstance label. All analyses were conducted with Python 3.9.

Results: The performance of our ML models varied depending on the label. K-fold CV suggested the SVM classifier had 95.4% specificity, an F1 measure of 71.3, and 89.4% accuracy in identifying whether female firearm suicide decedents had a recent dispute/interpersonal conflict before death (Table 1). 8 preceding circumstance labels were rare (<5% of cases). None of the ML models performed well in identifying these 8 labels.

Conclusions: Our NLP pipeline may help others automate the identification of interpersonal conflicts – mentioned in the narratives of NVDRS – preceding female firearm suicide. Understanding how these circumstances manifest among females may help inform future studies and interventions. Our NLP pipeline did not perform well for rare labels. Other identification methods may be more practical.

Table 1. Model performance metrics of the Naïve Bayes, Random Forest, and Support Vector Machine models using K-Fold Cross-Validation for Two Interpersonal Conflict Labels

Panel A Label: Recent dispute or interpersonal conflict

	Naïve Bayes		Random Forest		Support Vector Machine	
	Mean	SD	Mean	SD	Mean	SD
Accuracy (%)	78.1	1.4	90.2	1.0	89.4	0.9
Sensitivity (%)	75.0	4.7	57.7	8.9	64.8	4.8
Specificity (%)	78.8	2.1	97.3	0.5	95.4	1.5
F1	58.6	3.4	72.3	4.8	71.3	3.2
ROC AUC	80.2	2.8	93.8	1.0	90.8	1.4

Panel B Label: Problems with most recent/current romantic relationship

	Naïve Bayes		Random Forest		Support Vector Machine	
	Mean	SD	Mean	SD	Mean	SD
Accuracy (%)	69.9	2.9	83.7	2.1	83.6	2.8
Sensitivity (%)	60.5	7.4	30.0	6.1	51.6	9.3
Specificity (%)	72.4	2.1	89.3	7.4	88.0	3.9
F1	46.5	7.1	44.1	8.3	60.1	4.2
ROC AUC	72.4	4.5	89.2	3.1	84.1	0.3

Notes: ROC AUC is an abbreviation for the area under the receiver operator characteristic curve.

Mortality after 9/11 attacks among World Trade Center Health Registry (WTCHR) enrollees with cancer Jiehui Li* Jiehui Li Rebecca Kehm Erin Takemoto Janette Yung Baozhen Qiao Mark R. Farfel James E. Cone

While several studies have reported the association of 9/11 exposure with cancer risk, survival after a cancer diagnosis among the 9/11-exposed population is not well studied. In this longitudinal cohort study, we examined associations of 9/11-related exposures with mortality in 5,061 WTCHR enrollees (recruited 2003-2004) with a first-ever primary invasive (or *in situ* bladder) cancer diagnosed between 1995-2015 and followed through December 31, 2016. Enrollees were categorized into three groups by timing of cancer diagnosis(es): pre-9/11only (n=520, deaths=95), pre+post-9/11 (n=114, deaths=41), and post-9/11 only (n=4,427, deaths=1,066). The 9/11-related exposures of interest included 9/11-related probable PTSD (PTSD), any injury sustained, and number of traumatic events witnessed (witnessing) on 9/11. Person-time were from first cancer diagnosis to death or censoring (12/31/2016). Cox proportional hazards regression was used. Overall, PTSD was associated with 36% (adjusted hazard ratio (AHR)=1.36; 95% CI=1.11-1.65) higher risk of all-cause mortality in the post-9/11 only group, but not in those diagnosed with a cancer before 9/11. Further adjustment for initial treatment in the post-9/11 only group, PTSD (aHR=2.13, 95% CI=1.13-4.01) and witnessing ≥3 traumatic events (aHR=2.00, 95% CI=1.13-3.55) were associated with increased non-cancer mortality risk in rescue/recovery workers, but not in non- rescue/non-recovery workers. Injury was not associated with mortality risk in any cancer group. Our findings suggest that traumatic exposure and 9/11-related PTSD are associated with increased mortality in individuals subsequently diagnosed with cancer, particularly in those involved in the WTC rescue and recovery effort.

Associations of childhood socioeconomic status with colon cancer incidence and related health behaviors in adulthood: A prospective cohort study Anne-Josee Guimond* Anne-Josee Guimond Emily S. Zevon Reginald D. Tucker-Seeley Edward L. Giovannucci Claudia Trudel-Fitzgerald Laura D. Kubzansky

Background: Colon cancer is the third most common cancer in the US. While the socioeconomic status (SES)-health gradient is well-established, findings linking adult SES to colon cancer incidence specifically are mixed. Considering childhood SES and relevant risk factors, including related lifestyle behaviors, may provide more insight. **Methods:** At baseline in 1976, women from the Nurses' Health Study reported childhood SES as defined by parents' occupation when participants were age 16. Lifestyle-related factors (i.e., physical activity, body mass index, diet, alcohol intake, and tobacco consumption) were self-reported in 1988 or 1990, and every 4 years thereafter until 2016. Cox regression models estimated hazards ratio (HR) and 95% confidence intervals (CIs) of developing colon cancer in the entire analytic sample of colon cancer-free women at baseline (N=100,921) and adopting an unhealthy lifestyle among women who had a healthy lifestyle at baseline (N=22,507) across parents' occupation levels. Follow-up spanned from 1976 or 1990, depending on the outcome under study, through 2016. **Results:** During follow-up, 2,342 cases of colon cancer occurred. Compared to women whose parents were white collar workers, women whose parents were farmers had lower colon cancer risk (HR=0.84; 95%CI: 0.72, 0.98), but no differences were evident for women whose parents were blue collar workers in models adjusting for age and familial history of colon cancer. Using the same comparison group, risk of adopting an unhealthy lifestyle over follow-up was not significantly different in women with farmer parents (HR=0.96, 95% CI: 0.91, 1.02), while women with blue collar worker parents had slightly greater risk (HR=1.07; 95%CI: 1.03, 1.12) in age-adjusted models. **Conclusion:** Findings suggest the impact of childhood SES on colon cancer risk and likelihood of adopting an unhealthy lifestyle is modest and varies across outcomes and occupational status.

Cancer

Association between census-tract level diesel engine emissions and residence in a breast cancer hot-spot in Kentucky Stephie Abraham* Stephie Abraham Johnnie Newton Matthew Ruther Natalie DuPre

Background: Geographic differences in breast cancer incidence rates are observed across the US and within Kentucky counties. The geographic differences exist even after controlling for known breast cancer risk factors. Research on environmental pollutants on breast cancer risk has been inconsistent. The primary aim of this study was to evaluate the association between census-tract level diesel engine emissions in relation to residing in a breast cancer hot-spot in Kentucky.

Methods: The study population included Stage I-IV female breast cancer cases diagnosed between 1995-2018 from the Kentucky Cancer Registry (N=77011). The primary exposure was census-tract level diesel engine Particulate Matter (PM) emissions for each of the cases' residence at diagnosis obtained from the 2014 US EPA National Air Toxics Assessment. The outcome was whether the case resided in a breast cancer hot-spot determined by the Getis Ord Gi* statistic for age-standardized invasive breast cancer rates for KY census-tracts. Logistic regression analysis was done to calculate the Odds Ratio (OR) and 95% confidence intervals (CI). Additionally, effect modification was assessed by Metropolitan and non-Metropolitan counties based on the Beale code 2013.

Results: The odds of residing in a breast cancer hot-spot was 3.37 times higher for women living in the highest quartile of diesel PM compared to the lowest quartile after adjusting for age, race, family history, marital status, insurance, geographic area, smoking, menopausal status, and parity (95% CI: 2.77, 4.09). Additionally, for a standard deviation (SD, 0.219 µg/m^3) increase in diesel PM, the odds of being in a breast cancer hot-spot was significantly higher by a factor of 1.61 (95% CI: 1.54, 1.68). Results were similar among cases residing in Metropolitan and non-Metropolitan counties.

Conclusion: Census-tract level diesel engine emissions were associated with individuals residing in breast cancer hot-spot census-tracts in Kentucky.

A prospective study of hysterectomy, bilateral oophorectomy, and risk of breast cancer

Sharonda M. Lovett* Sharonda Lovett Dale P. Sandler Katie M. O'Brien

Background: Gynecologic surgery is hypothesized to reduce risk of breast cancer, but findings may be confounded by hormone use. We examined the association between history of gynecologic surgery and breast cancer risk considering the use of hormone therapy.

Methods: The Sister Study is a prospective cohort of women aged 35-74 years with a sister who had breast cancer but no breast cancer themselves. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between gynecologic surgery at the time of enrollment (no surgery, hysterectomy only, bilateral oophorectomy with or without hysterectomy) and incident breast cancer among 50,761 women. Effect modification and heterogeneity by race/ethnicity, family history of breast cancer, and breast cancer estrogen receptor status was also examined.

Results: History of gynecologic surgery was common, with 14% reporting hysterectomy and 18% reporting bilateral oophorectomy. During follow-up (median = 11.4 years), 3,919 breast cancer cases were diagnosed. Compared to no surgery, bilateral oophorectomy was inversely associated with breast cancer (HR = 0.87, 95% CI = 0.78, 0.96), especially when combined with estrogen only hormone therapy (HR = 0.81, 95% CI = 0.72, 0.92). Hysterectomy alone, versus no surgery, was positively associated with disease (HR = 1.08, 95% CI = 0.98, 1.20), with an even stronger association seen for hysterectomy with estrogen plus progestin hormone therapy (HR = 1.25, 95% CI = 0.98, 1.60). African American and Hispanic/Latina women were more likely to have had a hysterectomy, compared to non-Hispanic White women, though we saw no evidence of statistical heterogeneity in associations with breast cancer.

Conclusion: We observed an inverse association between bilateral oophorectomy and breast cancer risk. The positive association between hysterectomy and breast cancer may be limited to women also taking estrogen plus progestin hormone therapy.

Cancer

Survival differences by Charlson Comorbidity Index among early-stage NSCLC patients after stereotactic body radiotherapy. Meghann Wheeler* Meghann Wheeler Martin Tammemagi Michael Gould Gerard Sylvestri Christopher Slatore Yi Guo Jiang Bian Matthew Schabath Bruno Hochhegger Danting Yang Shama Karanth Dongyu Zhang Dejana Braithwaite

Purpose: To compare differences in overall survival (OS) by Charlson comorbidity index (CCI) among older adults with early-stage non-small cell lung cancer (NSCLC) who have received stereotactic body radiotherapy (SBRT).

Methods: Utilizing data from the National Cancer Database, we conducted survival analyses among patients aged 50 or older with primary stage I/II NSCLC who underwent SBRT between 2004 and 2018. A Kaplan-Meier lifetable analysis was used to evaluate OS by CCI (0, 1, and 2 or more) and multivariable Cox proportional hazards models were used to compare OS by CCI (CCI score of 0 as the referent) among the SBRT recipients. Subgroup analyses, in which CCI was treated as a binary variable (0 and 1 or more), were stratified by age (50-64, 65-74, and 75 or older) and sex. A Wald test was performed to assess if there was an interaction between CCI and sex or age in relation to OS.

Results: A total of 37,714 patients were included in the analysis. Among them, 54.6% had a CCI of 0, 25.8% had a CCI of 1, and 19.6% had a CCI of 2 or more. Mean age among all participants was 74.2 (SD=8.7) years, 53.1% were female, and 89.6% were non-Hispanic white. Median length of follow-up was 28.2 months. A total of 21,671 (57.5%) deaths were observed. Compared to patients with a CCI of 0 (HR: 1.00), patients with a CCI of 1 (adjusted hazard ratio [aHR]: 1.08, 95% CI: 1.05-1.11) or a CCI of ≥2 (aHR: 1.31, 95% CI: 1.26-1.35) experienced significantly worse OS. The subgroup analyses revealed significant interaction between CCI and sex (Male aHR: 1.12, 95% CI 1.08-1.17; Female aHR: 1.22, 95% CI 1.17-1.27, p-interaction<0.01). Effect measures did not differ substantially by age.

Discussion: Higher CCI is associated with increased risk of mortality among early-stage NSCLC patients receiving SBRT. Sex appears to influence the relationship between CCI and mortality, and women experienced higher risk of mortality versus men with the identical CCI level.

Cancer

The association between alcohol consumption and incident cancers: The KCPS-II Biobank and UK Biobank Keumji Jung* Keumji Jung Sun Ha Jee

Background: Worldwide, 3 million deaths every year result from harmful use of alcohol. There are several hypotheses that alcohol may increase the risk of cancer, but the mechanisms for this are not fully understood. In this study, we examined the association between alcohol consumption and cancer using data from Korea and the UK.

Methods: This study was conducted using the Korean Cancer Prevention Study-II (KCPS-II Biobank) and UK biobank. 160,000 KCPS-II Biobank and 500,000 UK Biobank enrolled participants were enrolled and followed up is ongoing. We used Cox regression model to examine an association of alcohol and incident cancers.

Results: Compared to non-drinkers, the overall cancer risk of drinkers was 10% higher in KCPS-II, and 13% higher in the UKB. In Korea, the risk of past drinkers was high, and in the case of alcohol-related cancer, it showed the J shape association. In esophageal and stomach cancers, the risk of cancer increased as the amount of alcohol consumption increased. Similarly, in the UK, the risk of past drinkers was high, and the cancer risk increased as the amount of alcohol consumed increased in head and neck cancer, breast cancer, and alcohol related cancer. In the case of thyroid cancer, the cancer risk decreased as the amount of alcohol consumed increased. However, when a sensitivity analysis was conducted, the association showed a tendency to weaken or disappear.

Conclusion: Alcohol consumption may be associated with incidence cancer in Korean population and UK population. However, the direction and intensity of the association showed different results depending on the cancer site and ethnicity. Therefore, further research considering each mechanism is needed.
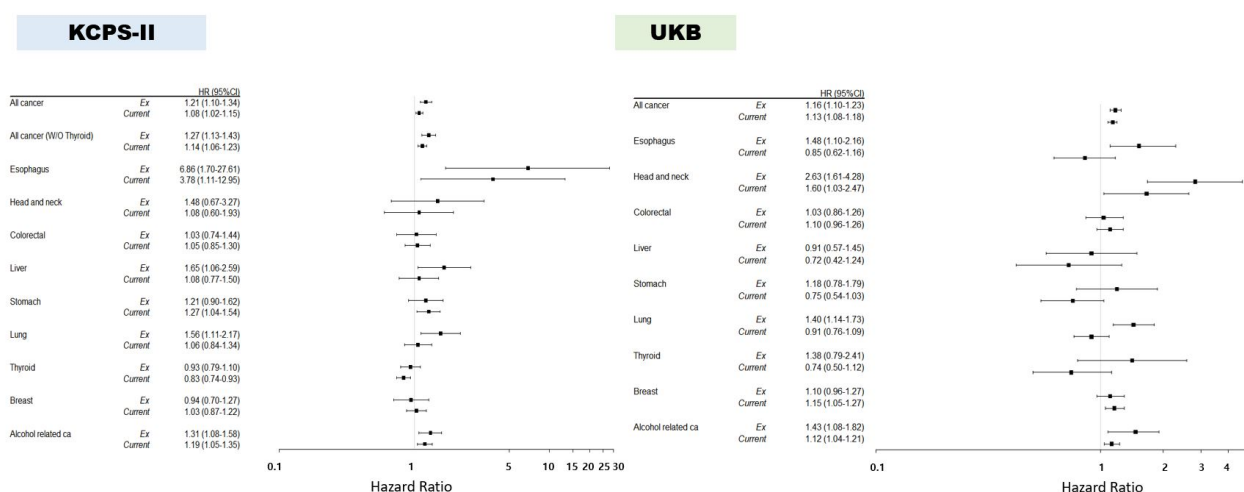
Adjusted for age, sex, BMI, smoking status, social economic status, family history of cancer

Employment Trajectories in Women and Cancer Onset at Older Age: A Multi-Country Cohort Study Bernadette van der Linden* Bernadette van der Linden Stefan Sieber Matthias Studer Arnaud Chiolero Stéphane Cullati

Different employment trajectories are associated with differences in lifestyles that can explain health gradients and chronic disease risk in the labor force. We assessed how employment trajectories relate to cancer in later life among women.

Data for 7477 women ≥ 50 years old included in SHARE were analyzed. Data was collected between 2004 and 2020 in 28 European countries and Israel. Participants filled out a life-calendar instrument to collect data on their past employment life. Employment trajectories were constructed using sequence analysis. Associations of the employment trajectories with later cancer onset (all types, breast, cervix, colorectal, lung, and skin) were assessed using Cox regression. Models were adjusted for age, birth cohort, attrition, body mass index, smoking, multimorbidity, and physical activity.

Preliminary analyses identified five different employment trajectories; C1) mainly inactive (n=2260), C2: mainly fulltime (n=2263), C3: fulltime to inactive (n=1299), C4: inactive to fulltime (n=600), and C5: fulltime to inactive to part-time (n=695). In total, 851 women were diagnosed with cancer. Risk of all types of cancer was increased for women in the C2, C3, and C5 trajectories compared to women in the C1 trajectory (hazard ratio (HR) = 1.48, 95%CI 1.24, 1.78; HR = 1.60, 95%CI 1.30, 1.98; HR = 1.80, 95%CI 1.41, 2.30, respectively). Results were similar for breast and colorectal cancer. For skin cancer, women in the C3 trajectory had a higher risk of skin cancer compared to the C1 trajectory (HR = 2.00, $p<0.05$). For cervix and lung cancer, no differences between the trajectories were found, but sample sizes of these cancers might have insufficient power to detect an association.

Women's employment trajectories seem to be associated with different cancer risk in later life. This may possibly be explained through different characteristics of the employment trajectories, such as health-related lifestyle and occupational health risks.

Cancer

Pre-diagnostic plasma 25-hydroxyvitamin D and mortality among women with breast cancer in the Nurses' Health Studies
Etienne Holder* Etienne Holder Serena Houghton Elizabeth Bertone-Johnson Jing Qian Zhenhua Liu Wendy Chen Michelle Holmes Rulla Tamimi A. Heather Eliassen Susan Hankinson

Background: 25-hydroxyvitamin D (25(OH)D) is an essential steroid hormone that is hypothesized to influence breast cancer prognosis by inhibiting breast tumor growth. While this has been observed in laboratory-based studies, findings from observational studies are inconclusive. We examined the association between pre-diagnostic 25(OH)D concentrations and both breast cancer-specific and all-cause mortality to explore the potential effects of vitamin D.

Methods: We evaluated this association among 1,312 women diagnosed with invasive breast cancer enrolled in the Nurses' Health Study 1 (NHS1) and 2 (NHS2) cohorts. In this analysis, women provided a blood sample from 1989-1990 and a second blood sample in 2000-2001 (NHS1) or a blood sample from 1996-1999 (NHS2). Women were diagnosed with breast cancer after blood collection up through 2016 (NHS1) and 2017 (NHS2) and censored at end of study or death. Cox proportional hazards models were used to estimate hazard ratios (HR) and 95% confidence intervals (95%CI) for mortality after adjustment for tumor characteristics, type of cancer treatment, and lifestyle factors. The competing risks HR for breast cancer-specific mortality was estimated using the Fine-Gray method.

Results: A total of 406 total deaths and 154 breast cancer-specific deaths occurred during follow-up through 2017. We observed a non-statistically significant 28% lower breast cancer-specific mortality rate among those with the highest, versus lowest, quartile of pre-diagnostic 25(OH)D levels (HR 0.72, 95%CI 0.41-1.20; p for trend=0.30), that did not vary significantly by estrogen receptor status of the tumor (p for interaction=0.61). Women in the highest vs. lowest quartile of plasma 25(OH)D experienced a 32% lower all-cause mortality rate (HR 0.68, 95%CI 0.51-0.92; p for trend=0.03). In cause-specific mortality analyses among non-breast cancer deaths, non-statistically significant decreases were observed for other cancer deaths and cardiovascular disease deaths.

Conclusion: Pre-diagnostic plasma 25(OH)D levels were not significantly associated with lower breast cancer-specific mortality among women with breast cancer. However, significant inverse associations were observed for total mortality, which supports a potential benefit of vitamin D among these women.
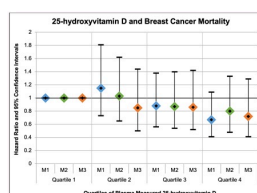
Figure 1: Competing risks model of breast cancer mortality by quartiles of pre-diagnostic plasma measured 25-hydroxyvitamin D.
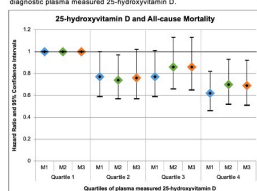

Figure 2: All-cause mortality by quartile of pre-diagnostic plasma measured 25-hydroxyvitamin D.

Cancer

Factors associated with non-attendance for cervical screening in England Dr. Karima Chiuri*
Karima Chiuri Prof. Dame Valerie Beral Dr. Isobel Barnes Dr. Siân Sweetland

Background

Previous studies have shown some differences in uptake of cervical screening by sociodemographic factors. However, available evidence on lifestyle, reproductive and hormonal factors is limited and inconsistent. We examined screening uptake in relation to personal factors by linking data from a large prospective cohort, the Million Women Study (MWS), with NHS Cervical Screening Programme (NHSCSP) records.

Methods

Using linked NHSCSP records for women before they were recruited into the MWS, participants were classified as non-attenders or attenders for routine cervical screening. Logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CI) of non-attendance versus attendance by deprivation status, smoking, body mass index (BMI), parity, age at first birth, oral contraceptive (OC) and menopausal hormone therapy (MHT) use. All analyses were stratified by year of birth and recruitment into the MWS and adjusted for other factors, where appropriate.

Results

Of 874,175 participants who were eligible to have been invited for screening 24,338 were non-attenders and 849,837 were attenders. The odds of being a non-attender were increased with deprivation (OR [95%CI] 1.41 [1.37-1.46] for most vs. least deprived tertile), obesity (1.46 [1.41-1.52] for BMI >30 vs. <25/kgm2) and smoking (1.18 [1.14-1.22] for current vs. never smokers). Nulliparous women were much more likely to be non-attenders (7.02 [6.84-7.22]) and women who were younger at first birth were also less likely to attend (1.17 [1.05-1.30] for <18 vs. 21-24 years at first birth). By contrast, women who had used OCs or MHT were much less likely to be non-attenders (0.43 [0.41-0.44] and 0.31 [0.30-0.32] for ever vs. never OC and MHT use respectively.

Conclusions

In this large cohort of women in England, attendance for cervical screening varied considerably, not only by deprivation, as had been reported previously, but also by lifestyle, reproductive and hormonal factors.

Cancer

Low-Dose Radiation Risks of Lymphohematopoietic Cancer Mortality in U.S. Shipyard Workers Xuguang (Grant) Tao* Xuguang (Grant) Tao Frank C. Curriero Mahadevappa Mahesh

Historically, radiation protection standards have relied heavily on radiation risk models derived from atomic bomb survivors. However, general population radiation exposures are more likely to occur from low, fractionated doses resembling exposures in industrial populations. The objective of this study was to examine risks and dose-response patterns of lymphohematopoietic cancer (LHC) and its subtypes associated with low radiation exposure among US shipyard workers. A retrospective cohort of 437,937 US nuclear shipyard workers, including 153,930 radiation and 284,007 non-radiation workers, was followed from 1957 to 2011. Time dependent accumulated radiation dose, lagged 2 years, was used in categorical and continuous dose analysis among radiation workers to examine the LHC risks and possible dose-response relationships based on Poisson regression models. The analyses controlled for sex, race, time dependent age, calendar time, socioeconomic status, solvent-related last job, and age at first hire. The results showed: 1) Controlling for sex, race, time dependent age, and calendar time, the LHC mortality for radiation workers was significantly lower than non-radiation workers (RR: 0.927; 95% CI: 0.865, 0.992). Among LHC subtypes, the risks for lymphoid leukemia and lymphomas in radiation workers were significantly lower than the risk in non-radiation workers with statistical significance. 2) For LHC, leukemia less chronic lymphocytic leukemia (CLL), acute myeloid leukemia, and Hodgkin's Lymphoma, there were RRs lower than 1.000 in the categories 0-<25 or/and 25-<50 mSv vs. 0 mSv. 3) The Poisson regression analyses among radiation workers using the time dependent radiation dose as a continuous variable showed a non-significant excess relative risks (ERR) for LHC at 100 mSv of 0.094, (95% CI: -0.037, 0.225). The ERRs and their linear trend for all subtypes were not statistically significant. In conclusion, the risks of LHC and its subtypes were not elevated among radiation workers as a group compared to non-radiation workers in US nuclear shipyards. For LHC, leukemia less CLL, acute myeloid leukemia, and Hodgkin's Lymphoma, a possible "hormesis" effect or a beneficial effect were suggested at a time dependent radiation dose less than 50 mSv.

Lifestyle factors and risk of progression from monoclonal gammopathy of undetermined significance to multiple myeloma Vicky C. Chang* Vicky C. Chang Ali A. Khan Wen-Yi Huang Hormuzd A. Katki Mark P. Purdue Ola Landgren Jonathan N. Hofmann

Background: Monoclonal gammopathy of undetermined significance (MGUS) is an obligate precursor of multiple myeloma (MM) and progresses to MM at an average annual rate of ~1%. Obesity is an established risk factor for MM; however, it remains unclear whether high body mass index (BMI) or other modifiable lifestyle factors are associated with progression from MGUS to MM. We conducted a nested case-control study in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial to evaluate associations between lifestyle factors and risk of MGUS progression to MM.

Methods: MGUS was characterized in prediagnostic sera from selected PLCO participants who did and did not subsequently develop MM or other hematologic malignancies during follow-up. Analyses were conducted among those identified to have non-IgM MGUS (N=488; including 164 MM cases and 324 non-progressing MGUS). Lifestyle characteristics were assessed at study baseline. Odds ratios (OR) and 95% confidence intervals (CI) were estimated overall and by sex using multivariable logistic regression adjusted for demographic and clinical characteristics related to progression.

Results: BMI was positively associated with progression from MGUS to MM (per 5-kg/m^2; OR 1.35, 95% CI 1.03–1.77), with a stronger association among women (OR 1.51, 0.97–2.34) than men (OR 1.29, 0.89–1.87). We also observed a nearly 3-fold, albeit not statistically significant, increase in odds of progression for women who were obese (≥30 vs 18.5–<25 kg/m^2; OR 2.82, 0.71–11.2). Furthermore, we found non-significant inverse associations with vigorous physical activity (≥4 vs <1 hours/week; OR 0.50, 0.11–2.30) in women and alcohol consumption in men (≥1 drink/day vs <1 drink/week; OR 0.55, 0.22–1.36).

Conclusions: High BMI or obesity may be a risk factor for progression from MGUS to MM, especially among women. Our findings, if replicated in larger studies, may have implications for clinical management and risk prediction among MGUS patients.

Residential proximity to dioxin emissions and risk of breast cancer in the NIH-AARP Diet and Health Study Jessica Madrigal* Jessica Madrigal Jared A. Fisher Mary H. Ward Rena R. Jones

Background: Residential proximity to industrial combustion facilities has been associated with increased levels of polychlorinated dibenzo-p-dioxins and dibenzofurans (PCDD/F) in homes. PCDD/Fs have been linked to breast carcinogenesis, but few studies have investigated this in non-occupational study populations. **Methods**: We evaluated residential PCDD/F exposure and breast cancer risk among female participants of the NIH-AARP Diet and Health Study, a prospective cohort (N=177,205; 11,859 cases) in 6 US states and 2 cities. We linked geocoded enrollment addresses (1995-1996) with an Environmental Protection Agency database of 4,478 historical PCDD/F sources (cement kilns, coal-fired power plants, industrial boilers, secondary copper smelters, and various waste incinerators) with emissions estimates (g TEQ). We computed two metrics at 3km and 5km from homes: proximity to any dioxin facility and a wind-adjusted distance- and toxicity-weighted average emission index (AEI [g TEQ/km^2]). We estimated associations (HR; 95%CI) with Cox models for all facilities and by type adjusted for demographic and lifestyle factors. **Results**: Having any facility within 3km or 5km was not associated with risk (3km HR=1.04, CI=0.98-1.09; 5km HR=1.03, CI=0.98-1.07). The 3km AEI was not associated with risk; however, risk was increased in the top quartile of the 5km AEI but the trend was not significant (HR$_{Q4vs0}$=1.08; CI=1.01-1.15; p-trend=0.23). Compared to those with no facilities nearby, risk was increased for medical waste incinerators at both distances (HR$_{3km}$=1.06, CI=1.00-1.12; HR$_{5km}$=1.04, CI=0.99-1.09), and risks were elevated with >median emissions from these facilities (3km HR$_{>median\ AEI\ vs.0}$=1.08, CI=1.00-1.16, p-trend=0.05 and 5km HR$_{>median\ AEI\ vs.0}$=1.06, CI 1.00-1.13, p-trend=0.04). We found no associations for other facilities. **Conclusions**: We found an increased risk of breast cancer with high residential exposure to PCDD/Fs from medical waste incinerators within 5km of homes.
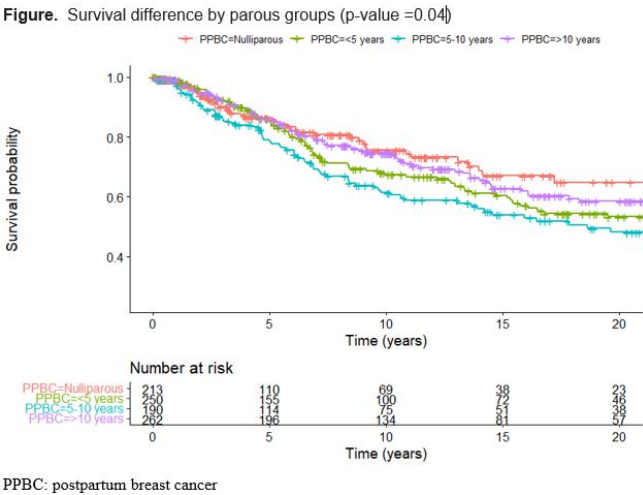
LATEBREAKER

Cancer

Impact of Time Since Last Childbirth on Survival in Young Women with Breast Cancer with BRCA1 and BRCA2 Mutations Zhenzhen Zhang* Zhenzhen Zhang Shangyuan Ye Heidi D Nelson D Gareth Evans Pepper Schedin

Background: Breast cancer diagnosis after childbirth in women ≤45 years of age is associated with increased metastasis and death. Women with germline *BRCA* mutations are more likely to be diagnosed with breast cancer at younger ages. Whether breast cancer outcomes in *BRCA* mutation carriers are influenced by the timing of childbirth is unknown. Our objective was to examine associations between breast cancer diagnosis time since last childbirth and all-cause mortality among *BRCA* carriers with breast cancer.

Methods: The study cohort includes 910 female *BRCA1* and *BRCA2* germline mutation carriers diagnosed with invasive breast cancer stage I-III at ≤45 years of age between 1936 and 2021 from northwest England. For the analyses, we compared nulliparous (n=226) versus parous cases diagnosed 0 to <5 years (n=228), 5 to <10 years (n=193) and ≥10 years (n=263) since last childbirth. Cox proportional hazard models were used to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs); and Kaplan-Meier curves were plotted to characterize survival differences across groups. Stratified analyses by estrogen receptor (ER) status and *BRCA* gene mutation (*BRCA1* vs *BRCA2*) were conducted.

Results: Breast cancer diagnosed 5 to <10 years after last childbirth was associated with an elevated risk for mortality [HR=1.48 (95% CI, 1.01-2.18)] compared to nulliparous cases. In stratified analyses, results were significant for ER-negative cases [HR=3.26 (95% CI, 1.27-8.35)] and *BRCA1* carriers [HR=1.80 (95% CI, 1.03-3.14)]. Trends for ER-positive and *BRCA2* carriers within 0 to <5 years after childbirth were observed but did not reach statistical significance.

Conclusion: This study shows poorer prognosis for *BRCA* carriers diagnosed with breast cancer within 10 years of childbirth, as previously reported for general populations. Further, a breast cancer diagnosis 5 to <10 years after last childbirth is an independent risk factor for mortality, especially among ER-negative and *BRCA1* patients. Clinical consideration of time between last completed pregnancy and breast cancer diagnosis in *BRCA* mutation carriers could improve the accuracy of prognosis in young-onset breast cancer patients.

Figure. Survival difference by parous groups (p-value =0.04)

PPBC: postpartum breast cancer

Differential association of low-density lipoprotein and breast cancer-specific survival among women with estrogen receptor-positive and estrogen receptor-negative cancers

Alexa Zimbalist* Alexa Zimbalist Bette Caan Wendy Y. Chen Elizabeth Cespedes Feliciano

Background: Estrogen receptor (ER)-negative breast cancer (BC) has worse prognosis and fewer treatment options than ER-positive BC. Identifying modifiable risk factors, such as cholesterol, could improve treatment and prognosis. While cholesterol is associated with BC risk, studies of survival have yielded inconsistent results. Despite evidence from cell and murine models that cholesterol contributes to ER+ vs. ER- BC progression via different pathways, few studies examine associations by ER status. This cohort study examined low-density and high-density lipoproteins (LDL & HDL) and BC survival among women with ER+ vs. ER- cancers.

Methods: 13,378 women diagnosed with stage I-III BC (11,164 ER+ and 2,214 ER-) from 2005-15 at Kaiser Permanente were included. Time-updated outpatient HDL and LDL values from diagnosis through 2019 or death were assessed. Risk of BC mortality by ER status was evaluated with Cox proportional hazards models adjusted for demographics, body mass index, diabetes, lipid and hypertension medications, glucose, triglycerides, and cancer treatment.

Results: Median follow-up was 8.58 years and 1,076 women died of BC (753 ER+ and 323 ER-). Those with ER- and ER+ cancers with low HDL (≤45 mg/dL) had higher BC mortality (HR, 1.73; 95% CI, 1.32-2.27; HR, 1.72; 95% CI, 1.45-2.05), whereas high LDL (>129 mg/dL) was associated with higher BC mortality only in women with ER- cancers (HR, 1.37; 95% CI, 1.07-1.75 in ER- vs. HR, 1.01; 95% CI, 0.85-1.20 in ER+; p-interaction = 0.03).

Conclusions: Low HDL evaluated over time is associated with higher BC mortality independent of ER status. High LDL is associated with higher BC mortality only among women with ER- tumors, which agrees with prior studies that show LDL induces proliferation of ER- BC cell lines, but not ER+ cells. Future studies should provide insight into the LDL mechanism in ER- BC cell lines and whether cholesterol-lowering agents can optimize BC survival among women with ER- tumors.

LATEBREAKER

Cancer

Financial worry among cancer survivors: Health behaviors and outcomes associated with it
Mimi Ton* Mimi Ton Salene Jones Rachel C Malen Jaimee L Heffner Polly A Newcomb

Understanding financial worries among cancer patients could contribute to improved survivorship care, especially during the COVID-19 pandemic. Few studies have investigated the association between financial worry and health behaviors. We ascertained financial worry within a population-based study of 1,539 cancer patients identified through the Puget Sound SEER cancer registry, 1,473 of whom answered questions on financial worry. We assessed financial worries as the frequency of serious financial worries in the past month. We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs) for the association of health behaviors and outcomes among cancer patients with financial worries compared to those without financial worries. We also used linear regression to estimate change in physical and mental quality of life (QOL) as measured by β and 95% CIs. Models were adjusted for material financial situation, income, health insurance, education, gender identity, sex, age, and cancer stage. 19% of study participants (N=279) reported financial worry. Patients with financial worry were more likely to report anxiety (OR [CI]: 2.99 [1.93-4.62]) and depression (OR [CI: 3.00 [1.86-4.86]). Those with financial worry reported lower physical (β [95% CI]: -2.84 [-4.05, -1.63]) and mental (β [95% CI]: -5.14 [-6.48, -3.80]) QOL. There were no significant associations between financial worry and problematic cannabis use, smoke status, problematic alcohol use, nor problematic prescription drug use. Overall, financial worry was associated with worse QOL and mental health. This suggests that financial worry is a significant burden among cancer patients and these characteristics could help us identify individuals who could benefit from interventions to reduce the burden of financial stress.

Metabolic Vulnerability Index and Mortality in Heart Failure: a Community Cohort Study

Katie Conners* Katie Conners Veronique L. Roger Hoyoung Park Jungnam Joo Sheila M. Manemann
Alan T. Remaley James D. Otvos Maureen Sampson Suzette Bielinski Anna Wolska Sarah Turecamo

Introduction: Heart failure (HF) is a prevalent syndrome associated with metabolic abnormalities and high mortality. Risk stratification remains challenging. Nuclear Magnetic Resonance (NMR) spectroscopy enables high-throughput analysis of metabolomics suitable for epidemiology research. The novel NMR Metabolic Vulnerability Index (MVX; range 1-100) is calculated using indicators of systemic inflammation (small HDL particles, GlycA) and metabolic malnutrition (leucine, valine, isoleucine, citrate). Its prognostic value has not been studied in HF. We tested the hypothesis that MVX was associated with mortality in a HF community cohort.

Methods: MVX scores in plasma were calculated from *NMR LipoProfile*® analyses conducted on the Vantera NMR analyzer platform using the LP4 deconvolution algorithm. Kaplan-Meier method estimated survival. Proportional hazard regression examined the relationship between MVX quartiles (Q) and mortality, adjusted for Meta-Analysis Global Group in Chronic HF (MAGGIC) score, a validated clinical risk score including ejection fraction, systolic blood pressure, BMI, creatinine, New York Heart Association class, sex, smoking status, diabetes, chronic obstructive pulmonary disease, HF diagnosis >18 months ago, beta blocker, angiotensin converting enzyme inhibitors and angiotensin receptor blockers.

Results: We studied a population-based cohort of 1,382 patients prospectively enrolled between 2003 and 2012 [median age 78 years (IQR 68-85); 48.3% women]. Median MVX score was 59.50 (IQR16.55). Higher MVX was associated with lower survival (figure). There was a graded positive association between MVX and death independently of MAGGIC score: (Q2 HR: 1.58, 95% CI 1.33-1.87; Q3 HR: 1.90, 95% CI 1.61-2.25; Q4 HR: 2.30, 95% CI 1.95-2.72).

Conclusion: In this cohort, the MVX score was significantly associated with mortality in HF, independently of MAGGIC score, suggesting that measures of metabolic vulnerability may contribute to risk prediction in HF.

Survival by MVX Quartiles

Cardiovascular
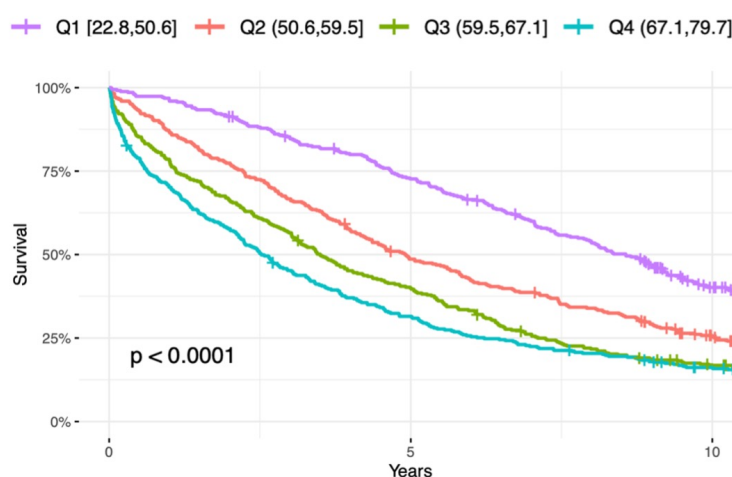
Serum vitamin D levels mediate the association between physical activity and blood pressure in adolescents Keisyanne de Araujo Moura* Keisyanne Moura Marcus Vinicius Nascimento-Ferreira Beatriz D. Schaan Katia Bloch Kênia Mara Baiocchi de Carvalho Felipe Vogt Cureau Augusto César Ferreira De Moraes

Keisyanne Araujo-Moura*; Marcus Vinicius Nascimento-Ferreira; Beatriz D. Schaan; Katia Bloch; Kênia Mara Baiocchi de Carvalho; Felipe Vogt Cureau; Augusto César Ferreira De Moraes

Background: Observational studies have revealed that movement behaviors and low vitamin D levels are associated with higher blood pressure (BP). However, few studies have investigated the role of vitamin d as a mediation factor. Thus, the aim was to examine the associations between 24-hour movement behaviors (physical activity, sedentary behavior and sleep time), serum vitamin D levels, and BP. Additionally, investigate whether vitamin D levels have a mediating effect between observed associations.

Methods: A sample of 1152 Brazilian adolescents aged 12 to 17 years a national school-based cross-sectional survey were included. Mainly exposure: 24-hour movement behaviors. Mediator: serum vitamin D (concentrations of 25-hydroxyvitamin). Outcome:blood pressure levels (diastolic and systolic). Multilevel linear regression models using fixed-effects intercept were applied to analyze the association between exposures and outcomes. To assess whether vitamin D mediate the relation between 24-hour movement behaviors and BP levels, structural equation modeling for mediation analyses were performed.

Results: We observed that 24-hour movement behaviors (screen time, sleep time, and physical activity) were not associated with blood pressure levels. In the mediation analyzes of the association of movement behaviors with high blood pressure, our study revealed that vitamin D mediates up to 12.9% of the association of physical activity with systolic blood pressure, with the direct effect of $\beta = 1.34$ (95%CI 0.50 to 2.17) ranging between and of.

Conclusion: Vitamin D mediates the association between physical activity and systolic blood pressure in adolescents; whereas, vitamin D is inversely associated with blood pressure in these adolescents. Thus, if additional studies are required, outdoor physical activity can promote double benefit, vitamin D serum level increases, and blood pressure controls.

Mediation Analysis

Proteomics Signatures in Heart Failure: a population-based study Kayode O. Kuku* Kayode O. Kuku Hoyoung Park Suzette J. Bielinski Nicolas B. Larson Jungnam Joo Véronique L. Roger

Background: Heart failure (HF) is a poorly understood heterogenous syndrome with persistently high mortality. Precision phenotyping is needed to improve management and survival. High throughput proteomics assays offers a novel and promising avenue for phenotyping HF.

Aim: We sought to identify proteomic signatures in a community cohort of HF patients with machine learning and examine its association with survival.

Methods: Plasma specimens were collected from a HF community cohort (Rochester Epidemiology Project in Southeastern Minnesota, 2003-2012). Proteomics were measured by the SomaLogic affinity-based technology SomaScan® containing 7335 protein targets. Using machine-learning, we performed a semi-supervised clustering of proteomic expressions. Kaplan-Meier survival curve evaluated survival by clusters. The association of the protein signatures with death was examined using Cox regression while adjusting for the Meta-analysis Global Group in Chronic Heart Failure (MAGGIC) score (age, ejection fraction, systolic blood pressure, BMI, creatinine, NYHA class, gender, current smoking, diabetes, chronic obstructive pulmonary disease, HF diagnosis > 18 months, Beta blocker and ACEi/ARB). The results were internally validated using 10-fold cross-validation and bootstrap approaches.

Results: We studied 1388 patients (mean age 75 ± 13; 52% male). Two distinct clusters were identified. Cluster 1 (n=722) included younger individuals (mean age 72 ± 14), 51% male, NYHA class III/IV:41%/26%; LVEF (47%±17); ischemic etiology in 42.2%; 13.2% were current smokers; 33.5% had diabetes mellitus (DM). Cluster 2 (n=666) was characterized by older age (mean age 79 ± 11), 52% male, NYHA class III/IV: 41%/31%, LVEF (48%±16), ischemic etiology 47%; 7.4% current smokers; 38.1% had DM. A total of 447 proteins (315 with HR ≥ 1; 84 with HR < 1) were associated with mortality. Cluster 2 was associated with an increased risk of death compared to Cluster 1 (internal validation HR:1.89; 95%CI [1.68 – 2.12])Figure 1. This association was independent of the MAGGIC score.

Conclusions: Machine learning applied to proteomics data in a HF community cohort identified two distinct protein signatures. Proteomics profile was strongly associated with survival and improved risk stratification over the MAGGIC score.
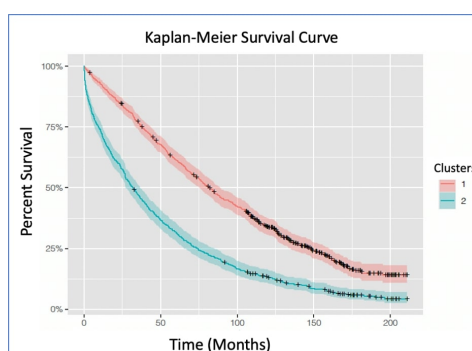
Hypothyroidism Treatment: A Regression Discontinuity Approach Manuel Hoffmann* Manuel Hoffmann Hsu-Hang Yeh Pascal Geldsetzer

Hypothyroidism is affecting millions of adults globally. It is the underproduction of thyroid hormone which manifests itself through symptoms such as fatigue, depression, and impaired memory. Hypothyroidism is diagnosed based on blood tests and commonly treated with the oral medication levothyroxine. To guide doctors when to diagnose and to prescribe, laboratories label their tests with recommended cutoffs which are evident to the physicians upon return. However, little is known whether the prescription for patients close to these cutoffs is beneficial. In this study, we use quasi-random laboratory test variation via a novel regression discontinuity approach to first provide clean evidence of a jump in prescriptions of levothyroxine around the cutoffs. In the second step, we estimate the local average treatment effect from levothyroxine on health outcomes and costs. We use an initial dataset of more than 3 million unique patients provided by the United States insurance company Optum. The laboratory blood tests span the years from 2003 to 2020. We select a conservative bandwidth of 1.25 mIU/L around normalized cutoff values from different laboratories where the cutoffs 4.5 mIU/L and 5.5 mIU/L capture over 85% of the tests. Dropping patients with prior hypothyroidism results in over 700,000 unique patients. Within 30 days after the blood test, we find a large 10 pp. (200%) jump in the prescription probability around the normalized cutoff (see Figure). We do not find any significant changes due to levothyroxine on one-, two-, three-, and five-year all-cause hospitalization and mortality. In contrast, we find that diagnoses of secondary hypertension and patient costs increase. We conclude that the prescription of levothyroxine may not provide substantial benefits and may even result in side-effects and only increase patient costs. Our study implies that prescription behavior should be re-evaluated, and higher laboratory thresholds may be beneficial to patients.

Figure: Thyroid stimulating hormone and Levoxythroxine uptake
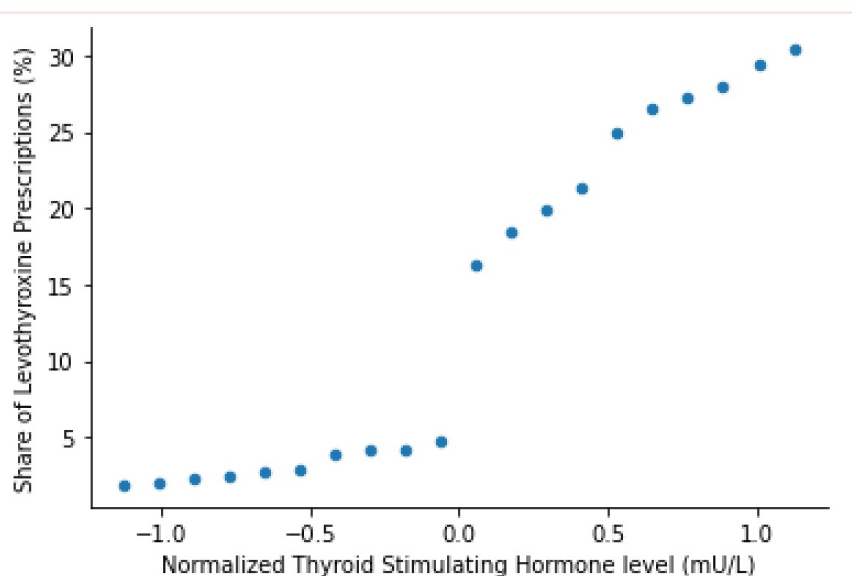
Explaining Different Types of Exchangeability in Causal Inference Haidong Lu* Haidong Lu
Jinghao Sun Forrest Crawford Gregg Gonsalves

In epidemiology, exchangeability is one of the key identification assumptions for estimating causal effects. While the term of "exchangeability" is often referred to as "comparability of treatment and control groups", different types of exchangeability assumptions have been proposed and inadvertently lead to confusion. Here, motivated by Sarvet et al (Epidemiology 2020) on graphical depiction of partial exchangeability, we extend to explain different types of exchangeability for dichotomous outcome Y and treatment A. Specifically, we use a "double-world intervention graph" (an adaptation from "single-world intervention graph") and sufficient component cause model (4 response types of causal, doomed, preventive and immune, and 8 covariate patterns) to explain the following types of exchangeability: marginal exchangeability where $Y^a \perp A$ for all a, and it only requires that the proportion of (causal and doomed) response types is the same among the treated and untreated groups, and the proportion of (preventive and doomed) response types is the same among the treated and untreated groups; full exchangeability where $(Y^{a=1}, Y^{a=0}) \perp A$, and it requires that the proportion of each response type is the same among the treated and untreated groups, and is a stronger assumption than marginal exchangeability; ultimate exchangeability where $(Y^{a=1}, Y^{a=0}, U) \perp A$ (note that U is covariates), and it requires that the proportion of each covariate pattern is the same among the treated and untreated groups, and is a stronger assumption than full exchangeability. Ultimate exchangeability holds in ideal randomized experiments with perfect compliance. We then demonstrate that while ultimate exchangeability requires full covariate balance between the treated and untreated groups, marginal and full exchangeability, which are sufficient as an exchangeability assumption for unbiased estimation of treatment effects, does not require full covariate balance.
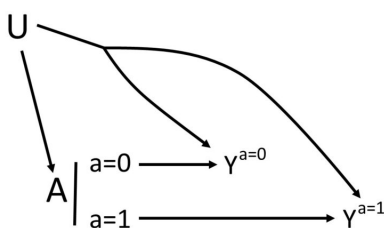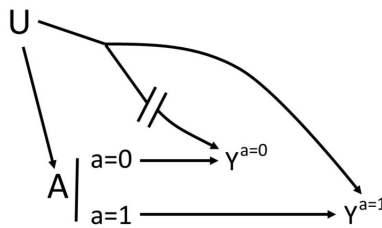
Causal Inference
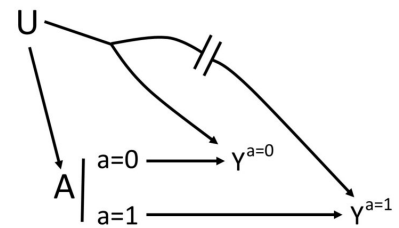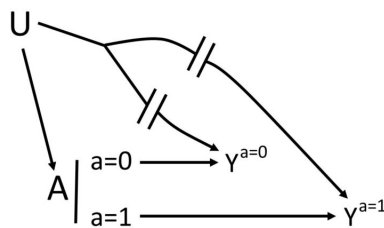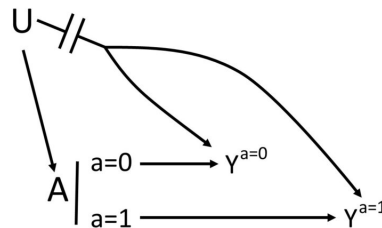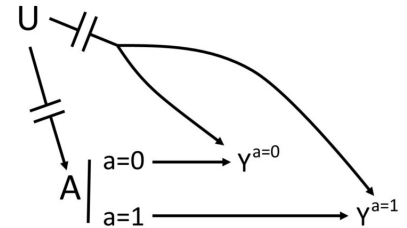
Attributable fraction and related measures: conceptual relations in the counterfactual framework Etsuji Suzuki* Etsuji Suzuki Eiji Yamamoto

Since the publication by Doll in 1951, attributable fraction (population) has specifically drawn much attention from a theoretical perspective and has been used extensively to assess the impacts of potential health interventions. Epidemiology textbooks offer several formulae to calculate attributable fraction (population), including the Levin formula introduced in 1953 and the Miettinen formula introduced in 1974. Despite its significance, however, there is much confusion about the concept and calculation methods of attributable fraction (population). In this presentation, we aim to discuss the concepts and calculation methods of attributable fraction and related measures in the counterfactual framework, providing their conceptual relations in a comprehensive manner. In general, attributable fraction is useful when the exposure of interest has a causal effect on the outcome. More properly, however, it is significant to understand that this statement applies to the exposed group. While the target population of attributable fraction (population) is the total population, the causal effect should be present not in the total population but in the exposed group. As related measures, we discuss preventable fraction and prevented fraction, both of which are generally useful when the exposure of interest has a preventive effect on the outcome, and we further propose a new measure termed attributed fraction. To avoid any confusion, attributable fraction and excess fraction should be clearly distinguished in the counterfactual framework, and we further propose to distinguish causal excess fraction and preventive excess fraction. Finally, we discuss the relations between the six measures and six possible patterns using a conceptual schema. As a prerequisite of the calculation of these measures, it is significant to have a clearer understanding of their definitions in the counterfactual framework, which would be essential to their proper interpretation in the real world.

Causal Inference

**Efficient estimation of modified treatment policy effects based on the generalized propensity score** Nima Hejazi* Nima Hejazi David Benkeser Iván Díaz Mark van der Laan

Continuous exposures have posed significant challenges for causal inference, including in formulating interpretable causal effects, identifying statistical estimands, and constructing robust and efficient estimators. Traditionally, methodological development has focused on techniques applicable to binary or categorical exposures with few levels, settings in which classical propensity score-based approaches can be applied with relative ease. Efforts to accommodate continuous exposures introduced the generalized propensity score (i.e., the conditional exposure density given covariates), a nuisance quantity required for the estimation of scientifically informative parameters like the causal dose-response curve and the causal effects of modified treatment policies (interventions shifting the "naturally" occurring value of the exposure). Unfortunately, conditional densities are challenging to estimate, and the vast majority of generalized propensity score estimators impose restrictive and unrealistic modeling assumptions, sharply limiting the real-world applicability of both inverse probability weighted (IPW) and doubly robust estimators alike. To overcome this, we present a flexible generalized propensity score estimator based on a nonparametric regression function (the highly adaptive lasso) with rate-convergence properties suitable for the construction of estimators with desirable asymptotic properties. Focusing on the causal effects of modified treatment policies, we present a class of nonparametric IPW estimators of such causal estimands, detailing statistical criteria for the targeted or global selection of asymptotically efficient IPW estimators, previously unavailable in the causal inference and non/semi-parametric estimation literature. Through numerical experiments, we demonstrate the competitive performance of several variants of our proposed IPW estimators relative to currently popular doubly robust estimation strategies.

Scaled bias of candidate IPW and DR estimators
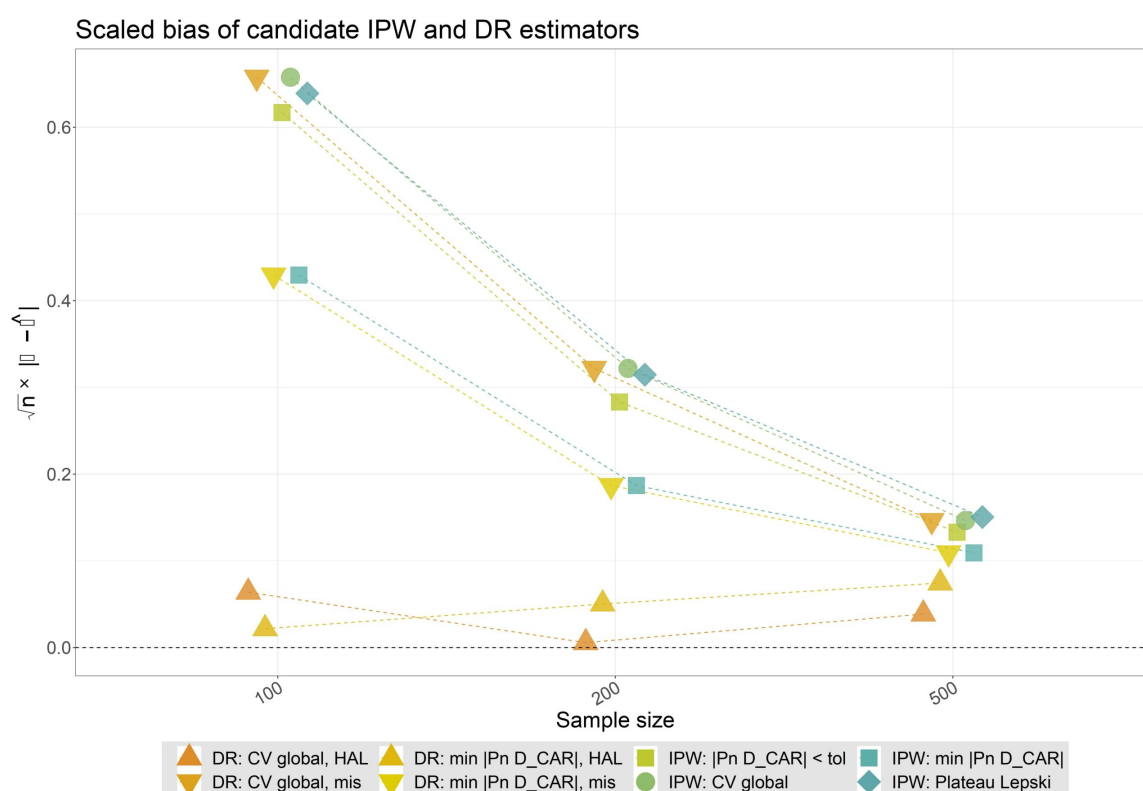
Different identification assumptions and estimation strategies of principal causal effect in randomized trials Elizabeth Sarker* Elizabeth Sarker Elizabeth Stuart Trang Quynh Nguyen

Often in randomized trials not everyone receives their assigned treatment – treatment group members may not fully participate, and control group members may get access to the treatment. In these cases, there is an interest in estimating the effect of actually receiving the treatment of interest, known as the "complier average causal effect" (CACE). The principal stratification framework deals with this "noncompliance" by forming principal strata defined by individuals' potential treatments received when assigned to the treatment and control groups. However, only one potential treatment received is observed in the data, leaving the principal strata membership unobservable. Additional assumptions are thus required to estimate principal causal effects such as CACE. There are many identification assumptions and corresponding estimation strategies in the literature. Though these assumptions are untestable, thoughtful consideration of the plausibility of the assumptions using scientific knowledge can serve as an indirect way to exclude the most unlikely assumptions and avoid incorrect inferences. In this talk, we explicate the causal structure of three such assumptions: Principal Ignorability (PI) from the principal score-based method, Exclusion Restriction (ER) from the two-stage least squares approach, and Auxiliary Independence (AI) assumption. We discuss the plausibility and potential threats for each assumption using directed acyclic graphs and use Baltimore Experience Corps trial data as an example to illustrate how researchers can think through which approach may be more appropriate for their data. We also present results from simulation studies, which showed the PI-based method to be the least sensitive and AI-based to be the most sensitive to its assumption. Our findings show the importance of examining the plausibility of different assumptions when choosing the approach that is most appropriate for a given research question and dataset.
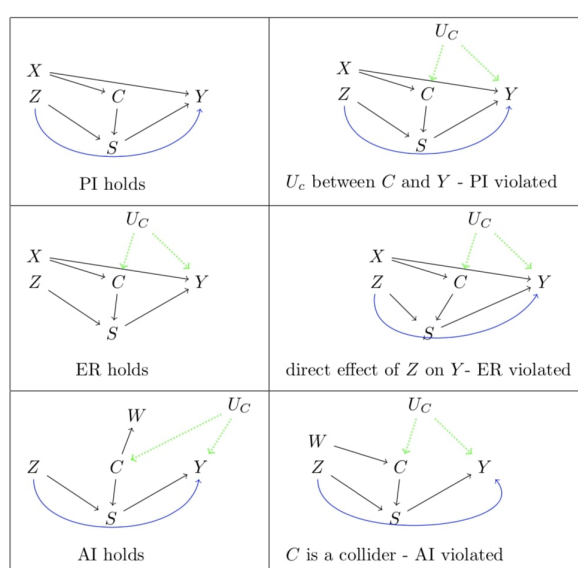
Directed acyclic graph demonstrating when assumptions hold (left columns) and when they are violated (right columns). Here X = baseline covariates, Z = treatment indicator, C = compliance, S = treatment received, W = auxiliary compliance instrument, Y = outcome, U_C = unobserved confounder

Chicken First or Egg First: Examining a Causal Effect of Depressive Symptoms on Metabolic Dysfunctions Sylvia Si Cheng* Si Cheng Stefanie Mayer Alejandro Schuler Rachael Philips Alan Hubbard Elissa Epel Barbara Laraia

Background: Metabolic disorders and depression are comorbid, but their causal relationships are yet to be elucidated. Moreover, effects from previous studies can be controversial due to lacking robustly defined intervention-specific counterfactuals in the light of longitudinal dynamics and racial disparity. We examined whether an increase in early-life depression has a causal effect on adult Metabolic Syndrome (MetS), using Longitudinal Targeted Maximum Likelihood Estimators (LTMLE) powered by machine learning, where shift counterfactuals were supported rigorously.

Methods: 418 women followed in the National, Heart, Lung, and Blood Institute Growth and Health Study (NGHS) over 31 years were included. Depression was measured at age 17 and 19 using the Center for Epidemiologic Studies Depression Scale, adopting 16 as the clinical cutoff score. MetS at age 41 was calculated using the National Cholesterol Education Program Adult Treatment Panel III 2005 version. We examined the causal effect by a marginal OR of having one more early-life depressive episode using LTMLE, with baseline covariates including household income, parental education, perceived stress, and time-varying covariates including stressful events, body mass index (BMI), physical activity, coping strategies, alcohol use and smoking frequency in the past 30 days. Time was discretized into 4 timepoints by year. We also conducted an alternative regression model where the exposure was the total depressive episodes, adjusting for baseline covariates including race.

Results: Analyses using LTMLE are currently ongoing. The logistic regression showed that the OR of one increased event of early-life depressive episodes is 1.06 (95% CI: 0.79, 1.42).

Conclusion: Preliminary results did not detect an effect of early-life depression on metabolic health in adulthood. The LTMLE analyses will help clarify the causal link between depression and metabolic disorders.

Issues of Discretization Scales in Causal Inference with g Methods for Trajectory Data

Jinghao Sun* Jinghao Sun Forrest W. Crawford

Under the Potential Outcome framework, causal inference methods for complex longitudinal data which track each individual repeatedly at different time points, e.g. Robins' g methods, extensively rely on the discretization scales (time interval between two consecutive data points), from the definition of potential outcome notations, causal identification assumptions, to the interpretation of the resulting causal estimands and estimates. However, the influence of such discretization scales on causal inference for trajectory data, whose data generating process is continuous-time, has been poorly understood. Consequently, the choice of discretization in the design and analysis phases of research studies is left unguided and even arbitrary in many situations. In this work, we discuss the issues of discretization, and quantify the influence of discretization scales on the identification bias of the g-formula estimand analytically and using simulations. In particular, we consider linear continuous-time causal data generating processes, and characterize the bias as a function of the number of repeated measurements, the treatment plan of interest, and the magnitude of the causal effect. Our results indicate that the discretization bias exists and can be severe when the number of repeated measurements is small, and suggest choosing denser discretizations when possible.
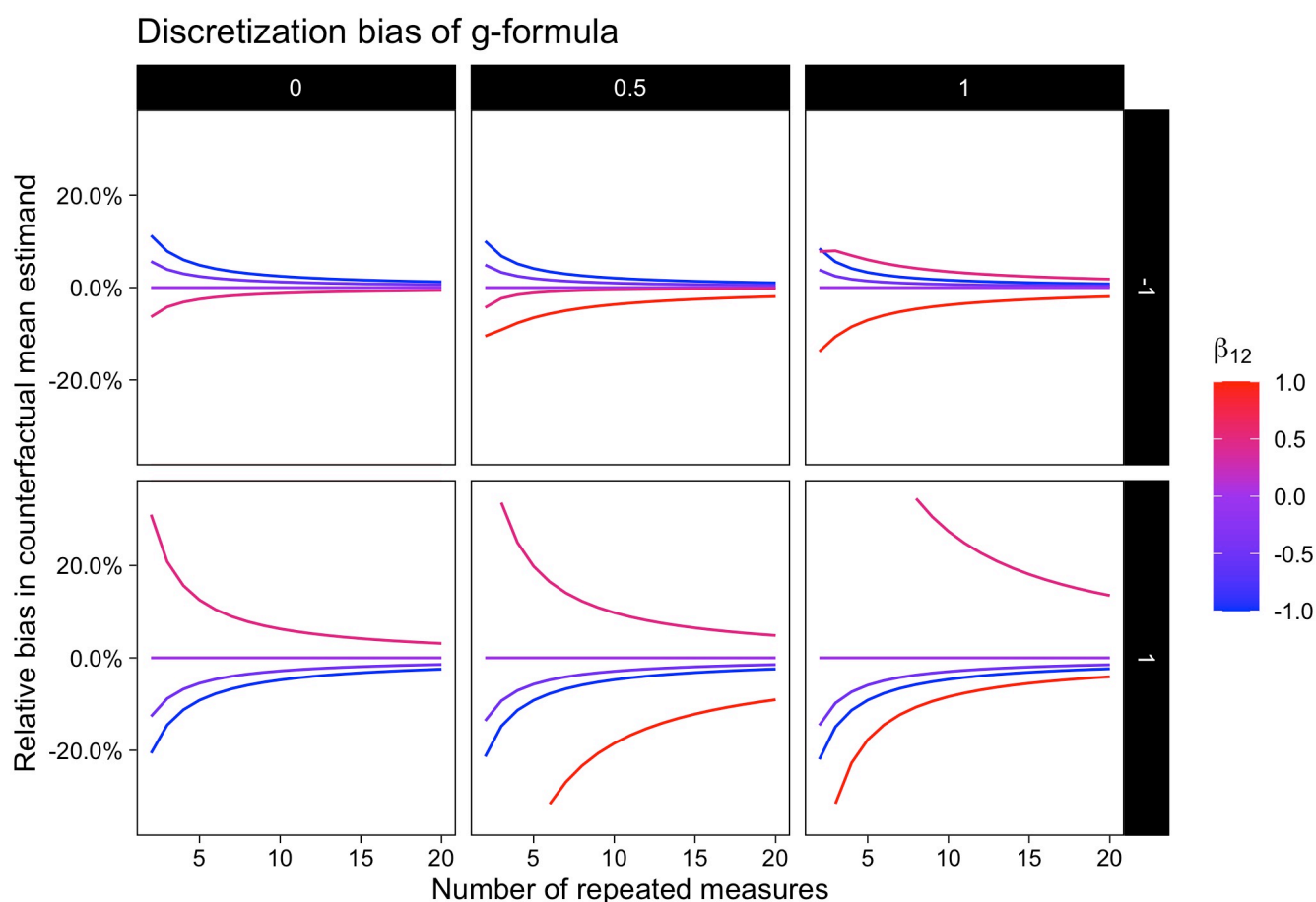
(Each row and column corresponds to different values of β_{21} and β_{11}. β's are parameters for causal DGP.)

Causal Inference

A novel principal stratification analysis of the birthweight paradox Jaffer Zaidi* Jaffer Zaidi

Yerushalmy noted that smoking was associated with a lower infant mortality among low birthweight infants of less than 2500 g. Other investigators have replicated this finding in different studies and now refer to this finding as the birthweight paradox as the direction of association is opposite to what is expected. We revisit a few suggested reasons for the paradoxical associations and previous counterfactual analyses of the problem. We provide a novel principal stratum analysis in which the seemingly paradoxical result largely dissolves. We conclude with future directions of research, including sufficient cause models and sensitivity analyses, that could further shed light on the paradox.

LATEBREAKER

Causal Inference

Causal Inference in Firearm Policy Research: A Scoping Review Camerin Rencken* Camerin Rencken Julia Schleimer Matthew Miller Sonja Swanson Ali Rowhani-Rahbar

Introduction: With over 45,000 firearm deaths in the US annually, there is an imminent need for rigorous firearm policy evaluation; however, existing evidence is mixed. This may be due to variation in the quality and appropriateness of research conducted using necessarily observational data. We conducted a scoping review of firearm policy research in the US with a focus on methodological considerations for causal inference.

Methods: We identified original, empirical articles indexed in PubMed from 1/1/2000-9/1/2021 that examined any of 18 pre-specified classes of firearm policies. Broadly, these policies regulate: 1) who may own, purchase, or possess firearms, 2) firearm sales and transfers, and 3) the use, storage, or carrying of firearms. We extracted key components of articles, including exposure (firearm policies); outcomes; study setting and population; unit of policy enactment and analysis; number of treated units, study design; statistical model; analytical framework; mention of causal identifiability assumptions (e.g., exchangeability); method of confounder selection if applicable; assessment of effect heterogeneity or mediation; bias analysis; and whether the authors stated that their goal was to estimate a causal effect.

Results: We screened 7733 articles, of which 126 were included. So far, we have extracted data from 15 articles. Ten articles (67%) used a composite policy score as the exposure, 3 (20%) mentioned estimating a causal effect, 15 (100%) examined state-level policies, and 8 (53%) used a cross-sectional design. The remaining results will be collated in the next 3 months.

Conclusion: Preliminary analyses suggest pervasive methodological problems in the firearm policy literature. The urgency of this public health crisis demands rigorous and transparent evaluations. Editors, reviewers and researchers should be aware of these methodological shortcomings and adopt higher publication standards.

Long-COVID symptoms and their interference among survivors who contracted infection three or more months ago Mandy S. Hall* Mandy S. Hall Horng-Shiuann Wu

Among the 57 million U.S. COVID-19 cases, it is estimated that 50-80% of survivors have long-COVID symptoms. Severity and daily interference of these symptoms over time remains unknown. Understanding the symptoms is essential in creating symptom management strategies. We investigated the presenting symptoms and their severity and interference among COVID-19 survivors ≥ 3 months after diagnosis. Data came from an on-going descriptive study on randomly sampled survivors from a hospital-based COVID-19 registry. Data were collected via telephone interviews using standardized survey questions for 22 long-COVID symptoms and the Patient-Reported Outcomes Measurement Information System (PROMIS) for fatigue, sleep disturbance, pain, depression, and cognitive function. Descriptive statistics were used to summarize symptoms occurrence, severity, and interference. The sample included 69 survivors who contracted COVID-19 an average(SD) of 8.8(2) months ago. Survivors' mean age was 49.8(17.7) years, 55% were male, and 74% were White. Forty-five reported ≥ one symptom [mean=6.4(3.5)]. Fatigue (43%), pain (36%), sleep disturbances (31%), difficulty remembering (29%), and depression (26%) were common symptoms. On scales of 1-9 and 0-9 (9 being the worst), the mean severity and daily interference of fatigue was 6.6(1.7) and 5.5(2.6), pain was 6.4(2.2) and 5.5(2.5), difficulty remembering was 6.3(2.3) and 5.5(2.8), depression was 6.3(2.0) and 5.3(2.6), and sleep disturbance was 6.2(2.2) and 5.1(3.0), respectively. Mean PROMIS T score was 61.1(10.3) for fatigue, 60.6(7.9) for sleep disturbances, 59.4(6.2) for depression, 53.4(10.2) for pain, and 38.9(6.3) for cognitive function; all worse than the US general population means of 50. Fatigue, pain, sleep disturbances, difficulty remembering, and depression are severe and interfering among COVID-19 survivors. Symptom management strategies are needed as the severity and burden of long-COVID symptoms can lead to disability in survivors.

Transmission prevention behaviors in households with SARS-CoV-2 cases Rebecca Rubinstein* Rebecca Rubinstein Wenwen Mei Caitlin Cassidy Jessica Lin Katie R. Mollan

Background: Households are ideal for transmitting SARS-CoV-2 given the challenges of distancing and wearing masks at home. Few studies have explored which household contacts are most likely to engage in behaviors that interrupt transmission or household-level structural barriers, including household living density.

Methods: We analyzed participant-reported data from the UNC COVID-19 Household Transmission Study, a community cohort in central North Carolina. Household contacts' behaviors were compared at cohort entry (median of 6 days from symptom onset of the index case) and Day 14 of observation using the Yang modification of Obuchowski's test for changes in paired binary data. Covariates associated with household contact mask use at home between Days 7-14 of cohort participation were analyzed using bivariate generalized estimating equations, with households handled as clusters and missing data excluded.

Results: Between April-October 2020, n=204 household contacts of 100 indexes were enrolled. Transmission risk behaviors decreased from entry to Day 14 (Figure 1). About 1 in 4 household contacts reported any mask use inside the home (Day 7: 24%; Day 14: 26%). Masking at home (between Days 7-14) was more likely among households with ≥6 members occupying 3 or fewer rooms (prevalence ratio [PR]=1.85, 95% CI 0.89, 3.85), Black, Indigenous, and People of Color (BIPOC), including Latinx participants compared to White participants (PR=1.97, 95% CI 1.07, 3.62), those with ≥4 days of symptoms between Days 7-14 (PR=1.87, 95% CI 0.97, 3.61), and those who observed or lived with an index case masking at home (PR=2.03, 95% CI 1.23, 3.35).

Conclusions: Masking in households affected by SARS-CoV-2 was infrequent and did not increase in the first weeks after diagnosis of a positive case. However, BIPOC-identifying participants and those with symptoms were more likely to mask, and masking clustered within households.
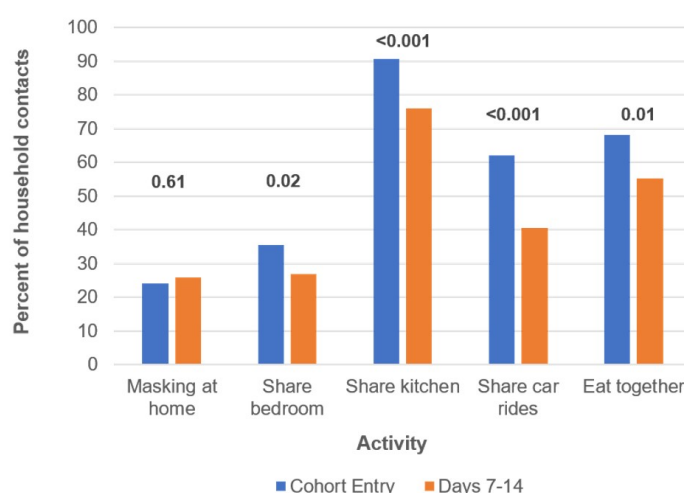
Figure 1. Proportion of household contacts that reported any mask use at home, sharing a bedroom, sharing a kitchen, sharing car rides, or eating with the index case in the 7 days prior to cohort entry and between days 7-14 of cohort participation. Values above bars represent p-values for each comparison.

Investigating Changes in Incidence and Severity of Pediatric Appendicitis During the COVID-19 Pandemic: An Interrupted Time-Series Analysis Francesca del Giorgio* Francesca del Giorgio Merieme Habti Joanna Merckx Jay S. Kaufman Jocelyn Gravel Nelson Piché Esli Osmanlliu Olivier Drouin

Since the onset of the COVID-19 pandemic, there have been concerns over potential delays in seeking medical attention for acute pediatric conditions, such as appendicitis. This study aimed to investigate whether there were changes in incidence and outcomes of pediatric appendicitis during the first year of the COVID-19 pandemic compared to previous years.

This was an interrupted time-series study using the computerized databases of the two tertiary care pediatric hospitals in Montreal, Quebec, with a combined census of 160 000 patients visits per year. Segmented Poisson regression adjusted for underlying baseline trend, seasonality, and site was used to estimate the change in bi-monthly incidence of children diagnosed with appendicitis at the onset of the COVID-19 pandemic (March/April 2020) and throughout the first 14 months of the pandemic (March 2020-May 2021), relative to the 4-year pre-pandemic trend at both hospitals (January 2016 to February 2020). In secondary analyses, change in average length of hospital-stay (LOS, measured via linear regression), and change in risk of perforated appendix and need for surgical drainage (measured via binomial regression) were used to quantify changes in outcome of patients relative to previous years.

From the regression analysis, there was a 14% increase in incidence of appendicitis cases at the onset of the pandemic (Incidence Rate Ratio (IRR)= 1.14, 95% CI= 1.01 ; 1.28). This increase remained stable throughout the first year of the pandemic (Figure 1). In secondary analyses, there was a decrease in average LOS during the pandemic (0.43 day decrease, 95% CI=0.14, 0.72), but no evidence of change in risk of perforated appendix (Risk Ratio= 0.96, 95% CI= 0.77; 1.20) or of requiring surgical drainage (Risk Ratio= 0.97, 95% CI= 0.71; 1.31).

These findings suggest no significant delays in presentation for appendicitis cases, but potential increase in triggers or changes in hospitalization use during the pandemic.
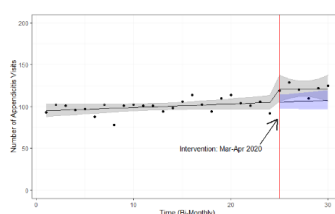
COVID-19 prognostic factors as predictors of delayed healthcare service among adults ≥ 50 years during the pandemic: 2006-2020 Health and Retirement Study Hind A. Beydoun, PhD, MPH* Hind Beydoun May A. Beydoun Brook T. Alemu Jordan Weiss Sharmin Hossain Rana S. Gautam Alan B. Zonderman

Background: Caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), the coronavirus disease 19 (COVID-19) was declared a global pandemic by the World Health Organization as of March 11, 2020. To date, few studies have examined the health behavioral impact of the COVID-19 pandemic. The purpose of this longitudinal study was to examine the relationship of established COVID-19 prognostic factors, with a focus on cardiometabolic risk factors and chronic conditions, with self-reported delayed healthcare services among adults, ≥50 years, in the United States.

Methods: Secondary analyses were performed using data from the 2006-2018 Health and Retirement Study (HRS) linked to the 2020 HRS Covid-19 Project. Socio-demographic, lifestyle and health characteristics were evaluated in relation to delayed surgical and/or non-surgical healthcare using logistic regression and machine learning algorithms.

Results: In fully adjusted logistic regression models, having 1-2 cardio-metabolic risk factors (vs. none) was associated with increased odds of delays in surgical and/or non-surgical healthcare services (OR=1.62, 95%CI: 1.07, 2.46) and non-surgical healthcare services (OR= 1.67, 95%CI: 1.10, 2.56). Being female, having College degree or higher, past smoker (vs. non-smoker) status, alcohol consumption (1-3 days per month vs. abstainer), fair or poor self-rated health and 1-unit increase in depressive symptom score were identified as key predictors of delayed surgical and/or non-surgical healthcare services. Super Learner modeling was better able to predict surgical as opposed to non-surgical delays in healthcare services.

Conclusions: Delays in surgical and non-surgical healthcare services may have distinct COVID-19 prognostic factors as predictors, with non-surgical delays more frequently observed among individuals with 1-2 cardiometabolic risk factors or chronic conditions. Further studies are needed to elucidate biopsychosocial mechanisms by which COVID-19 prognostic factors might influence utilization of healthcare services.

The Pattern of SARS-CoV-2 Seropositivity and Its Persistence among College Students Chen Chen* Chen Chen Molly Rosenberg Jonathan T. Macy Ming Li Christina Ludema

Background:

Much research has been done to study the persistence of SARS-COV-2 seropositivity (i.e., antibody positive), but few focused on college students.[1-7] Yet, they are more likely to cause community outbreaks and are within the age group where the highest percentage of cases were reported.[8-9] Therefore, a survey on college students can help us: (a). better understand SARS-COV-2 seropositivity persistence by providing data with this understudied group, (b) more accurately estimate the number of positive SARS-CoV-2 cases on campus, for it shows both diagnosed and undiagnosed cases, and (c) improve universities' virus control policies, as seropositivity protects students against reinfections and our results can thus be used to approximate their future infection likelihood.

Objective:

We aim to assess whether time since diagnosis of infection and initial symptomatic status are associated with seropositivity among college students.

Method:

We performed a longitudinal study to assess the seropositivity of SARS-CoV-2 in a sample population of Indiana University, Bloomington. A standard baseline questionnaire was used to collect the data for demographics, COVID-19 exposure, and RT-PCR testing history. Four follow-up surveys collected longitudinal data until the endline test visit. Two in-person point-of-care tests were used to collect seroconversion status (baseline and endline antibody test visits during September and November 2020). We used the t-test and Pearson Chi-square test to evaluate the persistence of the SARS-CoV-2 antibody and to estimate the modification effect by symptomatic status.

Result:

Overall, 1076 students completed baseline antibody test visits, and 850 completed endline tests. There were 131 samples who self-reported having a positive RT-PCR result of SARS-CoV-2: 42 were seropositive and 97 were seronegative. The means (SD) of the time interval between RT-PCR tests and antibody tests were significantly different (p-value = 0.02), which were 45 (31) days for the seropositive group and 61 (44) days for the seronegative group, respectively. 35.7% of students who were seropositive at baseline remained seropositive at endline. Additionally, there was no modification effect of symptomatic status on seroconversion status at the endline (OR = 2.04, 95% CI: 0.22, 17.65).

Conclusion:

A longer testing interval between positive RT-PCR and the antibody test resulted in a lower likelihood of seropositive results, regardless of the initial symptomatic status. Therefore, vaccination of SARS-CoV-2 and control strategies are strongly recommended for college students without infection, and also for those previously infected with SARS-CoV-2.

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Insecurity, social support, and family relationship in association with mental health disparities among U.S. adults during the COVID-19 pandemic Kexin Zhu* Kexin Zhu Siyi Wang Yihua Yue Joanne Zhang Ella Smith Dasang Dolma Eileen Wang Divya Goyal Jie Zhang Beth Smith Lina Mu

Objective: To examine the associations of insecurity (concerns about food, health insurance, or money), social support, and change in relationship with parents, children, or the significant other with mental health disparities.

Methods: We conducted a cross-sectional online survey between May-August 2020, recruiting 3952 adults in the US. Anxiety, depression, stress, and post-traumatic stress disorder (PTSD) were assessed by the Generalized Anxiety Disorder 7-item scale, the Patient Health Questionnaire-9, the Perceived Stress Scale 4, and the Primary Care PTSD Screen, respectively. Social support was measured by the Oslo Social Support Scale. We used multivariable logistic regression to examine the associations of insecurity, social support, and relationship change with mental health outcomes. We also performed stratified analyses by age, racial groups, and gender.

Results: The odds of mental health symptoms were higher among participants who had any worries about money, health insurance, or food compared to those who did not (anxiety OR=3.50, 95% CI 3.01-4.06; depression OR=3.01, 95% CI 2.60-3.49; stress OR=3.03, 95% CI 2.62-3.51; PTSD OR=2.92, 95% CI 2.41-3.53). Poor social support was associated with mental health symptoms (e.g., anxiety OR=1.61, 95% CI 1.21-2.14), and adults aged 18-26 years (OR=5.53, 95% CI 1.87-16.40) and those who identified as an underrepresented minority (UMR: Black, Hispanic, Native American, American Indian) (OR=3.65, 95% CI 1.55-8.58) were more susceptible. Participants who had changes (i.e., worse, better, mixed) in relationships with parents, children, or the significant other had worse mental health outcomes; the associations were stronger for UMRs and males.

Conclusion: Insecurity, poor social support, and worse family relationships were associated with worse mental health outcomes, with younger adults and UMRs being more affected. Targeted interventions to reduce disparities in COVID-19-related mental health problems are needed.

The development of a social vulnerability index for infectious disease emergencies in Canada Vinyas Harish* Vinyas Harish Amin Kharaghani Emmalin Buajitti Meghan O'Neill Muhammad Mamdani Kamran Khan Ashleigh Tuite Laura C. Rosella

Vulnerability to infectious disease emergencies arises at the intersection of various social determinants of health. Our objective was to develop a bespoke social vulnerability index (SVI) that can be deployed for infectious diseases emergencies in Canada.

Thirteen variables across five domains (socioeconomic status, household composition, minority status/language, housing/transportation, and employment) from the 2016 Census were used to create the SVI. Following Flanagan *et al.*'s (2011) rank-based approach, we converted the sum of the ranks across domains into percentile ranks at the forward sortation area (FSA) level. FSAs contain an average of 8000 households. We validated the SVI using publicly available data from Ontario. Moran's I was used to test for spatial autocorrelation in cases, hospitalizations/deaths, and the percentage of the population vaccinated as of March 28, 2021. The Lee test was used to test for spatial associations between the constructed SVI and the above COVID-19 metrics.

We generated the SVI for 1620 FSAs across the 10 Canadian provinces. Social vulnerability was concentrated in major urban areas such as the Greater Toronto Area (GTA). COVID-19 cases, hospitalizations/deaths, and vaccinations were spatially clustered in Ontario (Moran's I statistics 0.447-0.767, p<2.2e-16). There was a positive correlation between the overall SVI percentile and COVID-19 cases and hospitalizations/death rates in Ontario as a whole and within the GTA (Figure). There was a consistent, moderate spatial association between our SVI and cases and hospitalizations/deaths in both Ontario as a whole and in the GTA (L statistic 0.380-0.518, p<2.2e-16).

We developed a novel and comprehensive measure of social vulnerability for infectious diseases. This index has implications for not only supporting immediate response operations and pandemic preparedness, but also as a research tool to better characterize the impact of emergencies across vulnerable populations.

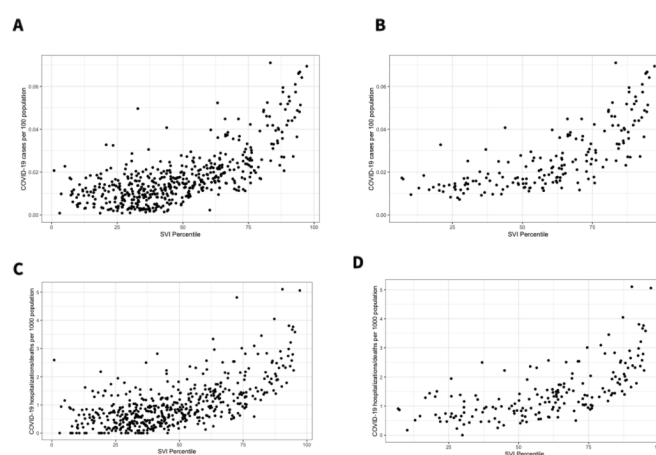**Figure:** *Scatterplots of the overall social vulnerability index against COVID-19 cases across all Ontario forward sortation areas (FSAs, panel A), cases in the Greater Toronto Area (GTA, panel B), hospitalizations/deaths across all Ontario FSAs (panel C), hospitalizations/deaths in the GTA (panel D). COVID-19 metrics are as of March 28th 2021. Note that the vertical axis scales in panels A and B are different than C and D.*

Financial hardship during COVID-19, coping through unhealthy behaviors, and the mediating role of resilience among a nationally representative sample of US Latinos: COVID-19's Unequal Racial Burden (CURB) Survey, 2020-2021 Stephanie Quintero* Stephanie Quintero Paula Strassle Stephanie Ponce Anna María Nápoles Anita Stewart

Background. Our objective was to examine the effect of financial hardship during COVID-19 on unhealthy behaviors and whether resiliency mitigates that effect among US Latinos.

Methods. We used the COVID-19's Unequal Racial Burden (CURB) online survey administered in English and Spanish to 5,500 adults (≥18 yo) from all major US racial/ethnic groups from 12/2020-2/2021. Eligible participants were proximity matched and weighted to be nationally representative within each racial/ethnic group. This analysis included 1,000 Latinos (500 English and 500 Spanish-speaking) and 113 multiracial Latinos. Financial hardship was defined as the number of hardships reported (e.g., having enough money to pay for healthcare), range 0-6. Alcohol consumption, smoking (cigarette and vaping), and unhealthy eating were dichotomized by frequency of use in the past month: any (alcohol/smoking) and at least once a week (unhealthy eating). Resiliency was captured using the Brief Resilience Scale. The association between financial hardship and unhealthy behaviors was estimated using multivariable logistic regression; interaction terms were used to assess whether resiliency mitigated this effect.

Results. Half of all Latinos reported financial hardship (substantial [4+]: 11.9%; some [2-3]: 20.4%; a little [1]: 16.8%); 15.7% had high resilience. Greater financial hardship was associated with smoking (OR 1.58, 95% CI 1.34-1.86), but did not impact alcohol consumption (OR 1.07, 95% CI 0.93-1.23) or unhealthy eating (OR 1.09, 95% CI 0.95-1.26). Resiliency didn't mitigate the effect of financial hardship on smoking, p>0.99, Fig.

Conclusion. Financial hardship due to COVID-19 was highly prevalent among US Latinos and was associated with more frequent smoking. Resiliency did not mitigate the effects of financial hardship on smoking in US Latino adults. Financial hardship is a complex experience and resiliency alone may not protect against tobacco product use in the face of such hardship among Latinos.

Overall Effect
1.58 (95% CI 1.34-1.86)

High Resilience
Normal Resilience
Low Resilience

p=0.998

0.1   1   10

Effect of Financial Hardship* on Any Cigarette or Vape Use OR (95% CI)

*Average effect of increasing financial hardship (e.g., none to a little; a little to some)
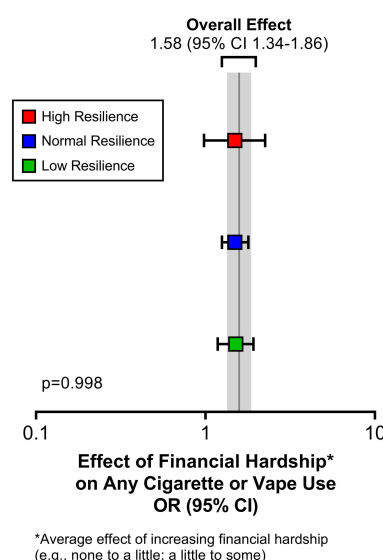
Association of Inpatient Statin Use with Inpatient Deaths of People with COVID-19 Admitted at Northwestern Medicine Health System Adovich Rivera* Adovich Rivera Omar Al-Heeti Janna Lynn Williams Matthew Feinstein Chad Achenbach Babafemi Taiwo Lucia Petito

Background: Observational studies on inpatient statin use and mortality in hospitalized COVID-19 patients have yielded inconsistent results. Differences may be due to statistical considerations (e.g., covariate imbalance, model misspecification) or issues from retrospective use of electronic health records (EHR) (e.g., selection bias, immortal time bias).
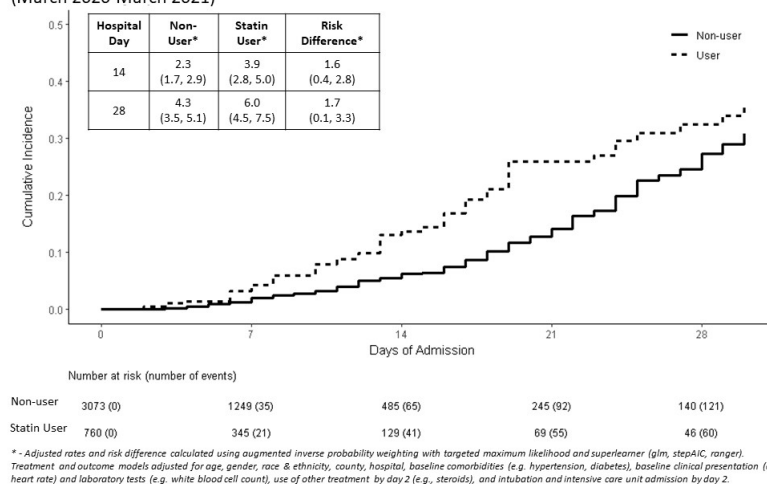
Objective: To estimate the association of inpatient statin initiation with inpatient death among statin-naive individuals admitted for COVID-19 at a large, regional health system in Chicago.

Method: We analyzed EHR from Northwestern Medicine Health System in Chicago (Mar '20-Mar '21), comparing rates of inpatient deaths at days 14 and 28 between inpatient initiators and never-users. Eligible individuals were ≥40 years old, admitted and alive for ≥48 hours, tested positive for COVID-19 in the 30 days before to 7 days after admission, and not on statins prior to admission. Inpatient use was defined as statin initiation within 48 hours of admission. We used augmented inverse probability weighting with targeted maximum likelihood estimation with ensemble learning to improve covariate balance and estimate the risk difference (RD) conditional on survival to 48 hours post-admission.

Results: This cohort included 3,833 adults (initiators: 760, non-initiators: 3073) in the analysis. Statin initiators tended to be older (60.4 vs 60.0 years), have comorbidities (e.g., diabetes 54% vs 27%), and longer median lengths of stay (6.4 vs 5.9 days) than non-users. Adjusted analysis showed a higher mortality risk (95% CI) in statin initiators than non-initiators for day 14 (RD: 1.6%, 95%CI: 0.4-2.8) and day 28 (RD: 1.7%, 95%CI: 0.1-3.3).

Conclusion: We did not detect lower inpatient death rates among statin initiators compared to non-initiators. Elevated risk may be due to residual unadjusted confounding related to worse baseline frailty of those who received statins rather than an actual adverse effect of statins on outcomes.

Figure 1. In-Patient Deaths among Admitted for COVID-19, Northwestern Medicine Health System (March 2020-March 2021)

Hospital Day	Non-User*	Statin User*	Risk Difference*
14	2.3 (1.7, 2.9)	3.9 (2.8, 5.0)	1.6 (0.4, 2.8)
28	4.3 (3.5, 5.1)	6.0 (4.5, 7.5)	1.7 (0.1, 3.3)

Number at risk (number of events)

Non-user	3073 (0)	1249 (35)	485 (65)	245 (92)	140 (121)
Statin User	760 (0)	345 (21)	129 (41)	69 (55)	46 (60)

* - Adjusted rates and risk difference calculated using augmented inverse probability weighting with targeted maximum likelihood and superlearner (glm, stepAIC, ranger). Treatment and outcome models adjusted for age, gender, race & ethnicity, county, hospital, baseline comorbidities (e.g. hypertension, diabetes), baseline clinical presentation (e.g. heart rate) and laboratory tests (e.g. white blood cell count), use of other treatment by day 2 (e.g., steroids), and intubation and intensive care unit admission by day 2.

Home or hospital? An observational study of what affects the place of death of people with COVID-19 Isaac Núñez* Isaac Núñez

Objectives: An increased number of out of hospital deaths has been reported during peak COVID-19 pandemic periods. Aside from COVID-19 severity, which variables are related to being hospitalized have not been properly studied. This study aimed to determine the association between several variables and dying out of a hospital due to COVID-19.

Methods: A case-control study was conducted using COVID-19 open data and the death registry from Mexico City, from March 2020 until February 2021. A causal model was pre-specified to identify the minimum adjustment set. Afterwards, adjusted logistic regressions were performed to determine strength of association with odds ratios (OR) between exposures of interest and dying out of a hospital due to COVID-19 (the outcome).

Results: Among 61 112 people who died due to COVID-19, 8080 died out of a hospital (cases). Older age (OR 3.49 age 90 vs 60), male sex (OR 1.18), later epidemiological week (OR 2.1 week 60 vs 40), and higher bed occupancy (OR 2.68 90% vs 50% occupancy) were associated with increased odds of the outcome (Figure 1). Conversely, having a comorbidity was associated with decreased odds (for example, OR 0.56 for having cancer).

Conclusion: These results are consistent with previous studies showing lack of hospital space related to less access to care. Older age could confer different patient wishes or less ability to look for healthcare. Lower odds seen among those with comorbidities could be due to previous healthcare contact and different attitudes towards it. Nonetheless, an unmet need for end-of-life care in out of hospital patients exists, and should be addressed.
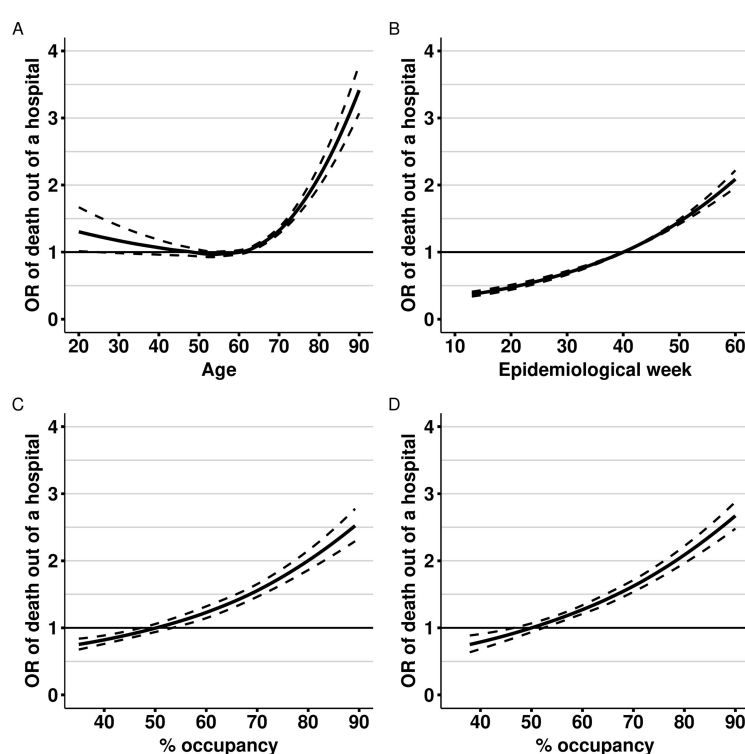
Association Between K-12 School Mask Policies and School-Associated COVID-19 Outbreaks
Megan Jehn* Megan Jehn J Mac McCullough Ariella P. Dale Matthew Gue Brian Eller Theresa Cullen Sarah Scott

CDC recommends universal indoor masking by students, staff members, faculty, and visitors in kindergarten through grade 12 (K–12) schools, regardless of vaccination status, to reduce transmission of SARS-CoV-2, the virus that causes COVID-19. Schools in Maricopa and Pima Counties, which account for >75% of Arizona's population, resumed in-person learning for the 2021–22 academic year during late July through early August 2021. School districts in both counties implemented variable mask policies at the start of the 2021–22 academic year. The association between school mask policies and school-associated COVID-19 outbreaks in K–12 public noncharter schools open for in-person learning in Maricopa and Pima Counties during July 15–August 31, 2021, was evaluated. A school was considered to have a mask requirement if all persons, regardless of vaccination status, were required to wear a mask indoors in school. A school-associated outbreak was defined as the occurrence of two or more laboratory-confirmed COVID-19 cases among students or staff members at the school within a 14-day period and at least 7 calendar days after school started, and that was otherwise consistent with the Council for State and Territorial Epidemiologists 2020 outbreak definition and Arizona's school-associated outbreak definition. Among the 999 (96.0%) schools included in the analysis, 210 (21.0%) had an early mask requirement, 309 (30.9%) had a late mask requirement enacted a median of 15 days after school started (interquartile range = 9–17 days), and 480 (48.0%) had no mask requirement. In the crude analysis, the odds of a school-associated COVID-19 outbreak in schools with no mask requirement was 3.7 times higher than those in schools with an early mask requirement (odds ratio [OR] = 3.7; 95% CI = 2.2–6.5). After adjusting for school county, enrollment size, grade levels present, Title I status, and 7-day COVID-19 case rate in the school's zip code during the first week of school, the odds of a school-associated COVID-19 outbreak in schools without a mask requirement were 3.5 times higher than those in schools with an early mask requirement (OR = 3.5; 95% CI = 1.8–6.9).

Living Alone and the Risk of Mental Health Problems During the COVID-19 Pandemic: An Electronic Healthcare Records and Longitudinal Study Analysis Kishan Patel* Kishan Patel Eoin McElroy Emily Herret Kathryn Mansfield Praveetha Patalay

Background: The COVID-19 pandemic and the associated viral suppression measures aimed to reduce social contact would have had different impacts on different groups of people. For example, the pandemic has changed the context of what it means to live alone, and the gap between lone and non-lone household mental health may have changed during the pandemic.

The use of both electronic healthcare records (EHR) and longitudinal studies offers a unique opportunity to quantify the effects, while triangulating evidence from different sources of data, of the pandemic on mental health outcomes among those living alone, compared to those not living alone, in the UK.

Methods: EHR and longitudinal studies were analysed in a co-ordinated approach, using the best methods for each of the different data sources.

The EHR analytical sample comprised of adults registered in English primary care. With the approval of NHS England, interrupted time series analyses were conducted within the OpenSAFELY platform. Separate analyses were carried out for each mental health outcome (depression, anxiety, self-harm, obsessive compulsive disorder, eating disorders, serious mental illness) and stratified by living alone status.

Data were also drawn from 10 UK longitudinal studies. Adjusted linear regression models were used to examine the relationship between living alone status and psychological distress before the pandemic, and at three timepoints during the pandemic. Analyses were conducted separately for each longitudinal study and pooled using a random effects meta-analysis.

Results from the EHR and longitudinal analytical samples are discussed together.

Findings: Early findings indicate a worsening of mental health over the course of the pandemic for those living alone. These results will have implications for policy, including the need for specific investment for support for those in lone households to mitigate the effects of the pandemic and measures to reduce isolation for this specific group.

Examining the role of distance to hospital services and county-level COVID-19 mortality
Gabriel Benavidez* Gabriel Benavidez Anja Zgodic

Introduction: Many individual-level factors have such as chronic diseases have been shown to be associated with COVID-19 mortality. However, there are likely several factors outside the control of the individual that are also likely to influence negative COVID-19 outcomes. Here we examine the association between county distance to the nearest hospital and COVID-19 mortality. **Methods**: Using data from the Johns Hopkins Coronavirus Resource Center we calculated county-level COVID-19 mortality rates for 96% of U.S. counties. We geocoded hospital facilities from the healthcare facilities database from the United States Department of Agriculture. We then calculated the straight-line distance in miles from population-weighted county centroids to the nearest hospital. Specialized hospitals (i.e., cancer centers and children's hospitals) were excluded assuming that they are not available to the general public. County sociodemographic characteristics were taken from the American Community Survey 5-year estimates. We then examined the relationship between distance to the nearest hospital and COVID-19 mortality rate per 100,000 using linear mixed-effects models with a state-level intrinsic conditional autoregressive random intercept to account for the spatial dependence and state-to-state variability. **Results**: A total of 3,025 counties were included in this analysis. Average distance to the nearest hospital was approximately 12 miles. After adjusting for race, rurality, car ownership, and proportion of residents lacking health insurance we found no significant association between hospital distance and county COVID-19 mortality (-0.03; 95% CI: -0.28,0.22). However, we did observe a significant association between lack of health insurance and COVID-19 mortality (5.27; 95% CI: 4.60,5.94). **Conclusion**: Distance to care may not be the most appropriate measure to use when attempting to examine healthcare access or utilization. Socioeconomic factors may play a stronger role in determining true access to healthcare, especially during the COVID-10 pandemic.

Identifying Symptom Clusters of Acute COVID-19 Illness and their Association with Long COVID Elizabeth Slocum* Elizabeth Slocum Yanmei Xie Jana L. Hirschtick Michael R. Elliott Patricia McKane Laura E. Power Nancy L. Fleischer

Background: A significant proportion of COVID-19 patients continue to experience persistent symptoms related to COVID-19 infection, referred to as Long COVID. In this study, we investigate the association between acute COVID-19 symptom clusters and Long COVID.

Methods: We used a symptomatic subset of a population-based probability survey of Michigan adults with COVID-19 onset between 6/1/20-11/15/20 (n=715). Symptom clusters were identified using latent class analysis (LCA) on acute self-reported symptoms during the first two weeks of illness, taking into account the complex sampling design. Goodness of fit indices was evaluated by considering Bayesian information criteria and entropy. Posterior probabilities for the final LCA model were used to assign participants to classes. Long COVID was defined as persistent symptoms ≥ 90 days post-onset. We used modified Poisson regression to produce adjusted prevalence ratios (aPRs) to assess association between symptom clusters and Long COVID, adjusting for sociodemographic factors.

Results: We identified five acute symptom clusters: 1) no distinct symptom pattern (n=105), 2) predominance of fatigue (n=241), 3) flu-like with fever (n=158), 4) flu-like without fever (n=71), and 5) respiratory and gastrointestinal symptoms (n=140). Compared to adults with no distinct symptom pattern, adults with respiratory and gastrointestinal symptoms (aPR=4.90, 95% CI: 2.44-9.83), flu-like symptoms with fever (aPR=2.31, 95% CI: 1.13-4.71), and flu-like symptoms without fever (aPR=3.38, 95% CI: 1.69-6.77) had increased prevalence of Long COVID.

Conclusions: This study identified distinct symptom clusters of acute COVID-19 illness and their associations with Long COVID. Understanding the landscape of acute COVID-19 illness may help identify clinical predictors of Long COVID among COVID-19 patients.

Associations between diabetes and COVID-19 severity within a cohort of U.S. Veterans: an application of inverse probability weighting to address potential collider bias Andrea R. Titus* Andrea Titus Rania Kanchi Samrachana Adhikari David C. Lee Aaron Baum Lorna E. Thorpe Mark D. Schwartz

Prior studies suggest that individuals with a history of diabetes mellitus (DM) are at increased risk for worse COVID-19 outcomes. However, these studies often face methodological challenges, in part due to differential uptake of COVID-19 testing. For example, unequal probabilities of testing among individuals with/without DM may lead to unequal probabilities of outcome ascertainment. On the other hand, restricting a study to tested individuals may introduce selection bias, if testing is a collider on the causal pathway between DM and COVID-19 severity. We used data from a pre-existing national cohort of U.S. Veterans (n=3,360,588) to explore associations between a history of Type II DM and COVID-19 outcomes (hospitalization, ICU stay, mechanical ventilation, and death). In our primary analysis, we used a nested sample design with inverse probability-weighted logistic regression, restricting the sample to Veterans with a positive COVID-19 test (to address ascertainment bias) and weighting the nested subsample to be representative of the full cohort (to address selection bias). We compared confounder-adjusted estimates from the primary analysis (n=178,042) to adjusted, unweighted estimates from the subsample and adjusted, unweighted estimates from the full cohort, to shed light on potential bias under alternative study designs. Within the weighted subsample, DM was associated with higher odds of COVID-19 hospitalization (AOR=1.74; 95% CI=1.67,1.82), ICU stay (AOR=1.92; 95% CI=1.80,2.05), mechanical ventilation (AOR=2.37; 95% CI=2.14,2.62), and death (AOR=1.38; 95% CI=1.29,1.47). AORs from the weighted subsample were smaller than AORs from the unweighted subsample or the full cohort (see figure). We found that DM was associated with higher odds of severe COVID-19 outcomes within a cohort of U.S. veterans. The changes in point estimates across models underscores the importance of considering bias in COVID-19 studies, given unequal probabilities of COVID-19 testing.

Adjusted ORs for associations between diabetes and COVID-19 outcomes
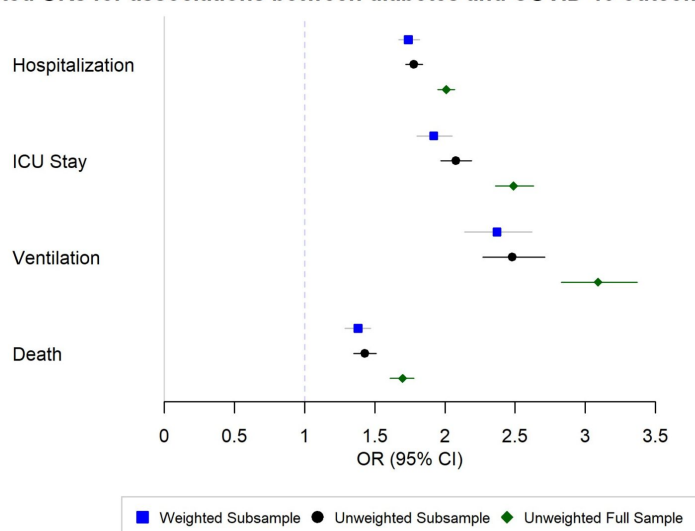
Obesity and weight change during the COVID-19 pandemic in children and adults: a systematic review and meta-analysis Laura Anderson* Laura Anderson Yulika Yoshida-Montezuma Jayati Khattar Vanessa De Rubeis Lauren Griffith Lawrence Mbuagbaw

Many obesity risk factors have increased during the COVID-19 pandemic, including physical inactivity, poor diet, stress, and poverty. The aim of this systematic review was to evaluate the impact of the COVID-19 pandemic, and associated lockdowns or restrictions, on weight change in children and adults. We searched 5 databases from January 2020 to November 2021. We included only longitudinal studies with measures from before and during the pandemic that evaluated the change in body mass index (BMI) or BMI z-scores for children, weight, or the prevalence of obesity. Random effects meta-analyses were conducted to obtain pooled estimates of the mean difference in outcome. Subgroups were evaluated for age, and diabetes or obesity at baseline. The certainty of evidence was assessed using the grading of recommendations assessment, development and evaluation (GRADE) approach. A total of 74 studies were included (1,081,498 total participants). In children, the pooled mean difference for BMI z-scores was 0.13 (95% C1: 0.10, 0.17; 20 studies), for weight it was 1.65 kg (95% CI: 0.40, 2.90; 9 studies) and the prevalence of obesity increased by 2% (95% CI: 1%, 3%; 12 studies). In adults, the pooled mean difference for BMI was 0.38 kg/m^2 (95% CI: 0.21, 0.55; 26 studies), for weight it was 0.93 kg (95% CI: 0.54, 1.33; 28 studies), and the prevalence of obesity increased by 1% (95% CI: 0%, 3%; 11 studies). Considerable heterogeneity was observed, and the certainty of evidence was very low. Pooled estimates suggested greater weight and BMI gain for children and people with obesity or diabetes at baseline. The first year of the COVID-19 pandemic was associated with small but potentially clinically significant increases in weight gain, BMI, and increased prevalence of obesity in both children and adults. Increases were greater in children, and in people with obesity or diabetes and targeted prevention interventions may be warranted.

Risk of herpes zoster following mRNA COVID-19 vaccine administration Ana Florea* Ana Florea Jun Wu Lei Qian Bruno Lewin Lina Sy Hung Fu Tseng

Introduction: Herpes zoster (HZ), or shingles, is caused by reactivation of varicella zoster virus. As the newly developed mRNA COVID-19 vaccines received emergency use authorization and were administered under real-world conditions, adverse events following immunization, including HZ, were reported post-vaccination. We conducted a cohort study to evaluate the association between mRNA COVID-19 vaccination and HZ among Kaiser Permanente Southern California (KPSC) members. **Methods**: The vaccinated cohort consisted of eligible KPSC members who received ≥1 dose of mRNA COVID-19 vaccine (hereafter, Moderna or Pfizer) between 12/2020 and 05/2021. Eligible unvaccinated individuals were randomly selected and matched 1:1 to the vaccinated cohort on age and sex and assigned an index date (vaccination date of vaccinated cohort). Incident HZ cases occurring within 90 days after the index date were identified by ICD codes and antiviral medications. Cox proportional hazards models were used to estimate adjusted hazard ratios (aHR) with 95% confidence intervals (CIs) comparing HZ incidence between the vaccinated and the unvaccinated. HRs were also estimated by age and history of zoster vaccine. **Results**: Our cohort included 1,052,362 Moderna recipients, 1,055,461 Pfizer recipients, and 1,047,779 matched comparators. The aHR for HZ up to 90 days after the 1st dose in Moderna-vaccinated vs. unvaccinated individuals was 1.06 (95% CI: 0.93-1.20), and 0.99 (0.86-1.15) for Pfizer. The aHR for HZ up to 90 days after the 2nd dose in Moderna-vaccinated vs. unvaccinated individuals was 1.12 (1.03-1.22), and 1.10 (1.01-1.20) for Pfizer. In those aged ≥50 years not vaccinated with zoster vaccine, aHR was also increased after the 2nd dose of Moderna (1.12 [1.01-1.24]) and Pfizer (1.11 [1.00-1.24]) vaccine vs. unvaccinated. **Conclusions**: Our findings suggest a 10% increase in HZ risk after a 2nd dose of Moderna or Pfizer both overall and in those aged ≥50 years not vaccinated with zoster vaccine.

Household food security during the COVID-19 pandemic Charlotte Talham* Charlotte Talham Francisco A. Montiel Ishino Faustine Williams

Background Since January 2020, the novel coronavirus (COVID-19) has caused 76.5 million cases and 900,000 deaths in the United States (US). However, the secondary effects of the COVID-19 pandemic aren't as immediately quantifiable. The spillover effects of COVID-19 on the economy have led to millions being unemployed. One consequence of this is a serious threat to food security and nutritional health among families across the US. Yet, food insecurity does not impact racial and ethnic populations equally. We aimed to assess the prevalence of food insecurity of US families during the COVID-19 pandemic and the inequities therein.

Methods We conducted a nationally representative survey of 5,938 US adults aged ≥18 from May 2021 to January 2022 on the physical and mental health impacts of the COVID-19 pandemic. We assessed food security using the USDA's US Household Food Security Survey Module: Six-Item Short Form. Food security status was assigned as high food security, low food security, or very low food security. Racial/ethnic subgroups were Hispanic/Latino, American Indian/Alaskan Native (AIAN), Asian, Black/African American, Native Hawaiian/Pacific Islander, White, and Multi-racial/ethnic.

Results Our sample population was majority White (42%) followed by Black/African American (22%), and Hispanic/Latino (18%). We identified stark disparities in food security by racial and ethnic subpopulation. For instance, 74% of Asian participants had high food security while only 49% of multi-racial/ethnic participants were deemed to have high food security. Additionally, the proportion of individuals reporting very low household food security was as high as 28% among AIAN participants and as low as 9% among Asian participants.

Conclusion The USDA reported that 10.5% of US households experienced food insecure in 2020. However, our findings indicate much higher levels of food insecurity.

Table 1. Household food security descriptive statistics (*N* = 5,556).

	High		Low		Very Low		Overall	
	n	%	n	%	n	%	n	%
Race/Ethnicity								
Hispanic/Latino	507	51.9	276	28.3	194	19.9	977	17.6
American Indian/Alaskan Native	73	50.7	31	21.5	40	27.8	144	2.6
Asian	409	74.2	94	17.1	48	8.7	551	9.9
Black/African American/African	642	52.2	324	26.3	264	21.5	1,230	22.1
Hawaiian/Pacific Islander	29	54.7	13	24.5	11	20.8	53	1.0
White	1,569	67.5	370	15.9	385	16.6	2,324	41.8
Multi-Racial/Ethnic	136	49.1	62	22.4	79	28.5	277	5.0
Gender								
Male	1,226	62.7	421	21.5	308	15.8	1,955	35.5
Female	2,025	59.4	705	20.7	682	20.0	3,412	61.9
Non-Binary/Other	89	61.4	34	23.5	22	15.2	145	2.6
Place of Birth								
US Born	2,553	58.9	912	21.0	871	20.1	4,336	78.0
Foreign Born	812	66.6	258	21.2	150	12.3	1,220	22.0
Unemployment Benefits								
No	2,906	65.1	878	19.7	681	15.3	4,465	80.7
Yes	446	41.8	287	26.9	334	31.3	1,067	19.3
Mental Health Status								
Fair/Poor	588	43.4	339	25.0	429	31.6	1,356	24.6
Good/Very Good/Excellent	2,754	66.2	818	19.7	586	14.1	4,158	75.4

Epidemiology of Renal Impairment Unrelated to Dehydration among Adults with Diabetes
Ayad* Ayad Ali

An analysis of administrative claims of about 12 million adults with type 2 diabetes mellitus (T2DM) and about 52 million persons of a general population without diabetes in the IBM MarketScan database between March 2015-2020 was used to describe the epidemiology of renal impairment conditions unrelated to dehydration. Patients with diagnosis codes reflecting dehydration conditions, gastrointestinal events potentially leading to dehydration, such as vomiting and diarrhea were excluded from the analyses. International Classification of Disease (ICD-9 and ICD-10) diagnosis codes were used to define renal impairment conditions, which included chronic kidney disease (CKD), renal failure, and acute kidney injury (AKI). The analyses showed that patients with T2DM (58 years mean age; 50% males; 3.7 years mean duration of T2DM since diagnosis) have higher prevalence and incidence rates of renal impairment compared to the general population (prevalence, 11.6% vs. 2.3%; incidence, 0.84 per 100 person-years vs. 0.60 per 100 person-years). Among any renal impairment conditions, patients with T2DM without dehydration events had CKD as the most prevalent condition compared to AKI (8.9% vs. 5.6%). Additionally, CKD contributed to the high incidence rate of renal impairment with 0.65 per 100 person-years rate. In conclusion, patients with T2DM are at risk for dehydration regardless of dehydration and should be considered as a potential comorbidity during T2DM management.

Diabetes

Reaching Optimal Glycemic Control Early and Throughout Pregnancy is Associated with Lower Risk of Perinatal Complications among Individuals with Gestational D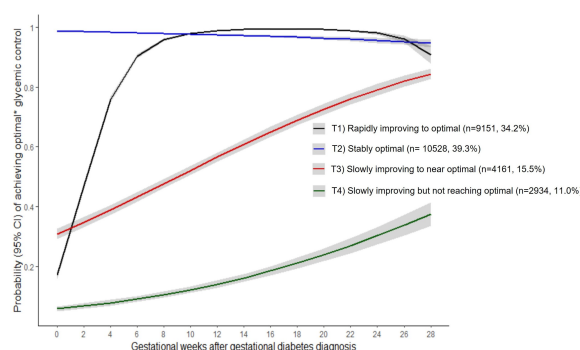iabetes: A Population-Based Study Rana F. Chehab* Rana Chehab Assiamira Ferrara Mara B Greenberg Amanda L Ngo Juanran Feng Yeyi Zhu

Glycemic control (GC) is the cornerstone of gestational diabetes (GDM) management. However, large-scale studies characterizing GC trajectories throughout pregnancy. We aimed to identify distinct GC trajectories and their associations with perinatal complications among individuals with GDM.

In a multi-racial/ethnic cohort of 26,774 individuals enrolled in a nursing monitoring program focused on GC at Kaiser Permanente Northern California (KPNC) from 2007-2017, we derived GC trajectories based on serial self-monitoring blood glucose (SMBG) measurements from GDM diagnosis to delivery using latent class modeling. Optimal GC was defined as ≥80% of all capillary SMBG measurements meeting the recommended capillary glucose targets. We examined associations of the GC trajectories with perinatal complications using Poisson regression models adjusting for multi-level sociodemographic, clinical, and GDM severity factors.

We identified four distinct GC trajectories: T1) rapidly improving to optimal (34.2%), T2) stably optimal (39.3%), T3) slowly improving to near optimal (15.5%), and T4) slowly improving but not reaching optimal (11.0%). Compared to individuals following T1, those following T2 had lower risk of Cesarean delivery [adjusted RR (95% CI): 0.93 (0.89, 0.96)], shoulder dystocia [0.74 (0.61, 0.91)], neonatal intensive care unit (NICU) admission [0.89 (0.82, 0.97)], and large-for-gestational age (LGA) [0.73 (0.68, 0.79)], and higher risk of small-for-gestational age (SGA) [1.10 (1.01, 1.20)]. In contrast, compared to individuals following T1, those following T4 had elevated risk of Cesarean delivery [1.19 (1.14, 1.25)], shoulder dystocia [1.41 (1.12, 1.77)], NICU admission [1.41 (1.28, 1.56)], LGA [1.49 (1.38, 1.61)], preterm delivery [1.32 (1.18, 1.48)], and NICU stay ≥7 days [1.25 (1.04, 1.50)], and lower risk of SGA [0.62 (0.52, 0.74)]. Individuals following T3 only had higher risk of LGA [1.13 (1.04, 1.22)] compared to those following a rapidly improving to optimal GC trajectory.

Reaching optimal GC levels earlier and throughout pregnancy was associated with lower risk of perinatal complications. This highlights the need to provide timely support to individuals with GDM to meet the glycemic targets. The association of GC with higher risk of SGA needs further investigation.

T1) Rapidly improving to optimal (n=9151, 34.2%)
T2) Stably optimal (n= 10528, 39.3%)
T3) Slowly improving to near optimal (n=4161, 15.5%)
T4) Slowly improving but not reaching optimal (n=2934, 11.0%)

*Optimal was defined as ≥80% of all self-monitored blood glucose measurements meeting the targets recommended by the American Diabetes Association guidelines and implemented at Kaiser Permanente Northern California.
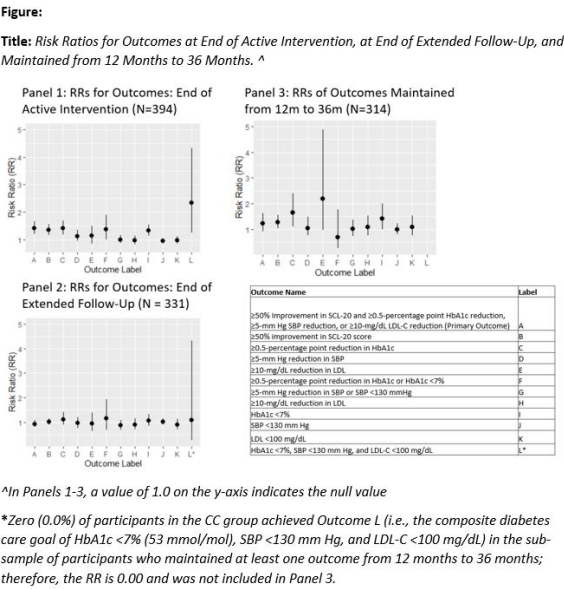
LATEBREAKER

Diabetes

Long-term Effects of a Collaborative Care Model on Metabolic Outcomes and Depressive Symptoms: The Integrating Depression and Diabetes Treatment Study Kara Suvada* Kara Suvada Mohammed K. Ali Lydia Chwastiak Shivani A. Patel

Background: Concurrent type 2 diabetes (T2D) and depression are increasingly prevalent. Collaborative care (CC) strategies may efficiently and effectively improve outcomes in this group. We examined the long-term effect of a year-long CC intervention on metabolic indicators and depressive symptoms among adults in India with co-morbid T2D and depression.

Methods: The primary outcome was the between-group difference in the percentage of patients with reductions since baseline of ≥50.0% Symptom Checklist Depression Scale (SCL-20) scores combined with at least one of: 0.5-percentage point hemoglobin A1c (HbA1c), 5 mmHg systolic blood pressure, or 10 mg/dL low density lipoprotein cholesterol. Intervention effects were estimated as the relative risk (RR) of achieving the primary outcome and its constituents using log binomial models with inverse probability weighting to account for attrition. Intervention effects were obtained at 12m (end of active intervention) and 36m (extended follow-up). We also examined the effect of collaborative care on maintenance of outcomes between 12m and 36m following randomization.

Results: While the CC group was more likely to achieve the primary outcome at 12m, this effect was not seen at 36m (CC, 57.0 % vs. usual care, 60.5%; RR: 0.93 [95% CI: 0.80, 1.09]). Patients in the CC group, however, were more likely to maintain sustained achievement of ≥50% improvement in SCL-20 score (54.9% vs. 40.9%; RR: 1.27 [95% CI: 1.04, 1.56]) and a ≥0.5-percentage point reduction in HbA1c (31.9% vs. 19.5%; RR: 1.64 [95% CI: 1.11, 2.41]) between 12m and 36m.

Conclusions: CC had no effect on composite depression and metabolic outcomes two years after the end of active intervention. The CC group, however, was more likely to maintain improvements in depressive symptoms and glycemic status two years after the end of active intervention. Continued and consistent exposure to CC may be needed to sustain multiple risk factor control in this high-risk group.

Figure:

Title: *Risk Ratios for Outcomes at End of Active Intervention, at End of Extended Follow-Up, and Maintained from 12 Months to 36 Months. ^*

Panel 1: RRs for Outcomes: End of Active Intervention (N=394)

Panel 3: RRs of Outcomes Maintained from 12m to 36m (N=314)

Panel 2: RRs for Outcomes: End of Extended Follow-Up (N = 331)

Outcome Name	Label
≥50% improvement in SCL-20 and ≥0.5-percentage point HbA1c reduction, ≥5-mm Hg SBP reduction, or ≥10-mg/dL LDL-C reduction (Primary Outcome)	A
≥50% improvement in SCL-20 score	B
≥0.5-percentage point reduction in HbA1c	C
≥5-mm Hg reduction in SBP	D
≥10-mg/dL reduction in LDL	E
≥0.5-percentage point reduction in HbA1c or HbA1c <7%	F
≥5-mm Hg reduction in SBP or SBP <130 mmHg	G
≥10-mg/dL reduction in LDL	H
HbA1c <7%	I
SBP <130 mm Hg	J
LDL <100 mg/dL	K
HbA1c <7%, SBP <130 mm Hg, and LDL-C <100 mg/dL	L*

^In Panels 1-3, a value of 1.0 on the y-axis indicates the null value

*Zero (0.0%) of participants in the CC group achieved Outcome L (i.e., the composite diabetes care goal of HbA1c <7% (53 mmol/mol), SBP <130 mm Hg, and LDL-C <100 mg/dL) in the sub-sample of participants who maintained at least one outcome from 12 months to 36 months; therefore, the RR is 0.00 and was not included in Panel 3.

Chronic cadmium exposure is associated with lower cognition among adults aged 60 and over in a representative US sample Tara Jenson* Tara Jenson Kelly Bakulski Keith Dookeran Ira Driscoll Amy Kalkbrenner
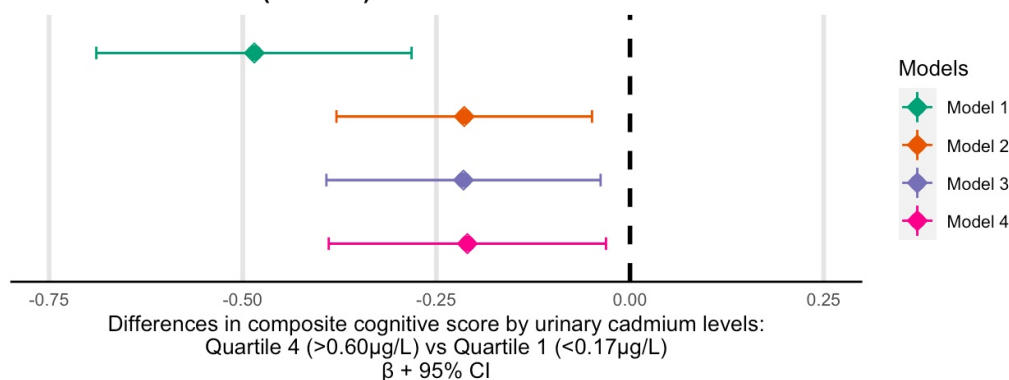
Background: Cadmium , a toxic heavy metal, has been linked to later-life cognitive function, but with inconsistencies in prior studies. We investigated this potential link, improving the consideration of confounding due to key cadmium sources (diet and tobacco) and a key co-pollutant: lead.

Methods: Participants >/= 60 years of age from the US were randomly sampled for urinary specimen collection (N=1091). Urinary cadmium reflects long-term exposure (10-15 years). Concurrent neuropsychological tests tapping memory, executive function, sustained attention and working memory were combined into a standardized z-score. We estimated patella bone lead levels, reflective of long-term exposure (10-15 years), with inputs of blood lead and other predictors. We classified cigarette smoking via self-report and cotinine, and used dietary survey data to quantify key dietary sources of cadmium. We used fully conditional multiple imputation to recapture substantial model observation drop-out (N=553) based on the underlying assumption of MAR pooled across five imputation iterations. We used linear regression to estimate differences in cognition, comparing the highest quartile of urinary cadmium levels (>0.60µg/L) versus lowest (<0.17µg/L).

Results: Adjusting for sampling weight and urinary creatine (measure of urine dilution), cadmium exposure was associated with 49% standard deviation lower cognitive score (95%CI: -0.69, -0.28). This association was attenuated to 21% lower cognition (95%CI -0.38, -0.05) after adjusting additionally for sex, age, race/ethnicity, marital status, education level, and poverty income ratio. Additional adjustment for smoking, bone lead, and diet did not further change results: 21% standard deviation lower cognitive z-score (95%CI: -0.39, -0.03).

Discussion: Cadmium exposure is associated with lower cognitive scores among older adults, even after accounting for confounding influences of diet, tobacco use, and lead exposure.

Figure 1. Unadjusted and Adjusted Linear Regression Estimates of Association Between Urinary Cadmium and Cognitive Performance in Adults Aged 60+ Years. NHANES 2011-2014 (N=1091)

Differences in composite cognitive score by urinary cadmium levels:
Quartile 4 (>0.60µg/L) vs Quartile 1 (<0.17µg/L)
β + 95% CI

Model 1: Adjusted only for NHANES MEC sampling weight and urinary creatinine

Model 2: Model 1 + adjusted for age, sex, race/ethnicity, poverty income ratio, marital status, education

Model 3: Model 2 + adjusted for smoking status; active smoker defined via self-report or serum cotinine >10ng/mL

Model 4: Model 3 + adjusted for estimated patella bone lead + quantified dietary intake of iron, fruit, dark green vegetables, red/orange vegetables, starchy vegetables, legumes, whole and refined grains, soy and nuts

Post-traumatic stress, depression, and diet among older survivors of the Great East Japan Earthquake and Tsunami Aki Yazawa* Aki Yazawa Ichiro Kawachi

Previous research has suggested an increase in cardiometabolic disorders among survivors of natural disasters. For example, Hikichi et al. (2019) reported increased risks of obesity 2.5 years after the 2011 Great East Japan Earthquake and Tsunami. A potential mechanism to explain this association is deterioration in dietary quality associated with trauma-related mental disorders, in particular post-traumatic stress and depression. Using the Brief Self-Administered Dietary History Questionnaire (BDHQ), validated in the Japanese population, we examined the association between posttraumatic stress symptoms (PTSS)/depression, relocation to temporary housing, and dietary habits among survivors (mean age 71.1 years) of the Great East Japan Earthquake and Tsunami. BDHQ data was collected from 1,531 survivors in 2019. A principal component analysis was performed to identify three dietary patterns: Pattern 1 consists of high intake of vegetables, soy products, and fruits; Pattern 2 consists of high intake of one-dish meals e.g., noodles and snacks/sweets; Pattern 3 consists of high intake of alcoholic beverages, meat, and seafood. Results revealed that individuals suffering from PTS symptoms were less likely to follow the Pattern 1 diet, and more likely to follow the Pattern 2 diet. Three-way interactions (PTSS/depression x relocation to temporary housing x gender) revealed that males with PTS symptoms living in temporary housing were more likely to follow the Pattern 2 diet, while men with depression living in temporary housing tended to follow the Pattern 3 diet. The association of disaster experiences with dietary habits appeared to vary by mental illness symptoms and men appeared to be more susceptible to unhealthy dietary patterns.
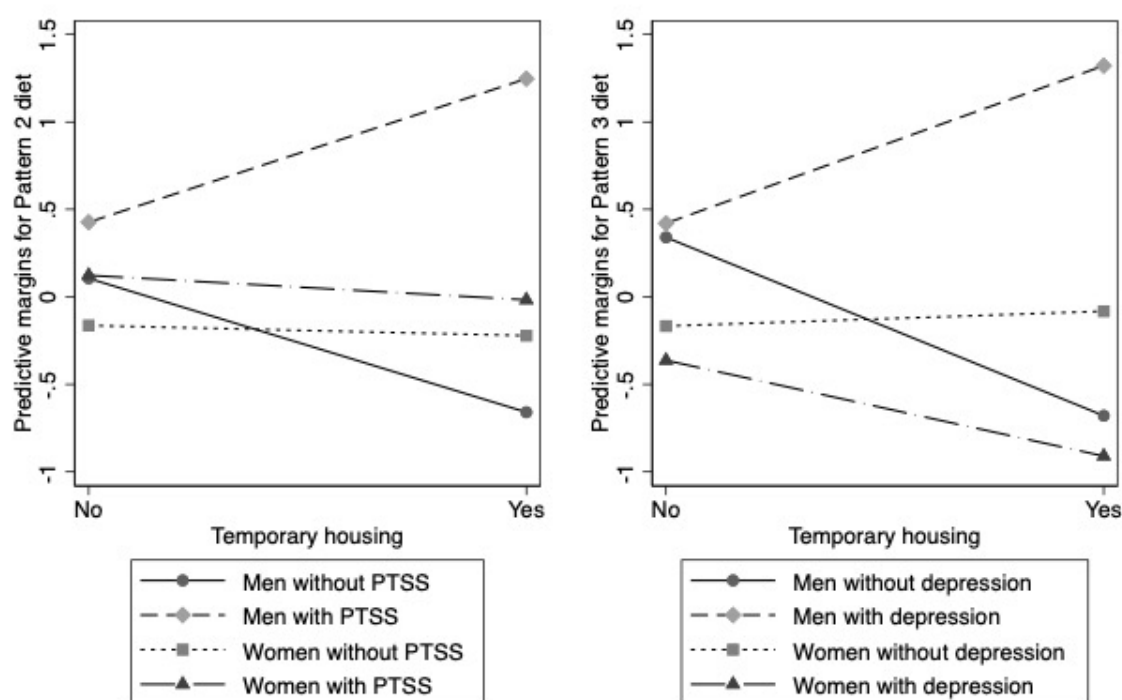
Birth sex ratio reduced by ambient temperature swing during early pregnancies Fang Guo*
Fang Guo Hualiang Lin Shengzhi Sun Linwei Tian

Background: Climate change as a major challenge worldwide that proves to threaten turtles by disrupting the sex ratios, may also impact humans via shaping the natural selection *in utero* against fetus sex. Several model-based studies on how temperature stress would potentially skew birth sex ratio (BSR) have generated inconsistent findings.

Methods: Here we applied a data-driven method, Empirical Dynamic Modeling (EDM), to examine the causality between temperature conditions and BSR dynamics in Hong Kong from 1984-2011. Based on state space reconstruction, EDM accommodates complex and likely changing causal relationships in nonlinear dynamical systems. Under EDM framework, with convergent cross mapping (CCM) harnessed to discover causal pairs, multivariate S-map (sequential locally weighted global linear map) quantifies the effect strengths.

Results: Using seasonal surrogate data to build a pointwise null distribution for significance test, CCM analysis with weekly data detected that short-term temperature variability, rather than temperature itself, had a potentially causal role in BSR, and such driving effect was realized at -37 to -36 lagged weeks, corresponding to 2~3 conception weeks. Consistently, CCM results of daily data further pinpointed a significant causal signal from temperature variability to BSR during the 17~20 days of early conception, a critical stage where embryos are selected for greater reproductive investment. Then, S-map analysis depicted a dynamic (non-static) but negative effect of temperature variability on BSR (i.e., a reduced ratio of male births) over the study period. The inverse effect strengthened first but waned with increasing temperature variability magnitude.

Conclusion: We found that ambient temperature variability can be a stressor during early pregnancies skewing BSR in favor of female offspring. This supports the classical "fragile boy" hypothesis that girls are favored during hard times for a higher chance to pass on the genes.
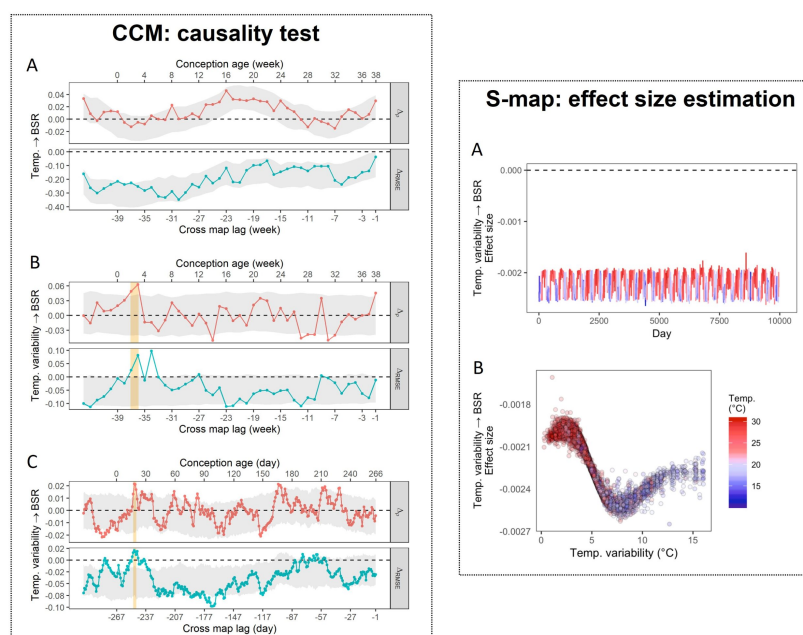
Red blood cell folate modifies the association between serum per- and polyfluoroalkyl substances and antibody levels in U.S. adolescents Yu Zhang* Yu Zhang Vicente Mustiele Yi-Xin Wang Yang Sun Zainab Bibi Nicole Torres Angela Slitt Carmen Messerlian

Background

Several per- and polyfluoroalkyl substances (PFAS) are considered immunotoxic and have been associated with reduced vaccine antibody response. Although red blood cell (RBC) folate has previously been associated with lower PFAS concentrations, no prior study assessed its role as an effect modifier between PFAS exposure and antibody levels.

Methods

We included 584 adolescents aged 12 to 19 years in the National Health and Nutrition Examination Survey 2003-2004 cycle. Concentrations of folate in RBC, four PFAS compounds [i.e., perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexanesulphonic acid (PFHxS), and perfluorononanoic acid (PFNA)], and measles, rubella, and varicella antibodies were determined in serum. We stratified the population into lower vs. equal or higher than median RBC folate levels (RBC folate < vs. ≥ median). We used multivariable linear regressions to estimate the covariate-adjusted percent changes (PCs) and 95% CIs of antibody levels in relation to a 2.7-fold increase in individual PFAS concentrations, for low and high folate groups, respectively. We used quantile g computation (QGC) and Bayesian kernel machine regression (BKMR) to examine the joint effect of total PFAS mixtures on antibody levels for each folate group. We further restricted the analyses to participants with seropositive antibody levels (about 95% of the total population).

Results

In the total population, we found negative associations between serum PFOS and PFHxS concentrations and rubella antibody levels in the lower folate group, while the results were null in the upper folate group. Associations among the lower folate group were strengthened by restricting to the seropositive subpopulation. We further found negative associations between serum PFOA and rubella antibody levels, and PFOS and varicella antibody levels only among the lower folate group in the seropositive subpopulation. QGC and BKMR showed consistent negative associations between the total PFAS mixture and rubella antibody levels among the lower folate group, while the upper folate group showed no meaningful mixture results (Figure 1). No associations were found between PFAS exposure and measles antibody.

Conclusion

In this U.S. representative cross-sectional study, we found negative associations between select PFAS and the total PFAS mixture and rubella antibody levels only among adolescents with lower than median RBC folate levels. If confirmed in mechanistic studies, the findings have important implications for using folate as a mitigating measure for adverse PFAS immune effects.
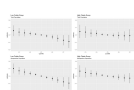
Wildfire exposure and health care use among people who use durable medical equipment in Southern California Heather McBrien* Heather McBrien Sebastian Rowland Tarik Benmarhnia Sara Tartof Joan Casey

Climate change-induced wildfires cause trauma, stress, and injury in affected communities, while exposing 70% of the US population to smoke $PM_{2.5}$ annually and exacerbating cardiorespiratory disease. Few studies examine wildfire smoke exposure in vulnerable populations, and none evaluate residence in an evacuation zone.

We identified 236,732 Kaiser Permanente Southern California members who used electricity-dependent durable medical equipment (DME). DME use is associated with respiratory illness and disability, indicating vulnerability to smoke exposure and difficulty evacuating disaster zones. Daily counts of outpatient, inpatient, and emergency healthcare visits made by DME users from 2016-2020 were linked with daily estimates of wildfire generated $PM_{2.5}$ by ZIP code. We used historical maps to identify evacuated ZIPs during the 2018 Getty and Woolsey fires. We performed negative binomial regression analyses using direct and lagged effects of wildfire $PM_{2.5}$ and difference-in-differences analyses to evaluate the association between wildfire $PM_{2.5}$, evacuation exposure, and health care visit frequency. We adjusted for temperature, temporal effects, non-wildfire $PM_{2.5}$, and spatial confounders.

Woolsey fire evacuation exposure was associated with fewer outpatient and more inpatient visits (RR = 0.98, 95% CI: 0.78, 0.87, RR = 1.45, 95% CI: 1.01, 2.11), while Getty fire evacuation exposure was not associated with visit frequency. In contrast, increases in wildfire $PM_{2.5}$ were associated with small and constant decreases in outpatient visits for six days after a change. Wildfire $PM_{2.5}$ was not associated with frequency of inpatient or emergency visits at any lag.

DME users, presumed vulnerable to wildfire smoke exposure, may have sheltered in place on smoky days or took other precautions. However, the Woolsey fire (which was much larger than the Getty) may have produced health concerns in those directly affected when evacuation was necessary and sheltering in place impossible.

Map of Southern California study area, shaded in grey, with counties labelled in black. Getty and Woolsey fire burn areas are filled in black, and evacuation zones plus 10 km buffer are in orange and red, respectively.
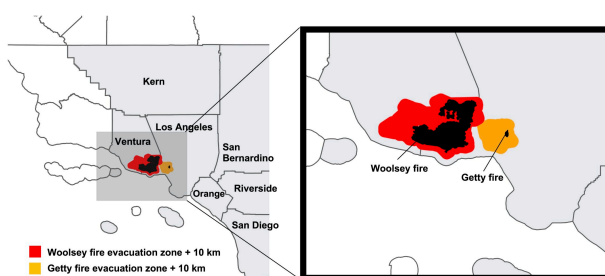
**Investigating Relationships between Asthma Mortalities, Environmental Factors, and Social Determinants in Chicago** Regan Cronk* Regan Cronk Molly Scannell Bryan Anastasia Montgomery Marynia Kolak Daniel Horton

Background: Chicago has one of the highest asthma mortality rates in the country, particularly among BIPOC communities. Previous studies have posited a host of underlying causal mechanisms for this disparity, including increased air pollutant exposure. However, a key limitation in these analyses is the lack of robust neighborhood-scale air quality data. Here, we employ a novel high spatial resolution air quality dataset and additional social determinants data to assess relationships between acute asthma mortality and social and environmental factors in Chicago.

Methods: We used the Cook County Medical Examiner Case Archive to quantify asthma mortalities on a community-area scale over a four-year period (2015-2018). To assess the potential influence of poor air quality, a newly developed neighborhood-scale resolution (1 km^2) fine particulate matter (PM$_{2.5}$) dataset from the University of Chicago's Spatial Lab was utilized. In addition, to assess other potential influences, we included demographic and housing data from American Community Survey, and a multidimensional summary index that estimates the effect of social determinates of health on community areas. A Zero Inflated Poisson Regression model was used to assess the relationship of each variable to asthma mortalities.

Results: We identity 268 acute asthma mortalities in this period, excluding those related to drug overdoses. We find that these deaths exhibit no seasonal trends. By using different variables in each regression, the effect of PM$_{2.5}$ without the possibility of confounding variables is assessed. We aggregated on a seasonal level, and examination of the coefficients and p-values inform the impact of each determinant.

Conclusions: Our results indicate that when conducting determinant analyses, synergistic and competing factors are often at work, thus care must be taken when interpreting results. We also discuss the overlapping effect of neighborhood characteristics in disease incidence.

Location of PM2.5 and Asthma Mortalities in Chicago, April 2015
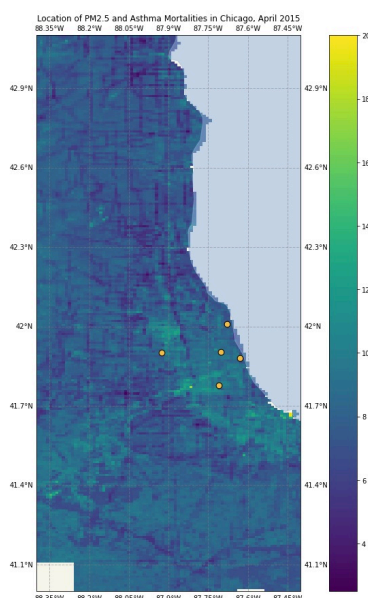
Identifying typologies of socio-environmental exposures Yue Ying* Yue Ying Belinda Nicolau Tracie Barnett

Background: Social factors are likely implicated in health outcomes. We sought to identify novel typologies of social environments by combining exposures from multiple domains including the Canadian census, on-site audits, and individual perceptions.

Methods: We used baseline data from the QUALITY cohort, an ongoing longitudinal study investigating the natural history of obesity in 630 children living in QC Canada. Children with ≥1 obese biological parent were recruited at age 8-10 years in 2005-2008. Relative material and social deprivation based on 2006 census data were computed for both residential and school neighborhoods based on Pampalon's method. Social disorder was based on on-site audits of 10 contiguous residential street segments and was defined as presence of ≥1 of the following signs: graffiti, vandalism, uncollected litter and abandoned buildings. Perceptions of residential neighbourhood safety and social capital were collected from parents in structured questionnaires. Neighborhoods were defined by 750 m walking buffers. All 7 variables were entered into hierarchical cluster analysis using the Gower method and average linkage.

Results: Four reasonably balanced clusters were identified, with a Silhouette score of 0.36. The least favourable type (n=187) was characterized by the most social deprivation both in residential and school neighborhoods, the most disorder, the lowest perceptions of social capital and safety, and moderate levels of material deprivation. Similarly, the most favourable type (n=85) was characterized by the most favourable values of all 7 variables. Two intermediate types exhibited more favourable census-based and unfavourable audit-based and perceived measures (n=149), or vice versa (n=209).

Conclusion: We identified meaningful contrasting social environment using measures from multiple domains. Future analyses will be modeling the association between typology membership and health outcomes using generalized estimating equation.

Perfluoroalkyl Substances and Fish Consumption in the Great Lakes Fish Consumer Study
Meghan Cerpa* Meghan Cerpa Mary Turyk Robert Sargis Saria Awadalla

Perfluoroalkyl substances (PFAS) are an emerging class of contaminants linked to various adverse health effects, including thyroid disease and dyslipidemia. One of the major sources of exposure is thought to be consumption of seafood harvested from contaminated waters. The objective of this study is to assess if serum PFAS levels are associated with self-reported fish meals in a cohort of frequent and infrequent Great Lakes sport fish consumers. Participants in the Great Lakes Fish Consumer Study (GLFCS) were recruited in the early 1990s from among licensed Great Lakes (GL) charter boat captains and persons with little or no GL fish consumption who lived in the same geographic areas of WI, IL, IN, MI, and OH as the captains. In 2004-2005, participants reported the number of fish meals eaten in the past year that were caught in one of the GL and those purchased commercially. Eleven PFASs were measured in stored serum from 473 participants. Log transformed PFAS were regressed on fish meals, adjusting for age, BMI, sex, and education. Participants had a mean age of 57.9 years and BMI of 29.6 kg/m^2; 70% were male; 70% completed at least some college. Participants ate a median of 10 (IQR=0, 30) GL sport fish and 15 (IQR=4, 52) commercial fish meals in the past year. An increase of 5 GL sport fish meals/year was significantly ($p<0.05$) associated with an increase in serum levels of several PFASs: PFUnDA (4.3%), PFDA (4.1%), n-PFOS (3.8%), PFNA (3.0%), PFHpS (1.8%), sm-PFOS and PFHxS (1.6%), and n-PFOA and MeFOSAA (1%). No significant associations were seen between GL sport fish consumption and EtFOSAA and FOSA. In contrast, significant increases in serum PFAS levels for an increase of 5 purchased fish meals/year were smaller, ranging from 0.8% for n-PFOS to 1.3% for PFNA. Both GL sport fish and purchased fish consumption were associated with significant increases in serum concentrations of several PFAS species, with larger increases for GL than commercial fish meals.

Association of Serum PFAS with Fish Meals in the Past Year in the Great Lakes Fish Consumer Study

Linear regression models adjusting for age, sex, BMI, education, n=468
Abbreviations: perfluorohexane sulfonate (PFHxS), perfluorononanoate (PFNA), perfluorodecanoate (PFDA), perfluoroundecanoate (PFUnDA), perfluoromethylheptane sulfonates (Sm-PFOS), n-perfluorooctane sulfonate (n-PFOS), n-perfluorooctanoate (n-PFOA), perfluoro-1-heptanesulfonate (PFHpS)

Sulfur dioxide reduction at coal-fired power plants in North Carolina and associations with preterm birth among surrounding residents Adrien A. Wilkie* Adrien Wilkie David B. Richardson Courtney G. Woods Marc L. Serre Thomas J. Luben Julie L. Daniels

Coal-fired power plants (CFPP) are major contributors of air pollution, including the majority of anthropogenic sulfur dioxide (SO_2) emissions, which have been associated with preterm birth (PTB). To address a 2002 North Carolina (NC) policy, 14 of the largest NC CFPPs either installed desulfurization equipment (scrubbers) or retired coal units, resulting in substantial reductions of SO_2 air emissions. We investigated whether SO_2 air emission reduction strategies at CFPPs in NC were associated with changes in prevalence of PTB in nearby communities. We used US EPA Air Markets Program Data to determine the implementation dates of intervention at CFPPs and geocoded 2003-2015 NC singleton live births. We conducted a difference-in-difference analysis to estimate change in PTB associated with change in SO_2 reduction strategies for populations living 0-<4 and 4-<10 miles from CFPPs pre- and post-intervention, with a comparison of those living 10-<15 miles from CFPPs. Reported average monthly SO_2 air emissions from the CFPP-scrubber group (N=7) in the pre- and post-intervention periods were 4,933 and 342 tons, respectively. The CFPP-retired group (N=7) emitted a monthly average of 909 tons of SO_2 pre-intervention versus <1 ton post-intervention. With the spatial-temporal exposure restrictions applied, 42,231 and 41,218 births were within 15 miles of CFPP-scrubbers and CFPP-retired groups, respectively. The estimated absolute prevalence of PTB decreased by 1.5% (95% CI: -2.6, -0.4) within 4-<10 miles from a CFPP after installation of scrubbers. When stratified by race/ethnicity, the absolute prevalence of PTB decreased for non-Hispanic (nH) Asian and nH white mothers by 8.2% (-14.1, -2.4) and 2.0% (-3.4, -0.6), respectively, with no change for nH Black [-0.4% (-3.2, 2.3)] and Hispanic [-0.0% (-2.6, 2.6)] mothers. Findings were imprecise and generally null among mothers living within 0-<4 miles regardless of the intervention type. This abstract does not represent EPA policy.

LATEBREAKER

Environment/Climate Change

The Impact of Historical Redlining on Air Toxics in Georgia Leah Moubadder* Leah Moubadder Susan Hoffman Jasmine Aqua Michael Kramer Lauren McCullough

Background: Historical redlining is the discriminatory practice of refusing home loans to neighborhoods based on their racial makeup. The systematic disinvestment and lack of political and social agency imposed upon redlined communities were exploited in the development of urban areas; resulting in contemporary patterns of zoning, highway location, and industrial emissions that produce local inequalities in toxicant exposure. This study examined the association between redlining and the National Air Toxics Assessment (NATA) in Georgia.

Methods: We evaluated the association between historical redlining and three present-day air toxics measures obtained from NATA at the EPA: cancer risk due to air toxics, respiratory hazard index ratio, and diesel particulate matter (DPM) levels. Redlining was defined according to the graded mortgage investment risk assigned by the Home Owners Loan Corporation (HOLC) in 1935, which assigned a grade to each neighborhood, ranging from A to D (Best, Still Desirable, Definitely Declining, and Hazardous, respectively). Because these boundaries do not align with current census tract boundaries, we used continuous HOLC scores that were weighted by graded land area. Census tracts were assigned grades A-D according to the following values: 1 – <2, 2 – <3, 3 – < 3.5, and 3.5 – 4, respectively. To determine if spatial autocorrelation exists in our study, we used Global Moran's I, a nonparametric statistic of spatial autocorrelation. Spatial autoregressive models with queen contiguity neighbors were used to calculate percent change in air toxics by redlining grade, adjusting for metropolitan area.

Results: A total of 154 census tracts from five historically redlined metropolitan areas in GA were included. The Global Moran's I values were significantly positive, indicating clustering by air toxics. Grade D census tracts experienced a 1.6% increase in risk of cancer due to air toxics compared to grade A tracts. Grade D census tracts also had a 1.5% increase in respiratory hazard index, compared to grade A census tracts. We observed no appreciable difference in DPM by redlining grade.

Conclusion: This research advances our understanding of how environmental hazards may result from historical practices that fail to center underserved communities in the adaptation of environmental amenities.
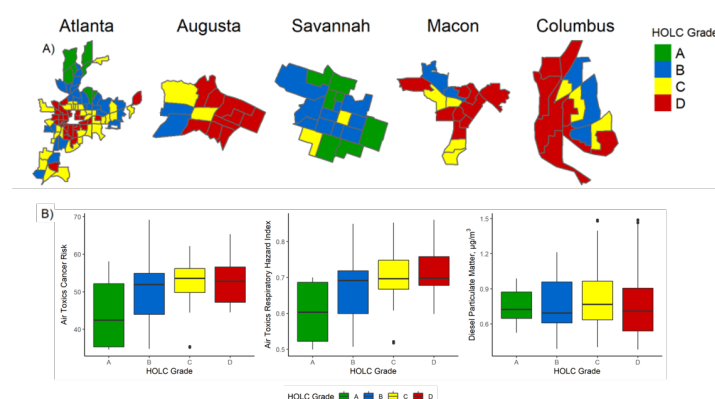
Figure 1. (A) Historical redlining by census tract by the five HOLC-graded metropolitan areas in Georgia. (B) NATA cancer risk, estimated as the lifetime (assumed to be 70 years) cancer risk from inhalation of air toxics, NATA respiratory hazard index, estimated as the ratio of exposure concentration to health-based reference concentration, and NATA diesel particulate matter levels in air, μg/m³ by historical redlining grade among all HOLC-graded metropolitan areas in Georgia.

Examination of newborn DNA methylation among women with and without self-reported polycystic ovary syndrome and hirsutism Kristen Polinski* Kristen Polinski Sonia L Robinson Diane L Putnick Raji Sundaram Erin Bell Paule Joseph James Segars Veronica Gomez-Lobo Weihua Guan Edwina H. Yeung

Objective: To assess associations of maternal polycystic ovary syndrome (PCOS) with and without hirsutism and DNA methylation (DNAm) alterations in the dried blood spots (DBS) of 830 neonates. **Methods:** Women enrolled in the Upstate KIDS cohort self-reported diagnoses of PCOS and hirsutism (i.e., excessive body hair) 4 months after delivery. Women were categorized as having PCOS with hirsutism, PCOS without hirsutism or no PCOS. DBS DNAm was measured using the Infinium MethylationEPIC BeadChip in singletons and one randomly selected twin of a pair. Multivariable robust linear regression was used to evaluate associations of PCOS with DNAm β-values. Minimally adjusted (infant sex, plurality, cell type count and batch effects) and fully adjusted models (inclusion of maternal characteristics) were considered. **Results:** Overall 12.3% (102/830) had a PCOS diagnosis (8.3% PCOS without hirsutism; 4% PCOS with hirsutism). These women were more likely to have a higher pre-pregnancy body mass index, gestational diabetes, or seek fertility treatment to conceive. Exposure to PCOS with hirsutism compared to no PCOS was associated with differential DNAm at cg08471713 near the *MEOX1* gene [β(SE):0.0768 (0.014); false discovery rate (FDR) p=0.04], which may have roles in somite development and hemopoietic stem cell differentiation. After adjustment for maternal characteristics, PCOS with hirsutism remained marginally associated with cg08471713 [β(SE):0.0716 (0.014); FDR p=0.12]. PCOS without hirsutism compared to no PCOS was not associated with individual CpG probes. **Conclusion:** The observed but limited effects among those exposed to PCOS with hirsutism suggests that excess circulating maternal androgens may potentially alter DNAm of offspring. This is supported by evidence from animal studies in which a hyperandrogenic state, such that is present in hirsutism, modifies offspring DNAm. Replication and further research are needed in additional cohorts.

Additive or interactive associations of food allergies with genotypes of GST genes (GSTM1, GSTP1 and GSTT1) in relation to ASD and ASD severity in Jamaican children Sepideh Saroukhani, MD, PhD* Sepideh Saroukhani Maureen Samms-Vaughan Jan Bressler MinJae Lee Courtney Byrd-Williams Manouchehr Hessabi Megan L. Grove Sydonnie Shakespeare-Pellington Katherine A. Loveland Mohammad H. Rahbar

Comorbidity of food allergies with Autism Spectrum Disorder (ASD) is increasing and oxidative stress has implications in both conditions. Using data from 344 pairs of age-and sex-matched ASD cases and typically developing (TD) controls, we assessed additive and interactive associations of food allergies with polymorphisms in three glutathione S-transferase (GST) genes (*GSTM1*, *GSTP1* and *GSTT1*) in relation to ASD, by applying conditional logistic regression models, and in relation to ASD severity measured by the Autism Diagnostic Observation Schedule-2nd Edition (ADOS-2) comparison scores (CSs), by fitting general linear models. After adjusting for child's age and history of breastfeeding, we found a marginally significant additive inverse association between allergy to yogurt and ASD [Matched OR: 0.36, P = 0.06], but there was no significant interaction between food allergies and GST genes in relation to ASD (all $P \geq$ 0.11). ASD cases with allergy to at least one non-dairy food had a higher ADOS-2 Restricted and Repetitive Behaviors (RRB) domain CS (9.1 vs. 8.2, P = 0.04), and a marginally significant higher total CS than those without allergy (8.0 vs. 7.3, P = 0.06). We also identified significant interactions between *GSTT1* and allergy to at least one dairy product (P = 0.04), as well as between allergy to cheese and *GSTP1* in relation to RRB CS (P = 0.02). Among ASD cases with *GSTT1* DD genotype, allergy to at least one dairy product was associated with higher mean RRB CS (10.0 vs. 8.1, P = 0.01), whereas this association was not significant among ASD cases with *GSTT1* I/I or I/D genotype (8.4 vs. 8.3, P = 0.72). In a dominant model for *GSTP1*, though marginally significant, allergy to cheese was associated with higher RRB CS in ASD cases with Val/Val or Ile/Val genotype (9.1 vs. 8.3, P = 0.05), whereas among ASD cases with Ile/Ile genotype, this association was in the opposite direction (6.4 vs. 8.0, P = 0.09). Our findings require replication in other populations.

Global Health

Identifying the Association between Neighborhood Walkability and Physical Activity among Adolescents Drawing from the Family Life, Activity, Sun, Health, and Eating Study Zili Zong* Zili Zong Cody Neshteruk Emily M. D'Agostino Jesse Troy

Although some evidence shows parents' and neighborhoods' influence on adolescent physical activity (PA), limited studies have examined the influence of the built environment on adolescent PA while accounting for both individual, interpersonal, and built environment factors. The purpose of this study was to examine the relationship between neighborhood age, density and adolescent weekly at school, out-of-school and weekend MVPA. Data were extracted from The Family Life, Activity, Sun, Health, and Eating (FLASHE) study (N=1179). Adolescent and parent moderate-to-vigorous physical activity (MVPA) was measured by self-report and accelerometer measurements were available for adolescents. Neighborhood factors were extracted by performing principal component analysis (PCA) for all census tracts in the U.S. Crude and adjusted linear regression models were fit to examine the association between each neighborhood characteristic and MVPA outcomes. Neighborhood density (8.29, 95% CI: 0.37, 16.21) and neighborhood age (6.58, 95% CI: -0.09, 13.25) were positively associated with adolescent at school MVPA after adjusting for adolescents' demographics and parent MVPA. Those living in high density (high residential density, high use of public transit and walking or biking) and old neighborhoods with the highest tertile had higher at school MVPA than those living in low density and young neighborhoods with the lowest tertile. After correction for false discovery, association between neighborhood density and adolescent at school MVPA after adjusting for adolescents' demographics persisted P-value<0.2. Further research could continue to investigate the association between residential density and adolescent at school MVPA. Efficient measures should be enacted to improve neighborhood walkability level.

Global Health

Influence of internal early migration on multimorbidity in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil) Letícia de Oliveira Cardoso* Leticia Cardoso Ana Luiza Gomes Domingos Aline Araújo Nobre Joana Maia Brandão Sandhi Barreto Isabela Bensenor Leonardo Bastos Arlinda Moreno Maria de Jesus Mendes da Fonseca Rosane Harter Griep

Introduction: Brazil has experienced an increase in the number of individuals living with multimorbidity. Migratory movements influence the occurrence of diseases among migrants and non-migrants, however, this relationship is scarcely investigated. **Objective:** The study aimed to evaluate the association between patterns of internal migration in early life and the prevalence of multimorbidity in adults in the Brazilian Longitudinal Study of Adult Health (ELSA-Brasil). **Methods:** Baseline data (2008-2010) from the ELSA-Brasil were analyzed, with a final sample size of 13.146 employees of both sexes aged 35-74 years. Participants diagnosed with ≥ 2 conditions from a list of 15 were classified with multimorbidity. A migrant was defined as an individual whose municipality of residence at the beginning of schooling (origin) was different from the municipality of residence at the study baseline (destination). All cities were classified according to the Brazilian cities' Regions of Influence (IBGE, 2018). Migration was categorized as nonmigrant, downward migrant, or upward migrant. Participants who migrated to a location of the same urban hierarchy classification were categorized as nonmigrants. We performed a logistic regression analysis for men and women to test the association of early migration with multimorbidity adjusting for age and maternal education. The nonmigrant category was considered a reference. The models were stratified by sex. **Results:** Of the total participants, 45.3% were migrants, and 69.6% had multimorbidity. After adjustments for confounding factors, we found a significant association between upward migration and multimorbidity in men (OR [95% CI], 0.88 [0.78 – 0.99]. For women, associations were found between upward (OR [95% CI], 0.84 [0.75 – 0.94] and downward migration (OR [95% CI], 1.43 [1.16 – 1.77] and multimorbidity. **Conclusion:** The results indicated a relationship between early internal migration trajectory and the prevalence of multimorbidity in adults from the ELSA-Brasil study.

LATEBREAKER

Global Health

Urinary Organophosphate and Neonicotinoid Metabolites in relation to Sex and Adrenal Hormones among Adolescents living in Ecuadorian Agricultural Communities Briana Chronister* Briana Chronister Denise Justo Dolores Lopez-Paredes Eduardo Gonzalez Jose Suarez-Torres Sheila Gahagan Danilo Martinez David R. Jacobs Jr. Harvey Checkoway Jose R. Suarez-Lopez

Background

Organophosphate (OP) and neonicotinoid (NNI) insecticides have caused adrenal and gonadal hormone disruption in animal and *in vitro* studies; limited epidemiologic evidence in humans exists. We assessed relationships between insecticide metabolites and these hormones in adolescents living in agricultural communities in Ecuador.

Methods

We examined 522 adolescents (11-17y, 49% male). We measured urinary concentrations of three OPs (3,5,6-trichloro-2-pyridinol [TCPy], malathion dicarboxylic acid [MDA], and *para*-nitrophenol [PNP]), two NNIs (acetamiprid-N-desmethyl [AND] and 5-hydroxy imidacloprid [OHIM]), and salivary 17β-estradiol (boys only), dehydroepiandrosterone (DHEA), testosterone, and cortisol. We imputed concentrations below the detection limit using multiple imputation. Linear regression models assessed associations between ln-metabolite and ln-hormone concentrations (β=% hormone difference per 50% increase of pesticide concentration). Bayesian kernel machine regression assessed interactions.

Results

The OP summary score was positively associated with testosterone (β=10.0% [95%CI: 1.5%, 19.2%]) with stronger associations in boys (β=14.1% [2.1%, 27.5%]). PNP was negatively associated with DHEA, overall (β=-7.3% [-14.3%, 0.1%]) and in boys (β=-11.0% [-21.9%, 1.4%]). MDA was borderline positively associated with cortisol (β=3.9% [-0.3%,8.3%]), with stronger association in boys (β=6.1% [-0.2%, 12.8%]) compared to girls (β=2.1% [-3.4%, 7.9%]). The NNI summary score (β=5.6% [0.14%, 11.4%]) and AND (β=3.9% [1.3%, 6.6%]) were positively associated with 17β-estradiol. Interactions were observed between OP metabolites on associations with DHEA and testosterone.

Conclusion

OP metabolites were positively associated with testosterone, and cortisol, and negatively associated with DHEA, with stronger associations in boys. NNI metabolites were positively associated with 17β-estradiol. Thus, OPs and NNIs may be endocrine disruptors in adolescents. Replication is warranted.
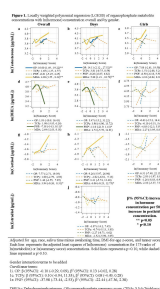
Trends in rural and urban cigarette smoking quit ratios in the United States, 2010-2020

Maria Parker* Maria Parker Andrea Weinberger Emma Eggers Erik Parker Andrea Villanti

Significance: Cigarette smoking prevalence is higher in rural versus urban areas of the United States (US) and the difference in smoking prevalence between these groups has widened over time. It is unknown whether there is a similar trend for a rural/urban difference in smoking cessation. The current study examined rural and urban cigarette quit ratios from 2010-2020 among US individuals.

Methods: Data were derived from the 2010-2020 National Surveys on Drug Use and Health, annual cross-sectional surveys of the non-institutionalized US population 12 years or older. Yearly rural and urban quit ratios (i.e., the proportion of former smokers among ever-smokers) were estimated from 2010-2020. Linear regression estimated trends in quit ratios over time.

Results: In 2020, the past-month smoking prevalence was higher for individuals living in rural areas (17.7%; 95% CI 15.7%, 20.0%) compared to urban areas (13.1%; 95% CI: 12.1%, 14.1%). In addition, quit ratios for those in urban areas (53.8%; 95% CI: 51.3%, 56.5%) were higher than the quit ratios for persons in rural areas (52.7%; 95% CI: 48.2%, 57.2%). Urban quit ratios were higher than rural quit ratios from 2010-2020 (OR: 1.18; 95% CI: 1.13, 1.23; $p<0.001$). This relationship was also seen after adjusting for background characteristics, (AOR: 1.14; 95% CI: 1.09, 1.20; $p<0.001$). Additionally, we saw a linear increase in quit ratios over time in both unadjusted (OR: 1.03; 95% CI: 1.03, 1.04; $p<0.001$) and adjusted (AOR: 1.02; 95% CI: 1.01, 1.02; $p<0.001$) analyses.

Conclusions: Smoking prevalence was higher in rural areas compared to urban areas. Quit ratios in rural areas were lower than those in urban areas and have increased over the past decade in the US. These updated findings highlight important rural-urban differences in smoking cessation that may contribute to differences in smoking prevalence. Interventions to increase cessation in rural areas are needed to stem disparities in tobacco use and its effects on the health of rural populations.
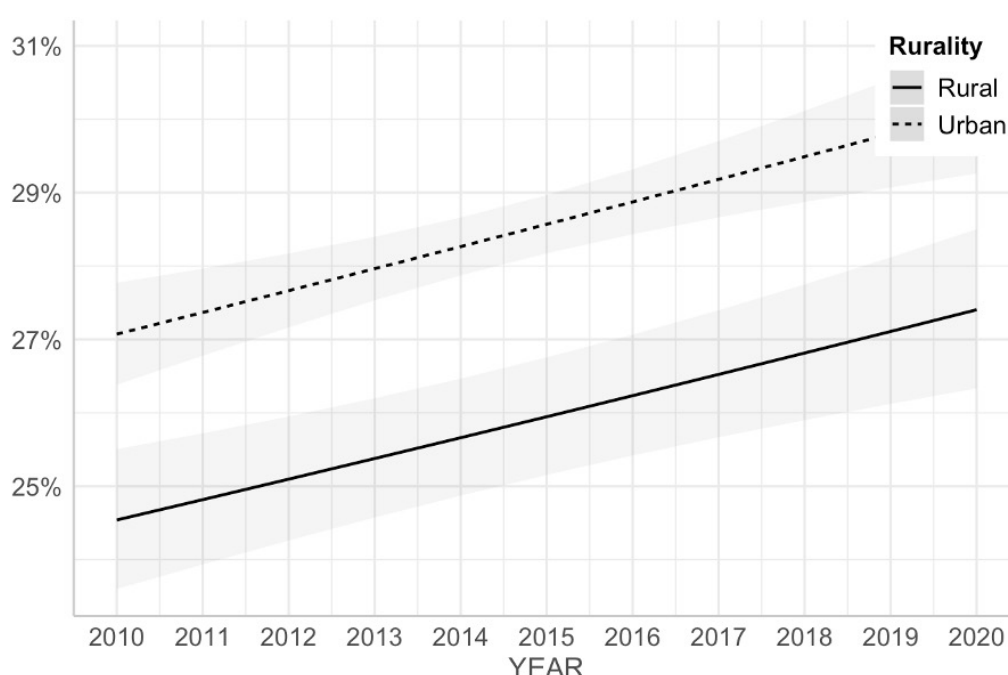
Trends in racial and ethnic disparities in HIV care continuum measures among U.S. adults in the North American AIDS Cohort Collaboration o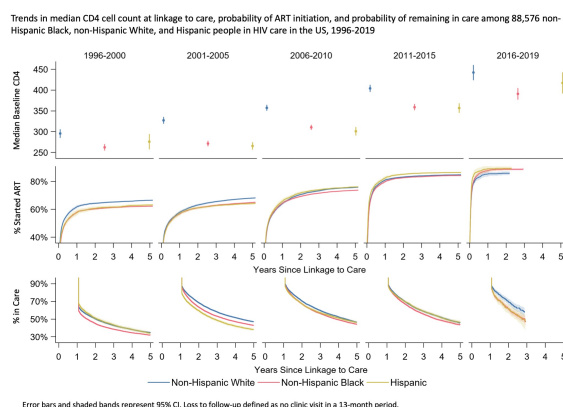n Research and Design (NA-ACCORD), 1996-2019 Lauren Zalla* Lauren Zalla Stephen R. Cole Joseph J. Eron Adaora A. Adimora Anissa I. Vines Michael A. Horberg Stephen Crystal Vincent C. Marconi Emily C. Williams Angel M. Mayor M. John Gill Keri N. Althoff Michael J. Silverberg Jessie K. Edwards for the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) of IeDEA

Identifying differences across racialized and ethnic groups in HIV severity at linkage to care, time to combination antiretroviral therapy (ART) initiation, and time to loss to follow-up (LTFU) may help inform interventions to reduce survival inequities among people with HIV (PWH).

We included 88,576 treatment-naïve PWH successfully linked to care (i.e., ≥2 clinic visits in 12 months) across all US states and territories from 1996-2019. We accounted for missing data using multiple imputation. We compared HIV severity at linkage to care among non-Hispanic Black, non-Hispanic White, and Hispanic PWH using median entry CD4 cells/mm^3. We compared time to ART initiation and LTFU across groups using the Aalen-Johansen estimator, accounting for the competing risk of death. To examine time trends, we stratified by calendar period at linkage to care (1996-2000, 2001-05, 2006-10, 2011-15, 2016-19).

Median entry CD4 was consistently lower among Black and Hispanic vs. White PWH from 1996-2015. From 2016-19, median entry CD4 was similar among Hispanic vs. White PWH (difference: -23 cells/mm^3; 95% CI -55, 9), but remained lower among Black vs. White PWH (-50; -74, -26). White PWH started ART earlier than Black or Hispanic PWH from 1996-2000. From 2001-15, time to ART initiation was similar or longer among Black and Hispanic vs. White PWH, despite lower entry CD4 and guidelines recommending ART initiation at <350 CD4 cells/mm^3. By 2016-19, ART uptake within 1 year of linkage to care was higher among Hispanic (+4%; 1, 7) and Black (+3%; 95% CI 0, 5) vs. White PWH. LTFU was more frequent among Black and Hispanic vs. White PWH. In 2016-19, 9% fewer Black (95% CI 4, 13) and 8% fewer Hispanic (2, 14) PWH attended a clinic visit within 13 months of successful linkage to care.

The persistent Black-White disparity in entry CD4 (likely associated with delayed diagnosis and linkage to care) and differential LTFU are potential targets for interventions to reduce survival inequities among PWH.

Trends in median CD4 cell count at linkage to care, probability of ART initiation, and probability of remaining in care among 88,576 non-Hispanic Black, non-Hispanic White, and Hispanic people in HIV care in the US, 1996-2019

Error bars and shaded bands represent 95% CI. Loss to follow-up defined as no clinic visit in a 13-month period.

Racial/ethnic disparities in hepatic steatosis, inflammation, and fibrosis in the U.S. Population (NHANES 2017-2018). Kevin Martinez-Folgar* Kevin Martinez-Folgar Usama Bilal Mariana Lazo

Liver disease mortality is a key contributor to recent declines in life expectancy in the US. We aimed to characterize racial/ethnic disparities in fatty liver disease manifestations (hepatic steatosis, inflammation, and fibrosis), liver disease risk factors and social vulnerability factors in a nationally representative sample of the US population. We included all adult participants in the 2017-2018 cycle of the National Health and Nutrition Examination Survey with complete data (N= 3255). We used elevated controlled attenuation parameter, elevated liver enzymes and elevated liver stiffness as definitions of hepatic steatosis, inflammation, and fibrosis, respectively. We included education, poverty, health insurance, and regular access to healthcare as social vulnerability; and adiposity, diabetes, viral hepatitis, and alcohol consumption as liver disease risk factors. We calculated age-adjusted prevalence of hepatic steatosis, inflammation, and fibrosis, and social vulnerability and liver disease risk factors, by race/ethnicity. We used Poisson regression models to estimate age- and gender- prevalence ratios of each outcome by race/ethnicity. We found an overall age-adjusted prevalence of hepatic steatosis, inflammation, and fibrosis of 22.8%, 15.4%, and 7.3%, respectively. Hispanics had the highest prevalence of all 3 liver outcomes (27.4%, 17.5%, and 9% for hepatic steatosis, inflammation, and fibrosis, respectively) (Figure), the highest prevalence of all social vulnerability factors, and very high prevalence of increased adiposity (45% obesity), diabetes (16.4%), and heavy alcohol drinking (18.7%). There are large racial/ethnic disparities in the prevalence and severity of fatty liver disease. Our results suggest that both social and proximal risk factors of liver disease cluster in populations with higher fatty liver disease supporting a syndemic model exacerbating racial/ethnic disparities.

Age-Adjusted Prevalence of Hepatic Steatosis, Inflammation, and Fibrosis and Prevalence Ratios (95% Confidence Intervals) for the Association between Race/Ethnicity with Liver Disease outcomes in the U.S. Population (NHANES 2017-2018)
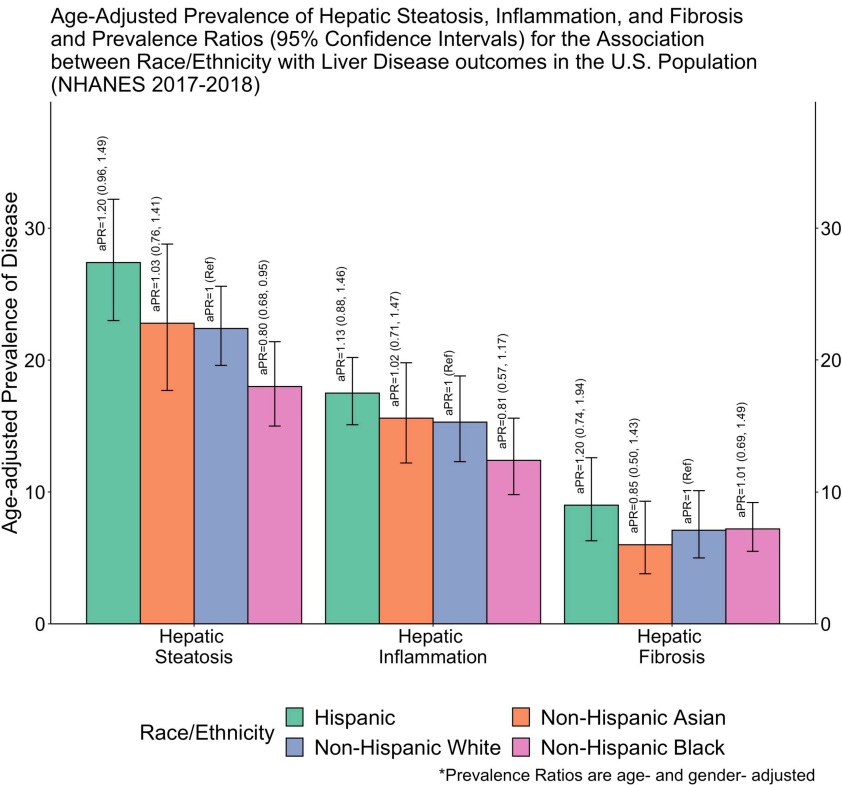
Black-White disparity in severe cardiovascular maternal morbidity: a systematic review and meta-analysis Ugochinyere Vivian Ukah* Ugochinyere Vivian Ukah Xinting Li Shu Qin Wei Jessica Healy-Profitós Natalie Dayan Nathalie Auger

Introduction: Racial disparities exist in adverse pregnancy complications but no study had quantified Black-White disparities in the occurrence of severe cardiovascular maternal morbidity. Our objective was to systematically review and synthesize existing evidence on Black-White disparities in the prevalence of severe cardiovascular maternal morbidity.

Methodology: MEDLINE, EMBASE, and CINAHL databases were searched until July 31, 2021 for studies comparing the risk of severe cardiovascular maternal morbidity between Black and White women. Severe cardiovascular maternal morbidity included stroke, acute myocardial infarction, and peripartum cardiomyopathy, occurring during pregnancy, delivery, or postpartum. Relevant information including adjusted and unadjusted effect estimates were extracted and the quality of included studies was assessed using the Newcastle-Ottawa scale. Random-effects models were used to estimate the pooled association between Black and White race and severe cardiovascular maternal morbidity.

Results: Eighteen eligible studies, which included a total of 7,656,876 Black women and 26,412,600 White women, were included in our systematic review and meta-analysis. Black women had an increased risk of any severe cardiovascular maternal morbidity (adjusted odds ratio, 1.90; 95% confidence interval, 1.54-2.33), compared with White women. Black women were also at increased risks of stroke (adjusted odds ratio, 2.13; 95% confidence interval, 1.39-3.26), acute myocardial infarction (adjusted odds ratio, 1.38; 95% confidence interval, 1.14-1.68), and peripartum cardiomyopathy (adjusted odds ratio, 1.71; 95% confidence interval, 1.51-1.94).

Conclusion: The risk of severe cardiovascular maternal morbidity is significantly higher in Black women than in White women, despite adjusting for confounders. Identifying effective ways to reduce Black-White inequality in serious cardiovascular maternal outcomes should be a priority for public health.

Selection Bias Masks Racial Differences in Age at Menopause: The Study of Women's Health Across the Nation

Alexis Reeves* Alexis Reeves Michael Elliott Carrie Karvonen-Gutierriez Sioban Harlow

Assumptions regarding "normative" aging, including average age at onset of disease, are often based on White populations. However, evidence suggests that Black and Hispanic populations may experience "weathering" or accelerated health declines compared to Whites due to the cumulative impact of social and economic marginalization. If "weathering" leads to a differential probability of inclusion into a cohort study, it will likely misinform understanding of aging in minoritized populations. Using the Study of Women's Health Across the Nation (SWAN), a longitudinal multi-ethnic cohort of midlife women, and its cross-sectional screening study, we quantified the extent of potential selection bias at study commencement and re-estimated racial/ethnic differences in age at menopause, the main outcome of SWAN, with adjustment for various forms of potential selection bias. Left truncation was corrected for using inverse probability weighting and right censoring using multiple imputation. Two selection mechanisms were identified, eligibility and participation. Black and Hispanic women had the lowest probability of eligibility stemming from a high prevalence of surgical menopause. Their eligibility rates decreased with increasing age faster than in White women. Correcting for selection biases showed that uncorrected analyses overestimated of the median age of menopause in Black and Hispanic women, thereby underestimating racial/ethnic disparities. After adjustment, Black women had earlier natural and surgical menopause (average 1.2 years) versus White women. Overall, this study found that failure to account for different forms of selection can lead to mis-estimation of racial/ethnic disparities in health and aging. Selection bias is particularly acute at study commencement, and particularly affects minoritized populations.

Adjusted Cox Proportional Hazard Models and Medians for Age at Final Menstrual Period

	Adjusted Model 1[ab] Unadjusted for Selection					Adjusted Model 6[cb] Fully Adjusted for Selection				
	Hazard	LCI	UCI	p-value	Median Age	Hazard	LCI	UCI	p-value	Median Age
Racial Group x FMP Type (ref = White, Natural FMP)										
Natural FMP										
White		*reference*			52.4 (52.1, 52.6)		*reference*			51.9 (51.8, 52.1)
Black	0.98	0.86	1.11	0.73	52.6 (52.4, 52.9)	1.13	1.00	1.26	0.04	51.5 (51.3, 51.6)
Chinese	0.88	0.73	1.07	0.21	52.7 (52.2, 53.5)	0.94	0.76	1.13	0.73	52.0 (51.6, 52.4)
Hispanic	1.04	0.81	1.33	0.77	52.1 (51.4, 53.1)	1.03	0.79	1.28	0.39	51.4 (51.2, 51.8)
Japanese	0.84	0.71	1.00	0.05	53.0 (52.5, 53.3)	0.83	0.69	0.98	0.99	52.4 (52.1, 52.8)
Surgical FMP										
White						1.58	1.19	1.98	0.01	48.9 (48.7, 49.4)
Black						3.21	2.80	3.62	0.00	47.2 (46.9, 47.6)
Chinese[d]						1.29	0.42	2.15	0.28	50.5 (46.8, 52.2)
Hispanic[d]						2.30	1.64	2.96	0.01	48.3 (47.9, 49.7)
Japanese[d]						1.43	1.02	1.85	0.04	51.4 (50.7, 51.7)

Note: [a]Model 1 - right censored for any missing FMPs and for observed surgical FMPs (nevents = 1653). [b]Adjusted for: baseline education, baseline self-reported health, baseline and last known prior to FMP waist circumference, baseline smoking status, baseline alcohol use, baseline physical activity score. [c]Model 6 - adjusts for all forms of selection by incorporating imputation and weights (nevents = 3302). [d]Chinese (n = 13), Hispanic (n = 39), Japanese (n = 16), all other groups > 90 observations.

Estimation of Racial Disparities in Influenza Vaccine Use among Nursing Home Residents

Joe B.B. Silva* Joe Silva Chanelle J. Howe John W. Jackson Barbara Bardenheier Melissa R. Riester Robertus van Aalst Matthew Loiacono Andrew R. Zullo

Disparities in influenza vaccination by marginalized racial group status and geography are significant. However, little is known about the geographic distribution of racial disparities in influenza vaccination among White and Black nursing home residents across states and hospital referral regions (HRRs). This nationally representative retrospective cohort study was conducted among short-stay (post-acute care) and long-stay (long-term care) United States nursing home residents across seven distinct influenza seasons from October 1, 2011, to March 31, 2018. Eligible residents were those aged ≥65 years and enrolled in Traditional Medicare. Race was measured using the Medicare Beneficiary Summary File Research Triangle Institute race variable. Influenza vaccination was obtained from resident Minimum Data Set assessments from October 1 through June 30 of a particular influenza season. Because residents could be represented across multiple seasons, we conducted our analyses at the person-period, or "resident-season," level. Using direct standardization accounting for age and sex, disparities were measured in aggregate by subtracting the proportion of Black residents vaccinated from the proportion of White residents vaccinated. The study included 7,807,187 short-stay resident-seasons (89.7% White, 10.3% Black) in 14,889 nursing homes and 7,308,111 long-stay resident-seasons (86.7% White, 13.3% Black) in 14,885 nursing homes. Wide geographic variation of racial disparities in influenza vaccination, ranging from no disparity to disparities in excess of 25 percentage points, was observed for both resident populations and across states/HRRs. The largest disparity was among short-stay residents in the HRR associated with Chicago, Illinois (26.57 percentage points). Understanding the distribution of influenza vaccine use by marginalized racial group status and geography can aid in the development of targeted interventions to increase vaccine uptake and promote health equity.

Figure: Directly Standardized Differences in Influenza Vaccination between Non-Hispanic White and Black Short-Stay (Post-Acute Care) and Long-Stay (Long-Term Care) Nursing Home Residents, by State and Hospital Referral Region, 2011-2018 Influenza Seasons.
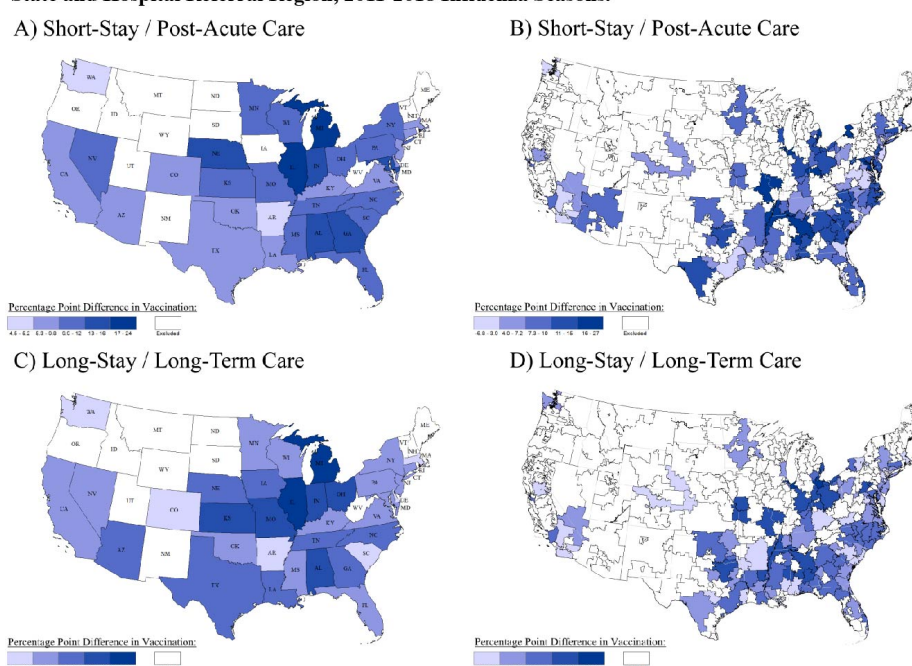
Racial/ethnic and socioeconomic inequalities in breast and cervical cancer mortality in the 100 million Brazilian cohort: an intersectional approach Joanna MN Guimarães* Joanna MN Guimarães Emanuelle Goes Ligia Gabrielli Conceição Almeida Sheila Alvim Mauricio Barreto Isabel dos Santos Silva Estela Aquino

Little is known about the impact of race/racism, and its intersection with socioeconomic status (SES), on mortality from breast (BC) and cervical cancer (CC). We examined racial and socio-economic status (SES) inequities, and their joint effects, on BC and CC mortality within the 100 Million Brazilian Cohort.

In all, 20,665,005 women aged 18-100 years were followed-up from January 1, 2004 to December 31, 2015, and their vital status and cause of death ascertained through linkage to the national mortality database. Poisson regression was used to assess cancer mortality associations with self-reported race (White/Brown/Black/Asian/Indigenous women) and SES (educational level and household conditions) in mutually-adjusted analysis with further adjustment for other potential confounders.

Both race and SES were independently associated with CC mortality. Relative to White women, CC mortality was 64% (fully-adjusted-rate ratio, aRR (95% CI): 1.64 (1.27-2.13), 62% (1.62, 1.19-2.21), 22% (1.22, 1.12-1.32) and 20% (1.20, 1.14-1.27) higher among Indigenous, Asian, Black and Brown women, respectively. Racial differences were less marked for BC, with Black women having higher mortality (1.17 (1.09-1.24)) than White women. SES gradients in mortality were also more marked for CC than BC (eg. aRR (95% CI) for ≤5 vs >9 education years: 2.63 (2.40-2.88) and 1.06 (1.00-1.13), respectively). Race differences in CC mortality were present within each SES strata but their magnitude was more marked among women of low education and poor household conditions (P for interaction=0.007 and 0.002, respectively). Consequently, Black and Brown women with ≤5 education years were ~3 times more likely to die from CC (2.90, 2.44-3.44 and 2.97, 2.54-3.46, respectively) than White women with >9 education years (Figure).

Low SES magnified racial inequities in cervical cancer mortality. The intersection between race and SES must be considered in any efforts to reduce racial inequities in health.

Figure. Joint effects of race/ethnicity and educational level on cervical cancer mortality in the 100 Million Brazilian Cohort, 2004-2015 (n=20,564,437 women aged 18-100 years). [Estimates for Asian and Indigenous women not shown due to small numbers].
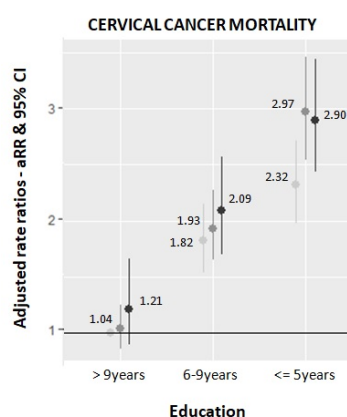
Income inequality, all-cause mortality, and self-rated health: a causal systematic review and meta-analysis

Michal Shimonovich* Michal Shimonovich Anna Pearce Hilary Thomson Mhairi Campbell Rachel Thomson Srinivasa Vittal Katikireddi

Background: This systematic review evaluated the relationship between income inequality and all-cause mortality (ACM) or self-rated health (SRH) in adults through a causal lens. **Methods**: We included multilevel studies evaluating income inequality and individual ACM or SRH and adjusted for individual-level socioeconomic position. Two reviewers independently screened records from Medline, ISI Web of Science, EMBASE and the National Bureau of Economic Research. We conducted a random-effects meta-analyses and explored pre-specified sources of statistical heterogeneity in meta-regressions and subgroup analyses. We assessed risk of bias (RoB) with Cochrane ROBINS-I tool, certainty with GRADE and causality with modified Bradford Hill viewpoints. **Results**: 53,722 studies were screened, 460 full texts assessed, and 91 met inclusion criteria with 55 meta-analysed: 36 cross-sectional SRH studies (2,108,209 individuals), and 19 ACM cohort studies (63,528,533 individuals). A 5% increase in Gini coefficient, an income inequality measure, was associated with poorer SRH (OR 1.07 (1.04–1.10)) and increased ACM (RR 1.02 (1.01–1.03)). Heterogeneity was high (SRH: I^2=97.9%; ACM: I^2=94.8%) and not explained by variations in time-lag, follow-up, area-level income inequality, or world region. Most SRH and ACM studies had serious-critical and moderate-serious RoB, respectively, due to confounding. Removing critical SRH and serious ACM studies slightly attenuated estimates. Unexplained heterogeneity and lack of evidence using causal methods to address confounding suggested low certainty of a causal effect. **Discussion**: The current evidence base shows a small negative association between income inequality and health, but causality has not been established. Natural experiment studies addressing confounding may be helpful, though in the absence of design-based approaches to evaluate this important relationship statistical tools to adjust for confounding in observational data should be used.

Multiple sleep dimensions and cardiometabolic multimorbidity by sex/gender and race: Findings from the Healthy Aging in Neighborhoods of Diversity across the Life Span Study

Erline E Martinez-Miller* Erline Martinez-Miller Dana M Alhasan Alyssa Gamaldo W. Braxton Jackson II Alan B Zonderman Michele K Evans Chandra L Jackson

Cardiometabolic multimorbidity (CM) is associated with poor health, complex care needs, and higher mortality. Although not yet an established risk factor, poor sleep has been associated with individual cardiometabolic conditions; greater insight into associations with CM – given its prevalence – can illuminate whether sleep is a key risk factor. Among 2,171 eligible adult participants of the Healthy Aging in Neighborhoods of Diversity across the Life Span Study (2013-2017), we examined cross-sectional sleep-CM (>1 condition consisting of obesity, hypertension, and diabetes). We assessed sleep using actigraphy-measured duration (<6, 6, 7-8, and 9 hours), Pittsburgh Sleep Quality Index (PSQI) overall score (>5=poor) and sub-categories (e.g. efficiency), and self-reported apnea diagnosis. We investigated sex (man, woman) and race (Black, White) as modifiers. Adjusting for sociodemographics and then health behaviors/conditions, we estimated PR (95% CI) using Poisson regression with robust variance. Most participants were women (59%), Black race (62%), aged ≥50 years (73%), obese (49%) and had hypertension (68%), diabetes (24%) and CM (47%). CM was more prevalent among women (53%) than men (38%). Overall, 52% had short sleep (≤6 hours), 63% had poor sleep, and 10% reported apnea. Adjusting for sociodemographics, CM was more prevalent among participants with poor overall sleep score (1.12 [1.02, 1.24]), disturbances (1.20 [1.10, 1.30]), insufficient duration (PSQI; 1.12 [1.04, 1.22]), poor efficiency (1.16 [1.07, 1.26]), poor quality (1.09 [1.01, 1.19]), and apnea (1.37 [1.28, 1.47]). The association was stronger among men (vs. women) with insufficient duration and apnea, and among Whites (vs. Blacks) with poor efficiency and apnea. Associations were attenuated with further adjustment for health factors, which may mediate the relationship. Adults with poor sleep had a higher prevalence of CM, highlighting the potential for sleep promotion to improve cardiometabolic health.
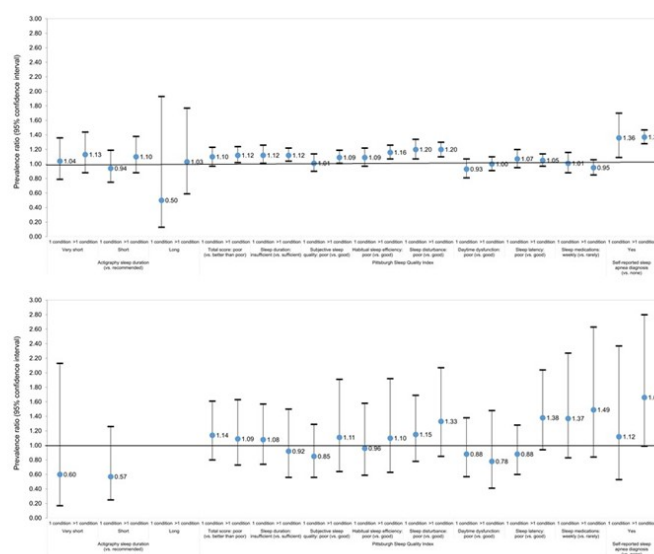
Figure 1. Adjusted[a,b,c] prevalence ratios (95% confidence intervals) for cardiometabolic multimorbidity[d] by sleep dimensions among adult participants of the Healthy Aging in Neighborhoods of Diversity across the Life Span Study, 2013-2017.
[a] Sociodemographic covariates adjusted for age, sex/gender, race, marital status, educational attainment, employment status, annual household income, poverty status, length of residence, and household composition.
[b] Health covariates adjusted for smoking status, alcohol consumption, physical activity, posttraumatic stress disorder, depressive symptoms, and sleep medications (via Pittsburgh Sleep Quality Index).
[c] Missing estimates non-estimable due to model nonconvergence.
[d] Cardiometabolic multimorbidity defined based on obesity (body mass index ≥30 via height and weight measurement), hypertension (≥130 systolic or ≥80 diastolic blood pressure measure, self-reported medical diagnosis, or record of medication), and diabetes (fasting plasma glucose concentration of ≥126 mg/dl [7.0 mmol/L], self-reported medical diagnosis, or record of medication).

The association between food insecurity and depression modified by the combined effect of nativity and social cohesion among New York City residents

Kelly Laurent* Kelly Laurent Elizabeth A. Kelvin

Neighborhood cohesion may decrease the risk of food insecurity and modify its impact on mental health. Immigrant and native-born populations may have different perceptions of neighborhood cohesion due to cultural differences with neighbors and language barriers. We looked at whether there was complex interaction among nativity, perceived neighborhood cohesion, and food insecurity in their association with depression among residents of New York City (NYC), where 40% of the population is foreign-born, using 2018 Community Health Survey data. Participants (N=10,076) included adults ages 18+ who lived in NYC. We conducted multivariable logistic regression adjusted for the complex sampling methods and weighted to the NYC population to estimate the association between food insecurity and depression and added all two- and three-way interaction terms among nativity, neighborhood cohesion, and food insecurity to the multivariable model to assess complex interaction. We found that food insecurity and depression had a significant dose-response relationship (severe food insecurity [OR=4.61; p<0.001], moderate food insecurity [OR=3.37; p<0.001], mild food insecurity [OR=2.57; p<0.001] versus food secure). The interaction among food insecurity, nativity, and social cohesion was statistically significant (p-value range: <0.001-0.954). In neighborhoods with high cohesion, there was a dose-response relationship between food insecurity and depression among both foreign- and US-born but it was stronger among those US-born. In neighborhoods with moderate social cohesion, there was a significant association between food insecurity and depression in a dose-response relationship only among those foreign-born, and in neighborhoods with low cohesion, the association between food insecurity and depression was stronger and significant only among those US-born. High community cohesion may decrease the impact of food insecurity on depression especially among those foreign-born.

Results of multivariable logistic regression model looking at the adjusted association between food security and depression stratified on nativity (Foreign versus US-born) and Level of Social Cohesion*
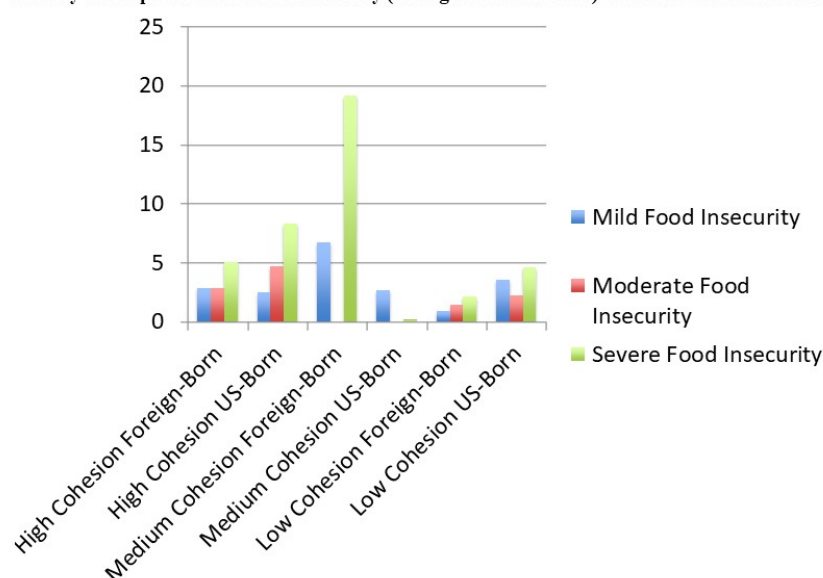
*Model is adjusted for age, sex, race/ethnicity, education, income, health insurance status, and marital status

Eliminating Racial Disparities in Dementia Risk by Equalizing Education Quality Chelsea
Liu* Chelsea Liu Audrey R. Murchland Tyler J. VanderWeele Deborah Blacker

Background: Higher risk of dementia among racial and ethnic minorities compared to White
populations in the U.S. has been attributed to lifecourse exposures to adverse conditions such as
lower educational attainment, but most studies have not considered additional disparities in
education *quality*. We aimed to determine the extent to which disparities in dementia would be
reduced if different racial groups had hypothetically received the same quality of education.

Methods: We conducted a literature review to assess whether and how measures of education
quantity and quality are utilized in normative data studies. In a separate search of the entire
psychometric literature, we identified parameter estimates of relationships between race, education
quality and dementia; and used a sensitivity analysis framework to calculate the adjusted association
between race and dementia had education quality been equalized between White and Black
participants.

Results: Few normative data studies included measures of education quality. Our literature search
identified the following relevant parameter estimates: 44.3% Black participants and 10.5% White
participants had "limited literacy" (<9th grade reading level), which was associated with a 53%
greater hazard of dementia compared with "adequate literacy" (>=9th grade reading level) after
adjusting for educational attainment. Applying these parameters to a hazard ratio (HR) of 1.37
(95%CI: 1.12, 1.67) for the risk of dementia among Black vs. White participants, we obtained an
adjusted HR of 1.17 (0.96, 1.43).

Discussion: Our work using available measures of education quality suggest that if measures of
education quality were equalized across groups by race without changing disparities in educational
attainment, racial disparities in dementia risk would be reduced substantially. Future studies should
seek to include and operationalize education quality in order to better understand the relationship
between race, education, and dementia.

Health Disparities

Neighbourhood income inequality, maternal depression, and child physical aggression at 5-years of age

Gregory Farmer* Gregory Farmer Roman Pabayo

Background

Pathways linking contextual income inequality and health have been hypothesized, with few studies identifying the role of potential mediators. The objective of the current study is to assess whether income inequality is linked to child physical aggression through maternal depressive symptoms.

Methods

We analyzed data from the All Our Families (AOF) longitudinal cohort located in Calgary, Alberta at 5-years postpartum. The analytical sample consisted of 1164 mother-preschooler dyads nested within 160 neighbourhoods. Income inequality was measured via the Gini coefficient. At 5-years postpartum mothers completed the Behavior Assessment System for Children, Second Edition (BASC-2), which assessed physical aggression symptoms. Maternal depression was assessed at 3-years postpartum using the Center for Epidemiologic Scales for Depression (CES-D). Generalized structural equation path models assessed the relationship between neighbourhood income inequality, maternal depression, and preschool physical aggression.

Results

The mean Gini coefficient across the 160 neighbourhoods was 0.33 (S.D = 0.05) and ranged from 0.23 to 0.56. Moderate income inequality was associated with maternal depression symptoms b = 1.26 (95% CI: 0.037, 2.48). Maternal depression was subsequently associated with preschooler physical aggression b = 0.26 (95% CI: 0.20, 0.34). Moderate income inequality was also associated with child physical aggression b = 1.26 (95% CI: 0.17, 2.34). Unexpectedly, high income inequality was not associated with either preschooler physical aggression b = 0.99 (95% CI: -0.08, 2.05) or maternal depression b = 0.15 (95% CI: -1.04, 1.33).

Conclusion

Moderate neighbourhood income inequality was associated with maternal depression and child physical aggression. However, no dose-response relationship was observed as high inequality was not associated with any outcomes. To corroborate this finding, future investigations should employ longitudinal methods.
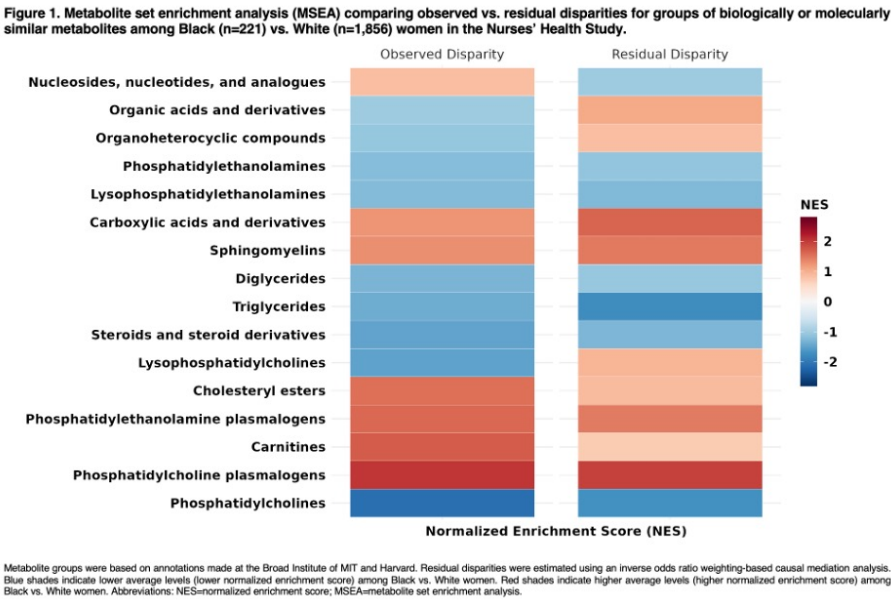
Disparities in Metabolomic Profiles Between Black and White Women Emma McGee* Emma McGee Oana Zeleznik Clary Clish Rulla Tamimi A. Heather Eliassen

Background: Black-White disparities in women's health represent a pressing public health issue. Metabolomic profiles are potential biomarkers of and risk factors for a variety of health conditions, yet many metabolomics studies lack racial diversity. We aimed to 1) describe observed Black-White disparities in metabolomic profiles and 2) estimate residual disparities after implementing hypothetical interventions.

Methods: We included 221 Black and 1,856 White women from the Nurses' Health Study. Plasma metabolites (n=321) were measured via liquid chromatography tandem mass spectrometry. We used linear regression to describe observed disparities and Metabolite Set Enrichment Analysis (MSEA) to assess disparities in metabolite groups. We estimated residual metabolomic disparities after hypothetical interventions to eliminate Black-White differences in disease risk factors using causal mediation analysis.

Results: A total of 64 metabolites had observed disparities |0.50| standard deviations**.** The largest disparity was observed for N6,N6-dimethlylysine (mean difference for Black vs. White women: -0.99 standard deviations, 95% CI: -1.12, -0.85). MSEA showed that, compared to White women, Black women had higher average levels phosphatidylcholine (PC) plasmalogens, carnitines, phosphatidylethanolamine plasmalogens, and cholesteryl esters and lower levels of PCs, lysoPCs, steroids, triglycerides, and diglycerides. Hypothetical interventions on lifestyle, reproductive, and contextual factors reduced some disparities, notably disparities in carnitines (MSEA score of 1.73 for observed disparity vs. 0.71 after hypothetical interventions) and cholesteryl esters (1.55 vs. 0.88).

Conclusions: Substantial disparities in metabolomic profiles exist between Black and White women. Interventions aimed at reducing differences in contextual, reproductive, and lifestyle features may mitigate some of these disparities. Work is ongoing to validate these findings in the Women's Health Initiative.

Figure 1. Metabolite set enrichment analysis (MSEA) comparing observed vs. residual disparities for groups of biologically or molecularly similar metabolites among Black (n=221) vs. White (n=1,856) women in the Nurses' Health Study.

Metabolite groups were based on annotations made at the Broad Institute of MIT and Harvard. Residual disparities were estimated using an inverse odds ratio weighting-based causal mediation analysis. Blue shades indicate lower average levels (lower normalized enrichment score) among Black vs. White women. Red shades indicate higher average levels (higher normalized enrichment score) among Black vs. White women. Abbreviations: NES=normalized enrichment score; MSEA=metabolite set enrichment analysis.

LATEBREAKER

Health Disparities

Inequity in timing of infection sharply limited benefits of declining SARS-CoV-2 case-fatality among minoritized populations Ramya Naraharisetti* Ramya Naraharisetti Rob Trangucci Krzysztof Sakrejda Nina B. Masters Ryan Malosh Emily T. Martin Marisa Eisenberg Joseph N.S. Eisenberg Jon Zelner

Introduction. Racial/ethnic disparities in mortality are a central feature of the COVID-19 pandemic in the United States. However, little is understood about how and why inequities in mortality from SARS-CoV-2 have changed over time.

Objectives. To understand how improvements in the clinical management and prevention of SARS-CoV-2 infection affected racial/ethnic disparities in mortality over time in relative rates of infection and case-fatality.
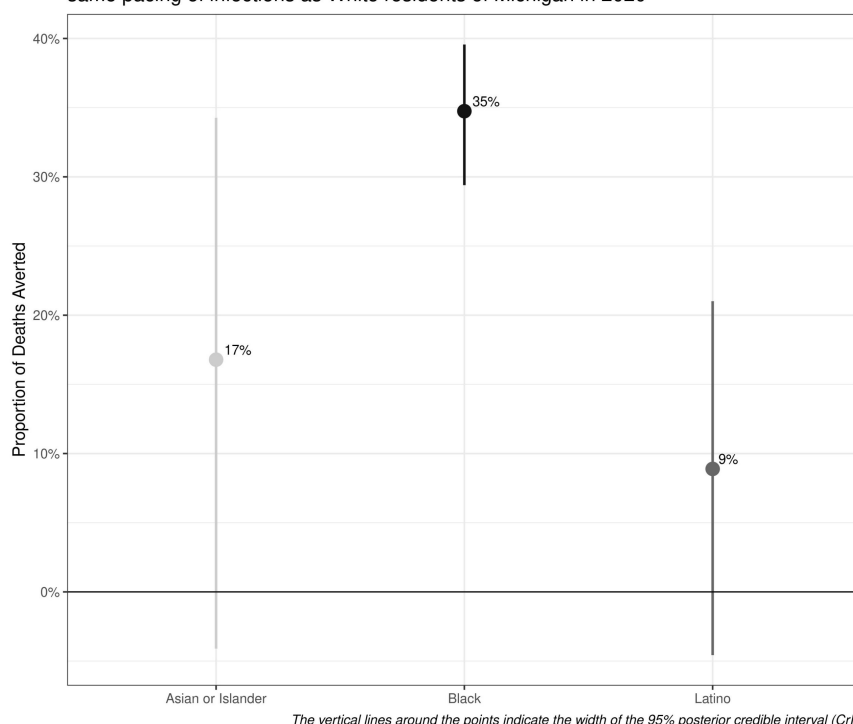
Methods. Utilizing detailed case data from the Michigan Disease Surveillance System, we estimated age- and group-specific SARS-CoV-2 incidence and case-fatality rates during three distinct periods of the SARS-CoV-2 pandemic during 2020 in Michigan.

Results. Throughout 2020, we observed a narrowing of disparities in infection risk between Black and White residents from an incidence rate ratio (IRR) of 4.98 (95% CrI = 4.90 – 5.07) in early 2020 to 0.79 (95% CrI = 0.78 – 0.80) at the end of the year. Because population-wide case-fatality rates also fell precipitously during this period, we estimate that 35% (CrI = 30% – 40%) of 2020 SARS-CoV-2 deaths among Black Michigan residents could have been prevented if the pace of infection in Black and White populations was equalized.

Conclusions. Structural inequalities allowed many White residents to 'wait out' infection when case-fatality rates were high, while residential and occupational segregation systematically denied this ability to Black and other non-White residents of Michigan.

Policy Implications. Preventing inequity in infection and death via structural remedies must become a key focus of pandemic preparedness.

Figure 1. Proportion of deaths averted if minoritized residents experienced the same pacing of infections as White residents of Michigan in 2020

The vertical lines around the points indicate the width of the 95% posterior credible interval (CrI).

Evaluating the Impact of the Medicaid Expansion Program on Diabetes Hospitalization: A Generalized Synthetic Control Method Approach. Fan Zhao* Fan Zhao Roch Nianogo

Objective

Diabetes is the most expensive chronic disease in the US, and hospital inpatient care accounts for 30% of the total medical care. Less is known about Medicaid Expansion's intermediate effect on diabetes hospitalization. This study investigated the impact of the Medicaid expansion on diabetes hospitalization by states and payer two years after the expansion.

Research Design and Methods

We limited to adults aged 19 to 64 years old and identified state-level data of twelve Medicaid expansion states (AZ, AR, CA, CO, IL, IN, KY, MD, MA, NV, NJ, and NY), and ten control states (FL, GA, KS, MO, NC, SC, TN, TX, UT and WI) from 2010 Quarter one to 2016 Quarter four. We performed generalized synthetic control method in this quasi-experiment study.

Results

The Medicaid Expansion decreased total diabetes hospitalization in most states, with an overall decrease of -0.03 per 1,000 population (95%CI -0.04, -0.02). The Medicaid share of diabetes hospitalization increased by 16.29% (95%CI 10.88, 21.69). The private insurance decreased by -2.86% (95%CI -5.71, -0.02). Uninsured share of diabetes hospitalization decreased by -14.17% (95%CI -19.52, -8.82).

Conclusion

Medicaid Expansion Program shifted diabetes hospitalization payer mix from private insurance and uninsured to Medicaid and had a moderate effect on decreasing total diabetes hospitalization.

Urban spatial accessibility of primary care and hypertension management in Chicago's South Side: a study from COMPASS cohort

Jiajun Luo* Jiajun Luo Briseis Aschebrook-Kilfoy Habibul Ahsan

Background: Hypertension is preventable. Understanding the relationship between spatial accessibility (SA) of primary care and hypertension helps develop interventions improving hypertension management. The study aims to investigate the association between SA of primary care and hypertension management.

Methods: Participants from the Chicago Multiethnic Prevention and Surveillance Study (COMPASS), a population-based cohort study, between 2013 and 2019 were analyzed. Locations of primary care providers in Chicago were obtained from MAPSCorps. A score were generated for SA of primary care. Higher score indicates better accessibility. The hypertension was defined as systolic blood pressure ≥130 mm Hg or diastolic blood pressure ≥80 mm Hg. Logistic regression was used to estimate OR and 95% CI.

Results: 5096 participants (mean age: 53.4±10.8) were included. The study population was predominantly non-Hispanic black (84.0%), over 53% reported an annual household income <$15,000, and 37.3% were obese. Measured hypertension prevalence was 78.7% in this population, among which 37.7% were uncontrolled and 41.0% were unaware. Higher SA score was associated with lower hypertension prevalence. Compared to the 1st quartile of SA score, the OR strengthened from 0.82 (95% CI: 0.67-1.01) for the 2nd quartile, to 0.75 (95% CI: 0.62-0.91) for the 3rd quartile, and further to 0.73 (95% CI: 0.60-0.89) for the 4th quartile. Similar associations were observed for both uncontrolled and unaware hypertensions. However, SA score was not associated with hypertension medication use among participants who self-reported hypertension. When stratified by neighborhood socioeconomic status, higher SA score was associated with lower rates of unaware hypertension in both disadvantaged and non-disadvantaged neighborhoods.

Conclusion: Better spatial accessibility of primary care can improve hypertension awareness and management.

Association between spatial accessibility score of primary care and hypertension management
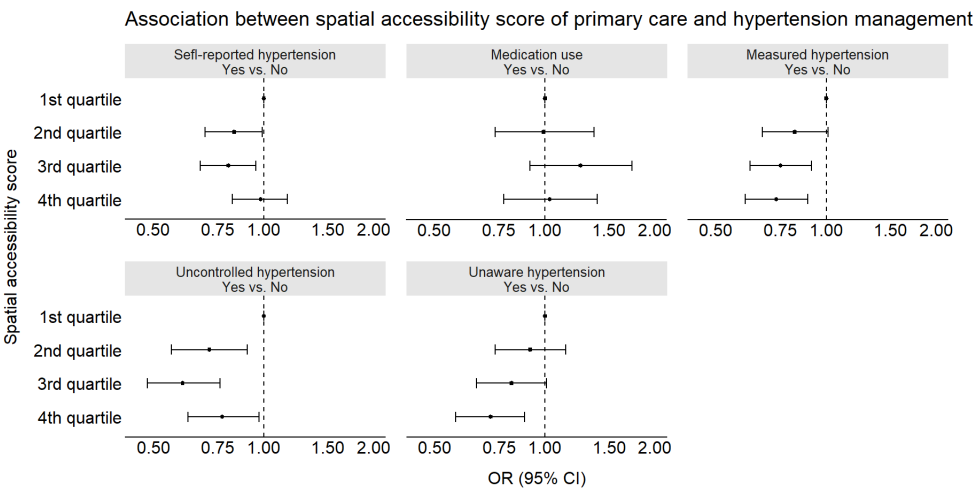
Trends in Scientific Publications on Ethics in Research and Ethics in Genomic Research

Ruchi Bhandari* R. Constance Wiener Ruchi Bhandari

Introduction: Ethics in research were codified in the U.S. with the Federal Policy for the Protection of Human Subjects, the Common Rule, in 1991. The Health and Human Services regulation, 45 CFR part 46, has guided research ethics. It was revised and published in the Federal Register in 2017. Publications regarding the importance of ethical conduct in research and specifically in genomic research have followed. The purpose of this research was to determine the trends in such publications.

Methods: Four major web browsers (Google Scholar, PubMed, Web of Science, and CINAHL) were queried with search terms "ethics in research" and "ethics in genomic research" for world-wide publications from 2011-2021.

Results: Google Scholar returned the most publications followed by PubMed, Web of Science and CINAHL for both the overall number of publications on ethics in research and those specific to genomic research. While in 2011, there were 929,955 overall publications on ethics in research this number significantly decreased to 290,924 in 2021. With linear regression analysis of year on publications on ethics, B=-0.931, p<.001. While in 2011, there were 31,551 publications on ethics in genomic research, in 2021 this number significantly increased to 82,289 publications (B=0.741, p<0.009).

Conclusion: There is a great need for research in ethics especially with the rapidly advancing technologies associated with genomic research. This has been observed in our study. However, there has been a threefold decline in overall publications on ethics in research. This is a concerning trend.

Health service use by home-care users with different six-month mortality risk profiles Maya Murmann* Maya Murmann Amy Hsu Michael Pugliese Doug Manuel Carol Bennett Sarah Beach Wenshan Li Rhiannon Roberts Peter Tanuseputro

Background: Palliative care is commonly misunderstood as only being relevant for people who are actively dying and in the final weeks or days of life. However, the relief of suffering through the provision of holistic and compassionate care is an essential component of care for all patients with a life- threatening illness. Clinicians, even palliative care specialists, often have difficulty estimating survival beyond a few weeks. The implementation of a palliative care approach requires accurate prognostication and understanding of the changing healthcare needs of a patient as they decline and approach death. The primary objective of this study was to describe health care service use for populations with different mortality risk profiles based on the Risk Evaluation for Support: Predictions for Elder-Life in the Community Tool (RESPECT), a prognostic tool previously developed and validated for home care users.

Methods: Using a cohort of 247,377 home care users in Ontario, Canada, patients were assigned to one of 61 mortality risk profiles using RESPECT. Service use was defined as total days per person-year within 6 months of a home care assessment using RESPECT. Services included any home care visit, palliative home care visit, hospitalization, emergency department visit and nursing home entry.

Results: The 6-month mortality within our study cohort was 14.3%. The mean predicted 6-month mortality risk ranged from 1.51% (95% CI 1.50%-1.52%) in the lowest risk group to 95.9% (95% CI 95.8%-96.1%) in the highest risk group. Nearly half of the cohort reported worsening capacity to perform activities of daily living. Regarding healthcare use, rates of hospitalizations and palliative home care use was highest in individuals with the highest mortality risk. Among the highest risk group, more days were spent in palliative home care than hospital while the opposite was observed among the lowest risk group.

Conclusion: Differences in health service use, including hospital care and palliative home care, were observed among home care users with varying mortality risk profiles, highlighting the value for prognostic indexes like RESPECT to inform care planning for individuals in the final years of life.

Effect of 2018 American College of Cardiology/American Heart Association Guideline on Statin Prescription for People Living with HIV Meng Pan* Meng Pan Afiba Manza-A. Agovi Ifedioranma Anikpo Esther Fasanmi Erika L. Thompson Jaquetta Reeves Rohit P. Ojha
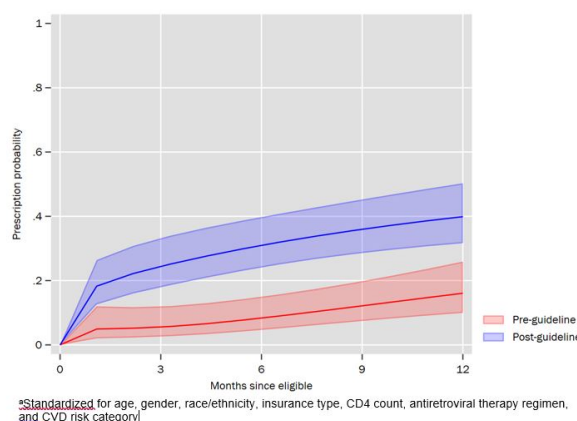
Background: People living with HIV (PLWH) have a high risk of cardiovascular disease (CVD). The American College of Cardiology (ACC)/American Heart Association (AHA) guidelines were updated in 2018 to explicitly include recommendations for statin use in primary CVD prevention among PLWH, but the effect of this guideline is unknown. We aimed to assess the effect of the 2018 AHA/ACC guideline on statin prescription among PLWH in an urban safety-net health system.

Methods: We emulated a single arm trial with historical comparison using data from our institutional HIV Care and Outcomes Registry (HIVCOR). PLWH eligible for this study were aged 40–75 years, engaged in HIV care between June 2016 and June 2021, had LDL cholesterol between 70 and 189 mg/dl, 10-year atherosclerotic cardiovascular disease (ASCVD) risk score ≥7.5%, no prior statin prescription, and no history of diabetes or ASCVD. Our intervention of interest was the 2018 AHA/ACC statin guideline. Our outcome was statin prescription, defined as a new statin prescription within 12-months of prescription eligibility. We used a flexible parametric model to estimate pre- and post-intervention standardized (marginal) prescription probabilities and corresponding risk difference (RD) with 95% confidence limits (CL), where standardization was based on age, gender, race/ethnicity, insurance type, CD4 count, antiretroviral regimen, and ASCVD risk category.

Results: Our study population comprised 194 PLWH (92 pre-guideline, 102 post-guideline), of whom 54% were aged <55 years, 86% were male, and 41% were non-Hispanic Black. The 12-month statin prescription probability was 16% (95% CL: 10%, 26%) pre-guideline and 40% (95% CL: 32%, 50%) post-guideline (RD=24%, 95% CL: 12%, 36%).

Conclusions: Assuming no substantial biases, our results suggest that the 2018 AHA/ACC guideline increased statin prescription among PLWH in an urban safety-net health system, but a sizable proportion of eligible PLWH were not prescribed statins.

Figure. Standardized[a] statin prescription probabilities among people living with HIV before and after the 2018 ACC/AHA guideline.

[a]Standardized for age, gender, race/ethnicity, insurance type, CD4 count, antiretroviral therapy regimen, and CVD risk category

Sexual Orientation and Sex of Sex Partners Among Men and Women with Primary and Secondary Syphilis, 2018-2019 Emily Learner* Emily Learner David Jackson Jeremy Grey Elizabeth Torrone

Introduction: Sexual orientation may not align with recent sexual behaviors, such as sex of sex partners (SOSPs), highlighting the importance of collecting both sexual orientation and sexual behaviors when examining disease disparities. Sexual orientation and SOSPs are collected for cases of sexually transmitted diseases reported via the National Notifiable Disease Surveillance System (NNDSS), but data are absent for most other NNDSS-reportable conditions. To inform potential collection of sexual orientation for other NNDSS-reportable conditions, we examined the intersection between sexual orientation and SOSPs among syphilis cases reported to NNDSS.

Methods: Primary and secondary (P&S) syphilis case notifications from 2018–2019 were extracted from the NNDSS. To minimize bias from incomplete reporting, we restricted the analysis to cases from states that reported sexual orientation and SOSPs for ≥70% of cases in both years. We calculated concordance between reported sex of sex partners in the past 12 months (men only, women only, both, unknown) and sexual orientation (gay/lesbian, straight, bisexual, unknown), stratified by current sex (male, female).

Results: From 2018–2019, 11,151 male P&S syphilis cases were reported by 7 states. Most men with only male sex partners (n=5,399) were reported as gay (82.2%), and most men with only female sex partners (n=2,948) were reported as straight (82.5%). Over half of men with male and female sex partners (n=828) were reported as bisexual (61.1%) (figure 1). Among 2,514 female P&S syphilis cases, most women reported only male sex partners (n=2,008), and of those, most were reported as straight (87.0%).

Conclusions: Among persons with P&S syphilis, sexual orientation and SOSPs did not align perfectly. Caution is needed in interpreting reported sexual orientation in NNDSS data, particularly when SOSPs data are not collected, as sexual orientation may not reflect recent sexual behaviors.
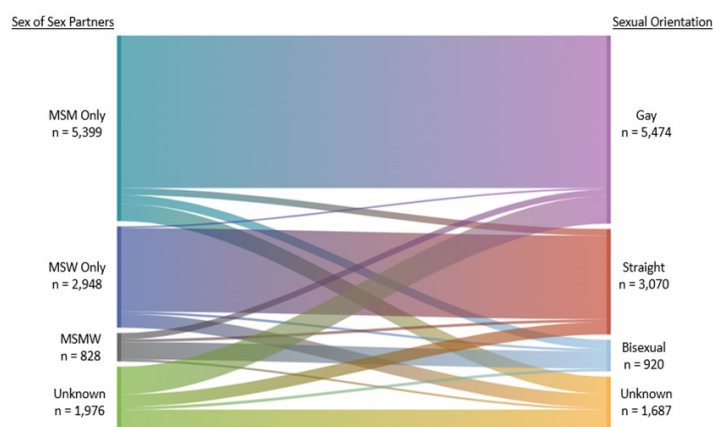
Figure 1: Concordance between sex of sex partners and sexual orientation for 11,151 male P&S syphilis cases from 7 jurisdictions in the US, reported via the National Notifiable Disease Surveillance System, 2018–2019.

A quantitative bias analysis to measure the effect of self-reported human papillomavirus vaccination on vaccine effectiveness estimates in a real-world setting Catharine Chambers*
Catharine Chambers Shelley Deeks Rinku Sutradhar Joseph Cox Alexandra De Pokomandy Troy Grennan Trevor Hart Gilles Lambert David Moore François Coutlée Daniel Grace Ramandip Grewal Jody Jollimore Nathan Lachowsky Rosane Nisenbaum Gina Ogilvie Chantal Sauvageau Darrell Tan Ann Burchell

Background: Self-report has ~80-90% sensitivity and ~75-85% specificity for adult vaccinations. We conducted a quantitative bias analysis (QBA) to correct vaccine effectiveness estimates for non-differential exposure misclassification associated with self-reported human papillomavirus (HPV) vaccination among gay, bisexual, and other men who have sex with men (GBM).

Methods: We recruited GBM aged 16-30 years in Montreal, Toronto, and Vancouver, Canada, from 2017-2019. Vaccine effectiveness (VE) was derived as (1 – adjusted prevalence ratio) x 100% for prevalent anal infection with quadrivalent HPV vaccine types (outcome) by self-reported receipt of ≥1 HPV vaccine dose (exposure). We conducted a multidimensional QBA for sensitivity and specificity values ranging from 70-100% (5%-unit increments) for non-differential exposure misclassification. We then conducted a probabilistic QBA assuming a trapezoidal distribution for sensitivity (min.=75%; mode=80%, 90%; max.=95%) and specificity (min.=70%; mode=75%, 85%; max.=90%) with 10,000 simulations.

Results: Among 608 participants, 40% self-reported ≥1 HPV vaccine dose and 26% tested positive for ≥1 HPV vaccine type. The uncorrected median adjusted VE against prevalent anal infection was 27% (2.5-97.5[th] percentile=−5-49%). Bias-corrected VE estimates were relatively stable across a range of sensitivity values but began to differ from the uncorrected estimate (>20% relative change) once specificity fell below 75% (Figure). In the bias-corrected analysis, the median adjusted VE was 38% (2.5-97.5[th] percentile=18-61%) considering only systematic error and 39% (2.5-97.5[th] percentile=2-65%) considering both random and systematic error.

Conclusions: Bias-corrected estimates were further from the null (indicating higher VE) when we corrected for non-differential exposure misclassification. A large proportion of GBM falsely reporting HPV vaccine receipt (specificity<75%) would be required to meaningfully change VE estimates.
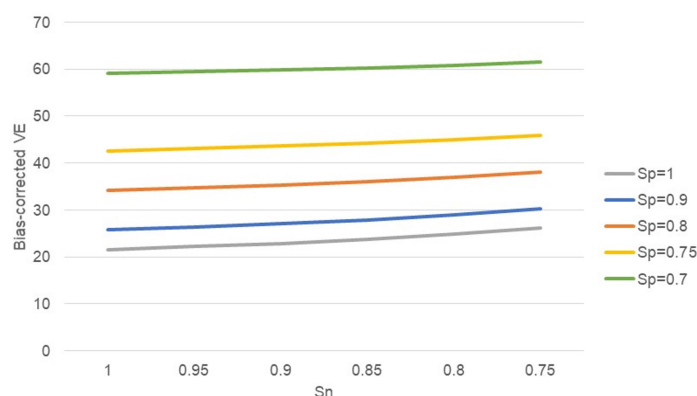
Figure. Bias-corrected vaccine effectiveness (VE) estimates across a range of sensitivity (Sn) and specificity (Sp) values for self-reported human papillomavirus vaccination status among gay, bisexual, and other men who have sex with men, Canada, 2017-2019

Effect of substance use on HIV viral suppression among persons living with HIV in San Francisco, USA Jason S. Melo* Jason Melo Sharon Pipkin Nancy A. Hessol Ling C. Hsu

The San Francisco (SF) Department of Public Health rapidly links people living with HIV (PLWH) to antiretroviral therapy (ART). However, not all PLWH benefit equally. People who use drugs (PWUD) may face challenges with retention in care, ART adherence, and maintaining HIV viral suppression (VS). SF's HIV surveillance program is unique in performing medical chart abstraction to identify illicit drug use among PLWH. We assessed the prevalence of substance use among PLWH in SF and its association with VS.

PLWH aged ≥18 years as of 12/31/2020 in the HIV case registry with a documented ART prescription and a medical record abstraction in 2020-2021 were included. Routine abstractions collected tobacco and illicit drug use history in the 12 months prior to their latest medical visit. We compared VS (most recent viral load <200 copies/mL in 2020-2021) for persons who inject drugs (PWID), persons who use non-injection drugs (PWNID), and non-drug using persons (NDU). We developed a logistic regression model to estimate ORs of VS, adjusting for associated demographics, housing status, tobacco use, and interaction between drug use category and tobacco use.

A total of 1940 PLWH were included, representing 12% of our case registry and overrepresenting those recently diagnosed. Most were men (86%), white (52%), 50-59 (33%) or 60-69 (25%) years old, and stably housed (84%). Thirteen percent were PWID, 23% PWNID, and 64% NDU. Among PLWH who do not use tobacco, PWNID and PWID had much lower odds of VS compared to NDU (Figure 1). These associations were significant but attenuated among PLWH who use tobacco (Figure 1). Among NDU, tobacco use was associated with lower odds of VS [OR=0.30, 95%CI (0.17,0.54)].

Despite established HIV care programs, lower odds of VS among PWUD suggests more efforts are needed to achieve health outcome goals in this population. Programs that treat HIV alongside substance addiction should be considered for future care initiatives.

Figure 1. Prevalence and odds ratios for viral suppression by substance use category among people living with HIV in San Francisco, USA, 2020-2021 (N=1940)
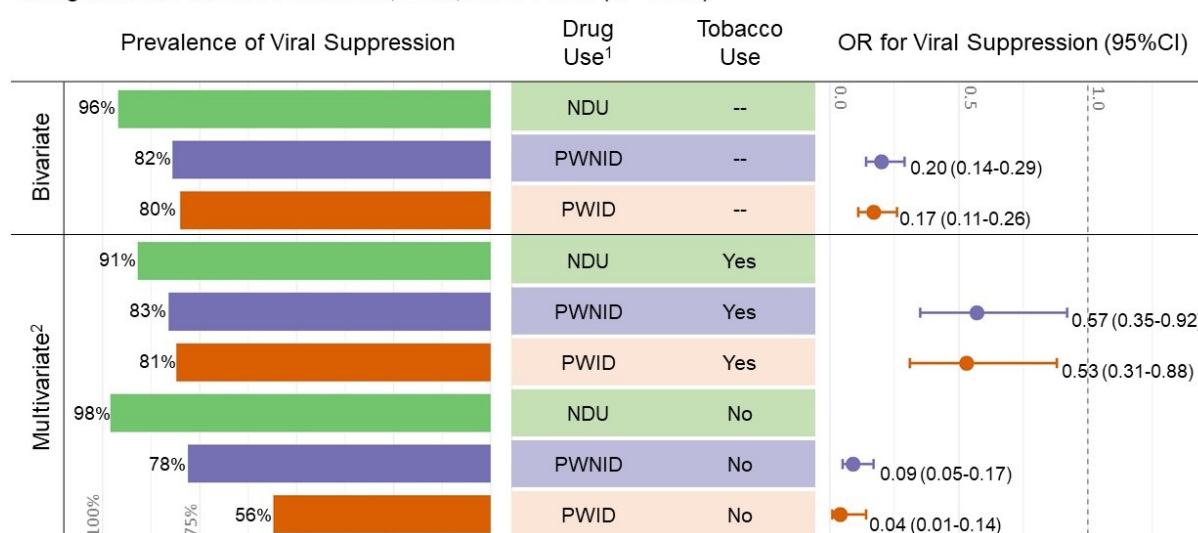
[1]Categorized as non-drug using persons (NDU), persons who use non-injection drugs (PWNID), and persons who inject drugs (PWID)
[2]The multivariate model adjusts for gender, race/ethnicity, age group, housing status, tobacco use, and interaction between tobacco use and drug use

Variability in County-level HCV Vulnerability Based on Publicly Available Measures of HCV in Ohio, 2018-2019 Daniel Brook* Daniel Brook Angela T. Estadt William C. Miller David M. Kline

Introduction

As a result of the opioid syndemic in the United States, the CDC conducted a vulnerability assessment of acute HCV using data from 2012-2013. This analysis has been replicated spatiotemporally, but variability in estimates of vulnerability by HCV categorization is unknown. As a home-rule state, there may be misclassification within Ohio's acute HCV data due to disparities in resources. We assessed HCV vulnerability in Ohio using total and acute HCV data from 2018-2019.

Methods

Replicating the CDC's backward selection method from their list of fifteen potential predictors, we conducted multivariable mixed-effects Poisson regression models controlling for year and including county as a random effect. Coefficients from the models were used to calculate county-level HCV vulnerability.

Results

Three predictors were included in our multivariable acute HCV vulnerability model: prescription opioid sales per 10,000 people (standardized prevalence ratio [sPR]: 1.4 [95% CI: 1.2, 1.7]), the percentage of the population living in poverty (sPR: 1.2 [95% CI: 1.0, 1.5]), and the percentage of the population that was non-Hispanic white (sPR: 1.2 [95% CI: 1.1, 1.4]). Two of these indicators (opioid sales and percent non-Hispanic white) were included in the CDC's model of six indicators. Four predictors were included in our multivariable total HCV vulnerability model: age-adjusted unintentional drug overdose deaths per 100,000 population (sPR: 1.2 [95% CI: 1.1, 1.2]), prescription opioid sales per 10,000 population (sPR: 1.2 [95% CI: 1.1, 1.3]), the percentage of households without a vehicle (sPR: 0.93 [95% CI: 0.87, 0.99]), and the percent of the population in poverty (sPR: 1.3 [95% CI: 1.2, 1.4]). We found that 2018-2019 total and acute HCV vulnerability differed from the analysis using national acute HCV data from 2012-2013 (Figure 1).

Conclusion

Estimates of HCV vulnerability may differ by HCV category, which may be biased by the resources available for surveillance.

Figure 1. HCV Vulnerability Maps by County in Ohio, 2018-2019

Infectious Disease
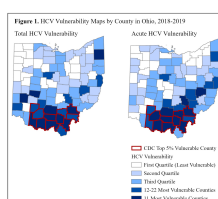
Characterization of patients receiving surgical versus non-surgical treatment for infective endocarditis: West Virginia multicenter study Ruchi Bhandari* Ruchi Bhandari Talia Alexander Noor Abdulhay Frank Annie Umar Kaleem R. Constance Wiener Jessica Rubenstein Andrew Meyer Melanie Fisher

Introduction: Infective Endocarditis (IE) is a severe infection affecting heart valves. Hospitalizations and surgical cases have sharply increased given the injection drug use epidemic in West Virginia. This study compares characteristics and outcomes among patients with IE receiving antibiotic treatment alone versus surgical treatment in West Virginia.

Methods: This study is a retrospective review of electronic medical records of all adults hospitalized for IE during 2014-2018 at the four major tertiary cardiovascular centers in West Virginia. Comparisons were made using Chi-square test or Fisher's exact test for categorical groups and Wilcoxon rank-sum test for medians. Bivariate and multivariable logistic regression analyses examined the association of surgery with discharge against medical advice (AMA) and mortality during hospitalization. Statistical analyses were conducted in R version 4.0.2. Statistical significance level was set at $p < 0.05$.

Results: Of the 780 patients hospitalized with IE, 37.82% had surgery. Patients with surgery were significantly younger, with 71.53% in the 18-44 age-group compared with 58.88% patients without surgery ($p < 0.001$). Compared with patients without surgery, a high proportion of patients with surgery were diagnosed with psychiatric disorders (30.99% vs. 57.29%), including, substance use disorder (19.01% vs. 45.08%), depression (15.91% vs. 28.81%), and anxiety (12.4% vs. 27.46%) (all p<.001); they also had significantly higher number of days in the intensive care unit (median=5 vs. 0, $p < 0.001$). The odds were significantly lower for patients with surgery for discharge AMA (Adjusted OR: 0.47; 95%CI: 0.30-0.74) and mortality during hospitalization (Adjusted OR: 0.457; 95%CI: 0.24-0.79).

Conclusion: Management of IE is complex and challenging. Findings showing differences in patient outcomes based on different treatment modalities can help improve future clinical management by reducing discharges AMA and in-hospital mortality.

Infectious Disease

Assessing the impact of influenza epidemics in Hong Kong Jessica Y. Wong* Jessica Y. Wong Justin K. Cheung Helen S. Bond Peng Wu Benjamin J. Cowling

Background: Influenza viruses cause a substantial burden of morbidity and mortality in Hong Kong and across the world. However, methodology for timely assessment of the impact of influenza virus infection is not standardized. As a result, there is a need to examine the validity of the methodology for the assessment of impact developed by the World Health Organization.

Methods: We estimated influenza-associated excess all-cause mortality from 1998 to 2019 in Hong Kong using linear regression models. We also collected severe influenza cases across different age groups. We assessed the influenza impact defined using World Health Organization's pandemic influenza severity assessment framework. We estimated thresholds using 2014 to 2018 data under the WHO averaging method and moving epidemic method, then applied the thresholds to the 2019 data.

Results: Our study estimated an annual influenza-associated excess all-cause mortality rate of 14.4 (95% CI: 11.1, 17.3) per 100,000 person-years. When thresholds were applied to the 2019 data, there was good agreement between excess mortality and severe influenza cases. Impact was characterized as moderate for all ages but high for individuals in the 45-64 years age group. In addition, there was good agreement between the WHO averaging method and moving epidemic method.

Conclusion: Our study assessed seasonal influenza impact using different data sources. The framework will be useful in monitoring circulating influenza strains that could potentially cause influenza pandemics.

Annual Trends in Prevalence and Incidence of Hepatitis-C Virus Infection in Manitoba with an Emphasis on Special Population Between 1998 and 2018 Sai Krishna Gudi* Sai Krishna Gudi Sherif Eltonsy Joseph Delaney Carla Osiowy Kelly Kaita Silvia Alessi-Severini

Background: Hepatitis-C virus (HCV) infection is a major cause of liver-related morbidity and mortality worldwide. Epidemiological data of HCV infection in the Canadian province of Manitoba are limited.

Objective: To determine trends in annual prevalence and incidence of HCV infection in Manitoba between 1998 and 2018 with an emphasis on special populations.

Methods: A population-based retrospective study was conducted using data from the Manitoba Centre for Health Policy (MCHP) repository. Using the test results provided by the Cadham provincial laboratory (CPL), individuals in Manitoba with any diagnosis (acute and chronic) of HCV infection (based on positive HCV RNA) were identified. Demographic characteristics of the population were described. Annual prevalence and incidence rates (crude and standardized) were calculated for the overall population and stratified by sex, regional health authority (RHA), residence area (urban vs. rural), income quintile and special population groups.

Results: A total of 8,721 HCV cases were diagnosed between 1998 to 2018 in Manitoba with a mean age of 40.5 years ± 13.6 (SD). The overall crude HCV incidence and prevalence were estimated at 0.03% and 0.37% during the study period, respectively. No significant change was observed in the standardized HCV incidence rate (per 100,000) during the study period (54.3 in 1998 and 54.8 in 2018). The standardized HCV prevalence (per 100,000) increased from 52.5 in 1998 to 655.2 in 2018. In all study years, an overall average incidence rate based upon sex, RHA, region, income and special population groups were observed to be higher in males (40.1), Winnipeg RHA (42.7), urban region (42.3), low-income quintiles (78.5) and pregnant women (94.3), per 100,000 population respectively.

Conclusions: Although incidence rates of HCV infection in Manitoba appeared to have initially declined, rates showed an upward trend by the end of the study period while prevalence increased steadily. These findings should be used to inform focused strategies to reduce HCV transmission in Manitoba.

LATEBREAKER

Infectious Disease

Double Negative Control of Hidden Bias in Test Negative Studies of Vaccine Effectiveness
Qijun Li* Qijun Li Xu Shi Wang Miao Eric Tchetgen Tchetgen

The test-negative design (TND) has become a standard approach to evaluate vaccine effectiveness against the risk of acquiring infectious diseases such as Influenza, Rotavirus, Dengue fever, and more recently COVID-19 in real-world settings. Despite TND's potential to reduce unobserved differences in healthcare seeking behavior (HSB) between vaccinated and unvaccinated subjects, it remains subject to potential biases. First, residual confounding bias may remain due to unobserved confounders. Second, because selection into the TND sample is a common consequence of infection and HSB, collider bias may exist. Third, generalizability of the results from the TND sample to the target population is not guaranteed. In this paper, we present a novel approach to identify and estimate vaccine effectiveness in the target population by leveraging a pair of negative control exposure and outcome variables to account for potential hidden bias in TND studies. We illustrate our proposed method with extensive simulation and an application to study COVID-19 vaccine effectiveness using data from the University of Michigan Health System.
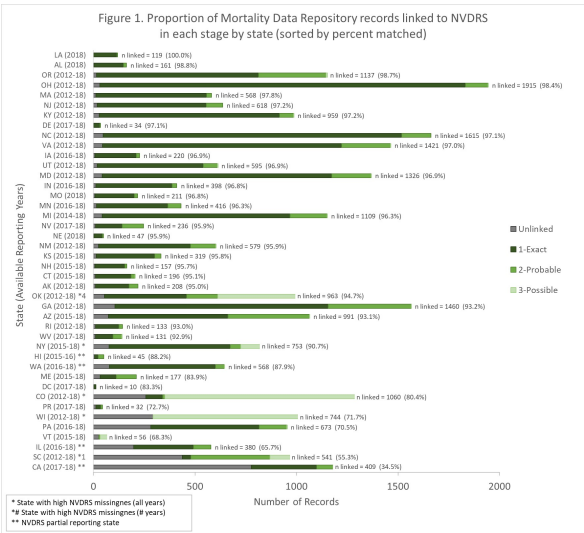
Harnessing national data systems to understand circumstances surrounding Veteran deaths by suicide and undetermined intent: Linking VA, DOD, and CDC data Laurel A. Gaeddert, BS* Laurel Gaeddert Talia L. Spark, PhD, MS Alexandra L. Schneider, BA Lindsey L. Monteith, PhD Claire A. Hoffmire, PhD

Background: US Veterans are at elevated suicide risk, yet research has focused on those using Department of Veterans Affairs (VA) healthcare, due to lack of data available for those not using VA healthcare. Linking VA and non-VA data sources may help to understand suicide risk among all Veterans. We linked VA, Department of Defense (DoD), and Centers for Disease Control and Prevention (CDC) data to understand circumstances surrounding suicide and undetermined deaths and explored quality and limitations to this approach.

Methods: We conducted a 1-to-1 linkage of VA-DoD Mortality Data Repository death records and the CDC National Violent Death Reporting System (NVDRS)-Restricted Access Database, which contains limited personal identifying information but no unique identifiers. A multi-variable, deterministic linkage approach within 189 state-year strata (42 contributing states, 2012-2018) was conducted in 3 stages: 1) *exact* (all key variables matched: age, sex, death date, underlying cause of death, birth day of month, last name first initial); 2) *probable* (all but one key variable matched); 3) *possible* (all but 2 key variables matched). Variables removed iteratively in Stages 2 and 3 were selected due to high NVDRS missingness. Duplicates were resolved manually. Accuracy of the NVDRS military history variable was assessed.

Results: Across all state-years, 23,690 matches (88.2% of 26,852 MDR records) were identified (64.7% exact, 14.5% probable, 9.0% possible; Figure 1). When high missingness (2+ key variables in >10% of records; n=23) or incomplete reporting (n=12) NVDRS state-years were excluded, 94.3% of MDR records matched (76.3% exact, 17.5% probable, 0.5% possible). The NVDRS military history indicator was accurate for 81.3% of matched records.

Conclusions: Linking VA, DoD, and NVDRS data is feasible. This novel dataset has potential to improve understanding of circumstances surrounding suicide and other violent deaths among Veterans to improve suicide prevention.

Figure 1. Proportion of Mortality Data Repository records linked to NVDRS in each stage by state (sorted by percent matched)

Evaluation of the In This Together program: Focused Therapy on Strengthening the Parent-Child Bond Michaela George* Michaela George Liliana Molina Cervantez Nancy Hernandez Meghan Kehoe Patti Culross

BACKGROUND

In the US a woman is beaten or abused every nine seconds, while about four million children witness domestic violence yearly. Previous research on survivor-parent–child group therapy is effective at targeting parenting skills to help prevent future abuse, decreasing harmful child behaviors, and allowing survivors to develop a higher self-esteem. The purpose of this study is to evaluate the "In This Together" program (ITT), to understand how the program is impacting the survivor-parent-child relationship, and empowering domestic violence survivors in Marin County, CA.

METHODS

Data was collected using a mixed methods approach including questionnaires, focus groups, and interviews. ITT was implemented for two cohorts over two 10 weeks sessions, each session covered unique clinical benchmarks. Both cohorts included 16 survivors and their children. ITT was administered by licensed therapists once a week via Zoom. After participants completed ITT, a follow-up questionnaire and interview were collected to determine the impact of ITT.

RESULTS

Based on preliminary analysis it is expected that participants will find ITT beneficial to their overall self-esteem and provide a safe space to express emotions with other survivors. From the analysis, several themes have emerged including: successfully dealing with emotions, removing obstacles in the way of making positive change, increasing parenting confidence, and diminishing the power of the abuser.

DISCUSSION

 ITT successfully empowered the emotional bond between the survivor-parent and child and decreased the likelihood of repeating the cycle of abuse over the six month study period. The survivor-parent-child bond is essential to maturity, academic success, and emotional well-being of the child. The public health implications of breaking the cycle of abuse are important to understand. In the future, we intend to implement ITT in a number of different clinical therapy settings with diverse populations.

The Relationship Between the Perceived Likelihood of Getting Ticketed and Self-Reported Distracted Driving Among Adults in the United States Nandi Taylor, MPH* Nandi Taylor

Background: Distracted driving is an important risk factor for motor vehicle crashes. Increased perception of punishment has been found to reduce several risky driving behaviors; however, its impact on distracted driving remains unclear. The current study examined the association between the perceived likelihood of getting a ticket and self-report distracted driving.

Methods: We used 2015 National Survey on Distracted Driving Attitudes and Behaviors, a nationally representative telephone-based survey, conducted by the National Highway Traffic Safety Administration. Multivariable logistic regression was used to assess the relationship between the perceived likelihood of getting a ticket and making a phone call while driving adjusting for age, race/ethnicity, education, previous history of a stop, support of distracted driving laws, and previous history of a crash. Modification by race/ethnicity was also assessed. Sampling weights were applied to create nationally representative estimates and all statistical tests accounted for complex survey design.

Results: A total of 4,194 respondents were included in our analysis. Of those, 2,033 (48%) drivers report engaging in making a call while driving. In the adjusted model, we found that the odds of reporting engagement in distracted driving were increased for those that perceived getting a ticket to be unlikely compared to likely (OR:1.31, 95% CI: 1.08, 1.59). We found no evidence of modification by race/ethnic groups.

Conclusion: A substantial proportion of drivers report engaging in distracted driving. The current study found that the perceived likelihood of getting a ticket was associated with engaging in distracted driving. Deterring behaviors by increasing the perception of punishment may be beneficial in reducing distracted driving behaviors. However, further research is needed to understand how effective this approach is among different demographic groups to create more equitable injury prevention interventions.

Men's Health

Disparities in Prevalence of Urinary Incontinence among a Nationally Representative Sample of Men, 2005-2016: Findings from the Urologic Diseases in America Project Julia Ward* Julia Ward Erline Martinez-Miller Brian Matlaga Lydia Feinstein

Age-related prostate problems commonly lead to loss of urinary control among men, which can profoundly impact quality of life. However, our understanding of urinary incontinence (UI) at a population level is limited given that UI is frequently underreported and underdiagnosed in the clinical setting. As part of the Urologic Diseases in America project, we analyzed data from 14,497 men aged ≥20 years who participated in the 2005-2016 National Health and Nutrition Examination Survey. Using self-reported symptoms, we estimated UI prevalence in the prior year, overall and by subtype (stress, urgency or mixed). Among men with UI, we additionally assessed symptom severity, using the validated Incontinence Severity Index, and impact on daily activities. All estimates were standardized to the age distribution of the 2010 U.S. Census. The 2005-2016 prevalence of any UI was 16%; 2% had mixed UI, 2% has stress only, and 10% had urgency only. UI prevalence remained relatively stable over the study period, ranging 14-17%. Overall UI prevalence was highest among men ages 60+ years (32%) compared to those ages 40-59 years (15%) and 20-39 years (6%). UI prevalence also differed by race/ethnicity and socioeconomic status over the study period. Non-Hispanic (NH) Black men had the highest UI prevalence (22%) compared to NH Whites (15%) and Mexican-Americans (16%). UI prevalence was also higher among those with less than a high school education (18%) and lower income (18%) compared to those with more than a high school education (15%) and high income (14%). NH Black men and those with a lower education and income level also reported worse UI severity, level of bother, and impact on daily activities compared to NH Whites and those with a higher education and income level. Our study demonstrates a high UI prevalence among a nationally representative population of men in the United States, with a disproportionate burden carried by those of a lower socioeconomic status and Black men.

Figure 1. Age-standardized prevalence of urinary incontinence in the National Health and Nutrition Examination Survey[a] among men overall and by type, 2005-2016[b]
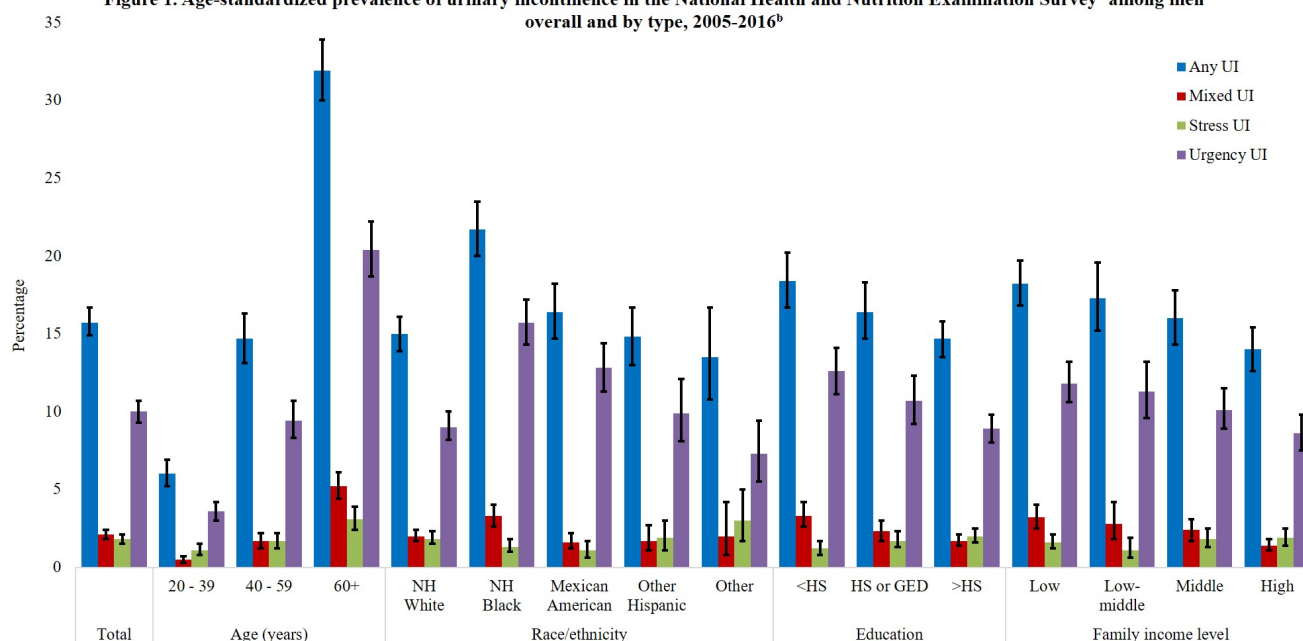
Abbreviations: NH=Non-Hispanic; HS=High School; UI=Urinary Incontinence
[a] Source: National Health and Nutrition Examination Survey, 2005-2016
[b] Standardized to the age distribution of the 2010 US Census. Due to small sample size in some cells, we used the Clopper-Pearson exact method to calculate all confidence intervals.

The association of sexual violence perpetration and victimization with depression, suicidal ideation, and suicide attempts among Korean adolescents Hyejin Kim* Hyejin Kim Sun Jae Jung Jae-Won Kim Ji Su Yang

Background: Few studies of sexual violence (SV) and mental health considered important confounders and the population who experienced both victimization and perpetration. This study aimed to observe the associations of depression, suicidal ideation, and suicide attempts with sexual violence victimization (SVV only), perpetration (SVP only), and both experiences (SVV & SVP) among Korean adolescents.

Methods: Using nationally representative cross-sectional data, Korea Youth Risk Behavior Web-Based Survey, we examined the self-reported experiences of depression, suicidal ideation, and suicide attempts within a year in Korean adolescents aged 12 to 18 (N=519,473). We compared the odds ratios for each outcome according to the self-reported SV experience types accounting for potential confounders. Adjusted potential confounders were as follows: age, sex, socio-economic status (city size, perceived economic position, residential status, and education of parents), body mass index, substance use (cigarette, alcohol, and drug), and sexual characteristics (early initiation of sexual activity and early puberty). We stratified the study population by sex and age groups after correction for multiple testings.

Results: All SV types were significantly associated with a higher odds of reporting depression, suicidal ideation, and suicide attempts, even after adjusting for all measured confounders and multiple testings (especially in the SVP only group: depression OR=1.57; suicidal ideation OR=1.61; suicide attempts OR=1.99). The distinct difference between sex was that the association of SVV & SVP with mental health was only significant in boys regardless of age.

Conclusion: SVP alone is associated with mental health regardless of age, sex, socio-economic status, body mass index, substance use, and sexual characteristics.
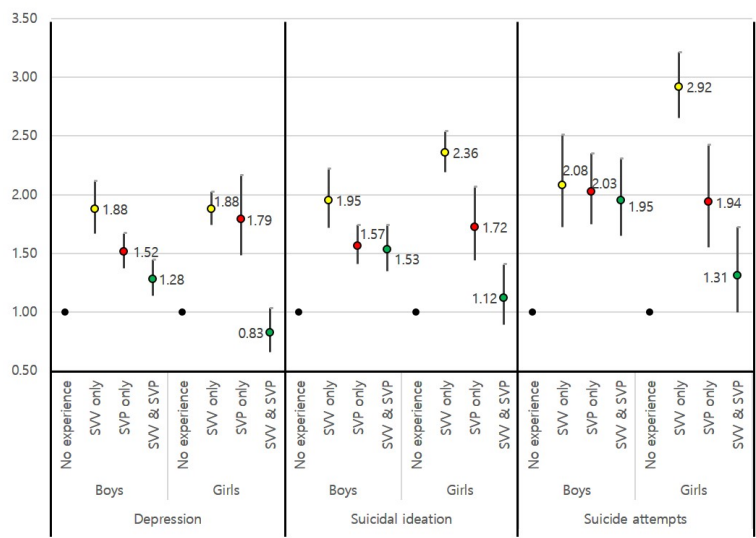
Figure. Association between types of experience of sexual violence and depression, suicidal ideation, and suicide attempts among Korean adolescents stratified by sex (2006-2012) (N= 519,470)
Odds ratios and confidence intervals are presented.
Yellow indicated OR for each outcome in the sexual violence victimization (SVV) only group compared to no sexual violence experience group.
Red indicated OR for each outcome in the sexual violence perpetration (SVP) only group compared to no sexual violence experience group.
Green indicated OR for each outcome in the SVV & SVP group compared to no sexual violence experience group.

Examining the association between history of heart attack and experiencing frequent mental distress among United States veterans and adult civilians: a national level study

Cristina Oancea* Jessica Passini Cristina Oancea

Frequent mental distress (FMD) is a health-related quality of life measure defined as poor mental health for any 14 or more days in the past month. While the prevalence and risk for PTSD, suicide, and depression have been shown to be higher among US veterans (USV) than US civilians (USC), little research has been done among USV regarding FMD. Anyone can experience stress and problems with emotions without necessarily being clinically depressed; therefore, examining FMD over clinical depression alone, more broadly captures the experience and burden of poor mental state on one's quality of life. This cross-sectional study used publicly available 2019 BRFSS data to explore the association between history of heart attack (HA) and FMD among USV compared to USC, which to our knowledge, has not be done to date. The final study sample size was 272,928 US adult residents: USV and USC. Weighted unadjusted and adjusted logistic regression models were conducted for the overall sample and by USV status. Overall results of this study indicated HA history increases the odds of experiencing FMD. We found health insurance and obesity status to be effect modifiers. Among USV with HA history who had health insurance and a healthy weight, the odds of experiencing FMD were 1.5 times significantly greater than the odds of experiencing FMD among insured, not obese USV without HA history, which was non-significant among USC. Among USC with HA history who were uninsured and obese, the odds of experiencing FMD were 3.5 times significantly greater than the odds of experiencing FMD among uninsured, obese USC without HA history, and marginally significantly lower among USV indicating a stark difference by USV status. Understanding the association between HA history and FMD will help inform policy for screening and prevention of mental distress post-heart attack to reduce the experience of FMD, as well as help identify another potential area of intervention to prevent and reduce suicide.

Mental Health

Early age at sexual debut, risky sex behaviors and depressive symptomatology among young adults in the United States Andrew Williams* Andrew Williams Amy

Background: In the United States, depression is most common among adults aged 18-29. Early sexual debut and risky sex behaviors may influence depression, but current evidence is mixed. We examined associations between sex behaviors and depression among US adults aged 20-25.

Methods: Data were from 2,580 adults aged 20-25 in the National Health and Nutrition Examination Survey(2005-2016). Depression was measured with the Patient Health Questionnaire-9(PHQ-9, (9 questions scored 0-3, range 0-27). Severe depression was PHQ-9 score >10. Three sex behaviors were assessed: early age at sexual debut(first sexual intercourse ≤age 16), chlamydia diagnosis in prior 12 months, and herpes diagnosis ever. Chlamydia and herpes diagnoses were considered proxies for lack of barrier protection during sex. Logistic regression models estimated odds ratios(OR) and 95% confidence intervals(95%CI) for the association between sex behaviors and severe depression, adjusted for demographic factors. Sensitivity analyses examined differences by gender and the effect of age at menarche.

Results: Early age at sexual debut and risky sex behaviors were associated with increased risk for severe depression. Compared to later sexual debut, early age at sexual debut was associated with two-fold higher risk for severe depression(OR:2.00 95%CI:1.99,2.01). Chlamydia diagnosis was associated with a 35% increase(OR:1.35 95%CI:1.35,1.37) and herpes diagnosis was associated with a 16% increase(OR:1.16 95%CI:1.15,1.17) for severe depression. In sensitivity analysis, early age at sexual debut was a stronger predictor of severe depression among women(OR:2.52 95%CI:2.51,2.53) than men(OR:1.29 95%CI:1.28,1.30)(p-interaction<.01). Age at menarche did not change results among women.

Conclusions: Risky sex behaviors increase risk of depression in young adults. Early age at sexual debut was the strongest predictor of depression and may be a stronger predictor of depression among women.

A systematic review and meta-analysis of chemical exposures and attention-deficit/hyperactivity disorder Lina V. Dimitrov* Lina Dimitrov Jennifer W. Kaminski Joseph R. Holbrook Rebecca H. Bitsko Brenna O'Masta Brion Maher Audrey Cerles Margaret Rush

Exposure to certain chemicals prenatally and in childhood can impact development and may increase risk for attention-deficit/hyperactivity disorder (ADHD). Leveraging a larger set of literature searches conducted to synthesize results from longitudinal studies of potentially modifiable risk factors for childhood ADHD, we present meta-analytic results from 63 studies that examined the associations between early chemical exposures and later ADHD diagnosis or symptoms. Studies were eligible for inclusion if the chemical exposure occurred at least 6 months prior to measurement of ADHD diagnosis or symptomatology. Included papers were published between 1975 and 2019 on exposure to anesthetics (n=5), cadmium (n=3), hexachlorobenzene (n=4), lead (n=22), mercury (n=12), organophosphates (n=7), and polychlorinated biphenyls (n=13). Analyses are presented for each chemical exposure by type of measure of association reported (categorical vs. continuous), type of ADHD measurement (overall measures of ADHD, ADHD symptoms only, ADHD diagnosis only, inattention only, hyperactivity/impulsivity only), and timing of exposure (prenatal vs. childhood vs. cumulative), whenever at least 3 relevant effect sizes were available. Childhood lead exposure was positively associated with ADHD diagnosis and symptoms in all analyses; the strongest association was for hyperactivity/impulsivity. Other statistically significant associations were limited to organophosphates ($r=0.11$, 95% CI:0.03–0.19 for continuous ADHD outcomes overall) and both prenatal and childhood mercury exposure ($r=0.02$, 95% CI:0.00–0.04 for continuous ADHD outcomes overall for either exposure window). Our findings provide further support for negative impacts of prenatal and/or childhood exposure to these chemicals and raise the possibility that primary prevention and targeted screening could prevent and mitigate ADHD symptomatology.

Mental Health

Is vitamin D level related to depression symptoms during adolescence? Abdullah Al-Taiar*
Abdullah Al-Taiar Reem Al-Sabah Lemia Shaban Ahmed N. Albatineh Reem Sharaf Alddin Praveen K. Durgampudi

Background and objectives: This study aimed to investigate the association between 25-hydroxyvitamin D (25(OH)D) and depression symptoms among adolescents in Kuwait, a country with a high prevalence of vitamin D deficiency.

Methods: A school based cross-sectional study was conducted on randomly selected 704 adolescents in middle schools. Data on depression symptoms were collected using the Children's Depression Inventory (CDI). Data on covariates were collected from the parents by self-administered questionnaire and from adolescents by face-to-face interview. Blood samples were tested in an accredited laboratory; and 25(OH)D was measured using liquid chromatography-tandem mass spectrometry.

Results: Of 704, 94 (13.35%; 95%CI:10.35-17.06%) had depression symptom (a score of 19 or more on the CDI). There was no significant difference in the median CDI score between different vitamin D status (p=0.366). There was also no correlation between serum 25(OH)D concentration and CDI score (Spearman's rank correlation=0.01; p= 0.825).There was no significant association between 25(OH)D and depression symptoms whether 25(OH)D was fitted as a continuous variable (crude analysis p=0.458 and adjusted analysis p=0.233), categorical variable as per acceptable cut-of points (crude analysis p=0.376 and adjusted analysis p=0.736), or categorical variable as quartiles (crude analysis p=0.760 and adjusted analysis p=0.549).

Conclusion: Vitamin D status does not seem to be associated with depression symptoms among adolescents in our setting. It is important to have sufficient vitamin D levels during adolescence for several other health benefits.

Food insufficiency and difficulty with expenses strongly associated with adverse mental health, regardless of poverty status and location, among Latinos in the United States during the COVID-19 pandemic Cara Frankenfeld* Cara Frankenfeld Carol Cleaveland

Identifying key contributors to mental health among vulnerable populations can be used to prioritize and target social services. Data from US Census Household Pulse Survey, covering April 23, 2020 to October 11, 2021, were analyzed. Latino individuals with available mental health data were included (n=209,384). Ordinal logistic regression was used to evaluate categorical frequencies (not at all, several days, more than half of days, and nearly every day) of anxiety, loss of interest, worry, and feeling down over previous two weeks, stratified by gender and poverty status. Demographic, household, financial, and work covariates were mutually adjusted, and jackknife replications and population weights applied. Feeling anxiety more than half the days or nearly every day was reported more frequently by males below poverty (36.8%) and females above (35.3%) and below poverty (41.4%), compared to males above poverty (27.5%). Often not having enough to eat was associated with feeling down (males above poverty: OR=4.9 (95% CI: 3.6-6.6); males below poverty: OR=5.36 (4.1-7.0); females above poverty: OR=4.10 (3.1-5.5); and, females below poverty OR=4.7 (3.5-6.3). Very difficult time with expenses was associated with anxiety (males above poverty: OR=3.6 (3.1-4.3); males below poverty: OR=4.5 (3.3-6.2); females below poverty: 3.5 (3.1-4.0); and females above poverty: 4.0 (3.1-5.3)). Some other characteristics also exhibited protective or adverse associations. For participants living in MSAs (n=96,869), food insufficiency and difficulty with expenses were consistently adversely associated with mental health across MSAs (Figure), with some protective associations of living quarters, receiving unemployment pay, and employment sector that varied across MSAs. Similar results were observed for other mental health outcomes. Across gender, poverty, and location, ensuring food sufficiency and financial resources may be pathways relevant in which to improve mental health in US Latinos.

Figure: Heat map of ORs from mutually adjusted mutual ordinal logistic regression of frequency of anxiety in relation to demographic, financial, household, and work characteristics in Latinos in the US surveyed from April 2020 to October 2021 in Latino participants (n=96,869) in the US Census Household Pulse Survey residing in 15 metropolitan statistical areas. Red indicates OR>1 and blue indicates OR<1, with darker coloration stronger magnitude.

		MSA 12060: Atlanta-Sandy Springs-Alpharetta, GA	MSA 14460: Boston-Cambridge-Newton, MA-NH	MSA 16980: Chicago-Naperville-Elgin, IL-IN-WI	MSA 19100: Dallas-Fort Worth-Arlington, TX	MSA 19820: Detroit-Warren-Dearborn, MI	MSA 26420: Houston-The Woodlands-Sugar Land, TX	MSA 31080: Los Angeles-Long Beach-Anaheim, CA	MSA 33100: Miami-Fort Lauderdale-Pompano Beach, FL	MSA 35620: New York-Newark-Jersey City, NY-NJ-PA	MSA 37980: Philadelphia-Camden-Wilmington, PA-NJ-DE	MSA 38060: Phoenix-Mesa-Chandler, AZ	MSA 40140: Riverside-San Bernardino-Ontario, CA	MSA 41860: San Francisco-Oakland-Berkeley, CA	MSA 42660: Seattle-Tacoma-Bellevue, WA	MSA 47900: Washington-Arlington-Alexandria, DC-VA-MD
Age	Age in 10 year	0.84	0.97	0.82	0.92	0.79	1.00	0.89	0.84	0.99	0.89	0.88	0.87	0.94	0.74	0.85
Race	White (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Black	0.91	1.06	0.89	0.89	1.28	0.86	1.11	0.91	1.01	1.07	0.61	0.80	0.78	2.18	0.86
	Asian	0.52	0.98	0.45	0.71	1.25	1.00	0.99	1.05	1.13	0.71	0.75	1.01	1.05	0.99	0.70
	Other	0.97	1.17	0.81	1.11	0.97	1.19	0.99	1.08	1.02	1.09	1.04	1.04	1.08	1.18	1.09
Education	Less than HS	1.05	0.84	0.91	0.83	1.19	0.74	1.06	1.12	0.63	1.02	1.11	0.82	1.30	0.73	0.87
	Some HS	0.76	0.61	0.91	0.69	0.48	0.81	0.90	1.11	0.91	1.13	1.01	0.83	1.44	1.26	0.93
	High school grad or equiv (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Some college	2.10	1.38	1.59	1.38	1.21	1.88	1.34	1.18	1.44	1.54	1.51	1.36	2.14	2.07	1.61
	Associate degree	2.57	1.23	1.85	1.48	1.44	1.76	1.28	1.14	1.56	1.60	1.42	1.65	2.11	2.55	1.55
	Bachelor degree	3.02	1.70	2.26	1.90	1.33	1.79	1.54	1.26	1.89	1.39	2.10	1.66	2.91	2.16	1.81
	Graduate degree	1.00	2.40	2.58	2.62	0.75	2.05	1.94	1.35	2.21	1.59	2.00	1.48	3.23	2.35	2.27
Marital status	Married (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Widowed	1.49	1.95	1.29	0.48	1.53	0.57	1.51	1.45	1.62	1.68	1.37	1.78	1.09	1.55	1.22
	Divorced	1.47	1.51	1.21	1.70	0.92	1.31	0.98	1.05	1.37	1.19	1.30	1.78	0.87	1.43	0.88
	Separated	1.16	1.43	1.15	1.16	0.78	0.93	1.03	0.91	1.36	0.86	1.26	1.44	0.82	1.15	1.56
	Never married	1.23	1.30	1.05	1.25	1.04	1.22	1.23	0.94	1.30	1.05	1.20	1.20	1.23	1.09	1.28
Household	Number of adults	1.01	0.93	1.05	1.06	1.10	0.94	0.99	1.03	1.01	1.05	1.00	1.00	0.87	0.90	0.97
	Number of children	0.93	0.88	0.96	1.01	0.89	1.01	0.87	1.01	0.98	1.03	0.99	0.94	0.95	0.78	0.90
Living quarters	Mobile home	1.37	1.00	1.84	0.78	2.70	0.87			2.33		0.57	0.85	1.82		0.74
	Single-family, detached (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Single-family, attached to other houses	1.14	1.29	0.79	0.72	1.21	0.97	0.86	0.74	0.97	0.92	0.90	0.79	0.73	0.77	1.01
	Building with 2 apartments	0.59	1.39	1.17	0.40	0.51	0.63	0.92	0.70	1.08	0.89	0.95	0.95	0.89	0.60	0.76
	Building with 3 or 4 apartments	1.26	0.86	1.13	0.76	1.88	1.00	0.89	0.92	1.04	1.33	0.98	0.84	0.96	0.89	0.84
	Building with 5 apartments	0.76	0.96	1.05	0.96	1.16	1.12	0.71	1.02	1.29	1.92	0.99	0.84	1.25	0.61	0.47
	Boat, RV, van, etc	0.97		0.33						0.49			0.47	1.03	2.65	1.63	6.47
	Phase 1, not asked	1.47	1.41	2.22	1.52	1.76	1.98	1.63	1.69	1.53	2.13	1.51	1.60	2.00	1.62	1.69
Food sufficiency in past 7 days	Enough of the kinds of food wanted (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Enough, but not always the kinds of food wanted	1.73	1.78	1.55	1.85	1.74	1.56	1.86	1.74	1.49	1.57	1.70	2.04	1.65	1.35	
	Sometimes not enough to eat	2.94	2.07	2.53	2.57	1.90	2.74	2.26	2.47	2.13	2.08	2.35	2.30	2.24	1.78	1.98
	Often not enough to eat			1.16									2.00	1.85	3.32	
Difficulty with expenses	Not at all (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	A little	1.96	1.12	1.76	1.88	1.37	2.10	1.85	1.82	1.45	1.63	1.77	1.67	1.63	1.62	1.90
	Somewhat difficult	2.08	1.77	2.14	2.36	3.30	2.41	2.21	2.67	1.90	3.43	2.48	1.94	3.20	1.58	2.46
	Very difficult		2.61													
Confidence paying mortgage or rent	Not at all	1.72	1.82	1.92	1.17	2.75	1.98	1.30	1.66	1.57	2.09	2.27	1.60	1.00	2.06	1.35
	Slightly	1.44	1.19	1.48	1.45	1.25	1.28	1.25	1.31	1.56	1.20	2.18	1.58	0.90	1.54	1.18
	Moderately	1.62	1.17	1.59	1.55	1.67	1.69	1.30	1.56	1.77	1.51	1.99	1.83	1.42	1.22	1.36
	Highly (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Payment deferred	1.12	1.17	0.71	1.27		1.18	1.43	1.05	0.77	1.63	1.38	0.93	3.99	1.62	1.26
Recent work loss	Yes	1.14	1.34	1.20	1.32	1.75	1.62	1.33	1.32	1.38	0.85	1.31	1.23	1.29	1.46	1.52
	No (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
Any work in past 7 days	Yes (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	No	0.61	2.00	0.81	0.95	0.38	1.13	1.70	1.16	1.09		0.60	1.04	0.59	1.15	1.07
Receiving unemployment pay	Yes, I use paid leave		0.74	0.45	0.67		1.26	1.26	0.73	0.89	0.83	0.90	1.11	1.53	1.63	0.45	0.79
	Yes, I receive full pay	1.79	0.93	1.60	0.85		0.76	0.84	0.98	0.47	1.11	1.53	1.63	2.39	1.19	
	Yes, I receive partial pay	2.45	0.76	1.26	1.08		1.07	0.81	0.78	0.56	0.53	0.90	1.01	0.38	1.20	1.96
	No, I receive no pay (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Not phase 1,2, or 3	0.64	0.95	0.92	0.50	0.67	1.04	1.01	0.87	0.75	0.67	0.60	1.01	0.74	1.06	0.89
Employment sector	Government	0.72	1.21	0.79	0.99	1.22	1.22	1.31	1.21	1.14	1.12	0.93	0.89	1.18	1.26	1.08
	Private company (reference group)	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00	1.00
	Non-profit organization	0.77	1.50	1.04	1.15	1.14	1.37	1.29	1.42	1.22	1.02	1.08	1.50	1.28	1.08	1.30
	Self-employed	0.91	1.14	0.89	0.65	0.92	0.81	1.14	1.03	0.62	1.46	0.67	0.92	0.86	0.75	1.10
	Working in a family business	0.52	2.37	1.06	1.28	1.08	0.50	1.39	1.12	0.71	0.76	1.91	0.80	1.26	2.54	0.68

Rates of psychopathology following traumatic events among immigrants and native-born individuals in Denmark Meghan L. Smith* Meghan L. Smith Vijaya Seegulam Erno Peter Szentkuti Erzsebet Horvath-Puho Sandro Galea Timothy L. Lash Anthony J. Rosellini Henrik Toft Sorensen Jaimie L. Gradus

Introduction. In European countries, immigrants tend to have more mental health problems than native-born individuals. An under-researched area is immigrants' posttraumatic psychopathology related to trauma in their country of resettlement.

Methods. We obtained data from a cohort of all Danish residents with 1+ traumatic events (e.g., accidents, assaults) recorded in medical and social national registries during 1994-2016. We calculated age- and sex-standardized rates of posttraumatic stress disorder (PTSD), depression, and any substance use disorder (SUD) within 5 years following trauma among native-born Danes, immigrants to Denmark, and immigrant subgroups defined by country of birth and recency of migration. We calculated standardized rate ratios (SRRs) and 95% confidence intervals (CIs) for immigrants vs. native-born Danes. Analyses were stratified by non-interpersonal [e.g., transport accidents] vs. interpersonal trauma [e.g., assaults].

Results. Following non-interpersonal trauma, immigrants were more likely than native-born Danes to be diagnosed with PTSD (SRR=6.3, 95% CI: 5.8, 6.7), about as likely to be diagnosed with depression (SRR=0.90, 95% CI: 0.87, 0.94), and less likely to be diagnosed with SUD (SRR=0.70, 95% CI: 0.67, 0.73). Results were similar following interpersonal trauma, except the SRR for PTSD was reduced in magnitude (SRR=2.4, 95% CI: 1.6, 3.8). There were some differences by region of birth. Additionally, immigrants who had been living in Denmark for ≥10 years when their trauma occurred had higher standardized rates of depression and SUD and lower standardized rates of PTSD, compared with more recent immigrants.

Conclusions. Immigrants to Denmark have high PTSD rates following trauma, possibly due to greater susceptibility to PTSD, the influence of pre-migration experiences, and/or a tendency of clinicians to diagnose PTSD in immigrants. Differences by recency of migration demonstrate immigrants' mental health needs may shift over time.

Mental Health

Children's Neurocognitive Development and Suicide Risk through Middle Adulthood Pablo Vidal-Ribas* Pablo Vidal-Ribas Theemeshni Govender Stephen E. Gilman

Background: Children's neurocognition is associated with psychiatric disorders, educational attainment, and socioeconomic status over the life span. It is uncertain whether childhood neurocognition is also associated with suicide mortality. In a large national cohort of children, we examined the association between childhood neurocognition and suicide deaths occurring through middle adulthood.

Methods: Vital status of 49,853 individuals born between 1959 and 1966 to participants in the Collaborative Perinatal Project (CPP) cohort was determined by a probabilistic linkage to the National Death Index, covering all US deaths occurring from 1979 through 2016. Cox proportional hazard models were used to investigate associations of intelligence (Wechsler Intelligence Scale for Children, WISC) and academic skills (Wide Range Achievement Test, WRAT) at age 7 with suicide death in unadjusted and adjusted models.

Results: By the end of 2016, 288 cohort members had died by suicide. Low reading and spelling skills (vs high) at age 7, but not general intelligence and arithmetic skills, were associated with suicide mortality (reading, HR=1.99, 95%CI 1.24-3.17; spelling, HR=2.02, 95%CI 1.10-3.75). Associations were still evident but attenuated after adjusting for prenatal and sociodemographic factors at birth (reading, HR=1.67, 95%CI 1.02-2.73; spelling, HR=1.71, 95%CI 0.91-3.22).

Conclusion: Lower reading and spelling skills in childhood increase vulnerability to suicide through middle adulthood independently from childhood sociodemographic conditions. Children's poor literacy is linked to the development of emotional distress, low self-esteem, and psychopathology. In contrast to arithmetic skills, it also predicts academic motivation in late adolescence, thus impacting educational attainment and adulthood socioeconomic conditions, which might increase the risk for suicide mortality.

Patterns and predictors of perinatal depressive symptoms among Kenyan women: a group-based trajectory analysis
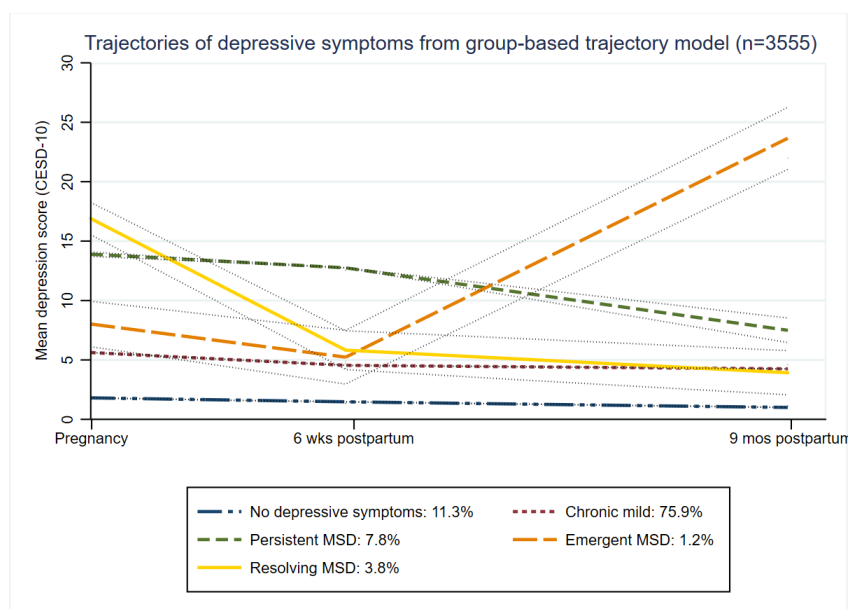Anna Larsen* Anna Larsen Jillian Pintye Mary M. Marwa Salphine Watoyi John Kinuthia Felix Abuna Barbra A. Richardson Lauren Gomez Julia C. Dettinger Grace John-Stewart

Introduction: We examined longitudinal patterns and predictors of perinatal depressive symptoms.

Methods: HIV-negative women were enrolled during pregnancy and followed through 9 months postpartum in 20 public sector maternal and child health (MCH) clinics. Study nurses serially assessed depressive symptoms using the Center for Epidemiologic Studies Depression Scale (CESD-10). Generalized estimating equations were used to identify correlates of moderate-to-severe depressive symptoms (MSD) (CESD-10 score $\geq$10) and group-based trajectory modeling (GBTM) identified patterns.

Results: Among 3555 women, median age was 24 years (IQR 21-29), 38% had low social support, and 8% reported intimate partner violence (IPV) in pregnancy. Prevalence of MSD was higher in pregnancy than postpartum (24$\bullet$5% vs. 16$\bullet$6%, $p<0\bullet001$). Five patterns of depressive symptoms were identified; persistent MSD in pregnancy and postpartum (8%), MSD in pregnancy which resolved postpartum (4%), MSD that emerged postpartum (1%), chronically mild symptoms (75%), and no depressive symptoms (11%). Emergent MSD was associated with older age. Emergent, persistent, and resolving MSD were associated with pregnancy IPV and prior pregnancy loss; persistent MSD with low social support ($p<0\bullet05$). MSD risk was 1$\bullet$3- to 2-fold higher with IPV, low social support, and partner HIV-positive status ($p<0\bullet05$); 28% of MSD was attributable to low social support.

Conclusion: One third of women had perinatal MSD; 13% had higher severity phenotypes of resolving, persistent and emerging MSD that may require tailored interventions. Perinatal women with comorbid psychosocial stressors such as IPV and prior pregnancy loss should be prioritized for mental health services that augment social support within routine MCH care.

Trajectories of depressive symptoms from group-based trajectory model (n=3555)

Legend:
- No depressive symptoms: 11.3%
- Chronic mild: 75.9%
- Persistent MSD: 7.8%
- Emergent MSD: 1.2%
- Resolving MSD: 3.8%

LATEBREAKER

Mental Health

The association between residential neighborhood surface temperature and depression among high school students living in Los Angeles County Catherine Gimbrone* Catherine Gimbrone Megan C. Finsaas Kira E. Riehm Ahuva Jacobowitz James W. Quinn Adam M. Leventhal Andrew G. Rundle Katherine M. Keyes

Rates of mental illness among adolescents have increased over the past decade, resulting in a growing crisis that remains poorly understood. As climate change progresses, disruptions to the physical environment may exacerbate these trends given that exposure to elevated temperatures can negatively impact mental health. Adolescents, who are at a critical period of mental development, may be particularly vulnerable to the psychological effects of hot temperatures. Further, those from socioeconomically privileged families may be more likely to be shielded from higher temperatures than those who are not, meaning that as climate change worsens so too may the mental health of disadvantaged adolescents. To assess how temperature impacts adolescent mental health, we linked fall 2016 Health and Happiness cohort data from 12th-grade students living in Los Angeles County to summer 2016 and 2018 Landsat Analysis Ready Data for each student's residential census tract. We employed negative binomial regression models with robust standard errors to account for clustering by schools to estimate the impact of categorical temperature on depressive symptom scores from the Center for Epidemiologic Studies Depression Scale (n = 2,432). We found that depressive symptoms were 27% higher for those living in tracts with surface temperatures above 110.76 °F compared to those living in tracts below 105.27 °F (Mean ratio (MR) = 1.27, 95% CI: 1.05, 1.53), and 15% higher for those living in tracts between 105.27 and 110.76 °F (MR = 1.15, 95% CI: 1.08, 1.24), when controlling for sex, race, ethnicity, receipt of free or reduced-cost lunch, and census tract demographics. Our results demonstrate that higher surface temperatures are significantly associated with increased severity of depressive symptoms among adolescents and suggest that the relationship between heat exposure and mental health warrants further investigation, especially considering ongoing climate change.

Circumstantial variables preceding female firearm suicides as reported in the National Violent Death Reporting System Julian Takagi-Stewart* Julian Takagi-Stewart Brianna Agnew Miriam Haviland Evan Goldstein Erin Morgan Stephen J Mooney Laura Prater

BACKGROUND: In part because firearm suicides are more common among men than among women, little is known about the circumstantial characteristics that precede female firearm suicides.

METHODS: The National Violent Death Reporting System (NVDRS) was used as a data source. All female deaths reported to be firearm suicides were extracted from all reporting states between 2014 and 2018. Of these cases, 18% (n=1,500) were randomly selected for manual coding of free-text medical examiner and law enforcement reports. Circumstantial variables were first selected a priori from scholarly literature; variables that emerged during an initial review of the case reports were then added. Four circumstantial variables were coded, including intimate partner conflicts, dementia, bullying and acting as a caregiver to an older adult. We conducted a bivariate analysis of each circumstantial variable using Chi-square (or Fisher's exact) tests as appropriate to examine whether circumstantial variables differed by age (less than 65 versus 65 and older).

RESULTS: 8,318 female firearm suicides were recorded in the NVDRS between 2014 and 2018. Of these cases, most (90.6%) were White, and the mean age was 47.2 years. Among the 1,500 cases sampled, 35 had missing narratives and 3 were miscategorized, leaving 1,462 cases for manual coding. Of these female firearm suicide decedents, 21.8% (n=319/1,462) experienced conflicts with their most recent/current intimate partner. As compared with women under age 65, older women were less likely to have reports of intimate partner conflicts and bullying but more likely to have reports of dementia (all p<0.05).

CONCLUSION: Acute relationship issues commonly preceded female firearm suicides, and more so among women <65 years old. Prominent circumstances contributing to stress prior to firearm suicide may vary across the lifespan.

Comparison of nested case-control and competing risk regression methodologies for analysis of outcomes in the presence of competing risks: associations of socioeconomic status and the risk of asynchronous contralateral breast cancer Hsiao-Ching Huang* Hsiao-Ching Huang Jenny S. Guadamuz Naomi Y. Ko Kent F. Hoskins Gregory S. Calip
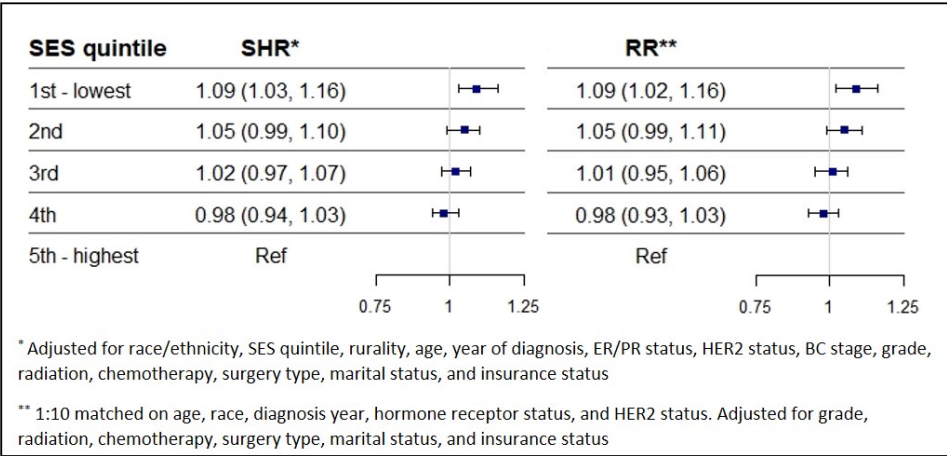
Introduction: Nested case-control(NCC) designs are increasingly used due to statistical efficiency, accommodation of time-varying exposure and approximation of the hazard ratio under risk set-based sampling conditions. However, the equivalence of NCC methods approximating cause-specific hazards and competing risk regression methods is not well documented. Our purpose is to compare results from analyses using Fine-Gray models and NCC-based conditional logistic models when evaluating the association between socioeconomic status(SES) and risk of contralateral breast cancer(CBC) accounting for non-CBC cancer and overall mortality as competing risks.

Method: We analyzed a cohort of adult women with unilateral Stage I-III breast cancer using SEER Database(2000-2016). We determined the association between SES and CBC using Fine-Gray regression models accounting for competing risks and estimated adjusted SHR and 95%CI. In the NCC approach, we used incidence density sampling without replacement to match women with CBC up to 10 women without CBC. Multivariable conditional logistic regressions were used to estimate adjusted RRs and 95%CI to determine the association between SES and CBC.

Results: In a cohort of 566,873 breast cancer survivors, the median age was 59(IQR 50-70) and 12% had Stage III unilateral BC. The Fine-Gray approach shows women living in the lowest SES quintile had a modest increased risk of CBC compared to the highest SES quintile(SHR1.09, 95%CI 1.03-1.16) after adjustment. For the NCC approach, the adjusted estimate was similar with nearly identical CI(adjusted RR 1.09, 95%CI 1.02-1.16).

Conclusion: We found that NCC analyses using risk set-based matching and cause-specific censoring were similar to an approach using Fine-Gray models. Both methods showed modest increased risk of CBC associated with lower SES. Our results align with literature that the NCC can be an alternative approach to cohort survival analyses, including in the presence of competing risks.

Figure 1. Comparing subdistribution hazard ratios (SHRs) from the Fine-Gray approach to adjusted relative risks (RRs) from the Nested Case- Control approach

SES quintile	SHR*		RR**	
1st - lowest	1.09 (1.03, 1.16)		1.09 (1.02, 1.16)	
2nd	1.05 (0.99, 1.10)		1.05 (0.99, 1.11)	
3rd	1.02 (0.97, 1.07)		1.01 (0.95, 1.06)	
4th	0.98 (0.94, 1.03)		0.98 (0.93, 1.03)	
5th - highest	Ref		Ref	

* Adjusted for race/ethnicity, SES quintile, rurality, age, year of diagnosis, ER/PR status, HER2 status, BC stage, grade, radiation, chemotherapy, surgery type, marital status, and insurance status

** 1:10 matched on age, race, diagnosis year, hormone receptor status, and HER2 status. Adjusted for grade, radiation, chemotherapy, surgery type, marital status, and insurance status

Impact of model misspecification on proportion mediated in causal mediation analysis Yi Li* Yi Li Maya B. Mathur Robert W. Platt Kazuki Yoshida

In causal mediation analysis, researchers might encounter circumstances where natural direct and indirect effects are in opposite directions, rendering proportion mediated (PM) outside [0, 1] and hence uninterpretable. Although this is possible under the true data generating process (DGP), it can also be caused by model misspecification. Based on the effect measure modification (EMM)-extended regression-based causal mediation approach, we conduct a simulation study to show how neglecting EMM impacts the range and the magnitude of bias in PM.

We randomly generate covariate (C), exposure (A), mediator (M), outcome (Y) and coefficients in mediator and outcome models. Assuming that covariate modifies exposure and mediator effects in the true DGP, we consider 4 model types (mediator and outcome models are linear or logistic) and 4 coefficient settings involving 3 main effects (exposure effect on mediator β_1, exposure effect on outcome θ_1, and mediator effect on outcome θ_2) when they are not in the same direction. First, we obtain the true PM. Then we fit correct and misspecified models. In misspecified models, we omit some EMM terms. We iterate the DGP 1000 times and calculate the probability of having true PM inside [0, 1] and estimated PM outside [0, 1], stratified by model type and coefficient setting. We further assess the magnitude of bias in PM when EMM terms are omitted, given true and estimated PM are both inside [0, 1].For linear outcome models, omitting EMM terms increases the probability of having PM outside [0, 1] by up to 10%; For logistic outcome model, the increase is less noticeable; overall, omitting M×C has the highest probability. For the magnitude of bias, omitting EMM terms increases bias for all model types (Figure 1); omitting A×C in mediator model and M×C in outcome model has the largest bias. These results suggest that researchers should be aware of potential EMM, as neglecting them may lead to significantly biased or even uninterpretable PM.
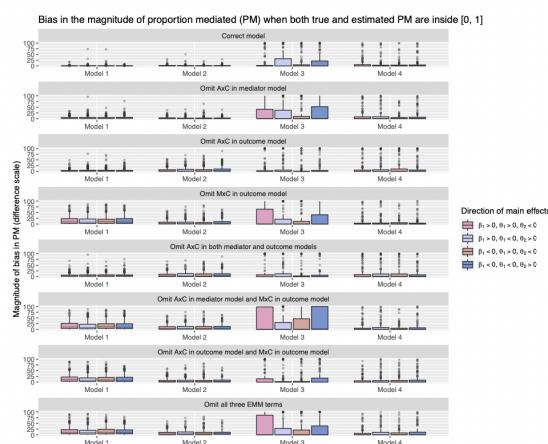

Figure 1: Bias in the magnitude of proportion mediated (PM) when both true and estimated PM are inside $[0, 1]$

(1) Mediation and outcome model configurations:

$$g_M(E[M|A = a, C = c]) = \beta_0 + \beta_1 a + \beta_2 c + \beta_3^T ac,$$
$$g_Y(E[Y|A = a, M = m, C = c]) = \theta_0 + \theta_1 a + \theta_2 m + \theta_3 am + \theta_4 c + \theta_5 ac + \theta_6^T mc,$$

where g_M and g_Y are link functions that can be either linear or logit.

(2) Four model types:
Model 1: linear mediator model, linear outcome model;
Model 2: logistic mediator model, linear outcome model;
Model 3: linear mediator model, logistic outcome model;
Model 4: logistic mediator model, logistic outcome model.

Marginal Structural Models for Causal Inference from Real-World Data: Recommendations from a Systematic Literature Review Ayad Ali* Ayad Ali Lisa Hess Yu Yan

Marginal structural models (MSM) are a class of causal models for the estimation of the causal effect of a time-dependent exposure in the presence of time-dependent covariates that may be simultaneously confounders and intermediate variables. We developed best practices for the application of MSM methodology to studies using real-world data. A systematic literature review was conducted of the Current Index to Statistics database and OVID's MEDLINE, Embase, and Cochrane database of systematic reviews using a combination of relevant search terms. The search was restricted to publications no earlier than 1997. A total of 31 methodological articles met the inclusion/exclusion criteria and were included in the review. Critical appraisal of the following aspects of MSM was conducted: causal effect analysis in time-dependent confounding scenarios; methodology assumptions; implementation in missing data; dynamic treatment regimens; targeted maximum likelihood estimator; and other applications of MSM in longitudinal data. Recommendations were developed for each aspect. In conclusions, MSM is used to account for time-dependent confounding and to estimate causal effects in real-world data. We developed recommendations for applying this methodology as best practice guidance for pharmacoepidemiolngists and outcomes researchers.

Standardizing to Specific Target Populations in Distributed Networks: A Proof of Concept
Michael Webster-Clark* Michael Webster-Clark Robert Platt

In distributed networks, a coordinating centre partners with multiple data nodes. The centre distributes an analytic protocol and/or code, nodes implement the protocol, and the centre compiles and disseminates results. If effect estimates differ across nodes of a network and the nodes are distinct and relevant populations, interpretation can be challenging.

We aimed to assess whether specifying target populations improved interpretability of distributed network analyses in four nodes of 10,000, 20,000, 40,000, and 80,000 individuals. Within nodes, we simulated a binary outcome Y and treatment X. Four confounders (C1-C4) differed in distribution across the nodes and were associated with the probability of Y and logit-linearly with the probability of X. The effect of X on Y was either uniform (no heterogeneity) or C2 and C3 interacted with X (heterogeneity) on the linear or log-linear scale. We estimated within-node effects of X on Y via inverse probability of treatment weights (IPTW) and used "naïve" inverse variance pooling (IVP) on within-node estimates to estimate a network effect. We also specified target populations (the full network, the smaller three nodes, or the smallest node), standardized node-specific estimates to each target via inverse odds weights (IOW), and then applied IVP. We compared results to a gold standard from analyzing each target population.

When no heterogeneity existed, all IVP estimates were unbiased. When heterogeneity existed, reweighting nodes to a target population greatly reduced differences in estimates between nodes (**Figure 1**). Naïve IVP resulted in estimates close, but not equal, to the full population target (mean naïve RD of 1.48% vs gold standard RD of 1.60% vs IOW RD of 1.62%; mean naïve RR of 1.146 vs gold standard RR of 1.152 vs IOW RR of 1.155). Specifying target populations facilitated comparison of the estimates produced by nodes of a distributed network and should be considered when effect estimates are heterogeneous.

Methods/Statistics
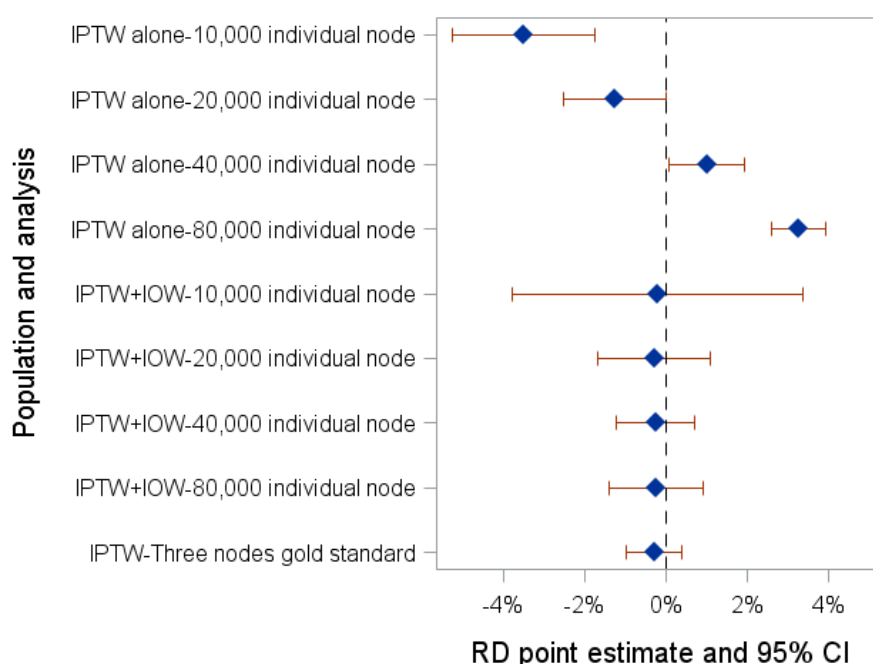
How many bootstrap samples do you need? A general approach Leah Sadinski* Leah Sadinski
Tiffany Breger Daniel Westreich

Suppose an investigator wishes to estimate the confidence interval for a difference in median systolic blood pressure between antihypertensive treated and untreated people. No closed form solution exists for estimating a variance for a difference in medians; one solution to this issue to bootstrapping. It is unclear in the published literature how many bootstrap samples must be drawn to stably estimate a variance. We propose a generalized approach to creating an algorithm to guide investigators on answering the question "how many bootstrap samples do we need?" Step 1 of our proposed algorithm is to identify: a) an initial number of bootstrap samples, b) a rule for increasing the number of bootstrap samples from round n to round n+1, and c) a stopping rule that indicates whether the variance has sufficiently stabilized. Step 2 is to draw the initial number of bootstrap samples indicated by (a) and calculate the variance. Step 3 is to increase the bootstrap sample size specified by (b), calculate the variance, and check if the stopping rule (c) is met; if it is not, then we repeat Step 3 until the stopping rule is met. Suppose that for our example (a) is 100, (b) is 50, and (c) is "stop when the variance changes ≤0.01 from round n to round n+1." Suppose in Step 2, the estimated variance for 100 bootstrap samples is 1.27. In Step 3, the estimated variance with 150 bootstraps is 1.23. Because the variance changed by more than the stopping rule, Step 3 is repeated. With 150+50=200 samples the estimated variance is 1.22, and since 1.23-1.22≤0.01 the investigator reports a variance of 1.22 estimated with 200 bootstrap samples. We will illustrate other potential rules for (a), (b), and (c) and compare results. Ultimately, this work can serve as a roadmap for employing bootstrapping and facilitate repeatable, transparent methods in epidemiologic studies.

Comparison of Bayesian Spatio-temporal models for estimating small-area level life expectancy: A simulation study Ikhan Kim* Ikhan Kim Hee-Yeon Kang Young-Ho Khang

Background: This study assessed the bias, variance, and normality of life expectancy values estimated with the three other Bayesian Spatio-temporal models, the Bayesian Spatial models, and the conventional method in the small-area application.

Methods: We hypothesized six scenarios, entire districts of Korea had the same population of 500, 1,000, 2,000, 5,000, 10,000, 25,000 during the study period (2013–2017), maintaining the actual age structure. We applied the Monte Carlo simulation method to create 1,000 hypothetical datasets for each scenario and calculated each district's life expectancy using hypothetical datasets by estimation methods. Setting the life expectancy calculated with the observed mortality for each district as true value, the magnitudes of bias and variance were compared among estimation methods for each scenario. The normality of the distributions of estimated life expectancy was also checked.

Results: The Bayesian Spatio-temporal models produced the lowest magnitude of bias, especially when the model assumed a non-linear association between age or time, and mortality. However, the Bayesian Spatio-temporal models estimated 95% uncertainty intervals overconfidently throughout all scenarios. The distributions of estimated life expectancy were against the normality assumption. We proposed 0.8 as a cut-off value when comparing life expectancy between small areas or time points using predictive posterior distribution from the Bayesian Spatio-temporal models.

Conclusions: The Bayesian Spatio-temporal models with non-linearity terms showed the most precise life expectancy estimates among the estimation methods. However, they produced overconfident uncertainty, and distributions of estimated values violated the assumption of normality. Therefore, a comparison of life expectancy between small-area or time points should be executed utilizing the posterior predictive distribution and appropriate cut-off value.
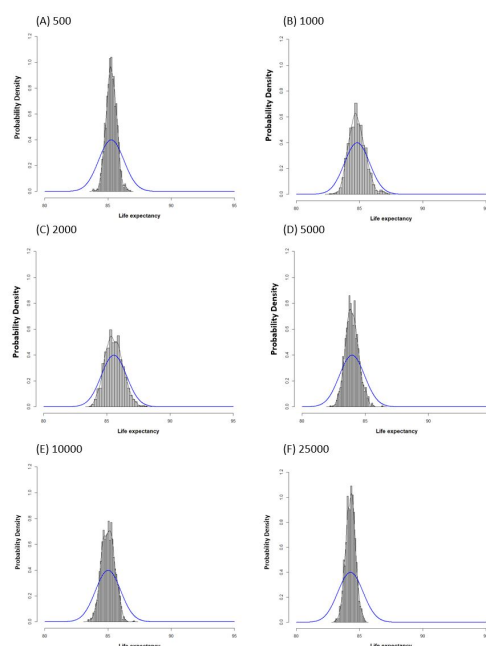
The use of multilevel modeling in meta-analytic studies investigating global health topics: accounting for clustering effects Kevin McIntyre* Kevin McIntyre Dr. Janet Martin Dr Saverio Stranges Dr Daniel Lizotte Dr Ava John-Baptiste Dr Yun-Hee Choi Jessica Moodie

Global health is a diverse and dynamic field that is developing an incredibly large literature base as the pace of scientific research accelerates across the world. To manage such vast amounts of information, evidence synthesis is a necessary tool for policymakers and other key stakeholders from the local through international levels. This reliance on evidence synthesis to guide policymaking presents many key challenges, one of which is how to best account for correlations between studies due to higher level clustering. We present a potential solution to this problem by recommending the use of techniques that account for such complex data generating procedures.

One such technique is multilevel meta-regression. This method views meta-analysis, and therefore meta-regression, as a special case of a multilevel model. Under this conceptualization, extending the model to include more levels and covariates is relatively straightforward. Extending a meta-regression to incorporate these aspects allows variables that could create clustering effects to be accounted for. One particularly important variable in the context of global health, is country. With a multilevel meta-regression, participants can be modeled as being nested within studies which are in turn nested within the country that the study was conducted in. This provides an elegant way for starting to address the inherent correlations in patient outcomes that may be expected due to national healthcare policies or other variables such as country income. Furthermore, covariates can be added at each of these levels. For example, aggregated individual outcomes can be modeled at the study level as proportions while country level factors such as the Human Development Index can be incorporated at that level. Accounting for such complex data structures will assist global health analyses in providing more reliable point estimates and interval coverage that may otherwise be biased by neglecting these hierarchical structures.

Sensitivity Analysis for a Biased Design Limitation Pin Li* Mara Epstein Pin Li Feifan Liu Christine C. Johnson George Divine

In a pharmacoepidemiology study of statin use and multiple myeloma risk at six Health Care Systems Research Network (HCSRN) sites, marginal structural modeling (MSM) was employed to address the impact of the exposure (statin use) and a confounder (serum cholesterol) when changes in both may influence the outcome as well as each other. Such a dynamic relationship means classic case-control analysis cannot properly control for the confounder. MSM can be analogous to survival analysis with time-varying variables. However, if diagnosis/index time is a matching variable, and control data after the index time is not collected, bias can be expected, since control observations are truncated, while cases' are not.

The issue of truncation and need for MSM was recognized in a nested case-control analysis assessing statin use on multiple myeloma risk using data extracted from the HCSRN Virtual Data Warehouse. To assess the bias due to truncation, sensitivity analysis was undertaken starting with a published multiple myeloma cohort with 2532 cases (47% >70 years old and 55% male), and 9805 matched controls. Hypothetical datasets were generated, with each control observation time extended by 1, 3, 6, 12 or 24 months. Analysis results for the extended datasets were compared to those originally obtained and published for all subjects and four subgroups.

We conducted 175 analysis variations. Risk Ratio (RR) estimates changed slightly in most, but moderately in some. The magnitude of change increased with greater control observation time. The RR estimates decreased up to 8.3% in all patients, 15.9% for under age 70, and 4.2% for over age 70. RRs changed about 7.5% for both males and females. The majority (98%) of changes to the 95% confidence intervals of the RRs did not change inclusion of the null (1.0).

In conclusion, after accounting for truncated observation of controls, overall conclusions of original analysis remain unchanged.

Conflict of Interest in the Peer Review Process: A Systematic Survey of Peer Review Reports Adham Makarem* Adham Makarem Rayan Mroue Halima Makarem Laura Diab Bashar Hassan Joanne Khabsa Elie Akl

Objectives: To assess the extent to which peer reviewers and journals editors address conflicts of interests (COI) and study funding. Also, we aimed to assess the extent to which peer reviewers and journals editors reported and commented on their own or each other's COI.

Study design and methods: We conducted a systematic survey of randomized controlled trials (RCTs) published in open access peer reviewed journals that also have open reports policy. Using REDCap, we collected data in duplicate and independently from journals' websites and articles' peer review reports.

Results: We included 115 RCTs published in 58 journals, with 263 associated peer review reports. While 90% of the studies were funded, 59% included a statement on the funder's role. At least 1 author reported a COI in 30% of articles. Out of 263 peer reviewers, 66% reported absence of COI, 4% reported presence of COI, while 30% did not report on COI. Only 2% of peer reviewers commented on the study funding source, 1% commented on the authors' COI, 1% commented on their own COI, and 0% commented on editor's COI. 13% of the articles had the editors' correspondence with the authors posted. Seven percent of editors commented on the study funding source. None of the editors reported on their own COI. While 7% of editors commented on the study funding source, none of them commented on the author's COI, the peer reviewers' COI, or their own COI.

Conclusion: The percentage of peer reviewers and journal editors who addressed authors' COI and study funding was extremely low. In addition, peer reviewers and journal editors rarely reported their own COI, or commented on their own or on each other's COI.

Correction for Unmeasured Confounding Using a Negative Control Outcome: a Case Study of Oral Quinolones and Tendon Rupture Phuong T Tran* Phuong Tran Michael Daniels Laura E. Happe Amie J. Goodin Almut G. Winterstein

Background

We can leverage the rich information in observational studies of automated healthcare data to find a valid negative control outcome (NCO), which can be used to assess and remove bias. Systemic quinolones are known to increase tendon rupture risk. However, recent studies did not find or found negligible magnitudes of this adverse effect, suggesting residual confounding due to channeling quinolones away from high-risk patients.

Objectives

To adjust risk estimates of oral quinolone-associated Achilles tendon rupture (ATR), using sports injuries as NCO to capture unmeasured physical activities.

Methods

We conducted a retrospective cohort study using 2005-2015 IBM® MarketScan Commerical Claims Databases. We formed 2 distinct acute sinusitis (AS) and urinary tract infection (UTI) cohorts of new quinolone users aged 18-64 years with active comparators to calculate HRs. We used a 1-year lookback period to measure baselines characteristics (e.g., diabetes, history of tendon rupture) and followed patients for 35 days or till they met censoring criteria (e.g., injuries). Inverse probability of treatment weighted (IPTW) Cox proportional hazard models were used to adjust for measured confounding. The corrected HR was the proportion of the adjusted HR of ATR over that of sports injuries.

Results

IPTW adjustment resulted in HRs of 1.02 (95%CI 0.30-2.59) for AS and 1.21 (0.54-2.68) for UTI. HRs for NCOs were 0.67 (0.21-2.13) for AS and 0.35 (0.15-0.84) for UTI. After adjusting for the departure of HRs of NCOs from 1, the corrected HRs were 1.52 for AS and 3.46 for UTI.

Conclusion

NCO-corrected results moved the ATR HR closer to risk estimates of early quinolone ATR studies when concerns about this adverse effect were just emerging and channeling effects less likely existed. Thus, NCOs enhanced traditional adjustments for confounding.

A systematic review of the reporting quality of studies that use Mendelian randomisation in UK Biobank Mark Gibson* Mark Gibson Francesca Spiga Amy Campbell Rebecca Richmond Marcus Munafo

Mendelian randomisation (MR) is a popular method of causal inference that uses genetic variation as an instrumental variable (IV) to account for confounding. While the number of MR articles published each year is rapidly rising, it is not currently known whether these articles report their analyses in enough detail for others to accurately replicate them. The aim of this systematic review is to assess whether studies which conduct MR in UKB provide the information necessary to perform a direct replication and whether this varies across different types of article. This study included 64 English language, fully accessible, full research articles that conducted MR using only individual-level UK Biobank data to obtain a causal estimate of the exposure-outcome association. These were identified from a search of four databases for terms relating to both UKB and MR conducted on 04/11/2020. Data were dual extracted on 17 items to do with reporting and methodological quality based on the STROBE-MR reporting guidelines. Information on article type and journal information was also extracted. Overall, the proportion of articles which reported complete information ranged from 1.6% to 96.9% across the different items. Information on palindromic variants, variant replication, associations between the IV and variables of interest, the code used and the three core assumptions of MR were often not reported on completely (<11%). There was no clear evidence that Journal Impact Factor, word limit or year of publication predicted percentage of article completeness across items, but there was evidence that the MR analysis being the sole primary versus a joint primary or secondary analysis did increase completeness. The results identify areas in which the reporting of MR studies needs to be improved and highlights that this is independent of journal prestige, year of publication or word limit.

Association of predictors with reporting quality across all data extraction items
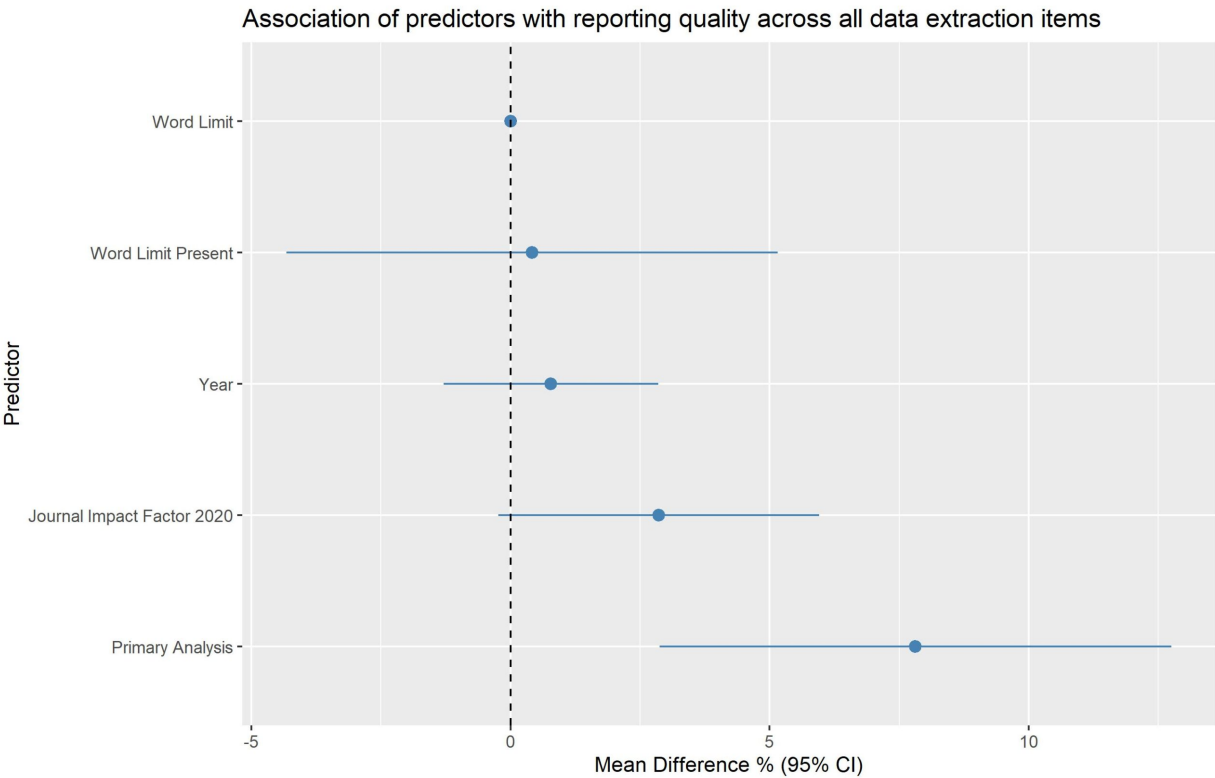
Circulating androgen and estrogen metabolites associated with urogenital menopausal symptoms in the Women's Health Initiative Observational Study Jessica Gorzelitz* Jessica Gorzelitz Britton Trabert Garnet Anderson Carolyn J. Crandall Margery Gass Ruth M. Pfeiffer Jean Wactawski-Wende Xia Xu Kara A. Michels

Background

Menopausal urogenital symptoms impact quality of life for many women. Lower estradiol levels are thought to contribute, but the role of other hormones is unclear. We compared circulating concentrations of over 30 markers of androgen and estrogen metabolism with urogenital symptoms in postmenopausal women.

Methods

Data came from a nested case-control study of ovarian and endometrial cancer in the Women's Health Initiative Observational Study (983 women not using hormone therapy (HT) at blood draw). Women reported the presence or absence of vaginal itching, dryness, and discharge in the month prior to baseline. We used sensitive LC/MS-MS assays to measure hormones in baseline serum samples. We performed linear regression to estimate percent differences in the geometric mean hormone concentrations associated with each symptom. We used weighting to correct for the oversampling of women who developed cancer during follow-up and adjusted for age, race, BMI, blood draw year, and recency/type of HT use.

Results

Compared to women who did not report the symptom, women who reported vaginal itching (n=177) had higher levels of conjugated estriol (21.9%, confidence interval [CI] 95% CI 0.4, 48.0%). Women with vaginal dryness (n=290) had lower levels of several androgens: dehydroepiandrosterone sulfate (-15.9% [-29.1, -0.2%]), androstenedione (-8.9% [CI -17.7, 1.0%]), dihydrotestosterone sulfate (-15.6%, [-26.1, -3.7%]), and etiocholanolone glucuronide (-16.6% [-30.8, -0.1%]); estrogens did not differ. Women with vaginal discharge (n=95) had higher levels of unconjugated 2-methoxyestradiol (40.4% [2.5-92.2%]).

Conclusions

While the onset of urogenital symptoms may coincide with the cessation of parent estrogen produced by the ovaries, other sex hormones were associated with these symptoms in our study. We did not consistently observe differences in the same hormones across the symptoms evaluated, suggesting that any hormonal contributions to their etiologies may be unique.

Epigenetic clocks and microRNAs among US firefighters Alesia Jung* Alesia Jung Melissa Furlong Jaclyn Goodrich Andres Cardenas Jefferey Burgess

Background: Epigenetic changes, including epigenetic (DNAm) age and microRNAs (miRNAs), have been proposed as biomarkers for measures of health. Accelerated DNAm age measured via DNAm clocks has been associated with adverse health outcomes and mortality. However, the intersection of DNAm clocks and miRNAs has yet to be evaluated, along with miRNA-based health implications of these associations.

Methods: Blood samples from 332 US firefighters at enrollment of two studies (2015-2018 and 2018-2020) were analyzed for DNA methylation profiles and miRNA expression. We considered seven measures of DNAm age (PhenoAge, GrimAge, Horvath, skin blood, Hannum, and extrinsic and intrinsic age acceleration). Excluding extrinsic and intrinsic age acceleration, we used residual values after regressing clocks on chronological age. Separate linear regression models were used to identify miRNAs associated with accelerated DNAm age adjusted for sex, race, chronological age, and cell type estimates. We used the miRNA Enrichment Analysis and Annotation Tool to investigate downstream effects (diseases and GO pathways) of miRNAs associated with accelerated DNAm age.

Results: On average, firefighters were 38 years, 88% male, and 12% non-Hispanic white. Of 798 miRNAs, we identified 181 associated with accelerated DNAm age at FDR<0.05 (PhenoAge=126, GrimAge=59, Horvath=1, skin blood=1) with no miRNAs present in all groups. Disease pathways significantly enriched for miRNAs associated with PhenoAge included arterial conditions, heart conditions, and cancers of the prostate, lung, lymphatic system, and digestive system. No pathways were significantly enriched for other DNAm age acceleration measures.

Conclusions: We identified miRNAs associated with measures of DNAm age in firefighters. PhenoAge had stronger associations with miRNAs than other clocks, with greater implications for miRNA-associated diseases. This clock may offer greater utility for measuring disease presentation.

Investigating the validity of GlycA as an inflammatory biomarker in the ALSPAC cohort and UK Biobank Daisy Crick* Daisy Crick Hannah Jones Joshua Bell Sarah Halligan Golam Khandaker Abigail Fraser

Background: Glycoprotein Acetyl (GlycA) is potentially a superior measure of chronic inflammation compared to other commonly used inflammatory biomarkers such as C-reactive Protein (CRP). This is because it reflects a composite measure of systemic inflammation rather than concentrations of individual acute phase proteins. Yet the validity of GlycA has not been examined well in large scale longitudinal population samples.

Objectives: To examine the validity of GlycA as an inflammatory biomarker.

Method: We used data from the UK general population Avon Longitudinal Study of Parents and Children (ALSPAC). GlycA and CRP were measured at ages 15y (n=3300), 18y (n=3114) and 24y (n=2957). We estimated and compared the intra-biomarker and inter-biomarker correlations across ages. We also investigated the short-term reliability of GlycA, in a subsample of participants who repeated the assessment within six weeks. Finally, we investigated unadjusted and adjusted associations of known determinants of inflammation (concurrent infection, BMI, maternal educational attainment (MEA), household social class (HHSS), smoking, drinking, asthma, sex, and age) with (log transformed and z-scored values of) GlycA and CRP. We ran inter-biomarker correlations using UK Biobank (UKB) (N=111,554) with logged CRP and GlycA.

Results: In the ALSPAC cohort the longitudinal intra-biomarker correlations were consistently higher for GlycA compared to CRP, e.g. 0.47 vs 0.33 between ages 15y and 18y for GlycA and CRP respectively. GlycA and CRP weakly correlated (≥ 0.50) at the different ages. Retest reliability correlations for GlycA were ≥ 0.44. The results of the multivariable analysis are presented in Figure 1. In UKB inter-biomarker correlation was 0.52.

Discussion: Our results demonstrate the short- and long-term reliability of GlycA. We found evidence associations between known inflammatory determinants and GlycA, supporting the use of GlycA to measure of chronic inflammation.
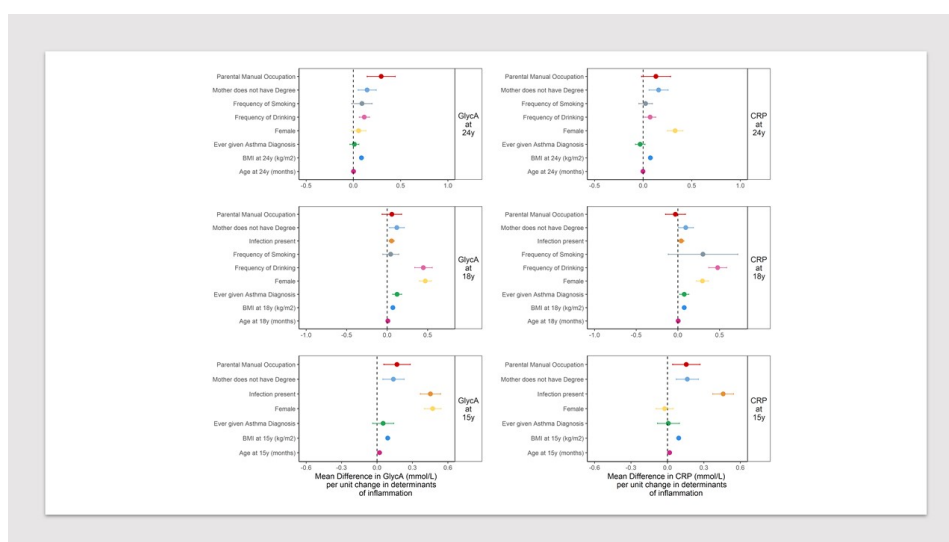
The association of neighborhood recreation centers and post-stroke outcomes Leanna
Delhey* Leanna Delhey Lynda Lisabeth Devin Brown Lewis Morgenstern Xu Shi Melinda A Cox Erin
Case

Objective: Determine whether neighborhood recreation centers are associated with post-stroke
outcomes.

Methods: This study used data from the Brain Attack Surveillance in Corpus Christi project, a
population-based surveillance cohort of stroke-survivors in Nueces County, Texas. We included non-
Hispanic Whites and Mexican Americans (MAs) with incident stroke. Number of centers (fitness,
golf, skiing, boating, bowling establishments) per square mile of the census-tract defined
neighborhood density of recreation centers. Outcomes at 90-days post-stroke included disability
(activities of daily living (ADL)/instrumental ADL (IADL)), cognition (Modified Mini-mental State
Exam), depressive symptoms (Patient Health Questionnaire-8), and quality of life (abbreviated
Stroke-Specific Quality of Life scale (SS-QOL)). We fit confounder-adjusted mixed linear models with
multiple imputation for each outcome and considered interactions with stroke severity (figure 1).

Results: The sample included 1,299 persons aged 45-95 years old (median=64, interquartile range
56-73), 53.6% male, and 62.9% MA. Residing in neighborhoods with greater density of recreation
centers (median = 1.70, interquartile range = 0.41-3.19) comparing 75th to 25th percentile was
associated with more favorable disability (mean difference in ADL/IADL= -0.12; 95% CI -0.22, -0.01;
range 1-4; higher scores worse) and quality of life (mean difference in SS-QOL= 0.13; 95% CI -0.004,
0.27; range 0-5; higher scores better) among those with moderate-severe stroke. We did not observe
these associations among those with mild stroke, or any associations with cognition or depressive
symptoms in either stroke severity group.

Conclusions: Availability of neighborhood recreation centers may affect post-stroke outcomes
related to disability and quality of life among those who suffer a moderate-severe stroke. Research
should confirm these findings and explore the mechanisms by which access to these centers may
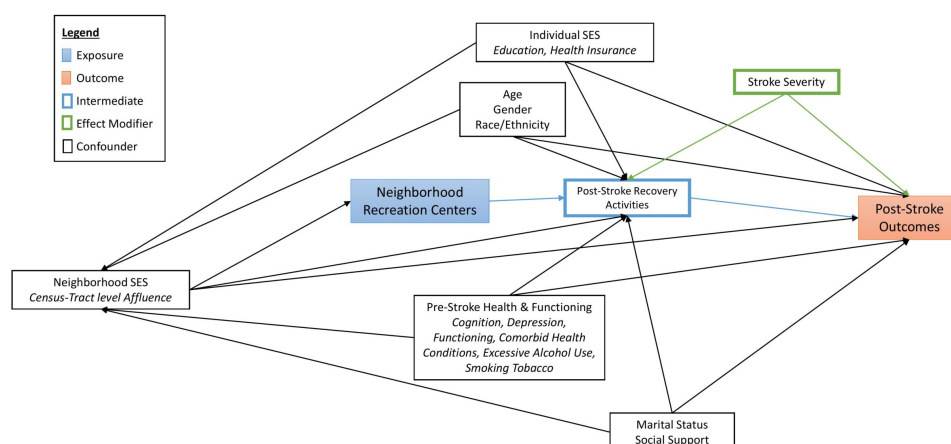promote recovery.

Figure 1. Directed Acyclic Graph (DAG) portraying effect of neighborhood recreation center density on post-stroke outcomes

The relationship of eating pattern and psychological distress among young adults during COVID-19-related quarantine Brigita Mieziene* Brigita Mieziene Ichiro Kawachi Arunas

Background. COVID-19 pandemic affected different domains of an individual life. The nutritional status of individuals has for long been considered an indicator of resilience in times of crisis. Previous studies showed that poor diet is associated with both physical and mental health. This study aimed to explore the relationships between eating patterns and psychological distress among young adults during the COVID-19 pandemic.

Methods. The study included 1214 participants. Among them, 61 percent were women. The mean age was 23 years. Eating habits were measured by the MEDAS scale. The Kessler 6 items scale identified psychological distress, and participants were distributed as having high and low distress.

Results. In total on the MEDAS scale, 50.1 percent had a poor diet, 47.7 percent had an average and only 2.2 percent complied with the recommendations of healthy eating. 44 percent of Lithuanian young adults had high distress during the COVID-19 pandemic. Those with low distress more often comply with a healthy diet at least on an average level (55 percent) than those with high psychological distress (44 percent). In particular, they consume more olive oil, eat more vegetables, prefer fish and white meat for red meat, consume less pastry, fast food, sugary drinks. Moreover, young adults with low psychological distress eat breakfast more often (72 percent) than those having high psychological distress (59 percent). However, the consumption of animal fats, fruits, wine, and eating out is similar between young adults with low and high distress.

Conclusion. Around the half of population of young adults have a poor eating pattern in times of crisis. Along, almost half of them also are prone to high psychological distress. At a community level, it is critical to provide social support to reduce the level of psychological distress and at a national level to spread awareness regarding the importance of healthy nutrition especially in times of crisis like pandemics.

Nutrition/Obesity

Caregiver concern about child overweight/obesity in grandparent vs. parent-headed households Samrawit F. Yisahak* Samrawit Yisahak Amrik S. Khalsa Sarah A. Keim

Objective: Grandparent-headed households (GPHH) are increasingly common in the United States and face unique economic and social challenges compared to parent-headed households (PHH). Caregiver concern about child overweight/obesity by household structure is understudied. We compared the prevalence of child overweight/obesity in GPHH vs. PHH in a national sample and determined the association of household structure with lack of caregiver weight concern.

Methods: Caregivers reported their relation to the child aged 10-17 years and the child's weight and height (National Survey of Children's Health 2016-20). Overweight/obesity was calculated using Centers for Disease Control and Prevention growth charts. Caregivers were asked, "*Are you concerned about this child's weight?*" with response options, "*Yes, too high*", "*Yes, too low*", or "*No, not concerned*". We used a 1:1 greedy matching algorithm with a caliper of 0.25 standard deviations for propensity score matching and estimated the association (prevalence odds ratio) of GPHH with lack of weight concern ("*Yes, too low*" or "*No, not concerned*") among matched children with overweight/obesity.

Results: Children with overweight/obesity lived in 41.15 (SE=2.05)% of GPHH and 29.68 (SE=0.42)% of PHH which includes children with obesity (25.87 (SE=1.99)% of GPHH and 14.53 (SE=0.34)% of PHH). Among children in the overweight/obesity category, 64.65 (SE=3.27)% of grandparents and 66.55 (SE=0.81)% of parents did not express concern about the child's weight status. Among children with obesity, it was 47.57 (SE=4.63)% and 50.96 (SE=1.28)%, respectively. GPHH was not significantly associated with caregivers' lack of weight concern (**Table 1**).

Conclusions: GPHH had a higher burden of child overweight/obesity but lacked appropriate weight concern as often as PHH. Overall, appropriate caregiver concern about child's weight status was strikingly low in both GPHH and PHH, though it increased slightly for children in the obese category.

Table 1: Associations of household structure with lack of appropriate caregiver concern among children with overweight and obesity, National Survey of Children's Health, 2016-2020

	Caregiver	Lack of appropriate caregiver concern[1] Odds ratio (95% CI)
Among children with overweight/obesity	Parent	Referent
	Grandparent	0.92 (0.76, 1.12)
Among children with obesity	Parent	Referent
	Grandparent	1.06 (0.82, 1.38)

Covariates used to estimate propensity scores include child's sex, race, ethnicity, age, as well as family poverty ratio, primary household language, highest level of education among reported adults, caregiver mental and emotional health, cash assistance from a government welfare program, child coverage by government assisted health insurance, and presence of sidewalks/walking paths in the neighborhood

1. Lack of appropriate caregiver concern defined as responding either "*No, not concerned*" or "*Yes, too low*" to the question, "*Are you concerned about this child's weight?*"

**Association between prenatal exposure to Perfluoroalkyl substances mixture and childhood obesity at age of 7 years** Shanyu Zhang* Shanyu Zhang Xiaoning Lei Qian Yao Chengyu Pan Yu Gao Ying Tian

Background: Perfluoroalkyl substances (PFAS) are considered as obesogens that cross placenta. However, few studies assess the joint effects of prenatal PFAS mixture exposure on childhood obesity.

Method: A total of 206 pairs of mother-children were enrolled in the Laizhou Wan Birth Cohort (LWBC) in Shandong, China. Ten PFAS were measured in serum of pregnant women during third trimester using HPLC-MS/MS. Body mass index (BMI), waist circumference (WC), waist to height ratio, fat mass, and percentage of body fat were ascertained for children as indices of obesity during 7-year-old follow-up. Multivariable linear regression and weighted quantile sum (WQS) regression were used to assess the associations of individual PFAS and PFAS mixture with children obesity.

Results: The detection rate of ten PFAS was more than 85%, and the highest PFAS was PFOA (45.14 ng/mL). Among all children, the mixture of PFAS was associated with decreased fat mass and percentage of body fat in WQS, and PFOSA was the greatest contributor. In individual PFAS analysis, PFHpA was associated with decreased WC (β= -4.97, 95% CI: -9.47, -0.46), and PFOSA (β= -9.05, 95% CI: -17.31, -0.79) was associated with decreased fat mass and percentage of body fat (β= -18.77, 95% CI: -34.84, -2.71). When stratified by sex, The mixture of PFAS and individual PFHpA, PFOSA were negatively associated with five obesity indices in boys, with PFHpA and PFOSA as the two greatest contributors in WQS. However, in girls, the positive associations were found between PFAS mixture and five obesity indices except percentage of body fat with the PFBS as the greatest contributor. In addition, individual PFHpA was also associated with increased BMI in single PFAS analysis.

Conclusion: Our study suggested that prenatal exposure to individual PFAS or their mixture was negatively associated with obesity indices in 7-year-old children. However, the direction of associations was contrast between different sex, with negative associations found in boys and positive in girls.
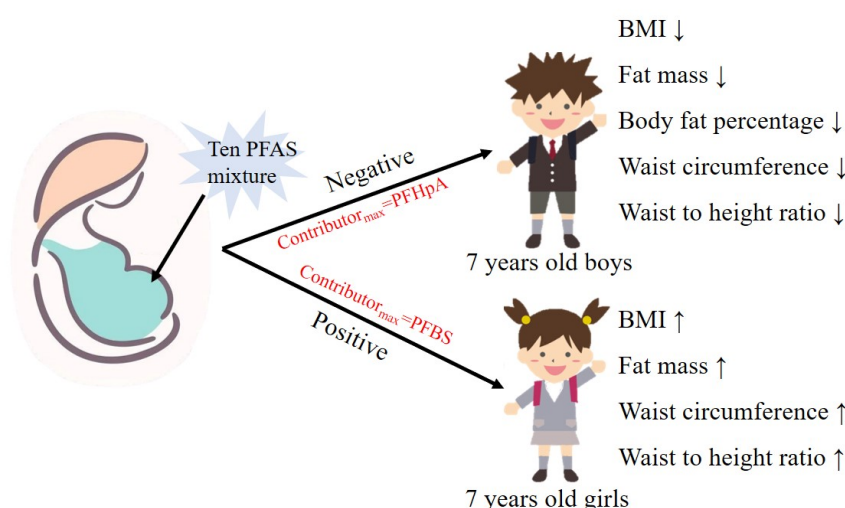
Examining the double burden of malnutrition among women of reproductive age and preschool children in low- and middle-income countries: A scoping review and thematic analysis of the literature Jason Mulimba Were* Jason Were Saverio Stranges Ishor Sharma Juan-Camilo Vargas-González M. Karen Campbell

Introduction: Many low- and middle-income countries (LMICs) are encountering the double burden of malnutrition (DBM). DBM appears to be common among preschool children and women of reproductive age. However, these population subgroups remain understudied.

Objectives: Which nutrition indicators have been used to operationally define the DBM at the individual, household and population levels among preschool children and women of reproductive age? What are the posited explanations for the occurrence of the identified DBM phenotypes at the individual, household and population levels among preschool children and women of reproductive age? What are the risk factors for the DBM at the individual, household and population levels among preschool children and women of reproductive age?

Methods: MEDLINE, LILACS, EMBASE, CINAHL, Scopus and ProQuest Dissertations & Thesis Global databases were systematically searched from inception to January 2022 to obtain literature discussing DBM concept in LMIC. Thematic analysis was conducted on extracted information from the literature to reveal emerging themes from included studies.

Results: Frequently used indicators for women were anthropometric indices and micronutrients measurements (e.g., overweight/obesity and anemia) and anthropometric indices (e.g., overweight/obesity and stunting) for preschool children: the following themes emerged as plausible explanations for the DBM phenotypes: diet transition; diet behavior; breastfeeding; biology and independence. Age, child sex, household wealth, women's education and urbanization were frequently occurring DBM risk factors. Of note was the use of the term 'double burden' as a buzz word.

Conclusion: The DBM phenomenon is loosely understood due to the varying operational definitions of the DBM construct. Emerging themes and common risk factors may provide target areas for public health interventions. Studies with robust designs are needed to succinctly understand the DBM phenomenon.

Docosahexaenoic acid and lifespan in men and women CM Schooling* CM Schooling MK Kwok

Background: Omega-3s have long been thought to have health benefits. Recent randomized controlled trials have suggested no overall benefit, but possibly a benefit for a precursor of eicosapentaenoic acid (EPA), raising questions about the role of other major omega-3s, such as docosahexaenoic acid (DHA). In addition, the trials were unable to assess differences by sex although intended to do so. To address these questions, we conducted a sex-specific Mendelian randomization study (MR) of DHA on parental longevity, so as to obtain estimates with little confounding or selection bias. Specifically, parental attained age from a cohort recruited in middle-age largely avoids selection bias due to the inevitable selection of survivors and has greater power than considering mortality of cohort members.

Methods: We conducted a one-sample MR study using two-sample methods in the UK Biobank. We obtained 44 strong (p-value $<5\times10^{-8}$), independent ($r^2<0.001$) genetic predictors of DHA from a genome wide association study (GWAS) in a randomly selected subset of 114999 UK Biobank participants. We applied these genetic predictors to GWAS of longevity, based on parental attained age (age at death or current age, n=415311 for fathers and 412937 for mothers). We used sensitivity analysis. We assessed the sex difference using a z-test.

Results: DHA was unrelated to maternal lifespan using inverse variance weighting (-0.17 years lost per standard deviation higher of DHA, 95% confidence interval (CI) -0.67 to 0.33) but was associated with shorter paternal lifespan (0.59 years lost, 95% CI 0.05 to 1.13), p-value for sex difference 0.04. Sensitivity analysis gave similar estimates.

Conclusions: DHA may have different effects by sex, including possible harms in men. Further verification and consideration of sex-specific dietary advice might be worthwhile.

LATEBREAKER

Nutrition/Obesity

Leisure time physical activity types and risks of all-cause, cardiovascular and cancer mortality Eleanor Watts* Eleanor Watts Charles E. Matthews Joshua R. Freeman Jessica S. Gorzelitz Hyokyoung G. Hong Linda M. Liao Kathleen M. McClain Pedro F. Saint-Maurice Eric J. Shiroma Steven C. Moore
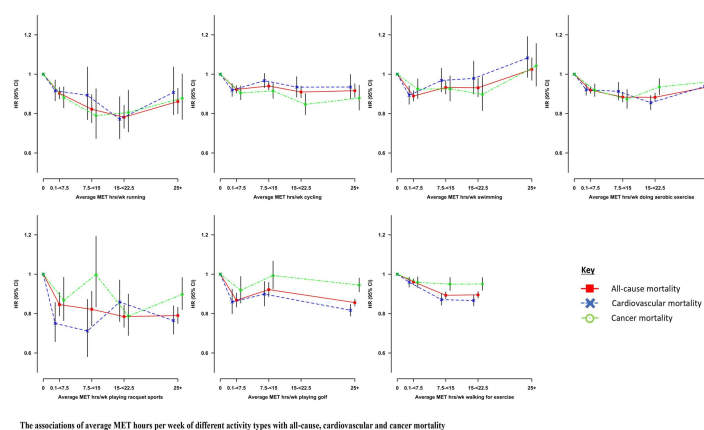
Physical activity is associated with increased longevity. However, less is known about how engaging in the same amount of different leisure time activity types are associated with mortality risks, and whether some activities are associated with a greater benefit than others.

We investigated whether achieving the recommended physical activity levels (7.5-<15 metabolic equivalent (MET) hrs/wk) through different activities (running, cycling, swimming, aerobic exercise, racquet sports, golf, and walking) was associated with mortality risk and examined the shape of the dose-response relationship.

We fitted multivariable-adjusted Cox proportional hazards regression models to estimate HRs and 95% CIs of mortality for each of the seven types of activities. Participants were 272,550 respondents from the National Institutes of Health-AARP Diet and Health Study, who completed the follow-up questionnaire which collected data on weekly durations of different types of physical activities. After an average of 12.4 years of follow-up, 118,148 participants (43%) died.

In comparison with those who did not participate in each activity, meeting the recommended range through racquet sports (HR=0.82,95% CI 0.75-0.89) and running (0.82,0.74-0.91) was associated with the greatest relative risk reductions for all-cause mortality, followed by aerobic (0.88,0.86-0.91), walking (0.89,0.88-0.91), golf (0.92,0.89-0.96), swimming (0.94,0.92-0.96), and cycling (0.94,0.92-0.96). Each activity showed a curvilinear dose-response relationship with mortality risk; meeting the physical activity recommendations for any activity type was associated with a large reduction in mortality risk, with diminishing returns for each increment in activity thereafter.

In conclusion, we observed small differences between different types of leisure time physical activities and mortality risks but meeting the recommended physical activity range through any activity was associated with lower mortality risks.

The associations of average MET hours per week of different activity types with all-cause, cardiovascular and cancer mortality

Occupational

The association between World Trade Center-exposure and obstructive sleep apnea in firefighters Ankura Singh* Ankura Singh Rachel Zeig-Owens David Appel David J. Prezant Mayris P. Webber

Background

Obstructive sleep apnea (OSA) is a common, potentially life-threatening condition. Prevalence increased in the last 2 decades, and was recently estimated to be 26% in adults, although estimates vary considerably. Previously, we reported that 44% of Fire Department of the City of New York (FDNY) World Trade Center (WTC)-exposed workers were at high risk of OSA based on a screening survey.

Objective

To estimate the association between WTC exposure and self-reported OSA diagnoses in WTC-exposed FDNY and non-WTC-exposed non-FDNY firefighters.

Methods

10,020 WTC-exposed FDNY firefighters and 3,513 non-WTC-exposed firefighters from the Chicago, Philadelphia and San Francisco fire departments who were employed on 9/11/01 were included in the analyses. Each completed a health survey that included questions about OSA diagnoses by a health professional and recency of a doctor visit. Multivariable logistic regression models estimated the OR of OSA in WTC-exposed vs. non-WTC-exposed firefighters, controlling for known risk factors.

Results

Overall, 33% of the WTC-exposed cohort reported an OSA diagnosis compared with 21% of the non-WTC-exposed. WTC-exposed firefighters had elevated OSA odds (OR=1.31; 95%CI=1.17-1.46) after controlling for age, sex, race, smoking, alcohol use, BMI, and self-reported hypertension and diabetes. Other statistically significant risk factors were male sex (OR=2.14; 95%CI=1.35-3.40), BMI (OR=1.14; 95%CI=1.14-1.16), hypertension (OR=1.51; 95%CI=1.39-1.65), and diabetes (OR=1.64; 95%CI=1.46-1.85). All FDNY firefighters and >90% of non-FDNY firefighters reported a doctor visit ≤2 years prior to survey completion.

Conclusion

WTC exposure conferred an increased risk of OSA diagnoses, although we cannot rule out the possibility of detection bias because FDNY physicians have heightened awareness of OSA based on its association with other WTC-related respiratory conditions. All of these conditions may be manifestations of chronic systemic inflammation.

Occupational

Association between county cannabis retail availability and subsequent county rates of occupational injury in Washington, 2014 – 2019 Vi Le* Vi Le Deborah Fulton-Kehoe Isaac Rhew

State-level analyses have found lower rates of workplace injuries following recreational cannabis legalization; however, cannabis laws are not homogenous between and within states. Examining within-state variability in retail access can provide information on the effectiveness of local jurisdictions in regulating cannabis. This study examines the association between county-level changes in cannabis retail availability and subsequent county-level occupational injury rates in Washington State (WA), where recreational cannabis sales began in July 2014. Annual data on occupational injuries were obtained from WA Labor & Industries, consisting of workers (≥18 years old) injured from 2014 to 2019 and covered under state-funded workers' compensation. We obtained data on licensed cannabis retail outlets between 2014 and 2019 from the WA Liquor Cannabis Board and calculated the annual number of licensed outlets per 10,000 residents for each of 39 counties. Associations between county-level retail availability and injury rates were examined using one-year lagged negative binomial two-way fixed effects models, with county and year fixed effects, adjusting for time-varying county poverty and unemployment rate. Secondary analyses examined association between county changes in retail availability and injury rates among workers in various industries. We observed no association between within-county increases in cannabis retail outlets and injury rates (IRR: 1.00; 95% CI: 0.98, 1.03). When examining industry types separately, a within-county increase of 1 retail outlet per 10,000 residents was associated with an 14% (95% CI: 3%, 26%) increase in injury rates among workers in transportation and warehousing. No associations were observed for workers in professional, scientific, technical services; educational services; manufacturing; and construction. Preliminary findings suggest county-level associations of cannabis availability in WA with occupational injuries may vary by industry.

Occupational

Metabolic profiling of night shift work – The Hormonit study Anna Palomar* Barbara Harding Debra J Skene Benita Middleton Ana Espinosa Gemma Castaño-Vinyals Kyriaki Papantoniou Manolis Kogevinas Marissa Baker

Introduction

Rotating shift work is increasingly common and has been implicated in a range of adverse cardiometabolic outcomes. Mechanistic studies are needed to provide insight into how rotating night shift work may perturb metabolism.

Methods

Plasma samples were collected from 49 male, rotating shift workers from a car factory in Barcelona, Spain. Samples were collected on two work-days per worker, both at the beginning and end of a night-shift (22:00-06:00) and a day-shift (06:00-14:00). Samples (n=196) underwent targeted LC-MS metabolomics using the AbsoluteIDQ® p180 metabolomics kit (Biocrates Life Sciences AG, Innsbruck, Austria). 130 quantified metabolites were retained for analyses. Values were log2 transformed and pareto-scaled. An elastic net model was used for dimension reduction to select the most influential metabolites for inclusion in linear mixed models, which were fit to examine within-person variation in metabolite levels at night shift end (06:00) compared to the referent day shift start (06:00).

Results

Participants had a mean age of 38 (SD ±9) years. Following elastic net model selection, 20 metabolites were incorporated into mixed models including several amino acids, acylcarnitines and glycerophospholipids. Night shift was associated with changes in concentrations of arginine (geometric mean ratio [GMR] 2.30, 95%CI 1.25, 4.23), glutamine (GMR 2.22, 95%CI 1.53, 3.24), kynurenine (GMR 3.22, 95%CI 1.05, 9.87), lysoPC18:2 (GMR 1.86, 95%CI 1.11, 3.11), lysoPC20:3 (GMR 2.48, 95%CI 1.05, 5.83), PCaa34:2 (GMR 2.27, 95%CI 1.16, 4.44), and PCae38:5 (GMR 1.66, 95%CI 1.02, 2.68).

Conclusion

Night shift work was associated with higher metabolite concentrations for several metabolites, including those with roles related to cardiovascular diseases, fatigue, immune function, neurological function and cancer. These findings may provide insight into mechanistic pathways explaining associations between night shift work and many common non-communicable diseases.

Ambient air pollution and birthweight, when is the sensitive window and who is vulnerable?

Zhongzheng Niu* Zhongzheng Niu Rima Habre Thomas Chavez Mark Johnson Brendan H. Grubbs Sandrah Proctor Eckel Kiros T. Berhane Jill Johnston Genevieve Dunton Deborah Lerner Laila Al-Marayati Fred Lurmann Shohreh F. Farzan Tracy Bastain Carrie Breton

Objective: To identify sensitive exposure windows in associations of air pollution with birth weight and to explore potential effect modification by perceived stress and neighborhood burden factors.

Methods: Among 628 full-term newborns in the MADRES study, daily estimated levels of ambient particulate matters (PM_{10} and $PM_{2.5}$), nitrogen dioxide (NO_2), and ozone (O_3) at residences were assigned using spatial interpolation. Weekly averages of exposure from 12 weeks before conception to 36 gestational weeks (GW) were calculated. Associations of each air pollutant with birth weight z-score (BWZ) for gestational age and sex were estimated using distributed lag models (DLM), adjusting for maternal and meteorological factors. We stratified the analyses by maternal perceived stress in pregnancy (dichotomized at the upper quartile on the Perceived Stress Scale, PSS), and by neighborhood burden factors using the total CalEnviroScreen 4.0 score (CES, dichotomized at the CA state median).

Results: DLM identified sensitive windows for associations of $PM_{2.5}$ and PM_{10} exposures with lower BWZ, which were further modified by PSS and CES scores. For participants with high PSS scores, the sensitive windows of $PM_{2.5}$ exposure were 0-6 weeks before conception, 13-18 and 33-36 GW, and PM_{10} was associated with lower BWZ in 9-19 GW. Similar associations and exposure windows were also seen in those with high CES scores. No significant associations were found among those with low PSS or low CES scores, or with other pollutants. The longest sensitive windows and the strongest effects for associations of $PM_{2.5}$ and PM_{10} with BWZ were among those with high PSS and high CES scores (**Figure**).

Discussion: Ambient $PM_{2.5}$ and PM_{10} were associated with lower BWZ with sensitive windows primarily in mid-pregnancy. Longer sensitive windows and stronger effects were seen in those born to mothers with higher perceived stress or higher neighborhood burden, suggesting greater vulnerability.
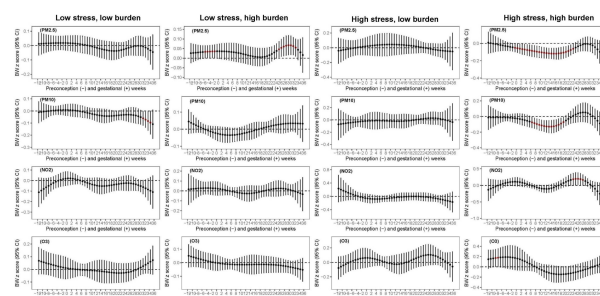
Figure. Stratification analysis by perceived stress and neighborhood burden for weekly associations of prenatal exposure to $PM_{2.5}$, PM_{10}, NO_2, and O_3 with birth weight-for-gestational age and sex z score. Panels from the left to the right show associations among 116 newborns whose mothers reported low-to-medium perceived stress and were resident in a neighborhood with a low-to-medium vulnerable-population burden, 207 newborns whose mothers reported low-to-medium perceived stress and were resident in a neighborhood with a high vulnerable-population burden, 39 newborns whose mothers reported high perceived stress and were resident in a neighborhood with a low-to-medium vulnerable-population burden, 56 newborns whose mothers reported high perceived stress and were resident in a neighborhood with a high vulnerable-population burden, respectively. Associations were adjusted for weekly temperature, maternal age, maternal pre-pregnancy body mass index, maternal ethnicity and nativity, marital status, and birth order in distributed lag models.

The effect of socioeconomic and demographic factors on racial disparities in antenatal depression diagnosis and treatment Abhismitha Ramesh* Abhismitha Ramesh Stephanie Radke Kelli Ryckman

Background: Recent data indicate that mental health treatment initiation after delivery is significantly lower for Black and Latina women compared to White women. It is evident that mental health disparities exist, but little is known about the relationships between socio-economic factors and barriers to depression care specifically during pregnancy. **Methods:** Compiled data from years 2015, 2017, and 2019 of the Iowa Prenatal Care Survey were used for analysis (n= 60,227). The main outcomes of this study include depression status, receipt of counseling for depression, and receipt of medication for depression. Exposure variables include age, education level, race/ethnicity, income level, and residence type (metropolitan, micropolitan, rural). Log-binomial regression was performed to examine the relationship between exposure variables and survey question responses. **Results:** Black, Asian, and Hispanic women were more likely to report perinatal depression diagnosis when compared to White women. These associations were attenuated when adjusting for sociodemographic factors. Depression treatment also had significant associations with race/ethnicity and residence type. Black (RR:1.29, CI: 1.18 – 1.41) and Hispanic (RR: 1.35, CI:1.24-1.46) women were more likely to report not being on medication for depression. Rural (RR: 1.10, CI:1.06-1.14) or micropolitan residents (RR:1.07, CI:1.02-1.11) were more likely to report not receiving counseling to treat their depression than metropolitan residents. **Conclusion:** This study confirms previous studies that there are higher rates of depression during and prior to pregnancy among Black, Asian, and Hispanic women; however, these associations are modified by socioeconomic status. Black and Hispanic women and those living in rural residences are less likely to receive common treatments for their reported depression. Further investigation is needed to determine the causes underlying lower utilization of treatments in these populations.

Ambient pollutants, gestational parent diet factors, and risk of preterm birth in North Carolina Kristen Rappazzo* Hanna Jardel Chantel Martin Catherine Hoyo Kristen Rappazzo

Toxicological work suggests gestational parent (GP) diet may modify the effect of ambient pollutants on birth outcomes. We assessed risk of preterm birth in humans in relation to fine particulate matter ($PM_{2.5}$), ozone (O_3), and nitrogen dioxide (NO_2) and whether associations vary by diet. Participants comprised 684 gestational parent-singleton infant pairs in the Newborn Epigenetics Study prospective birth cohort in central NC with data on GP diet, gestational age at birth, and residence at birth. Total energy intake, percent of energy intake from saturated fat, and percent of energy intake from total fat derived from a food frequency questionnaire were dichotomized at the 75th percentile. We assigned exposures from previously validated pollutant prediction models and residence at birth across trimesters. We used log binomial regressions to estimate risk ratios (RR (95%CI)) for preterm birth by pollutant interquartile ranges, including pollutant-diet interaction terms. We assessed departure from additivity using interaction contrast ratios (ICRs). The fully adjusted model controlled for age of GP at birth, pre-pregnancy body mass index, GP race/ethnicity, GP education, season of conception, household income during gestation, and each diet factor. We addressed missing covariate data with multiple imputation. Point estimates suggest that O_3 may be protective against preterm birth when exposure occurs in trimester 2 (min RR: 0.72, 95% CI: 0.34, 1.52), but may be harmful when exposure occurs in trimester 3 (max RR: 1.23, 95% CI: 0.53, 3.10). Additionally, $PM_{2.5}$ may be protective when adjusted for total fat and saturated fat in trimester 2. ICRs suggest departure from additivity (evidence of modification) with some pollutant-diet combinations. While confidence intervals are wide, we observed potential associations with preterm birth across different pollutants and time periods and potential modification of pollutant effects by dietary factors.

Child Mortality of Twins and Singletons among Late Preterm and Term Birth: A Study of National Linked Birth and Under-five Mortality Data of Korea Tammy Kim* Tammy Kim Seung-Ah Choe Young Shin Kim

Twins involve a higher risk of perinatal complications compared to singletons. We compared the risk of under-five mortality between twins and singletons among late preterm and term births. The national birth data of South Korea pertaining to the years 2010–2014 linked with the mortality record of children aged under five years in 2010–2019 was analyzed. The final study population were 2,199,632 singletons and 62,351 twins. We conducted a survival analysis of under-five mortality with adjustment for neonatal and familial factors. Overall under-five mortality rates during the study period were 3.6 and 2.0 for twins and singletons, respectively. Although the unadjusted overall under-five mortality was higher in twins (hazard ratio [HR] = 1.80, 95% confidence interval [CI]: 1.57, 2.06, overall risk), twin birth was associated with comparable or lower risk (HR = 0.70, 95% CI: 0.58, 0.85, overall; 0.70, 95% CI: 0.56, 0.87, excluding neonatal mortality; 0.59, 95% CI: 0.40, 0.86, excluding infant mortality) after controlling for both neonatal and familial factors. Twins born at a gestational age of 34–35 weeks showed a generally lower risk of under-five mortality than their singleton counterparts, regardless of model specification. Among late preterm and term birth, under-5 -year mortalities for twins were lower than singleton births when adjusted for neonatal and familial risk factors. This highlights the differential implication of gestational age at birth between twin and singleton in the child mortality.

Perinatal & Pediatric

The association between fetal sex and preeclampsia in a diverse cohort of nulliparous women Brandie DePaoli taylor* Brandie DePaoli Taylor Camillia Comeaux Ashley V. Hill Akaninyene Noah Maria J. Perez-Patron Abbey Berenson

Women with male fetuses have higher risk of pregnancy loss, preterm birth, and infant mortality. Differences in placental adaptations to maternal stressors may explain these epidemiologic findings. Interestingly, prior studies conducted in primarily non-Hispanic White and Asian populations suggest that female fetal sex is associated with preterm preeclampsia. Others have suggested that associations may vary by race and ethnicity. Our analysis included 12,689 singleton nulliparous pregnancies from an administrative database that recruits women from three urban hospitals. Women in this study are primarily on Medicaid/Chip (55.2%), are of Hispanic ethnicity (48.2%) and are married (68.2%). Outcomes included mild preeclampsia or preeclampsia with a term delivery >37 weeks, preeclampsia with severe features, and preeclampsia with preterm delivery (<37 weeks). Log-binomial regression was used to calculate relative risk (RRs) and 95% confidence intervals (CIs). Multivariable models adjusted for maternal age, race/ethnicity, marital status, and aspirin use. Relative excess risk due to interaction determine if there was an interaction between race/ethnicity and preeclampsia subtypes. Multiple imputations were used for missing data. Nulliparous women with a male fetus had higher risk of HELLP/eclampsia (RR_{adj}. 2.0, 95% CI 1.0-4.4) and preeclampsia with severe features (RR_{adj}. 1.2, 95% CI 1.0-1.4) compared to women with a female fetus. Male:female ratios displayed a male excess for all other preeclampsia subtypes (1.04-1.11). There was a significant interaction between Hispanic ethnicity and fetal sex (RERI 0.80, 0.10-1.51) for preterm preeclampsia and preeclampsia with severe features (RERI 0.90, 0.24-1.6) but not HELLP/eclampsia. In contrast to other investigations, our study found that male fetal sex was associated with severe forms of preeclampsia. This association was modified by Hispanic ethnicity. Population structure may influence the relationship between fetal sex and preeclampsia, possibly due to different underlying maternal stressors.

Prenatal Opioid Exposure and Well-Baby Care in the First 2 Years of Life – A Population-Based Study Andi Camden* Andi Camden Teresa To Joel G. Ray Tara Gomes Li Bai Astrid Guttmann

Background: Children with prenatal opioid exposure (POE) are at higher risk of health and developmental concerns, varying by type of POE. Well-baby care (WBC) is an important way to monitor development; however, the relationship between WBC and type of POE has not been examined.

Methods: This population-based cohort study comprised 22,455 infants with POE who were born in Ontario, Canada from Jan 2014-Feb 2018. We identified type of POE (<30 days analgesic, 30+ days analgesic, opioid agonist therapy [OAT], OAT + analgesic, unregulated opioid) from prescription records, maternal and newborn hospital care & outpatient visits. Outcomes included 5+ physician visits for WBC in the first 2 years of life and developmental screening at the 18-month enhanced well-baby visit (EWBV). We described WBC by type of POE and estimated aRR using modified Poisson regression comparing infants by type of POE to infants with <30 days opioid analgesic exposure, and by social, medical and healthcare factors.

Results: Overall, 56% of infants received 5+ WBC visits and 53% received developmental screening at the 18-month EWBV. Rates were highest among infants with <30 days and 30+ days of opioid analgesic exposure, respectively (5+ WBC visits: 61% & 54%; 18-month EWBV: 58% & 51%) and lowest among infants with OAT, OAT + analgesic or unregulated opioid exposure, respectively (5+ WBC visits: 35%, 35% & 37%; 18-month EWBV: 34%, 36% & 36%). Additional factors associated with being less likely to receive these care outcomes included: preterm birth, living in high deprivation neighbourhoods or rural areas, history of maternal social vulnerability or mental illness, and young maternal age at first birth (Figure). Infants with mothers with a usual primary care provider were more likely to receive 5+ WBC visits and 18-month EWBV.

Conclusions: Strategies to improve access to primary healthcare and strengthening recommendations for developmental health screening may be beneficial for children with POE.

Figure. Selected factors associated with 5+ physician visits for well-baby care in the first 2 years of life and developmental screening at the 18-month enhanced well-baby visits among infants with prenatal opioid exposure.
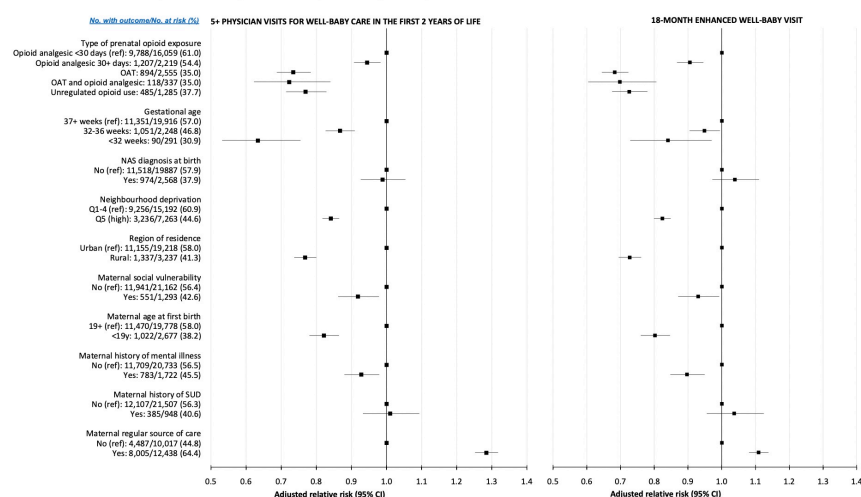
Proximity to immunization providers and vaccine series completion among children ages 0-24 months in Montana Rain E. Freeman* Rain Freeman Cindy S. Leary Jonathan M. Graham Juthika Thaker Alexandria N. Albers Bekki K. Wehner Annie Rechlin Matthew F. Daley Sophia R. Newcomer

Objective: To identify whether geographic factors, such as proximity to immunization providers, were associated with completion of early childhood vaccinations in Montana, a predominantly rural state.

Methods: Our analyses included children born in Montana between 2015-2017 with at least one vaccination record in Montana's immunization information system (IIS) after their first birthday. Using address data, we calculated distance in road miles from a child's residence to the nearest immunization provider. A multivariable log-linked binomial mixed model was used to identify factors associated with completion of the combined 7-vaccine series by age 24 months, with year of birth included as a random effect. Interactions between distance to immunization providers and rurality (using rural-urban commuting area codes) were also assessed.

Results: Among 26,085 children, 16,503 (63.3%) completed the combined 7-vaccine series by age 24 months. Distance to the nearest immunization provider ranged from 0 to 81.0 miles (median=1.7; IQR=0.8-4.1), with the majority (92.1%) of children living within 10 miles of the nearest immunization provider. Significant interaction occurred between distance to provider and rurality (p=0.02), with children living in isolated rural towns with medium (2-10 miles; adjusted prevalence ratio [aPR]=0.89; 95% CI=0.84-0.94) and long (>10 miles; aPR=0.90; 95% CI=0.85-0.96) travel distances less likely to complete the series, compared to children in urban cities/towns with short (<2 mi) travel distances. Visits to clinics with pediatric providers and lower Neighborhood Deprivation Index scores (at the census tract-level) were significantly associated with increased likelihood of series completion (p<0.05).

Discussion: Our novel analyses of state IIS data showed that while long travel distances are likely barriers to vaccination among children in isolated and small rural towns, access to pediatric providers and socioeconomic factors are also challenges.

Perinatal & Pediatric

Validity of gestational weight gain recalled up to 10 years postpartum among women in the Life-course Experiences and Pregnancy validation substudy Kriszta Farkas* Kriszta Farkas Sydney T. Johnson Lisa Bodnar Richard F. MacLehose Susan M. Mason

Pregnancy weight outcomes, including gestational weight gain (GWG), have important implications for the health of women and infants. However, many studies must rely on self-reports of GWG, which are prone to error. Using data from Life-course Experiences and Pregnancy (LEAP), a US-based pregnancy cohort linking survey- and medical record-based data on pregnancy weight outcomes, we assessed the validity of retrospectively self-reported GWG, in pregnancies occurring up to a decade prior, against data from prenatal and delivery medical records. Of 646 participants who had a singleton live birth, medical record data were abstracted for a subsample of 246 (38%), and 122 (19%) with complete survey and medical record data on GWG, gestational age, and prepregnancy body mass index (BMI) were included in the analysis. We calculated BMI- and gestational-age-specific GWG z-scores using the survey and medical record data and categorized them into low (<-1 standard deviation (SD)), moderate (-1 to 1 SD), or high (>1 SD) GWG. We calculated overall percent agreement and predictive values by self-reported GWG category, and we examined sources of error. Overall agreement between self-reported and medical record-derived GWG category was 73.8%. Predictive values varied by GWG category: 52.0%, 87.5%, and 41.2% for women classified by self-report into low, moderate, and high GWG, respectively. Misclassification of self-reported GWG category was driven by misreporting of total GWG rather than of prepregnancy BMI. Mean differences in self-reported and medical record-derived total GWG were 0.7 kg (SD: 3.4) for women correctly classified and -6.1 kg (4.3), 8.5 kg (4.5), and -1.4 kg (7.6) for women misclassified as having low, high, and moderate GWG, respectively. In comparison, prepregnancy BMI categories aligned for 81% of both women with correctly and incorrectly classified GWG category. Overall, long-term recall of total GWG is prone to misclassification, particularly at the extremes.

Testis growth and relative size from birth to 6 months in the Infant Feeding and Early Development Study Helen Chin* Thomas Amabile Helen B. Chin Andrea Kelly Walter J. Rogan David M. Umbach

Testis volume is an indicator of reproductive development in infancy, but no studies have longitudinally assessed ultrasound-measured testis size during this life stage. We used data from the Infant Feeding and Early Development study to describe infant testis growth and to assess whether individual boys maintain their relative ranking in the testis volume distribution. We followed this longitudinal cohort of 147 infant boys who had normal birthweight (2500-4500 grams) and term gestational age (37-42 weeks), after excluding those with hypospadias or cryptorchidism. We measured the testis with ultrasound at five ages from birth to 28 weeks; boys had to be observed within pre-defined intervals around each target age (e.g., ±30 days at 28 weeks). Our analysis used the average of the right and left testis volume from each study visit. We examined testis growth using smoothing splines and extracted predicted volumes for each boy at each of the 226 consecutive days spanning the maximum observation period to rank predicted volumes across boys on each day separately (range:1-147). The average testis volume trajectory exhibited monotonic growth over the study period (mean volume: 0.25 cm^3 at birth, 0.70 cm^3 at end of study). A boy's testis volume tended to stay in the same relative position with respect to other boys: across the 226 days, 61% of boys changed ranking within a range of 29 positions and 66% occupied fewer than 30 distinct rank positions (of 147 possible). These results suggest that boys who have a single small or large testis measurement have persistently small or large testis size relative to other boys across their growth trajectory. These findings add to the data on testis size in typically developing infant boys. Future directions for this work include creating a reference standard for age-specific testis size, developing a measure of the degree of within-boy tracking, and comparing these ultrasound measures to the more commonly used Prader bead method.

Epigenetic gestational age and the relationship with developmental milestones in early childhood: Upstate KIDS cohort Kristen Polinski* Kristen Polinski Sonia L Robinson Diane L Putnick Weihua Guan Jessica L Gleason Sunni L Mumford Raji Sundaram Pauline Mendola Stephanie London Edwina H. Yeung

Objective: DNA methylation clocks can estimate gestational age (DNAm GA) and deviations in observed and estimated DNAm GA may be useful markers in evaluating early childhood outcomes, such as identifying future developmental delay risk. We examined associations of measures of DNAm GA and probable developmental delay based on the Ages & Stages Questionnaire® (ASQ).
Methods: Data came from 855 singletons and one randomly selected twin of a pair whose parents completed the ASQ when their child was 4, 8, 12, 18, 24, 30 and 36 months of age. The ASQ is a validated screening instrument designed to detect whether a child has reached developmental milestones in 5 domains. We examined probable delays on specific ASQ domains as well as overall delay on any domain as outcomes of interest. Dried blood spot DNAm was profiled using the EPIC 850K BeadChip and DNAm GA was estimated using a cord blood DNAm GA clock specific to the EPIC 850K BeadChip (Haftorn 2021). In addition, gestational age acceleration (GAA) was calculated as standardized residuals from a linear regression of DNAm GA on observed GA. **Results:** Using generalized linear mixed models, each week increase in DNAm GA was protective of overall delay (OR 0.76; 95%CI 0.65-0.90) and delay in all domains except for problem solving skills after adjustment for maternal age, race, education, smoking or alcohol during pregnancy, prepregnancy BMI, plurality and child sex, i.e., fine motor (OR 0.71; 0.56-0.91), gross motor (OR 0.68; 0.53-0.89), communication (OR 0.74; 0.60-0.91), and personal-social (OR 0.75; 0.59-0.94). Associations remained in singletons (n=688) but not twins (n=167). Results were similar when restricted to term births (73%). However, no associations were observed with GAA. **Conclusion:** Longer gestational age is known to be protective of developmental delay. While DNAm estimated gestational age mirrored those known associations, GA acceleration was not associated with risk of early developmental delay.

LATEBREAKER

Perinatal & Pediatric

Perinatal health disparities between foreign-born and native-born women in Canada Melia Alcantara* Melia Alcantara Seungmi Yang Gabriel D Shapiro Tracey Bushnik

Background: Disparities in perinatal health by nativity status have been documented in various countries, whereby foreign-born mothers experience better perinatal outcomes than native-born mothers despite their lower socioeconomic positions. In this study, we updated a national study of maternal nativity with data on recent births. We examined differences in fatal and non-fatal perinatal outcomes between foreign- and Canadian-born women in a nationally representative sample of Canadian births.

Methodology: Using the 2016 Canadian Birth-Census Cohort dataset, we estimated the odds of preterm birth (PTB), small-for-gestational-age (SGA), large-for-gestational-age (LGA), stillbirth, and infant death by maternal nativity status, accounting for maternal ethnicity, education, income, and homeownership and paternal nativity, education, and employment as well as maternal age, marital status, activity limitations, and parity.

Results: A total of 129,229 singleton births were included. Foreign-born women had a higher risk of all outcomes except LGA births (RR: 0.67 (95% CI: 0.64-0.70)). The strength and direction of associations for non-fatal outcomes were consistent between nativity groups. For instance, the odds of PTB (95% CIs) for South Asian women were 1.43 (1.15-1.77) when native-born and 1.44 (1.25-1.66) when foreign-born compared to White women. Across non-fatal outcomes, South and Southeast Asian mothers consistently experienced higher odds compared to White women, regardless of nativity. For stillbirth and infant death, no associations were significant. Conclusion/Discussion: The results of this study do not support previous findings that foreign-born women experience better pregnancy outcomes than native-born women. Instead, foreign-born women consistently fared worse than native-born women, apart from LGA births. Our study suggests that disparities in perinatal health by maternal nativity in Canada may be due to factors beyond those examined in this study.

Prognostic Factors Associated with Survival in Patients Receiving Immunotherapy for First-Line Treatment of Advanced Non-Small-Cell Lung Cancer Mohsin Shah* Mohsin Shah
Sean Hennessy

Background: Novel anti-tumor agents such as programmed death or ligand-1 (PD-(L)1 pathway immune checkpoint inhibitors (ICIs) harness and modulate the immune system and improve overall survival in patients with advanced non-small-cell lung cancer (aNSCLC). However, a favorable response rate of ICIs in the first-line treatment setting is at best modest.

Objective: To assess baseline prognostic risk factors associated with overall survival in first-line ICIs alone or combination with chemotherapy in patients with aNSCLC.

Design, setting, and participants: We conducted a retrospective cohort study in the University of Pennsylvania Health System of aNSCLC patients initiating first-line ICIs alone or in combination with chemotherapy from March 4th, 2015, to August 25th, 2021. The primary outcome was overall survival, measured from the start of therapy (index date) to the date of death. Multiple imputation via chained equations with augmented regression was used to impute missing covariates. Multivariable Cox proportional hazards regression with pooled imputed data was used to estimate associations between risk factors and all-cause mortality. Patients with incomplete historical treatment data were excluded.

Results: Seven hundred and fifty-four patients met inclusion criteria. 53% of the cohort were female; median age at first-line therapy initiation was 68 years; 41% received ICI monotherapy (pembrolizumab, nivolumab, durvalumab or atezolizumab); 77% had non-squamous cell carcinoma; 89% had a history of smoking, 24% had a KRAS mutation and 5.3% had pre-existing autoimmune conditions. The median follow-up time from the index date was 10.3 months [IQR 4.7-22.4 months]. Male sex [HR 1.37; 95%CI 1.14-1.65] and higher ECOG performance status [HR 1.65; 95%CI 1.28-2.14] were associated with higher mortality, while having a higher PD1 expression (50-100%) [HR 0.63; 95% CI 0.45-0.89] and no history of smoking [HR 0.69; 95% CI 0.49-0.95] were associated with lower mortality.

Conclusions: Among aNSCLC patients receiving first-line ICIs alone or in combination with chemotherapy in routine practice, being a male and higher ECOG performance status appear to be associated with higher mortality, whereas higher PD1 expression and negative smoking history were associated with improved overall survival. Future studies are warranted to confirm these findings in a larger real-world data set.

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Potentially Inappropriate Medication utilization following Medicare Comprehensive Medication Review Ximena Oyarzun-Gonzalez* Ximena Oyarzun-Gonzalez Erin Abner Daniela Moga Anna Kucharska-Newton

Background: Medicare Part D was created including the requirement that sponsors provide Medication Therapy Management (MTM) programs to eligible beneficiaries (those with multiple chronic diseases, take multiple part D drugs, and likely to incur annual costs equal or greater than a yearly set threshold) through a Comprehensive Medication Review (CMR). One of MTM's principal aims is to prevent adverse events, such as those that may occur via the use of Potentially Inappropriate Medications (PIM).

Objectives: To evaluate the relation of CMR with mean PIMs among MTM enrollees over a 1-year period.

Methods: From a 5% random sample from Medicare Part D beneficiaries (2012–2016)(N=1,645,058), we excluded all beneficiaries with at least a month of dual eligibility (Medicare/Medicaid), those with original Medicare eligibility for any reason other than age, those not enrolled in the MTM program, and those with no PIM. Beers criteria (2015) were used to detect PIM. Incidence density sampling was applied to match MTM beneficiaries who chose to receive a CMR (n=34,901) to those who did not (n=54,378) on the time between MTM eligibility and receipt of CMR. Inverse probability treatment weighting was used to mitigate confounding, and balancing by demographics, comorbidities, and PIM at index date. Generalized estimating equations (GEE) were used to estimate the mean number of PIMs reported at 3, 6, 9, and 12 months post-index date.

Results: Beneficiaries who received a CMR were older, had fewer comorbidities, were using more medications at index date, and had more PIMs at index date and throughout the following year (Figure 1). There was no clear association between CMR receipt and change in mean PIMs, which declined in both groups.

Conclusions: These preliminary results suggest that factors associated with PIM use are not well understood. Additional studies, with longer follow-up and consideration of specific medications, are needed.

Figure 1a. Beneficiary characteristics at index (%)

	No CMR N=54,376	CMR N=34,901	p-value
Age*(Years)	74.98±6.90	76.44±6.97	<0.0001
Female	59.53	58.85	0.0435
Race			
White	90.27	89.45	0.0981
Black	6.23	6.89	
Other	3.51	3.67	
N° comorbidities*	3.65±2.91	3.33±2.85	<0.0001
N° Medications*	7.90±3.25	9.01±3.12	<0.0001
PIM	1.41±0.68	1.45±0.71	<0.0001

*Mean±SD

Figure 1b. Results of adjusted analysis for the N° of PIMs

Average Number of PIM over time
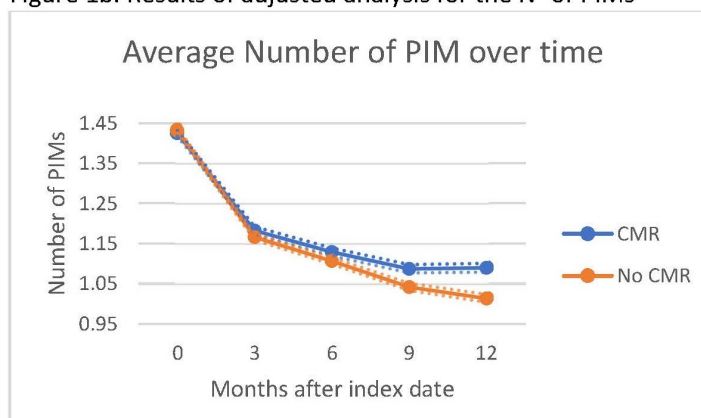
A national county-level profile of incarceration risk and unoccupied habitable housing

Nickolas Zaller* George Pro Brooke E.E. Montgomery

Introduction. Nearly 11 million individuals cycle through county jails each year and most are incarcerated for short periods (days to weeks). Many of these individuals face significant challenges transitioning from jail to their community, which are often co-located in the same county. We sought to explore the cross-sectional association between county jail incarceration rates and unoccupied habitable housing. This can inform local initiatives to make more equitable use of available housing for individuals being released from incarceration.

**Methods.** We used publicly available data to determine the jail admission rate per 100,000 county residents for 89% of US counties in 2018 (N=2,795 counties). We used the Distressed Communities Index to assess the percent of habitable housing that is unoccupied. We used linear regression to model jail admission rate (log-transformed), predicted by unoccupied habitable housing and adjusted for county-level indicators of race/ethnicity and rurality.

Results. The national average jail admission rate was 5,551 per 100,000 county residents. Unoccupied habitable housing was strongly associated county jail admissions(B=0.019, SE=0.003, p<0.0001). Nationally, 11.5% of habitable houses were unoccupied, which ranged from 2.2% (Summit County, CO) to 41.2% (Alexander County, IL). There were 420 counties that had both high rates of jail admissions and high rates of unoccupied habitable housing, and the majority of these were clustered in the US South (Figure 1).

Conclusion. Unoccupied habitable housing was positively associated with county level jail admissions, and the proportion of unoccupied habitable housing varied widely. We identified geographic clusters of counties with high rates of both jail incarceration and unoccupied habitable housing. Future research should examine how economic oppression and access to housing markets contribute to affordable housing shortages in communities with high rates of incarceration.

Figure 1
US counties demonstrating both high jail admission rates and high percentages of unoccupied habitable housing
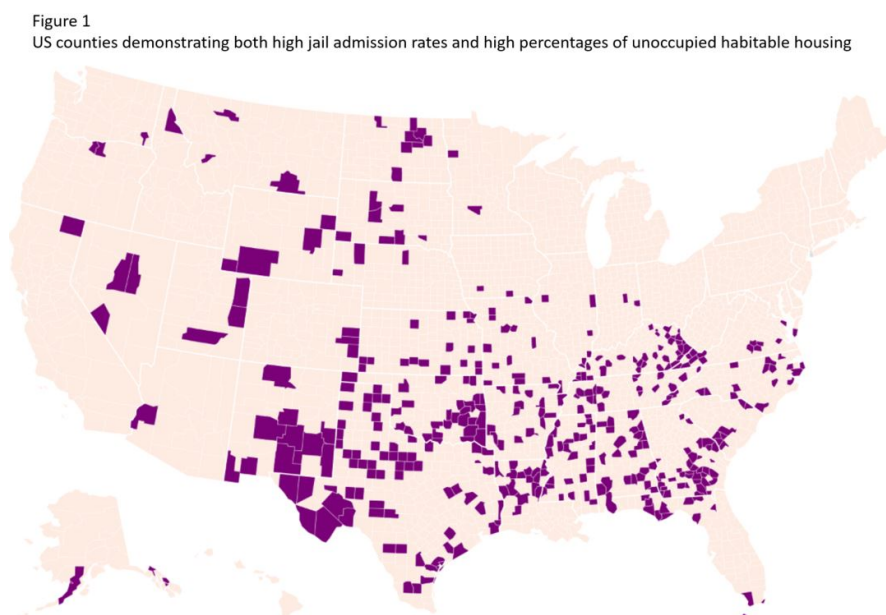
Note: High jail admission and high habitable housing were defined by counties in the upper tertile of each distribution; 240 counties

**Ovulation Tracking to Elucidate Length of Gestation and First-Trimester Growth** Ginna Doss* Ginna Doss Julie L Daniels Sunni L Mumford Charles Poole Anne Z Steiner Anne Marie Z Jukic

Background. Gestational age is approximated using observable measures like last menstrual period (LMP) and crown-rump length (CRL). Ovulation detection kits provide a more accurate estimate of the beginning of pregnancy. Our objectives were 1) to compare the proportion of births defined as preterm and postterm at delivery by LMP vs. by ovulation and 2) to present first trimester CRL growth curves when gestational age was defined by LMP vs. ovulation.

Methods. The Effects of Aspirin in Gestation and Reproduction (EAGeR) trial was a prospective time-to-pregnancy study that enrolled participants with a history of pregnancy loss. This analysis included singleton pregnancies conceived during prospective follow-up with known ovulation and LMP dates and with CRL measured at a first trimester ultrasound (n=464). Regression models for log-transformed and untransformed CRL with several functions of gestational age were fit for both ovulation and LMP-based gestational age assessment. Optimal models were selected by the highest adjusted coefficient of determination (R^2). Among participants who went on to have a live birth (n=406), we compared the proportion of births defined as preterm (<37 weeks) or postterm (>42 weeks) when gestational age was defined by ovulation or LMP. We report the weighted kappa for agreement between gestational age measures.

Results. A slightly larger proportion of births were assessed as preterm at delivery by ovulation (8.3%) than by LMP (6.9%) and as postterm by LMP (1.0%) than by ovulation (0.2%). The agreement between gestational age estimation methods was moderate, weighted kappa = 0.70 (95% CI: 0.56, 0.87). Using each method of gestation age estimation, we fit a model of first trimester growth (figure). The LMP-based model predicted smaller CRL than the ovulation-based model at later ultrasounds.

Conclusion. The comparison of LMP vs. ovulation-based gestational age at ultrasound and delivery suggest that LMP exhibits a slight tendency to overestimate gestational age relative to ovulation, potentially altering growth models. This is consistent with previous research.
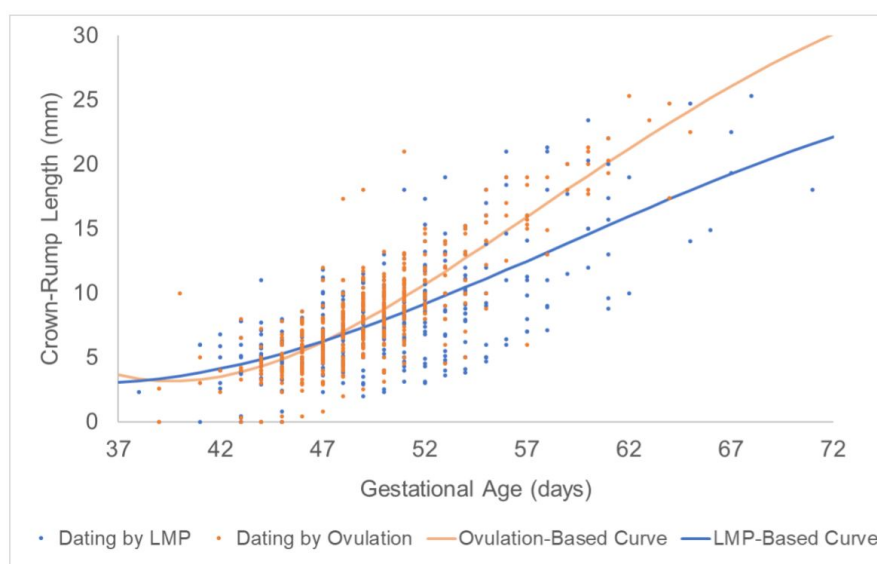
HPV vaccine and cervical cancer diagnosis, NHIS 2008-2018 Shanika Jerger Butts* Shanika Jerger Butts

Background

Human Papillomavirus (HPV) is the most common sexual transmitted disease in the United Sates with nearly 79 million people infected. The HPV vaccine was developed to prevent the infection of high-risk HPV that causes 70% of cervical cancers. Women between the ages of 35-44 years are most frequently diagnosed with cervical cancer. The vaccine is recommended for individuals ages 9-26 years, prior to the onset of sexual activity. The objective of this study is to examine the association of HPV vaccine and cervical cancer diagnosis.

Methods

Data from the National Health Interview Survey (2008-2018) were analyzed including only women older than age 18 years old. Weighted multivariate logistic regression was conducted using STATA to examine the association between HPV vaccination and cervical cancer diagnosis. Potential confounding variables investigated were age, race/ethnicity, education, insurance status, history of STD, history of cancer, alcohol consumption, smoking status and BMI.

Results

After adjustment, HPV vaccinated women had increased odds of receiving a cervical cancer diagnosis compared to unvaccinated women (OR: 1.24, 95% CI: 0.88-1.76). The odds of cervical cancer diagnosis were highest amongst women between the ages of 35-49 years old, which was statistically significant (OR: 2.17, 95% CI:1.07-4.44). Additionally, women who were uninsured also had increased odds of having cervical cancer compared to women who were insured (OR: 1.29, 95% CI: 1.09-1.51).

Conclusion

The results of this study suggests the age the HPV vaccine was administered effects the development of immunity to HPV, therefore modifies the association between HPV vaccination and cervical cancer diagnosis. Understanding the age, the HPV vaccine is administered would provide more context to future research in cervical cancer incidence.

| Table 3: Adjusted odds ratios (OR) and 95% Confidence Intervals (CI) for the association between age and cervical cancer diagnosis, 2008-2018, NHIS		
	Cervical Cancer Diagnosis	
	OR (Adjusted)	95% CI
Age		
18-34	1.29	0.81 -2.07
35-49	2.17	1.07 - 4.44
50-64	0.13	0.17 -0.96

Reproductive

Prenatal Exposure to Ambient Particle Radioactivity and Fetal Growth in Eastern Massachusetts

Veronica A. Wang* Veronica A. Wang Michael Leung Longxiang Li Anna M. Modest Michele R. Hacker Joel Schwartz Brent Coull Petros Koutrakis Stefania Papatheodorou

Background: Particle radioactivity (PR) is the radioactive component of particulate matter (PM) that mainly originates from the natural decay of PM-attached radon and has been previously associated with elevated glucose levels during pregnancy.

Method: We included 9,409 singleton pregnancies that had routine obstetric ultrasounds and delivered at Beth Israel Deaconess Medical Center in 2011-2016. Particle gross β-activity (mBq/m^3) representing PR exposure was estimated from an ensemble model and was assigned based on residential zip-code. We considered two exposure windows: first 16 weeks of pregnancy and conception until fetal growth measurement (cumulative PR). Standardized (z-score) biparietal diameter (BPD), head circumference (HC), femur length (FL), and abdominal circumference (AC) were examined on anatomic scans (<24 weeks' gestation) and growth scans (≥24 weeks' gestation), and weight was measured at birth. We used linear mixed models to examine the association of PR with fetal growth measurements and adjusted for maternal risk factors, meteorologic variables, and long-term trends. As a sensitivity analysis, we adjusted for PM ≤2.5 $\mu g/m^3$ ($PM_{2.5}$).

Results: An interquartile range (IQR) increase in cumulative PR was associated with reduced BPD (-0.06 [95% CI: -0.12, -0.01]) and FL (-0.06 [95% CI: -0.12, -0.01]) on anatomic scans and birth weight (-0.05 [95% CI: -0.11, -0.001]). While the association with AC was positive in early growth scans, it decreased with gestational age and was negative after week 35. First 16 weeks of gestation was not a critical window. Estimates were similar after controlling for $PM_{2.5}$.

Conclusion: Prenatal PR was associated with fetal growth, where the direction of the association depended on the fetal growth measure and the gestational age at measurement. Our findings are consistent with patterns previously observed among pregnancies complicated with gestational diabetes and bring awareness to a novel environmental exposure.
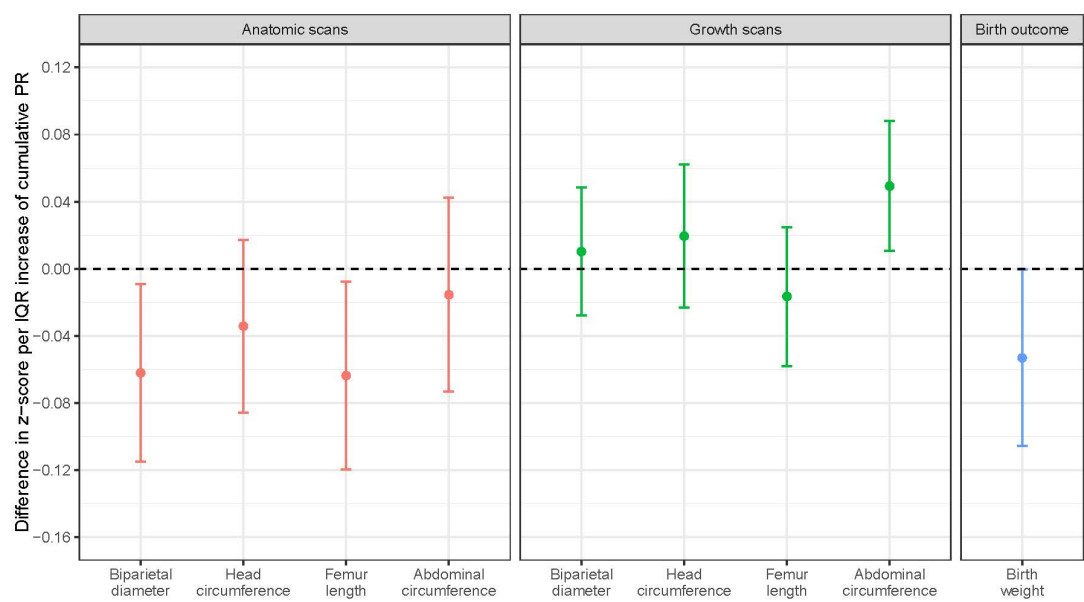
Infertility in relation to depressive symptoms and sleep deprivation among females of reproductive age in the general U.S. population Carmen Messerlian* Yu Zhang Vicente Mustiele Yi-Xin Wang Yang Sun Zainab Bibi Nicole Torres Alexandra Hillcoat Carmen Messerlian

Background

Previous research shows that women undergoing fertility treatment are more likely to report anxiety and depression. However, there are limited studies on the association between infertility and mental health in the general population setting.

Method

We included 2,973 females aged 20 to 45 years in the National Health and Nutrition Examination Survey (NHANES), 2013-2018 cycles. Infertility was self-reported as "having ever attempted to become pregnant over a period of at least a year without becoming pregnant." Depressive symptoms were measured by the Patient Health Questionnaire-2 (PHQ-2) brief screening instrument. Sleep was self-reported as the usual hours of sleep at night on weekdays or workdays. Sleep deprivation was defined as sleep ≤ 6 hours. We used multivariable logistic regressions to examine associations between infertility and depressive symptoms or sleep deprivation. Adjusted covariates included age, race/ethnicity, education, and household income to poverty ratio. We further examined effect modifications by race/ethnicity.

Results

Participants' mean age (SD) was 32.77 (7.55) years. The prevalence of infertility, depressive symptoms, and sleep deprivation was 11.87%, 9.65%, and 45.27%, respectively. Self-reported infertility was positively associated with depressive symptoms (OR: 1.54, 95% CI: 1.00, 2.37) and sleep deprivation (OR: 1.32, 95% CI:1.00, 1.75) in the study population. We found stronger associations among Non-Hispanic Blacks (OR for depressive symptoms (DOR): 1.59, 95% CI: 0.91, 2.78; OR for sleep deprivation (SOR): 1.84, 95% 0.95, 3.58) compared with associations among Non-Hispanic Whites (DOR: 1.24, 95%CI: 0.59, 2.61; SOR: 1.32, 95% CI: 0.89, 1.98).

Conclusion

In this U.S. representative study of reproductive-aged females, we found that infertility was positively associated with depressive symptoms and sleep deprivation. Causal relationships and directionality cannot be inferred due to the cross-sectional design of NHANES. Findings suggest that the general infertile population may be more vulnerable to adverse mental health with evidence of potential racial disparities.

Reproductive

Analgesic use during pregnancy and reproductive disorders in sons: Results from the Collaborative Perinatal Project Andrea A Florio* Andrea Florio Hannah B Mandle Barry I Graubard Armen A Ghazarian Jorge E Chavarro Mark A Klebanoff Katherine A McGlynn

Background: Testicular dysgenesis syndrome (TDS) is a group of male reproductive disorders that includes testicular germ cell tumors, impaired spermatogenesis, cryptorchidism, hypospadias, and inguinal hernia. TDS etiology is not well understood, though endocrine disruption, genetics, and environmental/lifestyle factors are likely mechanisms. Analgesics are commonly used in pregnancy and are associated with endocrine disruption and altered reproductive function. Prior studies of maternal analgesic drug exposure and outcomes in sons have resulted in inconsistent findings, however. Thus, the current study aimed to examine the association between maternal non-addicting analgesic drug use during pregnancy with cryptorchidism, hypospadias, and inguinal hernia among sons. **Methods**: 24,412 mother-son dyads from the Collaborative Perinatal Project, a prospective mother-child cohort, were included in the current analysis. Non-addicting analgesic exposure was categorized by frequency (none; low: 1-7 days, ≥1 month; high: >7 days, ≥1 month), trimester of use, and formulation (acetaminophen, phenacetin, aspirin). Multivariate logistic regression models were used to estimate ORs and 95%CIs and were adjusted for maternal age, body mass index, smoking, race/ethnicity, and gestational age. **Results**: High maternal analgesic exposure was associated with inguinal hernia (OR: 1.24, 95%CI: 1.07-1.44). This association persisted when examined by trimester (trimester 1 OR: 1.28, 95% CI: 1.10-1.49; trimester 2: 1.26, 95%CI: 1.09-1.46; trimester 3: 1.15, 95%CI: 1.00-1.34) and formulation (acetaminophen/phenacetin OR: 1.24, 95%CI: 1.05-1.47; aspirin: 1.26, 95%CI: 1.08-1.46). No associations were observed between analgesic use and either hypospadias or cryptorchidism. **Conclusion:** Non-addicting analgesic use during pregnancy may increase the risk of inguinal hernia in sons, regardless of trimester of use or formulation.

Neighborhood Evictions and Preterm Birth among Black Individuals Lea Ghastine* Lea Ghastine Shawnita Sealy-Jefferson Elizabeth S. McClure Catherine Hoyo Chantel L. Martin

Preterm birth (PTB), defined as delivery before 37 completed weeks of gestation, is the leading cause of infant mortality among Black infants. Evictions (involuntary displacement of occupants from a rented residence) are a key aspect of neighborhood housing instability, a neighborhood characteristic that impacts social cohesion and public health. Building upon previous findings suggesting familial distress as a potential driver of increased PTB among Black pregnant people exposed to high neighborhood eviction rates, this study explores whether the association of neighborhood evictions with PTB differs depending on the presence or absence of children in the household among 397 singleton births to Black pregnant people in the Newborn Epigenetics Study from 2009-2011. This study is based in Durham, North Carolina, which is experiencing a decades long eviction crisis that disproportionately affects Black residents. Using publicly available data, we calculated neighborhood eviction rates as evictions per 100 renter-occupied households in a census block group for the year of pregnancy. Presence of children in the household (0 or ≥ 1) was self-reported and PTB was abstracted from medical records. Logistic regression models were adjusted for maternal age at delivery, educational attainment, marital status, and neighborhood poverty. In our sample, 10% of births were preterm. A 1-SD increase in neighborhood eviction rate was associated with twice the odds of PTB among Black pregnant people with children in the household (OR=1.97, 95% CI: 1.14, 3.42). However, this association was not observed among those without children in the household (OR=0.85, 95% CI: 0.49, 1.39). These findings suggest that Black families with children are particularly vulnerable to neighborhood evictions. To reduce the disproportionate burden of PTB in Black communities, neighborhood level interventions to prevent evictions should prioritize Black families with children.

Respiratory

Exclusive, dual, and poly tobacco use is associated with the incidence of acute bronchitis among youth Luis Zavala-Arciniega* Luis Zavala-Arciniega Yanmei Xie Steven Cook Jana L Richa Douglas Arenberg Geoffrey D Barnes Rafael Meza Nancy L. Fleischer

Significance: Little is known about the health consequences of multiple tobacco product use. This study aims to evaluate prospective associations between exclusive, dual, and poly tobacco use and self-reported diagnosed bronchitis, pneumonia, or chronic cough among a nationally representative sample of US youth.

Methods: We used data (ages 12-17) from Waves 1-5 of the Population Assessment of Tobacco and Health Study (2013-19), including aged-up shadow youth and the Wave 4 replenishment sample. We categorized time-varying past 30-day tobacco use as exclusive use of 1) cigarettes, 2) electronic nicotine delivery systems (ENDS), or 3) other combustible products (OC; pipes, hookah, and cigars); dual use of 4) combustible products (cigarettes/OC) + ENDS or 5) cigarettes + OC; or 6) polyuse of all three tobacco product groups. We defined the outcome as an incident diagnosis of bronchitis, pneumonia, or chronic cough. We conducted weighted multilevel Poisson models (person n=17,546, 43,461 observations) to examine the longitudinal exposure-outcome relationship, adjusting for respondent's baseline covariates: sex, age, race/ethnicity, parental education, body mass index, secondhand smoke exposure, and household use of combustible products. We recalibrated cross-sectional sample weights into the conditional, scaled wave-specific Level-1 weights and the respondent-specific Level-2 weights to accommodate the PATH longitudinal hierarchy.

Results: About half of the sample were male and were 12 years old at baseline (due to the inclusion of aged-up youth). Compared to non-use, exclusive cigarette use (IRR=1.82, 95% CI 1.27-2.61), exclusive ENDS use (IRR=1.53, 95% CI 1.10-2.12), combustible products + ENDS dual use (IRR=1.87, 95% CI 1.19-2.95), cigarettes + OC dual use (IRR=1.90, 95% CI 1.12-3.21), and polytobacco use (IRR=2.79, 95% CI 1.54-5.05) were associated with a higher incidence of diagnosed bronchitis, pneumonia, or chronic cough.

Conclusions: We found an association between exclusive, dual, and polyuse and the incidence of acute bronchitis, pneumonia, or chronic cough among youth, this association was stronger for polyuse of tobacco products. These findings provide evidence that ENDS use among youth is associated with negative acute respiratory health outcomes.

Multilevel models predicting incidence of self-reported bronchitis, pneumonia and chronic cough among youth respondents (12-17), Population Assessment of Tobacco & Health Study (Wave 1-5, 2013-19) (n=17,546 persons, 43,461 observations)

|	Unadjusted			Adjusted		
	IRR	95% CI	p-value	IRR	95% CI	p-value
Time-varying poly tobacco use variable						
Non use	REF			REF		
Exclusive cigarette use	2.51	1.91	3.31	0.000	1.82	1.27	2.61	0.001
Exclusive e-cigarette use	1.62	1.17	2.23	0.000	1.53	1.10	2.12	0.011
Exclusive other combustible use	1.44	0.73	2.78	0.287	1.32	0.68	2.47	0.411
Dual use of cigarettes + ENDS/ Dual use of ENDS + OC	2.18	1.45	3.61	0.000	1.87	1.19	2.95	0.007
Dual use of cigarettes + other combustibles	2.51	1.59	3.91	0.000	1.90	1.12	3.21	0.017
Poly use of cigarettes+ ENDS + OC	3.91	2.92	6.44	0.000	2.79	1.54	5.05	0.001
Sociodemographic risk factors						
Age						
12	REF			REF		
13	1.01	0.84	1.21	0.944	0.59	0.84	1.19	0.937
14	1.15	0.96	1.41	0.144	1.11	0.91	1.35	0.314
15	1.33	1.11	1.66	0.003	1.29	1.05	1.58	0.017
16	1.60	1.28	1.88	0.000	1.37	0.99	1.64	0.058
17	1.98	0.73	4.80	0.174	1.79	0.72	4.96	0.215
Sex						
Male	REF			REF		
Female	1.07	0.94	1.23	0.299	1.10	0.96	1.39	0.160
Race/ethnicity						
NH White	REF			REF		
NH Black	0.75	0.60	0.93	0.100	0.74	0.60	0.95	0.009
Hispanic	0.68	0.58	0.81	0.000	0.71	0.60	0.85	0.000
NH Other	0.75	0.59	0.99	0.016	0.76	0.60	0.96	0.021
Parental education						
Less than high school	REF			REF		
High school	0.98	0.78	1.23	0.495	0.96	0.73	1.19	0.417
Some college	1.15	0.09	1.55	0.000	1.20	0.96	1.91	0.109
Bachelor's degree or higher	1.04	0.84	1.28	0.734	1.08	0.86	1.35	0.511
Baseline risk factors						
Second hand smoke exposure (30 hours)	1.10	1.06	1.15	0.000	1.06	1.02	1.09	0.003
Household use of combustible products						
No	REF			REF		
Yes	1.34	1.15	1.54	0.000	1.14	0.98	1.33	0.088
BMI - obesity						
Normal/underweigh	REF			REF		
Overweight	1.29	1.08	1.54	0.006	1.30	1.09	1.55	0.003
Obese	1.73	1.47	2.04	0.000	1.74	1.51	2.10	0.000

COPD-OSA overlap syndrome and leukocyte telomere length: the Korean Genome and Epidemiology Study Soriul Kim* Soriul Kim Inkyung Baik Chol Shin

Background: Chronic obstructive pulmonary disease (COPD) and obstructive sleep apnea (OSA) are both commonly prevalent, and thus the comorbidity of both disorders, often referred to as the overlap syndrome, had significantly greater amounts of hypoxemia and hypercapnia as well as increased mortality and cardiovascular risk than individuals with COPD or OSA alone. The aim of this study is to examine the association of COPD-OSA overlap syndrome with leukocyte telomere length, as one of the molecular mechanisms explaining cellular aging.

Methods: A total of 1795 participants of the Korean Genome and Epidemiology Study, who underwent both in-home polysomnography and leukocyte telomere length (at Exam6 [2013-2014] and about 6 years later [Exam9, 2019-2020]), were longitudinal analyzed. Participants were divided into six groups based on the presence of COPD and severity of OSA: no OSA (apnea-hypopnea index [AHI] <5), mild OSA (5≤ AHI <15), and moderate-severe OSA (AHI ≥15). We analyzed the association between the leukocyte telomere length and the overlap syndrome groups using the multivariate linear regression models.

Results: Based on linear regression model adjusting age, sex, BMI, smoking, alcohol consumption, hypertension, and diabetes, moderate-severe OSA with COPD was associated with greater telomere length decline over the prior 6 years than no OSA without COPD (β: -0.181, 95% CI: -0.342, -0.020). However, mild/moderate-severe OSA or COPD alone were not significantly associated with telomere length decline.

Conclusions: Individuals with COPD-OSA overlap syndrome had greater leukocyte telomere attrition than OSA or COPD alone. These findings suggest that severity of OSA with COPD are associated with accelerated biological aging.
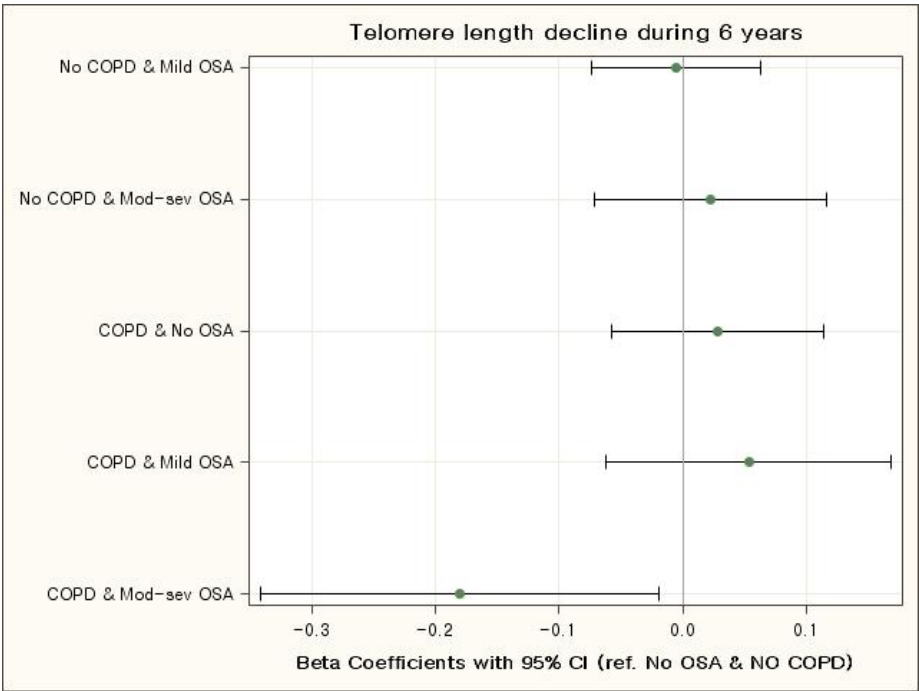
Screening

Screening test of health state for the young-adults at risk in susceptibility phase based on the natural history of diseases Hideo Yamazaki* Hideo Yamazaki Soichi Sakabe Xiao Qing Minako Danbara Hikaru Yamazaki Noriko Miyake

Introduction: Health promotion has been proposed as "the process of enabling people to increase control over their health and its determinants, and thereby improve their health" by the World Health Organization (WHO). In practical community health and public health nursing activities based on health promotion, a primary prevention is one of the most effective ways to prevent lifestyle-related diseases (LSRDs). In general, although the young-adults have a very low incidence rate in LSRDs, the cumulative exposure to behavioral disadvantage across stages of life may be strongly associated with predispose LSRDs. However, an appraisal way for health conditions in a susceptibility phase based on the natural history of diseases has not been established yet. The purpose of the present study was to examine the validity of a screening test of health state at risk in susceptibility phase on the natural history of diseases among the young-adults.
Methods: A self-report questionnaire consisted of 54 items was administered to the young-adults in Japan between 2016 and 2019. As analyzed data without defect values, 3,874 samples derived from university students. A principal component analysis (PCA) was applied to valid data.
Results: The PCA was applied to the sample in order to extract a semihealth index meant one's poor health condition in the susceptibility phase. Then the index score was calculated by the norm eigenvectors of the first principal component. Furthermore, a distribution of the young-adults with the semihealth condition was determined by using this score. As a result, the prevalence, sensitivity, specificity, positive predictive value, negative predictive value, and false positive rate showed 20.8%, 81.7%, 81.5%, 53.8%, 94.4% and 0.19, respectively.
Conclusions: Based on epidemiological indices, this method has shown to be useful for evaluating the semihealth state for the young-adults from a light of health promotion practice.

An Investigation of the Relationship between Income Inequality and Alcohol Consumption among Adolescents in Canada Sammy Lowe* Sammy Lowe Sujan Basnet Roman Pabayo

Objectives: To explore the association between census tract-level income inequality (CTII) and alcohol consumption among adolescents both cross-sectionally and over time.

Methods: This study utilized data from the Cannabis use, Obesity, Mental health, Physical health, Alcohol use, Smoking, and Sedentary behaviour (COMPASS) study of Canadian adolescents in junior and senior high school. 139,295 students captured in the 2016, 2017, and 2018 waves of the COMPASS study were analyzed cross-sectionally, while a subset of 19,759 students with case complete data at baseline were followed up from 2016 to 2020. Alcohol consumption was assessed as three distinct outcomes, including answering "yes" to having ever consumed alcohol, engaging in weekly binge drinking, and engaging in daily binge drinking. Multilevel logistic regression modelling was used in both cross-sectional and longitudinal analyses to quantify the relationships between CTII and adolescent alcohol consumption outcomes, adjusting for individual and area-level covariates.
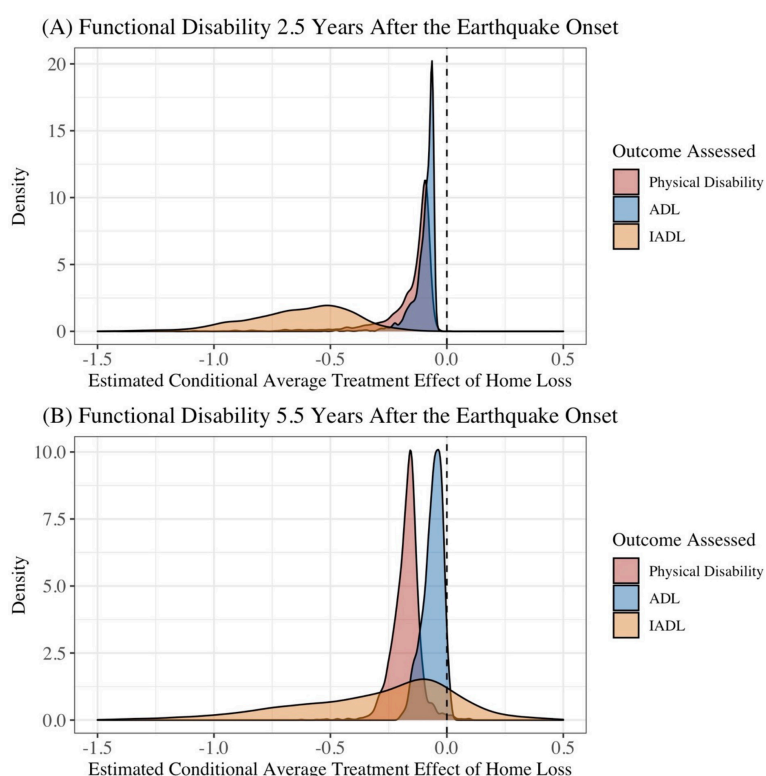
Results: For the cross-sectional analyses, CTII was significantly associated with daily binge drinking, indicating that adolescents had a 17% (OR=1.17, 95%CI=1.01, 1.35) increased odds of binge drinking daily for every one standard deviation increase in CTII. Unexpectedly, CTII was also significantly protective for overall alcohol consumption, with adolescents having a 19% (OR=0.81, 95%CI=0.74, 0.89) decreased odds of having ever consumed alcohol. There was no significant association between CTII and weekly binge drinking (OR=1.05, 95%CI=0.92, 1.19). When analyzed longitudinally, there was no evidence for a significant association between CTII and having ever consumed alcohol (OR=0.92, 95%CI=0.80, 1.06), weekly binge drinking (OR=1.13, 95%CI=0.90, 1.41), or daily binge drinking (OR=1.09, 95%CI=0.82, 1.45).

Conclusion: This study provides some evidence that alcohol consumption among adolescents is impacted by the level of income inequality of where they live. Future studies are needed to further clarify these associations and to help mitigate the adverse impacts of income inequality on population health.

Uncovering heterogeneous associations between disaster-related trauma and subsequent functional limitations: a machine-learning approach Koichiro Shiba* Koichiro Shiba Adel Daoud Hiroyuki Hikichi Aki Yazawa Jun Aida Katsunori Kondo Ichiro Kawachi

This study examined heterogeneity in the association between disaster-related home loss and functional limitations of older adults and identified characteristics of vulnerable sub-populations. Data were from a prospective cohort study of Japanese older survivors of the 2011 Japan Earthquake. Complete home loss was objectively assessed. Outcomes in 2013 (n=3,350) and 2016 (n=2,664) included certified physical disability levels, self-reported Activities of Daily, and Instrumental Activities of Daily Living. We estimated population average associations between home loss and functional limitations via targeted maximum likelihood estimation with SuperLearning and its heterogeneity via the generalized random forest algorithm. We adjusted for survivors' 55 characteristics from the baseline survey conducted seven months before the disaster. While home loss was consistently associated with increased functional limitations on average, there was strong evidence of effect heterogeneity for all functional limitations outcomes. Comparing the most and least vulnerable groups (top 10% versus bottom 10% of the distribution of the estimated effect), the most vulnerable group tended to be older, not married, living alone, and not working, with pre-existing health problems before the disaster. Individuals who were less educated but had higher income also appeared vulnerable. Our inductive approach for effect heterogeneity using machine learning algorithm uncovered large and complex heterogeneity in post-disaster functional limitations among Japanese older survivors.

(A) Functional Disability 2.5 Years After the Earthquake Onset

(B) Functional Disability 5.5 Years After the Earthquake Onset

Social

State-level unemployment and negative emotions throughout the COVID-19 pandemic in the United States Daniel Hagen* Daniel Hagen Alden Lai Emily Goldmann

Background:

The COVID-19 pandemic in the United States has been associated with the highest levels of unemployment since the Great Depression. Despite pre-pandemic research suggesting that unemployment is a key risk factor for poor mental health, this association has received little attention since pandemic onset.

Methods:

We obtained repeated cross-sectional respondent data for 52,879 members of the nationally representative Gallup Panel interviewed through Gallup's COVID-19 web survey, which was conducted daily from March to August 2020 and then monthly, and state-level unemployment data for each month from the Bureau of Labor Statistics. We used separate mixed-effects modified Poisson regression models to examine the association between state-level unemployment and the self-reported experience of 7 negative emotions during "a lot" of the previous day: sadness, worry, stress, anger, loneliness, depression, and anxiety, both overall and stratified by employment group, between April 2020 and July 2021. Adjusting models for individual-level covariates, average daily COVID-19 incidence, and state median income, we repeated analyses separately for April/May 2020 and June 2020 to July 2021 to account for emotional adaptation and policies to promote economic recovery.

Results:

Between June 2020 and July 2021, state-level unemployment was positively associated with increased prevalence of all negative emotions except depression in the overall sample ($p<0.01$); prevalence ratios (PR) for a 10% increase in unemployment ranged from 1.16 (stress) to 1.98 (anger) and were greatest among full-time employed, part-time employed, and retired respondents. In contrast, associations were either slightly negative (PR=0.90 to 0.95) or not significant at $p<0.05$ in April/May 2020.

Conclusion:

Area-level unemployment became a key determinant of mental well-being after the first wave of COVID-19 in the U.S., which may reflect growing concerns about long-term economic consequences of the pandemic.

Dead labor: classed, gendered, and racialized mortality inequities in the United States Jerzy Eisenberg-Guyot* Jerzy Eisenberg-Guyot Seth J. Prins

Introduction: Epidemiologic studies have seldom used relational social class measures based on control over productive property (i.e., capital) and others' labor when analyzing mortality inequities. Because such factors structure societal distributions of health-promoting resources and hazardous working conditions, this represents a substantial knowledge gap, which our study addresses. **Methods**: We used nationally representative data on respondents ages 25-64 to the 1986-2014 U.S. National Health Interview Survey with mortality follow-up until 2015 (n=841,624). First, we classified respondents' social class as worker, manager, petit bourgeois (PB), capitalist, or not in the labor force (NILF) based on their business ownership, managerial authority, and employment status. Next, using Cox models, we estimated class inequities in all-cause mortality. We also examined class-year, class-race, and class-gender interaction. Sensitivity analyses (in progress) will examine cause-specific mortality and subdivide workers and managers based on their authority, autonomy, and expertise. **Results**: We identified considerable class inequities (Figure 1), with the greatest mortality for workers and NILFs, which are the largest classes across races and genders and disproportionately consist of people of color (POC) and women. For example, relative to capitalists, the hazard ratios (HR) for workers and NILFs were 1.37 (95% CI: 1.31, 1.44) and 2.41 (95% CI: 2.30, 2.53), respectively; PBs also had an elevated HR (HR: 1.29, 95% CI: 1.23, 1.36). Inequities increased over time. For example, in 1986, the HR among workers relative to capitalists was 1.29 (95% CI: 1.21, 1.38); in 2014, the HR was 1.72 (95% CI: 1.38, 2.16). Inequities were similar within genders and races, although most POC classes had greater HRs than white workers. **Discussion**: We estimated considerable mortality inequities across classes, genders, and races, inequities that are increasing and that threaten population health.
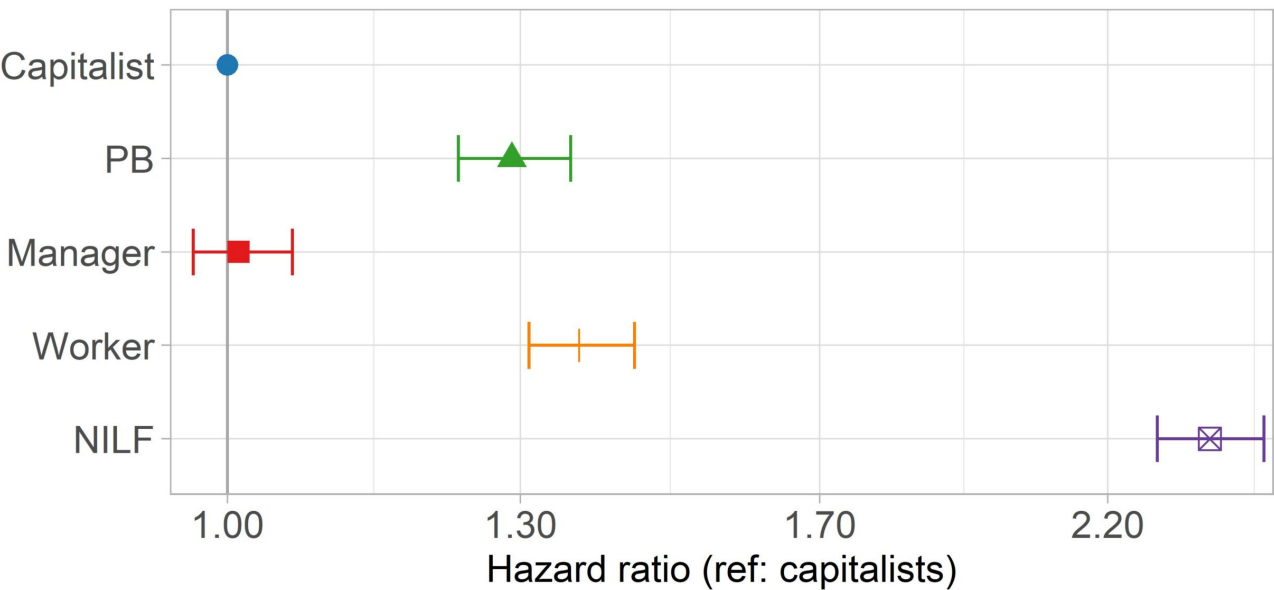

FIGURE 1. Mortality hazard for each class relative to the hazard for capitalists among 1986-2014 NHIS respondents ages 25-64 with f/u through 2015. NOTES: HRs from survey-weighted Cox models adjusted for gender, age, and year, with SEs calculated via Taylor series linearization.
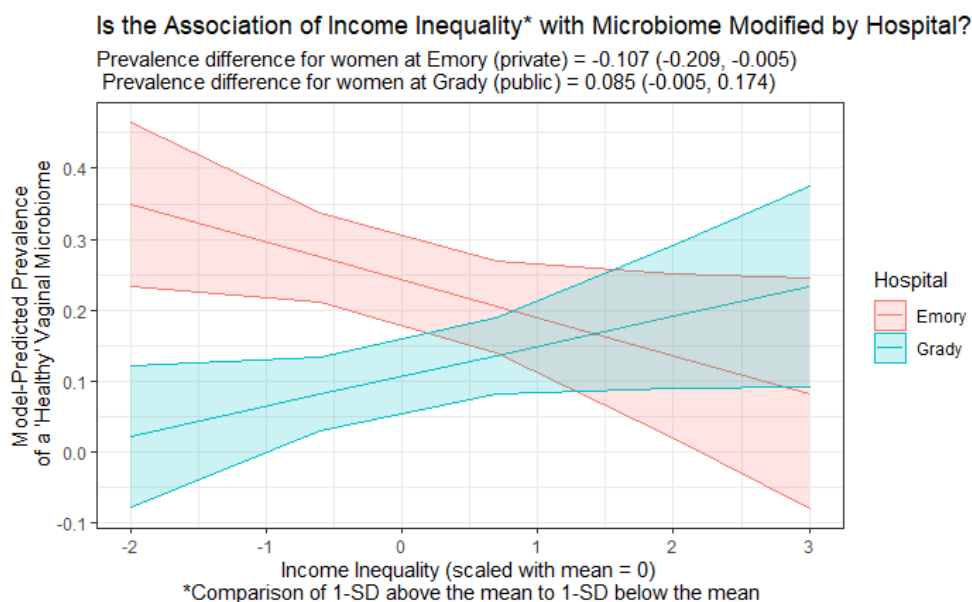
Does individual socioeconomic status modify the association between neighborhood context and vaginal microbiome composition? Meredith Dixon* Meredith Dixon Anne L. Dunlop Michael Kramer

Background: The vaginal microbiome is a dynamic ecosystem that is important for women's health. The composition of the vaginal microbiome, commonly conceptualized by community state type (CST) assignment, has been linked to risk for menopausal symptoms, sexually transmitted infections, gynecologic cancer, and preterm birth. Conventional risk factors for a vaginal microbiome linked with these health outcomes include sexual behaviors, hygiene practices, and individual socioeconomic status (SES). However, research on individual factors and vaginal microbiome has typically ignored the role of neighborhood context.

Methods: Socioeconomically diverse pregnant African American women in Atlanta, Georgia (n=436) provided residential addresses and first trimester vaginal swab samples, which underwent sequencing, taxonomic classification, and assignment into mutually exclusive CST. Linear probability models were used to estimate prevalence differences (PD) for the associations of neighborhood factors with vaginal microbiome CST and evaluate for effect modification by maternal level of education, health insurance, and recruitment hospital.

Results: Factors such as higher (vs. lower) maternal education, private (vs. public) insurance, and private (vs. public) hospital were associated with higher prevalence of healthy CST. Individual SES measures modified the relationship between CST and these community factors: census response rate, income inequality, and racial inequality. For women at a private hospital, neighborhood income inequality was associated with decreased prevalence of healthy CST (PD: -0.107, 95%CI: -0.209, -0.005); whereas, for women at a public hospital, neighborhood income inequality was associated with increased prevalence of healthy CST (PD: 0.085, 95%CI: -0.005, 0.174).

Conclusion: The association of certain community factors, such as income inequality and racial inequality, with the composition of the vaginal microbiome depends on individual SES indicators.

Is the Association of Income Inequality* with Microbiome Modified by Hospital?
Prevalence difference for women at Emory (private) = -0.107 (-0.209, -0.005)
Prevalence difference for women at Grady (public) = 0.085 (-0.005, 0.174)

Do school quality, spending per student, and class size modify gains in cognitive ability from education? Rebecca Stebbins* Rebecca Stebbins Stuart Ritchie

While research has consistently shown that education contributes to gains in cognitive ability, studies thus far have focused on narrow definitions of education: years in school or degree attained. However, evidence suggests that many other dimensions of education, including school quality, class size, or parental support, etc. can affect how much an individual benefits from their education. This issue is a violation of the consistency assumption—a central assumptions required for causal inference. By not considering quality domains, researchers have not defined the exposure to include all the causally relevant features. Therefore, research that investigates more nuances of education and their isolated impacts on cognitive ability is necessary to fully understand how education benefits cognitive ability. The objective of this project is to quantify how much the quality of mandatory education contributes to cognitive ability gains by considering as exposures multiple domains of educational quality. Using four waves of data on ~15,000 participants from the Millennium Cohort Study (MCS) and ~4000 in Growing Up in Scotland (GUS), two longitudinal birth cohorts of children born 2000-2002 and 2004-2005 respectively, we will use longitudinal g-computation to estimate the causal effects of average class size, spending per student, and Ofsted score (a measure of the overall effectiveness of a school) on individual cognitive ability at ages 14 and 17 while accounting for the time-varying nature of both the exposure and baseline/follow-up cognitive measures. **Figure 1** depicts a timeline of the cognitive measures collected in MCS and GUS from ages 5 through 17 and used in our analysis. We will include the following variables as confounding factors, determined to be a minimally-sufficient adjustment set via DAG analysis: race/ethnicity, sex, age, childhood SES, parental education, and baseline cognitive ability. This project is in progress and results are forthcoming.
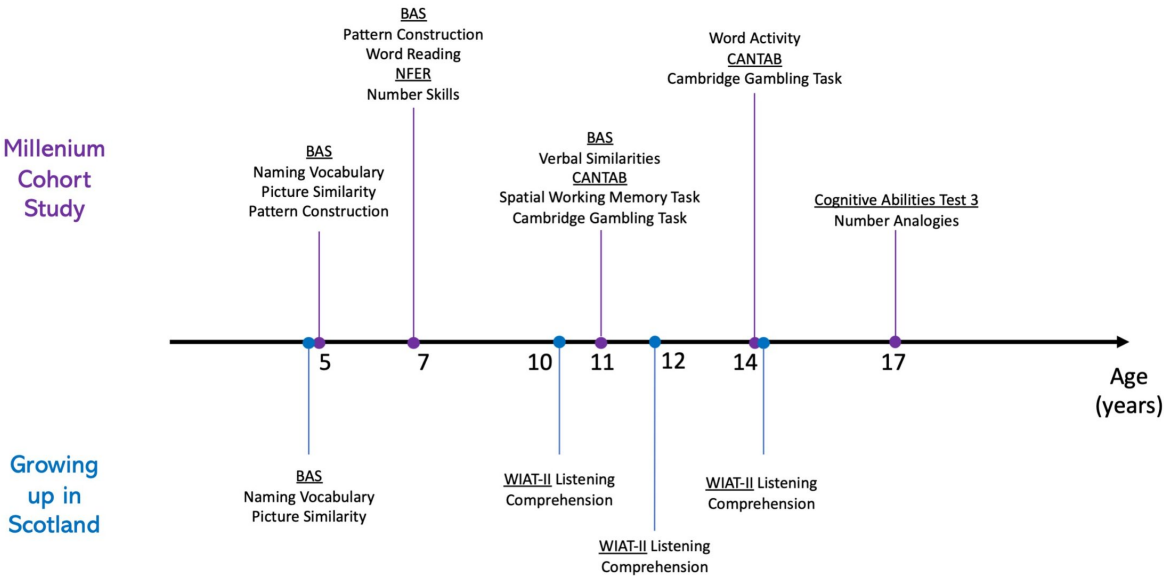

Figure 1. Cognitive Measures in the MCS and GUS by Age of Participant. BAS = British Abilities Scale; NFER = National Foundation for Educational Research; CANTAB = Cambridge Neuropsychological Test Automated Battery; WIAT = Wechsler Individual Achievement Test

Using Mobile Methods to Assess Time-varying Home and Neighborhood Environmental Exposures Related to Adolescent Sleep Stephanie Mayne* Stephanie Mayne Chloe Hannan Gabrielle DiFiore Uchenna Nwokeji Vicky Tam Tyler Martin Jonathan Mitchell Eugenia South Karen Glanz Alexander Fiks

Background: Growing evidence suggests home and neighborhood environmental exposures may influence adolescent sleep. Few studies have assessed these relationships using methods that account for time-varying exposures or multiple neighborhood contexts. We pilot tested the use of smartphone GPS tracking and ecological momentary assessment (EMA) to assess daily home and neighborhood exposures hypothesized to impact adolescent sleep.

Methods: A convenience sample of teens aged 15-17 years in Philadelphia completed 7 days of data collection. Smartphone GPS tracking was used to identify geocoded environmental exposures to neighborhood crime, litter, noise, and green space by linking teens' daily activity paths to geographic data from existing sources (e.g. crime records, Table). Daily EMA surveys assessed home sleep disruptors (e.g. noise, light). Sleep duration was assessed using actigraphy. We assessed feasibility by examining the number of days with valid GPS data and percentage of EMA surveys completed, and acceptability using Likert-scaled questions. We examined mean levels and variation in daily neighborhood exposures using descriptive statistics and linear mixed effects models.

Results: 25 teens (mean age 16, 56% male, 24% with household income <$50,000) participated. 159 days of GPS observation were available (median across teens: 7 days, range 0-7) and 78% of EMA surveys were completed (median across teens: 86%, range 29-100%). 96% of participants reported no privacy concerns due to GPS tracking and minimal burden due to EMA surveys. Mean sleep duration was 7.4 hours. 52% of teens reported ≥1 hypothesized home sleep disruptor (most common: uncomfortable temperature). Daily activity path-based neighborhood exposures varied (Table).

Conclusions: Results demonstrate the feasibility and acceptability of using mobile methods to assess time-varying home and neighborhood exposures relevant to adolescent sleep. Future work with larger samples is needed to examine associations.

Table. Daily Activity Path-Based Neighborhood Exposures of Adolescent Participants (n=25)

Daily activity path exposure[1] to neighborhood:	Definition/Unit (Directionality)	Mean (95% CI) across teens[2]	Range
Crime	Count of 2020 block-level crimes (higher = more crimes)	98.3 (66.8, 129.8)	4 – 537
Litter index	Quantity of litter on the block as assessed by trained raters; possible range 1-4 (higher = more litter)	1.8 (1.7, 2.0)	1.3 – 2.5
Percent parks	Block-level park coverage, percentage (higher = more parks)	13.7 (10.2, 17.1)	0.0 – 80.9
Percent tree canopy	Block-level tree canopy cover, percentage (higher = more trees)	15.3 (11.4, 19.2)	2.2 – 50.2
Noise	Block-level mean 24 hr A-weighted Leq sound level[2] (in decibels) from aviation, road, rail noise (higher = more noise)	51.4 (50.4, 52.4)	45.1 – 60.0

[1]Neighborhood exposures were calculated by overlaying each teen's GPS points on layers of geospatial data (aggregated at the block level, defined as 660ft radius) and calculating that teen's average value for each day for each neighborhood measure. Means and 95% confidence intervals were estimated using linear mixed effects models with participant random intercepts to account for clustering of days within teens.
[2]This reflects the average sound level in decibels, adjusted to reflect the sensitivity of the human ear.

Psychosocial Experiences Related to the 2019-2020 Protests In Lebanon Martine Elbejjani*
Martine Elbejjani Lynn Al Radi Sarah Badin Richard Dagher Tassnim Elhalabi Racha Ghoussaini
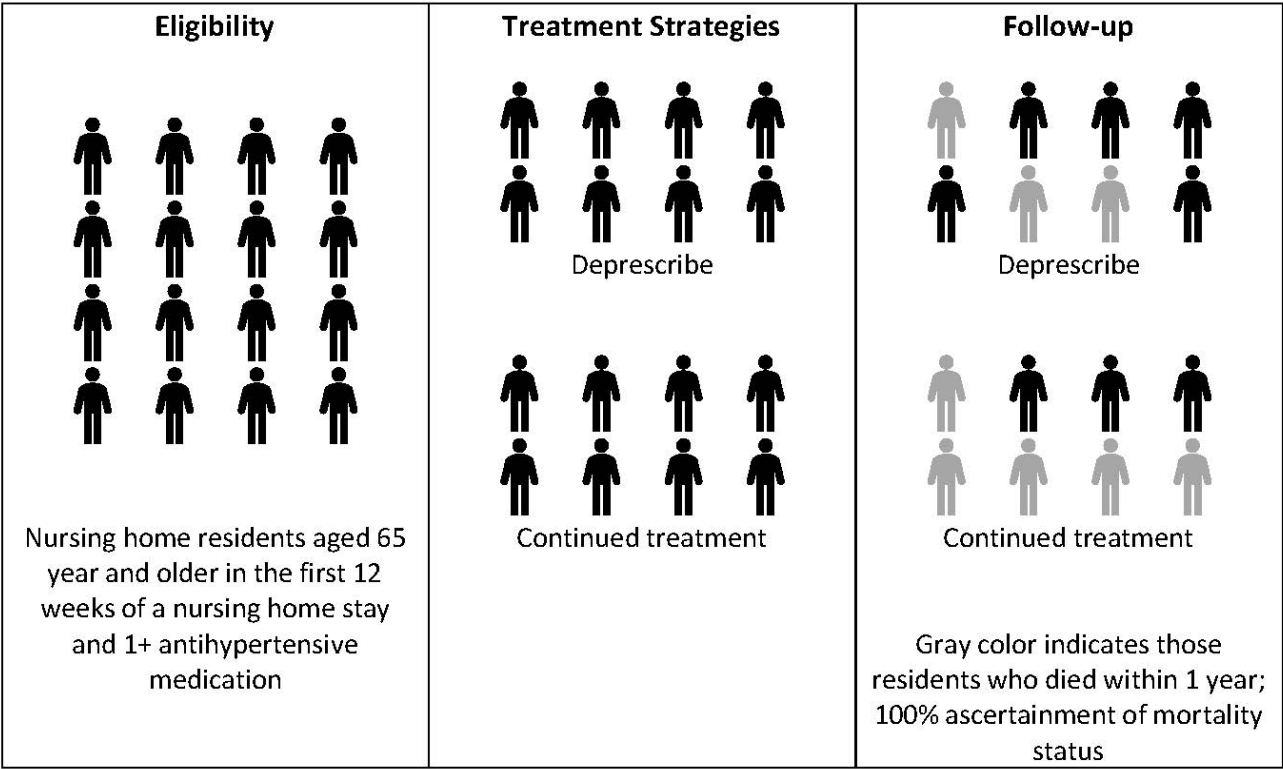Alice Recho Serge Yaacoub

Social movements have been growing globally in response to varying inciting factors, including racial discrimination and economic and political turmoil, and are expected to increase in the context of climate change and social struggles. While social and health aspects of collective events such as natural disasters or terrorist attacks have been studied, data on protests are limited. We studied characteristics of a nation-wide protest movement that began in Lebanon in October 2019 due to political and economic unrest. We assessed extent and form of direct and indirect participation, exposure to incidences of violence, changes in daily life, and affective perceptions related to the protests (International Positive and Negative Affect Schedule Short Form), via an online survey distributed to a random sample of students, staff, faculty, and alumni of the American University of Beirut, and on social media platforms (≥18y and residing in Lebanon in the 5 months (Oct-Feb) of regular protests).

Among respondents (n=794, mean age=32.2±13.6), 67% participated in the protests. Younger age (not gender or socioeconomic factors) was related to participation. Among protest participants, 81% experienced violent events (the most frequent were conflicts with the authorities and tear gas). Non-participants also reported witnessing violent events (>70%) in media coverage. Participation and non-participation were related to higher positive (mean difference=4.0, 95%CI=3.4, 4.6) and negative affective scores (1.9, 95%CI=1.2, 2.5) respectively. Protest participants and non-participants reported large disruptions in daily functioning (56%) and added socioeconomic (28%), interpersonal (25%), health (20%), and mental health (39%) difficulties; both groups also reported higher social engagement (51%) and cohesion (63%). Results show that exposure to violence was significant and that protests were highly emotionally experienced, and advocate for research on these large-scale collective events.

Target Trial Emulation for Medication Deprescribing: Recommendations and the Example of Antihypertensives Michelle Odden* Michelle Odden Xiaojuan Liu Yongmei Li Chintan Dave Bocheng Jing Kathy Fung Laura Graham

Deprescribing is the planned and supervised process of dose reduction or discontinuation of potentially harmful or ineffective drugs. Despite a growing interest in deprescribing in geriatric medicine, there is a paucity of evidence to guide practice. Target trial emulation based on electronic health records presents a viable alternative in the setting of limited trial data; however, this approach has been applied primarily in a new-user setting for medication initiation. First, we present methodologic recommendations for emulating a deprescribing trial using counterfactual theory. Second, we illustrate the implementation using the example of antihypertensive medication deprescribing on mortality in nursing home residents. Protocol components parallel those of a new-user design and include eligibility criteria, treatment strategies, assignment procedures, follow-up period, outcome ascertainment, and analysis plan. We recommend special consideration of eligibility criteria and treatment strategies in the setting of deprescribing. An important consideration is the indication for deprescribing which can be (i) therapeutic (no longer of benefit), (ii) in response to harm (such as an adverse event), or (iii) palliative (patient is near end of life). In our study, we are interested in therapeutic deprescribing and deprescribing in response to harm, thus we limited our eligibility criteria to include residents in the first 12 weeks of their nursing home stay and those who had at least a 6-month life expectancy. We define the treatment as a reduction in the number of medications or a 30% or greater reduction in the dose of a medication, sustained for a 2-week period. The comparison treatment strategy is continued treatment. In approximately 30,000 eligible nursing home residents, 30% were deprescribed antihypertensive medication. We will present the estimate of effects of deprescribing on mortality under varying assumptions.

Eligibility	Treatment Strategies	Follow-up
Nursing home residents aged 65 year and older in the first 12 weeks of a nursing home stay and 1+ antihypertensive medication	Deprescribe / Continued treatment	Deprescribe / Continued treatment / Gray color indicates those residents who died within 1 year; 100% ascertainment of mortality status

Study Design

Seeing the invisible: A novel study design in reproductive epidemiology. Marc Weisskopf*
Marc Weisskopf Michael Leung Sebastian Rowland Raanan Raz Brent Coull Ander Wilson Marianthi-Anna Kioumourtzoglou

When all events of an outcome cannot be counted, it may be impossible to identify risk factors associated with the outcome due to small numbers, or bias may be introduced if the events missed are non-random. An example is pregnancy loss because many of these events never come to medical attention, and some may not even be recognized by the mother. This greatly limits the research that can be done into risk factors for pregnancy loss. The few studies that have examined pregnancy loss as an outcome have relied on either a) medically-identified losses, which as a subset of all pregnancy losses is limited and could introduce unknown biases, or b) enrolling and tracking women intensively around conception (i.e., a preconception cohort), which are generally small and may not be representative.

We present a new study design to analyze exposure-pregnancy loss associations that considers all pregnancy losses, even those that go unrecognized by the medical community and even the mother. This approach relies on live birth records, which are generally much more widely available. This novel approach involves resorting live births by their estimated conception date, and then takes advantage of the fact that the total number of conceptions (TC) in a given period of time is the sum of live births that result from those conceptions (live birth-identified conceptions; LBIC) and those that are lost (pregnancy losses; PL). Put in simple mathematical terms, for a given period, e.g., week, TC = LBIC + PL.

Thus, for any risk factor that does not affect total conceptions, e.g. post-conception exposures, associations with total pregnancy loss can be inferred from associations with LBIC, which are identifiable.

Here we describe this novel, inferred-effects approach, its implementation, and assumptions required for causal inference. This new approach could be a powerful method to study effects on events that have to date been hidden to epidemiologists.

Substance Use and Firearm Access Among College Freshmen Bita Khoshhal* Bita Khoshhal
Samantha Karon Matthew E. Rossheim Lawrence J. Cheskin Pamela J. Trangenstein Cara L.
Frankenfeld Niloofar Ramezani Alison E. Cuellar

Background: Adult firearm owners in the United States have greater likelihood of recent binge
drinking, which is a known risk factor for violent behavior. Previous research documents high
alcohol and marijuana use rates among college students in the country, posing risks for violence and
other injuries to the users and surrounding community. However, less is known about college
students' access to firearms and associated substance use.

Objective: To examine rapid access to a firearm and associations with recent alcohol and marijuana
use among college students.

Methods: Cross-sectional data from first-year college students aged 18 to 24 (n=183) were obtained
from the spring 2019 wave of the *Mason: Health Starts Here* cohort study at George Mason
University in Virginia. A dichotomous measure was created for rapid access to a gun to distinguish
individuals who could get and shoot a gun within 15-minutes versus those who could not.
Multivariable logistic regression models evaluated rapid access to a firearm in relation to binge
drinking (≥ 4 drinks for females and ≥ 5 for males per occasion, past 30 days), marijuana use (any,
past 30 days), age, sex, and race.

Results: 10.3% of students could rapidly access a firearm, 53% of whom were current binge
drinkers, compared to 13% of those who could not rapidly access firearms. Non-Hispanic White
students (OR=4.1, 95%CI=1.3,12.7) and binge drinkers (OR=6.4, 95%CI=2.1,19.7) had significantly
greater odds of having rapid firearm access. Age, sex, and marijuana use, however, were not
significantly associated with rapid access to a firearm.

Conclusion: Despite being limited to a single college campus, our results indicate a notable
proportion of students with rapid access to a firearm and a strong association with binge drinking,
suggesting that similar surveillance data is needed for developing better campus policies and
prevention programs to address firearm safety, potential firearm violence and alcohol use behaviors.

Substance Use

Opioid agonist treatment as prevention against assisting others in initiating injection drug use: A longitudinal cohort study of people who inject drugs in Vancouver, Canada Zachary Bouck* Zachary Bouck Andrea C. Tricco Laura C. Rosella Matthew P. Fox Robert W. Platt M-J Milloy Kora DeBeck Kanna Hayashi Dan Werb

We conducted a longitudinal cohort study of 201 people who inject drugs (PWID) with suspected opioid use disorder from Vancouver, Canada to evaluate whether oral opioid agonist treatment (OAT) reduces the likelihood that PWID help others initiate injection drug use. Data were collected by questionnaire at semi-annual visits between December 2014–November 2017. At each visit, we assessed whether participants were currently on OAT (defined as present enrollment in methadone or buprenorphine/naloxone treatment) and had recently provided injection initiation assistance (defined as helping someone inject for the first time in the past six months). Additionally, we measured several baseline-fixed (age and gender) and time-varying covariates (history of providing injection initiation assistance, recent homelessness, recent incarceration, recent non-fatal overdose, and recent frequency of injection drug use). We estimated the average treatment effect of current OAT at a given visit on the provision of injection initiation assistance in the following six months—expressed as a relative risk (RR) with 95% confidence interval (CI)—using a repeated measures log-binomial generalized estimating equations model with inverse-probability-of-treatment-and-censoring (IPTC) weights to account for confounding and informative censoring by measured covariates. At baseline, participants were 45 years old on median (interquartile range=33–50), 67.2% were men, and 86.0% injected opioids in the past six months. Recent provision of injection initiation assistance was uncommonly reported irrespective of visit (range, 0.8%–8.5%). Based on the IPTC-weighted estimate, PWID currently on OAT were 81% less likely to provide injection initiation assistance in the following six months (RR: 0.19, 95% CI: 0.04, 0.85) versus PWID not currently on any medication for opioid use disorder. In conclusion, OAT may greatly reduce the likelihood that PWID with opioid use disorder facilitate first-time injections.

Substance Use

Association of marijuana/hashish and periodontal disease, NHANES 2009-2012 Ruchi Bhandari* R. Constance Ruchi Bhandari Nilanjana Dwibedi Chan Shen Patricia Findley Christopher Waters Usha Sambamoorthi

Introduction: To determine the interaction of smoking and marijuana/hashish use on periodontal health.

Methods: A cross-sectional design was used with National Health and Nutrition Examination Survey 2009-2012 datasets, the most recent datasets with available data. Participants were ages 30-59 years, with complete periodontal, cigarette smoking, and marijuana/hashish use data (n=4,193). Presence of periodontal disease was defined as at least 2 interproximal (IP) sites with attachment loss of ≥3mm and ≥2 IP sites with probing depths of ≥ 4mm which are not on the same tooth or ≥1 site with a probing depth of ≥5mm. Marijuana/hashish and smoking were self-reported Dose was calculated by the number of joints used per day times the number of years of use. Analyses included Chi-square and logistic regressions on periodontal disease.

Results: 42.5% of participants reported never using marijuana/hashish; 10.3% used marijuana/hashish within the previous month; 13.8% used within the previous year. There were 20.5% who smoked cigarettes;.39.8% had periodontal disease. In bivariate analysis, smoking and using marijuana/hashish were both risk factors for periodontal disease. In the adjusted logistic regression model on periodontal disease, there were higher odds for the combination of smoking and > 5 joint-years of marijuana/hashish (AOR= 2.58 (95% CI: 1.36, 4.87) and for smoking and ≤5 joint-years of marijuana/hashish (AOR: 2.85; 95% CI: 1.77, 4.61) as compared with non-smoking and >5 joint-years of marijuana/hashish use. Never/former smokers with nonuse of marijuana/hashish were not significantly different from the reference group, non-smoking and > 5 joint-years of marijuana/hashish use (AOR: 0.93; 95%CI: 0.62, 1.39).

Conclusion: Results indicate that marijuana/hashish use was initially significantly associated with periodontal disease in bivariate analysis, the effect was attenuated when smoking was considered.
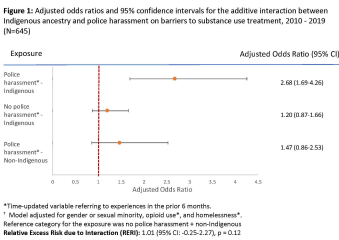
Violence, policing, and systemic racism as barriers to substance use treatment amongst marginalized women who use drugs: Findings of a community-based cohort study in Vancouver, Canada (2010-2019)

Shira Goldenberg* Shira Goldenberg Chelsey Perry-Ens Sarah Watt Brittany Bingham Melissa Braschel Kate Shannon

Background: Despite a high prevalence of substance use among women sex workers (SWs), rigorous epidemiologic data on the social epidemiology of substance use and treatment experiences among SWs remains limited. Given these research gaps and the disproportionate burden of criminalization borne by Indigenous SWs, we evaluated substance use treatment barriers and the interaction between policing and Indigenous ancestry on treatment barriers in a cohort of women SWs in Vancouver, Canada.

Methods: Baseline and follow-up data were from a prospective, community-based open cohort of women SWs (2010-2019). Bivariate and multivariable logistic regression with generalized estimating equations (GEE) modeled correlates of experiencing recent substance use treatment barriers. We developed a multivariable GEE confounder model to estimate the additive interaction between policing and Indigenous ancestry on treatment barriers.

Results: Amongst 645 SWs who used drugs (4342 observations), 32.1% reported being unable to access substance use treatment during the study period (354 events). In multivariable GEE analysis, participants who identified as a sexual or gender minority (AOR:1.91, 95% CI:1.38-2.65), used opioids (AOR:1.45, 95% CI: 1.09-1.94), were homeless (AOR: 1.69; 95%CI:1.31-2.19), and experienced police harassment (AOR: 1.48, 95%CI:1.02-2.16), and workplace (AOR:1.70, 95%CI: 1.22-2.36) or gender-based violence (AOR:2.09, 95%CI:1.49-2.95) faced higher odds of treatment barriers. In interaction analysis, Indigenous SWs who experienced police harassment faced the highest odds of treatment barriers, compared to non-Indigenous SWs who did not experience police harassment (Fig 1).

Conclusion: Findings suggest a need to scale-up culturally-safe and trauma-informed addictions, gender-based violence, and sex worker services, alongside urgently needed dismantling of systemic racism against Indigenous women across and beyond health and addictions services.

Figure 1: Adjusted odds ratios and 95% confidence intervals for the additive interaction between Indigenous ancestry and police harassment on barriers to substance use treatment, 2010 - 2019 (N=645)

Substance Use

Prevalence and Self-Reported Effectiveness of Alcohol in Treating Pain Among a Sample of Women with HIV Christina Parisi* Christina Parisi Hannah Gracy Robert L. Cook Natalie Chichetto

Background: Chronic pain and hazardous alcohol use are common among people with HIV (PWH) and are associated with negative health outcomes. It is unclear how drinking with intent to treat pain impacts alcohol use in this population. We aimed to 1) describe the proportion of people with chronic pain and their reported use of alcohol to treat pain in a sample of women with HIV (WWH) and 2) compare alcohol use patterns and problems among WWH who drink to treat pain to those who do not.

Methods: Cross-sectional data were from WWH with hazardous drinking (>7 drinks per week). The Brief Pain Inventory measured past-week chronic pain (0=no pain, 1-4=mild, 5-6=moderate, 7-10=severe). The AUDIT measured hazardous alcohol use. Use of alcohol to treat pain (yes/no) and perceived relief of alcohol to treat pain (0=no relief to 10=complete relief) were self-reported. The Short Inventory of Problems (SIP) identified alcohol-related problems. Group statistical comparisons were analyzed in SAS 9.4.

Results: Of 194 WWH (83% Non-Hispanic Black, mean age 48.3±8.7), 82 (42%) reported chronic pain. Among WWH with chronic pain, using alcohol to treat pain was common (70%) and 86% of those using alcohol to treat pain reported moderate or significant relief. There were no significant differences in AUDIT scores between WWH who drank to treat pain and those who did not (18.9 vs 14.9, p=0.242). However, WWH who drank to treat pain had a higher average SIP score (14.8 vs 11.6, p=0.047).

Conclusion: Over 40% of WWH with hazardous drinking reported chronic pain. Use of alcohol to treat chronic pain was prevalent with a high report of perceived relief. SIP scores were higher in WWH who drank to relieve pain although AUDIT scores were not different. Drinking with intent to treat pain may be a significant motivator to drink, especially among WWH. Future research will examine if self-medication to treat pain with alcohol influences long-term health outcomes and intervention success to reduce drinking.

Substance Use

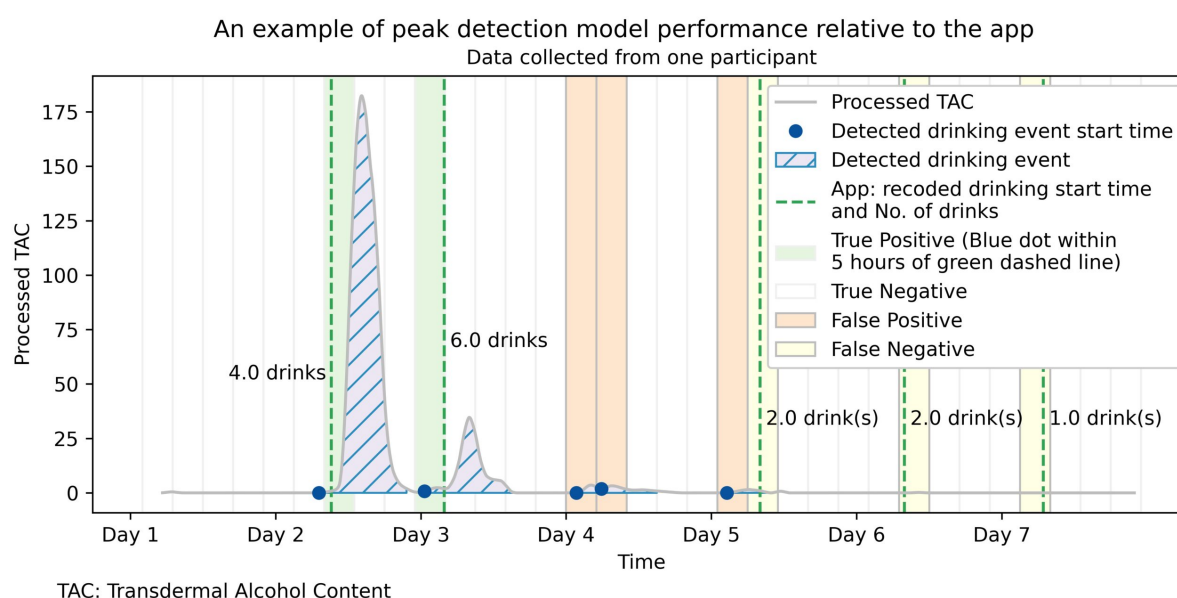## Development and validation of a model for measuring alcohol consumption from transdermal alcohol content data among college students Sina Kianersi* Sina Kianersi Christina Ludema Jon Agley Yong-Yeol Ahn Maria Parker Sophie Ideker Molly Rosenberg

Aim-Transdermal alcohol content (TAC) data collected by wearable alcohol monitors could potentially contribute to alcohol research, but data currently suffer from poor usability. We aimed to develop and validate a model that used TAC data to detect alcohol drinking event start times and number of standard drinks consumed.

Methods-In Spring 2021, we enrolled 84 college students to: 1) complete a baseline survey, 2) wear BACtrack Skyn monitors in their naturalistic drinking environments for 7 days, 3) record drinking start times in real-time for each of their standard drinks using an app, and 4) complete daily surveys. We used signal filtering, peak detection algorithm, linear regression, and hyperparameter optimization to develop a model. The predictor was unadjusted TAC and outcomes were drinking event start time and number of consumed standard drinks. We validated the model using daily surveys (internal validation) and data collected from 5 college students in 2019 (external validation).

Results-On the app, participants recorded 206 drinking events. Monitors collected 10,915 hours of TAC data. In internal validation, the model had a sensitivity of 73% (95% CI: 67%-79%) and a specificity of 67% (95% CI: 61%-72%) in detecting drinking events. The median absolute time difference between self-reported and model detected drinking start times was 66 minutes. Mean absolute error (MAE) for the reported and detected number of drinks was 3.3 drinks. In external validation, number of drinking events, sensitivity, specificity, median time difference, and MAE were 15, 67%, 78%, 65 minutes, and 1.6 drinks, respectively.

Conclusion-We developed and validated a model for detecting drinking event start times and drinking magnitude. Poor specificity in internal/external validation was potentially due to the inability of daily surveys to capture more than one drinking event start time in a day. Future research should consider using and modifying this model with their own alcohol data.

An example of peak detection model performance relative to the app
Data collected from one participant

TAC: Transdermal Alcohol Content

**The Association of Naloxone Co-Prescribing Mandates with Concurrent Naloxone Receipt in Patients with Cancer** Tarlise Townsend* Tarlise Townsend Spruha Joshi Magdalena Cerdá Corey Davis Fumiko Chino Amy S. B. Bohnert

Cancer patients and survivors experience high rates of pain. Opioids are a mainstay of pain management and can increase respiratory suppression risk. Co-prescribing the reversal agent naloxone can mitigate fatal overdose risk. In 2017-2018, four states (AZ, RI, VA, VT) mandated naloxone co-prescribing with opioids under high-risk conditions, e.g., high-dose opioids or concurrent opioids/benzodiazepines. Laws requiring prescribers to reference prescription drug monitoring programs (PDMPs) before prescribing opioids may also increase naloxone co-prescribing.

Using 2015-2018 Optum commercial claims data and staggered difference-in-difference models, we estimate the association between a) PDMP query mandates and b) naloxone co-prescribing mandates (NCMs) on naloxone fills among patients with any cancer-related diagnosis code in a given month.

Naloxone was dispensed within 7 days of only 0.15% of all opioid fills. Patients with documented past-year overdose or opioid use disorder were more likely to obtain it, but in no subgroup did the percentage of opioid fills with concurrent naloxone exceed 1%. PDMP query mandates were associated with a 42% increase in concurrent naloxone receipt (adjusted predicted means, no mandate: 0.09% of opioid fills, 95% CI: 0.08-0.10%; mandate: 0.13%, 95% CI: 0.11-0.15%). NCMs were associated with a 126% increase in naloxone filled with mandate-triggering opioids (adjusted predicted means, no mandate: 0.08% of triggering opioid fills, 95% CI: 0.08-0.09%; mandate: 0.19%, 95% CI: 0.13-0.25%). Still, rates remained very low. Results were robust to sensitivity analyses.

Low concurrent naloxone receipt likely reflects both low prescribing rates and patient-side barriers, e.g., stigma, cost, and pharmacy naloxone availability. PDMP query mandates and NCMs have been only minimally successful at improving low rates of naloxone access among this higher-risk group, raising concerns about whether clinicians are ensuring opioid safety in people with cancer.

Substance Use
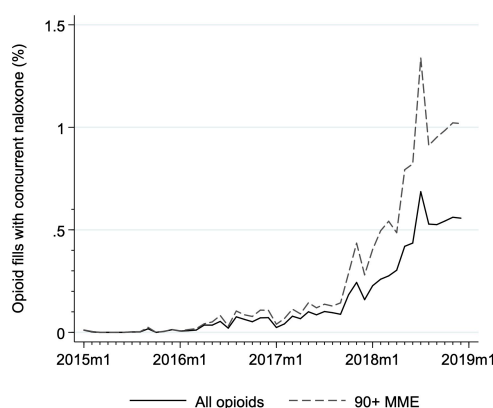
Expert consensus on the most beneficial and harmful opioid laws: A modified Delphi process Katherine Wheeler-Martin* Katherine Wheeler-Martin Leah Hamilton Corey S. Davis Silvia S. Martins Magdalena Cerdá

Evaluation of the United States opioid policy landscape is complex, as states have enacted numerous laws to address the opioid epidemic, often at the same time, and with widely varying provisions. To complement data modeling approaches, we conducted a modified Delphi process to assess expert opinions on the most impactful opioid laws and provisions, and the extent to which impacts were harmful or beneficial. This iterative consultation included a preliminary focus group (n=12) and two survey rounds (n=56, n=40) with experts representing all regions of the United States in the areas of policy research, clinical practice, criminal justice, advocacy, and public health. On a scale of 0 (very harmful) to 4 (very helpful), Good Samaritan laws received the highest average rating (3.62, 95% CI: 3.48-3.75), followed by naloxone access laws (3.37, 95% CI: 3.22-3.51), and pain management clinic laws (3.08, 95% CI: 2.89-3.26). Prescribing limits (2.83, 95%CI: 2.66-2.99), Medicaid coverage of medication for opioid use disorder (MOUD) (2.72, 95% CI: 2.55-2.89), prescription drug monitoring program (PDMP) laws (2.60, 95% CI: 2.44-2.77), and methadone laws (2.15, 95% CI: 1.91-2.38) averaged neutral ratings to somewhat helpful ratings, while drug-induced homicide laws were rated harmful to very harmful on average (0.88, 95% CI: 0.66-1.11). Impact ratings from 0 (no impact) to 4 (very impactful) aligned similarly, although Medicaid laws received the second highest overall impact rating. There were notable cases of divergent ratings within laws; Medicaid coverage of all forms of MOUD was rated the second most helpful provision (3.89, 95% CI: 3.82, 3.97) while Medicaid prior authorization for MOUD was rated the second most harmful provision overall (1.00, 95% CI: 0.72, 1.72). We are currently developing a state-by-state scorecard based on these expert ratings, which we will validate in regression models for opioid prescribing and opioid overdose mortality outcomes.

Substance Use

Drug treatment and crime: analysis of a population of 85,048 drug treatment patients between 2010 and 2019 in Chile Alvaro Castillo-Carniglia* Alvaro Castillo-Carniglia Andres Gonzalez-Santa Cruz Mariel Mateo

Background: Substance use can affect health and multiple social dimensions, including criminal behaviors and the likelihood of contacting the criminal justice system. Drug treatment is one possible intervention to reduce the risk of committing a crime, transiting through the judicial system, and being incarcerated. In this preliminary report, we estimated the prevalence of criminal offenses, by type of offense and result of the judicial process, among patients in drug treatment during 2010-2019 in Chile.

Methods: We used a registered-based retrospective cohort design of the population of people of 18+ years of age in publicly-funded treatments. We linked patient's information to National prosecutor's data of all criminal causes registered for this population in this period. Since the prosecutor's data was obtained in December 2021, we only reported descriptive results, aiming to estimate transition probabilities (i.e., multiple treatments and entries to the criminal justice system) and drug treatment effects on crime.

Results: There were 109,756 treatment episodes from 85,048 individuals during 2010 and 2019; 22% of treatments resulted in a therapeutic discharge. There were 324,858 criminal processes involving 74% of the patients. Of these, 52.4% were charged with a violent crime, 11.2% with a drug-related crime, and 91.8% for other charges (people can have multiple criminal charges). Thirty-seven percent of criminal charges resulted in full or partial (e.g., night) incarceration. Patients that completed their first treatment had, on average, 1.8 fewer criminal charges (0.3 for violent crimes) than those who did not complete their treatment; incarceration resulted in 30% of the times vs. 39%, respectively.

Conclusions: A large percentage of people in drug treatment have passed before, during, or after their treatment through the criminal justice system. People who complete their treatment have fewer criminal processes and a lower prevalence of incarceration.
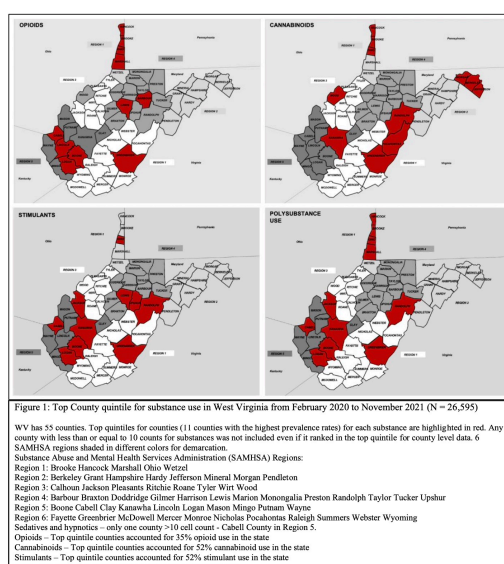
Substance Use

Patterns of substance use during pregnancy in West Virginia Amna Umer* Amna Umer
Christa Lilly Candice Lefeber Janine Breyel Collin John

Introduction: There is paucity of data on the types of substances and polysubstance used during pregnancy. West Virginia (WV) has one of the highest prevalence of substance use during pregnancy. The aim of the study was to examine the prevalence of substance(s) used during pregnancy in the state.

Method: The study used WV population level birth data from Project WATCH (February 2020 to November 2021). Prevalence of substance use was calculated for no substance used, opioids, cannabinoids, sedatives/hypnotics, stimulants, and polysubstance use (PSU). Highest prevalence of individual substances by SAMHSA regions (6 regions for WV) were identified. WV has 55 counties and top quintiles for counties (11 counties with the highest prevalence rates) for each substance was identified.

Results: There were 32,973 women who gave birth in the state of WV during the time period. Among all women, 12.44% used substances during pregnancy (one substance n = 3403, 10.32% and PSU n = 698, 2.12%). Among the 698 PSU cases, nearly a third were 'opioid and cannabis' (29.23%), 25.21% 'opioid and stimulants', and 19.63% 'cannabis and stimulants' use. 'Opioid, cannabis, and stimulants' were the highest category in 3-substances used (13.04%). Nearly 2% women (n = 14) used all 4 substances. The breakdown of individual substances used during pregnancy included cannabinoids (8%), opioids (4.5%), stimulants (2.1%) and sedatives/hypnotics (0.4%). SAMHSA region 1 had the highest prevalence of opioids (7.91%), cannabinoids (13.74%), and sedatives/hypnotics (0.9%) use and SAMHSA region 5 had the highest prevalence of stimulants (3.3%) use. Highest prevalence rates by counties (top quintile) for each substance are shown in Figure 1.

Conclusion: Types of substance use varied widely across the state among pregnant women who gave birth in WV. Data driven policies and interventions are needed to focus on regions and counties with the highest prevalence of substance and PSU during pregnancy.

Figure 1: Top County quintile for substance use in West Virginia from February 2020 to November 2021 (N = 26,595)

WV has 55 counties. Top quintiles for counties (11 counties with the highest prevalence rates) for each substance are highlighted in red. Any county with less than or equal to 10 counts for substances was not included even if it ranked in the top quintile for county level data. 6 SAMHSA regions shaded in different colors for demarcation.
Substance Abuse and Mental Health Services Administration (SAMHSA) Regions:
Region 1: Brooke Hancock Marshall Ohio Wetzel
Region 2: Berkeley Grant Hampshire Hardy Jefferson Mineral Morgan Pendleton
Region 3: Calhoun Jackson Pleasants Ritchie Roane Tyler Wirt Wood
Region 4: Barbour Braxton Doddridge Gilmer Harrison Lewis Marion Monongalia Preston Randolph Taylor Tucker Upshur
Region 5: Boone Cabell Clay Kanawha Lincoln Logan Mason Mingo Putnam Wayne
Region 6: Fayette Greenbrier McDowell Mercer Monroe Nicholas Pocahontas Raleigh Summers Webster Wyoming
Sedatives and hypnotics – only one county >10 cell count - Cabell County in Region 5.
Opioids – Top quintile counties accounted for 35% opioid use in the state
Cannabinoids – Top quintile counties accounted for 52% cannabinoid use in the state
Stimulants – Top quintile counties accounted for 52% stimulant use in the state
PSU – Top quintile counties accounted for 54% PSU in the state

Tick and tick-borne disease knowledge across frontline groups: a knowledge, attitudes, and practices meta-comparison Rebecca Smith* Rebecca Smith Lee Ann Lyons Samantha Crist Dawn Carson Nohra Mateus-Pinilla

Prevention of tick bites and tick-borne diseases (TBDs) is reliant on individual-level protection measures, such as use of repellants and frequent tick checks in high-risk areas. However, these require knowledge of local spatiotemporal risk, awareness of basic prevention measures, and concern sufficient to implement protection measures. Since 2018, we have conducted Knowledge, Attitudes, and Practices surveys within multiple populations for which ticks and TBDs are a concern in the state of Illinois, USA. These populations include employees of local public health departments (n=42), veterinary professionals (n=72), and medical professionals (n>300, closing in January 2022). We will compare knowledge scores, subscores and TBD concern levels among these different populations, and compare their responses to existing tick presence and abundance and TBD prevalence data at the county and regional level. For instance, veterinarians had a higher average tick knowledge score (49%) than public health officials (34%), but among veterinarians this score varied significantly by time since last training. These findings can serve as the basis of a One Health approach to tick prevention outreach and training for those at the front lines of TBD prevention.

Women's Health

Development and validation of predictive models of gestational diabetes mellitus and its onset Yi Zheng* Yi Zheng Hui Hu

Background: Gestational diabetes mellitus (GDM) affects a large proportion of pregnancies and contributes to both short- and long-term adverse health outcomes among women and their offspring. Previous studies have shown substantial under-reporting of GDM in the birth records data, a common administrative data source widely used to study GDM. More importantly, women with early-onset GDM (i.e., diagnosed <24 gestation weeks) have distinct maternal characteristics and a higher risk of worse health outcomes compared with those with late-onset GDM (i.e., diagnosed ≥24 gestation weeks). However, there is no information on the onset of GDM in birth records data. Real-world data such as electronic health records (EHR) can be used to accurately assess GDM and its onset, while the rich maternal, paternal, and infant information in the birth records data may be used to mitigate the measurement errors in GDM and determine the onset of GDM. **Methods:** Leveraging the statewide linked EHR-birth records data in Florida between 2012-2017, we trained several conceptually different machine learning models to determine GDM and its onset, using rich information from the birth records data as predictors, based on the "gold-standard" measures derived from the EHR. **Results:** A total of 193,677 pregnant women and 26,628 pregnant women with GDM were included to develop predictive models of GDM and early-onset GDM, respectively, with 145 predictors used. CatBoost had the best performance in classifying both GDM (AUC= 0.821, 95% CI: 0.817, 0.825) and early-onset GDM (AUC= 0.717, 95% CI: 0.705, 0.729). **Conclusions:** We successfully improved GDM measurements and enabled determinations of GDM onset in the birth records data, using machine learning algorithms, by leveraging the statewide EHR-birth records data. The models can be applied to the statewide birth records data and scaled up for future studies on GDM and its onset.

Women's Health

Hormonal Intrauterine Device Use and Incident Fibroids in the Study of Environment, Lifestyle, and Fibroids Mekhala Dissanayake* Mekhala Dissanayake Quaker Harmon Donna Baird

Background: Uterine fibroids, benign tumors of the uterine muscle, are associated with both pain and heavy menstrual bleeding. They are the leading indication for hysterectomy. Previous research suggests the progestin-only contraceptive shot (Depo) is associated with decreased fibroid incidence. However, the associated between progestin-only intrauterine device (IUD) and fibroid incidence has not been studied.

Methods: We analyzed data from the Study of Environment, Lifestyle, and Fibroids (SELF), a prospective cohort that enrolled African-American women in Detroit, Michigan between 2010 and 2012 aged 23-35 with no clinical diagnosis of fibroids. Four visits over 5 years included ultrasounds and questionnaires; 91% returned for final visit. Hormonal IUD use was categorized as never/ever use and cumulative duration of use. Fibroids >0.5 cm in diameter were detected via ultrasound. We fit crude and adjusted Cox proportional hazards models with age as the time scale to estimate the association between time-varying IUD use and incident fibroids. Adjusted models included time-varying covariates: parity, recent birth, employment, recent Depo use, and current smoking.

Results: Our analytic sample included 1,123 fibroid-free women followed for a median 4.7 years. At baseline, 134 (12%) women had ever used an IUD, and by the end of follow-up, 176 (16%) had. Crude and adjusted models showed an inverse association between ever IUD use and fibroid incidence (Hazard Ratio (HR): 0.69, 95% CI: (0.48,0.99); adjusted HR (aHR) (0.74, 95% CI (0.51,1.08)). We found stronger, but less precise associations among those who had used IUDs for 5+ years (aHR: 0.69, 95% CI (0.30,1.42)) than those who had used IUDs for <5 years (aHR: 0.80, 95% CI (0.52,1.22)), compared to never users.

Conclusions: We found an inverse association between IUD use and fibroid incidence among African-American women in SELF, providing further support for progestin-only contraception and decreased fibroid incidence.

Impact of Antepartum COVID-19 Vaccination on Pregnancy and Neonatal Outcomes: Results from an Ongoing New York City Cohort Erona Ibroci* Erona Ibroci Xiaoqin Liu Whitney Lieb Rebecca Jessel Frederieke Gigase Kyle Chung Mara Graziani Molly Lieber Sophie Ohrn Jezelle Lynch Juliana Castro Christina Marshall Rushna Tubassum Farida Mutawakil Nina Molenaar Rhoda Sperling Lotje de Witte Elizabeth Howell Teresa Janevic Veerle Bergink Siobhan Dolan Joanne Stone Anna-Sophie Rommel

In December 2020, pregnant persons were one of the first groups eligible to receive the coronavirus disease 19 (COVID-19) vaccine in New York City (NYC). Yet vaccination remains low as delayed recommendations, exclusion of pregnant persons from the initial clinical trials and misinformation influenced vaccine hesitancy. The objective of this study was to examine associations between prenatal COVID-19 vaccination and pregnancy and neonatal outcomes. In this analysis, we included pregnant persons enrolled in the Generation C Study at the Mount Sinai Health System in NYC who delivered a singleton between April 2020-November 2021, whose COVID-19 vaccination status (vaccinated or unvaccinated) was known and had complete covariate data (N=1,825). We excluded those eligible for vaccination with missing vaccine data. In this sample, 14% (n=251) received at least one dose of any COVID-19 vaccine during pregnancy and 86% were unvaccinated during pregnancy (n=356 received the first dose after pregnancy and n=1,218 delivered before December 2020). We used multivariable linear regressions to estimate the effect of COVID-19 vaccination during pregnancy on the continuous outcomes Apgar scores at 1- and 5-minute, delivery gestational age (days) and birth weight (grams); and log-binomial regressions for the categorical outcomes C-section delivery and neonatal intensive care unit (NICU) admission. In comparison to the unvaccinated, vaccination during pregnancy was not associated with Apgar score at 1-minute (β=0.06; 95% CI=-0.1, 0.3) and birth weight (β=44.6; 95% CI=-51.5, 140.7), but was associated with a borderline increased 5-minute Apgar score (β=0.1; 95% CI=0.0, 0.2) and delivery gestational age (β=2.4; 95% CI=0.0, 4.7). There were no increased risks of C-section delivery (RR= 0.9; 95% CI=0.7, 1.2) or NICU admission (RR=1.0; 95% CI=0.6, 1.7). Our findings further suggest that COVID-19 vaccination during pregnancy does not increase risk of adverse pregnancy and neonatal outcomes.

Women's Health

Sleep health in adulthood and incidence of uterine leiomyomata in the Study of Environment, Lifestyle and Fibroids Chad M. Coleman* Chad M. Coleman Traci N. Bethea Amelia K. Wesselink Quaker Harmon Ganesa Wegienka Donna D. Baird Lauren A. Wise

Disparities in sleep health by race and gender are well-documented, with Black women more likely to report poor sleep. Black women are also more likely to develop uterine leiomyomata (UL), or benign fibroid tumors of the uterus, than White women. Poor sleep health could influence UL risk through stress and endocrine biologic pathways; however, there have been no epidemiologic studies of this association. We examined the association between self-reported sleep health in adulthood and UL incidence in the Study of Environment, Lifestyle and Fibroids, a prospective cohort study of 1,693 Black women. Eligible participants were aged 23-35 years, resided in the Detroit, MI region, had no history of UL, and were recruited from 2010-2012. Participants reported their duration of sleep, frequency of sleep troubles, and sleep quality on self-administered questionnaires at baseline. UL incidence was ascertained using standardized ultrasounds at baseline and every 20 months through 80 months. We used Cox proportional hazards regression models to estimate adjusted incidence rate ratios (aIRR) and 95% CI for the association between baseline sleep health and UL risk. Among 1,246 participants without prevalent UL and with at least one post-baseline visit, 62% reported not feeling well-rested ≥4 days/week, 58% slept <7 hours/night on a typical workday, and 30% had trouble falling asleep or going back to sleep ≥5 nights/month. Preliminary findings indicate little association between sleep health and UL incidence. The aIRR for not feeling well-rested ≥4 days/week compared with <3 days/week was 0.99 (95% CI: 0.81-1.23), for sleeping <7 vs. ≥7 hours/night on a typical workday was 0.90 (95% CI: 0.73-1.10) and for sleep troubles 5-14 and ≥15 vs. 0 nights/month were 0.93 (95% CI: 0.69-1.26) and 0.89 (95% CI: 0.60-1.32), respectively. We will next perform latent class analysis to examine changes in sleep patterns during 80 months of follow-up with UL incidence.

Women's Health

The Appropriateness of Hysterectomy Treatment for Noncancerous Gynecologic Conditions
Maya Wright* Maya Wright

Introduction: Noncancerous gynecologic conditions are common and difficult to treat clinically. Hysterectomy cures many symptoms caused by these conditions, but permanently ends fertility. Defining appropriate hysterectomy care is important, however the most commonly cited recommendations were produced by RAND in 1997. The objective of this study was to use RAND and updated clinical recommendations to assess the appropriateness of hysterectomies performed at a large tertiary health system.

Methods: The study included patients aged 18-44 that received a hysterectomy for noncancerous, non-obstetric, and non-emergency conditions from 2014-2017. We used structured and unstructured data abstracted from electronic medical records to translate RAND recommendations into an appropriateness rating system (RAND ARS) (inappropriate/appropriate) and to develop a new appropriateness rating system (Wright ARS) (inappropriate/ambiguous/appropriate) based on updated recommendations from a panel of clinical experts. We characterized the missing criteria that led to an inappropriate or ambiguous rating. We then conducted sensitivity analyses to assess changes in appropriateness ratings due to potential misclassification of missing criteria.

Results: Using RAND ARS, 69% of 1,829 total hysterectomies were rated as inappropriate. The most prevalent type of inappropriateness was due to missing diagnostic procedures (44%). Using Wright ARS, 26% of hysterectomies were rated as inappropriate, 16% as ambiguous, and 58% as appropriate. Based on sensitivity analyses, when using Wright ARS, if 50% of the most prevalent missing criteria were misclassified, 20% of the hysterectomies would be rated as inappropriate, 10% as ambiguous, and 70% as appropriate.

Conclusion: Our sensitivity analyses suggest that the inappropriate ratings cannot solely be attributed to misclassification of missing criteria. Defining appropriate care for hysterectomy treatment is key to ensuring equity in clinical care.

Women's Health

County prevalence and geospatial trends of early-onset hypertensive disorders of pregnancy in Kentucky, 2008-2017 Courtney Walker* Courtney Walker Anna Kucharska-Newton Steven R. Browning W. Jay Christian

Early-onset hypertensive disorders of pregnancy (eHDP) are associated with more severe maternal and infant outcomes than later-onset disease; however, eHDP has had a limited evaluation of prevalence and geospatial trends. In this study, we used Kentucky certificates of live and stillbirth to assess county-level spatio-temporal trends and covariates associated with an increased prevalence of eHDP. We found that after adjusting for race (Black %), educational attainment (% completed college), maternal smoking (%) that counties with the highest obesity prevalence ($\geq$31.6%) had a 20% increase in eHDP prevalence compared to counties with the lowest obesity prevalence (<22.6%) (aOR=1.20, 95% CI: 1.00, 1.44). We also found counties with the highest proportion of primiparous mothers $\geq$34 years old (>6.1%) had a 26% increase in the prevalence of eHDP (OR=1.26, 95% CI: 1.04, 1.50), compared to counties with the lowest prevalence (<2.5%). We further identified two county-level clusters of elevated rates of eHDP in the Appalachian region. These trends may reflect poor reproductive literacy and poor community health.

Women's Health

Maternal Weight Change in Pregnancy and Associations with Women's Long-term Mortality Stefanie Hinkle* Stefanie Hinkle Sunni Mumford Katherine Grantz Pauline Mendola James Mills Edwina Yeung Anna Pollack Sonia Grandi Yan Qiao Rajeshwari Sundaram Enrique Schisterman Cuilin Zhang

Background: High pregnancy weight gain is associated with greater postpartum weight retention; yet the long-term implications remain unknown. We examined associations of pregnancy weight change with mortality after ~50 years of follow-up.

Methods: The Collaborative Perinatal Project (CPP) Mortality Linkage Study linked maternal participants in the CPP, a prospective pregnancy cohort (1959-1965), to the National Death Index and Social Security Death Master File for vital status through 2016 (n=46,042). Total gestational weight change (gain or loss) in the index pregnancy (last CPP singleton pregnancy) was the difference in recorded delivery weight and self-reported pre-pregnancy weight. All-cause and cause-specific mortality associations with quintiles of gestational weight change were estimated using Cox regression adjusting for index pregnancy age, pre-pregnancy body mass index (BMI), race, parity, smoking, marital status, income, education, site, study year, prior chronic conditions, and gestational week at delivery.

Results: Median (interquartile range) pre-pregnancy BMI of the sample was 21.8 kg/m^2 (19.9-24.6); 46% were white and 45% were black. Median total gestational weight change was 9.5 kg (6.4-12.2); 2.5% lost weight. Over a median follow-up of 52 years (45-54), 38.9% of women died. Adjusted HRs (95% CI) for mortality across quintiles 1 to 5 of weight change were 1.34 (1.28-1.40), 1.11 (1.06-1.16), 1.00 (Reference), 1.01 (0.96-1.07), 1.09 (1.03-1.15), respectively. Compared to quintile 3 (median weight gain 9.5 kg), quintile 1 (median 3.2 kg) was primarily associated with cancer mortality (HR=1.20 [0.99-1.46]), while quintile 5 (median 15.4 kg) was primarily associated with cardiovascular disease (HR=1.14 [1.03-1.27]) and diabetes mortality (HR=1.52 [1.20-1.92]).

Conclusions: Both low and high pregnancy weight change conferred long-term health implications for women, with elevated mortality risk over 50 years postpartum primarily due to chronic disease.

Women's Health

Breastfeeding duration and mortality among parous women in the Mexican Teacher's Cohort Susana Lozano-Esparz* Susana Lozano-Esparza Mishel Unar Munguía Britton Tabert Dalia Stern Ruy López Ridaura Martin Lajous

Objective: To estimate the relation of lifetime breastfeeding duration on the risk of all-cause and cancer-specific mortality in Mexican women.

Methods: Parous participants in the Mexican Teachers' Cohort were followed for over 13 years. We categorized lifetime breastfeeding from self-reports. Date and underlying cause of death were obtained from national mortality databases (2006-2019) and classified using the International Classification of Diseases 10th Revision as cardiometabolic (I00-I99, E08-E14), breast cancer (C50), ovarian cancer (C56), and other cancer (C00-D99 excluding C50 and C56). We estimated Cox proportional hazard regression models with time on study as the time scale adjusting for age (continuous), rural residence, indigenous ethnicity, socioeconomic status, age at first birth, parity, age at menarche, BMI at 18, recreational physical activity, and smoking. We evaluated cause-specific mortality using cause-specific Cox and Fine-Gray regression models.

Results: After a mean follow-up of 11.2 years (±1.3) 1,556 deaths occurred among 88,516 parous women (29% cardiometabolic, 9.6% breast, 2.8% ovarian and 28% other cancers). Compared with parous women that never breastfed, the hazard ratio for all-cause mortality among parous women with a lifetime breastfeeding of 24 months 0.80 (95%CI 0.67, 0.97). Comparing women who breastfed 6 or more months vs less than 6, the cause specific hazard risk of cardiometabolic mortality was 0.75 (95%CI 0.61, 0.91), breast cancer mortality 0.85 (95% CI 0.60, 1.20), ovarian cancer mortality 2.07 (95%CI 1.03, 4.13) and other cancer mortality 1.07 (0.87, 1.32).

Conclusions: Breastfeeding among parous women reduces their risk of all-cause mortality. The results suggest that breastfeeding could reduce cardiometabolic and breast cancer mortality while it seems to increase the risk of ovarian cancer.

Figure. Hazard ratios (95% CI) for cause-specific mortality comparing women by breastfeeding duration.
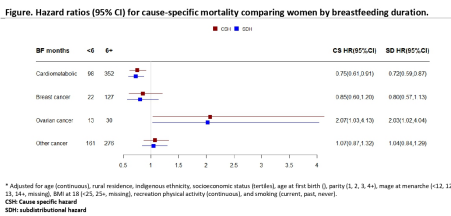
Does motherhood influence depression trajectories from late adolescence through adulthood?
Jessica K. Friedman* Jessica Friedman Darin J. Erickson Susan M. Mason

Background

This study assesses how women's parity (becoming a mother) is associated with changes in depressive symptom trajectories over time. Little is known about depressive symptom trajectories in women who become mothers beyond the postpartum period. Studies examining depression and motherhood report mixed findings with both decreases and increases in depressive symptoms related to motherhood.

Methods

A cohort of 971 women was surveyed approximately every 5 years over 5 waves of data collection, between 1999 (adolescence) and 2020 (adulthood) to assess health and wellbeing. Generalized Estimating Equations were used to evaluate changes in depressive symptoms by time-varying parity. Models compared population averages of Kandel Davies depressive symptom scores of parous and nulliparous women over follow-up after adjustment for sociodemographic factors (model 1) and additionally for relationship status (model 2). Multiple imputation was used to account for missing data.

Results

Approximately two-thirds of the women (n=646) became parous and n=325 remained nulliparous over follow-up. Results are reported as average predicted depressive symptoms (DS) stratified by parity. DS remained similar and steady between parous and nulliparous women through the third wave survey (DS$_{parous}$=19.28, 95% CI [18.65, 19.92], DS$_{nulliparous}$=18.98, 95% CI [18.62, 19.33]). Levels of DS diverged by the fifth wave, with parous women reporting lower DS (DS$_{parous}$=17.91, 95% CI [17.44, 18.38]) compared to nulliparous women (DS$_{nulliparous}$=19.19, 95% CI [16.64, 19.74]).

Conclusions

Parous women in this study reported decreased depressive symptoms over time compared to nulliparous women whose depressive symptoms remained stable over the same time period. These findings support earlier work that women who become mothers experience fewer depressive symptoms over time. These findings may also be associated with later life stages and influenced by relationship status.
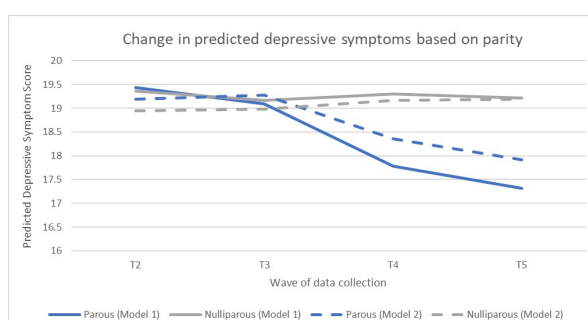
Can anthropometric measures be used as a surrogate for MRI-estimated visceral adiposity in the early 2nd trimester? Elizabeth M. Widen* Elizabeth Widen Sara Dube Jeffrey Luci Isaiah Janumala Megan Gray Celeste Sheppard Jaimie Davis Jack Virostko Adrienne N. Dula Stefanie N. Hinkle Amy N. Nichols Rachel Rickman Saralyn Foster Juan Pablo Robayo Jiminez Heather S. Jones Alison Cahill Michelle Wright

Greater visceral adipose tissue (VAT) during pregnancy increases the risk for preeclampsia and gestational diabetes. Yet, prenatal VAT assessment is challenging due to high cost of magnetic resonance imaging (MRI), tissue compression with ultrasound, and inability to use dual-energy X-ray absorptiometry (DXA). We sought to evaluate how VAT was associated with more accessible and inexpensive measures for epidemiologic research, and to evaluate for differences by BMI and high waist circumference (WC). Among 50 pregnant persons (88% White, 10% Asian, 8% American Indian/Alaska Native, 6% Black; 12% Hispanic) in the Mother Infant NuTrition Study (MINT) (2019-2022), body composition (anthropometrics and whole-body MRI including VAT) were measured at 14.9±0.8 wk gestation. A majority of people had healthy prepregnancy BMI (62%), and 38% had overweight or obesity. At 14 wk, mean±SD BMI, WC and VAT were 25.8±4.5 kg/m^2, 85.6±9.6 cm, and 1.0±0.6 kg, respectively; 26% had a high WC ≥85 cm. VAT was positively correlated with WC (0.59), mid-upper arm circumference (MUAC) (0.65), current BMI (0.65), and subscapular (0.67) and iliac crest (0.61) skinfold thickness. Mean VAT levels were 0.54 kg (95% CI: 0.85, 0.24) higher among those with WC ≥85 versus <85 cm. Except for WC, correlations with VAT were weaker for MUAC, and iliac crest and subscapular skinfolds among those with overweight and obesity (n=19, WC: 0.41, MUAC: 0.28, iliac -0.07, subscapular 0.39) compared to those with healthy BMI (n=31, WC: 0.40, MUAC: 0.49, iliac: 0.68, subscapular 0.61). Current BMI, MUAC and subscapular skinfold thickness were positively correlated with VAT and slightly stronger than WC and other measures. Although WC is a better measure of VAT outside of pregnancy, our data suggest that these other measures may better reflect VAT in the early 2nd trimester, and inclusion is warranted in studies of maternal health and adverse pregnancy outcomes.