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# Abstract Book

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Police exposure as a determinant of structural racism: An exploration of the association between preterm birth in neighborhoods with high police exposure Tongtan Chantarat*

Tongtan Chantarat Rachel R. Hardeman Morrison Luke Smith J'Mag Karbeah David C. Van Riper Dara D. Mendez

More frequent police contact for Black individuals and communities signals that in the eyes of the law they are seen as inherently criminal and dangerous, and combined with aggressive behavior that officers exhibit during these interactions is associated with higher reports of stress symptoms for people living in these communities. Given research demonstrating the association between stress and preterm birth (PTB), we assessed whether neighborhood police exposure is associated with differential rates of PTB among Blacks and Whites in Minneapolis, Minnesota. We used administrative and medical records from the largest health system in Minneapolis, population estimates for from the American Community Survey (ACS), and the all count Minneapolis Police Incident Report (2012-2016). The sample included 121 US-born Black, 193 foreign-born Black, and 745 White mothers of singleton births in 2016. We measured the association between exposure, defined as residence in tracts with high 5-year police incident count (4th quartile), and PTB. We conducted a multivariate multi-level regression controlling for the women's prenatal and socioeconomic statuses. An interaction term was used to test whether the effect of neighborhood exposure differ by the women's racial group. Lastly, we tested for the spatial correlation of the incident count and the proportion of Black residents in all Minneapolis census tracts. Our results suggest that high level of neighborhood police exposure increases the risk of PTB among women of all racial groups (OR=1.99, CI: 1.00-3.96; non-significant interaction term). Further, spatial correlation methods suggest there is clustering by proportion Black and police incident count (Moran's I=0.237, p=0.001). And local indicators of spatial association (LISA) suggest identifiable clusters (fig 1). The higher incidence of PTB in Black women may be partially attributed to racialized pattern of exposure rather than differential effect between the two groups.

Prop. Black - Incident count
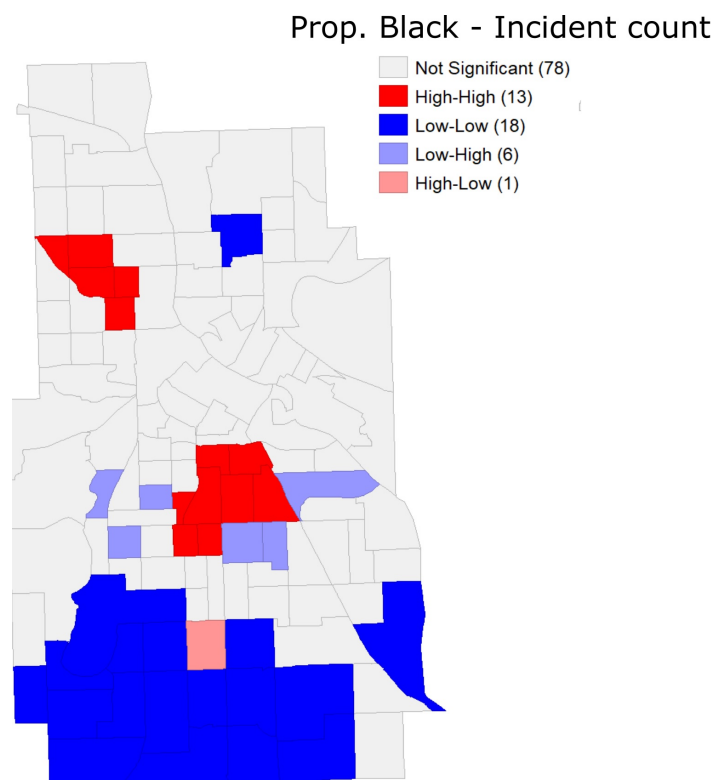
State- and county-level total and race-based hate crime in relation to cardiovascular risk factors among middle-aged adults: The National Longitudinal Survey of Youths 1979

Krisztina Gero or Daniel Kim* Krisztina Gero Ichiro Kawachi Christopher F. Baum Becky A. Briesacher Robert B. Wallace Daniel Kim

Background: Hate crimes are crimes based on a perpetrator's bias against a race, religion, disability, sexual orientation, ethnicity, or gender identity. Despite abundant research on the direct consequences of hate crimes on victims, little is known about how living in areas with higher hate crime rates may affect one's health including cardiovascular (CVD) risk factors. Methods: We used data from a nationally-representative sample of 7241 middle-aged Americans (age 45-53 years in 2010) in the National Longitudinal Survey of Youths 1979, and on hate crime from the Uniform Crime Reports. Multivariate logistic regression was employed to estimate the associations between changes in state- and county-level total and race-based hate crime rates (2000 to 2010) and individual-level incident diabetes, hypertension, obesity, and depression (2012 to 2016). All models controlled for individual-, state-, and county-level demographic and socioeconomic factors. Results: For each 1-standard deviation (SD) increase in the total and race-based hate crime rates at the state level, there was an associated 41% higher (OR 1.41, 95% CI 1.02-1.94) and 46% higher (OR 1.46, 95% CI 1.09-1.95) odds of incident hypertension, respectively. Compared to non-Hispanic/non-Blacks, these associations were weaker among Hispanics (p-interaction=0.02 for total hate crimes, 0.01 for race-based hate crimes) and Blacks (p-interaction=0.03 for total hate crimes, 0.04 for race-based hate crimes). At the county level, each 1-SD increase in the total and race-based hate crime rate was linked to 28% (OR 1.28, 95% CI 1.08-1.51) and 26% (OR 1.26, 95% CI 1.07-1.48) higher obesity odds, respectively. No associations were observed for diabetes or depression. Conclusions: Our findings suggest that living in regions with higher rates of hate crime, particularly race-based in nature, confer higher odds of hypertension and obesity. Investing resources into fighting hate crime may help reduce the national burden of CVD.

The association between state minimum wages, health, and health behavior among working-age adults, Panel Study of Income Dynamics 1999-2017 James Buszkiewicz* James Buszkiewicz Anjum Hajat Jennifer J. Otten Adam Drewnowski

Widening income inequities in the United States driven in part by stagnant federal wage growth has led many states to adopt higher minimum wage rates in an effort to improve the health and economic wellbeing of their residents. While much of the existing evidence evaluating the influence of minimum wage on health has shown some benefit, more recent work suggests that this relationship may vary across sociodemographic subpopulations. We employ a triple difference strategy using modified Poisson and linear regression to evaluate the association between minimum wage and obesity, body mass index, hypertension, self-reported health, moderate psychological distress, cigarette smoking, and alcohol consumption in adults age 25 to 64 years. Data from the 1999 to 2017 Panel Study of Income Dynamics was linked to state policies and characteristics to estimate the incident rate ratio, or mean difference for body mass index, associated with a \$1 increase in current and 2-year lagged minimum wage among less-educated adults overall, by race/ethnicity and gender, and by pay type (hourly or salary). Overall, we did not observe associations between current or 2-year lagged minimum wage and body mass index, hypertension, fair or poor health, moderate psychological distress, or daily cigarette consumption. However, we did find that higher 2-year lagged minimum wages were associated with a modest increase in the risk of alcohol consumption (IRR = 1.03, 95% CI = 1.01, 1.06) as well as obesity (IRR = 1.11, 95% CI = 1.01, 1.22). Subgroup models suggest an increased risk of obesity in women, a higher risk of moderate psychological distress in men of color as well as a reduced risk of moderate psychological distress and fair or poor health in non-Hispanic White women and men of color, respectively. Associations also varied by pay type. These results contrast with prior findings and provide evidence of a more nuanced relationship between minimum wage and health across race/ethnicity and gender.

**The impact of a hypothetical cash transfer intervention on racial/ethnic hypertension disparities in young adults** Audrey Renson* Audrey Renson Paul N Zivich III Alexander P Keil Robert A Hummer Kathleen Mullan Harris Allison E Aiello

Background: There are widening racial/ethnic disparities in cardiovascular disease. Few studies have evaluated socioeconomic interventions on cardiovascular health disparities, especially among young adults.

Methods: Add Health is US-representative cohort study of individuals who were in grades 7-12 in 1994. We used data on private financial transfers received within 12 months from caregivers when participants were aged 18-26, to estimate effects of a cash transfer policy on later hypertension prevalence disparities at ages 24-32. Using the parametric g-formula, we simulated two different cash transfer scenarios: (a) a universal $1000/year transfer (unconditional plan), and (b) a $1000/year transfer for individuals with parents' income at or below the whole-sample 25th percentile (targeted plan). We defined disparity as the hypertension prevalence difference between non-Latinx Blacks (NLB), Latinx Blacks (LB), and Latinx Whites (LW) on one hand, and non-Latinx Whites (NLW) on the other. Primary interest was in disparity differences (i.e. difference in prevalence differences) between each simulated scenario and the natural course (observed).

Results: Among 10,448 participants interviewed at Wave 4 and self-identifying as NLW, NLB, LB and LW, 5,134 received any private transfer, with NLW receiving on average $3-400 more than other races/ethnicities. NLW participants had the lowest observed hypertension prevalence (19%) followed by LW (20%), LB (21%) and NLB (22%). Adjusting for measured confounders and missing data, under the unconditional plan, estimated disparity differences were -1.1, -0.9, and -0.1 percentage points for LW, LB, and NLB, respectively. Under the threshold plan, the same disparity differences were -0.4, -0.5, and -0.1, respectively. 95% confidence intervals were wide (see Figure).

Conclusions: Our results suggest that racial/ethnic disparities in hypertension prevalence among young adults would likely be lessened via cash transfers in young adulthood.
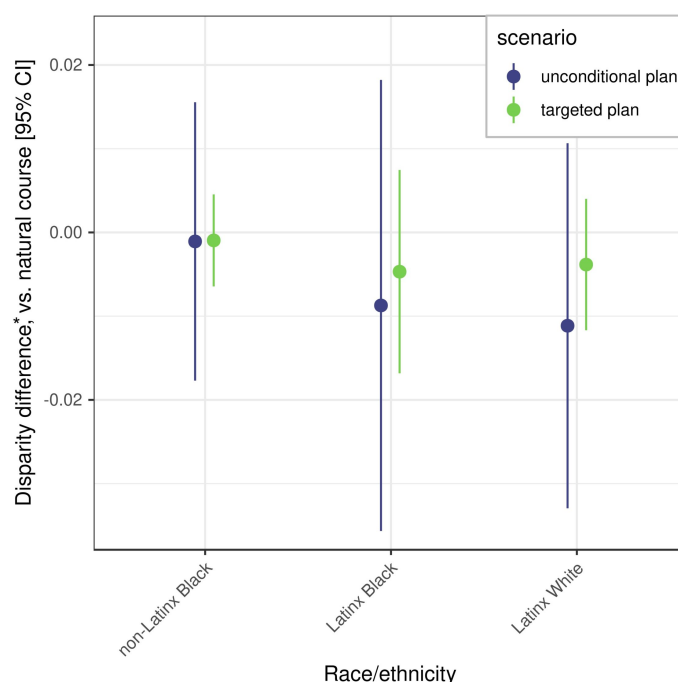
* Disparity is defined as the prevalence difference in hypertension between each other race/ethnicity and non-Latinx Whites. Disparity differences are the difference in prevalence difference between each cash transfer scenario and the natural course (observed).

Evaluating identifiability of the health effects of social policies in the presence of policy clustering Ellicott Matthay* Ellicott Matthay M. Maria Glymour

Extensive empirical research on the health effects of social policies takes advantage of the arbitrary timing and location of policy changes, often using variants of panel fixed effects designs. However, multiple social policies may be implemented simultaneously in the same locations, making it difficult or statistically impossible to disentangle individual policy effects. No prior epidemiologic research has documented the pervasiveness or consequences of policy clustering across diverse policy domains relevant to health. We review a systematic sampling of social policy databases (e.g., poverty reduction, education, firearms) and characterize the extent of policy clustering in each. Next, we assess whether sufficient variation ever exists to estimate individual policy effects, using R^2 in regression models of each policy regressed on the set of all other policies. Finally, we approximate impacts on precision by comparing SEs of estimated effects under the observed clustering to SEs expected if all policies were adopted independently. Findings indicate that policy clustering is the norm rather than the exception. The degree of policy clustering varies by domain, ranging from very high for firearm policies (Figure) to moderate for poverty policies. The impacts of clustering are substantial: for example, for 95% of firearm policies, greater than 90% of the variation across state-years in each policy is explained by other policies; under the null, this degree of clustering effectively increases the variance of effect estimates by at least 40%. Policy clustering is a major methodological challenge to rigorously evaluating the health effects of social policies and may explain surprising results in prior work. Statistical methods and data collection efforts to enhance statistical power for evaluating clustered policies or to circumvent the clustering are a high priority for future work.

Figure: Heatmap of covariation in state firearm policies across 50 states, 1991-2018

Policies are perfectly aligned

Policies vary completely independently

Each firearm policy is represented on the x and y axis. For a given column and row, the color of the cell indicates the degree of covariation between the two binary policies, measured by Pearson's Chi-squared statistic.

Equity Efficiency Tradeoffs in The Prevention of Coronary Heart Disease Among Non-Hispanic Black and White Americans
Gregory Cohen* Gregory Cohen Shailesh Tamrakar Sandro Galea

Heart disease, principally coronary heart disease (CHD) is the leading cause of mortality among US adults ages 35 and older. Disparities in CHD mortality between socially advantaged and disadvantaged groups, such as whites and blacks have persisted for decades. While these differences in disease burden have been well documented, there is a poor understanding of how to optimally narrow these differences while maintaining overall improvement in CHD mortality. An equity-efficiency tradeoffs (EET) framework may be a useful lens through which to consider this problem. We performed agent-based micro simulations to study the effects of pharmaceutical (Statins), and taxation ($1 and $2 tobacco tax) interventions on CHD mortality, and racial gaps in CHD mortality, incorporating efficiency as Years of Life Lost (YLL) averted per dollar spent. We initialized 4 cohorts of simulated agents including white non-Hispanic men and women, and black non-Hispanic men and women, ages 45-64, using demographic data from the American Community Survey and CHD risk factor data from NHANES. CHD mortality was estimated over a 10-year follow-up period using the SCORE algorithm. Compared to no treatment, statins were efficient among all groups; tobacco taxes were more efficient than statins for all groups except black non-Hispanic men, who experienced greater CHD mortality compared to no treatment. Among black compared to white non-Hispanic women, tobacco taxes were 4.3 to 4.4 times as effective, and statins were 2 to 2.1 times as effective in reducing absolute CHD mortality. Among black compared to white non-Hispanic men, statins were about 1.9 to 2 times as effective in reducing absolute CHD mortality. Tobacco taxes appear to exacerbate racial inequities in CHD among men, relative to statins. In contrast, relative to statins, tobacco taxes appear to be a progressive and optimal approach to decreasing racial gaps in CHD mortality among women, increasing equity without trading off efficiency.

Paternal mixtures of urinary concentrations of phthalate metabolites and phenols in relation to pregnancy outcomes among couples attending a fertility center. Lidia Minguez Alarcon* Lidia Minguez Alarcon Andrea Bellavia Audrey J. Gaskins Jennifer B. Ford Irene Souter Jorge E. Chavarro Antonia M. Calafat Russ Hauser Paige L. Williams

Few epidemiologic studies have evaluated the impact of paternal environmental exposures, particularly as mixtures, on pregnancy outcomes of their partners. We explored whether paternal urinary bisphenol A (BPA), parabens, and phthalates biomarker mixtures were associated with pregnancy outcomes among 300 couples undergoing 581 in vitro fertilization (IVF) or intrauterine insemination (IUI) cycles (2004-2017). Urinary biomarkers were quantified using tandem mass spectrometry (1urine/cycle). Principal component analysis (PCA) was used to identify underlying factors of biomarker concentrations. Multivariable Cox proportional hazards models for discrete survival time were used to estimate the odds ratios (ORs) and 95% CIs for the associations of PCA-derived factor scores with odds of not having a live birth (LB). Interactions were also included in the models to examine strength of associations over 3 vulnerable periods [embryo transfer (ET) to implantation (I), I to clinical pregnancy (CP), and CP to LB]. Models were adjusted for paternal and maternal ages and body mass indexes, paternal smoking, urine dilution and year of collection, infertility diagnosis, type of cycle (IVF/IUI), and other PCA factor scores. We identified three factors, representing di(2-ethylhexyl) (DEHP) metabolites, BPA and non-DEHP metabolites, and parabens, accounting for 57%, 15% and 9%, respectively, of the total variance explained. An interquartile range increase in the BPA/non-DEHP-related factor score was associated with elevated odds of failing prior to LB (OR=1.36, 95% CI: 1.05, 1.76); associations were similar across the 3 cycle-specific time windows. The overall ORs of failure for the DEHP-related and paraben-related factor scores were OR=1.28 (95% CI: 0.94, 1.74) and OR=1.19 (95% CI: 0.98, 1.45), and tended to be stronger in the CP to LB window. In summary, paternal mixtures of urinary BPA and non-DEHP metabolites were related to higher odds of couples' infertility treatment failure.

Associations of trimester-specific blood trihalomethanes concentrations with adverse birth outcomes Yixin Wang* Carmen Messerlian Yang Sun Yixin Wang Chong Liu Ying-Jun Chen Wen-Qing Lu Carmen Messerlian

Background: Toxicological studies in rodent species have demonstrated that trihalomethanes (THMs), a class of disinfection by-products in drinking water, adversely affect fetal growth and survival. Despite widespread human exposure, epidemiological studies in pregnancy are limited. We aimed to investigate the associations of blood THMs concentrations measured during early, middle and late pregnancy with adverse outcomes in a prospective birth cohort.

Methods: A total of 4086 blood samples were collected from 1660 Chinese mothers across trimesters of pregnancy and analyzed for chloroform (TCM), bromodichloromethane (BDCM), dibromochloromethane (DBCM) and bromoform (TBM). Birth outcome data (birth weight, gestational age (GA), infant sex) and demographic and covariate data were abstracted at delivery from medical records by study staff. We estimated hazard ratios (HR) and 95% confidence intervals (CI) of small for gestational age (SGA, 10th percentile for GA), low birth weight (LBW, <2500 g), and preterm birth (PTB, <37 completed GA weeks) by tertiles of biomarker concentrations using multivariable Cox models.

Results: After adjusting for a priori confounders, associations were found between blood TCM concentrations measured during middle and late pregnancy and risk of SGA [HRs comparing extreme tertiles = 2.55 (95% CI: 1.14, 5.73; p for trend= 0.03) and 2.12 (95% CI: 0.91, 4.91; p for trend= 0.10), respectively]. Blood BDCM concentrations in early pregnancy were associated with lower risk of SGA [HRs comparing extreme tertiles = 0.50 (95% CI: 0.25, 1.00; p for trend= 0.06)], but with higher risk of LGA [HRs comparing extreme tertiles = 1.37 (95% CI: 1.13, 1.67; p for trend= 0.002)]. There was no evidence of associations between blood THMs and LBW or PTB.

Conclusion: Our results suggest that exposure to THMs during pregnancy may have gestational age specific effects on fetal growth.

Prenatal Exposure to Perfluoroalkyl Substances and Behavioral difficulties in childhood at Age 7 and 11 years Jiajun Luo* Jiajun Luo Zeyan Liew

Background: Perfluoroalkyl substances (PFAS) are suggested to induce developmental neurotoxicity in animal studies but human evidence has been inconclusive. Most population-based studies have been limited by small sample size and neuropsychiatric outcomes assessed at a single time point. The study aims to assess the association between prenatal PFAS exposure and behavioral difficulties at age 7 and 11.

Methods: We combined biological samples in three studies originated from the DNBC and evaluated the associations between six types of PFAS in maternal plasma collected in early pregnancy and behavioral difficulties of the offspring assessed using Strength and Difficulties Questionnaire (SDQ), reported by parents at age 7 (n=2,421), and reported by parents (n=2,070) and by children themselves at age 11 (n=2,071). Composite SDQ scores above the 90th percentile was a priori defined to identify behavioral difficulties. We used logistic regression to estimate the OR for behavioral difficulties by doubling increase of PFAS concentration (ng/ml) adjusting for potential confounders.

Results: We found that prenatal perfluorononanoic acid (PFNA) was consistently associated with total and externalizing problems in all three SDQ measures reported by parents or children at age 7 and 11 years (ORs ranged from 1.43 to 1.67 for per doubling increase in PFNA and externalizing behavioral problems) while no consistent associations were observed for other types of PFAS. These associations appeared to be slightly mediated by maternal thyroid dysfunction during pregnancy.

Conclusion: Prenatal PFNA exposure was consistently associated with externalizing behavioral difficulties in childhood in repeated SDQ measures at age 7 and 11, while the associations found for other PFAS and child-reported internalizing difficulties at age 11 years. The slight mediation effects of maternal thyroid dysfunction warrant further evaluation.
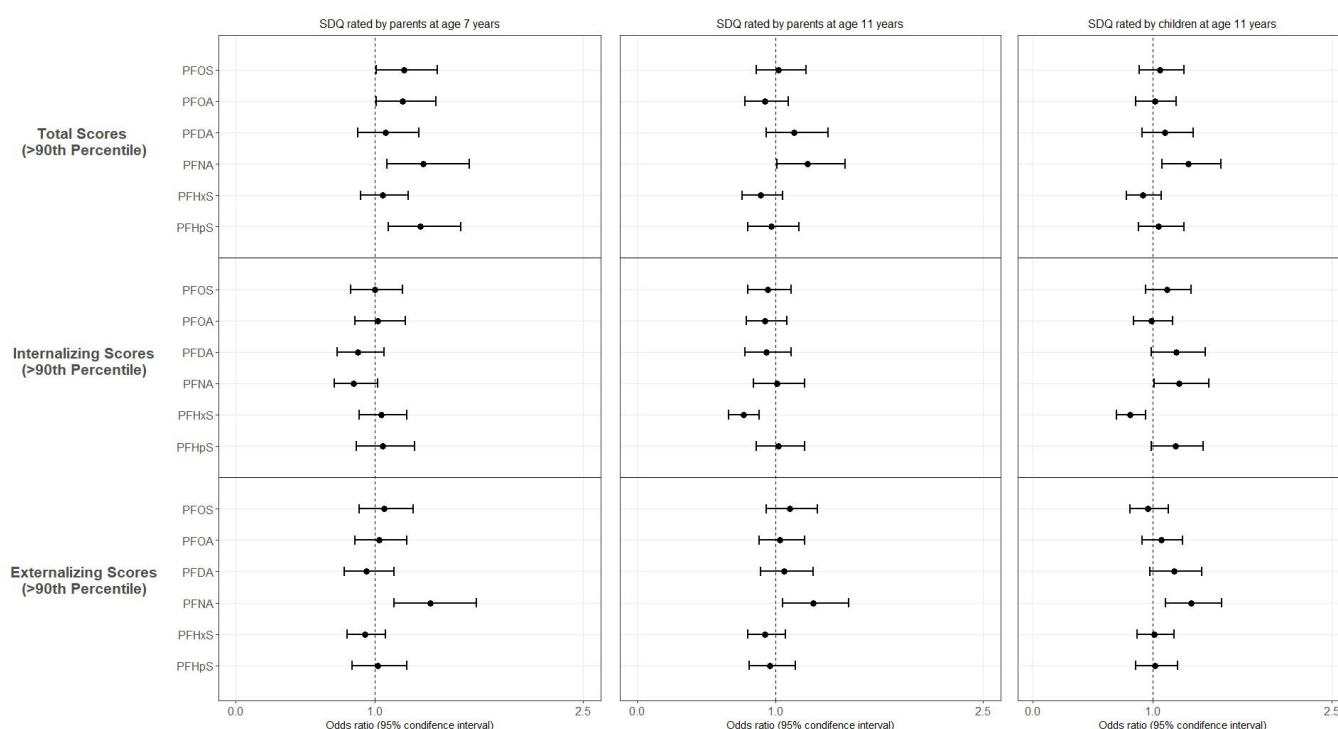
Environment/Climate Change

Prenatal exposure to mixtures of persistent endocrine disrupting chemicals and early menarche in British girls Kristin J. Marks* Kristin Marks Penelope P. Howards Melissa M. Smarr W. Dana Flanders Kate Northstone Johnni H. Daniel Antonia M. Calafat Andreas Sjodin Michele Marcus Terryl J. Hartman

Exposure to endocrine disrupting chemicals (EDCs) is ubiquitous. EDC exposure, especially during critical periods of development such as the prenatal window, may interfere with the body's endocrine system, which can affect growth and developmental outcomes such as puberty. Most studies have examined one EDC at a time in relation to disease; however, humans are exposed to many EDCs simultaneously. By studying mixtures, the human experience can be more closely replicated. We investigated the association of prenatal exposure to persistent EDCs (perfluoroalkyl substances (PFAS), polychlorinated biphenyls (PCBs), and organochlorine pesticides (OCPs)) as mixtures with age at menarche among female offspring in a nested case-control study within the Avon Longitudinal Study of Parents and Children (ALSPAC) (n=448). Concentrations of 52 EDCs were measured in maternal serum samples collected during pregnancy. Daughter's age at menarche was ascertained through mailed questionnaires sent annually. We used weighted quantile sum (WQS) regression to examine the association between prenatal exposure to EDC mixtures and age at menarche (<11.5 vs. ≥11.5 years) for each chemical class separately (PFAS, PCBs, and OCPs) and for all three classes combined. Models were adjusted for maternal age at menarche, education, parity, pre-pregnancy body mass index, age, smoking, and gestational week at sample collection. WQS regression models showed null associations between the WQS indices for mixtures (PFAS, PCBs, OCPs, and all three classes combined) and early menarche. For instance, the odds ratio for early menarche for one-unit higher of the WQS index (representing a one-decile increase in chemical concentrations) for all three classes combined was 0.94 (95% CI: 0.70, 1.18). While preliminary results suggest the overall effect of prenatal exposure to persistent EDC mixtures is not associated with early menarche, future analyses will explore effect modification and non-linear effects.

Environment/Climate Change

Endocrine-disrupting exposure profiles and early menarche among U.S. adolescent girls: application of unsupervised machine learning techniques Sabine Oskar* Sabine Oskar Susan Teitelbaum Mary Wolff Jeanette Stingone

Using non-traditional analytic approaches may enhance multiple exposure environmental epidemiologic investigations. We investigated whether unsupervised machine learning techniques may aid in hypothesis refinement to estimate the impact of exposure to multiple environmental chemicals on the timing of menarche. Data from 440 girls (12-16 years) from National Health and Nutrition Examination Survey with 30 biomarker measures of chemicals that may possess anti-androgen activity were analyzed. Menarche was dichotomized into "earlier" (≤11 years; 32% of girls) and "later" (≥12 years). Chemical mixture exposure profiles were identified using k-means clustering and effect sizes were estimated using regression models. A five-level categorical exposure variable was created based on the chemical exposure profiles identified from k-means clustering analyses. The majority of girls were classified in cluster 4 (82%). Girls in cluster 1 had higher mean concentrations of most phenols, lead, and two phthalates. Girls in cluster 2 had higher mean concentrations of most phytoestrogens whereas girls in cluster 5 had higher concentrations of the majority of phthalates. Compared to girls in cluster 4 who had lower mean concentrations of all the biomarker measures, girls in clusters 1 and 2 had a greater risk of earlier menarche in crude and covariate adjusted models (adjusted PR: 1.66, 95% CI: 0.84, 3.26; adjusted PR: 1.88, 95%CI: 0.67, 5.14, respectively). However, these associations were weak given the sample size in each cluster (n=8 and n=4, respectively). These results illustrate how unsupervised clustering methods can uncover the varied and distinct patterns of environmental chemical exposure profiles in adolescent girls. Further research is needed to understand what sources contribute to these distinct exposure patterns and how such exposures impact timing of menarche.

Intrauterine exposure to phthalate metabolites: A follow-up study assessing brain structure and white matter integrity in preadolescence Akhgar Ghassabian* Akhgar Ghassabian Michiel van den Dries Sander Lamballais Tessensohn Tonya White Anjoeka Pronk Leonardo Trasande Henning Tiemeier Mònica Guxens4

Exposure to phthalates, used in personal care products and food packaging, is ubiquitous. Despite growing concerns regarding their neurotoxicity, the underlying brain alterations are unclear. We used data from 908 mother-child pairs from a population-based birth cohort in the Netherlands (2002–2006) to examine associations of prenatal phthalate exposure with brain morphology and white matter integrity in preadolescents. Maternal urinary concentrations of 17 phthalate metabolites were measured at 25 weeks (T3) of gestation, and averaged across pregnancy. Outcome measures were brain global volumetric measures, subcortical volumes, cortical thickness, and cortical surface area; as well as fractional anisotropy and mean diffusivity in brain magnetic resonance imaging (mean age 9.8 years, SD=0.32). Maternal urinary concentrations of monoethyl phthalate (mEP) and phthalic acid in T3 were associated with smaller total brain and gray matter; whereas monobutyl phthalate (mBP) in T2 and T3 were associated with larger thalamus and caudate nucleus volumes, respectively. Di-2-ethylhexyl phthalate ([]DEHP) levels in T1 were associated with a smaller cerebellum white matter volume. We found associations between higher phthalate levels and thicker inferior parietal and mediolateral temporal cortices in the left hemisphere; whereas higher exposures were associated with a smaller surface area in the right hemisphere (e.g., mEP, mBP, and []DEHP in T3). Higher exposure to mono(3-carboxypropyl) phthalate averaged across pregnancy was associated with a larger surface areas in the lateral occipital cortex. There was no associations between phthalate exposure and measures of white matter integrity. Analyses stratified for sex revealed associations of higher phthalate levels with smaller white matter and subcortical volumes in girls only. These findings provide evidence on the contribution of prenatal phthalate exposure to impaired brain development in children.

Aging

Sedentary behavior (SB), brain-derived neurotrophic factor (BDNF) and brain structure in midlife: A brain Magnetic Resonance Imaging (MRI) sub-study of the Coronary Artery Risk Development in Young Adults (CARDIA) Xuan Zhang* Xuan Zhang Denise Gaughan Chengxuan Qiu Osorio Meirelles Lenore Launer

Introduction: There is evidence that sedentary time (ST) is associated with poor brain health but the underlying mechanisms are unclear. Studies suggest exercise increases BDNF levels, which plays a role in neurogenesis, and that low BDNF levels are associated with cognitive impairment. Limited population-based studies have examined associations among SB, BDNF, and brain structures. Here we explore the mediation of BDNF in the association of SB to brain health markers in middle aged cohort.

Methods: We included 625 participants from the brain MRI sub-study of the CARDIA study who had plasma BDNF data available at the Year 25 exam. SB was estimated by average ST hours/day from self-reported time spent in activities, including sitting while watching television, computer use, and riding transportation. Our outcome measures were total and selected regional brain volumes (cubic centimeter) related to cognition. General linear regression examined the following associations: SB and MRI measures; SB and BDNF; BDNF and MRI; and SB, BDNF, and MRI, adjusting for age, sex, race, and intracranial volume. BDNF levels were log-transformed. ST was categorized into quartiles.

Results: People in the upper 25%ile ST (>8.5 hours/day) had a decreased total brain (TB) volume of 11.6 (p=0.01) compared to the lower 25%ile (0.05). Controlling for the BDNF, the direct effect between ST and TB (β=-11.5, p=0.01), hippocampus (β=-0.2, p=0.01), and TGM (β=-7.4, p=0.03) were similar to the effect without BDNF adjustment.

Conclusions: Increased ST was associated with decreased TB, hippocampus, and TGM volumes. BDNF was not a mediator of the association of ST and brain structure in our study population. Larger sample size and more precise measures of SB may be needed.

Figure 1. The mediation effect of BDNF in the association between sedentary behavior and MRI measures
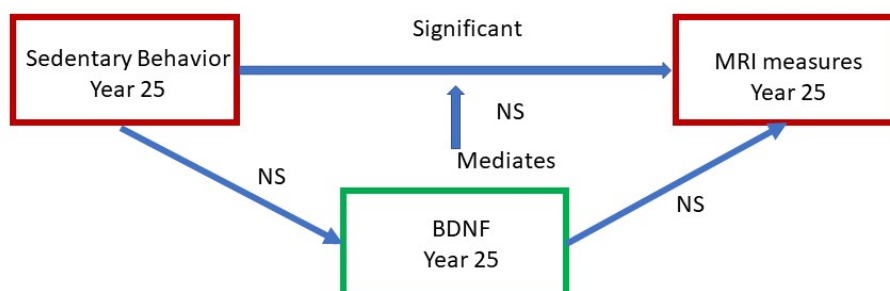
*NS: Not significant

Weekday-weekend sleep patterns and weight-related behaviors among adolescents Kaitlyn M. Berry* Kaitlyn Berry Aaron Berger Conrad Iber Melissa N. Laska Darin J. Erickson Kelsie Full Susan Redline Rachel Widome

Introduction: Sleep duration and timing are associated with weight related behaviors among adolescents, but the mechanisms linking chronobiology to weight are less clear. A driver may be inconsistency of sleep on weekends vs. weekdays resulting from: 1) Sleep debt: Most US adolescents get insufficient sleep on school nights and compensate by sleeping longer on the weekend. 2) Social jet lag: Many teens are also forced to wake earlier than their circadian timing on school days but not weekends, creating a difference in weekend and weekday sleep midpoint timing.

Methods: The START study (n=2134) follows a cohort of students from five Minnesota high schools to evaluate impacts of school start time changes. Sleep wrist actigraphs were worn for a week by a subsample of students at baseline (9th grade, schools started at 7:30-7:45am). Using data from this subsample (n=284), we examined sleep debt payoff (difference in weekend and weekday sleep duration) and social jet lag (difference in weekend and weekday sleep midpoints) and assessed whether these factors were related to weight and related behaviors.

Results: In our sample, 78.6% of teens had ≥1 hour of social jet lag and 60.9% had ≥1 hour of sleep debt. Social jet lag (SJL) and sleep debt payoff (SDP) had a correlation of 0.03. Neither measure was associated with eating breakfast ≥5 days per week (SJL: RR=1.02, 95% CI=0.92-1.14; SDP: RR=0.94, CI=0.87-1.01), eating fruit or vegetables daily (SJL: RR=1.00, CI=0.88-1.13; SDP: RR=1.04, CI=0.96-1.12), being active 6-7 days per week (SJL: RR=0.98, CI=0.86-1.12; SDP: RR=0.94, CI=0.86-1.03), or having a BMI above the 95th percentile (SJL: RR=1.01; CI=0.72-1.41; SDP: RR=1.04, CI=0.83-1.29).

Conclusions: Adolescents commonly live with both social jet lag and sleep debt, which appear to be distinct features of sleep. Though not associated with weight behaviors cross-sectionally, their impact on teen health over time remains an open question.
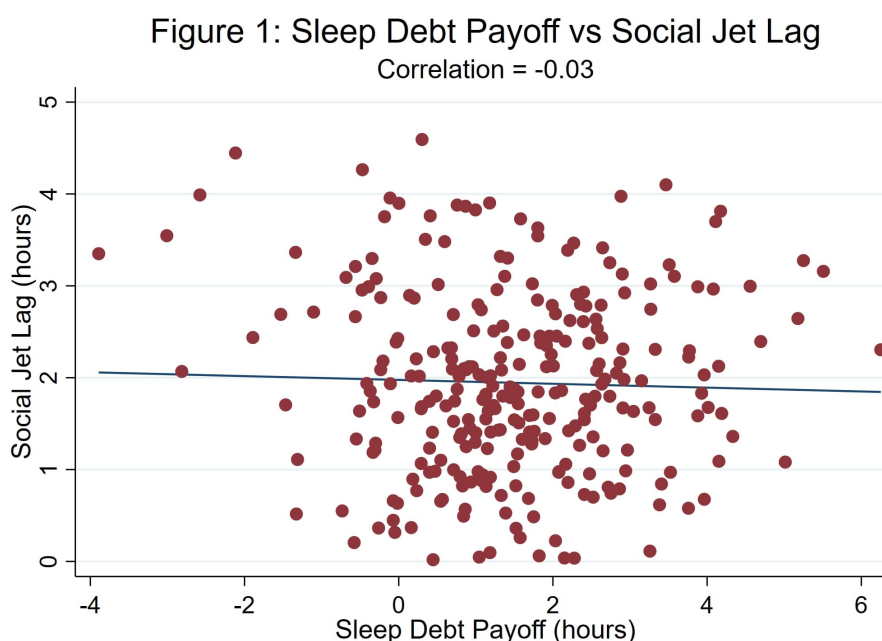
Figure 1: Sleep Debt Payoff vs Social Jet Lag
Correlation = -0.03

Diet quality and fecundability in a North American preconception cohort Sydney Kaye Willis*
Sydney Willis Elizabeth E. Hatch Amelia K. Wesselink Ellen M. Mikkelsen Anne Sofie D. Laursen
Katherine L. Tucker Kenneth J. Rothman Sunni L. Mumford Lauren A. Wise

Diet is a complex modifiable factor that has dramatically changed in both developed and developing nations over the last few decades. While many studies have examined the role of specific dietary nutrients or food groups in relation to fertility, there has been limited assessment of the effect of dietary patterns on fertility. We evaluated the association between diet quality and fecundability, the per-cycle probability of conception, in Pregnancy Study Online, a North American preconception cohort of pregnancy planners (2013-2019). After enrollment, female participants, aged 21-45 years, completed a baseline questionnaire to ascertain information on demographic and lifestyle factors. Ten days later, they were invited to complete the diet history questionnaire (DHQ) II, a validated food frequency questionnaire. We used the DHQ to calculate the Healthy Eating Index 2010 (HEI-2010), a diet quality measure based on USDA recommendations. Participants completed bimonthly follow-up questionnaires for up to 12 months to ascertain pregnancy status. We restricted our analyses to 8,701 women who were attempting pregnancy for ≤6 cycles at entry. We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% CIs, adjusted for age, body mass index (BMI), and lifestyle and demographic factors. Higher HEI-2010 scores, indicative of better diet quality, were associated with slightly increased fecundability (HEI-2010 score ≥90th (HEI-2010 score: 79) vs. <25th (HEI-2010 score: 57) percentile: FR=1.13, 95% CI: 1.00-1.28). We observed a dose-response relation between HEI-2010 score and fecundability when modeled using a restricted cubic spline (Figure 1). Results were slightly stronger among those with BMI <25 kg/m2 compared with BMI ≥25 kg/m2 and among those with attempt time at study entry <3 cycles compared with 3-6 cycles. These results support the hypothesis that overall diet quality is related to fecundability.

Figure 1. Association between HEI-2010 score and fecundability among 8,701 female PRESTO participants fitted by a restricted cubic spline. The reference level for the fecundability ratio is the lowest value in the data (HEI-2010 score: 11). The spline has 4 knot points at the 25th (HEI-2010 score: 57), 50th (HEI-2010 score: 65), 75th (HEI-2010 score: 73), and 90th (HEI-2010 score: 79) percentiles. Spline is adjusted for age, BMI, current smoker, alcohol intake, physical activity per week, hormonal last method of contraception, intercourse frequency, using method to improve pregnancy chances, daily use of prenatal or multivitamin, race/ethnicity, marital status, education, household income, intake of sugar sweetened beverages, and parity.
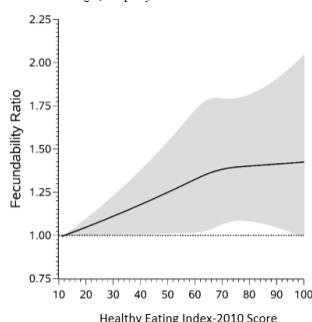
Role of physical activity in lowering racial inequalities in heart failure incidence: A Women's Health Initiative Study Sina Noshad* Sina Noshad Chanelle J Howe Michael J. LaMonte Charles B. Eaton

Background: African-American (AA) women have a higher risk of developing heart failure (HF) and on average, have lower levels of physical activity (PA). Given the etiologic role of physical inactivity on incident HF, longitudinal data from the Women's Health Initiative was used to investigate what proportion of racial inequality in HF incidence is mediated by PA.

Methods: Data were restricted to women with no missing values and negative HF history (12,557 AA and 120,476 Caucasian women). We defined HF as the first hospitalization episode. Death from any cause was considered a competing event. PA was defined as metabolic equivalent-hours per week (MET-h/wk). Covariates included demographic, lifestyle, and clinical factors. Given that many PA-HF confounders are affected by race, we used interventional analogs to the natural indirect effect (I-NIE) to estimate the proportion mediated (I-NIE/observed inequality). I-NIE was calculated by contrasting the 10-year HF risk among AAs under their observed PA distribution to their 10-year HF risk had these AAs had a PA distribution randomly chosen from PA levels among Caucasians. All confidence limits were calculated using the bootstrap method.

Results: During a median [lower quartile, upper quartile] follow-up of 8.0 [7.2, 9.0] years, 334 and 753 cases of HF and death occurred, respectively among AA women. Caucasians had higher levels of PA (median [lower quartile, upper quartile]: 9.0 [2.5, 18.6] vs 5.0 [0.7, 13.6] MET-h/wk). 10-year HF risk was 3.02% (95% CL: 2.69, 3.36) among AAs compared with 2.51% (95% CL: 2.40, 2.61) among Caucasians, showing observed inequality of 0.51 (95% CL: 0.16, 0.87). Changing the distribution of PA lowered 10-year HF risk by 0.20 (95% CL: 0.04, 0.36) among AAs suggesting that 39% (95% CL: 7.3%-117.7%) of the observed inequality may be mediated through PA.

Conclusion: Increasing PA levels among AA women to levels comparable with their Caucasian counterparts may reduce HF inequality by 39%.

The adverse impact of sleep quality on psychological resilience is buffered by the importance women place on healthy eating: an interaction analysis M Lauren Voss* Cheryl L Currie M Lauren Voss

Background: The ways in which women's daily habits may impact resilience is not well understood. The objective of this analysis was to examine how sleep quality over the past month may impact resilience among women, and how this association may by modified by the importance women place on healthy eating in their lives. Methods: This cross-sectional study collected in-person data from women living in a mid-sized city in western Canada in 2019 (N = 65; M age = 38 years). Resilience and sleep quality in the past month were measured using the Connor-Davidson Resilience Scale and the Pittsburgh Sleep Quality Index; respectively. One item assessed healthy eating importance (very important or less than very important). Linear regression models examined associations adjusted for age. Results: There was a significant interaction between sleep quality and the importance of healthy eating in a model that included these variables, their multiplicative interaction term, and age (standardized B = 0.8, p = 0.02). In a stratified model, sleep quality had no impact on resilience among women who reported healthy eating was very important in their lives (49% of sample; unstandardized B = 0.13, 95% CI -0.8, 0.6). Among women who reported that healthy eating was less than "very" important, every 1-point reduction in sleep quality was associated with a 0.8-point decrease in resilience (95% CI 1.4, 0.3). Sleep quality score explained 23% of the variance in resilience in this subgroup (R2 change = 0.23). Conclusions: In this community-based sample of women, placing an importance on healthy eating buffered the adverse impact that poor sleep quality had on psychological resilience.

Fig. 1: Associations between past-month sleep quality and resilience, stratified by healthy eating importance among women

blue = healthy eating "very" important,
red = healthy eating less than "very" important
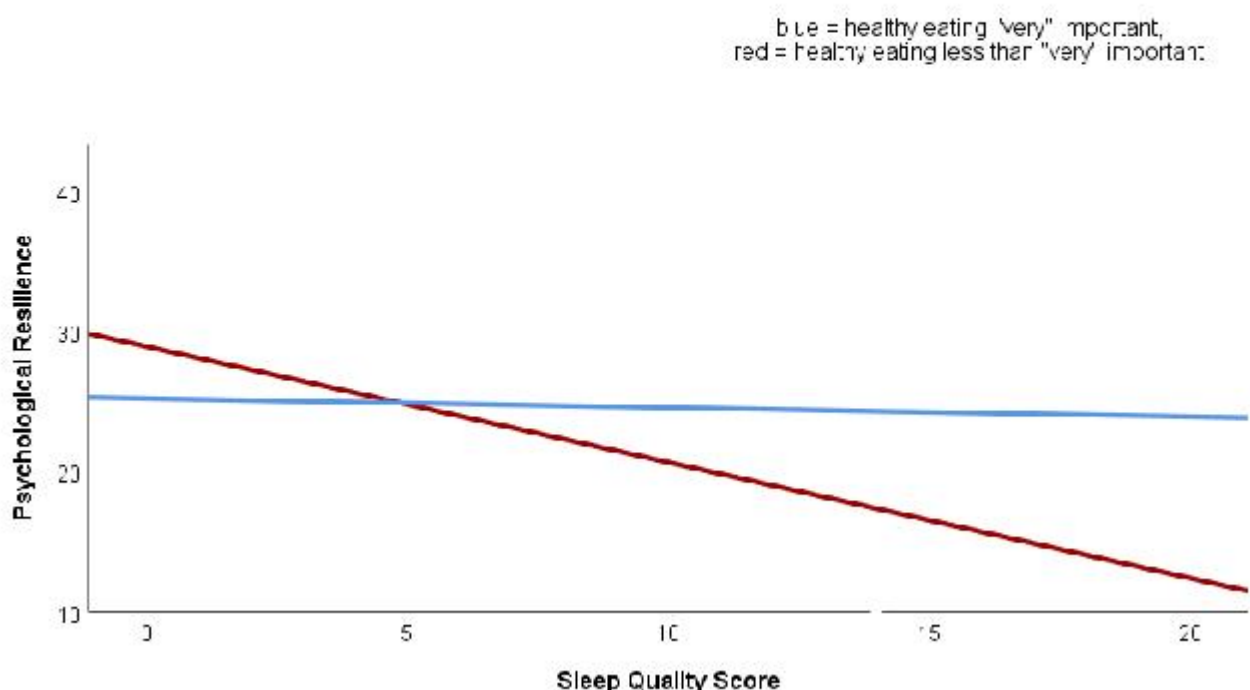
Interpregnancy interval and pregnancy outcomes: How important is the timing of confounding variable ascertainment? Laura Schummers* Laura Schummers Jennifer Hutcheon Wendy Norman Jessica Liauw Talshyn Bolatova Katherine Ahrens

Background: Estimation of causal effects of interpregnancy interval on pregnancy outcomes may be confounded by time-varying factors. These confounders should be measured at or before delivery of the first ("index") pregnancy, but are often only available at the subsequent pregnancy. Adjustment for confounders ascertained at the subsequent pregnancy may induce mediator adjustment or collider stratification bias. In this study, we quantify the bias induced by adjusting for time-varying confounders ascertained at the subsequent (rather than the index) pregnancy in estimated effects of interpregnancy interval on pregnancy outcomes.

Methods We analyzed linked records for all pregnancies in British Columbia, Canada, 2004-2014, to women with ≥2 singleton pregnancies (n=148,542). We used log binomial regression to compare short (<6, 6-11, 12-17-month) intervals to an 18-23-month reference for 5 outcomes: adverse fetal-neonatal composite; small-for-gestational age (SGA); preterm delivery (all, spontaneous, indicated). We calculated relative percent change between adjusted risk ratios (aRR) from two models with maternal age, low neighborhood income, body mass index, and smoking ascertained in the 1) index pregnancy and 2) subsequent pregnancy. We considered changes in aRR <5% minimal, 5-9% modest, and ≥10% substantial.

Results: Adjustment for confounders measured at the subsequent pregnancy modestly biased the fetal-neonatal composite aRR toward the null at <6 months (-6.3% change) and minimally biased the aRRs toward the null at 6-11 (-2.3%) and 12-17-months (-0.5%). For SGA, aRRs were minimally biased toward the null (from -0.9% to -0.4%); for preterm birth, aRRs were minimally biased away from the null (from 0.1% to 0.3% for spontaneous and 1.1% to 1.9% for indicated preterm).

Conclusion: Adjusting for time-varying confounders ascertained at the subsequent pregnancy induced minimal to modest bias in estimated effects of short interpregnancy interval on pregnancy outcomes.
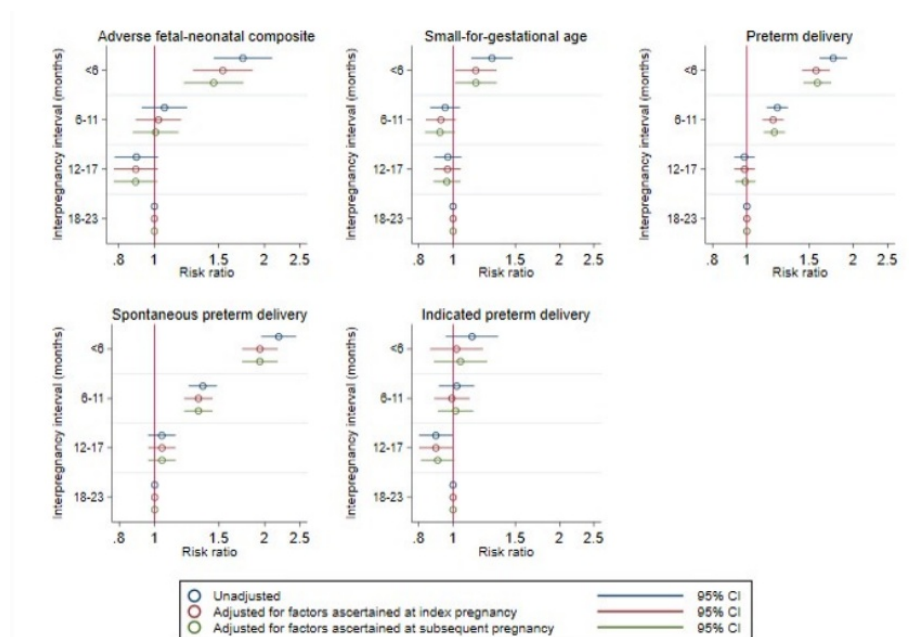
Increased Risk of Gestational Diabetes in Twin Pregnancies is Not Primarily Mediated by Gestational Weight Gain Michelle Dimitris* Michelle Dimitris Jay Kaufman Lisa Bodnar Robert Platt Katherine Himes Jennifer Hutcheon

Gestational diabetes, or glucose intolerance during pregnancy, is up to three times more common in twin versus singleton pregnancies. Although gestational weight gain is a known modifiable cause of gestational diabetes, and gestational weight gain is higher among twins, the extent to which increased gestational weight gain explains the relationship between plurality and gestational diabetes is unknown. We evaluated the extent to which increased risk of gestational diabetes in twin pregnancies is mediated by increased gestational weight gain. We leveraged previously-collected serial weights and glucose screening/diagnostic data abstracted from medical charts for 1397 twin and 2622 singleton pregnancies with normal or overweight pre-pregnancy body mass index (BMI) delivered between 1998 and 2013 at Magee Women's Hospital in Pittsburgh, Pennsylvania. We used causal mediation analyses to estimate natural indirect and direct effects, or those mediated and not mediated by gestational weight gain, respectively. We found that although odds of gestational diabetes were higher among twin pregnancies [marginal total effect=2.83 (95% CI 1.55;5.17) for normal weight and 2.10 (95% CI 1.17;3.75) for overweight pre-pregnancy BMI], there is limited evidence that this relationship is mediated by gestational weight gain [natural indirect effect=1.21 (95% CI 0.95;1.54) for normal weight and 1.06 (95% CI 0.90;1.24) for overweight pre-pregnancy BMI], and more evidence of mediation via other mechanisms [natural direct effect=2.34 (95% CI 1.25;4.39) for normal weight and 1.99 (95% CI 1.10;3.61) for overweight pre-pregnancy BMI]. We conclude that, while twin pregnancies experience nearly 200% increased risk of gestational diabetes relative to singletons, only approximately 10% of this is mediated by gestational weight gain. We recommend research that investigates alternative mechanisms, as well as the role of gestational weight gain in causing gestational diabetes specifically among twins.
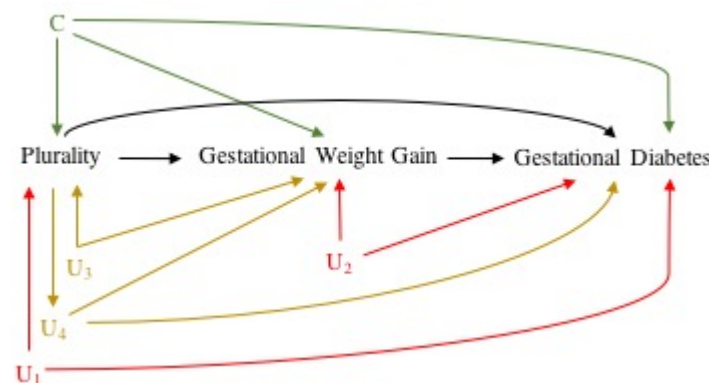
Fetal death as a competing risk for early neonatal death in California, 1989-2015 Tim Bruckner* Tim Bruckner Samantha Gailey Abhery Das Alison Gemmill Joan Casey Ralph Catalano Gary Shaw Jennifer Zeitlin

Introduction: Extremely preterm births (i.e., <28 weeks gestational age [GA]) account for less than 1% of all live births but over 40% of neonatal deaths. Some scholars argue that all fetuses which pass through a particular GA "starting point" represent a risk set of gestations at risk of ending with a neonatal death. Others, however, recommend against treatment of fetal death and early neonatal death as a composite indicator of competing risks. If the competing risk argument holds at the population level, then the risk of early neonatal death in the extremely preterm period should fall in pregnancy cohorts in which the risk of fetal death rises. We test this hypothesis in California over a 26-year period. Methods: We retrieved fetal death, live birth and infant death information on 89,276 extremely preterm deliveries from California linked birth and infant death cohort file, 1989 to 2015. Given well-documented differences in risk of fetal and early neonatal death by race/ethnicity and fetal sex, we stratified cohorts by maternal race/ethnicity and sex of gestation. We used ARIMA time-series methods to identify and remove well-documented patterns in neonatal death before calculating the cross-correlation coefficient between fetal and early neonatal death. Results: The cross-correlation coefficient is negative and shows a confidence interval (CI) that does not contain 0 (coef. = -.27, 95% CI= -.11, -.42). This inverse correlation indicates that, among extremely preterm deliveries, elevated fetal deaths in a particular year correspond with fewer early neonatal deaths among live births. Discussion: Elevated fetal death correlates with improved survival among live-born cohorts delivered extremely preterm in that same year. Findings support the competing risk hypothesis and should encourage inclusion of fetal deaths into cohort analyses of the etiology of neonatal death.
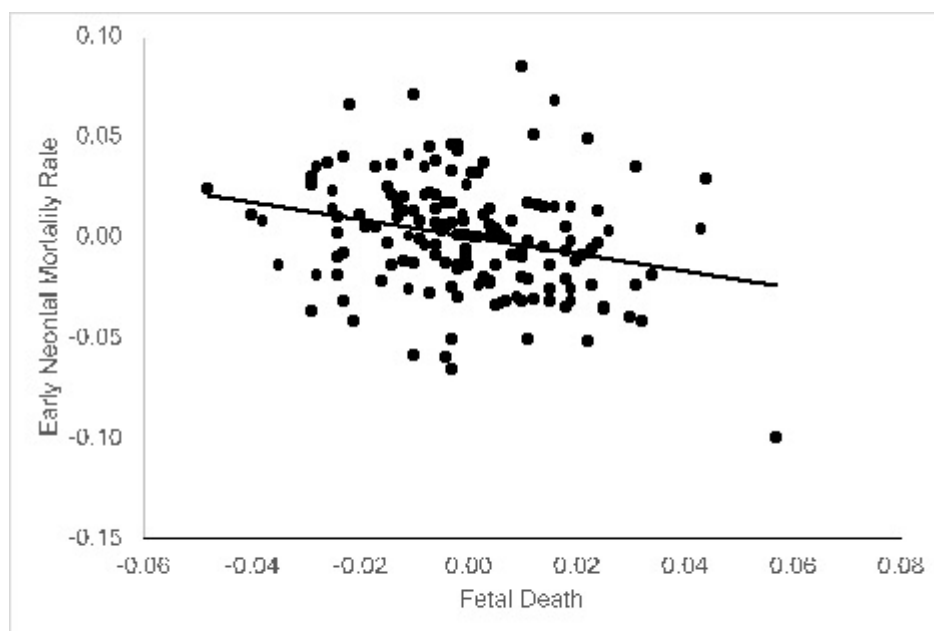
Figure 3: Scatter plot and best fitting line of detrended incidence of fetal death and early neonatal death for extremely preterm deliveries across 156 race/ethnicity-sex-year cohorts, 1989-2015.

Prospective Associations of Neighborhood Child Opportunity Index with Adolescent Cardio-metabolic Risk Izzuddin M Aris* Izzuddin Aris Sheryl L. Rifas Shiman Ling-Jun Li Marcia P. Jimenez Marie-France Hivert Emily Oken Peter James

Objectives
The Child Opportunity Index (COI) is a publicly available surveillance tool that incorporates both traditional (e.g. household income) and novel (e.g. access to health care facilities) attributes of neighborhood-based resources that may promote or inhibit healthy child development. The extent to which COI relates to individual-level cardio-metabolic outcomes later in life remains unclear. We investigated this relationship in Project Viva, a pre-birth cohort from eastern Massachusetts.

Methods
We geocoded residential addresses obtained from 995 participants in mid-childhood (mean 7.9 years) and linked each location with census-tract level COI data. We measured the change in cardio-metabolic outcomes from mid-childhood (between 2007 and 2010) to early adolescence (between 2012 and 2016; mean 13.1 years) and analyzed their associations with neighborhood-level COI in mid-childhood using mixed-effects models, adjusting for individual/family socio-demographics including race/ethnicity, sex, biparental educational level, household income, and maternal marital status.

Results
In mid-childhood, 37% (n=370) resided in areas of "very high opportunity" (COI score >80th percentile) while 14% (n=144) resided in areas of "very low opportunity" (COI score <20th percentile). Children who resided in areas of higher overall neighborhood opportunity in mid-childhood exhibited smaller gains in total fat-mass index (β -0.54 kg/m2 per 1-SD increase in COI; 95% CI -1.09,0.01), trunk fat-mass index (-0.33 kg/m2; -0.60,-0.06) and metabolic risk score (-0.16 SD units; -0.40,0.08) from mid-childhood to early adolescence. These associations were driven by certain components of COI such as proximity to high-quality childhood education centers and health care facilities.

Conclusion
Our findings suggest that more favorable neighborhood opportunities, reflected by the COI, in mid-childhood predict better cardio-metabolic health outcomes in early adolescence.
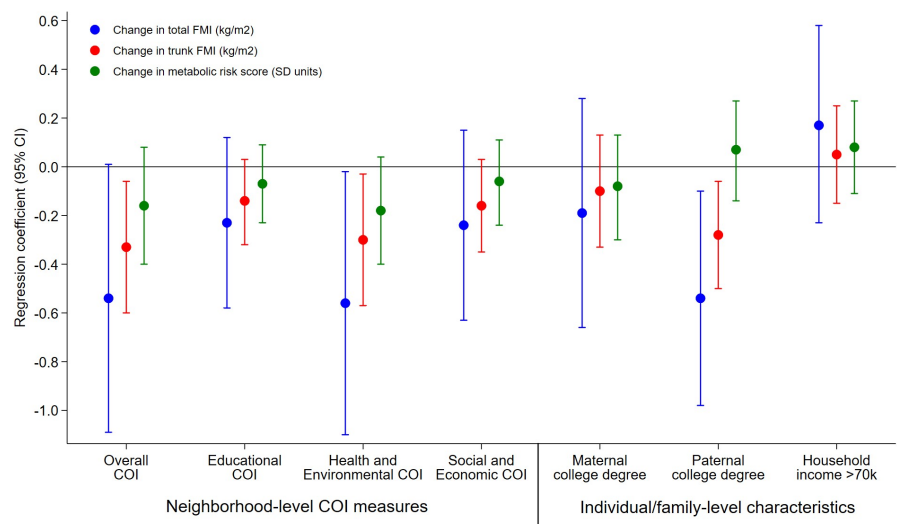
Examining variations in child development outcomes by gestational age at delivery among term births Jessica L. Gleason* Jessica Gleason Stephen E. Gilman Rajeshwari Sundaram Edwina Yeung Diane Putnick Yassaman Vafai Katherine L. Grantz

While preterm delivery is a known developmental risk factor, few studies have examined whether variation in gestational age at delivery among term births has any bearing on children's neurocognitive development. Children in the Collaborative Perinatal Project (CPP) were assessed for mental and psychomotor development at 8 months using the Bayley Scales of Development, 4 years using the Stanford Binet IQ (SBIQ) domains, and 7 years using the Wechsler Intelligence Scale for Children (WISC) and the Wide Range Achievement Test (WRAT). In adjusted linear mixed models using generalized estimating equations to account for sibling clusters, mean development scores were generally higher with each week of gestation from 37 weeks, with peaks at 40 or 41 weeks and declines in the post-term period (42+) (Figure 1). Delivery at 40 weeks was the reference group for all analyses. Children delivered at 39 weeks had lower Bayley mental (-0.77; 95% CI -1.38, -0.16) and psychomotor (-1.30; 95% CI -2.05, -0.55) scores, as well as lower WRAT spelling (-0.57; 95% CI -1.15, -0.01) and reading (-0.97; 95% CI -1.70, -0.25) scores. WISC scores did not vary by gestational age except at 37 weeks for verbal (-1.22; 95% CI -2.14, -0.30), performance (-1.43; 95% CI -2.48, -0.38), and full-scale IQ (-1.78; 95% CI -2.77, -0.79). In Poisson regression, children delivered at 37 and 38 weeks were also at higher risk for having below average scores on all domains across assessment times. Those delivered at 38 weeks had higher risk of being classified as suspect or abnormal on Bayley (RR=1.38; 95% CI 1.20, 1.59) and higher risk of scoring below average on the SBIQ (RR=1.12; 95% CI 1.01, 1.26) and WRAT spelling (RR=1.22; 95% CI 1.08, 1.38) and math (RR=1.20; 95% CI 1.04, 1.38) tests. While small, the improvement in development scores across assessment periods indicates that each week up to 40 or 41 weeks of term gestation is important for cognitive development.
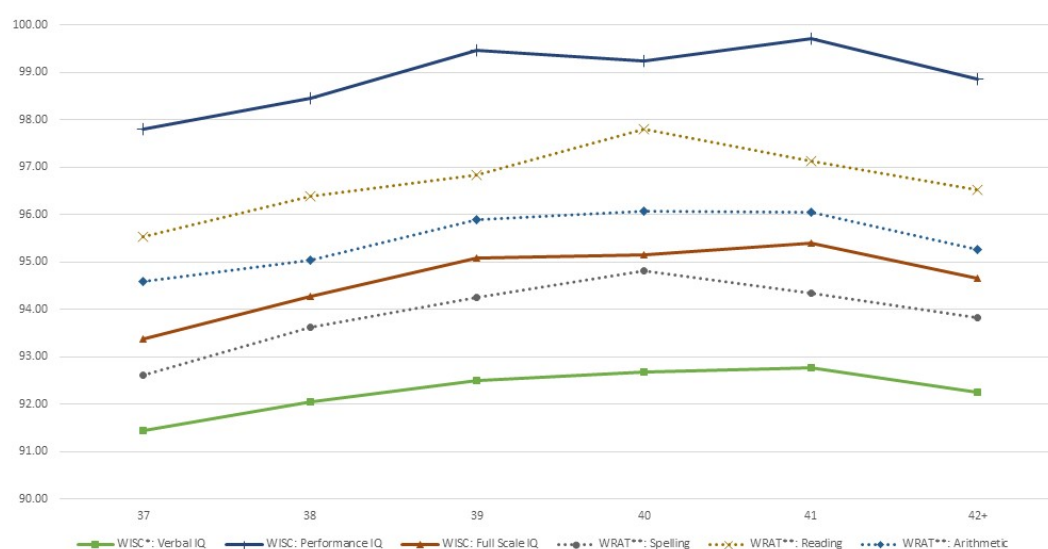

Figure 1. Adjusted mean scores for 7-year outcomes by gestational age.

Cancer

Coffee Intake and CRC Incidence and Mortality According to T-cell Response in Tumor Tissue

Tomotaka Ugai* Tomotaka Ugai Koichiro Haruki Rong Zhong Kenji Fujiyoshi Naohiko Akimoto Tzuu-Wang Chang Juha P Väyrynen Junko Kishikawa Kota Arima Shan-shan Shi Melissa Zhao Mai Chan Lau Marios Giannakis Jonathan A. Nowak Jeffrey A Meyerhardt Molin Wang Charles S. Fuchs Shuji Ogino

Observational studies have found conflicting evidence on the association between coffee consumption and the incidence and prognosis of colorectal cancer (CRC). While previous studies suggested that coffee influence adaptive immune response, the human data linking coffee to tumor immune response in CRC are lacking. We therefore hypothesized that the associations between coffee intake and CRC incidence and mortality may differ by immune cell densities in CRC tissue. During follow-up of 133,924 participants (3,585,019 person-years) in the Nurses' Health Study and Health Professionals Follow-up Study, we documented 908 CRCs with available data on T-cell densities in tumor tissue. We examined a differential association between coffee intake and the risk of CRC classified by T-cell densities (CD3+, CD4+, CD8+, CD45RO+ (PTPRC), and FOXP3+). We also evaluated a differential association between postdiagnosis coffee intake and CRC survival among documented CRC cases. Using covariate data of 4,420 CRC cases in total, inverse probability weighted Cox proportional hazards model was used to control for selection bias due to tissue availability and potential confounders, including stage, MSI status, KRAS, BRAF, and PIK3CA mutations. We did not observe a significant association between coffee intake and the risk of CRC incidence (Ptrend = 0.54). Differential associations between coffee intake and CRC by T-cell subset was not observed (Pinteraction > 0.30). Furthermore, there was no significant association of postdiagnosis coffee intake with the risk of CRC specific mortality for all cases (Ptrend = 0.85) or by each T-cell subset (Pinteraction > 0.10). Contrary to our hypotheses, the associations of coffee intake with CRC incidence and mortality did not significantly differ by T-cell densities in CRC. In this study, there is no sufficient evidence to conclude that coffee differentially influences the risk and mortality of CRC subtypes classified by T-cell infiltrates in tumor.

Gestational diabetes and young-onset breast cancer Kimberly A. Bertrand* Kimberly A. Bertrand Katie M. O'Brien Lauren B. Wright Julie R. Palmer William J. Blot A. Heather Eliassen Lynn Rosenberg Sven Sandin Wei Zheng Anthony J. Swerdlow Minouk J. Schoemaker Hazel B. Nichols Dale P. Sandler

Type 2 diabetes is associated with an estimated 20% increase in the risk of breast cancer. Gestational diabetes mellitus (GDM) may also impact breast cancer risk, particularly in young women, but results of the few prospective cohort studies are conflicting. To evaluate the association of self-reported history of GDM and young-onset breast cancer, we pooled data from >200,000 women aged 55 or younger from five cohorts (Black Women's Health Study, Nurses' Health Study II, Sister Study, Southern Community Cohort Study, and Women's Lifestyle and Health Study). Among parous women, we identified 4,889 incident breast cancer diagnoses over a mean follow-up of 14 years (0.1-24 years). We fit multivariable Cox proportional hazards regression models to estimate HRs and 95% CIs for risk of all breast cancer, invasive breast cancer, and breast cancer subtypes (estrogen receptor [ER] positive or negative), separately, in relation to history of GDM in any pregnancy. We used age as the time scale and stratified by study, adjusting for race, education, age at first birth, and body mass index at ages 18-24. Women accrued person-time from study entry until breast cancer diagnosis, study end, or age 55 years, whichever occurred first. Compared with parous women without GDM, parous women with a history of GDM were not at increased risk of breast cancer overall (HR: 0.90; 95% CI: 0.78, 1.03). Compared with nulliparous women, women with a history of GDM had a decreased risk of breast cancer overall (HR: 0.78; 95% CI: 0.67, 0.91); this decreased risk was restricted to ER+ breast cancer (HR: 0.81; 95% CI: 0.65, 1.00). Results of this analysis do not support the hypothesis that history of GDM is a risk factor for breast cancer in women under age 55. An inverse association of parity with ER+ breast cancer risk has been established, and our results suggest that the protective effect of parity on breast cancer risk persists even for pregnancies complicated by GDM.

Cancer

Comparative validation of the BOADICEA and Tyrer-Cuzick breast cancer risk models incorporating polygenic risk in a UK-based prospective cohort Parichoy Pal Choudhury* Parichoy Pal Choudhury Mark N. Brook Amber N. Wilcox Andrew Lee Penny Coulson Minouk Schoemaker Michael E. Jones Anthony J. Swerdlow Nilanjan Chatterjee Antonis C. Antoniou Montserrat Garcia-Closas

Background: The Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm (BOADICEA) model, originally developed to predict breast cancer risk for women with family history of breast cancer, has recently been extended to include reproductive and lifestyle factors and a 313-variant polygenic risk score (PRS) for applications in the general and high-risk populations. We conducted a comparative validation of the extended model with the Tyrer-Cuzick model including PRS in a population-based prospective cohort.

Methods: Five-year risks from both models were prospectively evaluated, separately for women younger and older than 50 years, in a nested case-control sample (619 cases, 718 controls) of women of European ancestry aged 23-75 years from the UK-based Generations Study. Calibration was assessed in terms of relative and absolute risk by comparing predicted and observed quantities overall and within risk categories. Discrimination was assessed using the Area Under the Curve (AUC).

Results: The original and extended BOADICEA models were well calibrated, particularly for women at the highest risk decile: expected to observed ratio (E/O) = 0.97 (95% CI = 0.62 to 1.53) and 1.09 (0.76 to 1.55) for younger and older women, respectively. Adding risk factors and PRS improved risk discrimination of the original model modestly in younger women (AUC 69.7% vs. 69.1%) and substantially in older women (AUC 64.6% vs. 56.8%). The Tyrer-Cuzick model with PRS showed similar risk discrimination (AUC 69.4% and 63.9% for younger and older women, respectively); but overestimated risk for women in the highest risk decile: E/O=1.54 (0.98 to 2.41) for younger and 1.73 (1.21 to 2.48) for older women.

Conclusion: The extended BOADICEA model identified women at elevated risk in a UK population more accurately than the Tyrer-Cuzick model with PRS. These analyses can inform choice of risk models for risk stratified breast cancer prevention among women of European ancestry.

Figure 1: Calibration and discrimination of five-year risk predictions of breast cancer for (A) women younger than 50 years and (B) women 50 years or older in the nested case-control sample of the GS cohort with risk categories based on deciles of five-year absolute risk.

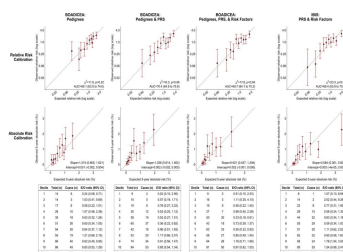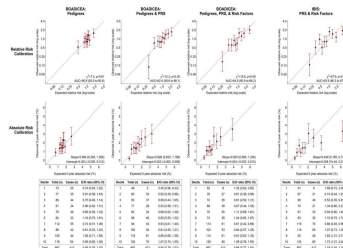AUC = area under the curve, GS = Generations Study, χ² = chi-square test, BOADICEA = Breast and Ovarian Analysis of Disease Incidence and Carrier Estimation Algorithm, PRS = polygenic risk score, E/O = expected to observed number of cases, CI = confidence interval.

Cancer

Trends in PSA Testing Across Nine Healthcare Delivery Systems Mara Epstein* Mara Epstein Hassan Fouayzi Richard Krajenta Stacey A. Honda Matthew P. Banegas Alanna K. Rahm Pamala A. Pawloski Debra P. Ritzwoller Robert T. Greenlee Lawrence H. Kushi R. Yates Coley Christine Y. Lu Christine Neslund-Dudas

Background: US Preventive Services Task Force (USPSTF) guidelines increasingly discouraged prostate-specific antigen-based (PSA) screening for prostate cancer in 2008 and 2011, despite evidence suggesting a benefit in high-risk men (e.g. African-Americans). We evaluated temporal trends in PSA testing using longitudinally-collected electronic health data from nine large, geographically diverse US healthcare delivery systems participating in the Cancer Research Network between 2000 and 2016.

Methods: Eligible men were 40-80 years old, without prostate cancer, and sought care at one of the healthcare systems. We identified one PSA test per person per year to approximate annual screening. PSA tests were identified in claims data by procedure (CPT) codes 84152, 84153, 84154, and G0103. Men were censored at prostate cancer diagnosis, disenrollment, death, or end of follow-up (December 31, 2016). Rates were examined by age group (40-54, 55-69, 70-80) and race (African-American, white, other). Joinpoint analysis examined changes in PSA testing over time overall and by age group and race.

Results: Across the nine sites, 926,871 men had at least one PSA test during the study period (42% of eligible men). Of those men, 61.4% were white, 4.6% African-American, and 34% men of other/unknown race. Most men were 40-69 years old (88%). All sites reported steady or increasing rates of PSA testing from 2000-2010, followed by a decline among all age and race groups from 2011-2016. Joinpoint analysis identified declines in PSA use from 2007-10 (Annual Percent Change [APC]=-0.98) and 2010-16 (APC=-8.71) in all men. Large declines in PSA use were observed from 2010-16 (APC=-10.19) in African-American men and 2009-16 (APC=-9.02) in white men.

Conclusion: This analysis of real-world electronic health data from nine large healthcare systems observed decreasing use of PSA testing from 2000 to 2016 among all men, with large declines in the years following changes to USPSTF recommendations.

Cancer

Global mental and physical health and 5-year mortality among older, long-term cancer survivors Chelsea Anderson* Chelsea Anderson Susan Gapstur Corinne Leach David Cella Lauren Teras

Brief measures of self-reported health have been associated with mortality in general population cohorts. However, little research has investigated whether such measures predict survival among people with a cancer history. We estimated associations between short mental and physical health measures and 5-year mortality among older, long-term cancer survivors (≥5 years post-diagnosis). Participants in these analyses were enrolled in the Cancer Prevention Study (CPS)-II Nutrition Cohort in 1992/1993 and had an incident cancer diagnosis as of 2006 (N=9,979). In 2011, global mental and physical health were assessed based on an adaption of four-item PROMIS® measures. Responses were summed, and scores of at least one standard deviation below the overall sample mean were considered to reflect poor health. Deaths through 2016 were ascertained via linkage with the National Death Index. We estimated age- and sex-adjusted hazard ratios (HRs) for all-cause mortality and subdistribution hazard ratios (sHRs) for cancer- and cardiovascular disease(CVD)-specific mortality within 5 years of survey. The median age among survivors at survey was 80 years (IQR=76-84), and 26% died within 5 years. Poor mental health (HR=2.40; 95% CI: 2.20-2.62) and poor physical health (HR=2.71; 95% CI: 2.49-2.93) were strongly associated with 5-year all-cause mortality. Associations were stronger for CVD-specific (mental sHR=1.90; physical sHR=2.17) than cancer-specific (mental sHR=1.22; physical sHR=1.74) mortality. In analyses according to cancer type, magnitudes of association for all-cause mortality were greatest for poor mental health among prostate cancer survivors (HR=2.68) and for poor physical health among lung cancer survivors (HR=3.80). Poor mental and physical health, as assessed by 4-item measures, were highly predictive of 5-year mortality in this sample of older, long-term cancer survivors. These measures may be clinically useful to help identify at-risk cancer survivors.

What quacks like a confounder and walks like an instrument? Michael A Webster-Clark*
Michael Webster-Clark Charles Poole

Directed acyclic graphs (DAGs) are potent tools for epidemiologists. Graphical rules for identifying minimally sufficient adjustment sets showed key exceptions to older definitions of confounders. That said, DAGs can be misleading when targeting specific populations. For example, researchers using propensity scores to estimate average treatment effects in the treated (ATT) may include variables associated with the outcome only in the treated (e.g. drug-drug interactions, hypersensitivity) in their models based on a DAG.
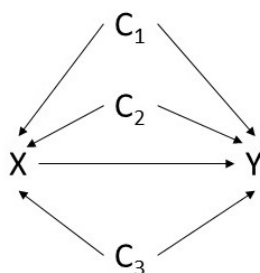
We aimed to show that such variables act like instruments for the ATT in that adjusting for them amplifies variance and unmeasured confounding.

We simulated populations with three independent binary variables (C1, C2, and C3), a treatment X, and an outcome Y. The probability of receiving X was a linear function of C1, C2, and C3, and the probability of experiencing Y was a linear function of C2, C3, and an interaction between X and C1. This interaction meant that C1 was associated with the outcome only in the treated, akin to an allergy to X. Figure 1 presents three DAGs: one for the full population, one for the treated, and one for the untreated.

Adjusting for C1 always amplified unmeasured confounding in and variance of ATT estimates. In one simulation with a true risk difference (RD) of 7.0%, the estimated RD after weighting the untreated to the treated based on C1 and C2 was 9.6% with a 95% confidence limit difference (CLD) of 2.8%, while the RD adjusting for C2 alone was 9.1% (CLD of 2.4%); adjusting for C1 amplified unmeasured confounding from C3 by 24%. Adjusting for C1, C2, and C3 yielded an unbiased RD with a CLD of 3.4% while adjusting for only C2 and C3 yielded an unbiased RD with a CLD of 2.6%. However, even a weak effect of C1 on Y reversed these results.

Confounders like C1 that are associated with the outcome only in the treated should be adjusted for when estimating population average treatment effects but act as instruments for the ATT.

A) Full population DAG   B) X=1 population DAG   C) X=0 population DAG
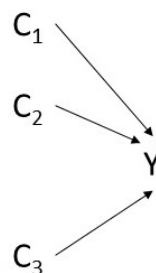
Regression model for the lifetime risk based on pseudo-values Sarah Conner* Sarah Conner Ludovic Trinquart

The lifetime risk measures the cumulative risk for developing a disease over one's lifespan. Regression modeling for the lifetime risk requires accounting for delayed entries, the semi-competing risk of death, and inference at a fixed timepoint. In addition, covariates may be associated with the cumulative incidence function but not with the lifetime risk. The Fine and Gray model ass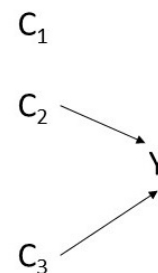umes proportional subdistribution hazards, thus predictions of the lifetime risk may be biased when the assumption is violated. We introduce a novel method to model the lifetime risk based on pseudo-values.

We define the pseudo-values of the Aalen-Johansen estimator at a fixed time point and accounting for delayed entry. We regress the logit-transformed pseudo-values on covariates with a generalized linear model. We derive the difference in lifetime risk and 95% confidence intervals with the multivariate delta method. We compared the performance of our method with the Fine and Gray model and with the Royston-Parmar flexible parametric model. We simulated semi-competing risks data with non-proportional subdistribution hazards. We estimated the mean bias, mean relative bias, mean squared error, and coverage for all methods, as well as the Type I error and power for the proposed method. Under the conditions of our simulation studies, we observed that our method performed well in all criteria in the majority of scenarios, and outperformed the other methods in scenarios with smaller sample size, greater delayed entry, and greater right censoring. Figure 1 depicts the mean bias across all scenarios and methods. Our method also demonstrated appropriate Type I error and high power. We illustrate our model by modeling the lifetime risk of atrial fibrillation in the Framingham Heart Study.
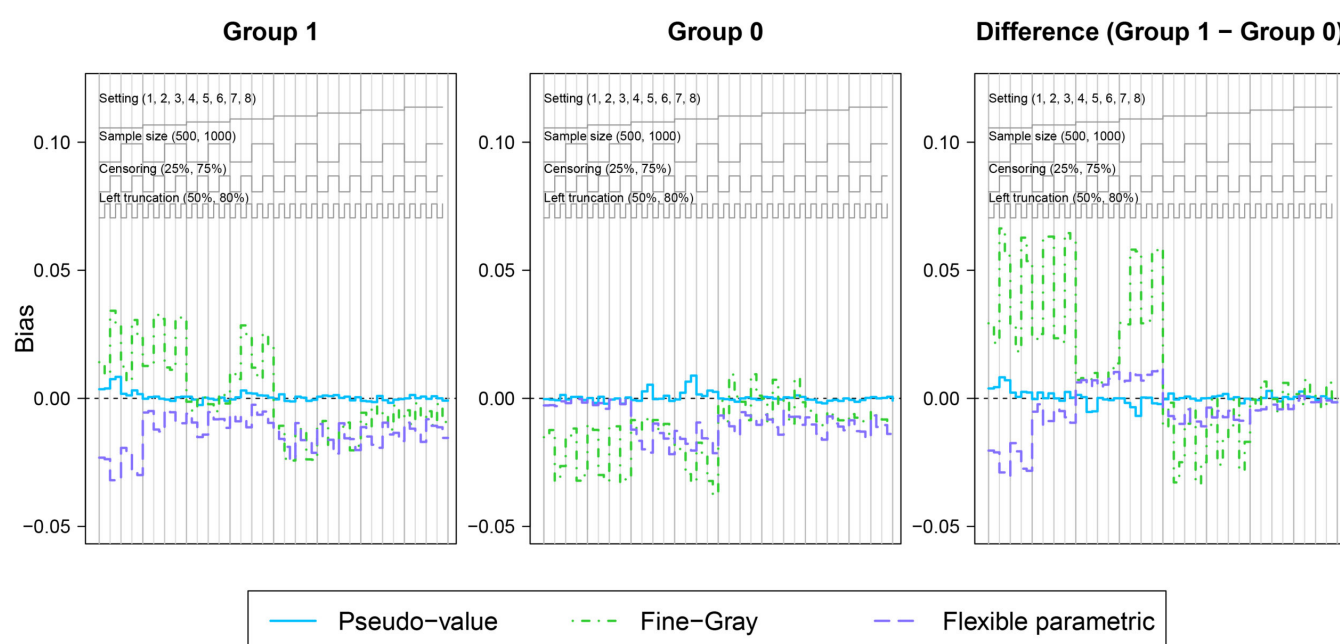
Leveraging the causal effects of stochastic interventions to evaluate vaccine efficacy in two-phase trials Nima Hejazi* Nima Hejazi Mark van der Laan David Benkeser Holly Janes Peter Gilbert

Causal inference has traditionally focused on the effects of static interventions, under which the magnitude of the treatment is set to a fixed, prespecified value for each unit. The evaluation of such interventions faces a host of issues, among them non-identification, violations of the assumption of positivity, and inefficiency. Stochastic interventions provide a promising solution to these fundamental issues by allowing for the target parameter to be defined as the mean counterfactual outcome under a hypothetically shifted version of the observed exposure distribution. Despite the promise of such approaches, real data analyses are often further complicated by economic constraints, such as when the primary variable of interest is far more expensive to collect than auxiliary covariates. Two-phase sampling schemes are often used to bypass such limitations – unfortunately, their use produces side effects that require further adjustment when formal statistical inference is the principal goal of a study. We present a novel approach for use in such settings: augmented targeted minimum loss and one-step estimators for the causal effects of stochastic interventions, with guarantees of consistency, efficiency, and multiple robustness even in the presence of two-phase sampling. We further propose a technique that utilizes the estimated causal effects of stochastic interventions to construct a nonparametric working marginal structural model to summarize the effect of shifting an exposure variable on the outcome of interest, analogous to a dose-response analysis. Using data from the recent HVTN 505 HIV vaccine efficacy trial, we demonstrate this technique by assessing the effects of changes in post-vaccination immunogenicity on HIV-1 acquisition across a range of possible shifts, outlining a highly interpretable variable importance measure for ranking multiple immune responses based on their utility as immunogenicity study endpoints in future HIV-1 vaccine trials.

TML estimates of mean counterfactual HIV-1 infection risk under shifted CD8+ polyfunctionality with pointwise confidence intervals and summarization via working marginal structural model ($\hat{\beta}_{TMLE}$ =-0. 013)
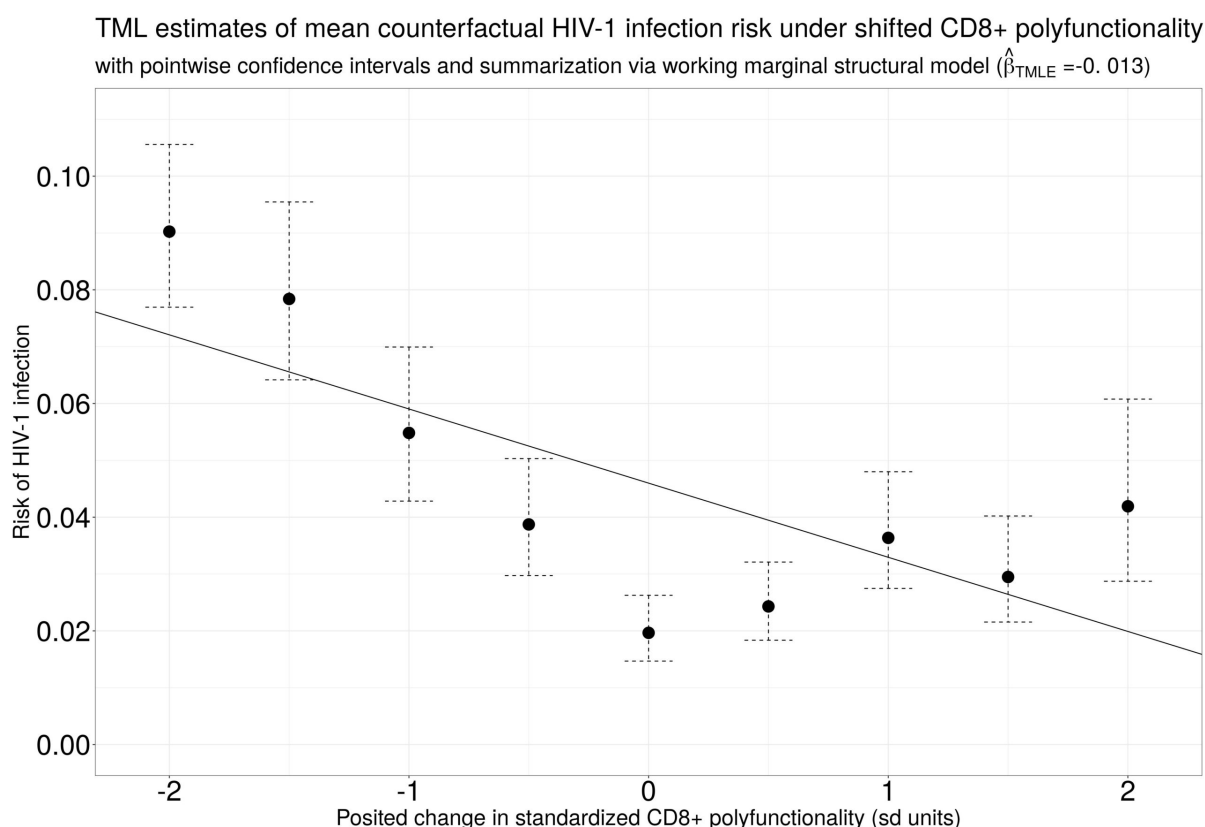
Comparing the performance of non-parametric doubly robust estimation to parametric doubly and singly robust estimation Jacqueline Rudolph* Jacqueline Rudolph Ashley Naimi

Inverse probability weighting (IPW) and g-computation are two singly robust methods that can be used to estimate the causal effect of an exposure on an outcome, in the presence of time-varying confounding, given certain assumptions have been met. One assumption is that the models are correctly specified. Both IPW and g-computation require the use of parametric, which may be misspecified. Nonparametric machine learning approaches can relax this assumption but do not work with singly robust approaches due to the curse of dimensionality. In contrast, machine learning can be used with double-robust methods, like augmented IPW and targeted minimum loss-based estimation (TMLE). However, nonparametric methods are less efficient than parametric methods when the latter are correctly specified. We sought to compare the performance of nonparametric TMLE against parametric TMLE, g-computation, and IPW with a survival outcome and time-varying confounding. We generated 200 simulations of 1000 individuals, who were followed over 5 time-points. Each individual was assigned a binary exposure, confounder, and outcome at each time-point. We estimated risk functions had all participants always been exposed versus never been exposed, and we quantified the risk difference at the end of follow-up. See the Figure for distributions of those risk differences for each approach. We found that all methods had low bias (<0.007) relative to the true risk difference of 0.236. IPW had the smallest average standard error (0.028), followed by g-computation (0.054) then parametric TMLE (0.055) and nonparametric TMLE (0.055). IPW was most efficient, but it was the only approach with less than nominal 95% confidence interval coverage (90.5%). This simple simulation demonstrates little cost of using a nonparametric double robust approach relative to the parametric options. More complex simulation settings may reveal alternative tradeoffs between parametric and nonparametric methods.
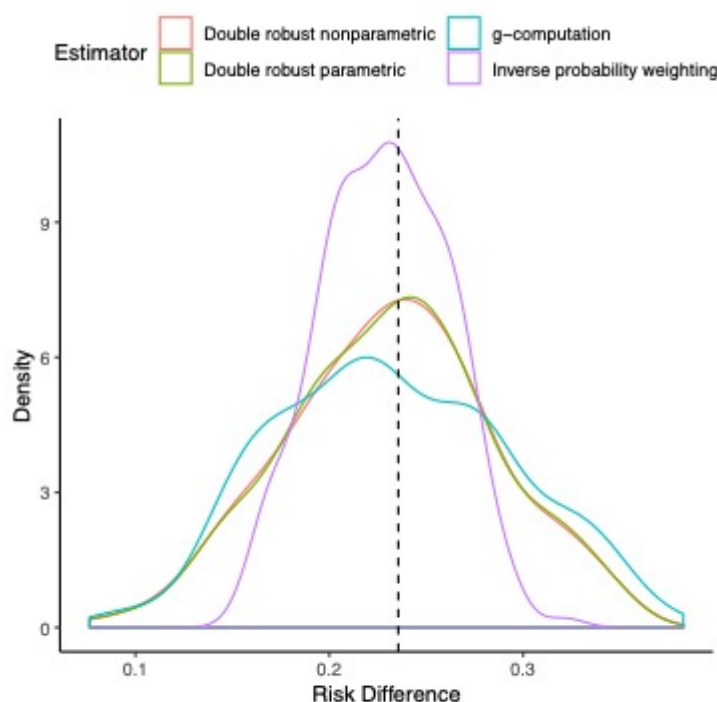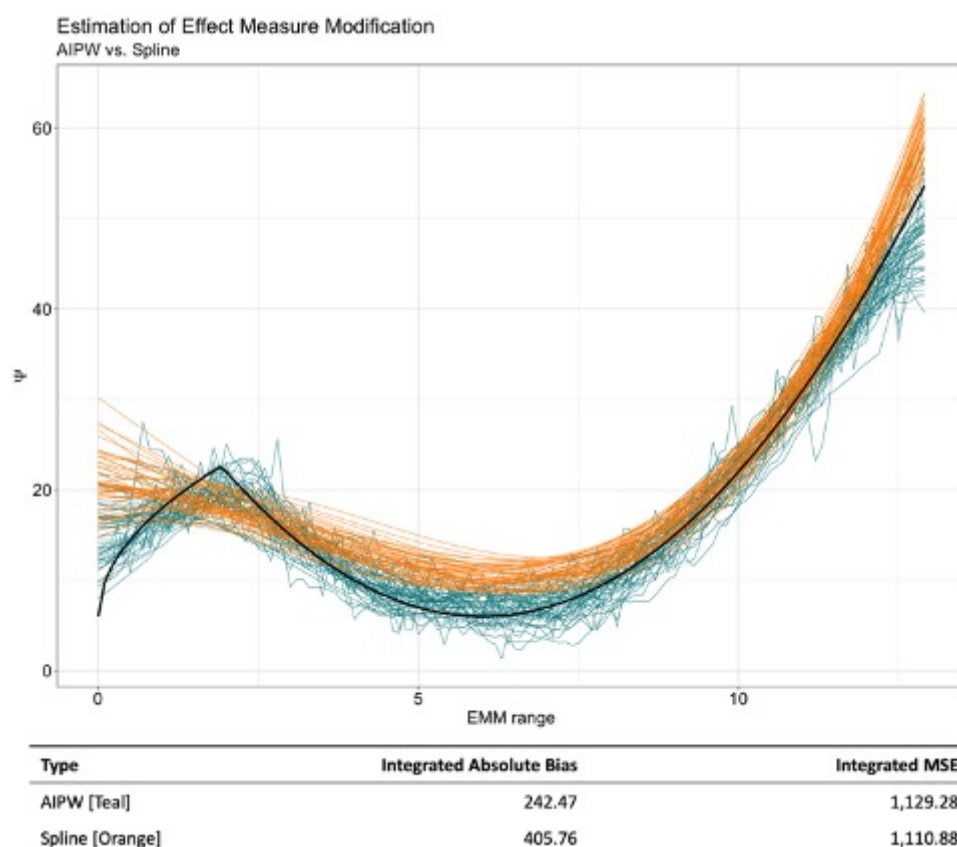

Figure. Distribution of risk difference estimates from the 200 simulations by estimator. The dashed line represents the true risk difference.

Non-parametric doubly robust estimators to evaluate effect measure modification Gabriel
Conzuelo* Gabriel Conzuelo Ashley Naimi Edward Kennedy Lisa Bodnar Abdus Wahed Maria Brooks

Evaluating effect measure modification (EMM) is subject to sample size limitations, even when
parametric models are used. Compared to correctly specified parametric models, doubly robust (DR)
nonparametric methods are less efficient. The extent to which this affects EMM estimation is
unknown. We simulated data to evaluate the tradeoff between parametric and non-parametric
methods for EMM with binary and continuous effect modifiers. Two independent standard normal
confounders were used to simulate a binary exposure and EMM, each with a marginal probability of
0.5. We generated a continuous outcome to yield a mean difference of 6 and 3 in each EMM stratum.
In binary case, each dataset was analyzed with: generalized linear model (GLM) with interaction
term (correct model); stratified GLM; targeted minimum loss-based estimation (TMLE); and
augmented inverse probability weighting (AIPW). In continuous case, the effect modifier was drawn
from a conditional uniform distribution, and the outcome was generated to have a complex
functional form as depicted via the black line in Figure 1. Continuous EMM data were analyzed with
a GLM including restricted cubic splines, and a DR influence function based estimator similar to
AIPW. All DR methods were fit using the SuperLearner. Performance was judged in terms of bias
(i.e. average of all estimates minus true value) for binary and continuous cases, and efficiency (i.e.
average of all SE divided by the SD of all estimates) for binary case. As expected, GLMs were
unbiased and fully efficient in both EMM strata. TMLE bias was 0.22 and 0.02, with efficiency of
0.65 and 1.84 in EMM stratum 0 and 1, respectively. AIPW was unbiased in both EMM strata, with
efficiency of 1.84 and 2.50 in EMM stratum 0 and 1, respectively. In the continuous EMM,
integrated absolute bias was lower with AIPW (242.5) compared to GLM (405.8). Results suggest
that both AIPW and TMLE are unbiased but less efficient than correct GLM model.

Estimation of Effect Measure Modification
AIPW vs. Spline

Type	Integrated Absolute Bias	Integrated MSE
AIPW [Teal]	242.47	1,129.28
Spline [Orange]	405.76	1,110.88

TMAO and cognitive function in the Boston Puerto Rican Health Study Tahani Boumenna*
Tahani Boumenna Tammy Scott Natalia Palacios Katherine L. Tucker

Background: Trimethylamine N oxide (TMAO) a small molecule generated by gut microbial metabolism of choline, carnitine and betaine, and has been implicated as a toxin and linked to increased risk atherosclerosis. Studies have implicated TMAO in AD disease and cognition. Objective: To examine associations between plasma TMAO and its plasma precursors, choline, carnitine and betaine, and the interaction of TMAO and age in relation to cognitive function in a cohort of older Puerto Rican adults.

Methods: In cross-sectional analysis, we examined whether plasma TMAO and its precursors, choline, carnitine and betaine, are associated with poor cognitive function in BPHS participants (n=715) (mean age 57.1 ± 7.9 y). Cognitive function was assessed via a battery of tests: Individual test scores were transformed to Z-scores and derived to a global cognitive function composite score. Multivariable linear regression was used to examine relationships between plasma TMAO, choline, carnitine and betaine and cognitive function.

Results: Plasma TMAO was positively correlated with plasma choline (Pearson corr P=<0.0001) but not with plasma carnitine or betaine. Naturally log transformed plasma TMAO was inversely associated with cognitive function after adjusting for age, sex and estrogen status (women), and APOE e4 (b =-0.07,P=0.05). After adjustment for BMI, physical activity, education, smoking, alcohol use and diabetes, this association was attenuated. The negative association of TMAO and cognitive function was more pronounced in older participants, compared to younger participants (p-int: 0.04). Natural log transformed plasma carnitine was borderline associated with poorer cognitive score (P=0.07) after adjusting for covariates. We did not observe an association between choline or betaine with cognitive function in this cohort.

Conclusion:Higher plasma TMAO concentration was associated with poorer cognitive function among older (>=56 y). Higher carnitine, but not choline or betaine, approached significance in relation to lower cognitive function. More studies are needed to understand whether these associations are related to food sources, or internal production or these metabolites.

Aging

Social Capital and Cost-Related Medication Nonadherence: A Retrospective Longitudinal Cohort Study Using the Health and Retirement Study Data, 2006-2016 Kayleigh R. Majercak*

Kayleigh Majercak Laurence S. Magder Ester Villalonga-Olives

Prescription drug spending and other financial factors (e.g. out-of-pocket costs) partially explain variation in cost-related medication nonadherence (CRN). Indicators of social capital such as neighborhood factors and social support may influence the health and well-being of older adults as they may rely on community resources and support from family and peers to manage conditions. Previous research on the relationship of social capital and CRN has limited evidence and contradictory findings. Hence, our objective is to assess the relationship of social capital indicators (neighborhood social cohesion, neighborhood physical disorder, positive social support, and negative social support) and CRN using a longitudinal design over multiple time periods, 2006 to 2016, in a nationally representative sample of older adults in the United States (US). The Health and Retirement Study is a prospective panel study of US adults aged ≥50 years evaluated every two years. Data was pooled to create three waves and fitted using Generalized Estimating Equation modelling adjusting for both baseline and time-varying covariates (age, sex, education, race, and perceived health status). The three waves consisted of 11,791, 12,336, and 9,491 participants. Higher levels of neighborhood social cohesion and positive social support were related with lower CRN (OR 0.90, 95% CI 0.87-0.93 and OR 0.74, 95% CI 0.67-0.81, $p<0.01$). In contrast, higher levels of neighborhood physical disorder and negative social support were related to higher CRN (OR 1.09, 95% CI 1.06-1.13 and OR 1.49, 95% CI 1.34-1.65, $p<0.01$). Interventions targeting social capital are needed, reinforcing positive social support and neighborhood social cohesion and diminishing neighborhood physical disorder and negative social support for older adults.

Adverse Childhood Experiences and Late Life Cognitive Performance Across Racial/Ethnic Groups: Results from the KHANDLE Cohort Erika Meza* Audra Gold Erika Meza Sarah F. Ackley Dan M Mungas Rachel Whitmer Elizabeth Rose Mayeda Sunita Miles Chloe Eng Paola Gilsanz M. Maria Glymour

Background:
Prior findings on adverse childhood events (ACEs) and late-life cognitive outcomes are inconsistent, with very little evidence from diverse racial/ethnic groups.

Methods:
Kaiser Healthy Aging and Diverse Life Experiences (KHANDLE) study baseline participants, aged 65 years and older (n=1,708; including 415 Asian-American, 348 Latino, 443 Black, and 502 White participants), self-reported experiences of 9 ACEs, including age of earliest occurrence (categorized as 0-6, 7-12, and 13-16 years). Verbal memory, executive function, and semantic memory were assessed with the Spanish and English Neuropsychological Assessment Scales. A mixed model indicated no evidence of domain-specific effects, so the 3 domains were combined into a z-scored composite. Using covariate-adjusted linear regression models, we assessed associations of exposure to any ACE, age of exposure, and type of ACE with global cognition overall and by race/ethnicity.

Results:
Most respondents (68%) reported experiencing one or more ACE, most frequently family illness (36%), domestic violence (23%), and parental divorce (22%). ACE count was not associated with cognition overall (b=0.01; 95% CI: -.02, .04, within any racial/ethnic group, or for any age-category of exposure. Among Asian Americans, each additional ACE was associated with slightly better cognitive scores for Asian Americans (b= 0.09; 95% CI, 02, .17). Overall, loss of job by parents was associated with better cognitive scores (b=0.14; 95% CI, 0.04, 0.25), while death of mother (b=-0.23; 95% CI, -0.41, -0.05), and death of father (b=-0.09; 95% CI, 0.23, 0.04) were associated with worse cognitive scores. There were no significant differences by race/ethnicity.

Conclusion:
A count of childhood adverse exposures did not predict worse cognition in older adults in a diverse sample, although parental death was associated with worse cognitive outcomes.

Figure 1. Prevalence of ACE Exposure by Race and Ethnicity

Aging
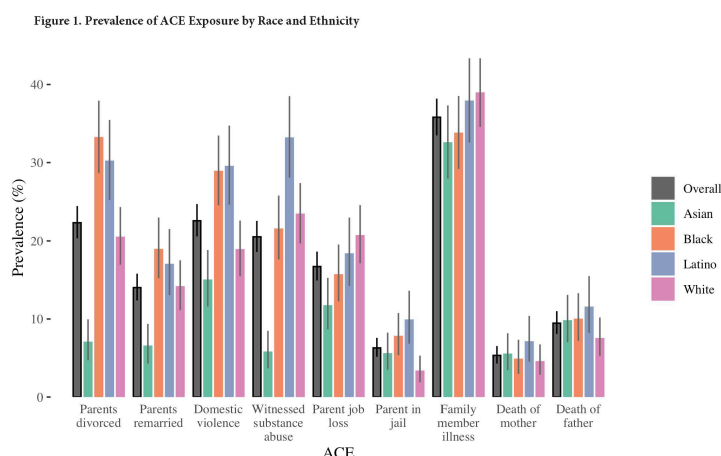
Relationship of socioeconomic factors on the relationship between the MIND diet and cognitive function in a minority cohort. Tahani Boumenna* Tahani Boumenna David Kriebel Katherine L. Tucker Natalia Palacios Tammy Scott Xiyuan Zhang

Background: Adherence to Mediterranean and DASH diets has been associated with better cognitive function. Socioeconomic measures such as education, poverty and job complexity have been associated with dementia and may modify the relationship between diet quality and cognitive impairment. Objectives: We examined whether adherence to the MIND (Mediterranean -DASH intervention) diet was associated with cognitive function in a cohort of Boston area Puerto Rican adults, and whether this association varied across levels of education, income to poverty ratio, and job complexity score. Methods: Cross-sectional analyses included 1,145 participants from the BPHS (mean age 57.1 ± 7.9 y). Cognitive function was assessed with a battery of tests and a global cognitive composite score was calculated. MIND diet score was derived based on 10 healthy food groups and 5 unhealthy ones. We used multivariable linear regression models, adjusted for age, energy intake, BMI, sex, physical activity, diabetes, education, smoking, APOEε4 gene and depression to assess associations between tertiles of MIND diet score and cognitive function. We examined whether the MIND-diet–cognition association was confounded or modified by SES measures. Results: Higher adherence to the Mind diet was associated with better global cognitive function after adjustment for SES measures and other factors (β =0.03, P trd=0.02). The association between MIND diet score and cognitive function was modified by education (P-int = 0.02) and was stronger among participants who had less than a high school education (P trd = 0.003) than among those with high school or greater education (P trd = 0.48). The association was modified by income to poverty ratio (P-int=0.045) and was stronger among those with low income to poverty ratio (P trd < 0.0001) than among those with high income to poverty ratio (P trd=0.96). Conclusion: Higher adherence to the MIND diet is associated with better cognitive status and was modified by education and by poverty.

Aging

Factors Associated with Recovery from Mobility Limitation in Middle Aged African Americans: The Jackson Heart Study Kendra D Sims* Kendra Sims Michelle C. Odden Roland Thorpe Yuan-I Min Mandip Dhamoon Mario Sims Adolfo Correa

Though mobility limitations are disproportionately prevalent among African Americans, there have been few investigations into factors associated with recovery. The present study investigated demographic, clinical, and social factors associated with recovery from incident mobility limitation within one year in the Jackson Heart Study, a cohort study of African Americans in Jackson, MS. Participants underwent three in-person examinations from 2000-2013. Mobility limitations were assessed during annual phone calls by self-reported limitations in walking half a mile or climbing stairs. The outcome of interest, recovery from mobility limitation, was defined as no mobility limitation the following year. Candidate predictor variables, assessed in logistic regression models, included demographic factors, behaviors, cardiovascular health measures, and chronic conditions. Multiple imputation using chained equations was used to address missing data. Among 5,276 participants [mean (SD) age = 55.4 (12.9) years], 1,759 (33%) had an incident mobility limitation over 12 years of follow-up, and 953 (54%) reported recovery from mobility limitation by one year later. Young women were more likely to recover from mobility limitation than young men. However, with increasing age, women were less likely to recovery from mobility limitation compared with men (p-value for age and gender interaction = 0.03). In adjusted models, being married was associated with a greater likelihood of recovering (OR: 1.26; 95% CI: 1.02, 1.55), whereas a history of heart failure and current statin use were associated with a lower likelihood of recovering (OR = 0.57; 95% CI: 0.34, 0.98 and 0.77; 95% CI: 0.61, 0.98, respectively). In conclusion, the majority of incident mobility limitations in this population of middle-aged African Americans was transient. Being married may support recovery from limitations by providing a form of structural social support. Cardiovascular health status appears to be an important factor in recovery.

Mental Health

The Protective Effect of Posttraumatic Stress Disorder on Suicide Attempt Risk: A Case of Collider Stratification Bias Tammy Jiang* Tammy Jiang Amy E. Street Erzsébet Horváth-Puhó Anthony J. Rosellini Timothy L. Lash Henrik T. Sørensen Jaimie L. Gradus

This study examined the association between posttraumatic stress disorder (PTSD) and suicide attempts. We conducted a case-cohort study using nationwide Danish registry data. Cases were all individuals who made a non-fatal suicide attempt between January 1, 1995 and December 31, 2015 (n = 22,974). The comparison subcohort was a 5% random sample of living individuals in Denmark on January 1, 1995 (n = 265,183). We estimated hazard ratios using Cox proportional hazards regression models to examine the association between PTSD and suicide attempt. We adjusted for age, sex, marital status, income, depression, anxiety, drug abuse, and alcohol abuse. We conducted analyses stratified by depression to assess the presence of interaction between PTSD and depression. The OR for the association between PTSD and suicide attempt in the depressed stratum was 0.89 (95% CI: 0.72, 1.1), and 5.2 (95% CI: 4.3, 6.3) in the non-depressed stratum. This suggests that having PTSD reduces the risk of suicide attempts among persons with depression, which is consistent with prior studies also finding a protective association among persons with depression. We use causal diagrams to show that these paradoxical findings may be explained by selection bias which arises due to stratification on a collider (depression). Depression may be a mediator on the causal pathway from PTSD to suicide attempt. Conditioning on an intermediate which has a common cause with the outcome may create downward bias, which may explain the observed protective association between PTSD and suicide attempt among persons with depression. Sorting out the temporal sequencing between onset of PTSD and depression is important when depression is likely both a common cause and mediator of the association between PTSD and suicide attempt.

Permissiveness of State Firearm Laws and Increased Suicides by Firearm in the US Abhery
Das* Abhery Das Parvati Singh Tim Bruckner

Background: The suicide rate in the US increased by more than 30% from 1999 to 2017. Suicides by
firearm account for more than half of all suicide deaths. Previous research finds access to firearms,
especially during periods of crisis, increases risk of suicide death. Permissiveness of state firearm
laws may increase suicides by firearm for those who own firearms, specifically non-Hispanic white
men, of which half (48%) own a firearm. We examine, across 50 states, from 2000 to 2016 whether
permissiveness of firearm laws at the state-level corresponds with an increase in county-level
suicides by firearm (1) overall and (2) among non-Hispanic white men.
Methods: We apply a fixed effects linear regression analysis with county and year fixed effects and
relevant covariates. We define our exposure as the annual rating of firearm permissiveness laws
(range: 0 as completely restrictive to 100 as completely permissive) across 50 states from 2000-2016
(from the Traveler's Guide to the Firearms Laws of the Fifty States). We use the National Center for
Health Statistics compressed mortality file to obtain the county-level counts and population rates of
suicides by firearm, by race and sex groups, from 2000 to 2016. Our total sample size comprises
528,774 county-years.
Results: Permissiveness of state firearm laws varies positively with risk of suicide death by firearm.
A one-unit increase in firearm law permissiveness corresponds with a 0.1% increase in suicide by
firearm per 100,000 population (95% CI [.0003, .0020]). This relation concentrates primarily among
non-Hispanic white men wherein a one-unit increase in firearm law permissiveness corresponds with
a 0.1% increase in suicide by firearm per 100,000 population (95% CI [.0002, .0018]).
Discussion: Stricter firearm policies at the state level, as a potential deterrent to suicide by firearm,
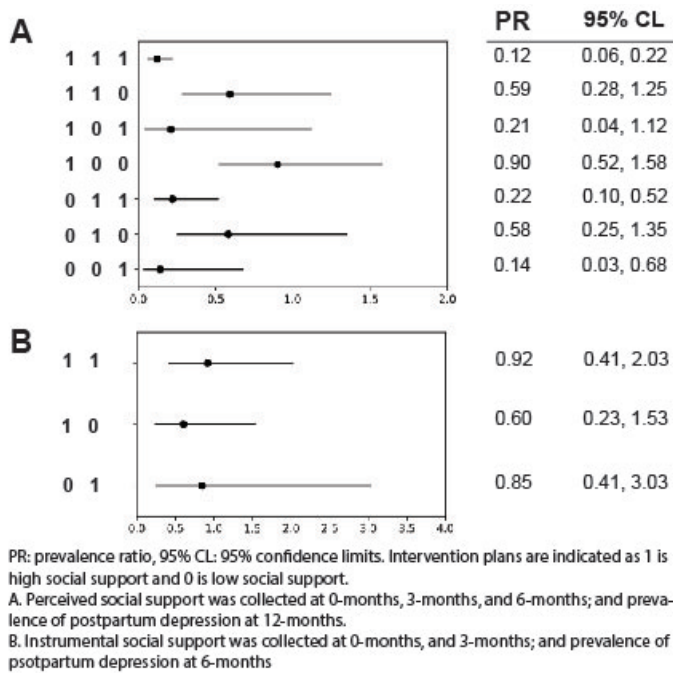warrant further investigation.
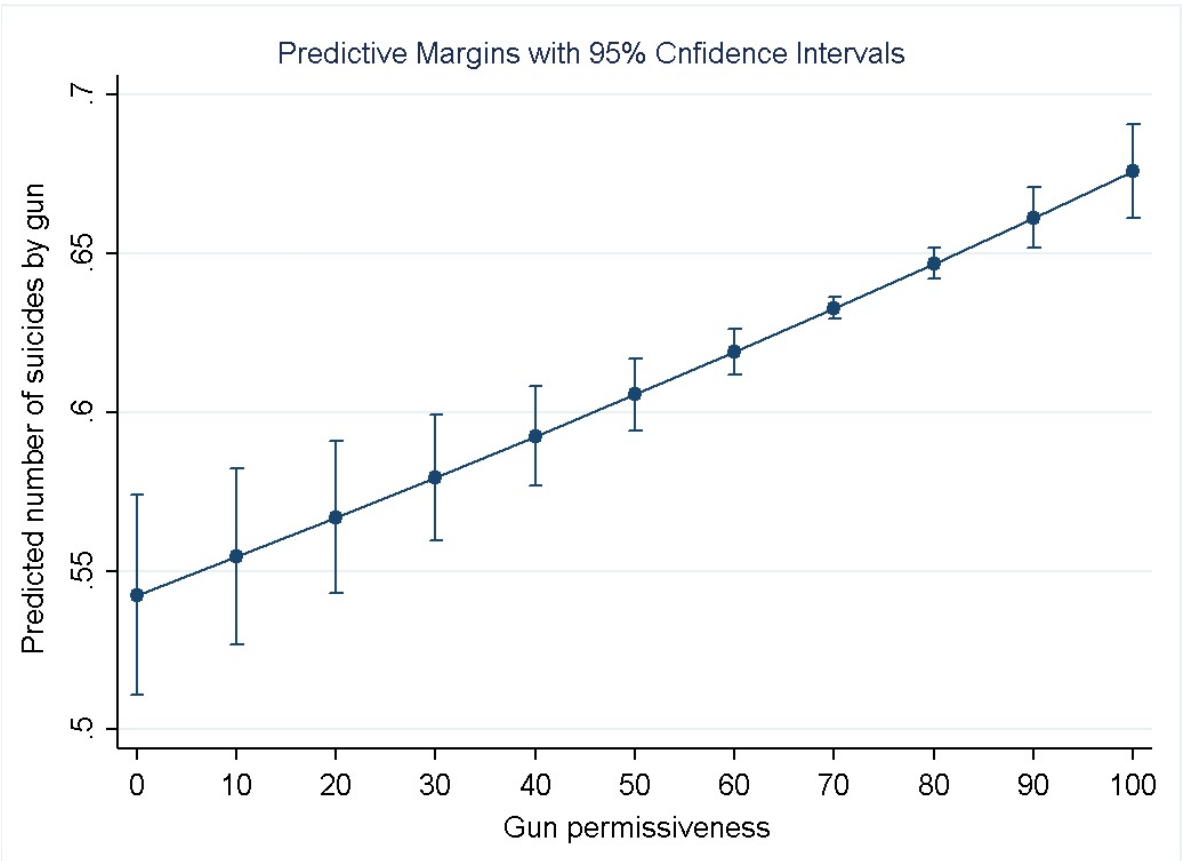
Using marginal structural models to estimate the causal association of social support from pregnancy to postpartum on maternal depression Katherine LeMasters* Katherine LeMasters Ashley Hagaman Paul Zivich Siham Sikander Joanna Maselko

Background: Perinatal depression (PND), depression symptom onset during pregnancy or within one year postpartum, imposes a high burden on women in low- and middle-income countries, and has implications for maternal and infant health. Social support (SS) is an established mechanism for protecting against PND, but the type and temporality of SS is unclear. This study evaluates perinatal SS and subsequent maternal depression at 12 months postpartum.

Methods: We assessed perceived and instrumental support and clinical depression (Structured Clinical Interview for DSM-IV) among women in rural Pakistan (n=780), recruited in their third trimester and followed at three, six, and 12 months postpartum. The average causal effect of SS (perceived; instrumental) on PND was estimated with inverse probability of treatment weights to account for confounders and inverse probability of censoring weights to account for informative loss-to-follow-up.

Results: In our sample, 66% had high perceived support at baseline, 71% at three months, and 63% at six months. Sixty-two percent had high instrumental support at baseline and 72% at three months. Thirty-seven percent of women had clinical depression at baseline, 15% at three months, 12% at six months, and 18% at 12 months. If all had high perceived SS until six months postpartum, the prevalence of depression at 12 months would have been 0.12 (95% CI: 0.06, 0.22) times that of low SS until six months postpartum. A protective relationship does not hold for instrumental support.

Conclusion: We find that it is not the timing of a singular instance of receiving SS, but sustained SS in reducing PND. These findings point to the importance of longitudinally assessing SS and PND, and doing so separately for SS constructs. Our work highlights the protective effect of sustained perceived support on clinical maternal depression. Interventions tailored to leveraging and maintaining this support may be particularly important in low-income settings.

PR: prevalence ratio, 95% CL: 95% confidence limits. Intervention plans are indicated as 1 is high social support and 0 is low social support.
A. Perceived social support was collected at 0-months, 3-months, and 6-months; and prevalence of postpartum depression at 12-months.
B. Instrumental social support was collected at 0-months, and 3-months; and prevalence of psotpartum depression at 6-months

Opioid overdose-related mortality and U.S. death certificate data: a quantitative bias analysis with expert elicitation of bias parameters

Elizabeth S. Goldsmith* Elizabeth Goldsmith Erin E. Krebs Richard F. MacLehose

Background: Opioid overdose-related mortality remains high in the U.S., and estimates rely on cause-of-death data from death certificates completed by health care providers and medical examiners. Opioid misuse and abuse among older adults are thought to be underestimated, with misclassification dependent on age. We conducted expert elicitation and quantitative bias analysis to assess the potential influence of age-related misclassification on U.S. opioid overdose-related mortality estimates.

Methods: We obtained de-identified cause-of-death data from the U.S. National Center for Health Statistics. We estimated crude opioid overdose-related mortality rates by age category (under 55, 55-64, 65+). We conducted brief structured interviews of 10 internal medicine physicians to elicit their beliefs on sensitivity of opioid overdose cause-of-death data from U.S. death certificates, by age-at-death category. We summarized the sensitivity estimates and applied resulting distribution parameters in simulation studies to conduct quantitative bias analysis assessing the potential influence of age-related differential misclassification.

Results: Physicians estimated lower sensitivity of U.S. death certificate data as an indicator of opioid overdose-related mortality among people aged 55 and older than among people under 55. Probabilistic bias analyses adjusting for physician-estimated misclassification yielded higher opioid overdose mortality rates, particularly among older U.S. residents.

Conclusions: We developed a method of quantitatively eliciting physician expert opinion on priors for sensitivity of a medical record-based indicator and applied findings in quantitative bias analyses adjusting for differential misclassification. Opioid overdose-related mortality rates may be underestimated in the U.S., particularly among people aged 55 and older, due to age-related misclassification in cause-of-death data from death certificates.

Meta-analysis of the total effect decomposition in the presence of multiple mediators: Integrating evidence across trials for schizophrenia treatment Yiwen Zhu* Yiwen Zhu Franca Centorrino John W. Jackson Garrett M. Fitzmaurice Linda Valeri

Causal mediation analysis can address mechanistic questions by decomposing and quantifying fine-grained effects operating through different pathways. There is growing interest in applying causal mediation analysis to disentangle the interplay between symptoms and side effects in clinical trials.

Because most individual trials are underpowered to detect mediating effects, we introduced an approach to meta-analyze causal mediation analyses with multiple mediators and interactions. Path-specific effects were estimated as functions of meta-analyzed regression coefficients capturing treatment-mediators and mediators-outcome associations across trials; standard errors were obtained using the delta method. We evaluated the performance of this approach in simulations and applied it to assess the mediating roles of positive symptoms of schizophrenia and weight gain in the treatment effect of an antipsychotic medication on negative symptoms across four efficacy trials (Figure 1).

The meta-analytic approach was unbiased and increased statistical power in simulations. In the application, we observed substantial mediating effects of positive symptoms (proportions mediated from fixed-effects meta-analysis:
PM6mg/d = 47%, PM9mg/d = 65%, PM12mg/d = 89%). Weight gain may have beneficial mediating effects; however, such benefit may disappear at high doses when metabolic side effects were excessive.

Meta-analyzing causal mediation analysis combines evidence from multiple sources and improves power. As shown in the application, targeting positive symptoms may be an effective way to reduce negative symptoms that are challenging to treat. Studies with longer follow-ups are needed to better understand the role of metabolic side effects in schizophrenia.

Figure 1. Directed acyclic graph (DAG) representing the causal relationships tested in the applied example, examining The Positive and Negative Syndrome Scale (PANSS) - positive symptoms and weight gain as mediators of the causal pathway between the treatment effect of an antipsychotic medication, paliperidone ER, and reduction in PANSS negative symptoms assessed at study termination.
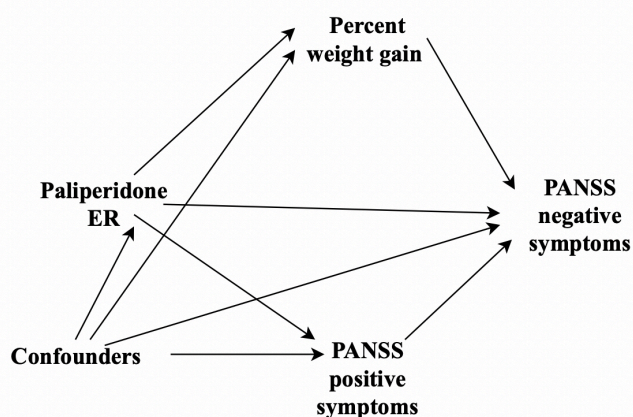
Estimating the Effectiveness of Childhood Vaccine Schedules Anne M. Butler* Anne M. Butler
Alexander Breskin John R. Sahrmann M. Alan Brookhart

Important questions exist regarding the real-world effectiveness of alternative childhood vaccine
schedules, however optimal approaches to study this complex issue are unclear. Adapting study
designs and analytic methods developed to estimate causal effects of dynamic treatment regimens,
we sought to estimate the comparative effectiveness of various rotavirus vaccine (RV) schedules for
the prevention of acute gastroenteritis (AGE)-related emergency department (ED) visits and
hospitalization. Using the IBM MarketScan® Commercial database (2006-2015), we identified
1,520,179 eligible infants who received a diphtheria-tetanus-acellular pertussis (DTaP) vaccine at
38-92 days of age. We assigned each infant's person-time – starting the day after DTaP - to separate
protocol-specific cohorts: 1-dose monovalent rotavirus vaccine (RV1), 2-doses RV1, 1-dose
pentavalent rotavirus vaccine (RV5), 2-doses RV5, 3-doses RV5 and no RV vaccine. Infants were
censored from protocol-specific cohorts when vaccination receipt deviated from that dictated by the
protocol. Inverse probability of censoring weighted estimation was used to address potentially
informative censoring by protocol deviations. In the observed data, the 2-year cumulative risks for
ED visits or hospitalization were 3.6% and 0.6%, respectively. Under a theoretical intervention to
fully vaccinate all infants, the 2-year risks of ED visits or hospitalization were 3.4% and 0.6%,
respectively. The risk differences comparing full to observed adherence were 0.21% (95% CI: 0.14%,
0.27%) for ED visits and 0.08% (95% CI: 0.05%, 0.11%) for hospitalization. Comparing outcomes
under varying adherence to recommended vaccine schedules generates important evidence about
the potential consequences of delaying childhood vaccines and the possible impact of interventions
to improve recommended vaccine schedule adherence.

Causal mediation analysis in the identification and establishment of correlates and mediators of protection for influenza vaccines Wey Wen Lim* Wey Wen Lim Nancy H. L. Leung Vicky J. Fang Eric J. Tchetgen Tchetgen Sheena G. Sullivan Benjamin J. Cowling

There has been increasing interest in identifying new immune correlates of protection (CoPs) for influenza vaccines to be used as predictors of effectiveness and potential targets for vaccine development. While past efforts have focused on establishing the association between a candidate CoP and protection, there is growing recognition of the importance of establishing a causal link between CoPs and protection. The hemagglutination inhibition (HAI) antibody titer is a widely accepted CoP for inactivated influenza vaccines (IIV). However, as the HAI antibody response represents only part of the overall immune response to current influenza vaccines, we aimed to estimate its contribution to influenza vaccine-induced protection. We reanalyzed data from a randomized controlled influenza vaccine trial to assess the efficacy of a seasonal influenza vaccine (SIV) in preventing laboratory-confirmed influenza virus infections in healthy children. We conducted a causal mediation analysis to estimate the total, direct, and indirect effect of vaccination on risk of infection using proportional hazards models with inverse odds ratio weighting and calculated the proportion of vaccine efficacy mediated by post-vaccination HAI titer. The total effect of influenza vaccination on protection against influenza A(H1N1) virus infections was 0.37 (95% CI = 0.20, 0.61), corresponding to a vaccine efficacy of 63% (95% CI = 39%, 80%). Of this, the effect mediated by increases in post-vaccination HAI titers against the influenza A(H1N1) vaccine strain was 0.77 (95% CI = 0.39, 1.67). The proportion of vaccine efficacy mediated by increases in post-vaccination HAI titers was 26% (95% CI = -0.5%, 118.0%). In conclusion, HAI titer is a partial mediator of influenza vaccine-induced protection against laboratory-confirmed influenza virus infections. Further investigation into protection mediated by other immune mechanisms is needed to identify additional correlates and mediators of protection.

HCV incidence and time-to-seroconversion among patients in an opioid agonist treatment program in New York City Ashly E Jordan* Ashly E Jordan Charles M Cleland Katarzyna Wyka Bruce R Schackman David C Perlman Denis Nash

Introduction
Hepatitis C virus (HCV) incidence has increased in the US in the current opioid epidemic. While opioid agonist therapy (OAT) with methadone has been associated with an average reduction of HCV incidence by 50%, there are gaps in data assessing the impact of individual and OAT-related factors on HCV incidence. We examined the impact of individual and OAT-related factors and their association with incidence to identify factors that could be leveraged to enhance the impact of OAT as HCV prevention.

Methods
In a retrospective observational open cohort of people in the largest not-for-profit OAT program in New York City between 1/1/2013–12/31/2016, HCV incidence was calculated among those HCV antibody tested >2 times. Incident HCV was defined as a new positive, after a previous negative, HCV antibody test.

Results
Among 8,352 patients, HCV prevalence was 48.7%. Among 2,535 patients seronegative at baseline, there were 108 seroconversions in 4,859 person-years of observation (PYO). HCV incidence was 6.70/100 PYO and 1.3/100 PYO among those reporting, and those not reporting, drug injection, respectively. Female gender (incidence rate ratio (IRR): 1.49), drug injection (IRR: 5.20), and lower OAT retention (IRR: 1.01) were associated with higher incidence. Female gender (adjusted hazard ratio (aHR): 1.52), drug injection (aHR: 5.98), and average methadone doses <60mg (aHR: 1.52) were independently associated with shorter time-to-seroconversion.

Discussion
While HCV incidence among those in OAT was lower than that generally seen in people who use drugs (PWUD) not on OAT, PWUD remain at risk of HCV. That females had a higher incidence suggests the potential value of gender-focused services. The finding that higher methadone doses and better OAT retention were associated with lower incidence suggests that interventions (at the patient-, provider- and policy-levels) may have the potential to improve the impact of OAT as HCV prevention.

Accuracy of chronic Hepatitis C diagnosis in the electronic medical record: implications for bias correction approaches Neal Goldstein* Neal Goldstein Deborah Kahal Karla Testa Igor Burstyn

Background: Health centers may wish to re-engage existing patients with known chronic hepatitis C virus infection (HCV) because of improved treatment response relative to the recent past. These patients can be rapidly identified by abstracting an HCV diagnostic code from the electronic medical record (EMR), but these may not be inaccurate.

Methods: We conducted a validation study within a cohort of 3,773 patients seen between 2016 and 2018 at an urban federally qualified health center that recorded the outcome of "risk-factor based" screening for HCV in its EMR. We validated an EMR diagnostic code of HCV through a combination of scrutinizing medical records and patient outreach. A second cohort of 1,445 patients without an indication of HCV in EMR was enrolled in 2019 and subjected to "universal" screening to provide estimates of HCV cases missed by a risk-factor based approach. The Figure depicts the study enrollment and decision steps to classify an individual's HCV status; dashed lines indicate estimated true HCV status for patients without laboratory testing using information on the negative predictive value from the universal cohort.

Results: In the risk-based cohort, 77 patients (2%) had HCV diagnostic code but HCV was only verified in 47 (1% of total cohort; 61% of those with a diagnosis). Among 341 patients who fulfilled an HCV lab order in the universal cohort, 5 patients (2%) had HCV. The positive and negative predictive values of risk-based screening were 61% (95% CI: 49%, 72%) and 99% (95% CI: 97%, 100%), respectively. The prevalence of HCV was estimated at 2% (95% CI: 2%, 3%) in the population served by the clinic.
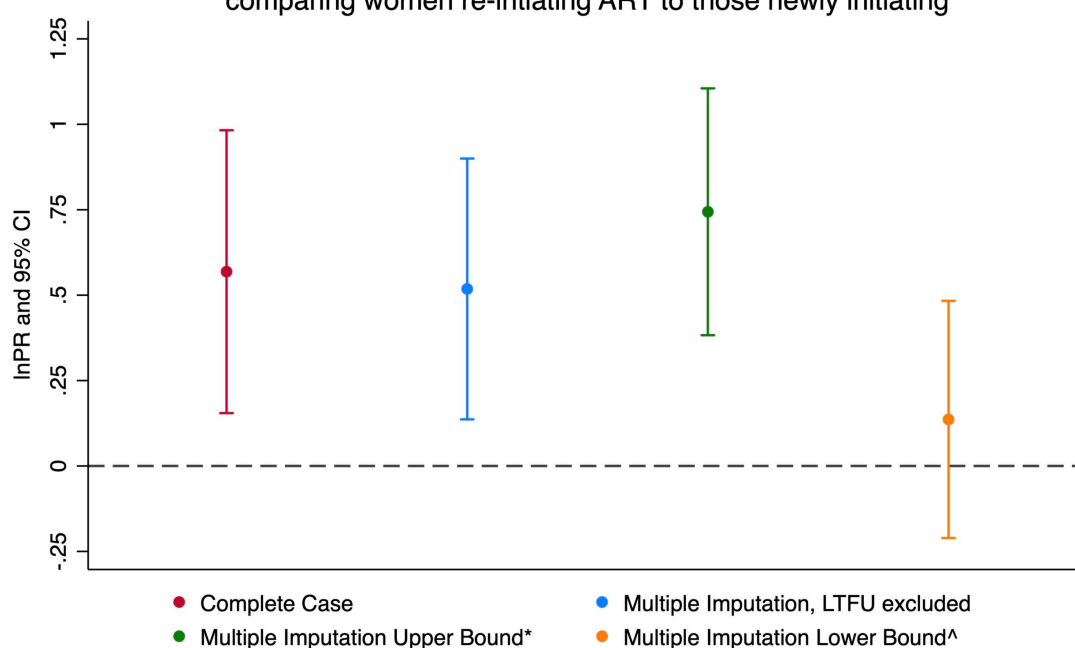
Conclusions: The risk-factor driven screening program underestimated the seroprevalence of HCV in the studied patients, affirming the need for universal screening in this population. Our work can also be used to inform parameters in quantitative bias analysis when investigators suspect misclassification of an HCV diagnosis.
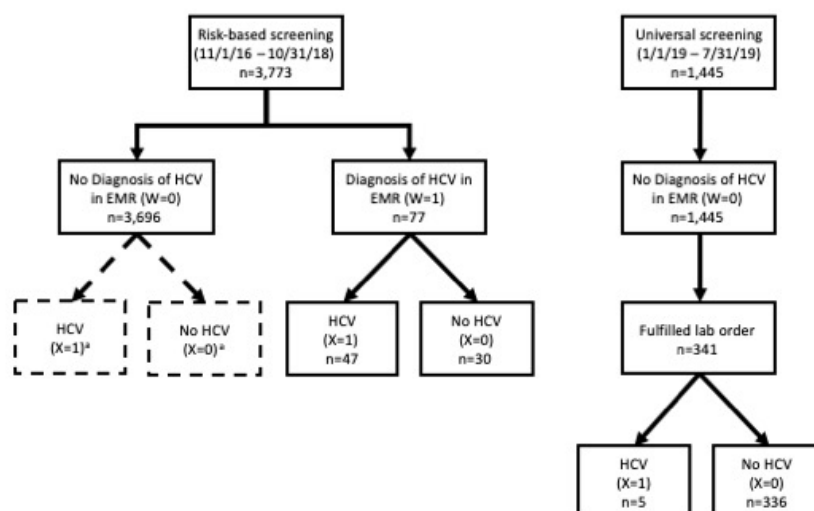
Viral suppression at delivery among women re-initiating or newly initiating antiretroviral therapy through Option B+ in Malawi Bethany DiPrete* Bethany DiPrete Emmanuel Singogo Laura Limarzi Shaphil Wallie Maganizo Chagomerana Aidan Walker Allan Jumbe Mina Hosseinipour

The success of Option B+ depends on women achieving and maintaining viral suppression (VS). We compared the likelihood of VS at delivery among women re-initiating antiretroviral therapy (ART) after a treatment interruption to women newly initiating ART. Women attending a first antenatal visit in Lilongwe, Malawi from 2015-2019 were enrolled into two sub-cohorts according to ART status: (1) newly diagnosed with HIV and initiating first line ART (tenofovir/lamivudine/efavirenz) (new initiators), and (2) previously initiated first line ART but off treatment >3 weeks (re-initiators). We used Poisson models with robust variance to estimate prevalence ratios (PR) of unsuppressed VL (≥1000 copies/ml) at delivery between cohorts, adjusting for age, education, CD4, and marital status. Sensitivity analyses included: (1) multiple imputation of missing VL (MI), excluding those lost to follow-up (LTFU) before delivery, and (2) MI, assigning re-initiators who were LTFU as unsuppressed at delivery and new initiators who were LTFU as suppressed (upper bound), and vice versa (lower bound). There were 449 women enrolled (299 newly initiating, 150 re-initiating). Outcomes were missing for 20% of women in each sub-cohort (n=62, n=31), one-third of which were due to LTFU. Among those with observed outcomes, 15% and 26%, respectively, had unsuppressed VL at delivery. In a complete case analysis, women re-initiating treatment were more likely to have unsuppressed VL than those newly initiating treatment (PR: 1.77, 95% CI: 1.17, 2.67). In sensitivity analyses (Figure 1), PR estimates ranged from 1.15 (95% CI: 0.75, 1.55) to 2.11 (95% CI: 1.34, 2.87). We found that women re-initiating ART after treatment interruption were more likely to have unsuppressed VL at delivery than those newly initiating ART. It is important to understand why women re-initiating ART had first discontinued treatment, which may inform how to keep women consistently on ART and suppressed after ART re-initiation.

Figure 1. Log prevalence ratios of unsuppressed VL at delivery comparing women re-intiating ART to those newly initiating

- Complete Case
- Multiple Imputation Upper Bound*
- Multiple Imputation, LTFU excluded
- Multiple Imputation Lower Bound^

*LTFU assigned as: re-initiating cohort=unsuppressed VL, newly initiating cohort=suppressed VL
^LTFU assigned as: re-initiating cohort=suppressed VL, newly initiating cohort=unsuppressed VL

Perceived discrimination and time to pregnancy Olivia R. Orta* Olivia Orta Amelia Alina Kenneth Elizabeth Lauren

Olivia R. Orta* Olivia Orta Amelia Alina Kenneth Elizabeth Lauren

Background: Perceived discrimination is a form of chronic stress associated with several adverse reproductive health outcomes. Its effect on fecundability is unclear.

Methods: We analyzed data from Pregnancy Study Online (PRESTO), a North American preconception cohort study. We followed female pregnancy planners until conception, fertility treatment initiation, loss to follow-up, or 12 menstrual cycles of attempt time, whichever came first. 2,599 participants reported retrospectively whether they experienced discrimination attributed to their race/ethnicity, sex/gender, or socioeconomic position in the year before baseline, and how they responded (talked to others v. kept to self, did something v. accepted as a fact). We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% CIs. Models included age, education, income, BMI, smoking, parity, contraception use, intercourse frequency, and multivitamin use.

Results: 47.2% participants reported experiencing discrimination, with the highest prevalence observed among non-Hispanic Black women (82.1%). Adjusted FRs for the association between discrimination (yes vs. no) and fecundability were 0.75 (CI=0.57-0.98) among the 296 minority women (non-Hispanic Black, Hispanic, Asian, or Other), and 0.96 (CI=0.88-1.05) among the 2,303 non-Hispanic White women. Among minority women, discrimination attributed to race/ethnicity was most strongly associated with reduced fecundability (FR=0.60, CI=0.41-0.87) and was weaker for those who responded by talking to others and doing something about it (FR=0.84, CI=0.56-1.25). We saw no trend in effect with increasing number of discrimination experiences.

Conclusion: Perceived discrimination was associated with reduced fecundability among North American women trying to conceive. The association was strongest among minority women who attributed their discrimination to race or ethnicity, and weaker among those who took action against such experiences.

Figure 1: Restricted cubic splines for the association between number of unfair treatment domains and fecundability among 1) 296 Minority[a] women and 2) 2303 non-Hispanic White women in PRESTO, (June 2013- August 2019)
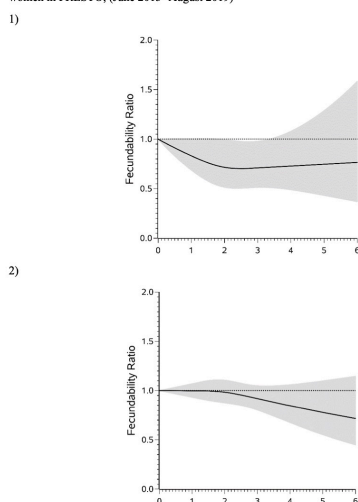
[a] Includes Non-Hispanic Black women (N=28), Hispanic women (N=121), Non-Hispanic Asian women (N=49), and mixed race or other racial and ethnic identities (N=98)
Models adjust for age, education, household income, body mass index, smoking status, number of previous births, last contraceptive method, intercourse frequency, and multivitamin use

1

Residential proximity to major roads and fecundability among North American pregnancy planners Amelia Wesselink* Amelia Wesselink Kipruto Kirwa Perry Hystad Elizabeth E. Hatch Adam A. Szpiro Joel D. Kaufman Jonathan I. Levy Ellen M. Mikkelsen Sabah M. Quraishi Kenneth J. Rothman Lauren A. Wise

Emerging evidence from animal and human studies indicates that exposure to traffic-related air pollution adversely affects fertility. Among 7,363 female pregnancy planners from the US and 1,455 from Canada, we examined the association between residential proximity to major roads (using A1, A2, or A3 roads in the US; expressways, highways, or major roads in Canada) and fecundability, the per-cycle probability of conception. From 2013 to 2019, women aged 21-45 years who were trying to conceive without fertility treatment completed an online baseline questionnaire and follow-up questionnaires every 8 weeks for up to 12 months. We geocoded residential addresses reported at baseline and over follow-up, and calculated distance to nearest major roads and length of major roads within buffers of 50, 100, 150, 300, and 400 meters around the residence as proxies for traffic-related air pollution. We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% CIs, adjusting for individual- and neighborhood-level characteristics. We followed women until pregnancy or the occurrence of a censoring event (cessation of pregnancy attempt, loss to follow-up, fertility treatment initiation, or 12 menstrual cycles). In the US, the FR comparing women who lived <50m with those who lived ≥400m from the closest major road was 0.87 (95% CI: 0.79, 0.95). Likewise, women in the highest category of length of major roads within a 50m around their residence had lower fecundability than women with no major roads within 50m of their residence (FR= 0.81, 95% CI: 0.69, 0.96); results were weaker when examining length of major roads within larger buffers. The associations among Canadian women were similar in magnitude, but less precise (corresponding FRs were 0.90 (95% CI: 0.72, 1.12) and 0.78 (95% CI: 0.48, 1.24)). These results support the hypothesis that traffic-related air pollution or other near road exposures may adversely affect fecundability.

Paternal Preconception Exposure to Plasticizers and Risk of Pregnancy Loss Carmen Messerlian* Carmen Messerlian Yu Zhang Stelios Smirnakis Irene Souter Russ Hauser Carmen Messerlian

Background: Evidence suggests that women's preconception exposure to plasticizers may increase the risk of pregnancy loss. However, the impact of men's preconception exposure to these chemicals on pregnancy loss is understudied.

Methods: We examined paternal preconception urinary concentrations of bisphenol A (BPA) and phthalate metabolites in relation to time from conception to pregnancy loss among 248 pregnancies (from 204 males) from the Environment and Reproductive Health Study, a prospective cohort of couples seeking fertility evaluation. The paternal preconception period was restricted to the 3 months preceding conception in order to model average exposure during spermatogenesis of the index conception. We estimated the hazard ratio (HR) of pregnancy loss (all conceptions not leading to live birth) for each log-unit increase in BPA concentrations, the molar sum of four di(2-ethylhexyl) phthalate metabolites (ΣDEHP), and the molar sum of seven anti-androgenic phthalate metabolites (ΣAAP) using mixed effects Cox regression, adjusted for covariates. We further adjusted for maternal preconception urinary biomarker concentrations.

Results: Among 248 pregnancies, 27% ended in a loss. Paternal preconception urinary ΣDEHP (HR: 1.19; 95%CI: 0.97, 1.44) and ΣAAP concentrations (HR: 1.27; 95%CI: 1.02, 1.57) were associated with increased risk of pregnancy loss. Associations for paternal ΣDEHP concentrations were attenuated after further adjusting for maternal preconception ΣDEHP (HR: 1.06; 95%CI: 0.84, 1.34), but remained for paternal ΣAAP concentrations (HR: 1.24, 95%CI: 0.99, 1.56). No association was found between paternal BPA exposure and pregnancy loss.

Conclusion: Paternal exposure to anti-androgenic phthalates in the preconception period may independently increase the risk of pregnancy loss. Mechanisms mediating these findings might include phthalate-induced epigenetic modifications and altered DNA methylation during the critical period of spermatogenesis.

Effects of lifestyle interventions on risk of pregnancy loss Alexandra Purdue-Smithe*
Alexandra Purdue-Smithe Elizabeth DeVilbiss Samrawit Yisahak Joshua R. Freeman Neil Perkins Lindsey Sjaarda Robert M. Silver Enrique F. Schisterman Sunni L. Mumford

Pregnancy loss affects up to 30% of conceptions, with roughly half of losses attributable to genetic abnormalities. Prior studies suggest that alcohol, smoking, and caffeine are among the strongest modifiable risk factors for pregnancy loss. However, prior studies did not account for time-dependent confounding by pregnancy symptoms, such as nausea, which may be affected by these behaviors and influence future exposure to these substances. Further, there is a need to understand the effects of changing these behaviors on pregnancy loss. Our aim was to estimate the risk of pregnancy loss, given a positive pregnancy test, under hypothetical lifestyle interventions initiated at different gestational ages (4, 7, and 12 weeks). Using the parametric G-formula, we estimated the risk of pregnancy loss under interventions of eliminating smoking, alcohol intake, and caffeinated beverage intake among 1,228 women without major medical disorders attempting pregnancy in the EAGeR trial. Among 797 pregnant women, the observed 20-week risk of pregnancy loss was 23.3%. Under a joint intervention initiated at earliest pregnancy detection (4 weeks' gestation), in which women quit smoking, alcohol, and caffeine consumption, the risk of loss was 18.6% (RD per 100 pregnancies versus natural course = -5.41; 95% CI = -8.02, -3.52). The risks of loss under single interventions initiated at 4 weeks' gestation were 22.0% for quitting smoking (RD = -1.99; 95% CI = -3.70, -0.92), 21.4% for quitting alcohol (RD = -2.52; 95% CI = -4.21, -1.15), and 21.0% for quitting caffeinated beverages (RD = -2.76; 95% CI = -5.41, 0.15). Later initiation of each intervention resulted in reduced benefit. Our findings suggest that in similar populations, nearly one-quarter of pregnancy losses could be prevented if all pregnant women quit smoking, alcohol use, and caffeine consumption starting at the earliest possible detection of pregnancy.

Selective serotonin reuptake inhibitor type and pregnancy loss Lindsey Sjaarda* Lindsey Sjaarda Jeannie G. Radoc Kerry S. Flannagan Sunni L. Mumford Keewan Kim Neil J. Perkins Robert M. Silver Enrique F. Schisterman

Objective: Selective serotonin reuptake inhibitors (SSRIs) have unclear links to miscarriage risk, and data on individual SSRIs are lacking. Therefore, we examined the association of urine-measured SSRI exposure during critical windows of pregnancy establishment with live birth and pregnancy loss for three common SSRIs.

Methods: A prospective cohort of 1228 women trying to conceive while enrolled in a clinical trial were included. SSRIs (fluoxetine, sertraline, escitalopram/citalopram) were measured in urine samples stored while trying to conceive, including 0 weeks' (i.e., last menstrual period) and 4 weeks' gestation for women who conceived during the study. Relative risks (RR) with 95% confidence intervals (CI) were estimated for 1) live birth among all women trying to conceive (SSRI exposed vs. no antidepressant exposure) and 2) pregnancy loss among those who conceived. Models of pregnancy loss used inverse probability weights to account for the probability of becoming pregnant and all models adjusted for potential confounders.

Results: 172 women (14%) were exposed to any SSRIs while trying to conceive. Live birth was lower in the total cohort of women trying to conceive exposed to fluoxetine (38% live birth), while exposure to the other drugs demonstrated similar birth rates (sertraline, 48%; citalopram/escitalopram, 52%), compared with those not exposed to any antidepressant (56% live birth) (RR 0.72; 95% CI: 0.53, 0.97). Among women who conceived, only fluoxetine exhibited increased risk for loss relative to unexposed women at gestational week 0 (34% vs. 24% loss; RR: 1.52, 95%CI: 1.01, 2.31) or week 4 (31% vs. 22% loss; RR: 1.66, 95% CI: 0.96, 2.87), while sertraline and citalopram/escitalopram indicated no elevated loss risk (Figure).

Conclusions: Fluoxetine, but not sertraline or citalopram/escitalopram was associated with an increased risk of pregnancy loss.

Funding: Intramural Research Program, Division of Intramural Population Health Research, NICHD.
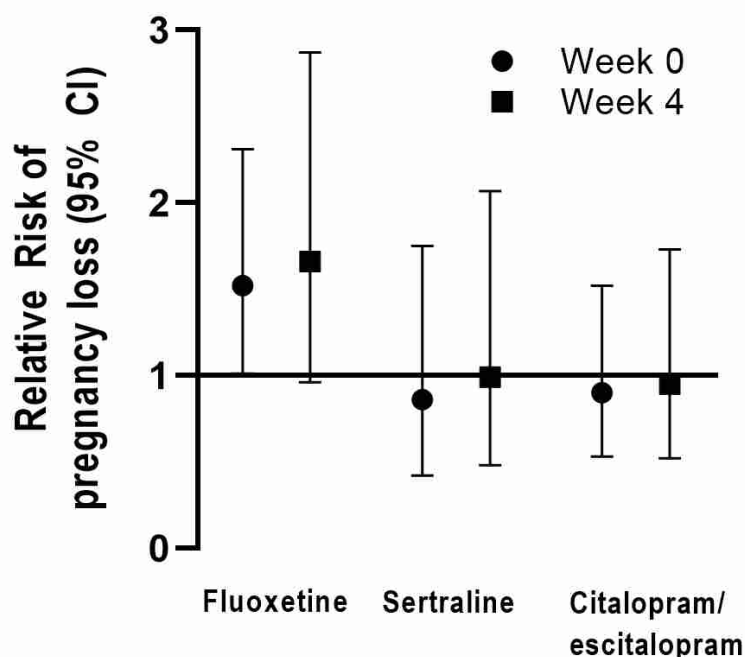
Higher levels of residential radon are associated with higher odds of PIH disorders in Massachusetts, USA Stefania Papatheodorou* Stefania Papatheodorou Weiyu Yao Carol Viera Michele Hacker Blair Wylie Joel Schwartz Petros Koutrakis

Background: Exposure to ionizing radiation has been associated with hypertension outside pregnancy, but the association between residential radon and pregnancy-induced hypertensive (PIH) disorders has not been evaluated.
Methods: We used the Massachusetts Birth Registry of Vital Records from 2001-2015 to study women with a singleton pregnancy without prior hypertension. The PIH disorders status was obtained from the birth certificates as a binary variable. Median zip code level measurements were used to estimate radon exposure at the lowest livable level of each place under closed-house conditions. We used a mixed-effects model adjusted for sociodemographic covariates, maternal comorbidities, PM2.5, temperature, and relative humidity. We examined effect modification by maternal age in two categories at the cutoff of 35 years.
Results: Of 990,364 women, 3.7% (37,027) of them developed gestational hypertension. The median zip code level ranged from 0.1 to 19.9 pCi/L. An interquartile range (IQR) increase in median zip code radon level throughout pregnancy was associated with a 3% increase in the odds of PIH disorders (95% CI 2% to 5%) in the full cohort. In women less than 35 years old, an IQR increase in medial residential zip code level radon was associated with a 4.1% increase in the odds of PIH disorders (95% CI 3% to 6%), while in women more than 35 years old, the association was null.
Conclusions: In this cohort, higher levels of residential radon are associated with increased odds of PIH disorders. After stratifying by age, this effect remained significant only in women less than 35 years old. Since the burden of pregnancy-induced hypertensive disorders is high and affects women's future cardiovascular health, the identification of modifiable risk factors is of great importance.

Late pregnancy oral corticosteroid dose and risk of preterm birth: Is early pregnancy exposure to oral corticosteroids a confounder or an instrumental variable? Kristin Palmsten*
Kristin Palmsten Gretchen Bandoli Jim Watkins Gabriela Vazquez-Benitez Christina D. Chambers

Background: Conditioning on an instrumental variable (IV), i.e. a variable associated with the exposure but not the outcome except through exposure, can bias point estimates. We share an example of adjusting for a covariate that may be a confounder or possible IV.
Methods: We used California Medicaid data linked to birth certificates (2007-2013), identifying women with systemic lupus erythematosus (SLE; n=1,174) and rheumatoid arthritis (RA; n=844). The exposure was time-varying oral corticosteroid (OCS) daily dose (≥10 mg/day of prednisone equivalent, <10, no OCS) after gestational day 139 and the outcome was preterm birth (PTB). We used early exposure to OCS cumulative dose before day 140 as a proxy for disease severity, identifying trajectory groups (high, low, no OCS) with k-means longitudinal. We adjusted exposure-outcome models for basic covariates including demographics and comorbidities. We further adjusted for early OCS exposure, i.e. the confounder or IV.
Results: Early OCS exposure was associated with later OCS exposure in both SLE and RA (among women with ≥10 mg/day after day 139, 51% and 73% were in the high dose trajectory for SLE and RA, respectively, vs 5% with no OCS for both SLE and RA). Early OCS exposure was associated with increased PTB for SLE but not RA (high dose trajectory and PTB HR 1.80 (1.34, 2.40) for SLE and 1.05 (0.59, 1.88) for RA). For SLE, increasing adjustment attenuated the association between ≥10 mg/day vs no OCS after gestational day 139 and PTB (unadjusted HR: 3.86 (2.68, 5.55); basic adjustment HR: 2.97 (1.97, 4.49); additional adjustment HR: 2.54 (1.60, 4.03). This pattern was not observed for RA (unadjusted HR: 3.18 (1.93, 5.24); basic adjustment HR: 1.88 (0.97, 3.64); additional adjustment HR: 2.42 (1.14, 5.18)).
Conclusions: When studying OCS use and PTB, earlier OCS exposure appeared to function as a confounder for the SLE subcohort (associated with exposure and outcome), and as an IV for RA (associated with exposure only).

The Association Between Prenatal Opioid Exposure and Neurodevelopmental Outcomes in Children. A large population-based study Dolapo Lawal* Oluwadolapo Lawal Xuerong Wen Nicholas Belviso Shuang Wang Kelly Matson Kimford J. Meador

Background. While negative fetal outcomes such as neonatal abstinence syndrome have been associated with maternal opioid use, little is known about the long-term effects of prenatal opioid exposure on the neurodevelopment of children.

Aim. We conducted retrospective analyses of a large administrative claims database to investigate the association between maternal opioid use and long-term neurodevelopmental outcomes in children.

Methods. Our study cohort included pregnant women, aged 12 – 55 years, with a live-birth between January 1, 2010 and December 31, 2012. Infants were considered exposed if their mothers filled at least one prescription of opioids during pregnancy. Following live-birth, infants born to eligible mothers were then followed from date of delivery till diagnosis of neurodevelopmental disorders, loss to follow-up, or end of study (December 31, 2017), whichever came first. We utilized propensity score by fine-stratification to balance for known and potential confounders. Hazard ratios (HR) and 95% confidence intervals (CI) were estimated with Cox proportional hazard models.

Results. The study population consisted of 53,400 mothers with their 54,875 live-born infants. About 10.5% (n= 5,518) infants were exposed to prescription opioids during pregnancy. Overall, 5099 children (9.3%) were diagnosed with neurodevelopmental disorders, with incidence rates of 42.6 and 35.9 per 1000 person-years in exposed and unexposed children respectively. Following adjustment for confounding, opioid-exposed children had 10% increased risks of neurodevelopmental disorders (HR: 1.10; 95% CI: 1.02, 1.20).

Conclusion. Approximately 9 in every 100 children was diagnosed with neurodevelopmental disorders, with increased risks associated with maternal opioid use. While further research is needed to confirm these findings, the benefits of prescription opioids may confer for pain management during pregnancy should be carefully balanced with the potential risks of neurodevelopment disorders in infants.

The impact of differential screening in studies of medication use and cancer risk Sophie E. Mayer* Sophie Mayer Jessie K. Edwards Til Stürmer

Use of certain medications has been indirectly associated with receipt of cancer screening through health-seeking behavior, underlying health status, and healthcare access or quality. Screening's ability to advance cancer detection may result in the appearance of non-causal relations between medication use and cancer risk, leading to spurious conclusions regarding drug safety or efficacy. Few studies have attempted to characterize the impact of differential cancer screening on findings in pharmacoepidemiology studies of cancer risk. We constructed a hypothetical cohort of 100,000 people in which "high healthcare access" was positively associated with both receipt of treatment and screening; true disease risk was independent of both treatment and healthcare access, leading to a true null treatment effect. Disease detection within 5 years was affected by 1) true disease status and 2) receipt of screening, with those receiving screening having a higher likelihood of detection than through clinical surfacing (85% vs. 40%). For the purposes of this study, we assumed 100% screening specificity. Using 2x2 tables, we calculated the RR based on detected cases only. When either screening or treatment was nondifferential with respect to healthcare access, there was no bias in the observed RR. We computed the maximum bias of the observed RR under our fixed detection parameters by making "access" a deterministic predictor of both treatment and screening, resulting in an observed RR of 2.13. A more realistic scenario examined the case where 90% of high-access and 40% of low-access individuals were treated. The observed RR ranged from 1.00-1.48 depending on the proportions screened. Consistent absolute differences in probability of screening produced larger impacts on the observed RR at low screening frequencies. The presence of shared predictors of treatment and outcome detection in observational research should be considered for regulatory decision-making and clinical practice.
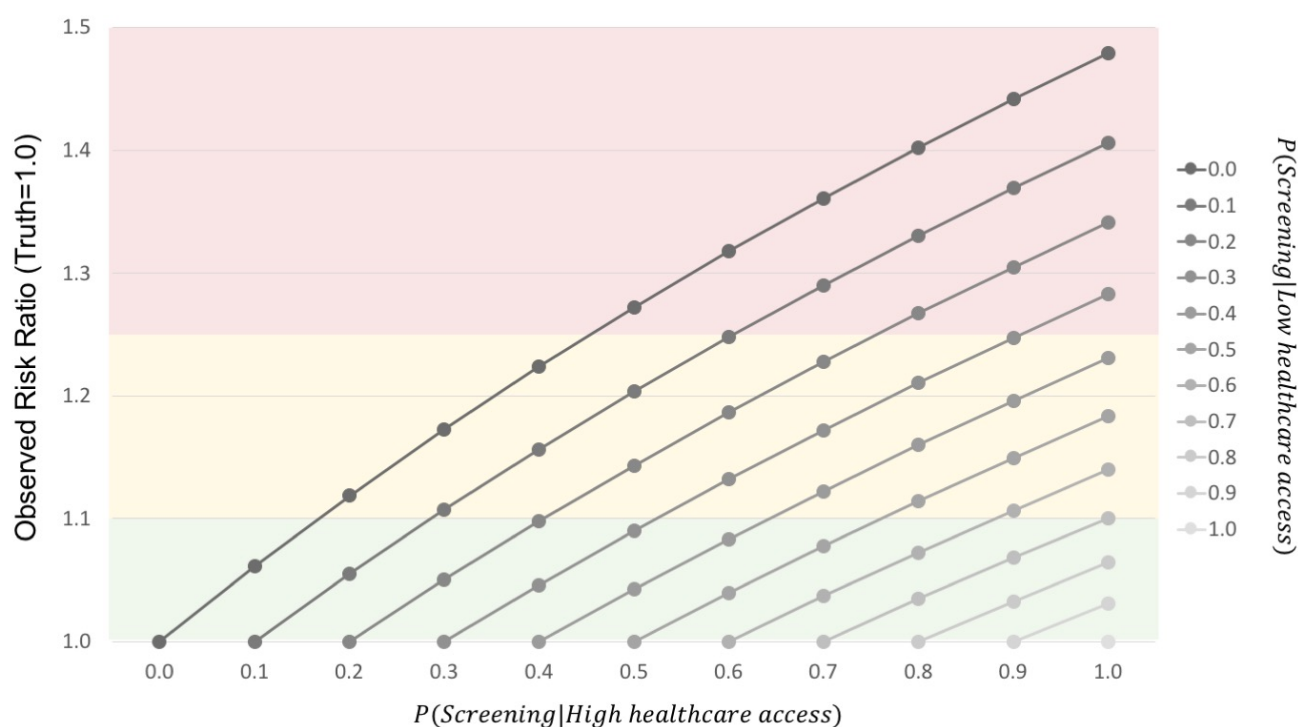
A good design is half the battle won: lessons learned for real-world evidence from trial replications using real-world data Xiaojuan Li* Xiaojuan Li Casie Horgan Soowoo Back Raghava Velagaleti Qoua Her Jessica G. Young Sengwee Toh

Epidemiologists have long used real-world data (RWD) to generate real-world evidence (RWE). There is increasing interest in using RWE to support regulatory decision making, but it is unclear when and how RWD can address the same questions traditionally answered by randomized trials. We used RWD from the OptumLabs® de-identified, linked claims and electronic health record data to replicate 2 published trials. Adapting the strict trial eligibility criteria, we used an active comparator new-user cohort design to identify adult atrial fibrillation patients who initiated rivaroxaban or warfarin during Nov 2011-Jun 2018 (trial 1), and adult type 2 diabetes, metformin-treated patients who initiated liraglutide or glimepiride during Jan 2010-Sep 2018 (trial 2). We used propensity score (PS) matching and weighting to adjust for potential confounders. We evaluated the trials' primary end points in unadjusted and PS-adjusted analyses: HRs of stroke or system embolism using a Cox regression (trial 1), and difference in A1C change at 6 months using a linear regression (trial 2). We assessed regulatory agreement (directional and statistical significance equivalence between the RWE and trial) and estimate agreement (the RWE estimate falls within the 95% CI of the trial estimate). We identified 11,088 rivaroxaban and 16,809 warfarin initiators (trial 1) and 2,700 liraglutide and 1,674 glimepiride initiators (trial 2). Balance was achieved in most covariates before PS-adjustment and in all covariates after PS-adjustment. Estimates from both RWD studies, including unadjusted and PS-adjusted analyses, achieved regulatory and estimate agreements with the trial findings, although the study populations did not fully reflect the characteristics from the trial populations. We successfully replicated the trial findings using nonrandomized RWD studies. Features of study design—active comparator new-user design and adapting strict trial eligibility criteria—removed much of the confounding.

Comparative effectiveness of systematic therapies for metastatic castration-sensitive prostate cancer: a parametric survival network meta-analysis of randomized controlled trials Lin Wang* Lin Wang Channing Paller Hwanhee Hong Caleb Alexander Otis Brawley

Background: Treatment decision-making for metastatic castration-sensitive prostate cancer (mCSPC) is challenged by unclear comparative effectiveness and widely varied costs of multiple competing strategies.

Objective: To compare the effectiveness and safety of systematic therapies for mCSPC.

Methods: Bibliographic databases, regulatory documents, and trial registries were searched for randomized controlled trials testing active drugs that added to androgen deprivation therapy (ADT) for mCSPC. Cochrane risk-of-bias tool version 2 were used to assess trial quality. Bayesian network meta-analysis (NMA) was used to estimate relative effects of competing strategies. In addition to combing published constant hazard ratios (HR), we reconstructed survival data from Kaplan Meier curves to enable parametric survival NMA and that allows time-varying HR.

Results: Seven trials with 7,236 patients were included. Risk of bias is a concern for trials with open label, missing data, or unprespecified analysis. Ordered from the most to the least effective, treatments that improved the overall survival are abiraterone, apalutamide, and docetaxel, HR (95% credible interval [CI]) 0.64 (0.56-0.73), 0.67(0.51-0.88), and 0.80 (0.72-0.89); treatments that improved radiographic progression-free survival (rPFS) are: enzalumide, abiraterone, apalutamide, and docetaxel, HR (95% C) 0.39 (0.30-0.51), 0.45 (0.40-0.51), 0.48 (0.39-0.59), and 0.67 (0.61-0.74). Allowing time-varying HR produced similar treatment rankings (Figure). Serious adverse events (SAE) were substantially increased for docetaxel and slightly increased for abiraterone, odds ratio (95%CI) 104.17 (24.85-1012.32) and 1.42(1.11-1.83).

Conclusions: Abiraterone provided the largest OS benefit with slightly increased risk of SAE. Apalutamide offered comparable OS benefit with abiraterone without increasing SAE risk. Enzalutamide, although delayed rPFS to the greatest extent, did not show OS benefit based on the available evidence.
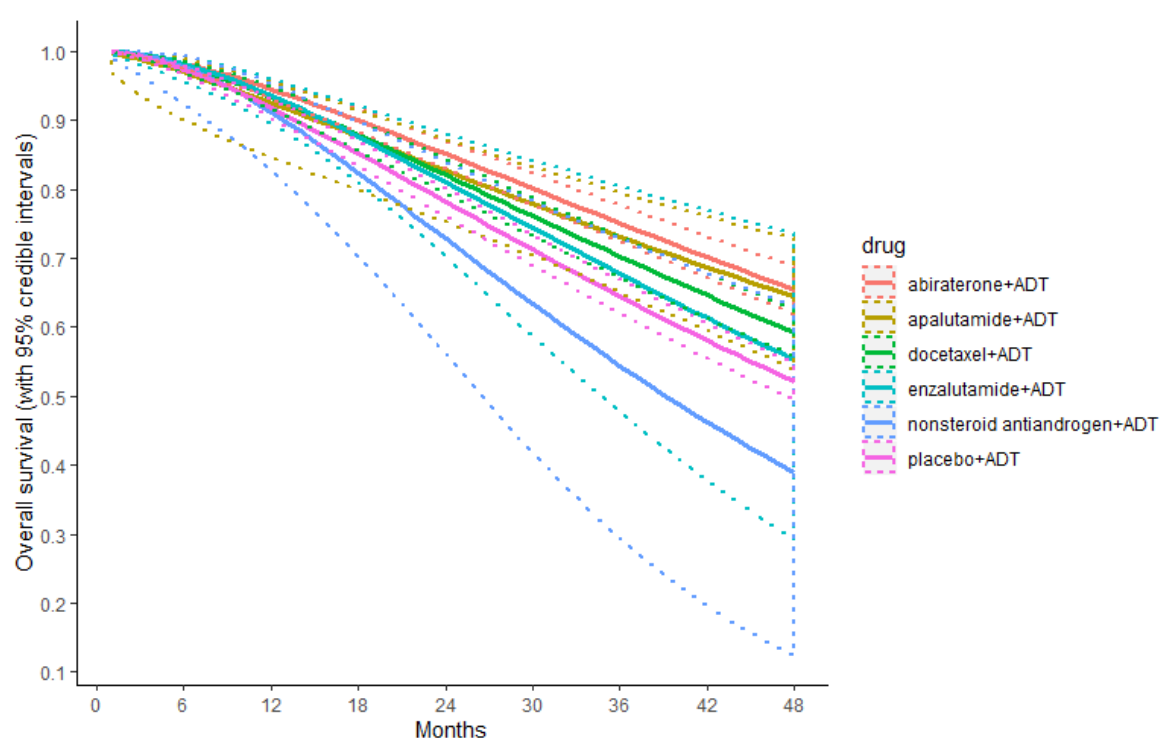
Associations of community socioeconomic deprivation with care processes and HbA1c values at time of type 2 diabetes diagnosis in Pennsylvania Annemarie Hirsch* Annemarie Hirsch Melissa N. Poulsen Cara Nordberg Joseph Dewalle Jonathan S. Pollak Carla Mercado Deborah B. Rolka Karen Siegel Brian S. Schwartz

Development of type 2 diabetes (T2D) can span more than 10 years before diagnosis. Microvascular disease progresses during this time, leaving individuals diagnosed later vulnerable to T2D complications. Community socioeconomic deprivation (CSD) is a risk factor for poor T2D control and complications, however it is unknown whether CSD disparities are present at diagnosis or occur later in disease. We conducted a retrospective cohort study of 15,888 individuals newly diagnosed with T2D to evaluate associations of CSD and care process and clinical measures at time of diagnosis. Participants were primary care patients of a Pennsylvania health system who had contact with the system at least 2 years before diagnosis. Process measures included presence/absence of glycated hemoglobin (HbA1c) and low density lipoprotein (LDL) laboratory testing in the electronic health record between 1 year prior to and 2 weeks after diagnosis; clinical measures were HbA1c (percentage of total hemoglobin) and LDL (mg/dL) values closest to diagnosis date. CSD was measured with U.S. Census indicators: proportion in poverty, unemployed, on public assistance, with less than high school education, and not in the labor force. We used logistic and linear regression to evaluate associations between CSD quartiles (Q) and process and clinical measures, respectively, adjusting for confounding variables. Analyses were stratified by community type (townships, boroughs, cities). Mean HbA1c values were 0.21% (95% CI: 0.01, 0.40) higher in the most (Q4) deprived versus the least (Q1) deprived townships at time of diagnosis. Residents of the most deprived townships (versus least deprived) were less likely to have been tested for HbA1c (OR: 0.84, 95% CI: 0.72, 0.98) and LDL (0.84, 95% 0.71, 0.98) in 1 year before and up to 2 weeks after diagnosis. T2D care and HbA1c levels differed at time of diagnosis by CSD, indicating disparities at the time of diagnosis in townships, but not in other community types.

Informing public health interventions using ethical criteria of health equity to reduce social inequities in type 2 diabetes: a modelling study using the Diabetes Population Risk Tool Brendan Smith* Brendan Smith Maxwell J. Smith Arjumand Siddiqi Christine Warren Sam Harper Nicholas King Adrian Viens Carlos Quiñonez Marian Kelly Laura Rosella

Background:Social inequities in diabetes remain in Canada, with uncertainty regarding which interventions will optimally reduce inequities. Little empirical evidence exists regarding how ethical criteria of health equity (e.g., 'sufficiency', 'equality') can inform public health interventions. The study objective was to model the effectiveness of public health interventions to reduce social inequities in diabetes according to distinct ethical criteria of health equity.
Methods:Using the validated Diabetes Population Risk Tool (DPoRT), ten-year diabetes risk was calculated for respondents to the nationally representative 2015-16 Canadian Community Health Survey (n=67,867, aged >28 years). Diabetes cases prevented or delayed was estimated across low (high school or less), medium (high school graduation) and high (post-secondary degree or higher) education groups according to two ethical criteria: 1) Equality (equalizing diabetes risk); 2) Sufficiency (reducing diabetes risk below the DPoRT high-risk threshold (≥16.5), beyond which remaining inequalities are not considered ethically important). Hypothetical percent weight-loss interventions in overweight and obese individuals were modelled for each ethical criterion, increasing until inequities were eliminated.
Results:Education was inversely associated with baseline diabetes risk (RR=1.68, 95%CI:1.63,1.73; low vs. high education). 'Equality' was achieved by implementing 20% and 15% weight-loss interventions in low and medium education groups. 'Sufficiency' was achieved by a 14% weight-loss intervention in high-risk individuals, however large social inequalities in diabetes remained (RR=1.52, 95%CI:1.48,1.56; low vs. high education). These interventions resulted in 246,923 and 267,690 diabetes cases prevented or delayed, respectively.
Conclusions:This study quantifies how the choice of two ethical criteria, which both aim to reduce diabetes inequities, can have disparate effects on social inequities in diabetes.

Supernatural beliefs intervention to enhance type 2 diabetes self-management in China: a pilot randomized controlled trial Stephen W. Pan* Stephen Pan Zihan Dong Qikai Wang Shiqiang Wu Yuxin Liang Wanqi Wang Mark A. Strand Amy Wachholtz Guofeng Zhou Dan Mao Yimei Tang

Background: China has over 100 million people living with type 2 diabetes mellitus (T2DM), many of whom experience adverse health outcomes due to suboptimal diabetes self-management. Interventions framed around pre-existing personal beliefs in the supernatural may improve T2DM self-management, but such interventions are lacking in China. This pilot randomized controlled trial (RCT) examined the feasibility of a full-size RCT to evaluate the efficacy of a supernatural beliefs-based intervention on T2DM self-management in China. Methods: In 2019, 62 T2DM patients were enrolled at two hospitals in Suzhou, China. Participants were randomly assigned to view a 30-second control or intervention video at baseline. The control video showed general diabetes self-management information. The intervention video showed identical information, but also indicated that some diabetics with supernatural beliefs have lower glycemic levels because their beliefs enhanced their confidence in diabetes self-management. Development of the intervention was guided by literature on spiritual framing health interventions. Baseline and follow-up measures after 2-12 weeks were assessed by interviewer-administered surveys in-person and by telephone, respectively. Diabetes self-management was assessed with the Diabetes Self-Management Questionnaire. Group differences were assessed with T-tests and Chi-square tests. Results: Comparable baseline characteristics between the control and intervention groups indicated that randomization was successful (Table). However, follow-up retention was low, especially for the intervention group (3% vs 31%, p<0.01). Conclusion: A full-size efficacy RCT using the current study design is unlikely to succeed. T2DM patients shown the supernatural beliefs-based intervention had significantly higher loss to follow-up that was insurmountable. Older T2DM patients in Suzhou, China may not be receptive to supernatural beliefs-based interventions delivered in clinical settings.

Table. Baseline participant characteristics (n=62)

	Control (n=32) (%)	Intervention (n=30) (%)	p-value
Sociodemographic Characteristics			
Age, mean (SD)	58.9 (11.0)	57.1 (11.5)	0.54
Sex			
Male (vs female)	53.1	43.3	0.44
Education			
None/elementary school	53.1	40.0	0.45
Middle school	28.1	43.3	
High school/vocational high school/vocational college	18.8	16.7	
Religious Affiliation			
None	78.1	70.0	0.52
Buddhist	15.6	26.7	
Muslim/Protestant/Catholic/other	6.3	3.3	
Belief in supernatural determinants of health score, mean (SD)	1.28 (0.63)	1.67 (1.06)	0.09
Diabetes			
Years since diagnosis, mean (SD)	7.67 (6.7)	7.8 (7.2)	0.93
Glucose control score, mean (SD)	11.0 (2.6)	11.0 (2.5)	0.99
Dietary control score, mean (SD)	8.6 (2.6)	8.9 (2.3)	0.66
Physical activity score, mean (SD)	6.8 (2.5)	6.1 (2.8)	0.27
Health-care use score, mean (SD)	5.7 (1.3)	5.1 (1.7)	0.09

Social

Religious involvement is associated with diabetes self-management among Chinese diabetes patients: a cross-sectional study Wanqi Wang* Wanqi Wang Shiqiang Wu Yuxin Liang Zihan Dong Qikai Wang Guofeng Zhou Dan Mao Yimei Tang Stephen W. Pan

Background
Diabetes prevalence is rising rapidly in China, but disease self-management among diabetes patients remains suboptimal. Research from Europe and the US indicates that religious involvement may be associated with more physical activity and healthy diet, but understanding of religious involvement among diabetes patient in China is limited. This study aimed to examine the influence of religious involvement on diabetes self-management among diabetes patients in Suzhou, China.
Methods
Participants were recruited from an endocrinology clinic in Suzhou, China. Eligibility criteria: >18 years old, no cognitive impairment, and diagnosed with diabetes by a physician. Diabetes self management questionnaire (DSMQ) were used as the outcome measure. Religious involvement was measured by the Duke University Religion Index. Multiple linear regression was used to evaluate the association between religious involvement and diabetes self management. Control variables included age, sex, diabetes duration, alcohol use, tobacco use, educational attainment, insurance type and living situation.
Results
The analytic sample size was 70. The DSMQ score significantly decreased by 0.45 for every unit increase in religious involvement ($\beta=-0.45$, $p<0.05$). Of the four subdomains of the DSMQ (Glucose Management, Dietary Control, Physical Activity, and Health-Care Use), religious involvement was significantly associated with physical activity ($\beta=-0.27$, $p<-0.01$), but not others. Stronger private religious activities and intrinsic religious beliefs were associated with less physical activity ($\beta=-1.06$, $p<0.05$; $\beta=-0.31$, $p<0.01$, respectively).
Conclusion
Religious involvement may be associated with inadequate physical activities and thus suboptimal diabetes self management among Chinese adults with diabetes. Further research is need to understand the mechanisms of how religious activities may be impacting diabetes self management in China.

Living in temporary housing increased the incidence of diabetes mellitus for men in 64 years or younger in tsunami affected area after the Great East Japan Earthquake Shuko Takahashi* Shuko Takahashi Kozo Tanno Ryohei Sasaki Seiichiro Kobayashi

Objectives: Previous study demonstrated temporary worsening of diabetes mellitus (DM) control immediate after the disaster. However, the association between incidence of DM and living conditions inside affected area has not been determined. We compared the incidence of DM between the people living in temporary housing (TH) and the people living in other types of accommodation (non-TH) five years after the Great East Japan Earthquake.
Methods: Longitudinal follow-up was conducted from 2011 to 2015 in a cohort of 7,491 residents (mean age, 61.6 years old, male, 36.0%). We calculated the odds ratios of new onset of DM in the TH group (n =2,372) compared with the non-TH group (n =5,119) using discrete-time logit models stratified by sex and age classes (64 years or younger, and 65 years or older).
Results: The TH group was significantly higher odds ratio (RR) for men in 64 years or younger (OR [95% Confidence interval (CI)], 1.71 [1.03 - 2.85]; P value =0.040), but that group was not significantly higher OR for men in 65 years or older. In women, the living condition was not significant in both age classes. The people who experienced the death of family member during the disaster was significantly higher OR than those who did not experienced it for women in 65 years or older (OR [95% CI], 2.83 [1.69 - 4.75] ; P value <0.001).
Conclusions: Survivors relocated to temporary housing appeared to be at increased risk of DM.

Neighborhood factors associated with diabetes control in a national sample of veterans with diabetes. Kelly Hunt* Kelly Hunt Melanie Davis John Pearce John Bian Brian Neelon

Background: We performed a retrospective analysis of a national cohort of veterans with diabetes to better understand neighborhood factors and racial/ethnic disparities related to diabetes control and treatment.
Methods: A retrospective cohort study was conducted in a 2015 national cohort of 1,140,634 veterans with diabetes, defined as two or more diabetes ICD-9 codes (250.xx) across inpatient and outpatient records. Exposures of interest included the Social Deprivation Index (SDI), the National Walkability Index (NWI) and a dichotomous variable identifying food deserts at the census track level. The main outcome measure was HbA1c level dichotomized at ≥ 8.0%.
Results: Mean SDI and NWI values were 52.8 (range 1 to 100) 7.9 (range 1-20), respectively with 44.7% of veterans living in a food desert. After adjustment for age, gender, race-ethnicity, service-connected disability, marital status, comorbidity index, diabetes medication use and adherence, access to care metrics and spatial effects, increased SDI was associated with increased uncontrolled diabetes [OR=1.05 (95% CI: 1.04, 1.06)] while increased NWI was associated with decreased uncontrolled diabetes [OR=0.97 (95% CI: 0.97, 0.99)]. Living in a food desert was not associated with diabetes control, but relative to whites, non-Hispanic blacks [OR=1.09 (95% CI: 1.07, 1.10)] and Hispanics [OR=1.32 (95% CI: 1.29, 1.35)] had higher odds of uncontrolled diabetes.
Conclusions: In a national cohort of veterans with diabetes, we found neighborhood level social deprivation and walkability indexes were independently associated with diabetes control even after adjustment for demographics; comorbidity burden; use of and adherence to diabetes medication; healthcare utilization, access metrics as well as spatial effects. Moreover, racial-ethnic differences in diabetes control persisted across the nation, with NHB and Hispanic veterans consistently having a higher odds of poor diabetes control than non-Hispanic veterans.

Nutrition/Obesity

Weight loss, stability and low weight gain during pregnancy among women with obesity are associated with preterm birth and smaller neonatal size Elizabeth Widen* Elizabeth Widen Amy Nichols Fei Xu Monique Hedderson

Few studies have examined whether associations between weight loss and low weight gain during pregnancy with birth outcomes vary by obesity class. Electronic health records of 35,011 women with obesity from Kaiser Permanente Northern California (2008-2013) were abstracted. Total pregnancy weight gain (GWG) was grouped into clinically meaningful categories [Adequate (reference, met Institute of Medicine (IOM, 5-9.1 kg)), Excessive (>IOM), Low (1-4.9 kg), Stable (+/-1 kg), Weight Loss (>1 kg)]. Associations between GWG and outcomes [preterm (8.2%), small- (7.3%)/large- (15.7%) for gestational age (SGA/LGA), NICU-admission (>72 hrs, 6.5%)] were examined using multivariable Poisson regression, evaluating effect modification by obesity class (I 30–34.9 kg/m2; II 35–39.9 kg/m2; III ≥40 kg/m2). A majority of women exceeded IOM (56.6%), 22.5% met IOM, and 12.6%, 3.5% and 4.7% had low GWG, weight stability and weight loss, respectively. Compared to adequate GWG, loss, stability and low GWG were associated with increased risk of preterm birth [RR: Loss=1.3, 95%CI: 1.1-1.5; Stable=1.2, 95%CI: 1.0-1.4; Low=1.2, 95%CI: 1.1-1.4]. Effects of GWG patterns on birth outcomes varied by class for LGA and SGA, but not preterm birth. Loss and low GWG were associated with lower risk of LGA [RR: Loss=0.6, 95%CI: 0.4-0.8; Low=0.7, 95%CI: 0.6.-0.8], while stability was associated with lower risk of LGA in class I (RR=0.49,95% CI: 0.33-0.72), but higher risk of LGA in class III (RR=1.8, 95%CI: 1.1-2.9). Loss and stability were associated with increased risk of SGA [RR: Loss=1.9, 95%CI: 1.6-2.5; Stable=1.7, 95%CI: 1.4-2.2)], while low GWG was associated with SGA only among class II (RR=1.3, 95%CI: 1.0-1.8). Only low GWG was associated with NICU admission (RR=0.85, 95%CI: 0.7-1.0). Among this large cohort of women with obesity, weight loss, stability and low GWG were associated with preterm birth among all obesity classes and smaller neonatal size with little variation by obesity class.

Estimating the effect of exclusive breastfeeding on risk of overweight and obesity in infants: A targeted maximum likelihood analysis. Sindiso Nyathi* Sindiso Nyathi Suzan Carmichael Michelle C. Odden

Incidence of childhood overweight and obesity in the United States has increased rapidly, with 18.5% of children obese in 2016. Recent work suggests that early-life exposures contribute to weight gain. Feeding behavior is an important early-life risk factor for weight gain in infancy. Breastfeeding and late introduction of solid food are associated with a protective effect against overweight and obesity. Causal estimates of the influence of breastfeeding on weight gain have been limited by the complexity of feeding behaviors and impracticality of controlled feeding trials. In this study, we use a doubly-robust estimator to estimate the influence of exclusive breastfeeding at 4-months on weight status at one year. Targeted maximum likelihood estimation (TMLE) uses information about treatment and outcome mechanisms and results in bias reduction if either model is correctly specified. We used data from the Infant and Feeding Practices Study, a longitudinal study of mother-infant pairs conducted from 2005-2007 across the United States. Data were self-reported by mothers via monthly mail questionnaires and included information on infant and maternal diet, demographics and sleep. Treatment was defined as exclusive breastfeeding at month 4 and the outcome was overweight status (weight-for-age >85th percentile) at 12 months. 1,391 mother-infant pairs were included in our analysis (mostly young, Caucasian and high-income). 32% (450) of mothers reported exclusive breastfeeding at month 4 and 23% (326) of infants were classified as overweight at 12 months. Exclusive breastfeeding was associated with a 48% decrease in the odds of overweight in infants (unadjusted OR=0.52, 95%CI 0.39–0.69). In the final marginal structural model with TMLE, treatment was associated with a 47% decrease in the risk of overweight (OR=0.53, 95%CI 0.36–0.70). Using a TMLE approach, we found that exclusive breastfeeding is associated with a reduced risk of overweight and obesity at 12 months.

Flexible approaches for modeling weight histories Hailey Banack* Hailey Banack Andrew
Stokes

Body mass index (BMI) and mortality have a well-known J- or U-shaped relationship: risk is highest
in the low and high values of BMI, with the nadir in the middle of the range. Despite the known
shape of the BMI-mortality curve, when BMI is used as an exposure variable, it is frequently
modeled as a dichotomous or categorical variable. This results in a loss of information regarding the
true exposure-outcome relationship, and potentially incorrect inferences about the mortality risks of
BMI. Moreover, most often, BMI is measured as a point exposure variable, which ignores important
information about weight history. The objective of this analysis is to demonstrate the use of two
flexible modeling approaches: locally weighted regression smoothing (LOWESS) and restricted cubic
splines, to compare the age-standardized mortality rate of current BMI, BMI 1-year prior to survey,
BMI 10-years prior to survey, and lifetime maximum BMI. We used data on adult participants from
the 1999-2012 waves of the National Health and Nutrition Examination Survey (NHANES;
n=29724). Mean values of BMI differed markedly across exposure variables. Results from the
LOWESS analysis are presented in the Figure. We found strong evidence of a J-shaped relationship
between BMI at survey and 1-year prior, but not BMI 10-years prior or lifetime maximum BMI.
Results from analyses using restricted cubic splines were very similar. These results raise the
question of whether the J-shaped BMI-mortality relationship can be attributed to reverse causality, a
type of bias due to disease related weight loss. This bias would be expected to affect current or
recent BMI but not historical BMI. Further research is needed to fully understand mortality risk in
the low BMI range (<24kg/m2), as the majority of research to date has focused on the risks of high
BMI. These findings speak to the importance of using flexible modeling strategies to understand the
complex BMI-mortality relationship.
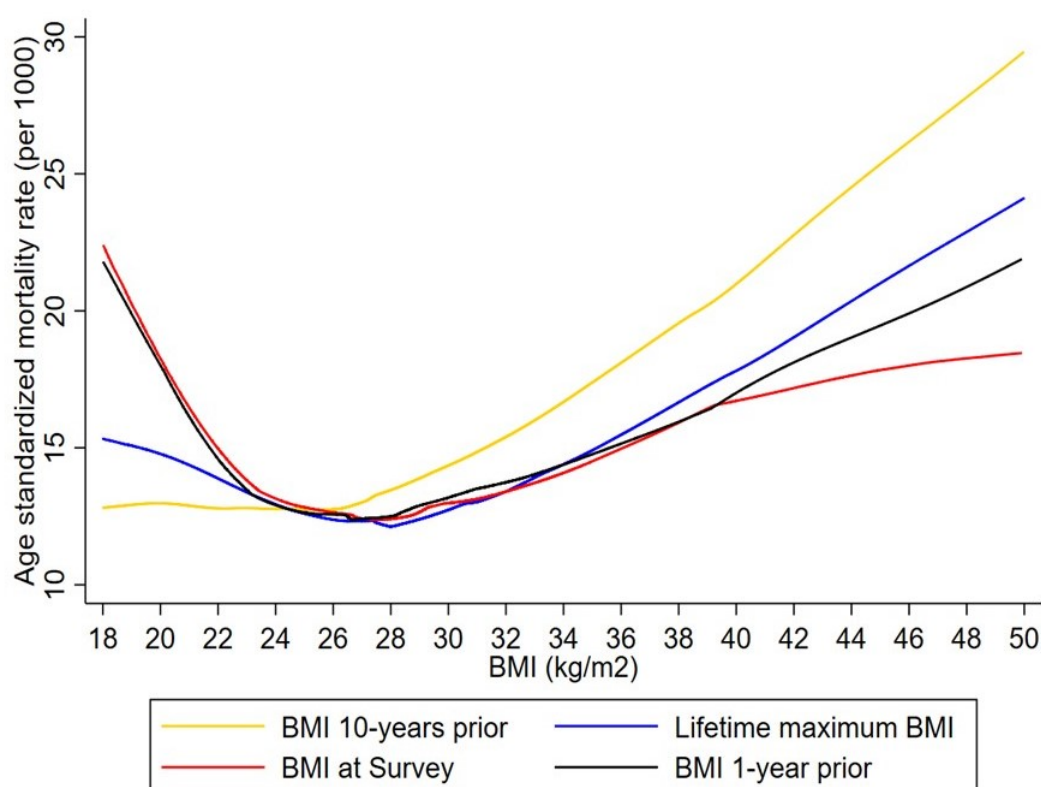
Comparative effectiveness of dietary interventions on the risk of cardiovascular diseases – estimates from Swedish populations Katalin Gėmes* Katalin Gėmes Alicja Wolk Maria Feychting Anita Berglund Miguel A. Hernán

Background: Explicitly causal approaches in nutritional epidemiology are rare. Most observational studies describe associations between different dietary items and health outcomes, which are hard to interpret causally. In contrast, the parametric g-formula can be used to compare the long-term risks of different health outcomes under hypothetical dietary interventions. We explored the feasibility of implementing the g-formula to Swedish population- and health-register data in order to quantify the risk of cardiovascular disease under hypothetical interventions on fish and red meat consumption.

Study population:
The Swedish Mammography Cohort (SMC) and the Cohort of Swedish Men (COSM) are two prospective cohort studies. The SMC was established in 1987 with women born between 1914 and 1948 in two Swedish counties. Of 90,303 women who were invited, 66,651 joined the cohort. Follow-up questionnaires were sent in 1997, 2008, and 2009 with questions on diet, lifestyle, and health. The COSM was established in 1997 with men born between 1918 and 1952 in the same counties. Of 100,303 who were invited, 48,850 joined the cohort. Similar follow-up questionnaires were sent in 1997, 2008, and 2009. Data from several national registers were linked to the individual level data through the unique Swedish Personal Identification number. Eligible participants were followed until major cardiovascular evens, death, non-return of the follow-up questionnaires or December 2017.

Results: Of 29,133 eligible women, 5796 experienced the outcome, and 7038 died due to other reasons during the follow-up. Of 31,229 eligible men, 8779 experienced the outcome, and 9384 died. The median weekly number of portions was 3 for fish, and 7-8 for red meat. Our findings suggest that there is enough information to use the parametric g-formula to estimate the effect of replacing dietary red meat by fish consumption on the risk of cardiovascular disease.

Causal differences in blood arsenic and mercury concentrations by following the dietary recommendation on seafood intake during pregnancy Pi-i D. Lin* Pi-i Lin Andres Cardenas Mohammad L. Rahman Marie-France Hivert Sheryl L. Rifas-Shiman Tamarra James-Todd Emily Oken

Background: Seafood can be a substantial source of exposure to toxic chemicals , such as methylmercury. The US Food and Drug Administration and the World Health Organization suggested pregnant women to consume up to 3 serving of seafood per week. In this study, we quantified the effect of following this dietary guideline on metal exposures to generate easily interpretable causal estimates for public health messages.

Methods: 1206 pregnant women in Project Viva (recruited 1999-2002 in eastern MA) reported dietary habits using a validated food frequency questionnaire and gave blood for metal concentration analyses in the first trimester. We performed a causal analysis to estimate differences in arsenic (As) and mercury (Hg) if all pregnant women followed a hypothetical intervention of eating ≤3 serving/week of seafood (fish and shellfish) compared to a scenario in which all of the pregnant women ate >3 servings/week. We applied Targeted Maximum Likelihood Estimation to estimate the marginal geometric mean (GM) difference in metals accounting for baseline covariates (age, parity, education, household income, marital status, race/ethnicity, pre-pregnancy BMI, smoking, hemoglobin level, sex of the child), and intakes of all other food groups .

Results: At median (IQR) 9.6 (2.1) weeks gestation, total erythrocyte As concentration was 0.8 ng/g (0.4, 1.6) and Hg concentration 3.3 ng/g (1.6, 6.6); 85.7% (N=1034) had seafood consumption of ≤3 servings/week. Under the hypothetical intervention where all women in the population followed the dietary recommendation of eating ≤3 servings of seafood per week, the marginal GM of As was 0.63 (95 CI: -0.93, -0.32) ng/g lower, and Hg was 3.39 (-4.68, -2.10) ng/g lower, than pregnant women consuming >3 servings of seafood per week.

Conclusion: Following the dietary guideline of consuming ≤3 servings/week of seafood during pregnancy may reduce exposure to arsenic and mercury.

Incident cancer diagnosis on subsequent risk of Alzheimer's disease-related dementia
Jonviea Chamberlain* Jonviea Chamberlain Carole Dufouil Geneviève Chêne

Background
Despite a preponderance of evidence supporting a protective effect of cancer on risk of developing Alzheimer's disease dementia, the high risk of survivor bias due to informed censoring remains. To date, few studies have accounted for the competing risk of mortality when investigating this association. Illness-death models (IDMs) could aid in assuaging this issue by accounting for mortality as a competing risk, while concurrently modelling risk of progression to AD dementia.

Methods
This study uses data collected in the Memento cohort, a prospective multi-center clinical cohort in France that follows individuals with cognitive deficits or isolated cognitive complaints up to five years post-inclusion. Incident cancer cases, excluding benign, were identified using terms from the Medical Dictionary for Regulatory Activities. An IDM was used to estimate transition-specific hazard ratios (HRs) and 95% confidence intervals (CIs), with attained age as the underlying time scale. Included confounders were sex, education, mini-mental state examination score, and APOE gene status.

Results
This study included 2,223 individuals. By study end, 201 individuals were diagnosed with AD dementia (8.7%), and 167 with incident cancer (7.2%); 79 cases died during follow-up. IDM results indicated cancer to be associated with a reduced HR for the transition from 'healthy' to 'AD dementia' (HR=0.4, 95% CI= 0.2-0.9). However, for the transition from 'AD dementia' to 'death', cancer was associated with an increased transition intensity (HR=3.1, 95% CI=1.7-5.5).

Conclusions
This study supports the inverse relationship observed between AD dementia and cancer. This relationship was not explained by potential survivor bias in the study population, which was taken into account in using an IDM. In light of these results, investigations into the potential mechanisms driving the observed relationship are needed so as to inform future research into therapeutic and preventative interventions.

Association of metabolic syndrome and cognitive function in a population-based cross-sectional study of adults aged 60 years or older Shama Karanth* Shama Karanth Erin L. Abner

Metabolic syndrome (MetS) is a clustering of cardiovascular risk factors, including diabetes, hypertension, high body weight, and hypercholesterolemia, which individually have been reported to associate with cognition. However, the association of (MetS) with cognition is not well established. The study aimed to explore the association of MetS with cognitive performance in a nationally representative study sample. Methods Cross-sectional data of the National Health and Nutrition Examination Survey (NHANES 2011-2014) were obtained for participants age $\geq$ 60 years. Cognitive performance was defined based on components of the Consortium to Establish a Registry in Alzheimer's disease (CERAD) neurocognitive battery. MetS was defined as per the American Heart Association of at least 3 of the 5 conditions. A composite cognitive z-score was calculated from CERAD component z-scores to denote global cognitive function, based on the NHANES sample (Fig1). To address missing data (19.5% of participants were missing at least one element of MetS or cognitive component), we imputed 20 datasets using multivariate imputation by chained equations, and survey statistics to account for the complex NHANES sampling design. Linear regression models were fit the imputed datasets to evaluate the association of cognitive performance and MetS. Results Participants (N=3181) were 69.4 years on average. MetS ($\geq$3 conditions) was present in 54.2% of participants. MetS was associated with almost a half standard deviation lower mean cognitive score compared to participants with no MetS factors (β= - 0.44; 95% CI -0.72, -0.15), while participants who did not meet criteria for MetS but had 1-2 MetS conditions had similarly lower scores relative to participants with none (β= -0.47 (95% CI -0.77, -0.16). Findings suggest that MetS was significantly associated with lower cognitive performance in adults $\geq$60 years. Dichotomous MetS classifications may obscure cognitive risks for those individuals who don't meet the MetS criteria.

Figure 1: Cognitive test scores before and after standardization
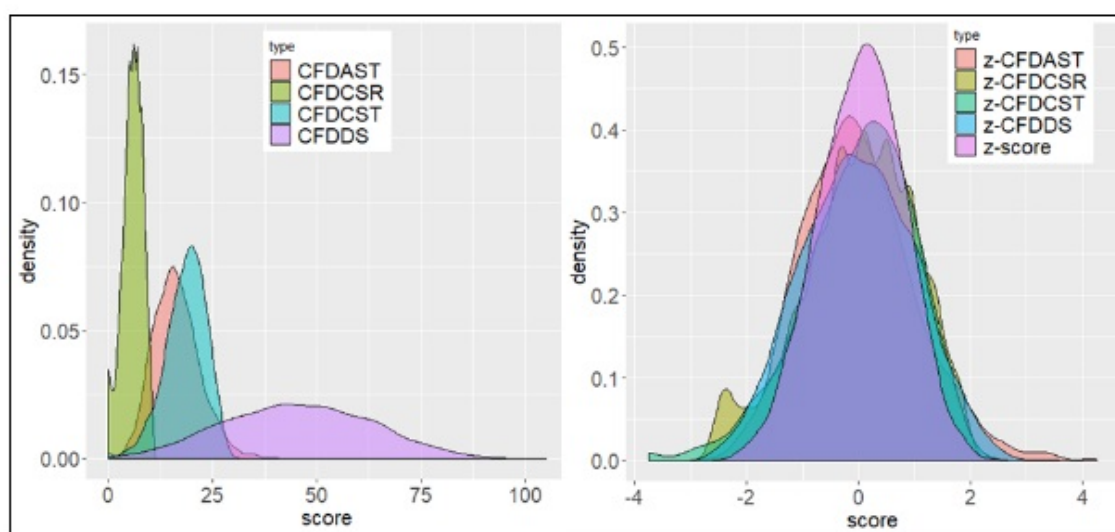
CFDCST test: CERAD word list learning.

CFDAST test: CERAD Animal Naming

CFDDS test: WAIS Digit-Symbol Substitution test

CFDCSR test: CERAD word list delayed recall

The Associations of Dietary Copper with Incident Dementia: The Atherosclerosis Risks in Community (ARIC) Study Jingkai Wei* Jingkai Wei Erin Bennett Eric A. Whitsel Xiaohui Xu Eun Sug Park Richard L. Smith James Stewart Qi Ying Melinda C. Power

Background: Copper may be involved in Alzheimer's disease pathogenesis. In particular, a combination of high dietary copper intake and high cholesterol may accelerate cognitive decline. We aimed to examine the associations of dietary copper intake in the presence of a high fat diet with incident dementia in a community-dwelling sample in the United States.
Methods: The Atherosclerosis Risks in Community (ARIC) Study was used for analysis. Dietary copper (including that from food and dietary supplements) and saturated fat intake were calculated as the average intake across the 1st (1987-1989) and 3rd (1993-1995) visits of the ARIC study, based on information collected from the 61-item Food Frequency Questionnaires. Dementia was ascertained based on in-person assessment, hospital discharge codes, and other supplemental methods throughout follow-up. Participants with diagnosed dementia at study baseline (Visit 4) were excluded from analysis. Cox proportional-hazards models were used to examine the associations of dietary copper (from food, supplements, total) with incident dementia. Potential interactions between dietary copper as continuous variables and high saturated fat intake (defined as the upper 25th percentile) were tested.
Results: A total of 9,492 participants (mean age: 62.9±9.7 years, 43.9% male, 17.5% African American) were included in the analysis, with an average follow-up time of 16.3 years. Each 1 mg/day higher intake of total dietary copper (hazard ratio (HR): 1.45, 95% confidence interval (CI): 1.02, 2.06) and copper from food (HR: 1.42, 95% CI: 1.04, 1.94) were associated with higher incident dementia among those with a high intake of saturated fat after covariate adjustment. Intake of copper from supplements was not associated with dementia.
Conclusion: The combination of a diet high in both copper and saturated fat may increase the risk of dementia among community-dwelling populations.

Neurology

A Comparison of Prediction Approaches for Identifying Prodromal Parkinson Disease Mark Warden* Mark Warden Brad Racette Susan Searles Nielsen Alejandra Camacho-Soto Roman Garnett

There is a growing interest in identifying people with Parkinson disease (PD) during the prodromal phase of disease to inform future research. Therefore, we derived PD cases and controls from a population-based case-control study of incident PD in 2009 among Medicare beneficiaries aged 66-90 enrolled in Medicare Part D. We used International Classification of Disease version 9 codes, procedure codes, prescription claims, and demographics to select variables and build predictive models using either penalized logistic regression or a random forest classifier. We considered whether the addition of Medicare Part D improved prediction above a model that used only the other claim codes. We compared the models using each model's receiver operator characteristic area under the curve (AUC). The random forest classifier favored common diagnoses/procedures/medications, including those with modest association with PD. The penalized logistic regression chose predictors with strong, occasionally rare, associations. All models showed good discrimination with AUCs between 0.824-0.835. The consistency of our results suggests we have obtained a robust final model approaching the limit of any model's predictive ability given this data structure. The identified predictive associations may guide further research into PD etiology.

Hypothetical blood-pressure-lowering interventions and risk of stroke and dementia L. Paloma Rojas-Saunero* L. Paloma Rojas-Saunero Saima Hilal Eleanor J. Murray M. Arfan Ikram Sonja A. Swanson

Introduction: Reducing blood pressure in later life is often proposed to reduce the risk of stroke and dementia. However, randomized trials and observational studies have given limited insights due to short follow-up, highly selected eligibility criteria, and lack of use of methods to control for time-varying confounding.

Aim: To emulate a target trial and estimate the effects of hypothetical interventions on systolic blood pressure (SBP) on the risk of stroke and dementia

Methods: We used data from 5113 individuals, aged 55-80 years, with no prior history of stroke, dementia or cognitive impairment, followed for 15 years within the Rotterdam Study, a population-based cohort. We defined the following sustained interventions on SBP: (1) maintaining SBP below 120 mmHg, (2) maintaining SBP below 140 mmHg, (3) reducing SBP by 10% if above 140 mmHg, (4) reducing SBP by 20% if above 140 mmHg, and a combined intervention of quitting smoking with each of these SBP-lowering strategies. Incident stroke and incident dementia were treated as outcomes. We applied the parametric g-formula to adjust for baseline and time-varying confounding.

Results: The observed 15-years risk for stroke was 10.7%. Compared to no specified intervention (i.e., the "natural course"), all interventions that reduced SBP were associated with a stroke risk reduction of about 10% (e.g., reducing SBP by 20% if above 140mmHg risk ratio: 0.88 [95% CI: 0.79-0.98]). Jointly intervening on SBP and smoking decreased the risk of stroke by 18%. None of the specified interventions were associated with a meaningful change in dementia risk.

Conclusions: Our study suggests that a joint intervention on SBP and smoking cessation may reduce stroke risk, while the potential benefits (or risks) for reducing dementia risk were not observed.

Risk of stroke and dementia in 15 years of follow up
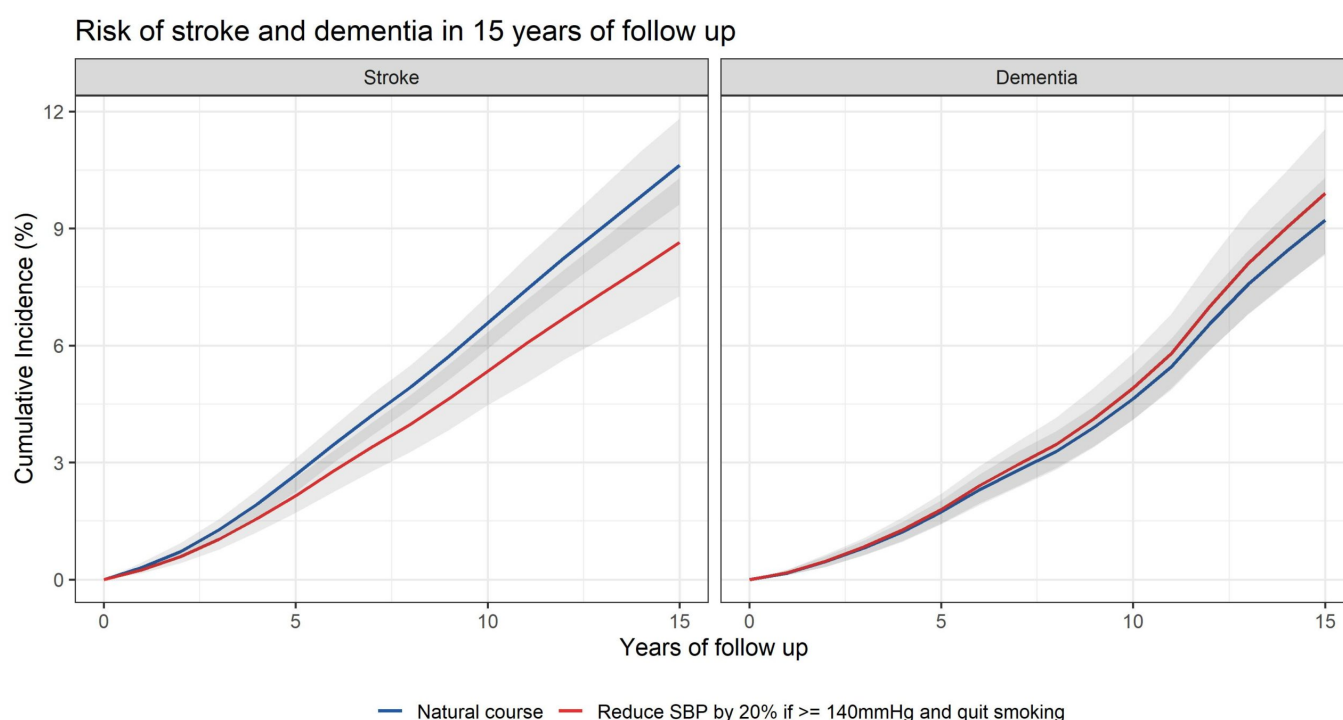
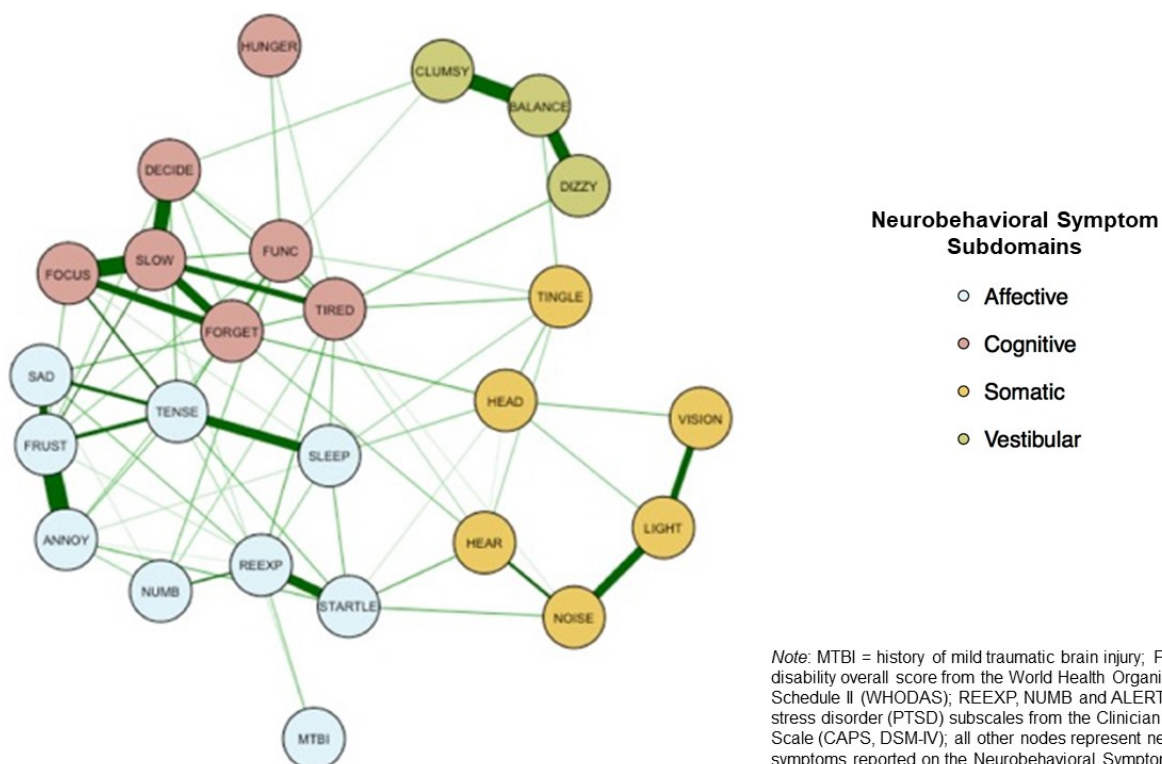## Mild traumatic brain injury, persistent neurobehavioral symptoms and functional disability in Post-9/11 Veterans: network analysis of a transdiagnostic sample Jennifer R. Fonda*

Jennifer Fonda Laura K. Levin Catherine B. Fortier William P. Milberg Regina E. McGlinchey

Post-9/11 Veterans are a clinically complex group; they often have several comorbid diagnoses including mild traumatic brain injury (mTBI), posttraumatic stress disorder (PTSD), and depression with overlapping neurobehavioral symptoms (NBS) such as poor concentration, irritability, and impaired sleep quality. Understanding the causal and indirect relationships between symptoms of physical and psychological trauma and measures of functional outcomes is critical to understanding the underlying drivers of impairment and has implications for treatment strategies. This study examined the relationships between NBS symptoms, mTBI, PTSD, and functional disability under the causal systems perspective. This approach posits that psychiatric comorbidity is a result of the interaction of symptoms that can directly influence other each other, as well as have their own unique or independent influence. Network analysis was used to model these complex relationships in which symptoms are modeled as "nodes" that are connected by "edges" representing the statistical relationships between them. By focusing on symptoms, network analysis revealed which symptoms (components) were most central to the propagation and maintenance of the overall psychopathology network and detect targets for interventions. Results showed that slowed thinking and anxiety NBS symptoms had the greatest node strength, a measure of how well a node is directly connected to other nodes, indicating that these symptoms were most influential in the model. Functional disability was most directly related to forgetfulness and impaired decision making as well as emotional numbness. History of mTBI was the weakest node, connected predominantly through its relationship with PTSD re-experiencing symptoms. These findings suggest that specific NBS are critically important factors in a complex constellation of symptoms in a highly comorbid population. Further, in a chronic sample, mTBI does not seem to be a determining factor.

Neurobehavioral Symptom Subdomains

- ○ Affective
- ● Cognitive
- ● Somatic
- ● Vestibular

Note: MTBI = history of mild traumatic brain injury; FUNC = functional disability overall score from the World Health Organization Disability Schedule II (WHODAS); REEXP, NUMB and ALERT are posttraumatic stress disorder (PTSD) subscales from the Clinician Administered PTSD Scale (CAPS, DSM-IV); all other nodes represent neurobehavioral symptoms reported on the Neurobehavioral Symptom Inventory (NSI).

Big Data

Improving prediction of outdoor active play using neighborhood images Randall Boyes*
Randall Boyes William Pickett Ian Janssen

Outdoor active play is a crucial source of physical activity for children with wide-ranging beneficial health impact. The built environment of a child's neighbourhood can influence their desire to engage in outdoor active play and can also indirectly influence ability to engage in outdoor active play by alleviating or worsening parents' safety concerns. Some of these important features are not easily measured at the national level from currently available data sources. We are exploring a new potential data source for measuring features of the built environment for use in prediction of children's time spent in outdoor active play.

Detailed physical activity data over a one-week period, parental assessment of neighbourhood features, and addresses were collected for 105 children between the ages of 10 and 13 from three different neighbourhoods in or near Vancouver, BC. Images from the area around these children's houses were collected using Google's Street View API. Semantic image segmentation of these images was completed using a deep neural network trained on ImageNet and the Cityscapes dataset. This process allows automated identification of features including tree cover, foot and bicycle traffic, vehicle traffic by type of vehicle, traffic calming features, and sidewalk type and quality. Initial tests suggest that the mean absolute error of prediction models using traditional data sources - such as points of interest, land use, green space, and street connectivity – can be reduced by 24% with the addition of these image-derived data.

This method of measuring features of the built environment offers potential benefits over traditional data sources. Accessing data through an API allows data to remain current and allows for modern knowledge translation in the form of a website interface. Using this data source, we can better understand the factors which influence children's physical activity and communicate this knowledge to the general population.

Big Data

Application of text mining methods to identify lupus nephritis from electronic health records Milena Gianfrancesco* Milena Gianfrancesco Suzanne Tamang Gabriela Schmajuk Jinoos Yazdany

Background: Lupus nephritis (LN), or chronic inflammation of the kidneys, is a frequent complication of systemic lupus erythematosus (SLE) and associated with higher overall morbidity and mortality. Accurate estimates of LN in the population remain limited due to the inability to capture this information through structured data fields in electronic health records. We aimed to develop a text mining pipeline to extract information on LN within clinical notes of a large, diverse university health system.

Methods: Individuals with a single diagnosis code for SLE (during June 2012 – February 2019 from electronic health records of a university health system were included (n=2,782). All clinical notes for patients were extracted and annotated using a clinical text-mining tool, the Clinical Event Recognizer (CLEVER), and a custom-built dictionary that included "lupus nephritis" and associated terms.

Results: A total of 18,354 positive and 9,293 negative mentions of LN were detected from over 68 million clinical notes. Positive mentions were captured for 834 unique individuals with SLE. When compared to a gold-standard set of chart-reviewed cases (n=161), our text mining tool detected LN with 94.4% sensitivity and 91.5% specificity. Estimates of LN by race and ethnicity mirrored patterns previously found in epidemiologic studies, with a higher prevalence of LN in African-American (35%), Asian (44%), other/mixed race (37%), and Hispanic (41%) patients compared to white patients (19%); however, our text-mining results showed a higher percent of LN across all race/ethnicity groups than those reported previously using ICD-codes in the Medicare population (Figure 1).

Conclusion: We conducted the first text-mining strategy to extract LN status from clinical notes. Additional evaluation on clinical notes of a national rheumatology registry is ongoing. Further refinement of the pipeline will allow us to determine factors associated with this important disease outcome.

Figure 1. Prevalence of Lupus Nephritis by Race/Ethnicity
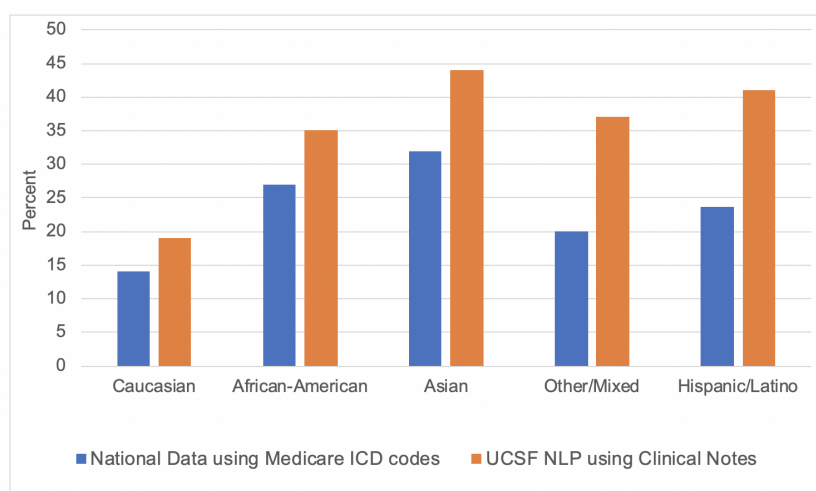
Prediction of Microclimates Using a Comparative Machine Learning Approach Rachel Sippy*
Rachel Sippy Diego Herrera David Gaus Ronald Gangnon Jorge Osorio Jonathan Patz

Microclimates are an important component of ecosystems and can impact human health through impacts on vector habitats. Aedes aegypti, the vector of dengue, chikungunya and Zika, is a highly localized species and its abundance is impacted by microclimate conditions. Our understanding microclimate stability is limited; there have been no attempts to predict microclimates.
HOBO Temperature/Relative Humidity Data Loggers were deployed in 4 sites per month for 1—24 days each month from September 2016 to August 2017 in a small community in rural Ecuador. Data were summarized for each 24-hour period. We assessed the variability of these summary microclimate measures across time and urban environments. We combined remotely-sensed and climate station data with urbanicity, elevation, and spatial components to predict summary microclimate measures across the entire community using machine learning. Machine learning algorithms were compared and best models were chosen based on predictive ability (highest root mean squared error (RMSE)) for a validation dataset.
We collected 287 log-days of data. Some microclimate measures were temporally stable, urban sites had warmer temperature measures and rural sites had higher relative humidity measures. We found that random forest algorithms best predicted many microclimate measures (temperature mean, median, minimum and relative humidity mean, median, RMSE: 0.61—0.65). Generalized boosting models fit temperature and relative humidity variance as well as minimum and maximum relative humidity, with good prediction (RMSE: 0.61—0.72). The best model for maximum temperature was a support vector machine, with moderate accuracy (RMSE: 0.53).
Our study was limited by a small sample size over time and space, and limited availability of prediction variables. Machine learning is a promising option for prediction of microclimates, though additional research with large datasets should be conducted for validation of model predictions.

Evaluating the health equity impact of a machine learning-based clinical prediction tool

Stephanie Teeple* Stephanie Teeple Corey Chivers Katherine Courtright

The construction, validation, and evaluation of clinical predictive models has been the purview of epidemiology for more than fifty years. However, there has been a persistent lack of validation for non-White/non-male populations and a more profound lack of 'impact studies' which examine the clinical impact of predictive models once implemented. These shortcomings have gained new urgency in the context of increasing public and scholarly concern about 'artificial intelligence' entrenching social bias in healthcare and other sectors. In this project, we evaluate a machine learning-based model already used in clinical practice (Palliative Connect, used to connect inpatients with palliative care consultation) to demonstrate an approach to subgroup validation and impact assessment.

For our subgroup validation analysis, we first fix the parameters of the Palliative Connect model and generate predictions for a new electronic health record (EHR) test dataset. We then partition copies of the test data according to strata of six patient attributes: racialization, sex assigned at birth, age quartile, insurance type, educational attainment and income. Using a nonparametric pairwise bootstrap weighted by number of encounters per patient, we generate CIs for performance metrics including accuracy, false positive and false negative rates, Brier score, c-statistic and integrated calibration index to compare predictive performance across patient subgroups. For our impact assessment approach, we utilize EHR data and an interrupted time series with synthetic control. We find that for several measures, predictive performance is equivalent or better in marginalized versus dominant patient groups. However, the inclusion of age as a predictor means that Palliative Connect has a higher false negative rate for several marginalized patient groups. More broadly, this project makes an important contribution to methods for evaluating the equity impacts of new predictive technology for health.

Race/ethnicity

group	n	accuracy	falsepos	falseneg	brier	cstat	eci
Non_hispanic_white	30195	0.81	0.16	0.38	0.09	0.81	0.02
Asian	874	0.81	0.17	0.35	0.10	0.82	0.05
Black	21962	**0.86**	**0.10**	**0.43**	**0.08**	0.82	0.01
Latinx	1123	0.85	**0.09**	**0.82**	**0.07**	0.76	**0.04**

Figure 1: Subgroup validation results by racialized group. Top row (non-Hispanic White) is the reference category. Bold face font indicates that the bootstrapped 95% confidence intervals did not overlap. For Black and Latinx patients, Palliative Connect performs similarly or better via accuracy, brier score, c-statistic and estimated calibration index. However, these groups have a significantly higher false negative rate (Palliative Connect fails to flag them for palliative care services) due in part to the fact that Black and Latinx patient populations are younger on average than the Non-Hispanic White patients.

Big Data

Approaches for the Inference of Mortality in Claims Data Dana Teltsch* Dawn Albright Feng Zhang Amanda MB Kelly Dana Y. Teltsch

Background
Deaths are often not completely captured in insurance claims databases, a common data source in pharmacoepidemiology studies. We hypothesized that machine learning can be used to identify likely mortality with sufficient precision to enable its use as an outcome in studies.
Objective
To assess the feasibility of inferring unreported deaths in claims data.
Methods
We used Optum's de-identified Clinformatics® Data , a nationally representative de-identified claims dataset with near-complete patient level mortality information before Sept/2011. We developed and assessed classifiers to identify deaths on training and testing sets prior to Nov/2011 using Apache Spark MLLib. Predictors included demographics, recorded diagnoses and medical procedures, and health services utilization, and were selected manually, from published studies, and automatically based on distributions. Models were developed from logistic regression and probabilistic machine learning approaches including random forest (RF) and gradient boosted trees (GBT).
Performance was evaluated based on sensitivity, specificity, positive and negative predictive values, and the area under the receiver curve (AUC) with bootstrapped-based standard deviations (StD).
Results
The cohort comprised over 36 million patients, and nearly 600,000 reported deaths. Several methods led to models with good properties, but GBT followed by RF performed the best. GBT classified deaths with a specificity of 0.99 when sensitivity was higher than 0.8, and AUC of 0.97 with a StD of 0.0017. Age, place of service, number of days in the hospital, total medical cost, as well as diagnosis codes indicating cardiac arrest and respiratory failure, or the count of diagnosis codes for hypertension, fatigue and shortness of breath were strong predictors of death.
Conclusion
Our results suggest that mortality events can be accurately inferred in claims data using machine learning approaches.

Cancer

mBCRM: a methylation-based risk prediction model for breast cancer Jacob Kresovich* Jacob Kresovich Zongli Xu Katie M. O'Brien Clarice R. Weinberg Dale P. Sandler Jack A. Taylor

Background: Current breast cancer risk models incorporate genetic and reproductive risk factors. The utility of epigenomic factors as predictors of risk has largely been unexplored. Here, we develop a methylation-based breast cancer risk model (mBCRM).

Methods: We profiled blood DNA methylation (DNAm) at over 450,000 CpGs among a case-cohort sample of 2,774 women enrolled in the Sister Study and calculated 41 previously-established, DNAm-based estimators of various physiologic metrics. These metrics included: 14 epigenetic age measures; 11 plasma protein concentrations; 10 blood cell components; and 6 complex traits. Women were randomly assigned into a training cohort (70%, n=1,941; 1,108 breast cancer events) and a testing cohort (30%, n=833; 471 events). In the training cohort, elastic net regularization was used to derive the mBCRM. The mBCRM was evaluated in the testing cohort and a publicly-available, nested case-control study of blood DNAm and breast cancer incidence.

Results: Fourteen DNAm-based estimators were selected into the mBCRM. In the testing cohort, after adjustment for a 313-SNP polygenic risk score (PRS) and Gail model lifetime risk score, the mBCRM was associated with breast cancer incidence (per 1-standard deviation [SD], HR: 1.58, 95% CI: 1.28, 1.95, P=2.2×10^{-5}). Compared to women with scores in the middle quintile, those with scores in the top quintile had twice the risk of breast cancer (HR: 2.07, 95% CI: 1.24, 3.46, P=0.006) and those in the lowest quintile had half (HR: 0.48, 95% CI: 0.28, 0.84, P=0.001). Combining the mBCRM, Gail, & PRS models significantly improved breast cancer risk prediction (Gail area under curve [AUC]: 0.53, mBCRM AUC: 0.59, PRS AUC: 0.63; combined AUC: 0.66). In the nested case-control sample, the mBCRM associations with risk and predictive utility were externally validated (per 1-SD, OR: 1.33, 95% CI: 1.06, 1.67, P=0.01; AUC: 0.59).

Conclusion: Blood methylation-based models can improve breast cancer risk prediction.

Transcriptome-wide prediction and association studies enriched for mediating biomarkers

Arjun Bhattacharya* Arjun Bhattacharya Michael I. Love

Traditional predictive models of gene expression for transcriptome-wide association studies (TWAS) consider only single nucleotide polymorphisms (SNPs) that are local to the genes of interest and perform parameter shrinkage based entirely on a regularization process. These approaches largely ignore the effect of distal SNPs to the gene of interest. Here, we outline a multi-omic strategy for transcriptome imputation from germline genetics for testing gene-trait associations. To identify trans-SNPs to be used in prediction, we identify mediating biomarkers (i.e. DNA methylation sites, microRNAs, or) that are highly associated with gene expression and train predictive models for these mediators using the genotype local to these mediators. Imputed values for mediators are then incorporated into the eventual model as fixed effects with cis-genotypes to the gene included as regularized effects. We then extend this strategy to prioritize trans-SNPs in the predictive model that show both direct and mediated effects on the gene of interest, borrowing from methods for trans-eQTL detection. We show the utility of these extensions through extensive simulations. Lastly, we train predictive models of gene in TCGA breast cancer data and in ROSMAP brain tissue data, showing average gains of 1-2% in total percent variance explained. These extensions to transcriptomic prediction can aid in increasing the power to detect gene-trait associations in TWAS. These methods are implement in an R package MOSTWAS, available at github.com/bhattacharya-a-b-t/MOSTWAS.

Genetic overlaps between birthweight and childhood obesity phenotypes Suvo Chatterjee*
Suvo Chatterjee Marion Ouidir Fasil Tekola-Ayele

Background: Lower or higher birthweight (BW) is associated with childhood obesity. Shared genetic factors may underlie these relationships. Although genome-wide association studies (GWASs) have identified genetic loci associated with BW, childhood obesity (COB), and childhood BMI (CBMI), the extent of shared genetic influence (genetic pleiotropy) on BW and childhood obesity traits (COB and CBMI) is unknown. We aimed to: 1) test whether there is significant shared genetic influence between BW and COB/CBMI, and 2) identify genetic loci with shared effect on BW and COB/CBMI.
Method: GWAS summary statistics data on approximately 9.8 million single-nucleotide polymorphisms (SNPs) for BW, COB, and CBMI were obtained from the Early Growth Genetics Consortium. A statistical approach that integrates summary statistics and functional annotations for paired traits was used to test for pleiotropy and enrichment of functional annotations. Combined Annotation Dependent Depletion and maps of DNase I hypersensitive sites were used as functional annotation of the variants. A Bayesian fine-mapping strategy was implemented to prioritize shared variants with potential causal variants.
Results: Genetic pleiotropy ($P < 1.09 \times 10\text{-}270$) and functional annotation ($P < 1.09 \times 10\text{-}128$) were enriched for BW and COB as well as BW and CBMI. At 5% false discovery rate (FDR), two loci (consisting 22 SNPs) were associated with BW and COB and 10 loci (consisting 340 SNPs) with BW and CBMI. The variants associated with lower birthweight were also associated with lower CBMI or lower COB risk, except for variants in the NCOA1 and EBF1 gene that regulates appetite and central adiposity. Out of the 12 loci, 11 loci have been associated with CBMI/COB but not with BW and one locus in the EBF1 gene was novel to both BW and CBMI.
Conclusion: We found significant genetic pleiotropy on BW and COB/CBMI, suggesting that shared genetic factors partly explain associations of birthweight and childhood obesity.

Beyond Mendelian Randomization: Using Genetic Information to Identify Earliest Manifestations of Alzheimer's Disease Willa D. Brenowitz* Willa Brenowitz Sarah F. Ackley Scott C. Zimmerman Stefan Walter Eric Jorgenson Thomas J Hoffmann Kristine Yaffe Rachel A Whitmer M. Maria Glymour

Background: Distinguishing early symptoms of a disease from potential causes of the disease can be challenging, particularly for conditions with long subclinical periods such as Alzheimer's disease (AD). We use a genetic risk score in an extension of Mendelian Randomization to study the natural history and early manifestations of AD, which may provide insight into critical windows for treatment and potential screening.

Methods: 408,942 UK Biobank participants aged 39-73without dementia and with Caucasian genetic ancestry were enrolled 2007-2010, including 18,362 with brain MRIs. We calculated an Alzheimer's disease genetic risk score (AD-GRS) as a weighted sum of 23 single nucleotide polymorphisms previously confirmed to be genome-wide significant predictors of late-onset AD. Cognition (verbal reasoning, numbers matching), hippocampus volume (from brain MRIs), and blood pressure all decline in the course of clinical AD and were assessed during UK Biobank enrollment or clinic visits. We modeled the age at which trends in each factor began to diverge for people with high AD-GRS using linear regression with linear and quadratic terms for age and including interactions with AD-GRS.

Results: Higher AD-GRS was associated with all 3 factors in adults aged 55+ (all, $p<0.05$) but not in adults age <55. Model based age-curves for people with high versus low AD-GRS scores began to diverge at age 46 for verbal reasoning, age 51 for numbers matching, age 50 for hippocampal volume, and age 54 for diastolic blood pressure. Differences by AD-GRS further diverged in older ages (Figure 1).

Conclusion: Genetic factors that increase late-onset AD risk predict divergence in cognition, hippocampal volume, and blood pressure by early 50s, decades prior to the average AD diagnosis (81 years). This likely reflects early manifestations of AD, which could not be detected using conventional study designs. Using genetic risk may be useful to examine the natural history of preclinical disease.

Figure 1. Age-based curves associated with the 10th (low) and 90th (high) percentile of Alzheimer's disease genetic risk score (AD-GRS)
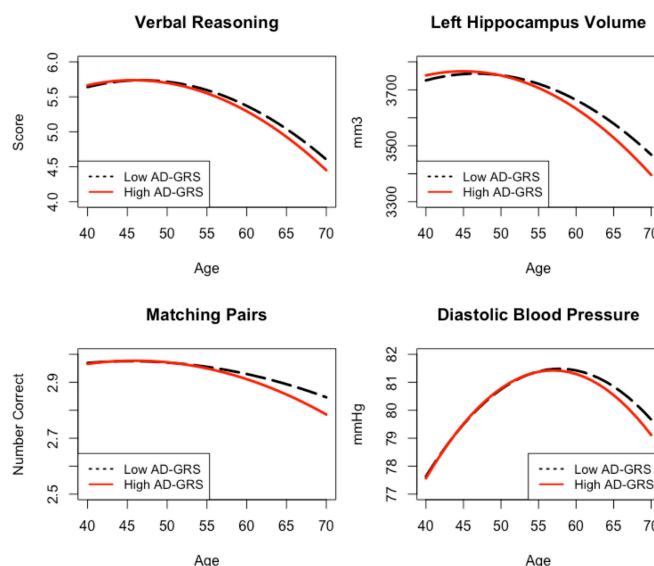
A comparison of analytical approaches to obtain Mendelian randomization estimates with longitudinal exposures Joy Shi* Joy Shi Sonja A. Swanson Peter Kraft Bernard Rosner Immaculata De Vivo Miguel A. Hernán

Background. Mendelian randomization (MR) is often used to estimate the effects of time-varying exposures on health outcomes using observational data. However, conventional methods for MR were designed to handle a single measure of exposure. As such, conventional MR effect estimates for time varying exposures are often difficult to interpret. We compared three analytical approaches to incorporate longitudinal measures of time-varying exposures in MR studies.

Methods. We used MR to estimate the effects of alcohol, high-density lipoprotein (HDL) cholesterol and low-density lipoprotein (LDL) cholesterol interventions on C reactive protein (CRP) levels, gamma-glutamyl transferase (GGT) levels and ankle-brachial index (ABI) using data from the Framingham Heart Study. We proposed weighted allele scores—based on genetic variants of alcohol consumption, HDL cholesterol and LDL cholesterol— as instruments. Multiple scores were generated for each exposure using different selection algorithms for genetic variants. We considered two exposure time points and used g-estimation to estimate parameters of structural mean models that (1) included each exposure time point separately; (2) included the average exposure across time points; or (3) included both exposure time points jointly.

Results. We observed increases in GGT levels and ABI as a result of increases in alcohol intake and LDL cholesterol across both time points. Effect estimates were similar regardless of the approach used, but the precision decreased with increasing number of time points included in the structural mean model and increasing correlation between weighted allele scores used for each time point.

Conclusions. This study demonstrates the first application of structural mean models to incorporate repeated exposure measurements to estimate the effect of a time-varying exposure on an outcome using MR. These methods provide a basis for considering time-varying exposures in future MR studies.

Bias from competing risk before recruitment in Mendelian Randomization studies of conditions with shared etiology CM Schooling* CM Schooling P Lopez SL Au Yeung JV Huang

Mendelian randomization, i.e., instrumental variable analysis with genetic instruments, is an increasingly popular and influential analytic technique that can foreshadow findings from randomized controlled trials quickly and cheaply even when no study measuring both exposure and outcome exists. Mendelian randomization studies can occasionally generate paradoxical findings different in direction from randomized controlled trial estimates. Despite robustness to confounding, Mendelian randomization studies are, like all observational studies, open to selection bias from sampling issues, such as selecting on exposure and outcome, or selecting on surviving until study onset, because of the gap between randomization (at conception) and recruitment, often decades later. What has been less considered is that biases due to selective survival on genetically predicted exposure can be compounded by selective survival on other diseases that share etiology with the outcome of interest, i.e., competing risk before recruitment. Many major causes of death, such as heart disease and stroke, share etiology. Here we show that, in the presence of survival on genetically predicted exposure, failure to account for competing risk of the outcome due to shared etiology can generate reversed Mendelian randomization estimates. We also explain when such selection bias is likely to occur. Mendelian randomization studies that do not take account of shared etiology of the outcome with survival likely have the greatest validity if the genetically predicted exposure does not cause death or when it does cause death the participants are recruited before many deaths have occurred from other diseases with which the outcome shares etiology.

Changes in the depression gender gap from 1992-2014: cohort effects and mediation by gendered social position Jonathan Platt* Jonathan Platt Lisa Bates Katie McLaughlin Justin Jager Katherine Keyes

The depression gap (i.e., women's excess of depression compared with men) represents an important mental health disparity in the US. The gap was historically reinforced by differences in gendered social position (i.e., social roles, responsibilities, and opportunities), which has been expanding for women since the mid-20th Century. The present study examined the evidence for a changing depression gap across birth cohorts, and tested the extent to which any cohort effects were mediated by changing gendered social position. Data were from the National Longitudinal Surveys. Using the Center for Epidemiologic Studies Depression Scale (CESD), the depression gap was defined as differences in mean depression scores for women vs. men. The analytic sample included 13,666 respondents interviewed from 1992-2014. Hierarchical mixed models estimated the magnitude of the gender depression gap over time, across 10-year birth cohorts (range: 1957-1994) and whether variation was mediated by gender ratios of: college degree attainment or more, full-time employment, and the average number of weekly hours spent doing housework, three indicators of gendered social position. There was a linear decrease in the depression gap by 0.18 points across birth cohort (95% CI= -0.26, -0.10), due mainly to CESD decreases among women (-0.41 points (95% CI= -0.63, -0.19). The mediation analysis estimated that an increasing ratio of college degree attainment mediated 39% of the gender depression gap across cohorts (95% CI= 0.18, 0.78). There was no evidence of mediation due to changing employment or housework ratios, indicating partial support for the hypothesis that variation in the depression gap is meaningfully related to changing social position. Understanding the social causes of the depression gap is important to reduce the present and future burden of the depression gap, and to understand the fundamental processes through which depression disparities may be perpetuated or attenuated over time.

Substance Use

Trends in U.S. women's mid-life binge drinking by socioeconomic status, 2006–2018 Sarah McKetta* Sarah McKetta Katherine M. Keyes

Background: Binge drinking causes injury and illness. Between 2006–2018, women in midlife (age 30-45) nearly doubled rates of binge drinking. These women were born approximately 1970–1990, and were among the first cohorts of women for whom attaining higher education and income (both associated with increased alcohol use) were highly prevalent. Understanding whether increases in binge drinking among women are concentrated among high versus low education/income groups can illuminate underlying trends and suggest etiologic factors.

Methods: We examined trends over time in binge drinking and abstaining using serial cross-sectional, nationally-representative National Health Interview Surveys (2006–2018) among women age 30-49 (N=107,088) according to their family income levels (= 200%) and educational histories (= college) controlling for race, marriage status, parenthood status, disability status, smoking status, BMI, and employment status.

Results: Binge drinking increased among all women from 2006 to 2018 (each additional year associated with 1.03 increased odds of binge drinking). Increases were stronger among women with high income compared to low income, from 23% in 2006 to 35% in 2018 (adjusted OR [aOR] 1.05, 95% CI 1.04–1.06) among higher income women, compared to an 14% to 19% increase among those with lower income (aOR 1.03, 95% CI 1.02–1.04). Similarly, women with higher vs. lower education had more pronounced increases in binge drinking (aOR for high education 1.05, 95% CI 1.04–1.06; for lower education aOR 1.02, 95% CI 1.01–1.03).). Two way tests for income x time (F_856^1= 10.44, p=0.001) and education x time (F_856^1= 28.85, p<0.001) showed that these trends have different slopes. Trends in abstaining from alcohol mirrored trends in binging drinking.

Conclusions: National increases in binge drinking are occurring across all levels of SES for women in the midlife, but they are the most pronounced among high SES women.

Transgender Mental Health in the U.S.: Results of a National Survey on College Campuses

Sarah Lipson* Sarah Lipson Julia Raifman Sara Abelson Sari Reisner

Transgender and gender nonconforming (TGNC) individuals have a gender identity or expression that differs from assigned sex at birth or does not fit the male-female binary. A small number of extant studies have documented a higher prevalence of mental health symptoms among TGNC adolescents and young adults relative to their same-aged cisgender peers. However, there is a lack of nationally representative data, which are critical for assessing the prevalence of symptoms and magnitude of disparities in TGNC populations.

The present study is the largest of its kind, and uses nationally representative data on a random sample of 1,237 TGNC and 63,994 cisgender students on 71 campuses. These data come from the 2015-2017 Healthy Minds Study, a web-based survey conducted annually on campuses across the U.S. Outcomes include symptoms of depression and suicidality based on validated screening instruments with standard cutoffs (e.g., Patient Health Questionnaire-9>10 for depression). Bivariable and multivariable analyses examine differences between TGNC and cisgender students. Another unique contribution is the examination of outcomes among TGNC students by assigned sex at birth. Survey response weights are applied in all analyses.

We find TGNC students have a significantly higher prevalence of symptoms across all mental health outcomes: 58% of TGNC students screen positive for depression and 35% report suicidal ideation, relative to 28% and 10% of cisgender students. TGNC status is associated with 4.3 times higher odds of screening positive for one or more mental health problem (95% CI=3.61, 5.12). Among TGNC students, nearly 90% of those assigned female at birth meet criteria for one or more mental health problem, making them a particularly high-risk sub-group.

Findings underscore the importance of recognizing and addressing TGNC mental health burdens, such as by screening and providing gender-affirming services for a growing number of students who identify as TGNC.

Psychological distress and substance use in transgender adults in the United States: An intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy

Ariel Beccia* Ariel Beccia Rodrigo Aguayo-Romero Sari L. Reisner

Transgender populations have elevated mental and behavioral health morbidity relative to the general U.S. population. However, no studies have comprehensively explored these disparities at the intersection of gender, race, and income. This study evaluated the intersectional effects of gender identity, race, and socioeconomic status (SES) on psychological distress and substance use (binge drinking, cannabis use, illicit drug use, cigarette smoking). Using data from the 2015 U.S. Transgender Survey, a national non-probability sample, we used intersectional multilevel analysis of individual heterogeneity and discriminatory accuracy (MAIHDA) to evaluate 25,443 transgender people nested within 48 intersectional social strata defined using gender identity (transgender women and men, non-binary assigned-male-at-birth and assigned-female-at-birth), race/ethnicity (American Indian, Asian, Black, Latinx, Bi/Multiracial, White), and SES (above, below the poverty line). For each outcome, three sequential multilevel logistic models were fit: a null model; an intersectional model adjusting for the additive effects of gender, race, and SES; and a model controlling for age, gender expression, and U.S. region. High rates of psychological distress and substance use were found. The predicted probabilities ranged from 26%-64% psychological distress, 21%-36% binge drinking, 19%-37% cannabis use, 7%-12% illicit drug use, and 16%-34% cigarette smoking. There was considerable variation across some intersectional strata and outcomes. After adjusting for additive effects, we found significantly lower predicted probabilities of cannabis use (19%) and cigarette smoking (17%) in White transgender women living above the poverty line. The intersectional MAIHDA approach is a feasible method to assess health inequalities in transgender people. By modeling intersectional social strata to identify those who are affected the most, findings can be used to guide public health policies and equity.

Expanding upon social stress theory in the context of the Black-White depression paradox: Testing alternative causal structures for the relationships between race, stress, and depression John R. Pamplin* John Pamplin Lisa M. Bates

Social stress theory posits that Black Americans, due to greater stress exposure, should experience worse mental health than their White counterparts. Yet epidemiologic studies consistently report depression prevalence among Blacks ≤ that of Whites – the so-called Black-White Depression Paradox. Extant evidence from efforts to explain the paradox suggests the causal structure implied by social stress theory may be incomplete. Two causal structures potentially consistent with observed patterns are effect modification (race modifies the effect of stress on depression) and inconsistent mediation (race increases depression risk via an indirect effect on stress exposure and there is a direct, protective effect of race on depression of greater magnitude). The present study tests the plausibility of these two causal structures to explain the paradox. Data are from the National Epidemiologic Survey on Alcohol and Related Conditions-III, a nationally representative sample of non-institutionalized U.S. adults (n = 26,960). Past-year major depressive disorder was assessed using DSM-5 criteria; stress was operationalized as the 75th percentile of a sum score of 16 major life stressors. We test effect modification using a cross product raceXstress term in a logistic model, and by calculating the relative excess risk due to interaction. We assess inconsistent mediation by estimating the pure direct effect and total indirect effect, using the R Mediation package. Models adjust for a minimally sufficient set of confounders. Preliminarily, results do not support effect modification. Black race is inversely associated with depression, even after adjustment for stress (OR: 0.6, 95% CI: 0.6, 0.7), but directly associated with stress (OR: 1.5, 95% CI: 1.5, 1.6) which is directly associated with depression (OR: 2.9, 95% CI: 2.7, 3.1). Early results support the inconsistent mediation structure and suggest that efforts to explain the paradox should prioritize non-stress-coping mechanisms.
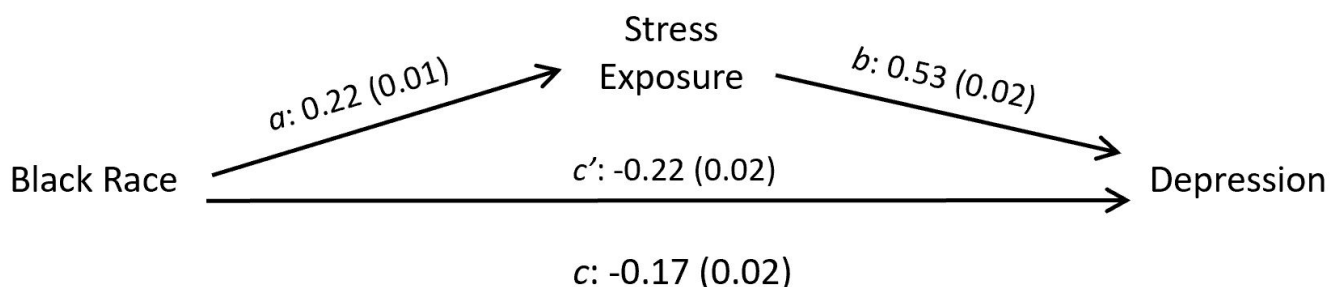

Figure 1. Estimated beta and standard errors for the paths of the inconsistent mediation model relating race, stress, and depression, in the National Epidemiologic Survey of Alcohol and Related Conditions – III (n = 26,960).

Racial Segregation and Treatment Capacity for Opioid Use Disorder in the United States

William Goedel* William Goedel Aaron Shapiro Magdalena Cerda Jennifer Tsai Scott Hadland Brandon Marshall

Treatment with methadone or buprenorphine is the current standard of care for opioid use disorder. Given the paucity of research identifying which patients will respond best to which medication, both modalities should be accessible to all patients. However, given differences in the historical contexts of their approval and initial implementation, access to each of these medications may vary along racial lines. In a cross-sectional analysis of all counties and county-equivalent divisions in the United States, we examined the extent to which capacity to provide methadone and buprenorphine vary with measures of resident segregation. Two county-level measures of racial segregation, including dissimilarity (representing the proportion of residents who would need to move census tracts to achieve a uniform spatial distribution of the population by race) and interaction (representing the probability that an African American resident will interact with a White resident and vice versa, assuming random mixing across census tracts) were calculated for each county. As of 2016, there were 1,698 facilities providing methadone (0.6 facilities per 100,000 population) and 18,868 facilities providing buprenorphine (5.9 facilities per 100,000 population). After adjusting for urbanicity and opioid-involved overdose mortality, capacity to provide methadone was higher in communities where African American residents are unlikely to interact with White residents while capacity to provide buprenorphine was higher in communities where White residents are unlikely to interact with African American residents. One's race and residential location may heavily determine whether they will be able to access methadone over buprenorphine when seeking treatment for opioid use disorder. Reforms to existing federal regulations governing the provisions of these medications are needed to ensure that both methadone and buprenorphine are equally accessible to all.

Frequent Police Stops, Parental Incarceration, & Mental Health: An Intersectional Analysis Among U.S. non-Hispanic Black and White Adolescent Girls and Boys

Jaquelyn Jahn* Jaquelyn Jahn Jarvis Chen Madina Agénor Nancy Krieger

Introduction: The adolescent mental health consequences of frequent interactions with police are largely understudied, and there are no federal data on police contact below age 16. No studies have examined whether these associations differ across gender and race/ethnicity, which is important given racialized notions of criminality that can bias which youth police decide to stop, gendered police behavior, and how those who are stopped may interpret these interactions.

Methods: We describe the distribution of police stops in the last 6 months stratified by both non-Hispanic Black and White race/ethnicity and gender in a nationally representative sample of adolescents ages 12-18 in the Panel Study of Income Dynamics 2002, 2007 & 2014 (n=2557). We used weighted race/ethnicity- and gender-stratified linear regression models to examine associations between the frequency of police stops and both depressive symptoms and subjective well-being (emotional, psychological, and social). We adjusted for several adolescent- and parent-level socioeconomic, geographic, and demographic covariates and tested for effect modification by parental incarceration.

Results: In each year 10% of adolescents were stopped 2+ times. Despite fewer police stops compared to boys, Black and White girls who were stopped 2+ times had more depressive symptoms relative to girls who were not stopped (Black: 2.13 95% CI: 0.73, 3.53, White: 2.17 95% CI: 1.07, 3.27) and these associations were stronger among girls whose parents had been incarcerated. Associations were larger among Black relative to White girls across all domains of subjective well-being. Black and White boys who were stopped 2+ versus no times had lower levels of emotional well-being (Black: -0.40 95% CI: -0.75, -0.04 White: -0.36 95% CI: -0.68, -0.04).

Conclusions: Policies that regulate youth-police contact have different mental health consequences across race/ethnicity and gender and youth may benefit from less contact with police.

Changes in Opioid prescribing after implementation of mandatory registration and proactive reports within California's prescription drug monitoring program: a quasi-experimental study Alvaro Castillo-Carniglia* Alvaro Castillo-Carniglia Andrés González-Santa Cruz Magdalena Cerdá Chris Delcher Aaron B. Shev Garen J. Wintemute Stephen G. Henry

Background: In 2016, California updated its prescription drug monitoring program adding two key features: proactive reports to prescribers and mandatory registration for prescribers and pharmacists. We evaluated the joint effect of these two features on county-level prescribing practices in California.

Methods: We generated a county-level quarterly dataset from 2012 to 2017 for California and two control states (n=3280 county-quarter). We considered seven prescribing practices related to both overall opioid supply (opioid prescription rate per 1,000 state residents; patients' mean daily opioid dosage in milligrams of morphine equivalents[MME]; prescribers' mean daily MME dosage prescribed; prescribers' mean number of opioid prescriptions per day) and high-risk prescribing (percentage patients getting >90 MME/day; percent days with overlapping prescriptions for opioids and benzodiazepines; multiple opioid provider episodes per 100,000 state residents). Using the generalized synthetic control method, we estimated the average treatment effect on the treated (ATT) for the implementation of proactive reports and mandatory registration in counties in California, compared to counties in Florida and Washington.

Results: Proactive reports and mandatory registration were associated with a decrease in three out of the seven outcomes considered: -9.3% in MME in patients' mean daily opioid dosage (ATT= -7.7; 95%CI: -11.4, -2.9); -13.7% in the percentage of patients getting >90MME per day (ATT= -1.8; 95%CI: -2.3, -0.9); -9% in prescribers' mean daily MME dosage prescribed (ATT= -6.3; 95%CI: -10.0, -1.3). Robustness checks through standard fixed-effect difference-in-difference models yielded the same conclusions.

Conclusions: Implementation of proactive reports and mandatory registration was associated with reduction in mean opioid dose prescribed in California, though some risky prescribing measures (e.g., overlapping prescriptions of opioids and benzodiazepines) remained unchanged.
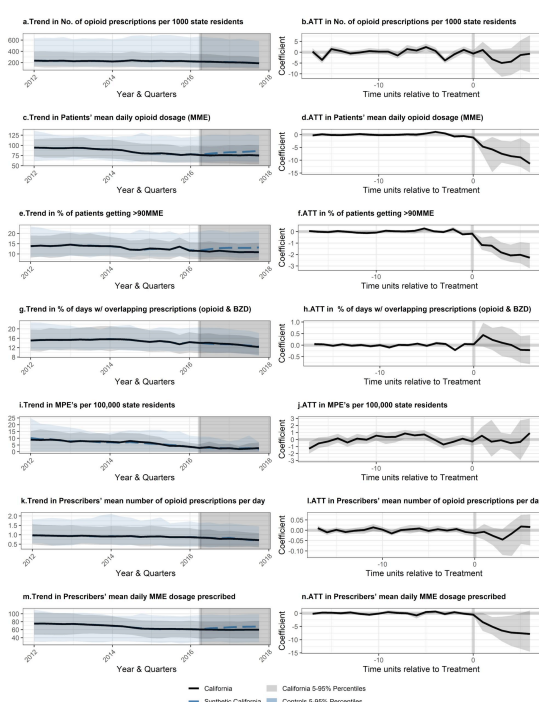
What impact have pain management clinic laws had on opioid overdose deaths in the United States?
Magdalena Cerda* Magdalena Cerda Katherine Wheeler-Martin Emilie Bruzelius William Ponicki Paul Gruenewald Christine Mauro Stephen Crystal Corey Davis Katherine Keyes Deborah Hasin Silvia Martins

Aims: Pain management clinic laws (PMC), enacted by 11 states since 2006, are one of the leading responses to the opioid overdose crisis in the United States, yet their impact on opioid overdoses is inadequately understood. We evaluated their impact on overdose deaths involving opioids in 2010-2017.
Methods: We scored states 0-3, according to the number of key PMC provisions enacted, including restrictions on cash payments, permitting inspection of the clinic, and imposing criminal penalties on facilities that violated the law. We examined the county-level change in rate of overdose deaths, by opioid type, following change in state PMC laws, adjusting for contemporaneous trends in counties in states that did not change PMC laws. We used spatiotemporal Bayesian hierarchical models, adjusted for year, state-level fixed effects, county-level demographic characteristics, county-level random intercepts and slopes, and state-level policy changes (prescription drug monitoring programs, initial prescribing limits, marijuana legalization, Good Samaritan laws, and naloxone access laws).
Results: After 3 years, counties in states that adopted all three provisions saw a 29% greater decrease in the rate of opioid-related overdose deaths (any opioid, RR: 0.71; 95% CI: 0.62, 0.81). This included a decrease in overdoses involving natural/semi-synthetic (e.g., oxycodone) opioids (RR: 0.63; 95% CI: 0.55, 0.73), and an increase in non-methadone synthetic opioid (e.g., fentanyl) overdoses (RR: 1.33; 95% CI: 1.05, 1.68) and heroin overdoses (RR: 1.52; 95% CI: 1.14, 2.03).
Conclusion: PMC laws that restrict cash payments, permit clinic inspection, and impose criminal penalties on violating facilities are associated with substantial reductions in opioid overdose deaths, driven by a decrease in natural/semi-synthetic opioid overdose deaths. At the same time, the increase in overdoses involving heroin and synthetic opioids raises concerns about unintended consequences.

Health Services/Policy

Do TRAP laws close abortion clinics? Nichole Austin* Nichole Austin Sam Harper

Background: The number of abortion clinics in the US decreased substantially from 2011 to 2017. Given contemporaneous declines in abortion rates, this trend is likely partially attributable to reduced demand for abortion services. However, Targeted Regulation of Abortion Providers (TRAP) laws may also lead to clinic closures, potentially impacting access to care. In this paper, we aim to quantify the relationship between these policies and clinic availability.

Methods: We merged data on TRAP policies with publicly available data on state-level counts of abortion clinics from 2008 to 2017. We used Poisson models and a difference in differences approach to compare changes in the number of clinics in states that enforced new TRAP policies to states that did not, accounting for temporal trends in clinic availability common to all states. Given compelling evidence from Texas that TRAP laws likely lead to a decrease in clinics, we used a Bayesian approach and specified models with both weakly and moderately informative priors for the policy effect. We conducted several sensitivity analyses.

Results: TRAP enforcement resulted in 3.7 fewer clinics (95% credible interval: -6.03, -0.82) in a model with a weakly informative prior. Including a more informative prior (assuming laws reduce clinics by 10-20%, on average) yielded a weaker, but more precise, estimate (-2.48, 95% credible interval: -4.23, -0.67). Pre-policy trends in provider availability were comparable in exposed and unexposed states, supporting the validity of a difference in differences approach in this context.

Conclusion: Our results suggest that TRAP enforcement leads to the closure of anywhere from 1 to 6 clinics, on average. This is above and beyond any demand-based declines occurring simultaneously, which has important implications for the accessibility of abortion.

Health Services/Policy

Impacts of the Smoking Ban Policy on the Sales of Billiard Halls in Seoul, South Korea: Using Objective Sales Information from Credit Card Companies Ki-Bong Yoo* Ki-Bong Yoo Jin-Won Noh

Background: In January 2018, the Korean government imposed a total ban on smoking in in-door sports facilities by law. The purpose of this study is empirically investigating the economic impacts of the smoking ban for billiard halls, one of the indoor sports facilities.

Methods: Credit/debit/check card sales information on the largest card company in South Korea was used. The information data period is from January 2017 to September 2018. Three districts in Seoul were selected; Nowon district (533,498 population in 2019), Secho district (430,697 population in 2019), and Songpa district (675,843 population in 2019). There are 23 dongs, which are submunicipal level administrative unit in the districts.
The monthly sales data in 23 dongs was used. Unit of analysis is dong-month. log(billiard halls' sales) and log(the number of the transactions) were used as dependent variables. The models were analyzed by OLS regression, fixed-effects model(FE), a regression model with panel corrected standard errors (PCSE).

Results: The coefficients of the smoking ban policy varied by the models and the regression methods, but there were no negative results. In the model with the highest R-squared ($R^2=0.977$), the smoking ban policy showed a significant positive association with the billiard halls' sales (estimate=0.115; p=0.037), but not significant association with the number of transactions (estimate=0.056; p=0.278).

Conclusions: Despite the owners' expectations of the negative impacts on the sales of billiard halls, we found that the negative effects of the smoking ban policy on billiard halls had not been confirmed. Smoking ban policies can produce better health outcomes without negative economic impacts. Credit/debit/check card sales information is better choice to identify the impacts on retail stores as well as sport facilities sales because it is not biased by the owners.

Graphs by id
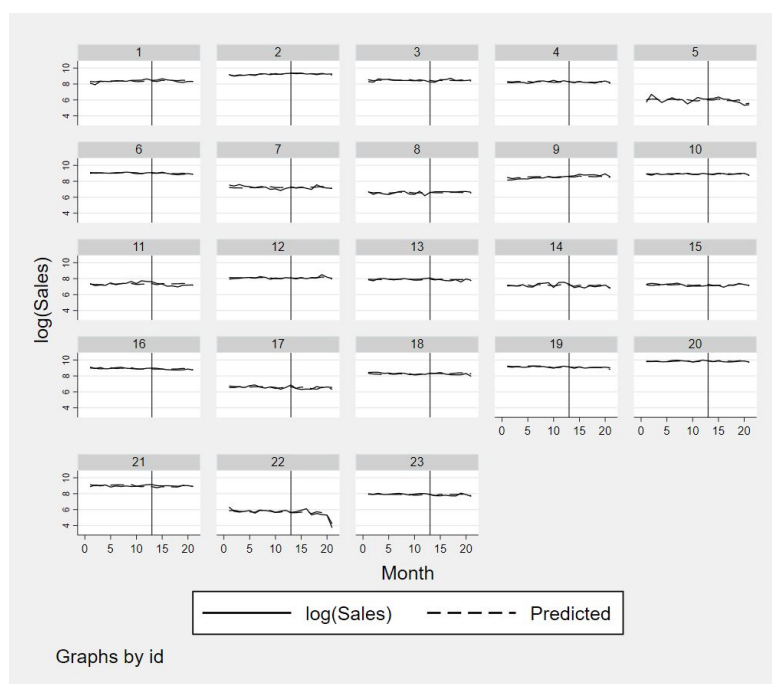
Combining weights for missing data and confounding Rachael K Ross* Rachael Ross Alexander Breskin Daniel Westreich

Inverse probability weighted estimators are increasingly used in epidemiologic analysis. Weighting can be used to adjust for confounding, selection, missing data, and sampling, or for generalizing or transporting results. Estimation and application of a single weight is well discussed in the literature. When an analysis requires multiple weights, added complexities emerge regarding the estimation and combination of the weights. We examine combined weights for confounding and for missingness in a time-fixed setting. There are two variations that can be used to construct the weights: the inverse of (a) the probability of treatment conditional on covariates among those with complete data, multiplied by the probability of no missing data conditional on covariates, or (b) the probability of treatment conditional only on covariates, multiplied by the probability of no missing data conditional on treatment and covariates. In (a), the treatment probability is calculated from the complete cases (i.e. conditional on no missing data) and thus estimation can occur prior to correcting for missing data. Conversely, in (b), the treatment probability is estimated in the full data and therefore either the covariates must be fully observed (i.e. only outcome data are missing) or their distribution must be recoverable by applying the weights for missingness when estimating the treatment probabilities. The missingness probabilities in (a) and (b) are also different and, if the covariates are not fully observed, each requires a different assumption about the independence of the covariates and missingness. Using a simulated scenario, we illustrate each estimator and show that without examination of the formulas, one may mistakenly combine the treatment probability estimated among the complete cases with the missingness probability estimated conditionally on treatment and covariates. This combination of the treatment weight from (a) and the missingness weight from (b) is generally biased.
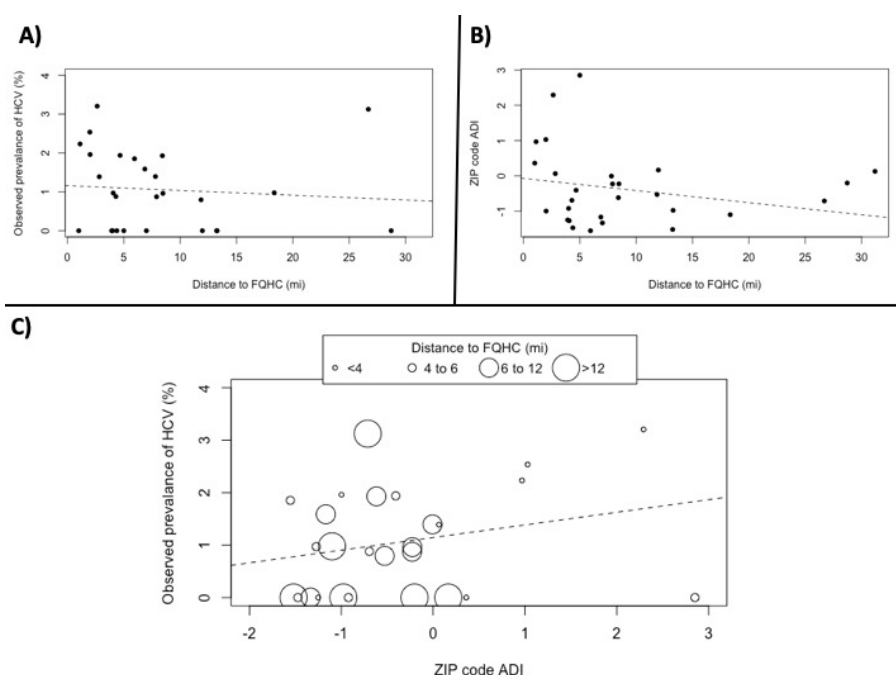
Catchment and selection bias in an outpatient electronic medical record study of community deprivation and chronic Hepatitis C virus infection Neal Goldstein* Neal Goldstein Deborah Kahal Karla Testa Igor Burstyn

The catchment area of a healthcare facility defines the geographic and demographic expectations under which the typical patient arises. However, if the catchment population differs from the source population, inference made from a cohort study drawn from this facility may be prone to selection bias. In this study, we demonstrate such an occurrence by assessing whether community deprivation (measured as the ZIP code level area deprivation index, ADI) is associated with chronic Hepatitis C virus infection (HCV) using a retrospective cohort drawn from a federally qualified health center's electronic medical record.

ZIP code-level ecological plots of the cohort demonstrated that there was a pattern of the ADI exposure, the HCV outcome, and distance to the health center (intuitive proxy for being within catchments) suggesting the possibility of selection bias. As distance to the health center increased, prevalence of HCV (Figure panel A) as well as ADI score (corresponding to less deprivation, Figure panel B) decreased. Figure panel C suggested an ecological association between ADI and prevalence of HCV

We then created a multilevel catchment model that attempted to define the probability of selection into the cohort on the basis of three distance thresholds - 75%, 80%, 90% - of patients in the cohort from the health center. Using the inverse of this probability, we compared naïve unweighted and weighted mixed effects regression models to demonstrate the impact of selection bias. The naïve analysis found that moving towards an area with greater deprivation resulted in 1.25 times odds of HCV (95% CI: 1.06, 1.48), whereas the weighted analysis found no statistical evidence of such an effect.

We observed that the catchment processes may induce selection bias in a study of community deprivation and HCV; this potentially can be mitigated through inverse probability weighting.

Lessons Learned from Use of Inverse Probability Weighting to Adjust for Selection Bias in Molecular Epidemiology Shuji Ogino* Shuji Ogino Tomotaka Ugai Rong Zhong Koichiro Haruki Mai Chan Lau Melissa Zhao Tsuyoshi Hamada Carino Gurjao Edward L. Giovannucci Marios Giannakis Jonathan A. Nowak Mingyang Song Jooyoung Lee Li Liu Daniel Nevo Tyler J. VanderWeele Molin Wang

Molecular pathological epidemiology (MPE) provides integrative methods that can examine associations between exposures and specific pathobiological molecular signatures. MPE research often relies on biospecimen availability, which causes selection bias. To address this limitation, we developed methods of applying inverse probability weighting (IPW) to tissue bio-data-bank within prospective cohort studies. The weight was the inverse of the probability of biomarker data availability estimated by the logistic regression model. In proof-of-principle MPE studies, we utilized IPW-adjusted duplication-method Cox proportional hazards regression models to evaluate etiologic heterogeneity by disease subtypes. In an example study, we assessed smoking status and risk of colorectal cancer (CRC) subtypes by tumor neoantigen loads (high vs. low), using 4,420 CRC incident CRC cases including 571 cases with available tumor neoantigen data, within prospective cohorts of 173,229 participants (followed since 1976). In analyses without IPW, compared with never smokers, 20-39 and ≥40 pack-years of smoking were associated with hazard ratios (HRs) (with 95% CI in parentheses) for neoantigen-low CRC of 0.83 (0.52 to 1.31) and 1.02 (0.65 to 1.60), and HRs for neoantigen-high CRC of 1.86 (1.26 to 2.73) and 2.04 (1.38 to 3.01), respectively (P for subtype heterogeneity = 0.001). In the IPW-adjusted analyses, the corresponding HRs were 0.85 (0.54 to 1.35) and 1.06 (0.68 to 1.66) for neoantigen-low CRC, and 1.97 (1.33 to 2.91) and 2.06 (1.40 to 3.02) for neoantigen-high CRC, respectively (P for subtype heterogeneity = 0.003). Various other MPE studies have confirmed feasibility of our method, and provided a sanity check to ensure a small degree of selection bias in our tissue-available dataset. Our integrative methods of causal inference plus MPE can have a potential to enhance biomarker research for precision medicine and public health.

Reweighting to address non-participation and missing data bias in a longitudinal electronic health record study Milena Gianfrancesco* Milena Gianfrancesco Charles McCulloch Laura Trupin Jonathan Graf Gabriela Schmajuk Jinoos Yazdany

Background: Generalizability and validity of study findings may be threatened due to decreasing participation rates, with study populations failing to mirror their target population. Taking advantage of a unique study cohort in which all patients attending a clinic were invited to participate, we examined whether weighting according to the probability of participating in a research study could explain longitudinal differences in disease outcomes between research participants and non-participants with rheumatoid arthritis (RA).

Methods: We included 377 individuals with RA from 2013-2017. In order to account for differences between research participants and non-participants, we estimated the probability of not being in the research study and constructed weights using inverse probability weighting. Longitudinal disease outcomes were analyzed across the entire population, and amongst research participants only using multivariate mixed effects models.

Results: There were no differences in RA disease outcomes between research participants and non-participants at baseline; however, longitudinal effect estimates differed between groups, specifically with respect to race/ethnicity. Weighting research participants according to demographics of non-participants did not result in any meaningful changes in disease outcomes over time. For example, black, non-Hispanic race/ethnicity was associated with a 0.40 and -1.25 change in disease activity in the unweighted and weighted participant population, respectively, in comparison to 3.77 higher disease activity score in the analysis including both research participants and non-participants.

Conclusions: Non-participation in longitudinal studies may not be fully accounted for using techniques such as inverse probability weighting with demographic variables. In our example, we underestimate the effect of race/ethnicity on RA disease outcomes for minority groups if we only consider the participant population, even after reweighting.

Taking 'steps' to explore selection bias due to missing accelerometry data Erin Delker* Erin Delker Hailey Banack John Bellettiere

Accelerometers are hip- or wrist-worn devices that can be used to obtain valid and reliable measures of physical activity (PA). Wearing accelerometers can be a burden, leading some participants to not wear devices. Consistent evidence suggests that the participants who choose not to wear accelerometers are less active and have poorer health than those who choose to wear devices. Excluding participants due to incomplete or missing PA data can lead to underestimates of the true association between PA and health outcomes. Using simulations, we illustrate how the association of meeting PA guidelines and hypertension (HT) might be impacted by this exclusion. Based on the observed prevalence of PA and HT in an ongoing cohort study, we simulated data on 2000 participants, with 40% not meeting PA guidelines and 10% having HT. We set the "true" association between not meeting PA guidelines and HT at 1.9 (95% CI=1.5, 2.5). We then simulated scenarios to show the impact of four different patterns of missing accelerometer data: A) Missingness independent of PA and HT; B) Missingness associated with PA only; C) Missingness associated with HT only; D) Missingness associated with PA and HT. For each scenario, we conducted complete case analyses using logistic regression to assess associations between meeting PA guidelines and HT. Results are described in Figure 1. Odds ratios (ORs) in Scenarios A, B, and C were unbiased. ORs in Scenario D underestimated the magnitude of the "true" association and were increasingly attenuated as the relationship of PA and HT with missingness strengthened. This demonstrates that accelerometer measurement that results in missing data can lead to selection bias if the missingness is associated with both the exposure and outcome. Efforts to minimize missing PA data should be prioritized. Carefully considering the structure of missingness will inform quantification of potential bias, analytic strategies, and interpretation of findings.

Methods/Statistics
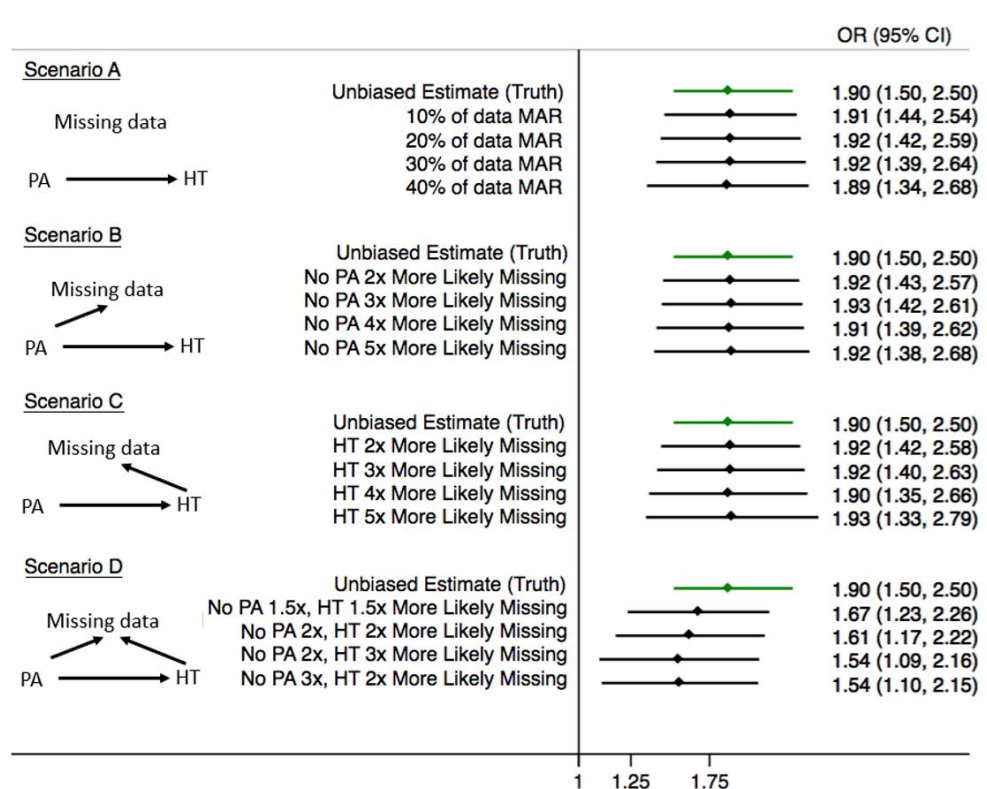
Covariate missingness, complete case analysis, and transportability, oh my! Michael A Webster-Clark* Michael Webster-Clark Jessie K Edwards

Interest in transporting study results to external target populations is increasing. While work has addressed differing distributions of effect measure modifiers (EMM), little attention has been paid to missing EMM data. The appropriateness of complete case analysis may depend on whether missingness is completely at random (MCAR), at random with respect to observed covariates (MAR), or not at random with respect to EMM value (MNAR).

We assessed performance of inverse odds of sampling weighting to estimate effects of dabigatran vs warfarin on stroke in real-world patients when data on EMM were missing. Specifically, we reweighted Randomized Evaluation of Long-Term Anticoagulation trial participants to resemble new users of oral anticoagulant therapy in a random sample of US Medicare patients. We then estimated intention-to-treat hazard ratios in the weighted trial. Next, we added missingness to trial or target populations in history of transient ischemic attack (TIA), an EMM, and re-estimated treatment effects. Missingness was a logit-linear function of age and past warfarin use (if MAR) and TIA (if MNAR), evaluated in 21 scenarios with differing model coefficients. We report the median (confidence limits: 2.5th, 97.5th) of 1000 bootstraps.

Figure 1 shows the truth and complete case results from 21 scenarios. Trial MCAR, MAR, and MNAR increased variance but added minimal bias, even with strong associations between covariates and missingness; in the target, however, MAR and MNAR covariate data appeared capable of adding bias (particularly with strong associations with missingness) with little increase in variance.

When transporting estimates from randomized trials to external populations, using trial complete cases may be acceptable if the study population is large even if covariate data is MAR or MNAR. Taking complete cases in the target population, however, may add some bias if data is MAR or MNAR because the distribution of EMM can differ from the full target.

A) Covariate missingness created in the trial

B) Covariate missingness created in the target
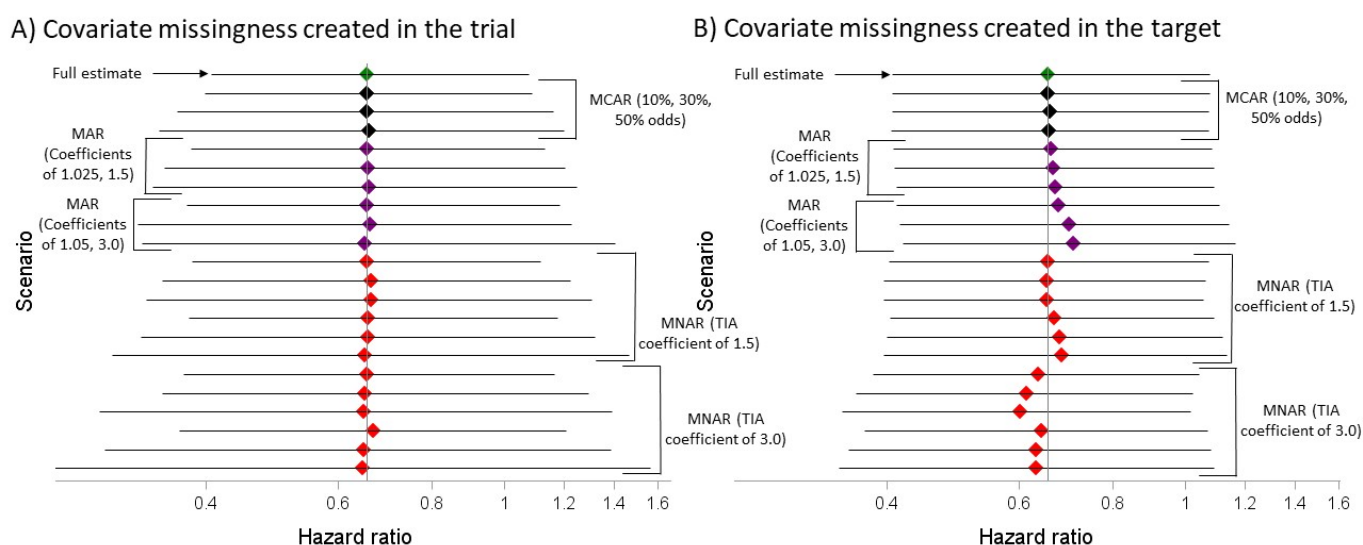
Does amyloid-beta reduction improve cognitive outcomes? Integrated evidence from randomized trials of amyloid targeting therapies Sarah F. Ackley* Sarah Ackley Scott C. Zimmerman Willa D. Brenowitz Audra Gold Eric J. Tchetgen Tchetgen Jennifer J. Manly Elizabeth Rose Mayeda Teresa Filshtein Melinda C. Power Fanny Elahi Adam M. Brickman M. Maria Glymour

Reduction of amyloid beta has been a primary focus of new therapies for prevention or treatment of Alzheimer's Disease (AD). No amyloid-targeting therapies have progressed sufficiently to receive FDA approval, bringing into question amyloid's hypothesized role in AD development. Trials of these drugs have been analyzed individually to validate specific therapies but have not been fully leveraged to evaluate whether and on what time scale reductions in amyloid are likely to improve cognition. In this analysis, we pool summary information from 13 randomized trials of amyloid-targeting therapies to estimate the effect of amyloid reductions on cognitive change. We reviewed ClinicalTrials.gov to identify randomized controlled trials of therapies for prevention or treatment of AD targeting an amyloid mechanism. Analyses included trials for which we could obtain information on both change in brain levels of amyloid measured with amyloid-PET and change in at least one cognitive test score reported for each randomization arm. Using randomization as an instrument, we used maximum likelihood to estimate the effect of amyloid reduction on cognitive change. Aggregated results from all trials were more precise and indicated that reducing amyloid by 0.1 standardized uptake value ratio units induces a change in the Mini-Mental Status Exam of 0.1 points, 95% CI: (-0.2,0.4). Using a mixed-effects model with a random effect by drug of the effect of reducing amyloid on cognition, we fail to find evidence of heterogeneity across drugs (p=0.57). We provide an R Shiny app allowing for the re-estimation of our results when new data become available, and to illustrate the magnitude of the new evidence that would be necessary to achieve a pooled estimate supporting benefit of amyloid reduction. Pooling evidence from all available trials reporting both amyloid reduction and change in cognition, we find that amyloid reduction strategies, in aggregate, did not substantially improve cognition.

Effect of 0.01 decrease in SUVr on change in MMSE
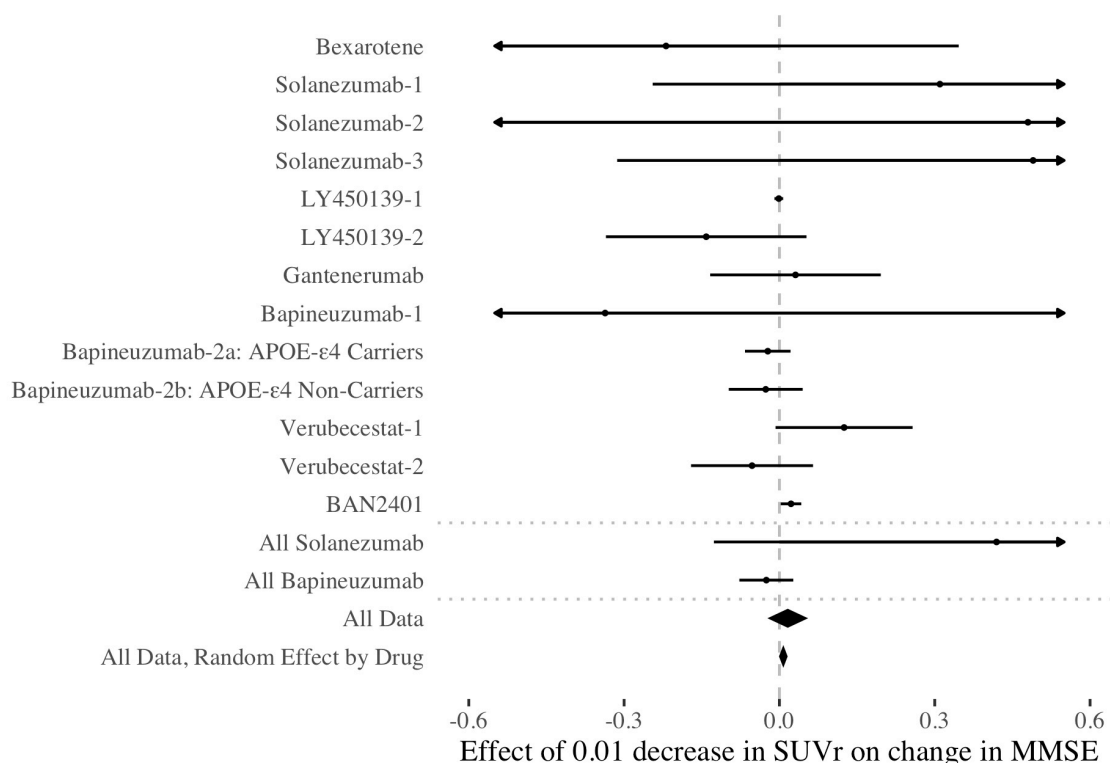
Assessing the generalizability of findings from the Alzheimer's Disease Neuroimaging Initiative to the Atherosclerosis Risk in Communities Study cohort Kan Gianattasio* Kan Gianattasio Jingkai Wei Erin Bennett Megha Mehrotra M. Maria Glymour Thomas Mosley Rebecca Gottesman Elizabeth Stuart Michael Griswold David Couper Melinda Power

Introduction
The Alzheimer's Disease Neuroimaging Initiative (ADNI) collects and shares high quality imaging, biomarker, genetic, and clinical data. Whether findings from ADNI generalize broadly is unclear, given its highly-selected, predominantly white and well-educated participants. We compared associations estimated in ADNI to those estimated in the Atherosclerosis Risk in Communities (ARIC) study, which initially recruited participants randomly from four US communities, to examine the potential generalizability of ADNI findings.

Data and Methods
We identified common risk factor, cognitive, and imaging variables at the ADNI screening/baseline visits and ARIC Visit 5. Data were pooled to estimate associations between risk factors and cognitive or imaging data, and between cognitive and imaging data, using adjusted linear and logistic regression models. Models included a term for cohort and its interaction with the variable of interest, allowing for cohort-specific estimates and statistical evaluation of cohort differences. We repeated analyses on data subsets defined by race and cognition. Sensitivity analyses accounted for cohort differences in the impact of confounders by including cohort by covariate interactions.

Results
The proportion of estimated associations that differed significantly by cohort (interaction p-value<.05) in primary analyses was 42% (range 25-42% across subset and sensitivity analyses). Many differences were substantively meaningful (e.g. OR for APOE-4 on amyloid positivity in ARIC: OR=2.75; in ADNI: OR=8.44).

Conclusions
The proportion of associations that differed significantly between ADNI and ARIC was substantially higher than would be expected by chance. Differences may stem from inherent differences in the populations from which participants were recruited. This has implications for the generalizability of highly selected samples, including deeply phenotyped samples typically used for biomarker research.

Aging

**Decreased complexity and increased variability in systolic blood pressure are associated with elevated long-term risk of dementia: The Rotterdam Study** Yuan Ma* Yuan Ma Junhong Zhou Maryam Kavousi Lewis A. Lipsitz Francesco Mattace-Raso Berend E. Westerhof Frank J. Wolters Julia W. Wu Brad Manor M. Kamran Ikram Jaap Goudsmit Albert Hofman M. Arfan Ikram

Background Blood pressure (BP) is a key player in the vascular etiology of dementia, but their relationship is not fully elucidated. The current BP control paradigm focuses on BP levels, but real-time BP is highly dynamic, involving simultaneous interactions of numerous neural and vascular feedback mechanisms. We hypothesized that early subclinical disruption in BP dynamics, captured by complexity and variability, contributes to dementia risk, above and beyond BP levels.

Methods In a prospective cohort study since 1997 involving 1,877 dementia-free community-based participants (59 % women; mean [SD] age, 70.9 [6.3] years), we investigated whether BP variability and BP complexity were associated with the risk of dementia. The primary exposures were BP complexity (quantified by sample entropy) and BP variability (quantified by coefficient of variation) derived from continuous beat-to-beat BP series of 300 beats. The primary outcome was incident dementia during follow-up until January 1, 2016.

Results Of 1,877 participants (59 % women; mean [SD] age, 70.9 [6.3] years), 333 developed dementia over 20 years. Reduced systolic BP (SBP) complexity was associated with a higher dementia risk (HR comparing extreme quintiles: 1.53 [95%CI: 1.08, 2.17], P=0.008). Increased SBP variability was also associated with a higher risk of dementia (HR comparing extreme quintiles: 1.57 [95% CI: 1.11, 2.22]; P=0.017). When considered jointly, individuals with both high variability (within the top quintile) and low complexity (within the bottom quintile) had a significantly higher risk of developing dementia compared with those with both high complexity and low variability in SBP (HR: 2.16; 95%CI: 1.28-3.65, P=0.003). These findings were observed after adjusting for age, sex, APOE genotype, mean SBP, and traditional vascular risk factors.

Conclusion Decreased complexity and increased variability of beat-to-beat systolic blood pressure are potential novel risk factors for dementia.
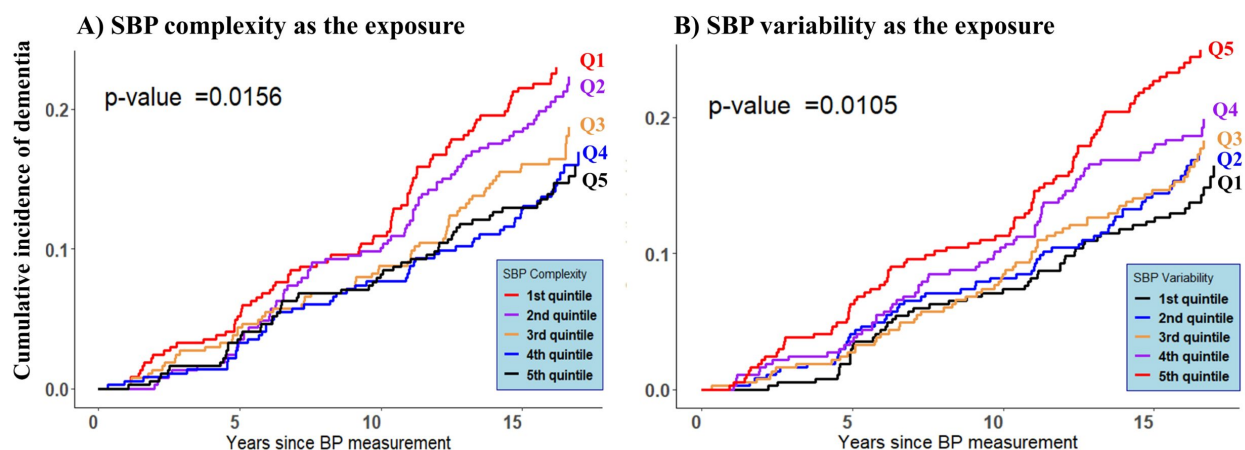
Figure. Cumulative incidence of all-cause dementia by quintile of SBP complexity (A) and variability (B)

* SBP=Systolic Blood Pressure; Q1-Q5 represent 1st~5th quintiles of the corresponding measures.

Competing risks in studies of air pollution and dementia: A demonstration of multiple approaches to account for informed censoring due to death Sindana Ilango* Sindana Ilango Tarik Benmarhnia

Adverse health effects of air pollution are well-documented and may affect neurocognitive outcomes, including dementia, through inflammation and oxidative stress. One challenge in studying the effect of chronic exposure to air pollution on aging-related outcomes is the presence of informed censoring due to competing events such as death. In studies of older adults, premature death may prevent or "compete with" a neurocognitive outcome of interest. Different approaches to account for informed censoring have been described in epidemiologic literature but are underutilized in air pollution studies. In this study, we demonstrate and compare several approaches to account for informed censoring due to death in a cohort study in France examining the relationship between air pollution and dementia. In most studies of air pollution and dementia, death is typically censored. This analytic decision implicitly assumes death occurs independently of exposure. However, since there is substantial evidence linking air pollution to premature death, and death can "compete" with a dementia diagnosis, this assumption is likely violated. It is thus important to account for informed censoring to avoid a selection bias that may underestimate the true effect. In this study, we demonstrate three approaches to account for competing risks, each with unique assumptions. First, a Fine and Gray approach will be applied to consider sub-distribution hazards. Second, inverse probability weights will be applied to correct for time-varying informed censoring. A model-averaging technique will be applied to these weights to simultaneously consider multiple hypothesized sets of covariates that predict death. Finally, a causal mediation framework approach recently proposed by Young et al where death is considered a mediator on the causal pathway from air pollution and dementia will be applied to account for informed censoring due by estimating a controlled direct effect. Assumptions and estimates generated from the approaches are compared.

Can the competing risk of death or selective survival explain the inverse association between cancer and dementia? A simulation study Eleanor Hayes-Larson* Eleanor Hayes-Larson Sarah Ackley Scott Zimmerman Rebecca E. Graff John S. Witte Monica Ospina-Romero Lindsay C. Kobayashi M. Maria Glymour Elizabeth Rose Mayeda

Robust literature supports an inverse association between diagnoses of multiple cancer types and dementia incidence (incidence rate ratio, IRR≈0.7). The substantive relevance of these findings depends on whether they can be accounted for by the competing risk of death (cancer death precludes dementia) or selective survival (collider bias). We used simulations to determine their plausibility to explain the inverse cancer-dementia association. We developed a continuous time multistate simulation model (Figure, arrow thickness shows relative magnitude of incidence rates) to follow a cohort of 65-year-olds cancer- and dementia-free at baseline. Age-specific transition rates were calibrated to cancer (all types) and dementia incidence from Surveillance, Epidemiology, and End Results (SEER) and the Adult Changes in Thought study, respectively, and US lifetable mortality rates. In all scenarios, cancer had no effect on dementia. Competing risk of death was introduced by setting higher mortality in individuals with cancer (SEER data). To introduce selective survival, we set a portion of the initial cohort (10-50%) to have characteristic U that reduced cancer mortality and dementia incidence (IRRs 0.5-0.9). Under competing risk of death, the cumulative incidence ratio (CIR) for cancer on dementia was protective (CIR 0.53), but IRRs were unbiased (null). With selective survival, both the CIR and IRRs were biased. For example, when prevalence of U was 50% and U halved both cancer mortality and dementia incidence rates, the CIR was 0.72, and there was more bias in IRRs at older ages as the cohort became more highly selected for U (e.g., IRR=0.98 ages 65-75 and IRR=0.77 ages 95-105). Despite biasing the CIR, the competing risk of death alone cannot explain protective IRRs for cancer on dementia. Selective survival resulted in small protective associations. Other explanations (e.g. shared biological basis) are needed to fully explain the inverse cancer-dementia association.
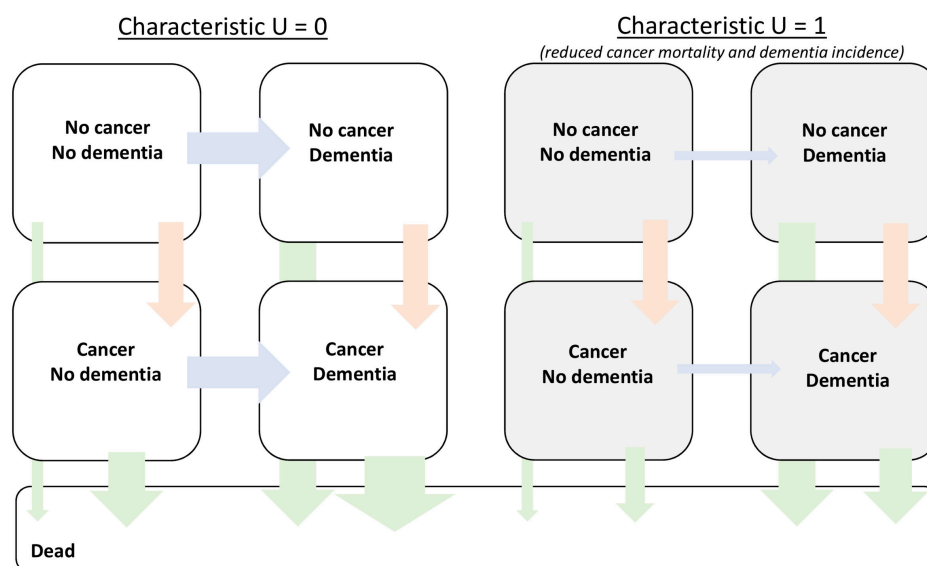
Figure. Schematic of multistate simulation model

Choosing a Target Population for American Indian data: Standardization, not Assimilation

Madison D Anderson* Madison Anderson Winnie Lindstrom Charlie Bouverette Michael Mudgett

Choosing a target population for standardization that produces meaningful results is critical, especially when working with data pertaining to American Indians. Given that there are over 570 federally recognized tribes, all with their own unique culture and traditions, it is wrong to assume homogeneity across American Indian populations. Using the Tribal Tobacco Use Project survey II (TTUP II) data, we will demonstrate the importance of choosing an appropriate target population when standardizing tribal-specific data. The Tribal Tobacco Use Project surveys a representative sample of American Indians in Minnesota across eleven tribes and two urban samples on topics related to commercial and traditional tobacco. Using tribal-specific data for the target population when standardizing provides results that are more informative. It is more appropriate to use tribal-specific data for our target population than it is to use statewide American Indian demographics or nation-wide American Indian demographics. There are unique considerations when working with American Indian data and researchers should be cautious when choosing their target population when standardizing data.

Translational & Implementation Science

Finding those who need us most: Data-driven efforts toward enrollment and engagement of US Veterans in VA services Courtney D. Shelley* Courtney Shelley Jodie Trafton Suzanne Tamang

There are approximately 18.2 million military veterans in the US, but only one third receive healthcare services at US Department of Veterans Affairs (VA) facilities. Veterans often do not engage with VA health services until they need them; those who do receive care are older and suffer more chronic illness than do the population of veterans more broadly. Thus, the locations of current healthcare facilities and who they serve may not be helpful in determining future outreach efforts, which can only be directed by the current demographic knowledge of younger, healthier veterans who will eventually seek out services. The American Community Survey (ACS) is conducted annually by the US Census Bureau to understand detailed population dynamics. In addition to many demographic questions, the survey asks both whether a person is a veteran and, if so, whether they currently receive services through the VA. This information can guide VA outreach efforts to identify underserved populations and, when combined with additional health survey data and the VA's own records, can identify locations where people are "at risk for risk" for diseases of despair such as substance abuse, Type 2 diabetes, homelessness, and suicide. Iterative proportional fitting (IPF) allows for the inference of joint probabilities at a population level given completely enumerated samples from census data, thereby creating a synthetic US population with features matching the geographic, demographic, and health characteristics of the overall population. This allows the VA to identify currently underserved populations, populations with multiple risk factors for complex chronic diseases and the interventions that will likely require based on risk factor profiles, and to plan for future outreach efforts and facility locations. This work is supported by the Million Veteran Program (MVP), US Department of Veterans Affairs.
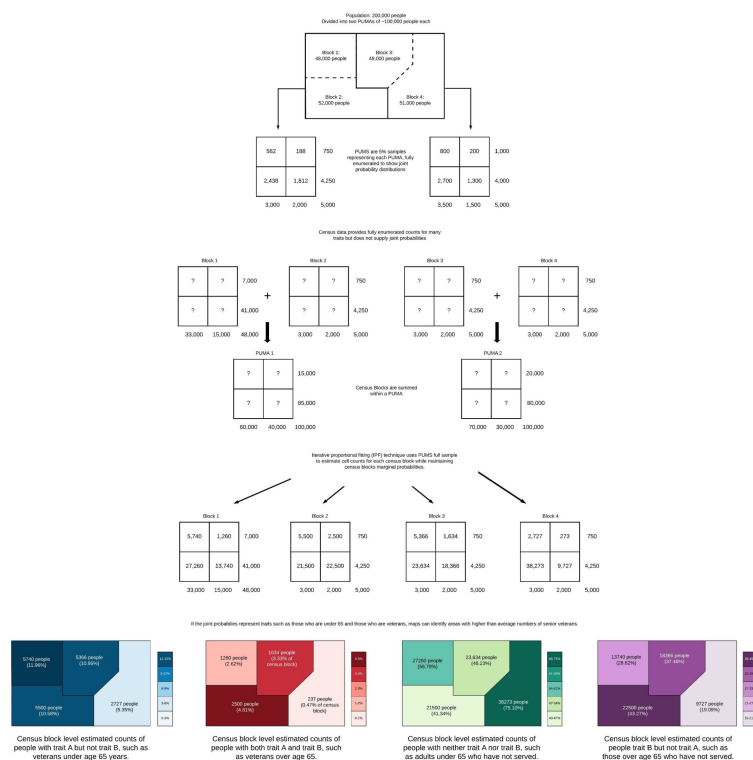
Figure: Iterative Proportional Fitting Method and Hypothetical Results. Iterative proportional fitting (IPF) allows for the inference of population-level joint probabilities using full census data and fully enumerated joint probability samples of the population-level census data. This information includes a geographic component, which can be leveraged to guide policy, such as the ideal location for future healthcare services to reduce patient travel distance, or guide outreach to subpopulations which may be in need of unique outreach messages.

Missing Sexual Orientation and Gender Identity Data in the Behavioral Risk Factor Surveillance System, 2014-2018: Sources, Magnitude, and Correlates Bill Jesdale* Bill M. Jesdale

Purpose: To describe sources, magnitude, and correlates of missing data in the Behavioral Risk Factor Surveillance System (BRFSS) Sexual Orientation and Gender Identity (SOGI) module.
Methods: Missing data from the BRFSS SOGI module fielded from 2014 to 2018 were ascribed to 4 sources: the optional nature of the SOGI module, out-of-state cellphone respondents, interview termination, and item non-response. The prevalence of missing-ness at these 4 stages was examined in relation to sociodemographic factors and survey process factors.
Results: Of 2,280,474 BRFSS respondents from 2014-2018, 1,178,052 (44.2%, weighted) were in states that did not administer the SOGI module. Among 551,387 cell phone interviews in states administering the module, 12.7% (weighted) were out-of-state. Among 1,102,422 potential respondents, 8.6% (weighted) terminated the interview before SOGI module administration. Among 970,520 administered the module, 3.5% did not answer the sexual orientation item, and 1.3% were missing gender identity. In states administering the SOGI module, 20.3% of respondents were missing sexual orientation data, and 18.5% were missing gender identity information. Correlates of missing-ness varied considerably at each stage.
Conclusions: Missing BRFSS SOGI data are much more prevalent than item non-response alone would suggest. Analytic techniques that consider only item non-response, such as complete case analysis, risk producing biased findings. Including the SOGI module in the core demographics section would greatly reduce the amount and complexity of missing data.

Social

A systematic review of the use of race and ethnicity in U.S. medical and epidemiologic research

Rae Anne Martinez* Rae Anne Martinez Nafeesa Andrabi Andrea N. Goodwin Rachel E. Wilbur Natalie R. Smith Paul N. Zivich Allison E. Aiello Robert A. Hummer

Despite robust documentation of racial and ethnic disparities in health outcomes, the conceptualization and measurement of race and ethnicity in medical and epidemiologic literature may be suboptimal. This study aims to assess whether the conceptualization, operationalization, and utilization of race and ethnicity has changed over time in leading journals that likely shape discourse around race, ethnicity, and health. We systematically reviewed randomly selected articles from prominent medical (Annals of Internal Medicine, JAMA, Lancet, NEJM, BMJ) and epidemiology journals (AJE, Annals of Epidemiology, Epidemiology, Journal of Clinical Epidemiology, Journal of Epidemiology and Community Health). Within these, all original human-subjects research conducted in the US was eligible for review. Articles were randomly selected within five periods: 1995-99, 2000-04, 2005-09, 2010-14, 2015-19. Information on theoretical justification (conceptualization), measurement/coding (operationalization), and use in analysis (utilization) was extracted. From medical literature, we reviewed 900 articles, including 213 (23.7%) in analyses. Primary reasons for exclusion were non-US research and commentaries. The proportion of studies in medical journals that measured race or ethnicity increased over time, but plateaued in 2005-09. In 1995-99, 40.0% of studies reported measuring race and 17.5% reported on ethnicity; after 2005-09, this grew to 71.1-75.0% and 39.5-47.7%, respectively. Regardless of period, the measurement of race and ethnicity was unclear in the majority of studies. No studies explicitly conceptualized race or ethnicity; just one study justified racial coding schemas. Data collection and analyses are ongoing for the epidemiologic literature. This review is timely given the continued emphasis on racial and ethnic health disparities, which constitute a major threat to health and well-being. Future work will consider medical sociology for added cross-disciplinary comparisons.
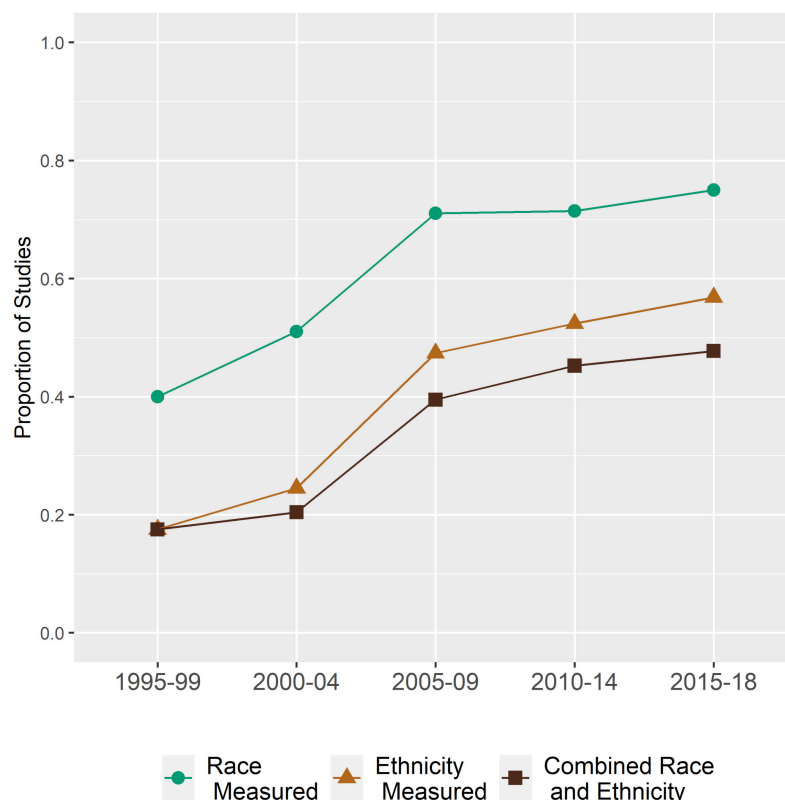
Filling in the Gaps: Feasibility of using Electronic Health Record data to study uninsured populations Dawn G. Albright* Dawn G. Albright Elizabeth C. Dabrowski Liza R. Gibbs Nicolle Gatto Dana Y. Teltsch

Background
Claims data provide rich information on large populations, but by definition do not have information on uninsured individuals. This limits generalizability of Real World Evidence (RWE) studies towards the employed population. Electronic Health Records (EHR) such as Optum® de-identified Electronic Health Record dataset can potentially be used to study uninsured populations. EHR data can capture insurance type as part of an observation, but lack start and end information for coverage type. Individuals may also have more than one insurance type and uncovered services.

Objectives
To estimate the size of the uninsured population within Optum EHR.

Methods
We used Optum® de-identified Electronic Health Record dataset from Jan 2007 to March 2018. The main analysis focused on the 42,454,224 individuals who had 3 or more encounters with an insurance type other than "Other" or "Unknown", out of the 91,028,176 total. See figure below for distribution. Insurance types were summarized in 3 month periods to describe insurance type coverage and assess the level of type overlap.

Results
In the study cohort over all documented activity,17,498,467 (41%) had at least one "Uninsured" encounter. 25,746,337 (60%) had only one type of insurance recorded, allowing for unambiguous insurance type assignment. 5,729,801(13%) individuals were uninsured with an average of over 17 observations per patient. In addition, 14,291,351 patients had time spans with =>80% activity as uninsured.

Conclusions:
Optum EHR documents a substantial amount of medical activity that is not covered by insurance. Such EHR data can offer a window into learning about this understudied population.

Distribution of observations by insurance type
(10th, 25th, 50th, 75th, 90th percentiles)

*Of those with three or more visits, excluding insurance types of "Unknown" and "Other Payor"

Infectious Disease
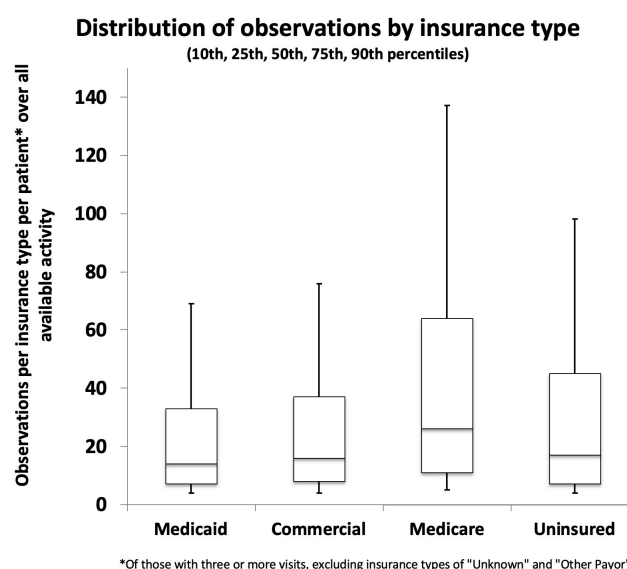
Exploring the impact of clustering of unvaccinated individuals on risk of measles infection at herd-immunity vaccination levels Nina Masters* Nina Masters Jon Zelner Marisa Eisenberg Matthew Kay Paul Delamater Matthew Boulton

The past decade has witnessed an increasing number of measles outbreaks, with 2019 experiencing the most measles cases in the US in 25 years. The 2019 outbreaks occurred despite 94.7% of kindergarteners being vaccinated against measles, exceeding the calculated critical vaccination fraction (CVF) required to reach herd immunity (94%). Such outbreaks illustrate the flaws inherent in calculating the CVF, which assumes homogeneous vaccination coverage and mixing of individuals, when in reality, clusters of non-vaccinated individuals can permit ongoing transmission. This study employed a spatial, compartmental susceptible-infected-recovered (SIR) measles model on a 16 x 16 grid. The overall vaccination rate was fixed at 94%, and only the spatial location of non-vaccinated individuals was varied using nested probability distributions to generate 625 unique 'motifs'. The clustering of each motif was characterized by the global Moran's I, an overall measure of spatial autocorrelation, and the SIR model was run for one year using each motif as initial conditions. All simulations met the CVF overall, yet the clustering of the initial conditions greatly impacted whether or not an outbreak occurred. There were no secondary cases from an introduced case when non-vaccinators were homogeneously distributed, but as the environment grew more clustered, outbreaks did occur. A simulation in the motif with the highest Moran's I (0.866) yielded 9,729 total cases, representing 63% of the initial susceptible population becoming infected over one year. This highlights that the assumptions underlying the CVF calculation are flawed, and clustering may allow for outbreaks to occur even when aggregate vaccination coverage meets or exceeds the CVF. Such mounting evidence that clustering of non-vaccination can impact disease dynamics motivates finer-scale surveillance in elimination contexts to identify susceptible clusters before they can lead to outbreaks.

90-day time-lapse of spatial measles SIR model in environment with 94% overall vaccination coverage, but with 85% of non-vaccinators located in top-left quadrant (initial infection dropped in center of that quadrant)
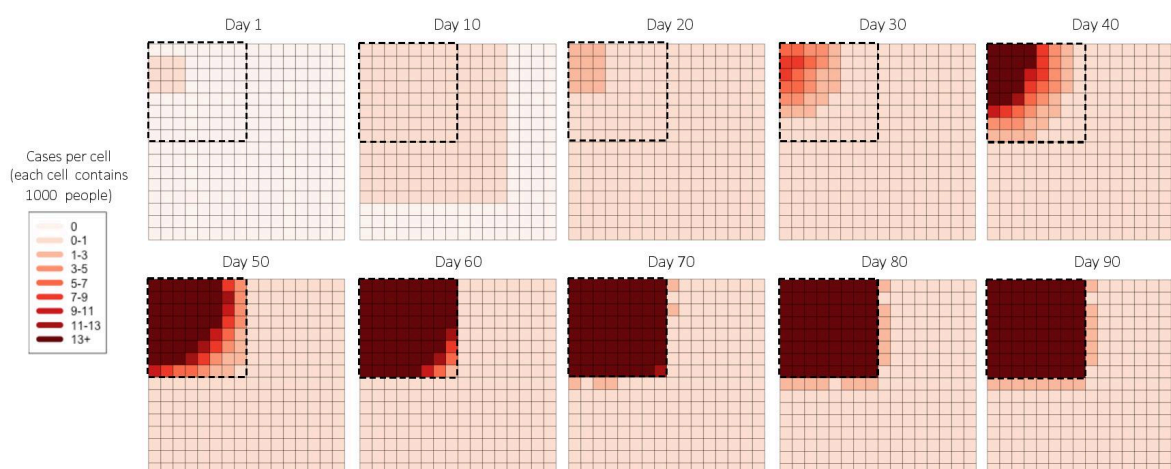
The causal interpretation of "overall vaccine effectiveness" in test-negative studies Ben Cowling* Ben Cowling Shuo Feng Eric Tchetgen Tchetgen Sheena Sullivan

The test-negative studies are increasingly used to estimate influenza vaccine effectiveness (VE). In a typical study, "overall VE" is estimated based on data from all participants. However, the patients enrolled into this type of study may not be representative of the underlying population, and there may be heterogeneity in VE particularly by age, which challenge the causal interpretation of "overall VE". We therefore discuss the potential for a weighted average of age-specific VE estimates to provide a more meaningful measure of "overall VE". We illustrate this perspective first using simulations to evaluate how "overall VE" would be biased when a certain age group was over-represented. We found unweighted "overall VE" estimates tended to be higher than weighted VE when children were over-represented and lower when elderly were over-represented. Then we extracted published estimates from the US Flu VE network, in which children are overrepresented, and some discrepancy in unweighted verses weighted "overall VE" was observed. Differences in weighted versus unweighted "overall VE" could translate to substantial differences in the interpretation of individual risk reduction in vaccinated persons, and the total averted disease burden at the population level. Weighting overall estimates should be considered in VE studies in future.

Assessing the Reporting and Misclassification of Arboviruses in the National Surveillance System of Colombia (2014-2017) Mabel Carabali* Mabel Carabali Gloria Isabel Jaramillo Vivian A. Rivera Neila Julieth Mina Berta N. Restrepo Kate Zinszer

Surveillance systems are vital components of disease control programs to understand disease burden, trends, and to detect outbreaks. However, underreporting can bias estimates and greatly reduce surveillance data utility. Chikungunya, dengue, and zika are three different arboviruses, which have similar symptoms and are a major public health issue in Colombia. Despite the mandatory reporting of these arboviruses to the National Surveillance System in Colombia (SIVIGILA), it has been reported that the system captures less than 10% of diagnosed cases in some cities. To assess the scope and degree of arboviruses reporting, we conducted an observational study using the capture-recapture approach in three Colombian cities from 2014-2017. We used registries of cases from healthcare facilities and surveillance offices in each city, to identify cases that were diagnosed at the healthcare facilities (capture) and those that were reported to SIVIGILA (recapture). We fit robust Poisson regressions to identify predictors of reporting and estimated the predicted probability of reporting by disease and year. To account for the potential misclassification of clinical diagnosis, we used the simulation extrapolation for misclassification (MC-SIMEX) method. A total of 266,549 cases were examined across the three study sites between 2014-2017. The overall reporting of arboviruses varied in magnitude depending largely on age and year of diagnosis. Dengue was the most notified disease (21-70%) followed by zika (6-45%) and the highest reporting rate for all arboviruses was 2016, an epidemic year. Regardless of the correlation matrix used for MC-SIMEX, naïve estimates were consistently lower than the corrected results, indicating underestimation of the reporting due to the potential misclassification bias. These findings reflect important challenges for estimating arboviral disease burden in Colombia as well as in other endemic settings with similar surveillance systems.
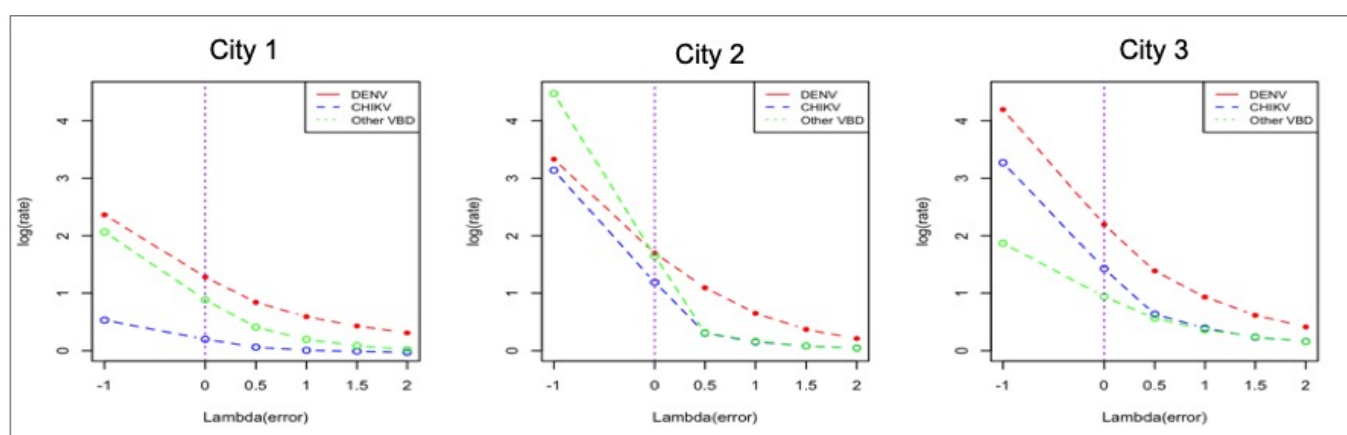
Simulation Extrapolation results: Measurement Error estimation of the reporting by disease, adjusted by age and year of notification in three Colombian cities (2014-2017). Results presented in the log scale: the degree/change of misclassification error on the X axis and the log-rates of reporting on the Y axis . The dotted line at error level zero in the X axis (purple dotted line) indicates the naïve estimated rates and the estimates at error level -1, indicate the extrapolated misclassification-corrected rates. Estimates from error level (lambda) 0.5 to 2, indicate the change in the estimated rates of reporting by adding different levels of misclassification error. DENV=Dengue; CHIKV=Chikungunya, and Other VBD= Other Vector-Borne Diseases including Zika.

A machine learning approach to predict mortality from severe dengue in Colombia Andre Filipe de Moraes Batista* Andre Filipe de Moraes Batista Farley Liliana Romero Vega Fredi Alexander Diaz-Quijano Alexandre Dias Porto Chiavegatto Filho Mariane Furtado Borba Juliana Maria Trindade Bezerra Mariângela Carneiro

Dengue is an endemic public health issue in regions with tropical and subtropical climate within the Americas. In Colombia, persistence of its transmission vector, and the number of deaths associated to severe dengue, are a growing concern to the local authorities. Predictive tools identifying cases with the highest risk of death, can improve decisions about adequate and effective care to prevent severe dengue mortality. For this study, we tested the predictive performance of machine learning algorithms such as random forests, gradient boosted trees and artificial neural networks to predict mortality among patients with severe dengue, using as predictors routinely collected data from local healthcare facilities. We used national surveillance data from 2010 to 2015 for training the machine learning models (n = 16,236), and then unseen data from 2016 (n = 2,148) was used to test their future real-world performance. The highest predictive performance for this new data (2016) was obtained by the gradient boosted trees algorithm, with an Area Under the Curve of the Receiver Operating Characteristic (AUC ROC) of 0.854. The top 20% patients with of the highest predicted risk provided by the best model included 66.05% of total deaths of the cohort. In conclusion, machine learning models are able to predict mortality risk for patients with severe dengue in Colombia by using only routinely collected data from local healthcare facilities. Applications of predictive machine learning methods can bring agile and assertive insights for severe dengue cases that require differentiated protocols for hospitalization and care.

Differences in the target parameter could explain contradictory results between observational and intervention studies of the effect of improved sanitation on child growth

Elizabeth T. Rogawski McQuade* Elizabeth T. Rogawski McQuade Daniel J. Westreich Jade Benjamin-Chung Benjamin F. Arnold

Background

Improved sanitation has been associated with improved child growth in observational studies. However, recent trials of sanitation interventions failed to show an impact on linear growth. Residual confounding of the observational associations is often cited as an explanation. We aimed to assess to what extent differences in the target parameter being estimated in the two study designs (average treatment effects, ATE, in observational studies and population intervention effects, PIE, in trials), could help explain the contradictory results.

Methods

We estimated the effect of providing improved sanitation compared to current sanitation coverage in control arms from two large sanitation trials (WASH Benefits, n=3204), a multisite prospective cohort study (MAL-ED, n=640), and cross-sectional DHS data from 8 countries (n=109,438). We compared these PIE to the usual ATE in the same data. Effects on mean length-for-age z-score among children under age 2 were estimated using parametric g-computation and linear regression.

Results

The PIE was always smaller than the ATE, though the magnitude of difference varied, depending on the baseline prevalence of improved sanitation (Figure 1). Three of 8 DHS sites, 2 of 3 MAL-ED sites, and both WASH Benefits sites had ATEs greater than 0.15 z-scores, a clinically meaningful difference. In the Nepal and Pakistan DHS sites, the PIE were 20% of the ATE (PIE: 0.07, 95% CI: 0.02, 0.11 and 0.06, 95% CI: 0.00, 0.11, respectively). In MAL-ED and WASH Benefits, the PIE were only slightly smaller than the ATE.

Conclusions

Because the PIE in some sites were smaller than effect sizes recent large intervention trials were powered to estimate, incongruence between observational associations and null trial results may in part be explained by expected differences between the ATE and PIE. Using ATEs from observational data to inform intervention trials may overestimate expected PIE. Intervention effects should be more routinely estimated.
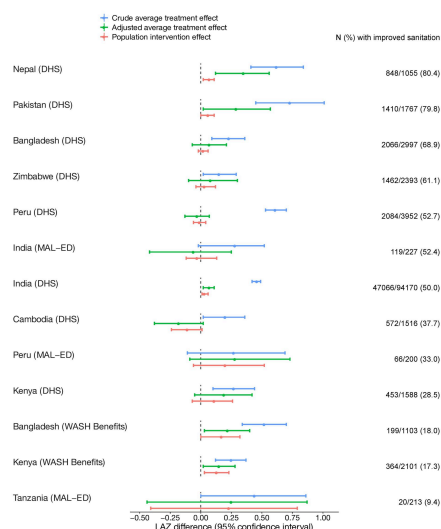
Figure 1. Estimates of the average treatment effects and population intervention effects for improved sanitation on mean length-for-age z-score (LAZ) among children under age 2 in WASH Benefits (n=3204), MAL-ED (n=640), and Demographic Health Survey (DHS) data from 8 countries (n=109,438). Effects are ordered from highest to lowest baseline prevalence of improved sanitation and are adjusted for age, sex, socioeconomic status, maternal education, household size, drinking water source and treatment, and livestock ownership.

Perinatal & Pediatric

Maternal Diet in Pregnancy and Child Blood Pressure: Results from the Conditions Affecting Neurocognitive Development and Learning in Early Childhood (CANDLE) Study

Yu Ni* Yu Ni Christine Loftus Frances Tylavsky Adam Szpiro Mario Kratz Annette Fitzpatrick Jennifer Sonney Kaja LeWinn Nicole Bush Sheela Sathyanarayana Robert Davis Catherine Karr

Background: The intrauterine environment may influence offspring blood pressure, with effects possibly extending into adulthood. The associations of maternal dietary patterns and micronutrient status during pregnancy, alone or in combination with other sociodemographic or behavioral factors, with offspring blood pressure are unclear. Methods: The CANDLE study includes a racially and socioeconomically diverse birth cohort in the Mid-South of the U.S., with 60% of women identifying as Black. Mother-child dyads (N=858) who completed an age 4 visit were included. Child systolic (SBP) and diastolic blood pressure (DBP) percentile incorporating sex, age and height were calculated, and further categorized as high blood pressure (HBP) (≥ 90th percentile) or normal. Maternal dietary patterns were assessed by the Healthy Eating Index (HEI) based on the Food Frequency Questionnaire during the 2nd trimester, and plasma folate was determined during mid to late pregnancy. We conducted linear and Poisson regressions with adjustment for sociodemographic, anthropometric measurements, behavioral factors, maternal stress and child diet. Interactions between nutrient indices and child sex, maternal race, maternal smoking, breastfeeding and maternal weight status were explored. Results: Mean HEI and folate were 60.1 (11.3) and 23.2 (11.1) nmol/L respectively. 29% of the children were defined as HBP based on measurements at one visit. Maternal HEI and plasma folate were not associated with child BP percentile and HBP in the full cohort. We found a significant interaction between maternal race and HEI in the association with SBP (P = 0.024). Among non-Blacks, each one unit increase of HEI was associated with 0.44 lower SBP percentile (95%CI: -0.79, -0.09). Conclusion: Using two indices of maternal diet, we found little evidence for effects of maternal diet on childhood BP. Optimal maternal dietary patterns were associated with lower child BP in non-Blacks.

Patterns of Complementary Feeding Behaviors Predict Diet Quality in Early Childhood

Karen Switkowski* Karen Switkowski Véronique Gingras Sheryl Rifas-Shiman Emily Oken

Infancy may be a "sensitive period" for learning new taste preferences and establishing healthy dietary behaviors that may track later in life. Among 1,162 children in the U.S. prospective cohort study Project Viva, we examined associations of complementary feeding (CF) behaviors around 1 year with diet quality in early childhood (median age 3.2y, range 2.8-6.3y). We identified patterns of CF using latent class analysis and compared mean total and individual component scores on the Youth Healthy Eating Index (YHEI) among latent classes. We identified four distinct CF patterns (latent classes). The primary outcome was total YHEI score in early childhood (overall mean 52.7 points out of 80). Total YHEI scores were highest in the class characterized by "breast milk and delayed sweets and fruit juice" and lowest in the "picky eaters" class (difference of 6.62 points, p<0.0001). The classes defined as "late flavor introduction and delayed sweets" and "early flavor introduction and more fruit juice" had similar, moderate scores. These associations were similar within strata of various participant characteristics (maternal education and BMI; household income; child race/ethnicity and breastfeeding status in infancy). We also conducted a series of secondary analyses to determine whether different CF patterns in infancy were associated with specific dietary components in early childhood, measured using 9 individual components of the YHEI. The highest mean score (indicating better diet quality) for vegetables was observed in the "early introduction and more fruit juice" class, and the "picky eaters" class had the lowest scores on the vegetable and whole fruit components. The "breast milk and delayed sweets and fruit juice" had the highest scores on the snack, soda/drinks, and meat components. Infancy CF patterns that increase food acceptance and discourage innate preference for sweetness may influence diet quality into childhood.

Figure 1: Comparison of adjusted[1] mean YHEI total and component scores among latent classes of complementary feeding behaviors
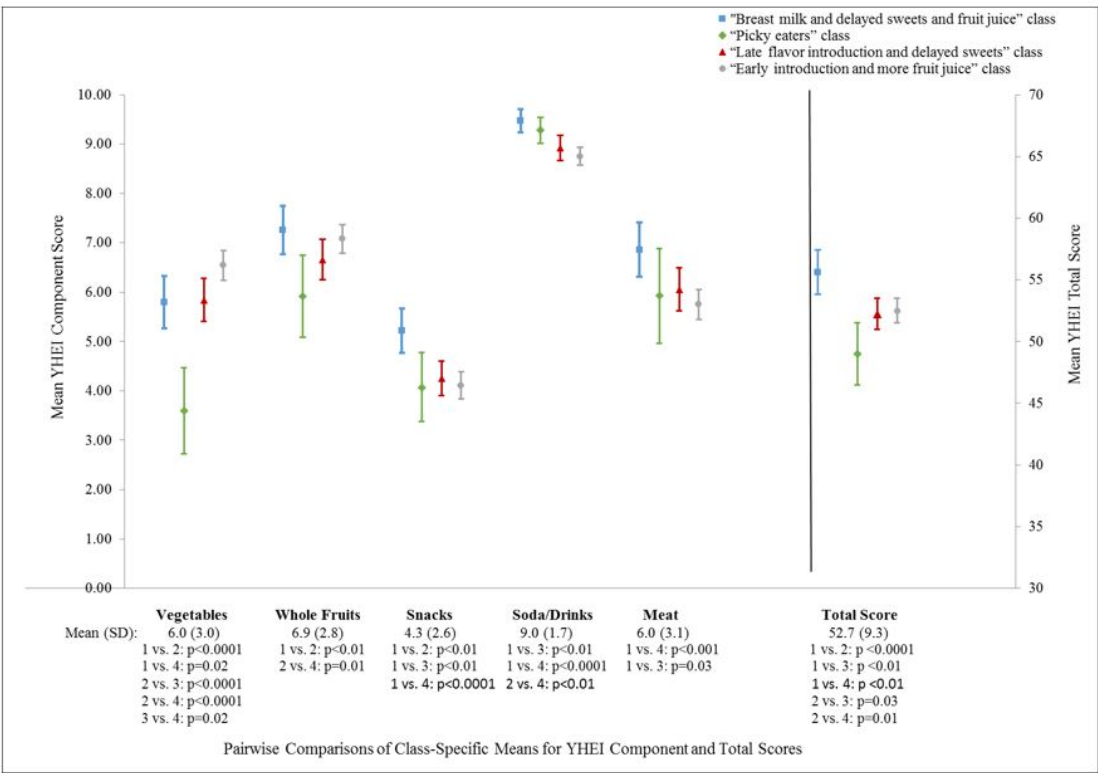
1 Means were adjusted using the "Bolck, Croon, and Hagenaars (BCH)" approach, which applies weights that are inversely related to the probabilities of classification error to obtain unbiased estimates

Changes in association between school meals and children's dietary quality during implementation of the Healthy, Hunger-Free Kids Act of 2010 Aaron T Berger* Aaron Berger Rachel Widome Darin J. Erickson Melissa N. Laska Lisa J. Harnack

Introduction. The Healthy, Hunger-Free Kids Act of 2010 (HHFKA) reformed all foods served in schools in the United States. We sought to evaluate the effects of its implementation on the dietary quality of all US school-aged children, and to examine if the effect of implementation differed by income/age group.

Methods. We leveraged a natural experiment within the 2007-2016 National Health and Nutrition Examination Survey, to estimate changes in the effects of eating school foods on children's dietary quality, measured with the Healthy Eating Index-2010 (HEI-2010). We used survey regression to estimate the proportion of energy intake from school foods, and the association between greater dietary intake from school food intake and dietary quality, before and after HHFKA passage/implementation. We used inverse probability weighting to account for temporal changes in the US population. We estimated the effect of HHFKA implementation on dietary quality by multiplying the change in the association between school food intake and dietary quality, by the proportion of dietary intake from school foods.

Results. US children's school food intake was stable during HHFKA implementation. The association between school food intake and dietary quality more than doubled during implementation. Scaled to the proportion of children's dietary intake from school foods, HHFKA implementation improved the dietary quality of all US children by 0.74 HEI points per day (95% CI: 0.17, 1.3), and by 2.6 HEI points (95% CI: 0.6, 4.5) on days when children ate school meals.

Conclusions. HHFKA implementation appears to have measurably improved total dietary quality of US children, particularly children eligible for free/reduced-price meals. US children would benefit from increased school meal intake. HHFKA regulations should not be relaxed.

a Pre-Passage (2007-2010)

b Implementation Period (2013-2016)

HEI-2010 (Day 2 - Day 1)

% of calories from school cafeteria food (Day 2 - Day 1)

The impact of Health Canada's Voluntary Sodium Reformulation Targets on educational inequalities in sodium intake: a modelling study using the 2015 Canadian Community Health Survey-Nutrition Brendan Smith* Salma Hack Douglas Manuel Mahsa Jessri JoAnne Arcand Lindsay McLaren Mary L'Abbé Laura Anderson Erin Hobin David Hammond Heather Manson Laura C. Rosella Brendan T. Smith

Background: High sodium intake is a leading modifiable risk factor for cardiovascular diseases. Sodium reformulation of processed foods, a World Health Organization 'best-buy' intervention, has been successful globally and encouraged in Canada to reduce excess population sodium intake. The study objective was to estimate the effectiveness of achieving Phase 3 of Health Canada's Voluntary Sodium Reformulation Targets on educational inequalities in sodium intake.
Methods: A modelling study was conducted using cross-sectional 24-hour dietary recall data from respondents of the 2015 Canadian Community Health Survey-Nutrition, Canada's most recent nationally representative nutrition survey (n=13,519 >19 years, 47% males). Sodium content in reported foods were quantified using the 5690 unique foods from the 2015 Canadian Nutrient File. Phase 3 was modelled by replacing sodium levels in foods with sodium reformulation targets. Weighted multivariable linear regressions were used to estimate sodium intake and 95% confidence intervals according to educational attainment (less than high school; high school; certificate or diploma from a trade, college; bachelor degree or higher) adjusted for age, energy, and misreporting.
Results: Educational inequalities in mean sodium intake were observed at baseline, with intake higher in the "less than high school" group [men: 399 mg/day (95%CI: 172, 626), women: 122 mg/day (95%CI: 6, 239)] compared to the "bachelor degree or higher" group. After modelling Phase 3 targets educational inequalities were eliminated and mean sodium intake was reduced across all education groups in men (Phase 3: 2745mg/day to 2918mg/day) and lowered intake below the 2300 mg/day tolerable upper limit in women (Phase 3: 2067mg/day to 2119mg/day).

Conclusion: Achieving Phase 3 sodium reformulation targets was estimated to be both effective in reducing population-level sodium and eliminating educational inequalities in sodium intake in Canadians adults.

Association between dietary patterns and urinary phthalate exposure among postmenopausal women Gabriela Vieyra* Gabriela Vieyra Katherine

Phthalates are synthetic additives used in food packaging materials. Prior research has identified diet as a major source of phthalate exposure, yet such studies relied on single measurements of diet and urinary phthalate biomarkers and did not examine specific dietary patterns. We evaluated associations between adherence to the Mediterranean diet (MED) and Dietary Approaches to Stop Hypertension (DASH) diet and urinary phthalate biomarker levels. Among a subset of the Women's Health Initiative participants, we included 2 to 3 contemporaneous measurements collected over a 3-year period of diet (assessed by a standard food frequency questionnaire) and urinary phthalate biomarkers (measured using HPLC-MS-MS) per woman. We modeled associations between each diet pattern and natural log transformed phthalate biomarker concentration (ng/mL) using generalized estimating equation models with adjustment for urinary creatinine, age, body mass index, race, clinical site, education, income, smoking status, and physical activity. Among 1,024 postmenopausal women, higher MED scores were associated with lower concentrations of diethylhexyl phthalate (DEHP) (β=-9.69 p=0.03), monobenzyl phthalate (MBzP) (β=-13.52, p=0.01), and monoethyl phthalate (MEP) (β=-12.32, p=0.05). Similarly, higher DASH scores were associated with lower DEHP (β=-22.68, p=0.05) and MBzP (β=-40.18, p<0.01) but not MEP (β=-7.49, p=0.6). MED and DASH scores were not associated with other phthalate biomarkers. Adherence to dietary patterns that are rich in fruits and vegetables and limit processed foods were associated with lower concentrations of specific urinary phthalate biomarkers. Future work will identify specific food items that significantly contribute to phthalate exposure. These results identify adherence to MED and DASH diets as a potential means of reducing dietary phthalate exposure.

Challenges and Approaches for Causal Inference in Studying the Long-term Health Effects of Disaster Koichiro Shiba* Koichiro Shiba Ichiro Kawachi

Introduction
Two frequently encountered challenges for causal inference in studying the long-term health effects of disaster include: (a) time-varying effects of the exposure and (b) selection bias due to loss-to-follow-up. We describe approaches to overcome these challenges using a real-world example from the 2011 Great East Japan Earthquake.

Methods
We used longitudinal data of older adults aged >=65 years who were directly affected by the 2011 earthquake and tsunami (n=4857). For the challenge (a), we examined the association between residential distance from the coast (a proxy of housing damage from the tsunami) and mortality. We compared results from Cox regression assuming proportioinal hazards vs adjusted parametric survival curves allowing time-varying hazard ratios. For the challenge (b), we examined the association between proximity to the coast and depression in 2013 and 2016. Since the analytic sample was restricted to respondents of the follow-up surveys (n=3567 for 2013, and n=2781 for 2016), we corrected for potential selection bias via inverse probability attrition weighting (IPAW) and survivor average causal effect (SACE) estimation.

Results
Adjusted Cox regression showed no strong evidence that proximity to the coast is associated with mortality. However, the adjusted parametric survival curves showed that risk of death was significantly higher among those who lived closer to the coast for the first 3 years after the disaster. For selection bias, while IPAW did not differ from the multivariable Poisson model (RR of depression in 2013 =1.67, 1.34-2.04 for those less than 1000m of the coast), SACE indicated a much greater risk (RR=1.93, 1.44-2.68). Only SACE continued to show significantly elevated risks of depression in 2016 for those who lived closer to the coast (RR=1.90, 1.21-3.11).

Conclusion
Analytic approaches that ignore time-varying effects and selection bias due to attrition may substantially underestimate the long-term health effects of disaster.
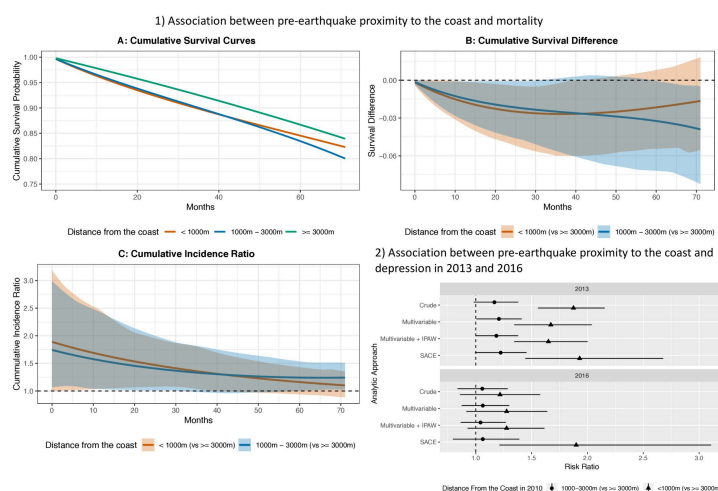
Potential for preterm birth to mediate the relationship between maternal exposure to air pollution and childhood academic achievement. Arin A. Balalian* Arin A. Balalian Katharine H. McVeigh Jeanette Stingone

Abstract
Introduction
Previous research has observed relationships between higher prenatal exposure to air pollutants and neurodevelopmental and academic outcomes later in childhood. However, mechanisms of these associations are unclear. We aimed to investigate if previously observed associations between prenatal exposure to common urban air pollutants, diesel and perchloroethylene (perc), with 3rd grade standardized test scores was mediated through increased risk of preterm birth.
Methods
Data from the 1994-1998 birth cohorts within the Longitudinal Study of Early Development were included in this analysis. The exposure was determined by linking the mother's residence at the time of delivery to EPA's 1996 National Air Toxic Assessment of estimated ambient concentrations of pollutants. Children's third grade standardized math and language score tests were selected as outcome. The missing data on covariates were imputed by multiple imputation methods. We excluded the participants with missing information on gestational age and school test scores. We employed linear regression models and causal mediation analysis to examine the mediation by preterm birth. We also explored possible exposure and mediator interaction.
Results
In total 187,401 participants were included in the analysis. We found that exposure to the fourth quartile of diesel was associated with 2% (95%CI: -0.03 , - 0.01) of a standard deviation lower math score than exposure in the first quartile. Similarly, exposure to the highest quartile of perc was associated with a 2% difference in the math score (95%CI: -0.04, -0.01). We did not find evidence of mediation by preterm birth or exposure-mediator interaction in our models.
Conclusion
We found no evidence that observed relationships between prenatal exposure to air toxics and standardized test scores in childhood was mediated through an increased risk of preterm birth.

Impacts of Exposure to Oil and Gas Drilling during Pregnancy on Markers of Intrauterine Growth Restriction among Term Infants: A Difference-in-Differences Analysis Mary D. Willis* Mary Willis Elaine L. Hill Andrew Boslett Molly L. Kile Susan Carozza Perry Hystad

Background: An estimated 17.6 million people live <1.6km of an active oil or gas drilling site in the United States, yet the health impacts of this industry are largely unknown. A growing body of literature examines impacts of drilling activity on markers of intrauterine growth restriction (IUGR), but these analyses primarily use traditional epidemiological methods. Studies to date focus on unconventional gas drilling, a small subset of potential exposures, and overlook population-level socioeconomic changes that occur during an industrial boom. We implement a difference-in-differences design to disentangle impacts of drilling-related pollution on term IUGR from economic gains and demographic changes.

Methods: We leverage a population-based retrospective term birth cohort (37-42 weeks gestation) from 1996-2009 in Texas with mothers (n=2,598,025) living <10km from an oil or gas site and link addresses to active drilling sites between 1985 and 2019. We compare two markers of term IUGR (birth weight and small-for-gestational-age (SGA)) among infants from pregnant women residing <1km of a site pre-drilling vs. post-drilling. We then create a contemporaneous counterfactual population by comparing to pregnant women residing 3-10km away pre-drilling vs. post-drilling. We apply linear and logistic regressions with sociodemographic, maternal health, and spatial-temporal covariates.

Results: After including sociodemographic and maternal health covariates, we see that maternal residence <1km of 1+ drilling site during pregnancy is associated with a -4.2g (95% CI: -8.3, -0.1) reduction in term birth weight and a 1.06 (95% CI: 1.03, 1.10) increased odds of term SGA. However, after accounting for regional spatial confounding, we find no evidence of associations.

Conclusion: Using a robust difference-in-differences framework with controls for unmeasured spatial confounding, we find no associations between exposure to drilling during pregnancy and markers of IUGR among term infants.

Figure 1: Schematic of spatial and temporal components of the difference-in-differences analytical design
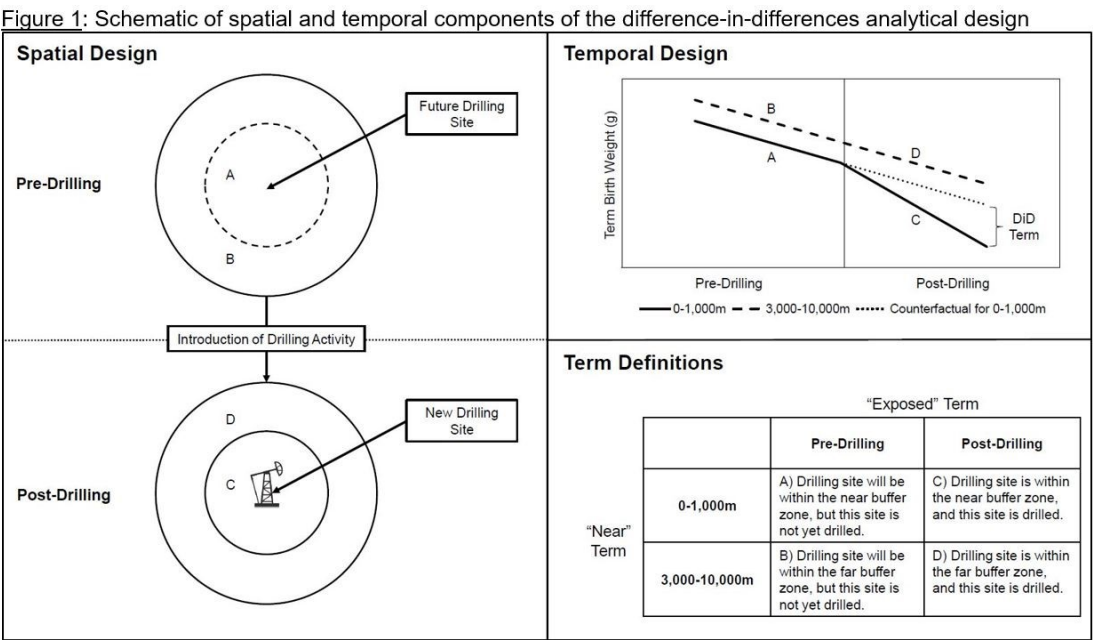
Spatio-temporal patterns of associations between deforestation and malaria incidence in Lao PDR. Francois Rerolle* Francois Rerolle Emily Dantzer Andrew Lover John Marshall Bouasy Hongvanthong Hugh Sturrock Adam Bennett

Background
Given the importance of forest-based malaria transmission in the Greater Mekong Sub-region (GMS), understanding the relationship between deforestation and malaria incidence is essential for malaria programs in the region to assess and meet their elimination goals.

Methods
Village-level monthly malaria incidence between 2013 and 2016 was estimated from health facility malaria surveillance data from 4 northern and 4 southern districts of Lao PDR. Deforestation was defined as the percent area within 1, 10 or 30 km of villages that experienced complete removal of their tree crown cover in the previous 1 to 5 years. A negative binomial spatio-temporal model was used to assess the relationship between varying spatio-temporal definitions of deforestation and village-level monthly incidence, adjusting for environmental variables.

Results
Deforestation, defined as a 0.1% increase in forest loss within 1 or 10 km of a village, was not associated with monthly malaria incidence in either the south or the north, regardless of the temporal lag. However, within 30 km of a village, deforestation in the previous 1 and 2 years was associated with higher malaria incidence rates (e.g, 1 year lag: IRR [95% CI] = 1.23 [1.16; 1.30] in the south and 1.02 [0.94; 1.10] in the north), whereas deforestation in the previous 3, 4 or 5 years was associated with an approximately 5% lower malaria incidence rate (see figure). These associations became stronger when restricting deforestation to densely forested areas only and differed between malaria parasite species.

Conclusion
Deforestation was associated with higher malaria incidence in the first two years but lower long-term malaria incidence. The association between deforestation and malaria incidence was stronger when considering larger areas around villages and more densely forested areas, reinforcing the importance of forest-going populations, traveling between villages and forested areas, on malaria transmission.

Associations between malaria incidence and a 0.1% increase in the area that experienced deforestation within 1, 10 or 30 km (left-right) of a village in the previous 1 to 5 years (top-down) in Lao PDR
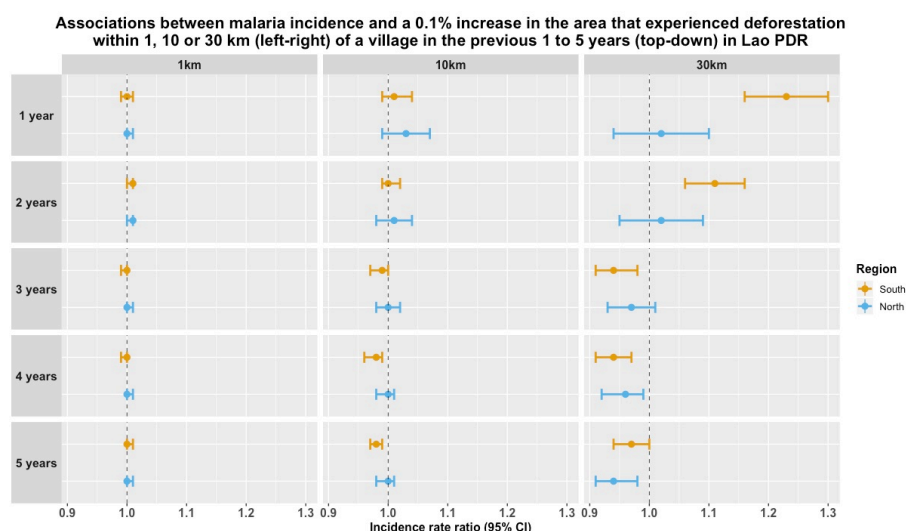
Birth outcomes and pregnancy complications after the 2013 Calgary flood: a difference in difference analysis Erin Hetherington* Erin Hetherington Kamala Adhikari Lianne Tomfohr-Madsen Scott Patten Amy Metcalfe

Background: In June 2013, the city of Calgary, Alberta sustained significant flooding which resulted in the evacuation of over 75,000 people and caused downtown to close for one week. Floods can cause significant levels stress which may negatively impact perinatal outcomes. Previous studies have found increases in preterm birth and low birthweight after natural disasters, but results are inconsistent, and study design often does not account for baseline differences in affected and unaffected areas, or time trends.

Research Question: Did the 2013 Calgary flood negatively impact pregnancy health and birth outcomes?

Methods: Administrative data including all births in the province of Alberta between 2012 and 2014 were used. Outcomes included preterm birth (< 37 weeks gestation), small for gestational age, new diagnoses of preeclampsia or gestational hypertension. Data were analyzed using a difference in difference design, comparing nulliparous women in the flood area and a non-flood area in 2012 and 2013. Multivariable log binomial regression models were used to estimate risk ratios, adjusted for maternal age. Additional analyses included examining timing of exposure (trimester of pregnancy) and stratifying by plurality and infant sex.

Results: Participants included 18,266 nulliparous women. Adjusted difference in difference analyses showed no effect for preterm birth (RR: 1.00 CI: 0.82, 1.22), small for gestational age (RR 0.98 CI: 0.85, 1.13), or new cases of preeclampsia (RR 1.00 CI: 0.77, 1.30). There was a small increase in new cases of gestational hypertension (RR: 1.29 CI: 1.07, 1.55) due to the flood. There were no differences by plurality, infant sex or gestational age at flood.

Conclusion: The flood had no effect on birth outcomes, and only a minor increase in gestational hypertension. Universal prenatal care and a coordinated disaster response strategy may have minimized impacts of the flood on pregnant women.

Mediating role of metals in the associations between dietary behaviors and growth-related traits in Bangladeshi children aged 5-7 years Yu-Hsuan Shih* Yu-Hsuan Shih Mohammad Hasan Shahriar Tariqul Islam Alauddin Ahmed Golam Sarwar Molly Scannell Bryan Mary Turyk Arden Handler Hua Yun Chen Krista Christensen Farzana Jasmine Muhammad Kibriya Victoria Persky Habibul Ahsan Maria Argos

Background: Previous studies suggest associations between exposures to metals and metalloids and growth of children as well as independent associations of dietary intake with growth. Given that consumption of food or water is a major source of exposure to both trace and toxic metals, we hypothesize that the association of diet with growth is mediated by metal exposures.

Objectives: We sought to evaluate the mediating role of metal exposures in the association between dietary patterns and growth in 491 children aged 5-7 years from the Bangladesh Environmental Research in Children's Health cohort.

Methods: Latent dietary patterns were identified by exploratory factor analysis of 10 food classes, with diet characterized as score above or below the median for the study population. For anthropometric traits (i.e., height, weight, body mass index, and waist circumference), sex- and age-adjusted z-scores were modeled as continuous outcomes. Linear regression was used to evaluate associations between dietary patterns, 17 toenail metals, and anthropometric outcomes, adjusting for confounding variables. For anthropometric outcomes associated with dietary patterns, analyses were conducted to evaluate mediation by metal exposures.

Results: We identified 4 major dietary patterns (i.e., varied diet, traditional diet, sweet & water diet, and protein diet). While all patterns showed positive associations with growth, the associations of the varied diet with increased waist circumference, height, and weight were significantly mediated by greater toenail selenium concentration. Selenium explained 13.6%, 10.3%, and 5.6% of the variance in the growth outcomes, respectively.

Conclusions: The varied diet (rich in juice, milk, beans, fruit, and meat) may be beneficial to Bangladeshi children. The positive mediating association with selenium may be due to an independent positive impact on growth, but also due in part to mitigation of the detrimental effects of arsenic exposure.

Differences in the Distribution of Tract Level Ambient Air Toxics by Race/Ethnicity and Segregation in the Metro Chicago Breast Cancer Registry Alpana Kaushiva* Alpana Kaushiva Garth H Rauscher Serap Erdal

Introduction: Ambient air toxics are associated with breast cancer. Compared to non-Hispanic Whites (nHW), African Americans (AA) and Hispanics are disproportionately burdened by most ambient air toxics. The magnitude of observed differences varies by geographic location and segregation. We examined disparities among women in the Metro Chicago Breast Cancer Registry. Methods: Census tract level measures of 49 ambient air toxics were obtained from EPA National Air Toxics Assessments (NATA) conducted in 2002, 2005, 2011, and 2014. We sampled 238,923 nHW (66%), AA (24%), and Hispanic (10%) women. Addresses for 228,028 (95%) women were geocoded to the tract and linked to NATA by year of first breast imaging exam. Census tracts with >=90% AA individuals were defined as segregated. A combined patient race and tract level segregation variable was created as follows: 1) nHW, 2) AA living in non-segregated tracts, and 3) AA living in segregated tracts. Quintiles for each ambient air toxic were created and modeled as the dependent variable in ordinal logistic regression against race/ethnicity and race/segregation while adjusting for age. Results: In age-adjusted models, minority women were more likely to reside in tracts with high levels of ambient air toxics. For over 50% of chemicals (26/49), AA women resided in tracts with the greatest burden, while this was the case for 37% of chemicals (18/49) in Hispanics (Q5 vs Q1, $p<0.0001$ for all). Chemicals with the highest levels were acrylamide, cadmium, manganese, 4,4'-Methylenebis(2-chloroaniline), and propylene oxide. Among AA women, those who lived in segregated tracts fared worse than those who did not for 84% of ambient air toxics (41/49, $p<0.0001$ for all).
Conclusion: AA and Hispanic women in the metropolitan Chicago area tend to reside in census tracts with higher levels of ambient air toxics than their nHW counterparts. AA women living in segregated tracts fare worse than those living in non-segregated tracts.

The role of spatial accessibility in presenting for care at Breast Imaging Centers of Excellence Jenna Khan-Gates* Jenna Khan-Gates Shannon Zenk Jan Eberth Michael Berbaum Sarah Friedewald Garth Rauscher

Introduction: Patients presenting at Breast Imaging Centers of Excellence (BICOE) are more likely to have a screen detected, early stage breast cancer (BC), and less likely to experience diagnostic delays. We sought to understand whether geospatial accessibility to BICOE facilities could explain why ethnic minority patients were less likely than non-Latina (nL) whites to receive screening mammography, diagnostic mammography, and biopsy at BICOE facilities in the population-based Breast Cancer Care in Chicago study (BCCC).
Methods: In the BCCC (N=989), drive and public transit times were used to define standardized geospatial BICOE accessibility scores via the Enhanced 2 Step Floating Catchment Area (E2SFCA) method, taking into account both capacity and demand for BICOE facilities nearby each patient's residence. We ran logistic regression models to examine whether BICOE spatial accessibility scores mediated presentation at BICOE facilities.
Results: Minority women, women of lower socioeconomic status, and those without insurance were less likely to present for care at BICOE facilities. For mammography, BICOE accessibility scores were lower for nL black and Latina than nL white patients (Drive time: -0.40 and -0.13 vs. 0.47, p<0.001; Public transit: -0.38 and -0.36 vs. 0.56, p<0.001). Similar differences were observed for biopsy. In adjusted mediation analyses, drive and public transit-based accessibility scores together accounted for 33% (p=0.05) of the racial/ethnic disparity in presentation at BICOE facilities for screening mammography. Results were not significant for diagnostic mammography and biopsy.
Conclusion: Spatial accessibility to BICOE facilities plays an important role in determining who presents for BC screening at these highly accredited and comprehensive imaging and diagnostic facilities. Inequitable spatial accessibility to BC screening at BICOE facilities in this population has downstream implications for racial/ethnic disparities in BC outcomes.

Cancer

Liver cancer mortality disparities between Hispanics and Non-Hispanics Whites in 126 US cities Kevin Martinez-Folgar* Kevin Martinez-Folgar Usama Bilal Mariana Lazo

Background: There are wide racial/ethnic disparities in liver cancer mortality but little is known about the variability of these disparities across cities. We aimed to compare the spatial and temporal variability of liver cancer mortality among Hispanics (H) and Non-Hispanic Whites (NHW) in US cities. Methods: We included all metropolitan statistical areas (MSA) with a population average equal or greater than 100,000 residents and at least 10% Hispanics. We used vital statistics to estimate the age-adjusted liver cancer (ICD10: C22) mortality rates (MR) in H and NHW men and women in two time periods (2005-2011 and 2012-2017). We operationalized the disparity as the rate ratio (RR=H/NHW) and rate difference (RD=H-NHW). We used the coefficient of variation (CV) between cities, as a measure of variability. All analyses were stratified by gender. Results: A total of 126 MSAs were included. Compared to NHW women, H women had consistently higher liver cancer MR per 100,000 people (5.6 and 6.1 in H vs. 3.0 and 3.5 in NHW, for 2005-2011 and 2012-2017, respectively). RR and RD were both large but constant over time (RR=1.89 and 1.77, and RD=2.65 and 2.66, for 2005-2011 and 2012-2017, respectively). In men, similar trends were observed, but the absolute MR and RD were larger (MR=12.7 and 13.4 in H, MR=7.3 and 8.2 in NHW, and RD=5.38 and 5.14, for 2005-2011 and 2012-2017, respectively). The spatial variation in liver cancer mortality rates was higher in H as compared to NHW, especially among women. Discussion: We found large and sustained disparities in liver cancer mortality rates between Hispanics and non-Hispanic whites men and women. Furthermore, these disparities are highly heterogeneous between cities. Understanding the different risk factors of liver cancer within Hispanics and across cities may be key to design interventions to reduce this disparity.
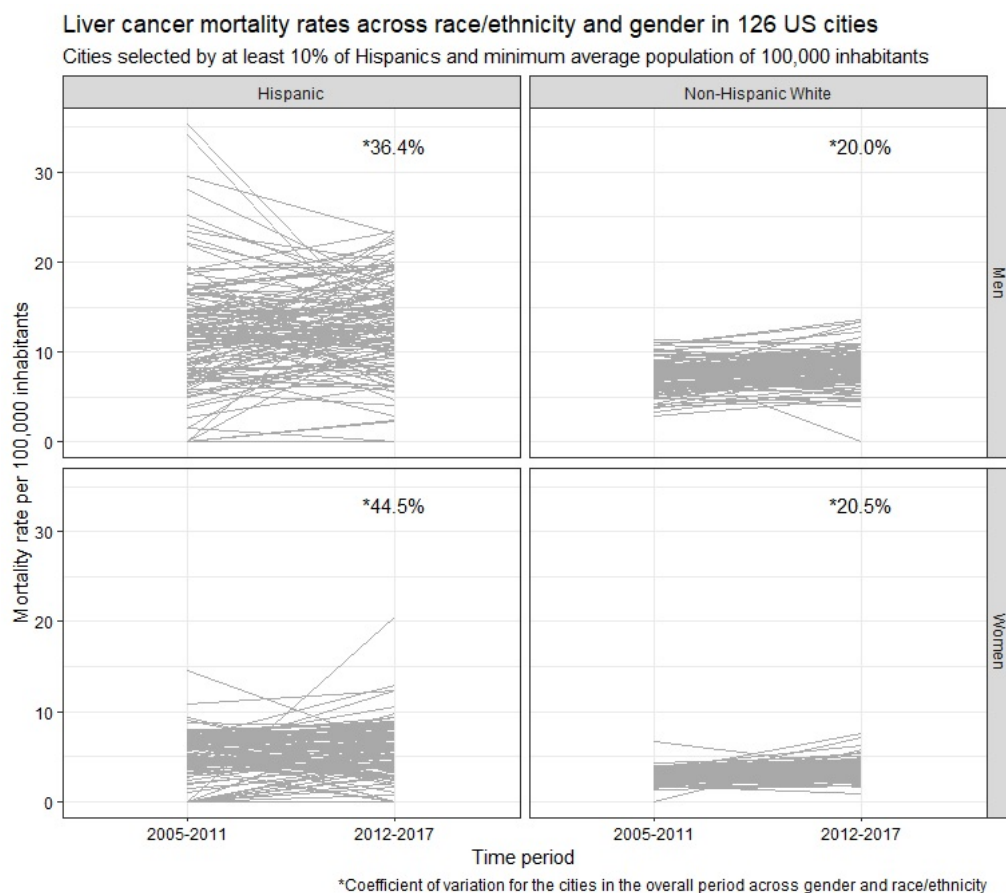
Liver cancer mortality rates across race/ethnicity and gender in 126 US cities
Cities selected by at least 10% of Hispanics and minimum average population of 100,000 inhabitants

Financial toxicity is associated with increased breast cancer mortality: the role of structural racism on disparities in outcomes Lindsay J Collin* Lindsay J Collin Anne Gaglioti Kristen Beyer Yuhong Zhou Miranda A Moore Rebecca N Nash Jeffrey M Switchenko Jasmine M Miller-Kleinhenz Kevin C Ward Lauren E McCullough

Background: Neighborhood-level redlining and lending bias influence where people live and can adversely impact health outcomes. This study sought to evaluate the role of neighborhood redlining and lending bias on breast cancer (BC) mortality and determine whether differences emerge by race among women diagnosed with BC in the metro-Atlanta.
Methods: Using data from the Georgia Cancer Registry, we included 4943 non-Hispanic white (NHW) and 3580 non-Hispanic black (NHB) women with a stage I–IV first primary BC diagnosis in metro-Atlanta (2010–2014). Redlining and lending bias—the odds of mortgage denial for NHB applicants compared to NHW applicants—were derived for each census tract using data from the Home Mortgage Disclosure Act database, which collects information on mortgage lending practices. We used Cox proportional hazard regression to calculate the hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between current day redlining and lending bias on BC mortality, and explored race-stratified effects.
Results: Overall, 20% of NHW and 80% of NHB women lived in redlined census tracts, and 60% of NHW and 26% of NHB women lived in census tracts with pronounced lending bias (≥ 3 vs. <3). In multivariable-adjusted models, living in a redlined census tract was associated with a nearly 60% increase in BC mortality (HR=1.58, 95%CI=1.37–1.82). The association between lending bias and BC mortality was null (HR=0.99, 95%CI=0.85–1.15). Race-stratified models showed a slight increase in the hazard of BC mortality (HR=1.13, 95%CI=0.97–1.08) among NHB women living in redlined census tracts; among NHW women the association was more pronounced (HR=1.39, 95%CI=1.09–1.78).
Conclusion: These findings highlight the association between area-level measures of structural racism related to housing and breast cancer mortality. The role of financial toxicity in health outcome is an important unexplored area that offers innovative interventions to address disparities.

Identification of Breast Cancer Spatial Structures Based on the Wisconsin Women's Health Study Maria Kamenetsky* Maria Kamenetsky Ronald Gangnon Amy Trentham-Dietz Polly Newcomb

Geographic health data are frequently aggregated into administrative units, e.g. counties. This makes the identification of geographic hot spots of disease at high resolution challenging. Our objective is to map fine spatial structures of breast cancer risk using case-control data, based on a unique series of 5 population-based case-control studies of Wisconsin women aged 20-79 years old spanning 1988-2004. Here, we focus on the Milwaukee Metropolitan Area. Cases were identified through the Wisconsin mandatory registry. Controls were randomly selected from driver's license lists (<65 years old) and from Medicare beneficiary files (65-79 years old), age-matched to cases in 5-year age groups. Using data aggregated to a high-resolution (1-km) grid, we identified 12 overlapping geographic hotspots (clusters) using the least angle absolute shrinkage and selection operator (LASSO) applied to quasi-binomial logistic regression. Using unaggregated data on case (n=3,668) and control (n=3,205) women, we then used logistic regression to estimate geographic variations in risk [odds ratios (OR)] adjusting for individual-level risk factors. In age-adjusted models, breast cancer risks were elevated in 3 regions [OR (95% confidence interval)]: near Brynwood [1.29 (1.04, 1.60)], Waukesha [1.47 (1.20, 1.81)] and Whitefish Bay [1.78 (1.40, 2.27)]; lower in 1 region: Roosevelt Grove [0.69 (0.50, 0.95)]. After adjustment for age, family history of breast cancer, parity, and age at first birth, the odds ratios in 3 of the original 4 regions remained elevated (Brynwood [1.36 (1.07, 1.73)], Waukesha [1.50 (1.20, 1.88)], Whitefish Bay [1.95 (1.48, 2.59)]), as well as in a new region in West Allis [1.19 (1.00,1.42)] (Figure 1). These results indicate that hot spots of elevated breast cancer risk in the Milwaukee metro area persist even after adjustment for known individual-level risk factors. In future work, we will extend these analyses to the entire state of Wisconsin.
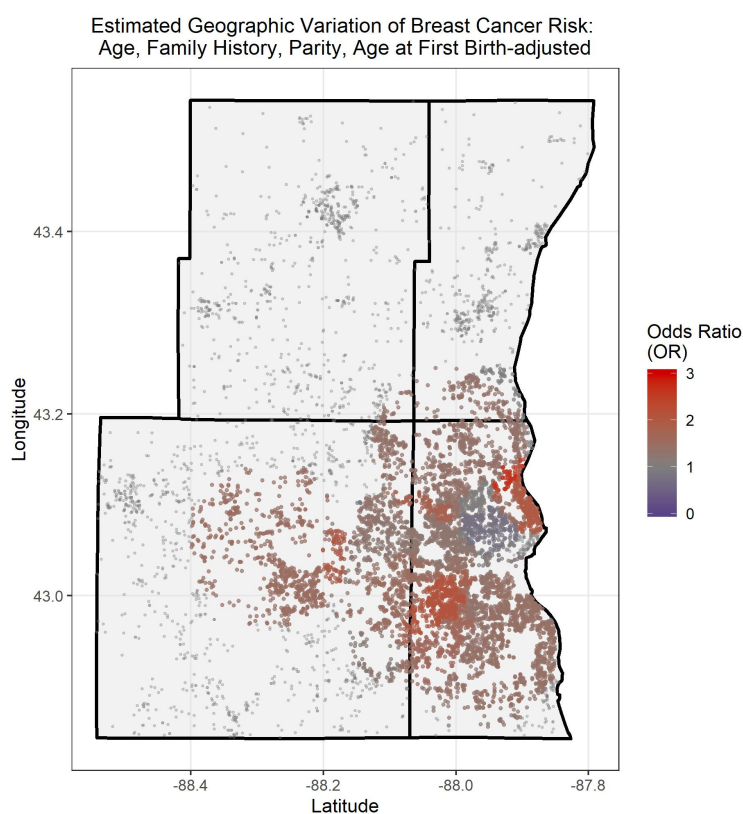
Figure 1: Estimated odds ratios after full adjustment for age, family history, parity, and age at first birth.

Substance Use

Changes in marijuana use disorder treatment utilization following medical marijuana law enactment, 2004-2014 Pia Mauro* Pia Mauro Melanie Askari Silvia Martins

Aim: While medical marijuana laws (MML) have been associated with marijuana use among adults, downstream effects of MMLs remain uncertain. We tested the impact of MML enactment on marijuana use disorder (MUD) treatment utilization in the United States.

Methods: We used data from people ages 12+ in the 2004-2014 National Survey on Drug Use and Health restricted dataset with state-level indicators. Time-varying MML enactment indicators differentiated state-years before and after MML enactment, and states without MML by 2014. Needing MUD treatment was defined as meeting past-year DSM-IV MUD criteria or reporting last/current treatment episode for marijuana. Multi-level logistic regressions with random state intercepts estimated odds of last/current (a) any MUD treatment and (b) specialty MUD treatment by MML status among people who needed treatment. Models adjusted for year, sex, age, race/ethnicity, education, income, nativity, urbanicity, insurance, self-reported health, other drug use disorders, and state-level census covariates.

Results: Of the ~25,600 people ages 12+ (1.78%) who needed MUD treatment, 13.6% reported any MUD treatment and 10.2% reported specialty MUD treatment in their last/current treatment episode. MUD treatment use was higher in states without MML, compared to states that passed an MML by 2014 (14.2% vs. 13.4%). Adjusted odds of any MUD treatment decreased by 13% (aOR=0.87, 95% CI=0.75, 1.01), and adjusted odds of specialty MUD treatment decreased by 22% (aOR=0.78, 95% CI=0.65, 0.94), comparing people in states after MML enactment vs. before MML enactment.

Conclusion: After MML enactment, people were less likely to report MUD treatment in their last/current treatment episode, controlling for individual- and state-level differences. This could be due to changing perceptions of treatment need or coerced treatment. Next steps will examine potential mechanisms of change and test the effects of recreational marijuana laws in 2015-2018.

The association between prescription opioid misuse and suicidality in United States adolescents: NSDUH 2015-2017 Luis Segura* Luis Segura Natalie Levy Alexander Perlmutter Julian Santaella-Tenorio Silvia Martins

Background: In 2017, 6,769 adolescents and young adults (10 – 24 years old) died by suicide in the United States, making suicide the second leading cause of death after unintentional injury in this age group. Feelings of isolation, sleep deprivation, psychosocial distress, and substance use, in particular prescription opioid misuse, are associated with increased suicides in adolescents.

Methods: Using 2015-2017 United States National Survey on Drug Use and Health data (N=41,579), we estimated the association between any past-year prescription opioid misuse and past-year suicidal ideation/attempts in adolescents ages 12-17. We estimated survey-weighted prevalence ratios using modified Poisson regression adjusted for sex, race/ethnicity, urbanicity, survey year, past-month binge/heavy alcohol use, past-year other substance use, and receipt of past-year mental health services for behavioral/emotional problems not caused by alcohol or drugs.

Results: The prevalence of past-year suicidal ideation and attempt increased from 14.4% in 2015 to 15.4% in 2017 and from 3.4% in 2015 to 4.0% in 2017, respectively. Among adolescents who misused any prescription opioid in the past year 21.0% in 2015 and 23.8% in 2017 reported past-year suicidal ideation and 6.28% in 2015 and 9.24% in 2017 had a suicide attempt. Among those who did not misuse prescription opioids, the prevalence of past-year suicidal ideation was 12.4% in 2015 and 13.7% in 2017 and the prevalence of past-year suicide attempt was 2.50% in 2015 and 2.88% in 2017. The prevalence of suicidal ideation and attempt were 1.33 (1.17–1.52) and 1.67 (1.29–2.16) times higher for adolescents who misused prescription opioids in the past year than those who did not.

Conclusion: Our results provide initial insights into the potential role of opioid misuse in suicidality among adolescents.

Substance Use

Prenatal cannabis exposure and adverse neonatal outcomes Gretchen Bandoli* Gretchen
Bandoli Rebecca Baer Laura Jellife-Pawlowski Christina Chambers

Background: There has been a rapid expansion in cannabis use, yet there remains little empirical
evidence regarding the effects of prenatal cannabis exposure to the developing fetus. The objective
of this study was to estimate the association between prenatal cannabis exposure and adverse
neonatal outcomes.

Methods: We queried a retrospective California birth cohort of 3 million singleton, live births
between 2011-2017 created from linked birth certificates and hospital discharge summaries.
Cannabis use was identified from ICD-9/10 codes. We performed multivariable log-linear regression
to estimate risk estimates of preterm birth [(PTB), <37 weeks gestation], very preterm birth [(vPTB),
<32 weeks gestation], small for gestational age [(SGA), <10th centile] and neonatal intensive care
unit (NICU) admission. Models were adjusted for maternal factors listed in Figure 1. Additionally, we
estimated the effects of cannabis alone, cannabis and tobacco only, and cannabis with polysubstance
use compared to women with no indication of cannabis use.

Results: There were 29,112 women with documented prenatal cannabis use (949/100,000
deliveries). Women with cannabis use were more likely to be young, non-Hispanic White or Black,
use public insurance, have a diagnosis of a mental health disorder, use tobacco, and use alcohol or
other substances during pregnancy than women without cannabis use. Of women with cannabis use,
52% used only cannabis, 23% used cannabis and tobacco, and 25% had polysubstance use. Women
who used cannabis were at a 20-40% increased risk of PTB, vPTB, and an SGA infant or infant
requiring NICU admission (Figure 1). Cannabis alone conferred the lowest risk, while cannabis with
polysubstance use conferred 2-3 fold higher risk for all outcomes (Figure 1).

Conclusions: Prenatal cannabis use was associated with an increased risk of all four adverse
outcomes. Additional work is needed to assess risk associated with dose and duration of exposure.
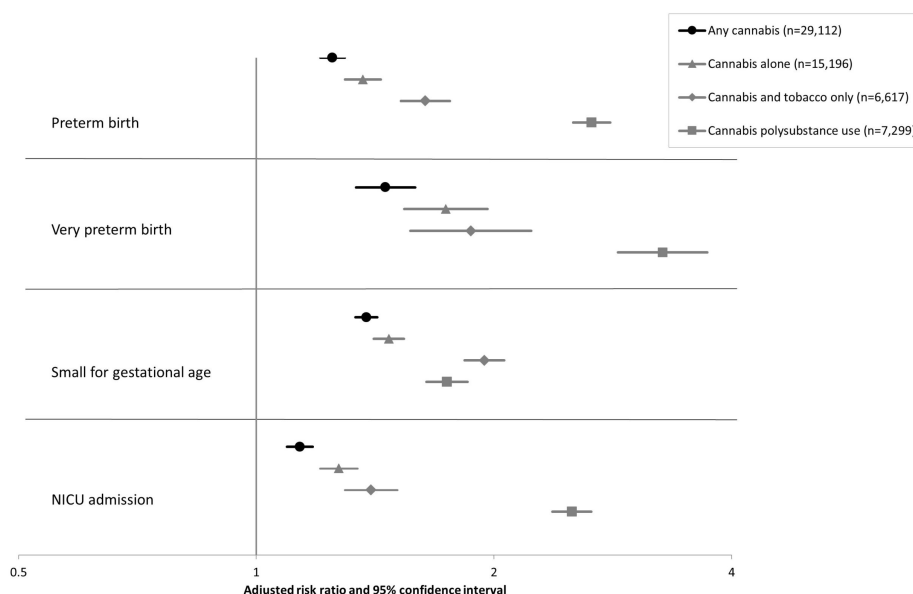
Figure 1. Adjusted risk estimates for cannabis use and adverse neonatal outcomes. Models were adjusted for pre-pregnancy BMI, race and ethnicity, payer
source, anxiety, depression, bipolar disorder, diabetes, maternal age and education. 'Any cannabis' estimates were further adjusted for tobacco, smoking, and
other substance use.

Association between public injection and syringe sharing frequency in a cohort of people who inject drugs in San Francisco and Los Angeles Elizabeth Kinnard* Elizabeth Kinnard Shelley Facente Ricky Bluthenthal Lynn Wenger Barrot Lambdin Jimi Huh Alex Kral

Aim: People who inject drugs (PWID) in public have higher risk of homelessness, rushed injection, and overdose than people who do not inject drugs publicly. There is limited research on the relationship between public injection and syringe sharing, a risk factor for infectious disease transmission. The aim of this study was to investigate longitudinal associations between frequency of public injection and syringe sharing among PWID in San Francisco and Los Angeles.

Methods: PWID (N=984) were recruited using targeted sampling and surveyed during three study visits (baseline, 6-month, and 12-month) from 2016 to 2018. The explanatory variable was frequency of injecting in public (never, occasionally/sometimes, or usually/always), and the outcome variable was number of times using previously used syringes in the past six months. Explanatory and outcome variables were measured across all three timepoints. We examined this association using a negative binomial mixed-effects model.

Results: At baseline interview, 83% reported current homelessness, and 78% of participants had injected publicly in the past six months, with 38% of the sample reporting they usually/always injected publicly. Over a quarter (26%) had injected with a previously used syringe in the six months preceding baseline, reporting an average of 20.9 instances of receptive syringe sharing. Our longitudinal analysis showed that occasionally/sometimes and usually/always injecting publicly were associated with a 3.12 (95% CI: 1.11, 3.63) and 6.21 (95% CI: 2.54, 7.18) times higher rate of receptive syringe sharing over the past six months, respectively, compared to those who never publicly injected, controlling for age, gender, and time-varying homelessness, stimulant injecting, opioid injecting, and binge drinking.

Conclusion: An increase in public injection frequency is associated with a higher frequency of receptive syringe sharing, suggesting the need for safer environment interventions, such as supervised consumption sites.

The association between marijuana use and initiation of pain reliever misuse during young adulthood in a legal marijuana context Isaac Rhew* Isaac Rhew Christine Lee Katarina Guttmannova Jason Kilmer Mary Larimer Brittney Hultgren Charles Fleming

The current opioid crisis in the US has occurred during a period of shifting societal attitudes towards and legal context of marijuana (MJ). With some ecological-level studies suggesting that opioid overdose fatality rates are lower in states with legal medical MJ, there has been speculation that MJ could act as a substitute for opioids. More research at the individual-level is needed to understand the relation between MJ and opioid use. This study examines whether recreational and medical MJ use is associated with initiation of pain reliever misuse among young adults in Washington State, where recreational MJ use is legal. Preliminary analyses used longitudinal data collected over five annual surveys starting in 2014 from 1,329 participants aged 18-25 at baseline (with future analyses incorporating data from additional cohorts). At each study wave, participants reported their past year frequency of use of MJ, cigarettes, alcohol, and pain relievers "to get high." We used discrete time survival analyses to examine associations between baseline MJ use and onset of pain reliever misuse among those who had not yet initiated. Models adjusted for regular (≥weekly) alcohol use, past year cigarette use, and sociodemographic covariates such as baseline age, race, and sex. The cumulative incidence of pain reliever misuse during the study period was 5.6%. At baseline, 37.6% reported any past year and 17.9% reported ≥monthly "recreational" MJ use, and 10.7% reported any past year and 7.9% reported ≥monthly medical MJ use. Associations with initiation of pain reliever misuse were observed for past year (OR = 3.55; 95% CI: 1.99, 6.47) and ≥monthly recreation MJ use (OR = 4.04; 95% CI: 2.33, 6.98). There was also a statistically significant association between past year medical MJ use and onset of pain reliever misuse (OR = 2.15; 95% CI: 1.03, 4.51). Results suggest that young adult recreational and medical MJ users may be at elevated risk for initiating prescription opioid misuse.

Why Do the Majority of US High School Seniors Still Not Use Marijuana? Prevalence of Self-Reported Reasons Across Four Decades Spruha Joshi* Spruha Joshi Deborah D. Kloska Jennifer L. Maggs Megan E Patrick

Historical changes toward increased legality and pro-marijuana public discourse surrounding marijuana use have led to public health concerns about adolescent marijuana use. The majority of secondary school students, however, continue to be never- or rare-users of marijuana. This paper documents reasons given by US high school seniors for not using marijuana investigates whether these reasons for marijuana abstention have changed across the last four decades and examines whether they differ by gender. Data are drawn from the Monitoring the Future study, an annual nationally representative study, which included approximately 15,000 seniors in 130 high schools in the contiguous US. Our sample was restricted to students in 1977-2018 who indicated no lifetime use of marijuana and no intention to use marijuana in the next year (n=46,072). Time-varying effect modeling was used to assess historical change in the prevalence of 14 reasons to not use marijuana, overall and by sex. TVEM is a regression-based method that allows for examination of changes in outcomes associations over continuous time without the assumption of a parametric form (e.g., linear or quadratic). In 2018, the most prevalent reasons for not using marijuana were not feeling like getting high (62.1%), parental disapproval (55.4%), and concerns about possible psychological damage (52.7%). Least prevalent reasons were lack of availability (9.6%) and price (16.8%). Across the study period, almost all reasons showed variability, with a majority of them declining. (see Figure 1.) The overall patterns for boys and girls were similar, but the prevalence of endorsements varied. We found that not feeling like getting high, parental disapproval and concerns about possible psychological damage reasons were frequently endorsed, inaccessibility and price reasons were quite rare as reasons not to use marijuana. Marijuana preventive interventions may increase awareness of these reasons to not use marijuana use.
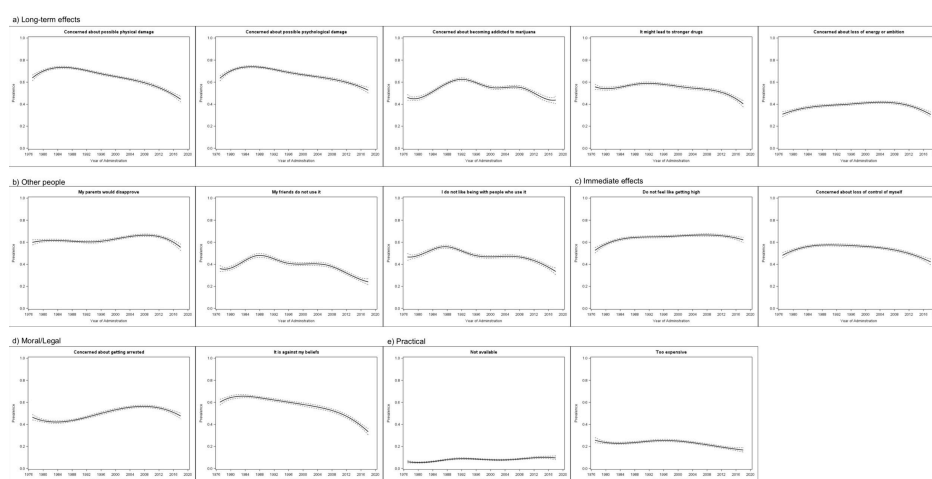
Exploring Paternal Preconception Windows of Vulnerability on Offspring Birthweight in Relation to Bisphenol and Phthalate Exposure Carmen Messerlian* Carmen Messerlian Yu Zhang Vicente Mustieles Paige Williams Stelios Smirnakis Irene Souter Russ Hauser Joseph Braun Carmen Messerlian

Background: Paternal preconception environmental chemical exposure has been associated with reduced offspring birthweight. However, the specific window of vulnerability during the paternal preconception period remains unknown.

Methods: We examined paternal preconception urinary concentrations of bisphenol A (BPA), the molar sum of four di(2-ethylhexyl) phthalate metabolites (ΣDEHP), and the molar sum of seven anti-androgenic phthalate metabolites (ΣAAP) in relation to birthweight among 189 singletons from the Environment and Reproductive Health Study, a prospective preconception cohort of subfertile couples. The paternal preconception window was modelled as >3 months vs. ≤3 months of the index pregnancy, based on the duration of spermatogenesis (~90 days). Birthweight was abstracted from delivery records. Associations of natural-log urinary concentrations of BPA, ΣDEHP, and ΣAAP with birthweight were examined using multiple informant models, simultaneously evaluating both windows while adjusting for covariates. We further adjusted for maternal preconception urinary biomarker concentrations.

Results: Each log-unit increase in paternal urinary BPA, ΣDEHP and ΣAAP concentrations within ≤3 months of the index pregnancy was associated with a 166 g (95%CI: -289, -43), 49 g (95%CI: -92, -6) and 64 g (95%CI: -109, 19) decrease in birthweight, respectively. Less consistent patterns were found for paternal urinary concentrations at >3 months of the index pregnancy (BPA: 63 g; 95%CI: -8, 135; ΣDEHP: -19 g; 95%CI: -59, 22; ΣAAP: -37 g; 95%CI: -79, 5). Associations differed significantly between the two windows, and remained after adjustment for maternal preconception exposure.

Conclusion: Paternal exposure to BPA and DEHP within 3 months before conception was associated with decreased birth weight. The spermatogenesis period resulting in a successful conception seems the most relevant window for evaluating paternal preconception exposure to non-persistent chemicals.

Experience of multiple hardships prior to and during pregnancy and fetal growth: Extending environmental mixtures methodology to social exposures
Dana Goin* Dana Goin Monika Izano Stephanie Eick Amy Padula Erin DeMicco Tracey Woodruff Rachel Morello-Frosch

Background: Women can be exposed to a multitude of hardships prior to and during pregnancy that may affect fetal growth, but previous approaches have not analyzed them jointly as social exposure mixtures.

Methods: We evaluated the independent, mixture, and pairwise joint associations between self-reported hardships and birthweight and birthweight for-gestational age z-scores in the Chemicals in Our Bodies-2 prospective birth cohort (N=510) using G-computation. We examined financial hardship, food insecurity, job strain, poor neighborhood environment, low perceived social status, caregiving, stressful life events, and unplanned pregnancy collected via questionnaire administered in the second trimester of pregnancy. We used propensity score-based restriction to ensure our analyses had sufficient data support and estimated absolute differences in outcomes. Analyses were adjusted for maternal age, race/ethnicity, educational attainment, and pre-pregnancy body mass index.

Results: Food insecurity and job strain were most strongly associated with reduced birthweight individually, with absolute differences of -155 g (95% confidence interval [CI] -316, 6) and -178 g (95% CI -347, -9), respectively. The pattern of association with birthweight for gestational age z-scores was similar for food insecurity, with an absolute difference of -0.20 (95% CI -0.49, 0.09), while the association for job strain was attenuated [-0.03 (95% CI -0.34, 0.28)]. Accounting for co-exposures resulted in similar findings. The pairwise joint effects on birthweight were strongest for food insecurity in combination with unplanned pregnancy [-305 g (95% CI -580, -29)] and stressful life events [-354 g (95% CI -612, -95)].

Conclusions: Experiencing food insecurity and job strain during pregnancy may affect fetal growth, and experience of multiple hardships may exhibit stronger effects on this health outcome.
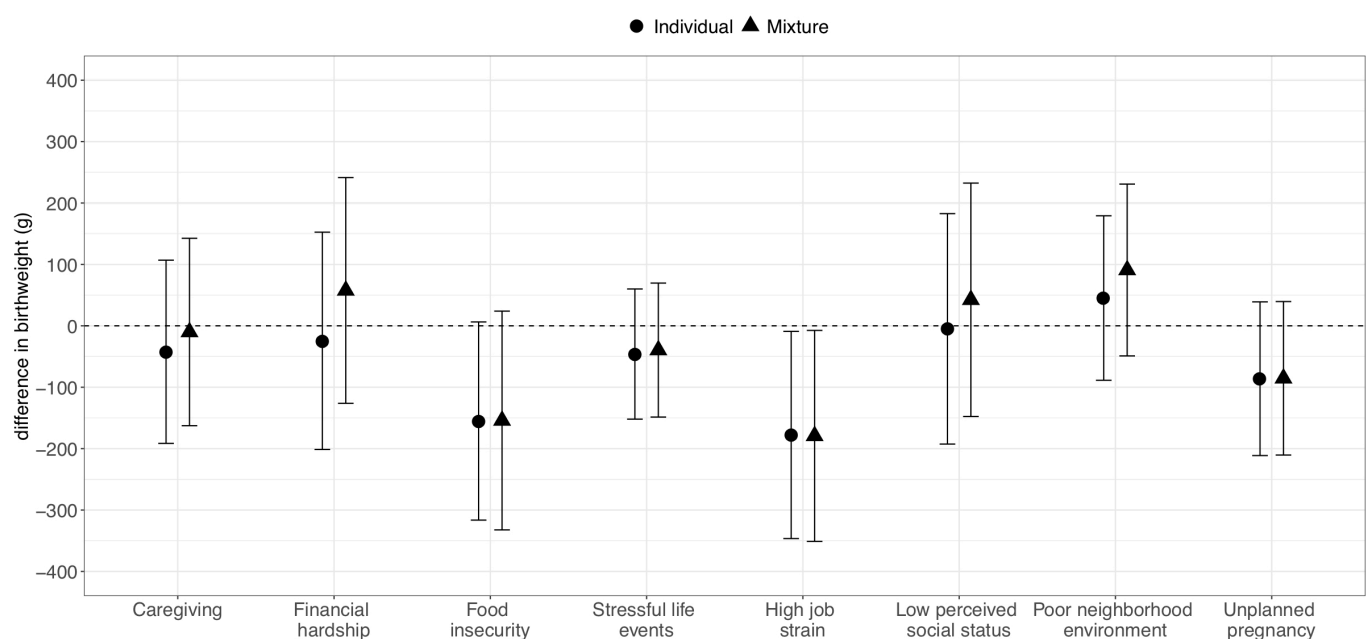
Association of Maternal Electronic Cigarette Use Before and During Pregnancy with Impaired Fetal Growth in Offspring Buyun Liu* Buyun Liu Yang Du Yuxiao Wu Yangbo Sun Jean M. Kerver Mark K. Santillan Donna A. Santillan Wei Bao

Background: While conventional cigarettes are known to affect fetal growth, the influence of e-cigarettes remains unknown. This study examined the association of maternal use of e-cigarettes and/or conventional cigarettes before and during pregnancy with small for gestational age (SGA) in offspring.

Methods: We used data from a nationwide population-based study (the Pregnancy Risk Assessment Monitoring System). Mothers aged 18 years or older who delivered a singleton live baby in 2016-2017 in 37 states of the United States, were surveyed. Participants were categorized as dual users of e-cigarettes and conventional cigarettes, exclusive e-cigarette users, exclusive conventional cigarette users, and non-users before and during pregnancy, respectively.

Results: Among the 62,561 women included, the rate of dual use of e-cigarettes and conventional cigarettes, exclusive e-cigarette use, and exclusive cigarette use during pregnancy was 0.7% (95% CI 0.6%-0.8%), 0.4% (0.3%-0.5%) and 7.2% (6.9%-7.5%), respectively. Compared with women who used neither e-cigarettes nor conventional cigarettes, the adjusted risk ratio (95% CI) of SGA was 2.31 (1.76-3.04) for dual users, 1.43 (0.86-2.40) for exclusive e-cigarette users, and 2.19 (1.97-2.43) for exclusive cigarette users. The association of e-cigarette and/or conventional cigarette use with SGA was stronger in whites than in non-whites. Similar results, but of lower magnitudes, were observed for maternal use of e-cigarettes and/or conventional cigarettes before pregnancy and SGA.

Conclusions: Dual use of e-cigarettes and conventional cigarettes before and during pregnancy was associated with higher risk of SGA. More research is needed to clarify the safety and health effects of e-cigarette use during pregnancy.

Maternal Vegetarian Diets and Fetal Growth: Findings from the NICHD Fetal Growth Studies Samrawit Fikru Yisahak* Samrawit Yisahak Sunni L. Mumford Stefanie N. Hinkle Mengying Li Katherine L Grantz Cuilin Zhang Jagteshwar Grewal

OBJECTIVE: A vegetarian diet during pregnancy may influence fetal growth, but prior evidence relies solely on neonatal size at birth. In a prospective multi-racial/ethnic cohort of U.S. pregnant women, we compared in utero fetal growth trajectories by maternal vegetarianism.
METHODS: Maternal diet among 1,585 women was assessed at 8-13 weeks' gestation using a food frequency questionnaire. Vegetarianism was self-defined and diet-based (based on servings of meat, poultry, and fish (MPF) intake: full vegetarian = MPF < 1 per month; semivegetarian = MPF ≥ per 1 month and < 1 per week). Fetal biparietal diameter (BPD), head circumference, abdominal circumference (AC), humerus length, and femur length were measured by ultrasound ≤6 times during pregnancy. Estimated fetal weight (EFW) was calculated using a Hadlock formula. Fetal growth curves were estimated using linear mixed models with cubic splines. Median fetal measures at each gestational week were compared by vegetarian status, after adjustment for maternal age, race, pre-pregnancy BMI, total energy, and diet quality.
RESULTS: Ninety-nine (6.1%) self-defined, 32 (2.0%) full, and 300 (18.8%) semivegetarians were identified. There were no statistically significant differences in the overall trajectories of fetal measures except for BPD that was smaller in self-defined vegetarians than nonvegetarians (global p=0.01) (Figure). At gestational week 40, adjusted median BPD was 92.5 mm in self-defined vegetarians and 93.2 mm in nonvegetarians (p= 0.64). Diet-based semivegetarians had significantly lower EFW and AC than nonvegetarians, but only in weeks 18-25.
CONCLUSION: BPD was the only fetal measure that varied by self-defined vegetarianism. Although there was a divergence in EFW and AC in the second trimester by diet-based vegetarianism, these curves mostly converged by the end of pregnancy. It remains to be seen whether these minor differences in fetal growth curves are of clinical significance.

Figure: Median Fetal Growth Measures by Gestational Age and Vegetarianism: A) Estimated Fetal Weight by Self-defined Vegetarianism; B) Estimated Fetal Weight by Diet-based Vegetarianism; C) Biparietal Diameter by Self-defined Vegetarianism; D) Abdominal Circumference by Diet-based Vegetarianism
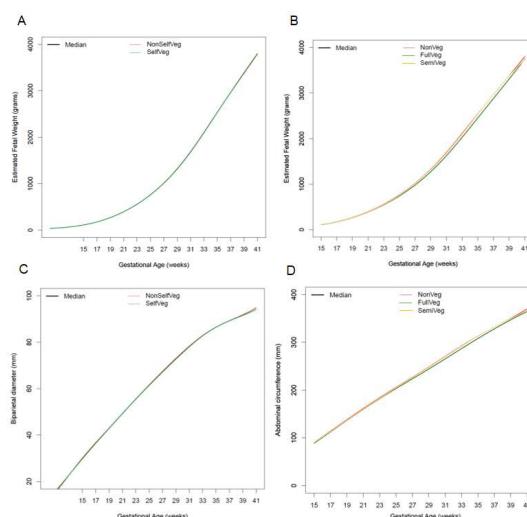
Maternal Marijuana Use and Emotional and Behavioral Functioning among Children at Age 9-10 in The Adolescent Brain Cognitive Development (ABCD) Study Jiajun Luo* Jiajun Luo Jingyuan Xiao Haoyu Zhang Zeyan Liew

Background: Cannabis is legalized in more regions worldwide. Psychoactive ingredients in cannabis can cross the placenta affecting fetal neurodevelopment, but epidemiological studies on long-term impacts of maternal pregnancy cannabis use are still sparse. This study aims to estimate the association between maternal cannabis use and child behaviors.

Methods: The Adolescent Brain Cognitive Development (ABCD) is an ongoing longitudinal study on child health and brain development across the US. Data of 8,176 children enrolled at aged 9-10 (baseline) were analyzed in this study. Child's biological mothers reported preconception and prenatal cannabis in structured questionnaires at the baseline. We analyzed measures of child's internalizing and externalizing behavior included in the Child Behavior Checklist reported by parents and the Brief Problem Monitor reported by teachers. We used linear mixed model to estimate the difference (β) in child's internalizing and externalizing behavioral scores, adjusting for the study-site and other potential confounders including parental socio-demographic factors and maternal tobacco use.

Results: Maternal cannabis use during pregnancy was associated with externalizing behaviors in both scales ($\beta=5.8$, 95% CI: 3.4, 8.1 for parent-report, and $\beta=2.1$, 95% CI: 0.4, 3.7 for teacher-report) compared with never users. Maternal cannabis use before pregnancy and not during pregnancy was associated with parent-report externalizing problem in a smaller magnitude of effect size ($\beta=2.4$, 95% CI: 1.2, 3.6) compared with never users, but the associations were null for outcomes reported by teachers.

Conclusion: Maternal cannabis use during pregnancy is associated with externalizing behaviors in children at age 9-10 years. The association for child's externalizing behavior was weaker or null if mothers used cannabis before but not during pregnancy. Our results raise concerns regarding cannabis exposure on fetal neurodevelopment.

Initial HIV treatment with efavirenz and risk of suicidal thoughts and behaviors: transporting results from trials to routine care Angela Bengtson* Angela Bengtson Katie R. Mollan Steven Xu Jessie K. Edwards W. Christopher Mathews Conall O'Cleirigh Ellen F. Eaton Daniel J. Westreich Camlin Tierney Stephen R. Cole Brian W. Pence

Efavirenz (EFV) is an HIV medication. EFV increased the risk of suicidal thoughts and behaviors in a pooled analysis of 4 randomized trials (HR 2.3, 95% CI 1.2-4.4), while an observational cohort found little evidence of increased risk (HR 1.2, 95% CI 0.7-2.3). To understand these disparate findings, we transported the effect of EFV in the original 4 trials to a target population in routine HIV care, represented by the CFAR Network of Integrated Clinical Systems cohort. Trial participants were US adults with HIV enrolled in 2001-2007 to 4 trials comparing initiating EFV to other therapy regimens. The trials were not nested within the cohort. Cohort participants were HIV-infected adults initiating therapy from 1999-2015 who met modified trial inclusion criteria. We used inverse odds weights of participation weights to transport the effect of initiating EFV on risk of suicidal thoughts/behaviors from the trials to the cohort. Thirty imputations were used to address missing baseline covariate data (0.3% trials; 9% cohort). We fit weighted Cox models to estimate intention-to-treat HR, and bootstrapped 95% confidence intervals. The incidence rate difference (IRD) was estimated from a weighted Poisson model. We included 3949 trial and 8291 cohort participants. Sex, race-ethnicity, age, and viral load were similar between the trial and cohort participants. Antidepressant prescription (19% vs 13%) and injection drug history (16% vs 10%) were more common among cohort participants. When transporting trial results to the cohort, the relative EFV effect was somewhat muted (HR 1.8, 95% CI 0.9-4.5), while the IRD (5.4, 95% CI -0.6, 12.1) was similar to the trials (IRD 5.1, 95% CI 1.6, 8.7). Findings for relative and absolute effects differed when transporting effect of EFV on suicidal thoughts/behavior from 4 trials to adults in routine care. Outcome ascertainment, study population, measurement error and unmeasured confounding may account for the remaining relative differences.
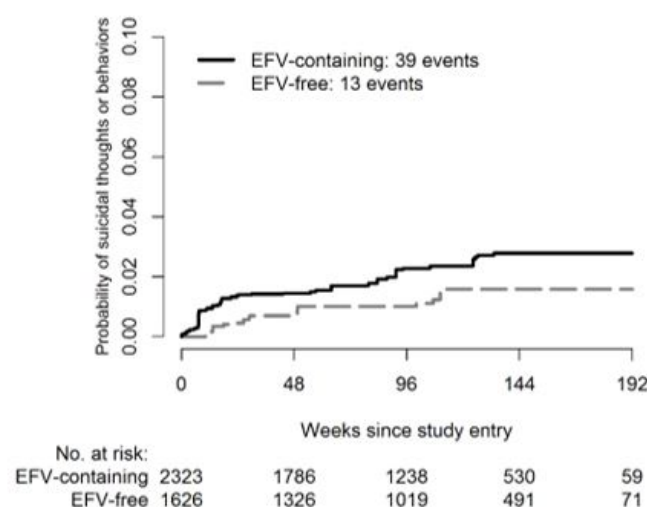
Figure. Cumulative probability of suicidal thoughts and behaviors.
Probability was estimated as 1 minus a weighted Kaplan-Meier estimate. The unweighted number at risk is shown. 30 multiply imputed datasets were constructed, and the resulting 30 weighted estimates were averaged at each respective time point.

Modeling Pre- and Post-Prophylactic Doxycycline in Preventing Syphilis Infection Among Urban Men Who Have Sex with Men in the Context of Condom Use Nguyen K. Tran* Nguyen Tran Neal D. Goldstein Seth L. Welles

Introduction: Primary, secondary, and early latent syphilis (i.e., infectious syphilis) have consistently increased in the past decade for men who have sex with men (MSM) in the U.S. Pre- and post-exposure prophylactic doxycycline (doxy PrEP and PEP) may be effective tools for preventing infection. This study compares the differences between doxy PrEP and PEP in preventing syphilis incidence among urban MSM.

Methods: Network-based mathematical models of HIV and infectious syphilis transmission were used to determine the percentage of anal/oral syphilis infections averted due to doxy PrEP/PEP. Data were simulated to resemble the demographic characteristics of MSM living in Philadelphia for up to 10 years of follow-up. Scenarios varied doxy PrEP/PEP uptake (range: 0% to 100% by 10% intervals), modified by medication adherence and within the context of condom use and HIV seroadaption.

Results: Models were calibrated to surveillance data of HIV and syphilis diagnoses in Philadelphia. With 10% uptake of doxy PrEP, 5% of anal and 28% of oral syphilis infections would be averted over the next decade. For doxy PEP, uptake by 10% of MSM led to 6% of anal and 36% of oral syphilis infections averted. The percentage of anal/oral infections averted more than doubled when uptake of either doxy PrEP/PEP was at 50%. Comparing prevention strategies, doxy PrEP/PEP was inferior to condoms in preventing anal infections at all levels of uptake. For oral syphilis, condoms prevented the greatest number of infections when doxy PrEP/PEP was at 10%.

Discussion: Implementation of doxy PrEP/PEP appeared to be more effective in reducing oral syphilis compared to anal syphilis infections. However, the effect of these biomedical tools was approximately equivalent to each other. Syphilis prevention strategies should consider scaling up doxy PEP as a supplement to condoms, given the greater level of tolerability compared to doxy PrEP, to prevent the greatest number of syphilis infections among MSM.

Percent of Infections Averted by Doxy PrEP/PEP Uptake Level
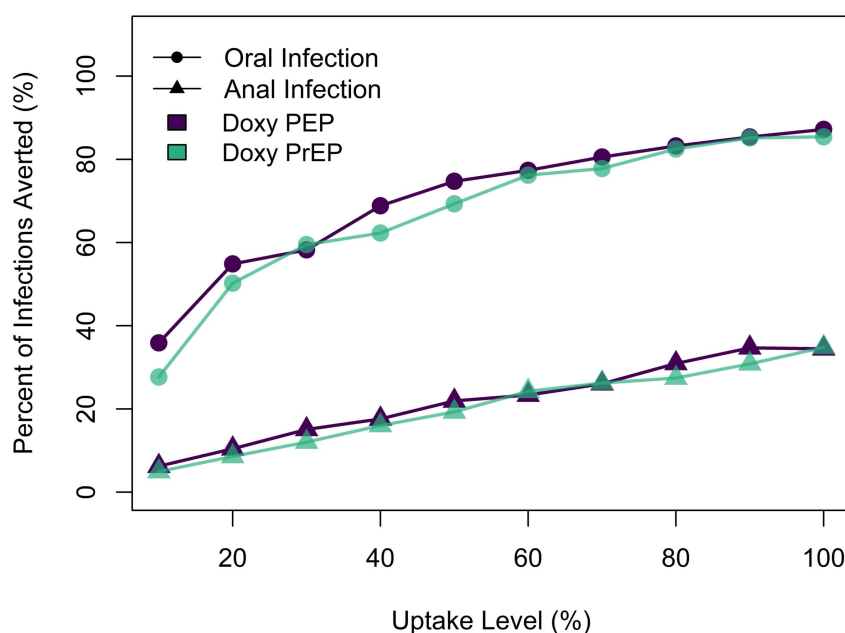
All-cause mortality under modeled interventions on substance use among HIV-positive women in the United States, 1998 – 2017 Tiffany L. Breger* Tiffany Breger Jessie K. Edwards Stephen R. Cole Daniel Westreich Brian W. Pence Mackey R. Friedman Alison G. Abraham Kara W. Chew Adaora A. Adimora

Compared to the general US population, people with HIV experience a higher prevalence of multimorbidity, accelerated aging, and decreased life expectancy. Yet, the improvement in survival that may be achieved by targeting non-AIDS risk factors among those who initiated ART remains unclear. We estimated 8-year risks of all-cause mortality among women with HIV in the Women's Interagency HIV Study (WIHS) under prompt initiation of modern ART combined with hypothetical interventions on alcohol consumption and smoking using the parametric g-computation algorithm. In Strategy 1, we modeled an intervention in which all women initiated modern ART within 6-months of study entry. In Strategy 2a, we also eliminated alcohol consumption of >1 drink/week, while in Strategy 3a, we also eliminated smoking. We also estimated risks under more realistic strategies in which ART was combined with interventions reducing, but not eliminating, alcohol (Strategy 2b) and smoking (Strategy 3b) to obtain generalized intervention contrasts. Among 1003 women participating in the WIHS between 1998 and 2017, 58% reported smoking and 15% reported consuming >7 drinks/week at baseline. The 8-year risk of all-cause mortality in the observed data was 22% compared to 12% had all women initiated modern ART under Strategy 1. The 8-year risk of mortality was 11% when ART was combined with eliminating consumption of >1 drink/week and 9% when ART was combined with 100% smoking cessation, representing an 8% and 25% reduction in the risk of all-cause mortality respectively. Under strategies in which the prevalence of alcohol consumption and smoking were reduced based on the expected efficacy of existing interventions, reductions in the 8-year risks of mortality were attenuated. While targeting alcohol and smoking may further improve survival in the modern HIV treatment era compared to intervening on ART alone, more effective interventions are needed to eliminate these risk factors (particularly smoking).

Risk of all-cause mortality under hypothetical interventions to eliminate (Panel A) or reduce (Panel B) non-AIDS risk factors in the Women's Interagency HIV Study, 1998 – 2017.

HIV / STI
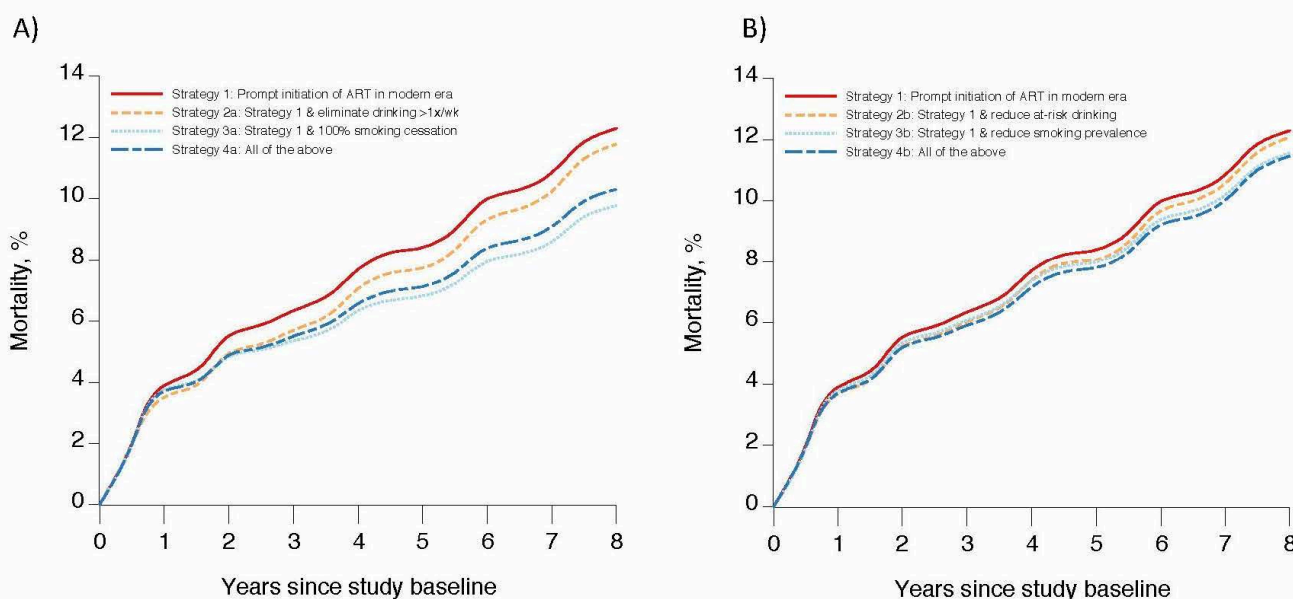
Variation in estimated viral suppression associated with the definition of viral suppression used Catherine Lesko* Catherine Lesko Geetanjali Chander Richard D. Moore Bryan Lau

Background: The proportion of people living with HIV with suppressed viral load is a key indicator of the HIV care continuum. Yet viral load is a dynamic, continuous variable; implications for how viral load across a calendar year is dichotomized into suppressed or not have not been well-described. Methods: We calculate the proportion of the Johns Hopkins HIV Clinical Cohort who are virally suppressed each year, 2010-2018, based on different definitions of the study population (the denominator for each proportion); thresholds for suppression; and strategies for summarizing multiple viral load measurements. We included in the denominator: persons with ≥1 viral load measurement in the prior year AND in the current year; persons with ≥1 viral load in the current year; and persons with ≥1 viral load measurement in the prior year, assuming a missing viral load in the current year is equivalent to non-suppression). To estimate proportion suppressed we counted in the numerator persons with any lab, ≥50% of labs, last lab, or all labs below some threshold (≤20, ≤50, ≤200, or ≤400 copies/mL). We also calculated 5-year risk of all-cause mortality associated with each classification of viral suppression.
Results: Proportion classified as virally suppressed ranged from 51.8-92.5%, depending on the definition used. Requiring more labs below the threshold; using a lower threshold; and assuming persons lost to follow-up were not suppressed ("stricter definitions") resulted in a lower proportion estimated to be suppressed. Suppression by stricter definitions were associated with better 5-year survival.
Discussion: The range in the estimated proportion suppressed using different definitions was greater than the improvements in viral suppression over the 9-year study period. Measures of durable viral suppression, and low-level viremia (20-400 copies/mL), should be considered in describing the health of people with HIV, in addition to the standard estimates of suppression.
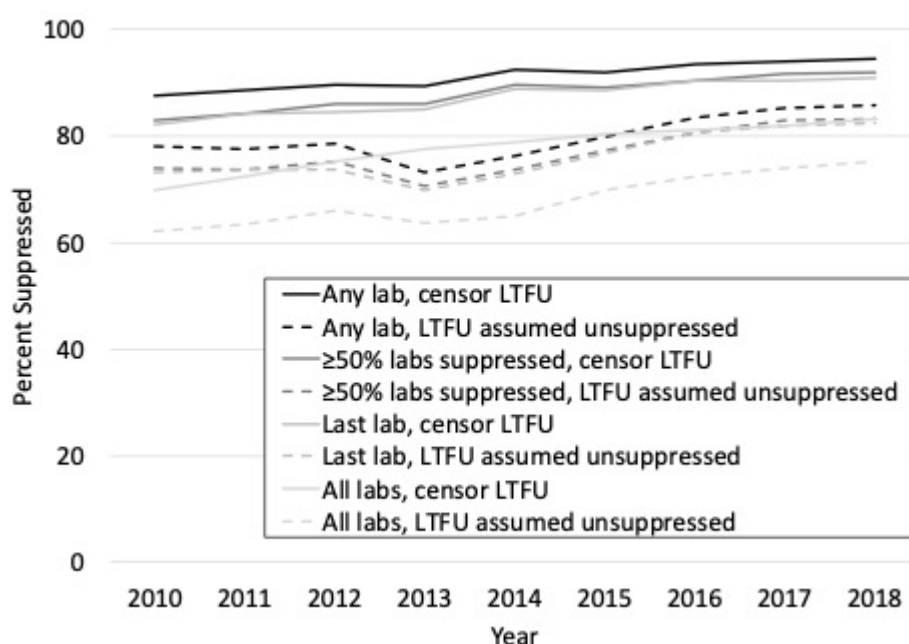
Evaluation of Enhanced Gonorrhea Partner Services in Two Jurisdictions in the US, 2018

Emily Learner* Emily Learner Jamie Black Christina Thibault Robert Kirkcaldy Karen Schlanger

Background: Antibiotic resistant gonorrhea (GC) is an urgent emerging threat. A strategy to halt the spread of GC is standard partner services, which involves: (1) interviewing persons with GC to elicit information about recent sex partners, (2) locating and testing these partners, and for those diagnosed with GC (3) locating and testing their partners. We evaluated outcomes of enhanced partner services, a novel prevention strategy in which, in addition to the process above, partners of persons in step 2 (above) who tested negative for GC were also located, interviewed, and screened. Methods: We used data from two jurisdictions conducting enhanced partner services through participation in CDC's Strengthening the U.S. Response to Resistant GC (SURRG) project. In each jurisdiction, persons with GC with reduced susceptibility to select antibiotics ("index cases") were identified by local antibiotic susceptibility testing. Index cases and partners were interviewed by local investigators. We mapped sexual networks using partner services data and classified persons as either index cases, partners who would be identified with standard partner services only, or partners who would be additionally identified with enhanced partner services. Results: In 2018, 77 index cases were identified, and 30 named at least one partner. Through standard partner services, 68 sexual partners were identified, 54 of whom had not been screened recently for GC. Of those, 37 were referred for screening, 16 of whom were screened and seven were newly diagnosed. Through enhanced partner services, an additional 28 partners were identified, 25 of whom had not been screened recently for GC. Of those, 16 were referred, four of whom were screened and two were newly diagnosed. Conclusions: In some situations, enhanced partner services might have potential to help slow the spread of GC by further enumerating sexual networks and locating and screening persons who might have otherwise been missed.
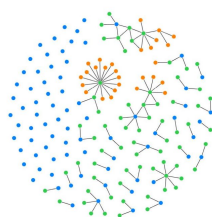
Figure 1: Enhanced gonorrhea partner services in two jurisdictions in the U.S. in 2018. Nodes (dots) are persons and edges (lines) are sexual partnerships. Blue nodes represent persons with gonorrhea with reduced susceptibility to select antibiotics identified by local antibiotic susceptibility testing ("index cases"). Green nodes represent sexual partners identified through standard partner services. Orange nodes represent sexual partners additionally identified through enhanced partner services.

Cognitive development, literacy and math achievement in 6-8-year-old children with HIV, children HIV-exposed but uninfected, and children HIV-unexposed Rachel S. Gruver* Rachel Gruver Jane D. Kvalsvig Chris Desmond Justin R. Knox Sumaya Mall Claude A. Mellins Leslie L. Davidson

Background: Perinatally-acquired HIV infection (PHIV) is associated with delays in cognitive development. Less is known about cognitive outcomes in children perinatally HIV-exposed but uninfected (CHEU), particularly in low-to-middle income countries. Previous findings from the population-based Asenze cohort study in KwaZulu-Natal, South Africa showed that children aged 4-6 years with PHIV (CPHIV) were cognitively delayed, but CHEU were not (adjusted for preschool attendance). Two years later, we compared cognitive outcomes and math and verbal achievement in CPHIV and CHEU to children HIV-unexposed and uninfected (CHUU).
Methods: Asenze children, age 6-8 years (CPHIV=34, CHEU=218, CHUU=553) were assessed using the South African-validated Grover-Counter Scale of cognitive development, subscales of the Kaufman Assessment Battery for Children II, the Hopkins Verbal Learning Test, the Wide Range Achievement Test 3 (WRAT3) for arithmetic, and the Takalani literacy test. HIV status of children and mothers was determined previously by HIV tests or by caregiver report. Multivariable linear regression was used to compare developmental outcomes by HIV exposure status.
Results: On all outcomes, CHEU and CHUU groups had comparable scores. The CPHIV group scored lower than the other two groups (some significantly), but in analyses adjusted for preschool, only the WRAT3 differences were significant (adjusted means: CPHIV=11.16[10.6-11.7], CHEU=13.3[13.1-13.5], CHUU 13.7[13.6-13.9]).
Conclusions: CHEU and CHUU groups had similar outcomes to one another at ages 6-8, consistent with our prior findings at ages 4-6. Although they had scored lower at 4-6 years, CPHIV had similar cognitive outcomes to the other groups when adjusted for preschool, with the exception of arithmetic achievement. Thus, early differences in cognitive performance between CPHIV children and CHUU may attenuate by school age, but CPHIV may require preschool and/or additional academic support to improve achievement.

Cardiovascular

Early Experiences of Emotional Maltreatment and Favorable Cardiovascular Health in Young Adulthood Sakurako S.Okuzono* Sakurako Okuzono Farah Qureshi Scott Delaney Julia Boehm Laura D. Kubzansky

Background: Despite robust evidence on the adverse effects of childhood physical maltreatment on health in adulthood, the life-course impact of emotional maltreatment remains understudied. We examined whether early experiences of emotional maltreatment are associated with a lower likelihood of favorable cardiovascular health (FCH) in early adulthood.

Methods: Data are from 12,240 participants in the National Longitudinal Study of Adolescent to Adult Health. We measured FCH in early adulthood (mean age 31) as having healthy levels of blood pressure, cholesterol, and body mass index, having no diagnosed diabetes, and being a non-smoker. At the same age, participants retrospectively reported how frequently they experienced emotional maltreatment before age 18 (never, 1 or 2 times, > 2 times) and the age of their first experience (never, childhood, early adolescence, late adolescence). We assessed associations between both the frequency and the timing of first maltreatment and FCH using logistic regression adjusted for adolescent sociodemographics, health conditions, and health behaviors.

Results: 42.4% of our sample reported early emotional maltreatment, and 4.7% had FCH. After adjusting for covariates, participants with versus without maltreatment experiences were less likely to have FCH (OR=0.80 95% CI [0.62, 1.03] for 1 or 2 times; OR=0.67, 95% CI [0.53, 0.86] for > 2 times). Those with a first experience in early adolescence versus those with no maltreatment experience had significantly lower odds of FCH (OR=0.59, 95% CI [0.44, 0.80]). Associations with first experience in childhood or later in adolescence were weaker: childhood, OR=0.75, 95% CI [0.53, 1.07]; late adolescence, OR=0.72, 95% CI [0.50, 1.02].

Conclusion: Childhood emotional maltreatment, especially during early adolescence, is associated with a lower likelihood of having FCH in early adulthood. Findings suggest the impact of emotional maltreatment on health differs based on developmental stage.

Cardiovascular

Secular trends in the association between newly-diagnosed atrial fibrillation and the excess risk of death

Ludovic Trinquart* Ludovic Trinquart Nicklas Vinter Qiuxi Huang Morten Fenger-Grøn Lars Frost Emelia Benjamin

Background: Atrial fibrillation (AF) is associated with increased mortality but data on secular trends are lacking. We examined temporal trends in the association between newly-diagnosed AF and death.

Methods: We selected Framingham Heart Study participants free of AF and aged 45 to 95 years in each pre-specified epoch: 1972-1985, 1986-2000, and 2001-2015. We ascertained newly-diagnosed AF (or atrial flutter) and followed participants until death, last follow-up, or end of epoch. For each epoch, we used a matched cohort design to estimate adjusted difference in restricted mean survival times (RMST) between AF cases and matched referents at 10 years after AF diagnosis. We estimated hazard ratios (HR) for the association between time-varying AF and all-cause mortality with adjustment for time-varying confounding factors. We tested for linear trend in HR and RMST over epochs with meta-regression.

Results: We selected 5,671 participants in epoch 1; 6,177 in epoch 2; and 6,174 in epoch 3. Ten years after AF diagnosis, the adjusted difference in RMST between AF cases and matched referents decreased by 26%: from -2.7 years (95%CI -3.0, -2.3) in epoch 1, -2.3 years (-2.5, -2.0) in epoch 2, to -2.0 years (-2.2, -1.7) in epoch 3 (ptrend=0.002). All-cause mortality adjusted HRs were 1.8 (95%CI, 1.6, 2.1) in epoch 1, 1.4 (1.3, 1.5) in epoch 2, and 1.7 (1.4, 1.9) in epoch 3 (ptrend=0.70).

Conclusions: The mean number of life years lost to AF at 10 years has significantly improved but there is still a 2-year gap as compared to individuals without AF

Cardiovascular

Conception by Infertility Treatment and Blood Pressure in Early Childhood Edwina Yeung*
Edwina Yeung Pauline Mendola Diane Putnick Akhgar Ghassabian

Background: Conception by assisted reproductive technologies (ART) appear to be associated with higher offspring blood pressure, potentially due to developmental programming, including the use of culture media. However, evidence on ovulation induction (OI) without embryo culture is lacking, even though exposure to supraphysiological levels of hormones is a plausible biological pathway.
Methods: Upstate KIDS oversampled newborns conceived with infertility treatment based on birth certificate data. At baseline (4 months postpartum), mothers reported ART, which we previously saw had high sensitivity (93%) and specificity (99%) compared to linkage with the Society for Assisted Reproductive Technology Clinical Outcomes Reporting System. Therefore, self-reported infertility treatment (i.e., no treatment, ART, OI) was used in all analyses. At 8-10 years of age, 559 children from 448 families (333 singletons and 226 twins) attended a clinic visit. Anthropometry, blood pressure (BP) and arterial stiffness by pulse wave velocity (PWV) were measured. Multiple linear regressions (with generalized estimating equations for twins) were used to estimate mean differences (95% CIs) adjusting for child age sex, and height, maternal age, race, education, insurance, pre-pregnancy BMI and clinic site. Due to statistical interactions, models were stratified by plurality.
Results: 220 singletons and 99 twins conceived without treatment served as reference for mean outcome differences in Figure 1. Singletons conceived by treatment did not differ in BP or PWV. Conversely, twins conceived with infertility treatment had lower blood pressure (e.g., systolic BP difference for OI twins: -5.14; -8.74, -1.53 mmHg and for ART twins: -6.10; -10.19, -2.13 mmHg). OI twins had higher arterial stiffness (0.37; 0.08, 0.66 m/s).
Conclusion: In general, infertility treatment was not associated with elevated blood pressure. Isolated association of PWV among OI twins requires further evaluation.

Figure 1. Infertility treatment and childhood cardiovascular measures
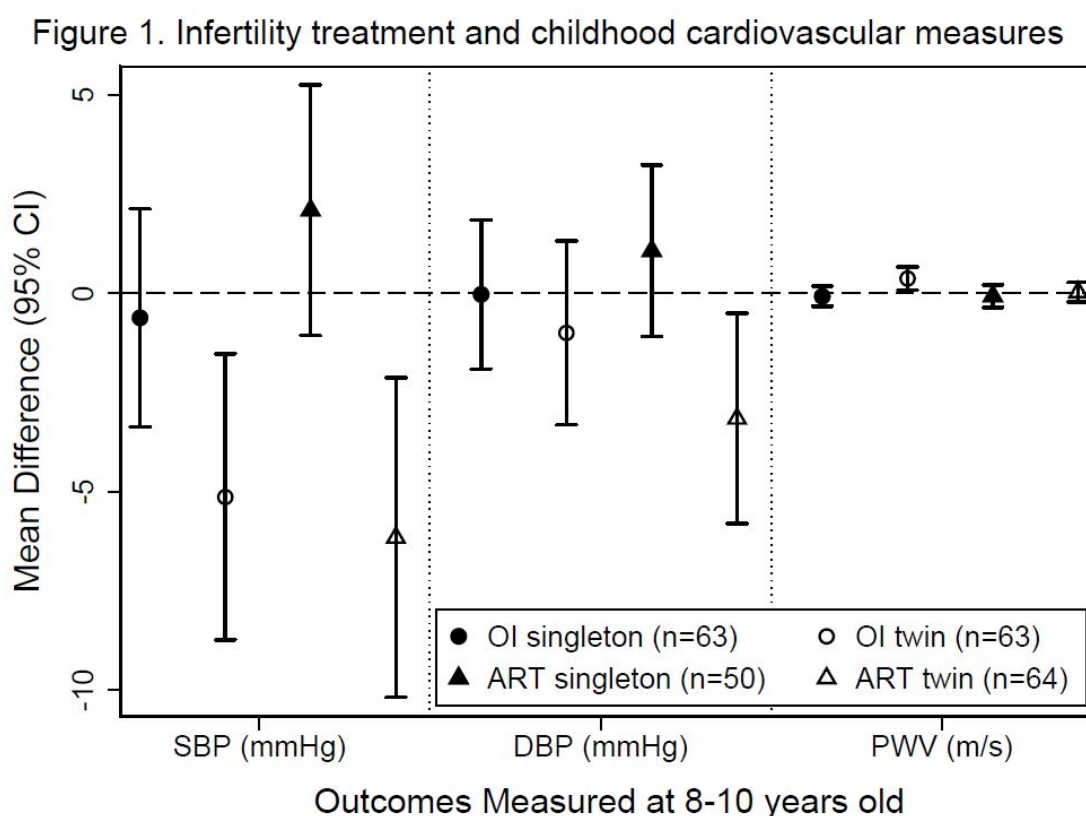
Preterm Birth and Subsequent Risk of Coronary Heart Disease in Black Women Samantha Parker* Samantha Parker Max Brock Nisha Parikh Janet Catov Julie Palmer Lynn Rosenberg

Background: Adverse pregnancy outcomes, such as preterm birth, are associated with an increased risk of coronary heart disease (CHD) and may serve as an early-warning signal for its development decades later. Existing studies have not examined this association among Black women, who notably have higher rates of preterm birth and CHD compared to White women.
Methods: We examined the association between preterm birth and incident CHD in the Black Women's Health Study (1995-2015), a prospective cohort of 59,000 women in the US. Information on preterm birth (<37 weeks) and indication, if any, was collected via biennial questionnaires administered from 1997-2003. Incident CHD was defined as self-reported myocardial infarction (MI) or coronary revascularization procedures through 2015. Reports of CHD (n=2,054) were adjudicated using medical records when available (n=518) and 65.6% were confirmed as definite MI or coronary revascularization; 77.4% including probable MI. We estimated incidence rate ratios (IRRs) and 95% confidence intervals (CIs) using Cox proportional hazards regression, adjusted for questionnaire cycle, age, family history of MI, hypertension, education, smoking, and BMI. We also examined preterm birth with and without hypertensive disorders of pregnancy.
Results: Among 7,857 women reporting pregnancies during follow-up, there were 66 self-reported incident CHD cases, and 18% had a preterm birth. Preterm birth was associated with a 62% increase in the rate of CHD (IRR: 1.62, 95% CI: 0.96, 2.72). For early preterm births (<34 weeks), the IRR was 1.71 (95% CI: 0.91, 3.20). IRRs for preterm birth with or without hypertensive disorders were 3.11 and 1.36, respectively. Results restricted to confirmed CHD were similar.
Conclusions: In a large cohort of Black women, preterm birth was associated with an increased incidence of CHD, which was strongest for preterm births with a history of hypertensive disorders of pregnancy, but remained for normotensive births.

Acute ambient temperature changes and risk of cardiovascular events among low-risk women associated with singleton delivery Pauline Mendola* Jenna Kanner Danielle Stevens Carrie Nobles Matthew Rohn Sandie Ha Tuija Mannisto Marion Ouidir Pauline Mendola

Background: Cardiovascular events are one of the leading causes of death for pregnant women in the United States. Temperature and seasonality are associated with changes in blood pressure and risk of cardiovascular events (e.g. MI, stroke) in the general population, but potential risk for pregnant women is unclear. We assessed acute risk of cardiovascular (CV) events in association with exposure to high and low ambient temperatures during the week prior to delivery in a low-risk population.

Methods: A case-crossover study design evaluated 191 women with cardiovascular events derived from electronic medical record data from 51,086 women with 112,203 singleton deliveries in the Eunice Kennedy Shriver National Institute of Child Health and Human Development Consecutive Pregnancies Study (Utah, 2002-2010). We assessed the impact of ambient temperature on cardiovascular event risk at labor/delivery. Using conditional logistic regression models, we estimated the odds ratio (OR) and 95% confidence interval (CI) for each 1° Celsius (2.8°F) change in temperature during the week prior to delivery. We stratified the analyses by season, adjusting for time-varying environmental factors: humidity, ozone, and fine particulates.

Results: CV events during the delivery admission included acute myocardial infarction (n = 1), stroke (n = 29), heart failure (n = 7), cardiac arrest (n = 118), and unspecified cardiovascular event (n = 39). For every 1°C increase during the warm season, CV event risk increased 9% (95% CI: 1.02, 1.18) and for every 1°C decrease in temperature during the cold season, risk increased 6% (95% CI: 1.00, 1.13).

Conclusion: Acute exposure to high and low temperatures was associated with increased risk of cardiovascular events at labor/delivery. Cardiovascular events during pregnancy are serious and can result in death or life-long morbidity. Further research about temperature exposure periods associated with the greatest risk is warranted.

Longitudinal Association between Residential Segregation and Incident Hypertension: the Multi-Ethnic Study of Atherosclerosis Xing Gao* Xing Gao Kiarri N. Kershaw Sharelle Barber Pamela J. Schreiner D. Phuong Do Ana V. Diez Roux Mahasin S. Mujahid

Extant, mostly cross-sectional literature has found an association between racial/ethnic segregation and hypertension (HTN) in Black populations, but the relationship is less clear among other minority groups. Longitudinal studies are needed within a multi-racial cohort and to explore whether neighborhood environments modify association between segregation and HTN. We used race/ethnicity-stratified Cox models to examine the association of time-varying segregation with incident HTN, defined as systolic blood pressure greater than 140 mm Hg, diastolic blood pressure greater than 90 mm Hg, or reported antihypertensive medication use, in 1945 adults free of HTN at baseline. Using Getis-Ord Gi*, a spatially-weighted measure of how neighborhood racial composition deviated from the larger surrounding area, participants were categorized as segregated and non-segregated. We used a robust covariance matrix estimator to account for clustering within neighborhoods and assessed effect modification by neighborhood social or physical environment. The sample's mean age was 58 years and included 465 Chinese, 699 Black, and 781 Hispanic participants. Over an average follow-up of 8.25 years, 41% Chinese, 56% Black, and 46% Hispanic participants developed HTN. Adjusting for sociodemographic and health factors, Black and Hispanic residents in segregated neighborhoods were more likely to develop HTN (Black: HR=1.29, CI=1.05-1.58; Hispanic: HR=1.30, CI=1.02-1.68). Results were similar but not significant among Chinese residents (HR=1.66, CI=0.89-3.12). Among Black residents, neighborhood social environment significantly modified the relationship such that worse social environment was associated with larger impact of segregation on HTN (see figure). This study underscored the importance of continued investigations of groups directly impacted by the health consequences of racial residential segregation while taking contextual neighborhood factors, such as social environment, into account.

Racial Residential Segregation and Risk of Incident Hypertension among Black Participants, by Neighborhood Social Environment: the Multi-Ethnic Study of Atherosclerosis, 2000-2012
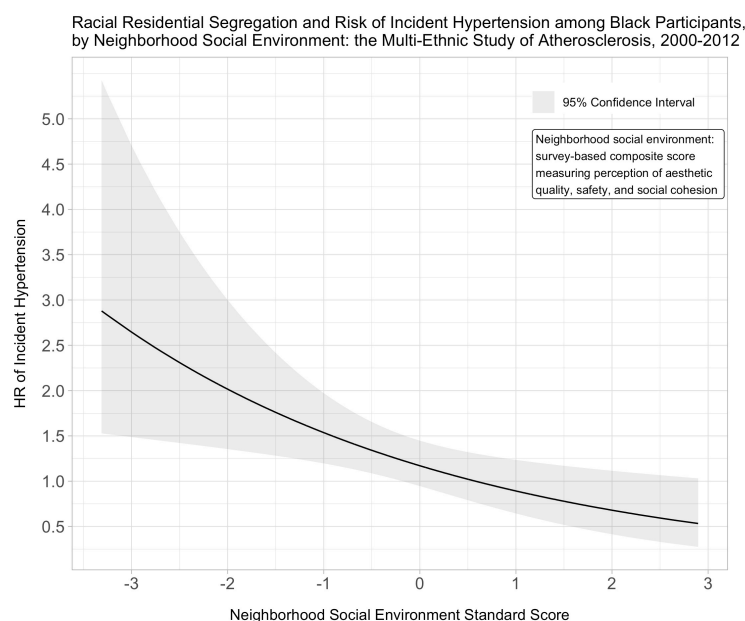
This figure displays the relationship between changes in standard deviations of neighborhood social environment and hazard ratios of incident hypertension comparing segregated to non-segregated Black residents, adjusting for baseline age, sex, education, and time-varying income, BMI, physical activity, and smoking. A higher score indicates better neighborhood social environment. As the neighborhood social environment worsens, the risk of incident hypertension associated with segregation is greater. For example, moving from the 75th to 25th percentile of social environment score (0.61 and -1.19, respectively), the HR increases from 0.99 (CI: 0.8-1.3) to 1.62 (CI: 1.2-2.1).

The Effects of Age and Time on Risk of Violent Crime Associated with Driving Under the Influence Christopher McCort* Christopher McCort Kagawa, Rose M. C. Wintemute, Garen J.

Background.

Firearm violence poses a serious threat to health in the US. Recent research suggests firearm purchasers with convictions for driving under the influence (DUI) are at elevated risk for being charged with a violent crime, but the length of time that this risk remains is unknown. Our objective is to identify the time it takes for the elevated risk for violence following a DUI conviction to return to levels of risk comparable to purchasers with no DUI convictions.

Methods.

We conducted a retrospective, longitudinal cohort study of all legal handgun purchasers, aged 21-49, in California in 2001. Purchasers were followed through 2013. Exposure was defined as having a DUI conviction prior to first purchase in 2001. The primary outcome was time to a violent crime charge. We modeled associations using Cox proportional hazards, controlling for individual and community covariates, and tested interactions between DUI conviction, decades elapsed from DUI, and age (decades) at purchase.

Results.

There is a significant interaction with age and DUI conviction. The AHR (95% CI) of a DUI conviction for a 21 year old is 3.0 (2.0, 4.3). For subjects without a DUI, one additional decade of age corresponds with an AHR of 0.65 (0.62, 0.67). Subjects with a DUI have about half the relative decrease with higher age, AHR: 0.82 (0.68, 1.00). Their risk does decrease with decade elapsed since the DUI, AHR 0.81 (0.66, 0.99). The AHR for a decade of both combined is 0.67 (0.55, 0.81), such that the decrease in risk associated with both is similar to that of aging among those without a DUI.

Conclusion.

Given two subjects of the same age and with the same measured covariates at purchase, the one with a DUI has significantly elevated risk no matter how long ago the DUI was. A 45 year old with a DUI who was convicted of DUI at 16 has similar hazard as a 21 year old (highest risk) without a DUI.

AHR for DUI subject
vs.
21 year old w/o DUI
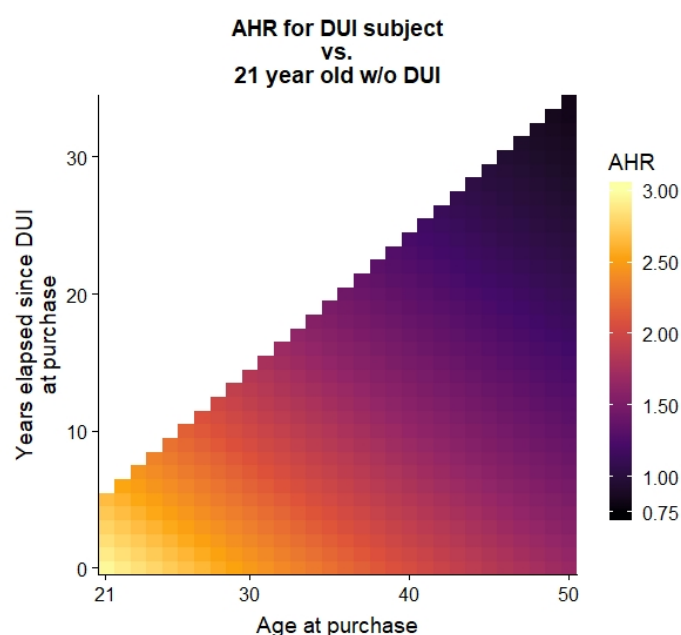
The modifying effect of sex/gender on police reporting patterns pre- and post-#MeToo: An investigation of male and female survivors of sexual assault Erin Erwin* Katherine Muldoon Erica Erwin Kathryn Denize Melissa Heimerl Kari Sampsel

Background: In October 2017, the trending #MeToo hashtag sparked a public social movement that brought unprecedented attention to the scope and severity of sexual assault and harassment. This study was designed to examine routinely collected crime data to examine gendered patterns of police-reported sexual assault pre- and post-#MeToo.

Methods: This study uses a quasi-experimental design with data from the Victim Crisis Unit of the Ottawa Police Service, a unit designed to offer support and services to complainants or victims of crime. The study uses 11 months of data from pre-#MeToo (1nov16 to 31sep17) and 11 months post-#MeToo (1nov17 to 30sep18). Cases seen in October 2017 were excluded to account for delayed effects. Log binomial regression was used to measure Risk Ratios (RR) and 95% confidence intervals (CI), comparing police-reported sexual assault cases pre- and post-#MeToo. Analyses were sex stratified to assess effect modification.

Results: During the study period, there were 13,333 complainants seen in the Victim Crime Unit, 6507 (48.80%) pre-#MeToo and 6826 (51.20%) post-#MeToo. There were 273 cases of sexual assault with a cumulative incidence of 1.68% pre-#MeToo and 2.40% post-#MeToo. Compared to the pre-#MeToo period, the relative risk of police-reported sexual assault post-#MeToo was 1.43 (95% CI:1.12-1.82); however, sex stratified analyses revealed an 89% increase in risk among females (RR:1.89, 95% CI: 1.45-2.48) and a 59% decrease (RR:0.41, 95% CI:0.22-0.77) among males.

Conclusion: This study identified diverging patterns of police-reported sexual assault cases, where post-#MeToo, increased reporting was documented among female survivors and decreased reporting was documented among males. #MeToo was heavily focused on violence against women. These findings suggest that more gender inclusive efforts are needed to improve police reporting and violence prevention for male survivors of sexual violence.

Ridesharing and Motor Vehicle Crashes in New York City: A Spatial Ecological Case-Crossover Study of Trip-Level Data Christopher Morrison* Christopher Morrison

Background. Ridesharing services (e.g. Uber, Lyft) have facilitated over 11 billion trips worldwide since operations began in 2010, but the impacts of ridesharing on motor vehicle injury crashes are largely unknown. Methods. This spatial ecological case-crossover study used highly spatially and temporally resolved trip-level rideshare data and incident-level injury crash data for New York City (NYC) for 2017 and 2018. The space-time units of analysis were NYC taxi zone polygons partitioned into hours. For each taxi zone-hour we calculated counts of rideshare trip origins and rideshare trip destinations. Case units were taxi zone-hours in which any motor vehicle injury crash occurred, and matched control units were the same taxi zone from precisely one week before (-168 hours) and one week after (+168 hours) the case unit. This study design accounts for unknown vehicular traffic flow through the small space-time units of analysis, which could confound associations between rideshare trips and injury counts. Conditional logistic regression models estimated the odds of observing a crash (separated into all injury, motorist injury, pedestrian injury, and cyclist injury crashes) relative to rideshare trip counts. Models controlled for taxi trips and other theoretically relevant covariates (e.g. precipitation, holidays). Results. Each additional 100 rideshare trips originating within a taxi zone-hour was associated with 5% increased odds of observing any injury crash compared to the control taxi zone-hours (OR=1.05; 95%CI:1.03,1.06). Associations were detected for motorist injury crashes and pedestrian injury crashes, but not cyclist injury crashes. Taxi trips were not associated with injury crash incidence. Findings were substantively similar for analyses conducted using trip destinations (instead of origins). Conclusions. Ridesharing contributes to increased injury burden due to motor vehicle crashes, particularly for motorist and pedestrian injury crashes at trip nodes.

Total Injury Crashes per Taxi Zone 2017 and 2018
1 - 156
157 - 299
300 - 486
487 - 804
805 - 1626
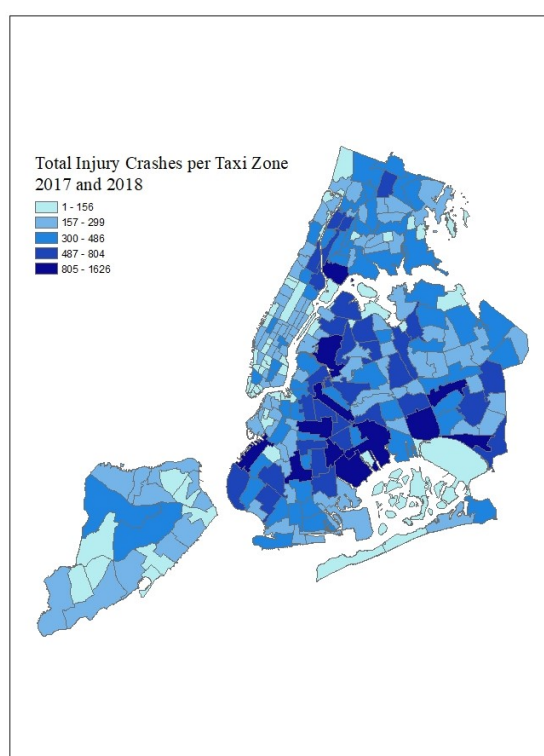
Association between minimum age handgun purchase and possession laws and homicides perpetrated by youth 18-20 years old Miriam Haviland* Miriam Haviland Caitlin Moe Andrew Bown Ali Rowhani-Rahbar Fred Rivara

Background: In 1994 the U.S. government established a minimum age of 21 to purchase a handgun from a licensed dealer, 18 to purchase a handgun from an unlicensed dealer, and 18 to possess a handgun. Since then some states have enacted laws that raise the minimum age to purchase a handgun from all dealers to 21 and/or the minimum age to possess a handgun to 21. The effect of these stricter laws on the rate of homicides perpetrated by youth aged 18-20 is unknown.

Methods: In this study we reviewed purchase and possession laws and identified states that raised the minimum age to purchase and/or possess a handgun above the minimum established by federal law. We excluded states that had stricter minimum age requirements to purchase and/or possess a handgun before 1994 from our analysis. Our outcome of interest was the rate of homicides perpetrated by youth aged 18-20. We obtained outcome data from the Federal Bureau of Investigation's Supplementary Homicide Report. We used a linear regression model with a generalized estimating equation to compare the homicide rate between states that did and did not implement stricter minimum age laws, adjusting for state-level demographic variables and minimum age laws to purchase and/or possess a long gun.

Results: From 1994-2017 Massachusetts, Maryland, New Jersey, New York, and Wyoming increased the minimum age to purchase a handgun from all dealers from 18 to 21. Except for Wyoming, all of these states also increased the minimum age to possess a handgun from 18 to 21. There was no difference in the rate of homicides perpetrated by youth 18-20 (IRD: 0.11 per 100,000 people; 95% CI: -0.01, 0.23) between states that implemented stricter minimum age laws to purchase and/or possess a handgun (IR: 0.52 per 100,000 people) and the 33 states that did not (IR: 0.40 per 100,000 people).

Conclusion: State laws that increase the minimum age to purchase and/or possess a handgun may not impact the rate of homicides perpetrated by youth 18-20.

Applying Directed Acyclic Graphs (DAGs) to Analytic Criminology: A Framework for Causal Inference Haylea Hannah* Haylea Hannah Ross Matsueda Ali Rowhani-Rahbar

Directed acyclic graphs (DAGs) can be used to depict causal relationships and identify adjustment variables in statistical models to obtain a valid causal estimate. Many criminology studies evaluate the causes of criminal behavior using statistical models. DAGs may provide a useful framework for identifying adjustment variables and be used to produce unbiased estimates of causal effects. We examined a published criminology study evaluating the association of borderline personality disorder (BPD) symptoms with opioid use in adulthood using data from the Pathways to Desistence study, which followed 1,354 adolescent offenders for 84 months after adjudication for a serious offense. The original study (OS) adjusted for gender, race, socioeconomic status (SES), age, self-control, depression, deviant peer association, and baseline opioid use, and a secondary analysis controlled for witnessed violence and direct victimization as mediators. The present study (PS), informed by a DAG, replicated all other elements of the OS but only adjusted for age, gender, and SES as the additional variables above were believed to be on the causal pathway. Both studies found that having more BPD symptoms is associated with increased odds of opioid use, however, the magnitude of the relationship in the OS was attenuated as compared to the PS. When adjusting for mediators, the OS reported a non-significant 20% reduction in the BPD and opioid use relationship. When replicating this approach, the PS found that the strength of the relationship did not attenuate and maintained its statistical significance. These differences may be due to the bias associated with this approach or an underestimation of the total effect in the OS. A DAG-informed approach resulted in different conclusions than the alternative, thus signifying the potential utility of DAGs in selecting adjustment variables to obtain valid causal estimates in criminology studies.

Table. Comparison of results between a DAG-informed and general regression approach: Models 1 and 2

	Original Study Additionally adjusted for race, self-control, depression, deviant peer association, and baseline opioid use		Present Study DAG-informed approach	
Model 1: No adjustment for direct victimization and witnessed violence				
	Odds Ratio	**95% Confidence Interval**	**Odds Ratio**	**95% Confidence Interval**
Borderline personality T-score	1.047	1.008-1.088	1.078	1.050-1.106
Age	1.037	0.732-1.449	0.998	0.748-1.315
Gender	0.330	0.074-1.467	0.236	0.056-1.000
Mean SES	1.027	0.993-1.062	1.010	0.973-1.048
Model 2: Adjustment for direct victimization and witnessed violence				
Borderline personality T-score	1.038	0.998-1.079	1.065	1.036-1.094
Age	1.011	0.719-1.423	0.998	0.756-1.319
Gender	0.496	0.107-2.303	0.031	0.071-1.318
Mean SES	1.030	0.995-1.065	1.012	0.975-1.051
Direct Victimization	1.792	0.783-4.105	1.427	0.679-3.001
Witnessed Violence	3.743	1.512-9.265	3.631	1.697-7.772

The role of sex-specific risk factors for the prediction of cardiovascular disease in women of reproductive age Sonia M Grandi* Sonia Grandi Kristian B. Filion Jennifer A. Hutcheon Graeme N. Smith Robert W. Platt

INTRODUCTION: Currently available cardiovascular disease (CVD) risk scores were developed in older age populations and do not incorporate sex-specific factors, which limits their ability to provide accurate estimates in younger women. This study aims to contrast the performance of nested prediction models that do and do not include sex-specific risk factors to estimate the risk of CVD in women of reproductive age.
METHODS: We created a cohort of 262,891 women aged 15-45 years with a recorded delivery from 1999-2017 in the UK's Clinical Practice Research Datalink. Women with a history of CVD, prior pregnancy, and <1 year of medical history prior to cohort entry were excluded. The primary outcome was incident CVD. Three models were developed using candidate predictors identified based on substantive knowledge. A base model including traditional CVD risk factors was compared to a base model and pregnancy-related factors and a base model and sex-specific factors. An accelerated failure time model was used to estimate CVD risk. Internal validation via bootstrapping was used to estimate the optimism-corrected measures of accuracy and performance.
RESULTS: 943 women (0.81 per 1,000 person-years) experienced an event over a median follow-up of 3.8 years (IQR: 1.5-7.9). Sex-specific risk factors including gestational hypertension and diabetes, preterm birth, and depression provided important contributions to the prediction of survival free from CVD (Figure). The traditional predictors found to be important were hypertension, age, and BMI. The model containing traditional and sex-specific factors was found to have the best accuracy and overall performance (C-statistic: 0.695; calibration slope: 1.04; Nagelkerke R2: 0.03).
CONCLUSIONS: The findings highlight the importance of sex-specific risk factors for the prediction of CVD risk in women of reproductive age and the need to consider these factors when assessing the risk of CVD in this patient population.
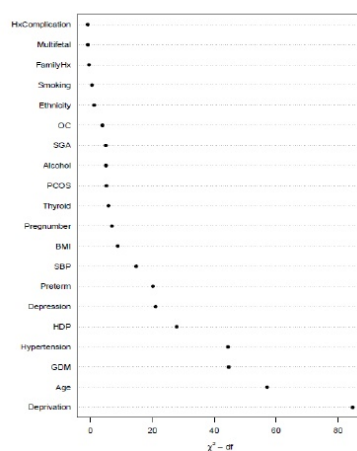
The Relative Contribution of Predictors to Survival Time.
The relative contribution of predictors plotted on the x-axis is calculated as the chi-squared statistic penalized for the number of degrees of freedom used to model the respective predictor. A value > 10 suggests that the predictor provides important contributions to the overall prediction of survival time. Abbreviations: BMI: body mass index; FamilyHx: Family history of CVD; GDM: gestational diabetes; HDP: hypertensive disorders of pregnancy; HxComplication: prior history of a pregnancy complication; OC: oral contraceptive; PCOS: polycystic ovary syndrome; SBP: systolic blood pressure; SGA: small-for-gestational-age.

Tubal ligation, hysterectomy, and serum androgen and estrogen metabolism among postmenopausal women in the Women's Health Initiative Observational Study Ashley M. Geczik* Ashley Geczik Michels KA Anderson GL Farland LV Manson JE Shadyab AH Pfeiffer RM Xu X Trabert B

Background Prior research has shown that hysterectomy status is associated with changes in hormone levels in postmenopausal women, but the effect of tubal ligation is unknown. To further evaluate this relationship, we explored whether circulating concentrations of androgens and estrogens differ by tubal ligation and hysterectomy status in postmenopausal women from the Women's Health Initiative (WHI)-Observational Study (OS).

Methods We examined associations of prior tubal ligation and hysterectomy status to serum androgens/androgen metabolite and estrogen/estrogen metabolite levels measured in a cross-sectional study of 1,783 postmenopausal women from the WHI-OS. Hormone geometric means (GM) and 95% confidence intervals were estimated using inverse probability sampling weighted linear regression to account for the selection criteria for our study and to represent the WHI-OS cohort. Models were adjusted a priori for potential confounders and stratified on menopausal hormone therapy (MHT) use at blood draw.

Results Circulating levels of 12 androgen/androgen metabolites (nmol/L) or 20 estrogen/estrogen metabolites (pmol/L) were not different by tubal ligation status (ever vs. none). Across both never/former and current MHT users, we observed lower levels of adrenal androgens among women reporting prior hysterectomy compared with no hysterectomy [testosterone GM:0.46 vs 0.62 never/former; 0.37 vs 0.43 current MHT users]. Among never/former MHT users, estrogen metabolites were higher among women with hysterectomy compared with no hysterectomy [e.g., 2-methoxyestradiol:1.8 vs 1.5; 4-methoxyestradiol:14.7 vs 12.3; estriol:21.7 vs 17.2; p-values≤0.04].

Conclusion Our work suggests that postmenopausal women reporting prior hysterectomy have lower circulating levels of adrenal androgens and higher estrogen metabolites, which may have implications for cancer risk. Prospective studies are needed to evaluate associations of hysterectomy and tubal ligation status with hormones.

Hypertensive Disorders of Pregnancy and Racial/Ethnic Differences in Risk of Incident Kidney Disease Five Years Following Delivery
Angela M. Malek* Angela Malek Dulaney A. Wilson Tanya Turan Julio Mateus Daniel T. Lackland Kelly J. Hunt

Introduction: Hypertensive disorders of pregnancy (HDP) are related to maternal morbidity and mortality including kidney disease. There is, however, little knowledge regarding racial/ethnic disparities. Our objective was to examine the association between HDP and pre-pregnancy hypertension with maternal kidney disease within five years of delivery by race/ethnicity.
Methods: A retrospective cohort study conducted in South Carolina (2004-2016) included 13-49-year old women with live, singleton births. HDP (pre-eclampsia, eclampsia, gestational hypertension) were defined by birth certificates or hospitalization/emergency department (ED) visit data as was pre-pregnancy hypertension. Fatal and nonfatal incident kidney disease (chronic kidney disease, end-stage renal disease [ESRD]) was defined by hospitalization/ED visit data or death certificates.
Results: Of 433,333 women (58.7% non-Hispanic white, 31.8% non-Hispanic black, 9.5% Hispanic), 68,131 (15.7%) were diagnosed with HDP without pre-pregnancy hypertension (HDP alone), 1,587 (0.4%) with pre-pregnancy hypertension without superimposed HDP (pre-pregnancy hypertension alone) and 10,001 (2.3%) with both conditions (superimposed HDP) during at least one pregnancy. Compared with normotensive women (n=353,614; 81.6%), those with superimposed HDP (HR=5.57; 95% CI: 4.17-7.45), HDP alone (HR=3.00; 95% CI: 2.44-3.69) or pre-pregnancy hypertension alone (HR=1.75; 95% CI: 0.56-5.48) had significantly higher risk of incident kidney disease. Race/ethnicity interaction was statistically significant (p=0.028). The HR for Non-Hispanic Black and Hispanic women with HDP was significantly higher than in Non-Hispanic Whites, and the HR for Non-Hispanic Black women with superimposed HDP was significantly higher than in Non-Hispanic Whites (Table).
Discussion: Within five years, women with HDP or pre-pregnancy hypertension were at higher risk of kidney disease including ESRD and related mortality with notable racial/ethnic disparities.

Table. Association of hypertensive disorders of pregnancy (HDP) with maternal fatal and nonfatal incident kidney disease within five years of delivery by racial/ethnic group [*,†]

Incident kidney disease	Non-Hispanic White	Non-Hispanic Black	Hispanic
	HR (95% CI)		
Neither pre-pregnancy hypertension nor HDP	referent	Referent	referent
Pre-pregnancy hypertension alone	3.15 (0.77-12.9)	0.96 (0.13-6.95)	--
HDP alone	2.39 (1.75-3.26)	3.51 (2.63-4.69)	9.76 (3.18-30.0)
Superimposed HDP	2.63 (1.39-5.00)	7.51 (5.25-10.7)	8.64 (0.89-84.0)

Abbreviations: HDP, Hypertensive disorders of pregnancy; HR, hazard ratio; CI, confidence interval.
[*] Adjusted for sociodemographic (maternal age, education, rural/urban residence, median income, payer, WIC), behavioral (pre-pregnancy smoking, smoking during pregnancy), and clinical characteristics (pre- and post-pregnancy BMI, gestational age, mode of delivery, induced labor, previous cesarean, previous pre-term delivery, Revised Graduated Index of Prenatal Care Utilization [R-GINDEX], and pre-pregnancy or gestational diabetes).
[†] p-value=0.028 for interaction between HDP and pre-pregnancy hypertension and racial/ethnic group.

Child abuse and adult cardiovascular disease: mediation by post-traumatic stress disorder and depression Anna K Poon* Anna Poon Jennifer J Stuart Karestan C Koenen Laura D Kubzansky Andrea Roberts Janet W Rich-Edwards

Background: Childhood physical and sexual abuse are associated with cardiovascular disease (CVD) in adulthood. This relationship may be mediated by post-traumatic stress disorder (PTSD) and depression, but their role as mediators is undetermined.

Methods: We included 49,337 women followed from 1989-2015 in the Nurses' Health Study 2. Physical abuse before age 18 was defined as none, mild, moderate, or severe. Sexual abuse before age 18 was defined as none, sexual touching, or forced sex. PTSD was defined by trauma history and ≥4 symptoms. Depression was assessed by self-reported symptoms and report of symptoms to a clinician. CVD, including coronary heart disease (non-fatal MI, fatal MI, or fatal CHD) and stroke (non-fatal or fatal), were confirmed by medical record review. Cox proportional hazards models were used to estimate hazard ratios and 95% confidence intervals (CI). The difference method was used to determine the proportion and corresponding 95% CI of the main effect of child abuse mediated by PTSD or depression. Models were adjusted for age and childhood characteristics.

Results: Of the 8% of women (n=4,088) that reported severe physical abuse during childhood, 45% (n=1,827) reported PTSD and 68% (n=2,781) reported depression. Of the 11% (n=5,402) of women that reported forced sex during childhood, 42% (n=2,264) reported PTSD and 66% (n=3,541) reported depression. A total of 787 CVD events occurred during 26 years of follow-up. Women with vs without a history of severe child physical abuse had a 37% higher rate of CVD (CI:1.09-1.72); PTSD and depression accounted for 61% (CI: 24-88%) of this association. Women with vs without a history of forced sex had a 39% higher rate of CVD (CI: 1.13-1.71); PTSD and depression accounted for 50% (CI: 26-75%) of this association.

Conclusions: The relationship between early abuse and later CVD may be partly mediated by PTSD and depression, suggesting that early trauma and psychological distress may exacerbate CVD risk.

Is infertility associated with an increased risk of future cardiovascular disease in females?

Zoe Cairncross* Zoe Cairncross Sofia Ahmed Sandra Dumanski Kara Nerenberg Amy Metcalfe

Background: Cardiovascular diseases (CVD) are the leading causes of death in women globally. In recent years, attention has turned to pregnancy-related events and infertility as early markers for CVD development and cardiovascular mortality. We examined whether infertility is associated with the development of increased cardiovascular risk factors and events.

Methods: The Study of Women's Health Across the Nation is an ongoing longitudinal cohort study of women's health. Eligible women were aged 42-52 with a uterus and at least one intact ovary, a menstrual period, and no hormone medications within three months prior to enrollment. Infertility was self-reported and defined as no pregnancy after 12 months of trying to conceive, or use of fertility medications for >1 month. Study outcomes included development of metabolic syndrome as a proxy for CVD risk, and any CVD event (stroke, myocardial infarction, or angina) over 7 and 10 years of annual follow-up, respectively. Cox proportional hazards models were used to calculate hazard ratios (HR) for each study outcome in women with infertility, compared to those without infertility, with adjustment for covariates, both categorical (race, family history of CVD, insurance, continuous oral contraceptive use from age 25-35) and time-varying (hypertension, body mass index, smoking, income, menopausal status).

Results: 2,370 participants were included in the analysis of metabolic syndrome risk. Women with self-reported infertility did not have a higher risk of developing metabolic syndrome (HR=0.87, 95% CI 0.70-1.07). In the analysis of CVD event risk (n=2,809) we found no higher risk of CVD events in women with infertility compared with referent after adjustment for covariates (HR=0.79, 95% CI 0.52-1.21).

Conclusion: No association was found between infertility and development of metabolic syndrome or CVD events. Future studies should investigate the effects of specific causes of infertility and treatments on CVD outcomes.
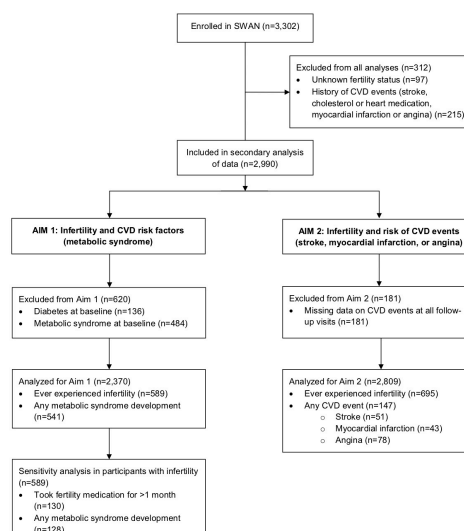
The impact of (forced) job separation on self-injury mortality in a cohort of autoworkers; application of a novel causal approach Sally Picciotto* Suzanne Dufault Kevin Chen Sally Picciotto Andreas Neophytou Ellen Eisen

In 2018, the U.S. Centers for Disease Control and Prevention reported a 30% increase in the suicide rate over the last two decades. Further, unintentional poisonings, commonly due to opioid overdoses, nearly tripled. The phrase "deaths of despair" has been used to link these increasing death rates to the deterioration of economic and social stability in middle aged men and women. Though this phenomenon was observed nationally in the early 2000s, the American auto industry experienced these same pressures beginning in the 1980s with the emergence of a competitive global market. Using the Michigan General Motors – United Autoworkers cohort as a case study, we examine the impact of precariousness of employment on risk of self-injury mortality (suicide combined with unintentional poisonings).

For 27,498 autoworkers employed on or after January 1, 1970, we estimated the causal effects of hypothetical interventions to reduce the annual odds of leaving work, under assumptions. We applied incremental propensity score interventions to examine how shifting the odds by a series of multiplicative factors (δ between 0.5 and 1.2) would have affected the cumulative incidence of self-injury mortality. In order to develop a comprehensive picture of the relationship we estimate a curve for the incremental effect on self-injury over a range of possible intervention sizes.

The cumulative incidence of self-injury mortality was 0.76% (210 cases) at the observed odds of leaving work (δ = 1). Cumulative incidence rose monotonically to 1.2% as we incrementally increased the odds of leaving work to 1.2. It fell when the odds were decreased: the estimated cumulative incidence of self-injury mortality dropped by 90%, to 0.078% (95% CI: [-2.4%, 2.6%]) when the odds of leaving work were reduced by 30% (δ = 0.7). These results suggest that forced job separation, as is the case when local industrial plants close, increases the risk of death due to suicide or drug overdose.

Occupational
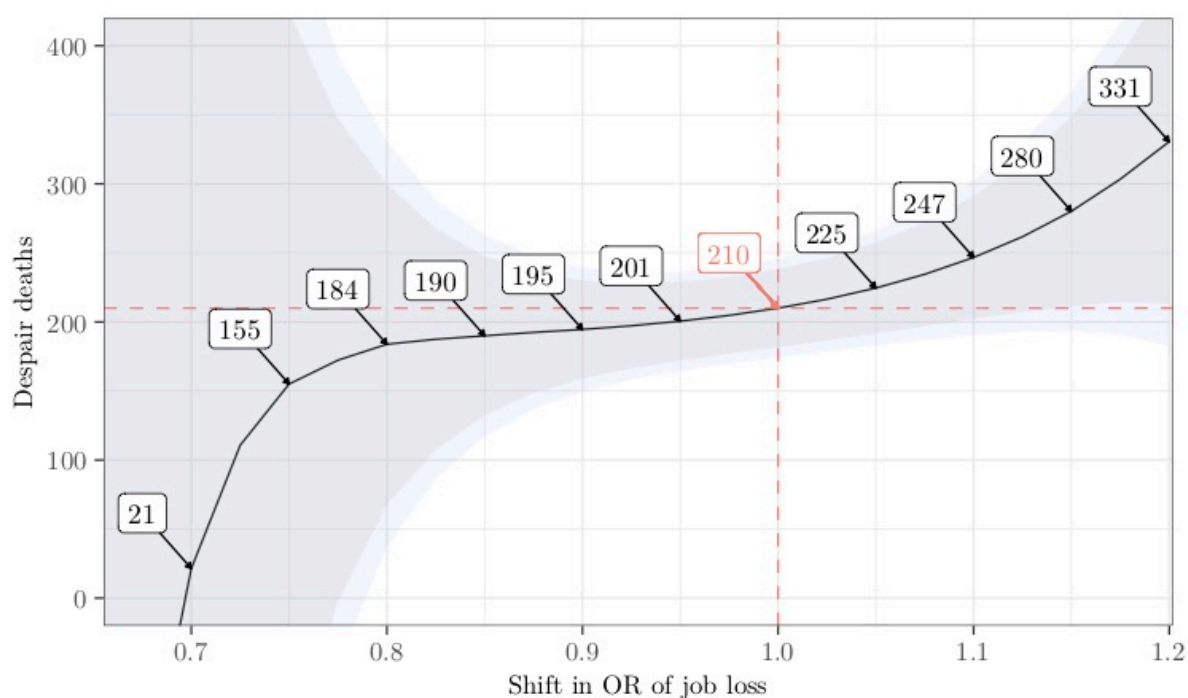
Investigating the impact of job insecurity and managerial status on sleep index using longitudinal population-based data Sukhdeep Kaur* Sukhdeep Kaur Antony Chum

Background: Given the net growth of non-standard/short-term employment contracts over the last two decades, job insecurity is becoming a chronic issue in most OECD countries. Organizations are also flattening, which results in heightened risk for middle managers to be made redundant. These shifts in labour market trends are work-related stressors that may have an impact on sleep quality.
Methods: Using the UK Household Longitudinal Study (n=43575), we examined the longitudinal relationship between job insecurity (the likelihood of losing your job over the next 12 months), managerial status (upper,middle and non-management) and sleep quality. A multidimensional index of sleep quality was computed based on Pittsburgh Sleep Quality Index survey (PSQI) with higher scores indicating poorer sleep quality. The longitudinal associations between sleep quality and the predictor variables (job insecurity and managerial status) were analyzed using mixed model. We adjusted for demographic characteristics including age, gender, household income, marital status and self reported health.
Results: A change from high to low job insecurity is associated with an improvement in sleep quality (Sleep Index -0.31. 95% CI -0.49 to -0.17, p <0.0001). Similarly, a change from non-management employment position to middle management is associated with a decrease in sleep quality (Sleep Index 0.14. 95% CI 0.059 to 0.221, p <0.0001).
Conclusion: Job insecurity and middle management employment was a risk factor for poor sleep. Although there have been some studies exploring the association between different work-related stressors and sleep, few have explored the impact of job insecurity and managerial status on multidimensional measures of sleep quality. Since our work environment is changing rapidly, it is important to have large scale studies that track the impact of these changes on sleep at the population level to produce evidence to inform public health policies.

Occupational

Impact of early opioid prescribing practices on long-term disability among injured workers in Washington State John R. Haight* John Haight Jeanne M. Sears Deborah Fulton-Kehoe Thomas M. Wickizer Gary M. Franklin

Background: Opioid prescribing practices have changed dramatically across the last two decades. This study sought to estimate the association between early opioid prescribing practices and longer-term work-related disability outcomes using Washington State workers' compensation claims data.
Methods: Washington State injured workers aged 18-56 years with a primary care provider and at least one filled opioid prescription within the first six weeks of injury from July 1, 2002, through August 30, 2013, were included. Logistic regression models were used to test the association between early high-risk opioid prescribing and time lost from work, receipt of total permanent disability (workers' compensation pension), and a surrogate measure for receipt of Social Security disability benefits. Early high-risk opioid prescribing was defined as exposure to of any of the following prescribing practices: (1) more than seven days' supply within the first six weeks after injury, (2) more than 50 milligrams morphine equivalent daily dose within the first 90 days, (3) 60 or more total days' supply of opioids within the first 90 days, or (4) at least one day of concurrent opioid and sedative prescribing within the first 90 days.
Results: In separate adjusted models, exposure to high-risk opioid prescribing was associated with a 3.12 times higher odds (95% CI 2.97, 3.27) of having more than 90 days of time loss, a 2.88 times higher odds (95% CI 2.71, 3.06) of having more than a year of time loss, a 3.11 times higher odds (95% CI 2.39, 4.05) of total permanent disability (pension), and a 2.76 (95% CI 2.26, 3.38) times higher odds of Social Security disability benefits, on average, than those exposed to low-risk opioid prescribing.
Conclusion: Exposure to high-risk opioid prescribing practices during the first 90 days after injury was significantly and substantially associated with risk of long-term temporary and permanent disability.

Are there gender inequities in editorial decisions by EPIDEMIOLOGY? Chrystelle Kiang*
Chrystelle Kiang Stephanie J. London Hailey R. Banack Sonja A. Swanson Jay S. Kaufman Emily
DeVoto William C. Miller Andrew F. Olshan Timothy L. Lash

Background: Emerging evidence suggests that manuscripts authored by women scientists may be
more often rejected without review, are reviewed less favorably, and face longer time to editorial
decision. It has been suggested that journals perform systematic evaluation of possible gender bias,
but reports of such analyses are rare. We evaluated these possible inequalities in a general interest
epidemiology journal.

Methods: Among 2,618 original research articles submitted to EPIDEMIOLOGY in 2015-2018, we
compared editorial decisions by imputed gender of first and last authors. We imputed gender from
authors' first names using the publicly available Genderize.io script and for a small number, by
internet research. Editorial decision categories were proportion rejected without review, rejected
with review, and accepted. Other metrics were time to decision, proportion sent for second review,
and successful appeal for reconsideration. One of us, who is otherwise not involved with the journal
as an author or editor, completed all the analyses.

Results: Among all authors of original research articles, 47% (95% CI: 45%-49%) of first authors and
36% (95% CI: 35%-38%) of last authors were women. These proportions varied little within
categories of editorial decision and gender was not related to time to decision. Men were more likely
than women to request repeal of an editorial decision: 78% of 27 appeals were by men. The decision
was reversed for 3 of 21 men and 2 of 6 women.

Conclusion: At a leading general interest epidemiology journal, authors' gender did not appear to
have a strong influence on editorial decisions or timeliness. More requests for reconsideration were
received from men than from women; success rates were comparable.

Evidence of diagnostic bias by sex from a randomized experiment of U.S. rheumatologists

Julia Simard* Julia Simard Yashaar Chaichian Nada Rizk Candace Feldman

Background: Systemic lupus erythematosus (SLE) is considered more prevalent in females and racial minorities. We tested whether implicit bias in clinical decision making might contribute to diagnostic delays and/or missed diagnoses that result in disparities in outcomes by sex.

Methods: U.S. rheumatologists were invited to participate in a survey via email including 5 clinical case vignettes: 2 SLE (1 mild SLE and 1 lupus nephritis, to vary severity) and 3 "control" rheumatologic cases (gout, ankylosing spondylitis, and sarcoidosis). We randomly assigned sex and race of each vignette holding constant all other features. Each case's true diagnosis was compared to each participant's response (primary outcome). Response time was a secondary outcome measure of implicit bias. We calculated the number of correct and incorrect assessments stratified by case vignette variant for each case and mean response time.

Results: 296 rheumatologists (6%, N=4909) completed surveys. The participating rheumatologists were generally similar to the reported rheumatology workforce. The 3 control cases were answered correctly >93% of the time for all variants. However, Black female cases were most likely to be diagnosed with SLE (89%), followed by White females (86%), Black males (84%), and lastly White males (77%). The pattern was similar for our secondary outcome: among the respondents ultimately answering correctly, the response time was longer for the White male v. Black female SLE vignette (36 v.16 sec).

Discussion: Cognitive heuristic shortcuts in clinical decision making influence how clinicians diagnose patients, which feeds into the future evidence base. We noted that the proportion correctly diagnosed with SLE was commensurate with the evidence base (e.g. respondents took longer and were less likely to diagnose SLE in White males), suggesting that implicit bias might contribute to delayed or missed diagnoses in cases that do not look like "the average".

Social

Adherence to Gender-Typical Behavior as a Determinant of Occupational Health: Gender and Occupational Differences in Associations Between Gender Adherence and C-Reactive Protein in a Nationally Representative Cohort Nicky Tettamanti* Nicky Tettamanti Sarah Andrea Janne Boone-Heinonen

Background: The gender composition of one's peers within their occupation as well as gendered duties required by occupation type (e.g., customer service, caretaking) may contribute to observed higher levels of C-reactive protein (CRP), a marker of systemic inflammation, among women. Moreover, workers who do not adhere to gender-typical behaviors may experience differential exposure and vulnerability to workplace stressors. Our objective was to investigate differences in the association between adherence to gender-typical behaviors (AGB) and CRP by occupational gender composition and job class.

Methods: Using data from the National Longitudinal Study of Adolescent to Adult Health, we linked Wave IV self-reported occupation (2007-2008; age 24-33 years) to Bureau of Labor Statistics gender composition data. In gender-stratified multivariable linear regression, we modeled log-levels of CRP as a function of AGB and confounders. AGB is an empirically validated measure quantifying the concordance of a one's behaviors relative to others of the same gender. We subsequently examined percent women in occupation and job class (blue-collar, white-collar, service) as modifiers of the association between AGB and CRP in gender-stratified models.

Results: For women, greater femininity was associated with higher CRP regardless of occupation (β: 0.005 log mg/ml; 95% CI: 0.002,0.009 for every 1% increase in AGB). For men, job classification modified the association between AGB and log-CRP. Greater femininity was associated with lower CRP for men in the service industry, while greater femininity was associated with higher CRP for men in white-collar occupations.

Conclusion: In a nationally representative sample, femininity was associated with inflammation among men in white-collar occupations and among women irrespective of occupation. Workplace policies aimed at the equitable distribution and valuation of feminized labor may be beneficial to worker health.

A Systematic Review of Methods Used to Study Intersections of Sex and Social Circumstances on Older Adults' Health Afshin Vafaei* Afshin Vafaei Susan Phillips Siu Yu

Background: Gender and other social circumstances are known determinants of health, particularly amongst older people. Usual approaches to their study assess heterogeneity between social groups (eg race, income) but embed within-group homogeneity in analyses. Intersectionality theory posits that the impact of, for example, being a woman of color is not simply the combined effect of each. Our aim was to examine how multidimensionality and interdependence within social strata are addressed in quantitative studies. We did this via a systematic review of methods used in gender and health outcomes research on older adults, that is, by examining methods used to study intersectionality and health.

Methods: Following PRISMA, we conducted a systematic review (2014- July 24, 2019) of peer-reviewed, quantitative, health outcomes studies among adults older than 45. The main inclusion criterion was incorporation of sex and at least one social factor. Abstract and full-text screenings were performed in duplicate followed by extraction of data on health outcomes, analytic methods, and social factors.

Results: After abstract review of 9214 citations and 711 full-text reviews, 501 articles met our inclusion criteria (figure 1). Most studies used regression methods and adjusted for (250) or stratified by sex (116). More advanced analyses included multilevel (25), mediation (17), structural equation modelling (25), decomposition (9), growth models (19), propensity score matching (2) and calculation of inequality indices (3). No study employed regression tree or any other discrimination analytic method.

Conclusions: Epidemiologic literature on the health of older adults uses a life-course framework and acknowledges the centrality of sex and social factors however rarely considers intersections between these determinants. Despite theoretical developments in social sciences, epidemiologic measures of intersectionality rely primarily on sex-stratified analyses.

Results of full-text review
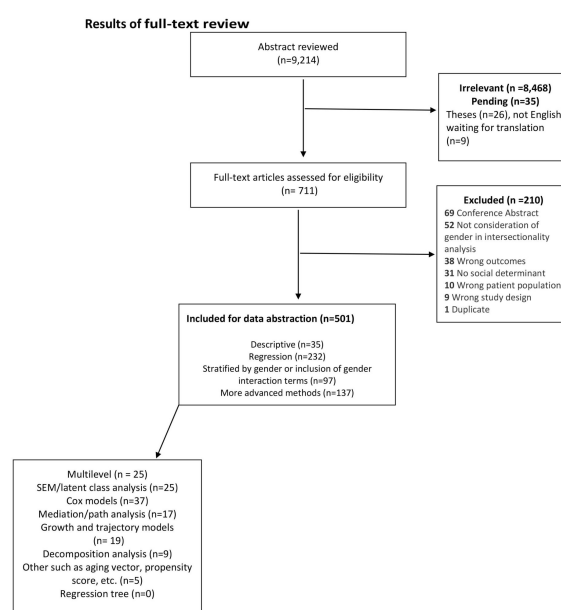
The relationship between maternal adverse childhood experiences and child physical and socioemotional development in rural Pakistan
Esther Chung* Esther Chung Katherine LeMasters Elissa Scherer Lisa M. Bates Ashley Hagaman Brooke S. Staley Elizabeth L. Turner Siham Sikander Joanna Maselko

Background: Adverse childhood experience (ACE) are associated with poor adult mental and physical health. Yet, intergenerational effects of ACEs are understudied, particularly in low- and middle-income countries. We examined the relationship between mothers' own ACEs and their 3-year old's development in rural Pakistan.

Methods: Data came from the Bachpan birth cohort (n=877). Maternal ACEs were measured with an adapted ACE International Questionnaire and operationalized as the number of ACEs (continuous, binary, categorical) and as grouped domains (neglect, family distress, home violence, community violence). Outcomes included child growth z-scores and socioemotional development using the Ages and Stages Questionnaire: Socioemotional (ASQ: SE). A lower ASQ score indicates better development. We used adjusted linear mixed effects models accounting for clustering and missingness.

Results: A majority of mothers (58%) reported experiencing at least one ACE, with the most common items being emotional (32%) and physical abuse (23%) and emotional neglect (15%). We found largely null effects for maternal ACEs on child growth z-scores (Figure 1A, 1B). Any maternal ACE (vs. none) was associated with worse child socioemotional development [Figure 1C. Mean difference (95% CI): 3.22 (0.95, 5.48)]. Children with mothers who experienced three or more ACEs (vs. none) had greater socioemotional problems [4.29 (1.17, 7.42)]. When grouped by broader domains, community violence and neglect were associated with worse ASQ scores [3.30 (-0.04, 6.65); 2.31 (-1.35, 5.98) respectively], adjusting for all other domains and covariates.

Conclusions: Maternal ACEs may affect the next generation's socioemotional development, but we found no associations with physical growth. Potential mechanisms include maternal mental health and parenting practices and ongoing analyses will examine this further. Targeted interventions to mothers with ACEs may have substantial effects across generations.

Figure 1. Maternal adverse childhood experiences (ACE) and child growth and development (n=877)
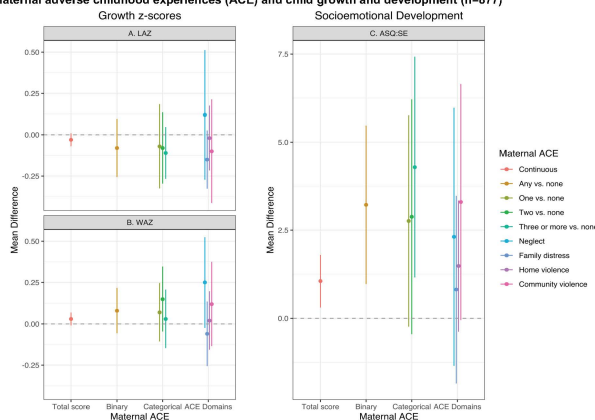
All models accounted for clustering and included probability weights to account for unequal sampling. *A priori* confounders included maternal age, education, trial arm, and assessor and baseline covariates that predicted missingness at 36 months: grandmother co-residence, number of living children, and people per room.
ACE domains were included in one model after separate models showed no substantive differences in estimates and precision. *Neglect* included physical and emotional neglect; *Family distress* included parental separation / divorce / death, alcohol / drug abuse, a household member with chronic depression, and an incarcerated household member; *Home violence* included a violent treatment of a household member, physical, and emotional abuse; *Community violence* included bullying, community violence, or collective violence.
Abbreviations: Length-for-age z-score (LAZ); Weight-for-age z-score (WAZ); Adverse Childhood Experience (ACE); Ages and Stages Questionnaire Socioemotional (ASQ: SE)

Are there birth cohort effects in socioeconomic disparities in child obesity? Felice Le-Scherban* Felice Le-Scherban Jeffrey Moore Irene Headen Christopher B. Forrest

Background: Children belonging to the same birth cohort (i.e., born in the same year) experience shared exposure to a common obesity-related milieu during the critical early years of development—e.g., secular beliefs and feeding practices, adverse chemical exposures, food access and nutrition assistance policies—that set the stage for a shared trajectory of obesity as they mature. Fundamental cause theory suggests that inequitable distribution of recent efforts to stem the rise in child obesity may exacerbate cohort-based disparities over time.

Methods: Using longitudinal electronic health record data spanning 2007–2016 on 170,373 children aged 2–19 from a large pediatric care network linked with birth records, we used hierarchical age-period-cohort models to investigate cohort effects in maternal-education-based disparities in child obesity. Disparities were measured as absolute difference in prevalence (%) compared to maternal college degree. Disparity cohort effects were changes in disparity per 5 birth years. We hypothesized that socioeconomic obesity disparities were larger among more recent birth cohorts.

Results: In sex-stratified models adjusted for race/ethnicity, obesity disparities increased with lower maternal education and with age. Disparities for the lowest levels of maternal education were larger among more recent cohorts. Among girls, this disparity cohort effect was larger at young ages (at age 4, disparity for maternal education < high school increased by 4 [2–6] percentage points per 5 birth years) while among boys it was larger at older ages (at age 16, disparity for < high school increased by 6 [2–10] percentage points). Among boys, disparities decreased by birth year among young children for maternal some college and high school.

Conclusions: There may be widening socioeconomic disparities in child obesity by birth cohort but only in some age and sex subgroups.

Estimated obesity disparities[a] among (a) girls and (b) boys, and cohort effects for obesity disparities[b] among (c) girls and (d) boys at different ages from hierarchical age-period-cohort models[c], by maternal education level
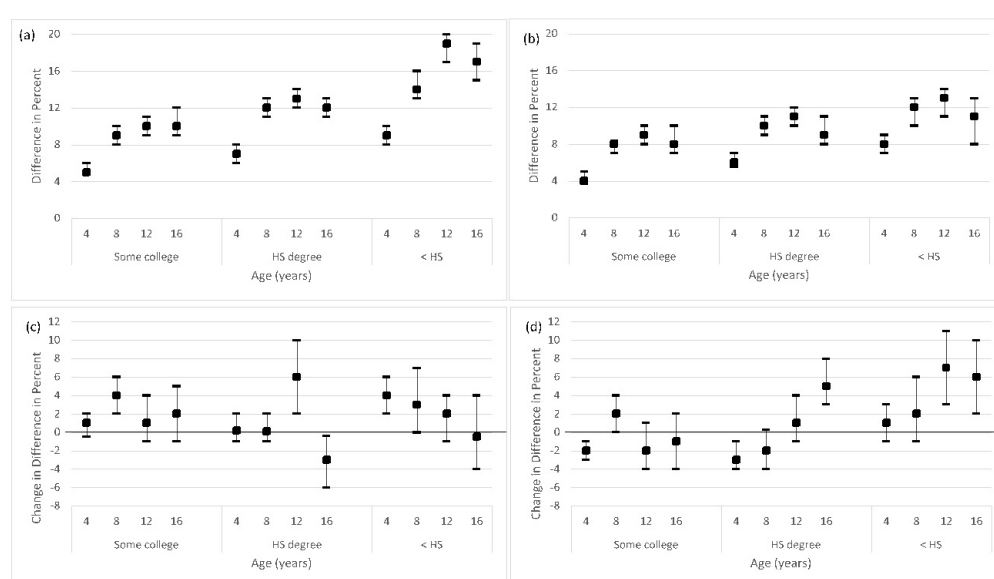
Error bars indicate 95% confidence intervals; markers may appear uncentered because of rounding.
[a] Obesity disparity is defined as the mean difference in obesity prevalence compared to maternal bachelor's degree or higher.
[b] Change in the obesity disparity per 5-year difference in birth year (e.g., disparity among 4-year-old children born in 2005 − disparity among 4-year-old children born in 2000).
[c] Adjusted for race/ethnicity.

Data-adaptive methods for high-dimensional mediation analysis: Application to a randomised trial of tuberculosis vaccination Margarita Moreno-Betancur* Margarita Moreno-Betancur Nicole L Messina Kaya Gardiner Nigel Curtis Stijn Vansteelandt

Statistical methods for causal mediation analysis are useful for understanding the pathways by which a certain treatment or exposure impacts health outcomes. While there have been many methodological developments in the past decades, there is still a scarcity of feasible and flexible, data-adaptive methods for mediation analysis with respect to high-dimensional mediators (e.g., biomarkers) and confounders. Existing methods necessitate modelling of the distribution of the mediators, which quickly becomes infeasible when mediators are high-dimensional. To avoid such high-dimensional modelling, we propose novel methods for estimating the indirect effect of a randomised treatment that acts via a pathway represented by a high-dimensional set of measurements. The proposed methods are doubly robust, which allows us to achieve (uniformly) valid statistical inference, even when machine learning algorithms are used for the two required models, as is desirable in a high-dimensional setting. This work was motivated by the Melbourne Infant Study: BCG for Allergy and Infection Reduction (MIS BAIR), a randomised controlled trial investigating the effect of neonatal Bacillus Calmette–Guerin (BCG) (tuberculosis) vaccination on clinical allergy and infection outcomes in the first years of life. The hypothesis of the trial was that the heterologous effects of BCG on innate immunity have beneficial effects on the developing immune system, resulting in improved outcomes (see Figure). We illustrate the proposed methods in the investigation of this hypothesis, where immune pathways are represented by a high-dimensional vector of cytokine responses under various stimulants. We moreover confirm adequate performance of the methods in an extensive simulation study.
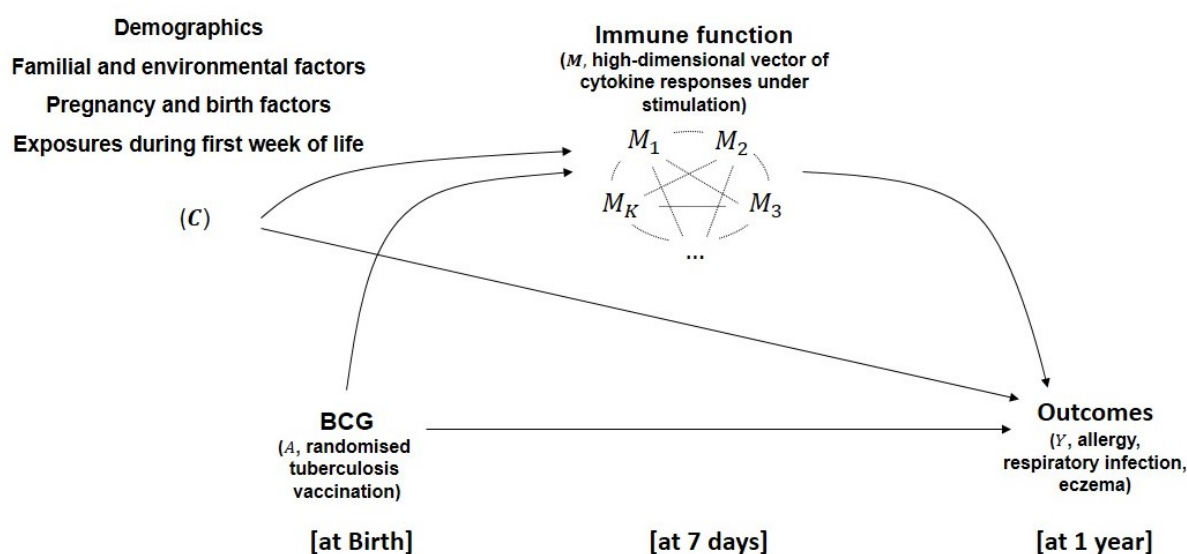
Extending inferences of experimental results with entropy balancing Kevin Josey* Kevin Josey
Seth Berkowitz Debashis Ghosh Sridharan Raghavan

In a randomized controlled trial (RCT), the population from which the random sample is collected, the trial population, often differs from the population of interest, the target population, yielding biased estimates of the average treatment effect in the target population. Methods for generalizing or transporting RCT results from a trial to a target population are thus essential. We show how entropy balancing can be used for transporting or generalizing experimental treatment effects from the trial population to the target population. This method is doubly-robust in the sense that if either the outcome model or the probability of trial participation is correctly specified, then the estimate of the target population average treatment effect is consistent. Furthermore, we only require the sample moments from the target population to consistently estimate the target population average treatment effect. We compared the finite sample performance of entropy balancing with several alternative methods for transporting treatment effects between populations. We found that entropy balancing is more robust to violations of the positivity assumption relative to the other methods while remaining efficient in each of the scenarios we tested. We also examine the results of our proposed method in an applied analysis of the Action to Control Cardiovascular Risk in Diabetes (ACCORD) blood pressure RCT transported to the National Health and Nutrition Examination Survey (NHANES) cohort.

Methods/Statistics
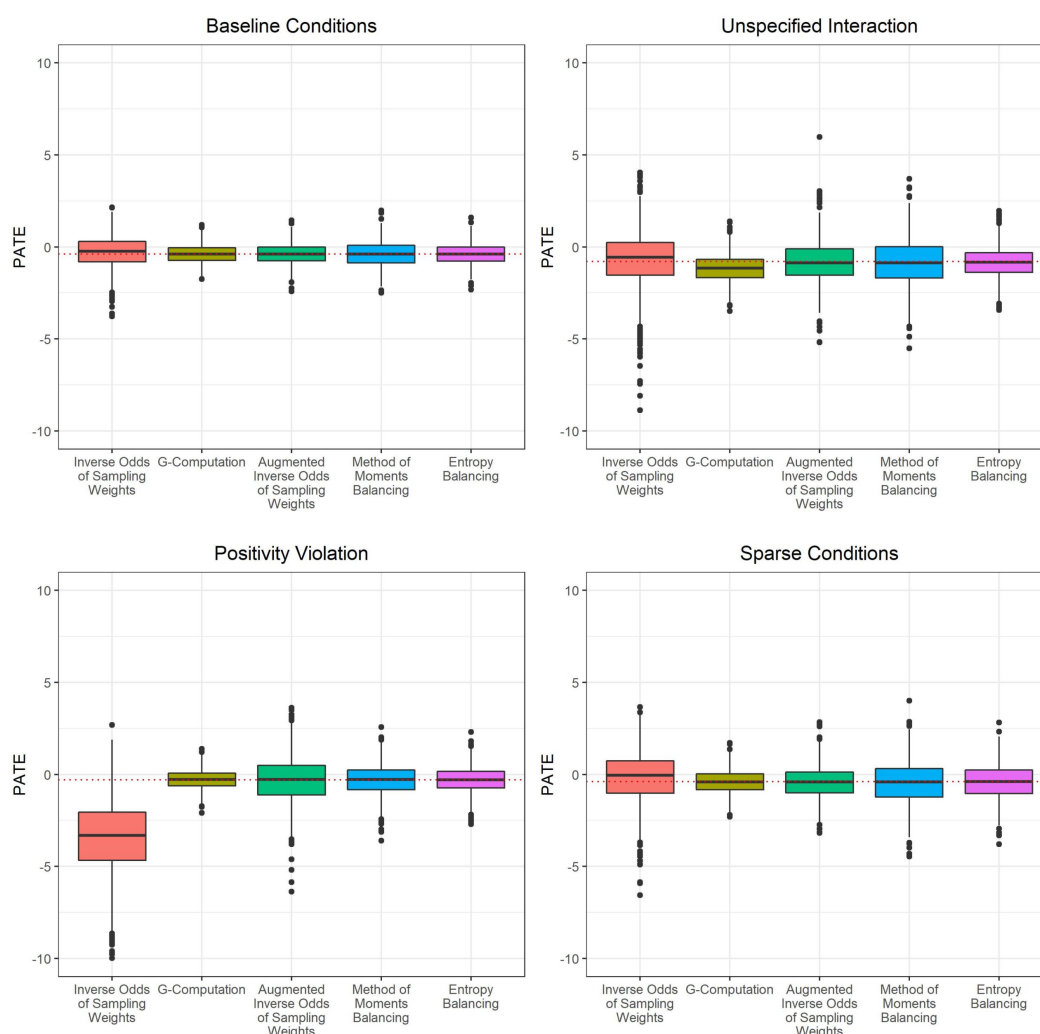
Examining the utility of targeted maximum likelihood estimation for network data Paul N Zivich* Paul Zivich David Weber Michael Hudgens M. Alan Brookhart James Moody Allison E Aiello

The assumption of no interference (i.e. that an individual's potential outcome is independent of all other individuals' treatments) is violated in many substantive areas of epidemiology, most clearly highlighted in infectious disease epidemiology with the concept of community protection. While less often discussed, concerns of interference and network dependence extend to a variety of other substantive areas in epidemiology, as recently demonstrated in re-analysis of the Framingham Heart Study for cardiovascular outcomes and mortality. One contemporary methodological approach for estimation with observational network data and interference is targeted maximum likelihood estimation (TMLE).

We conducted a simulation study of TMLE using randomly generated and observed networks in the context of three scenarios: (1) potential outcomes depend only on individual treatment status, (2) potential outcomes depend only on direct contacts' treatment, and (3) potential outcomes depend on both individual and direct contacts' treatment. We examined bias and confidence interval coverage of various stochastic interventions. TMLE allows for estimation of the sample average treatment effect under stochastic interventions with dependent observational data by allowing for dependence between individuals connected in a known network through summary measures, where potential outcomes depend only on the treatment status of direct contacts through a known summary measure. All summary measures were correctly specified in simulations.

When interference is present but ignored, TMLE that assume observations are independent results in biased estimates. By using a TMLE that allows for interference, estimates are unbiased and confidence interval coverage is at nominal levels. Ignoring interference may result in erroneous conclusions regarding interventions. Methods that allow for interference to occur, like TMLE, should be more often considered by epidemiologists.
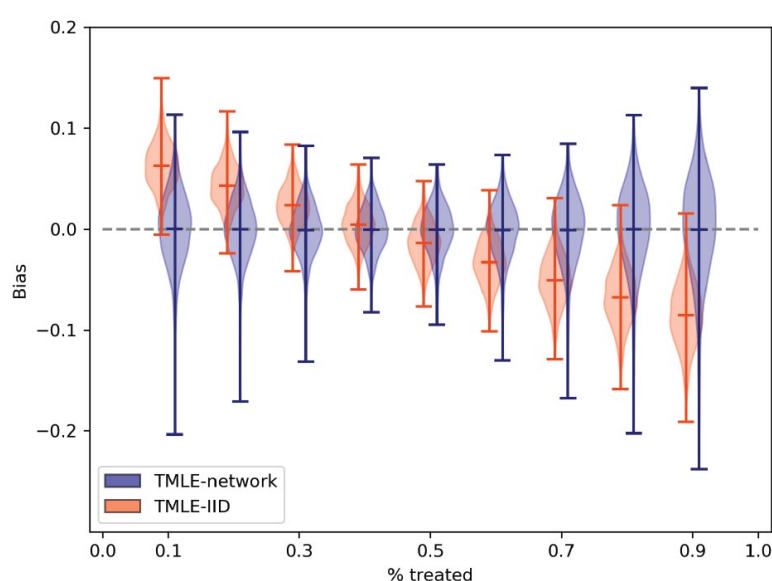
TMLE: targeted maximum likelihood estimation, IID: independent and identically distributed.
Bias was defined as the estimated incidence minus the true incidence under the specified proportion of the population treated (% treated). The shaded region is the density of centered estimates and the horizontal line indicates the mean.
Based on 1,000 simulations with a sample size of 500 with the network and confounder distribution held constant, and potential outcomes depend on both individual and direct contacts' treatment.

New estimands for conditional causal effects Mats Julius Stensrud* Mats Stensrud Miguel A. Hernán Jessica G. Young

Many epidemiologic studies aim to assess treatment effects on outcomes in individuals characterized by status on a particular post-treatment variable. For example, we may be interested in the effect of cancer therapies on quality of life, and quality of life is only well-defined in the those individuals who are alive. Similarly, we may be interested in the effect of vaccines on post-infections outcomes, which are only of interest in those individuals who become infected. In these settings, a naive contrast of outcomes conditional on the post-treatment variable does not have a causal interpretation, even in a randomized experiment. Therefore the effect in the principal stratum of those who would have the same value of the post-treatment variable regardless of treatment, such as the survivor average causal effect, is often advocated for causal inference. Whereas this principal stratum effect is a well defined causal contrast, it cannot be identified without strong untestable assumptions, and its practical relevance is ambiguous because it is restricted to an unknown subpopulation of unknown size. Here we formulate alternative estimands, which allow us to define the conditional separable effects. We describe the causal interpretation of the conditional separable effects, e.g. in settings with truncation by death, and introduce three different estimators. As an illustration, we use data from a randomized clinical trial to estimate a conditional separable effect of chemotherapies on quality of life in patients with prostate cancer.

Epidemiology and risk factors of child stunting in low-resource settings: new insights from pooled analyses of 31 longitudinal cohorts and over 62,000 children Jade Benjamin-Chung*

Jade Benjamin-Chung Andrew Mertens John M Colford, Jr Alan E Hubbard Mark J van der Laan Jeremy Coyle Oleg Sofrygin Wilson Cai Anna Nguyen Nolan Pokpongkiat Wendy Jilek Esther O Chung Sonali Dayal Nima Hejazi Ivana Malencia Haodong Li Ryan Hafen Vishak Subramoney Jonas Häggström Thea Norman Kenneth H. Brown Parul Christian Benjamin F. Arnold members of the ki Child Growth Consortium

Prior meta-analyses of cross-sectional data suggested that the period from birth to age 24 months is the critical window in which to intervene to prevent childhood stunting. Our aim was to estimate the age-specific incidence of stunting onset and identify risk factors associated with stunting onset. We performed an individual participant meta-analysis of 31 longitudinal cohorts in low- and middle-income countries that measured anthropometry from birth to 24 months (N=62,993 children and 463,802 measurements). Incident stunting was defined as a reduction in length-for-age Z-score (LAZ) below –2 within pre-specified age windows. For risk factors preceding stunting onset, we estimated population attributable fractions (PAF) as the reduction in cumulative incidence of stunting at birth, 6, and 24 months if a risk factor was reduced to the level with the lowest incidence in the entire population. We estimated adjusted PAFs in each cohort using targeted maximum likelihood estimation with ensemble machine learning and pooled estimates using random effects models with restricted maximum likelihood estimation. Over half of incident stunting episodes occurred before age 6 months. The cumulative incidence of stunting was 12% (95% CI 8%, 18%) at birth, 27% (95% CI 22%, 32%) by age 3 months, 35% (95% CI 30%, 40%) by age 6 months, and 65% (95% CI 55%, 74%) by age 24 months. PAFs were largest for maternal height and weight and child birth length. Population-level increases in maternal weight (to >= 58 kg) or height (to >= 155 cm) were associated with an approximately 20% reduction in stunting incidence at 24 months, and an increase in birth length (to >= 50 cm) was associated with an approximately 30% reduction (Figure). Risk factors associated with stunting incidence at birth and 6 months were similar. Our findings emphasize the pre-natal and early post-natal windows as targets for preventative interventions and the need for maternal interventions to reduce stunting onset.
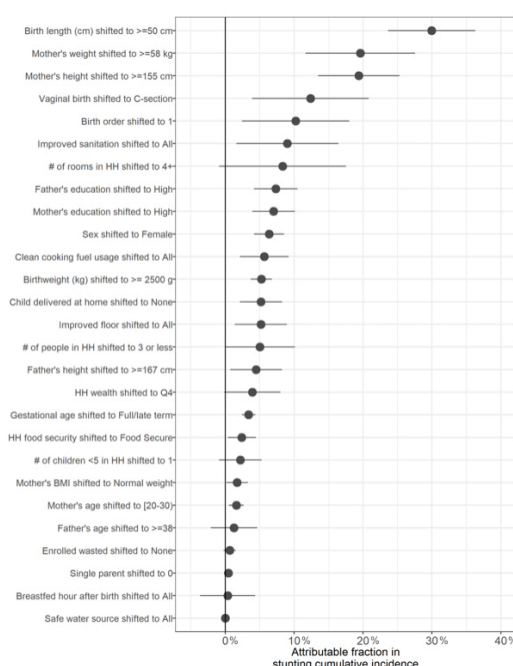
Association between parental preterm birth and low birth weight and autism spectrum disorder (ASD) risk in their offspring: A population-based multigenerational cohort study in Denmark Jingyuan Xiao* Jingyuan Xiao Yu Gao Yongfu Yu Gunnar Toft Yawei Zhang Jiajun Luo Yuntian Xia Jørn Olsen Jiong Li Zeyan Liew

Objectives: To evaluate whether parental preterm birth or low birth weight was associated with autism spectrum disorder (ASD) risk in offspring.

Design/Setting: Nationwide register-based multigenerational cohort study in Denmark.

Participant: Danish parents born since 1978 who have had singleton live-born offspring registered in Denmark during 1994 -2013. We identified 230,174 mother-child pairs and 157,926 father-child pairs.

Exposure: Gestational age and birth weight of parents obtained from the Danish Medical Birth Register.

Main Outcome: ASD diagnoses in offspring, obtained from the Danish Central Psychiatric Registry. We estimated ORs and corresponding 95% CIs for offspring ASD according to parental preterm (<37 weeks) and low birth weight (<2500 grams) status comparing with gestational weeks ≥ 37 weeks or birth weight ≥ 2500 grams as the reference, with or without adjustment for grandmaternal sociodemographic factors including age, parity and education level. Mediation analyses were conducted for selected parental health and pregnancy-related factors of the index child.

Results: Offspring of mothers or fathers with adverse birth outcomes had about 31-43% higher risk for ASD (maternal preterm birth, OR=1.31, 95% CI= 1.12,1.55; maternal low birth weight, OR=1.35, 95% CI: 1.17,1.57; paternal preterm birth, OR=1.43, 95% CI=1.18, 1.73; paternal low birth weight, OR=1.38, 95% CI= 1.13, 1.70). Parents born very preterm (<32 weeks) marked a nearly 2-fold increase in offspring ASD risk. These associations were slightly attenuated upon adjustment for grandmaternal sociodemographic factors. Mediation analyses suggested a small magnitude of indirect effect estimated for parental social-mental wellbeing and perinatal risk factors for the child, especially for maternal birth outcome associations.

Conclusions: Offspring of parents born with adverse outcomes had elevated risk for ASD. Transgenerational ASD risk through maternal and paternal factors should be considered in future research.

Patriarchal norms and intimate partner violence in India: The use of national and state-level data to examine temporal and spatial patterning and associations Kathryn M. Barker*
Kathryn M Barker Abhishek Singh Kaushalendra Kumar Praveen Chokhandre Lotus McDougal Anita Raj

Introduction: Patriarchy is a social system in which men hold primary power and predominate in roles of political leadership, moral authority, social privilege and control of property. In India, patriarchy is internalized as an ideology, expressed as stridharma or pativaratadharma, or the duties and obligation of women, and is evidenced by power relations within households. Previous evidence suggests that rigid norms regarding gender roles, family, and marriage contribute to men's use of violence against partners. Methods: We use three waves of data (1992–1993, 2005–2006, and 2015–2016) from the Indian National Family Health Survey (NFHS) and a novel composite measure, the Patriarchy Index, to quantify the construct of patriarchal norms and to examine historic and geographic variation of patriarchy in India and its association to intimate partner violence among married females (ages 15-49). Results: Preliminary results suggest significant variation in patriarchy by state, and slowly changing trends in patriarchal norms within India. Findings also demonstrate a strong correlation between patriarchy and incidence of intimate partner violence. Conclusion: Results offer empirical evidence to suggest that addressing patriarchal norms may be an avenue to enable improved health outcomes among Indian women.

Impact of Marijuana Legalization in Uruguay on Use of Other Substances Among the General Population Ariadne Rivera-Aguirre* Ariadne Rivera-Aguirre Alvaro Castillo-Carniglia Magdalena Cerdá

Background: In 2013, Uruguay removed the prohibition and regulated the sale, cultivation, and distribution of marijuana. The new regulation is a non-commercial legalization model, where the state controls production and sales of marijuana, prohibits advertisement, and sets limits on the quantity and potency of marijuana Uruguayans can purchase. With expanded access to marijuana, Uruguayans could substitute other substances for marijuana, thus producing a decrease in the use alcohol, tobacco and cocaine, or could see a complementary increase in use of other substances.
Aim: To evaluate whether a non-commercial model of national marijuana legalization in Uruguay is associated with changes in the prevalence of past month use of alcohol, tobacco and cocaine.
Methods: We used a quasi-experimental comparative case study design using the synthetic control method. To create the synthetic control group for Uruguay we used data for comparable regions in Chile (n= 15) and Argentina (n= 24) from cross-sectional nationally representative surveys on drug use of individuals aged 15-64 in urban areas for years 2002-2018. We fitted models for two groups separately; individuals aged between 15-25 and 26-64 years old.
Results: In 2014-2018, following legalization, among people 15-25 years, past month prevalence of alcohol use was associated with an absolute increase 3.9 percentage points, while past month tobacco and cocaine use decreased 6.9 and 1.2 percentage points, respectively. For Uruguayans aged 26-64, alcohol decreased 22.2%, tobacco increased 0.22%, and cocaine decreased 0.6% when compared to its counterfactual. However, none of these results were statistically different from the null.
Conclusion: Legalization of marijuana in Uruguay is not associated with short-term changes in the use of alcohol, tobacco, and cocaine. Questions remain about potential changes in substance use given a longer-term follow-up following full implementation of the legalization model in Uruguay.

Substance Use

The impact of prescriber networks on opioid agonist treatment retention: A retrospective population-based analysis

Megan Kurz* Megan Kurz Jeong Eun Min Lindsay Pearce Joan Hu Bohdan Nosyk

Background: While care models fostering physician collaboration to support long-term engagement in opioid agonist treatment (OAT) have been introduced to improve care quality, evidence of the potential benefits of such interventions are sparse. We aimed to describe the OAT prescriber network characteristics over time in British Columbia (BC), Canada, and determine their association with treatment retention.

Methods: We conducted a retrospective study using four health administrative databases to define the population of physicians prescribing OAT and their clients receiving treatment in BC from January 1st 1996 to November 30th 2017. We constructed prescriber networks based on shared OAT clients and measured the number of shared clients, the prescriber's centrality within the network, and the number of connected prescribers for each OAT prescribing physician. We performed regression analysis under a generalized linear mixed effects model with the probit link to determine the effects of the characteristics of the prescriber, the prescriber's clients and their network on the percentage of a prescriber's clients retained in treatment for at least 12 months.

Results: A total of 2,069 unique prescribers and 173,926 person-years of OAT from 43,930 clients were included in the analysis. After adjusting for prescriber and client characteristics, we found that increased connectivity of prescribers was associated with a 0.29% increase in a prescriber's 12-month retention rate for each 10% increase of connectivity, while the number of clients that prescribers share was associated with a 0.52% decline for each additional prescriber.

Conclusion: Increased connections between prescribers had a positive impact on treatment outcomes providing evidence to support the development of care structures that promote connectivity; however, ongoing monitoring is still required to determine optimal connectivity and client load as clients seeing multiple prescribers had poorer outcomes.

November 1997   November 2007   November 2017

OAT client load:
Median (P25-P75): 5 (1-28)
Maximum: 133

OAT client load:
Median (P25-P75): 26 (6-61)
Maximum: 250

OAT client load:
Median (P25-P75): 2 (1-28)
Maximum: 573

1 OAT client   11–50   101–200
2–10 OAT clients   51–100   201–573
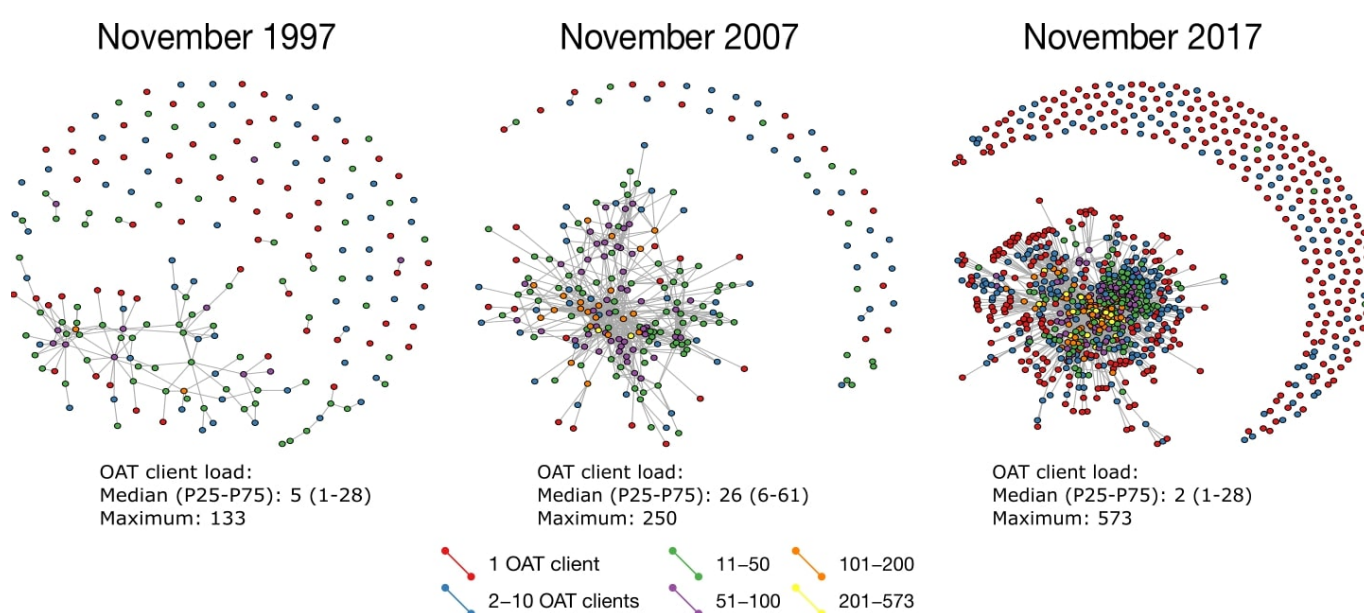
Legend: Each circle represents a single prescriber. The connecting lines (ties) imply they share atleast one client with a range of 1 to 120. Keeping ties of weight=1 was important due to the large number of prescribers who only saw 1 client. The node color is based on how many clients the prescriber treated during the calendar month.

Association of Marijuana Use History with Current E-cigarette Use among Adults in the United States Buyun Liu* Buyun Liu Yang Du Linda G. Snetselaar Robert B. Wallace Wei Bao

Background: In the United States, ever use of marijuana is common in adults, and many of them initiated marijuana use during adolescence. While marijuana use has been linked to tobacco use among adults, its relation with e-cigarette use, which has become a public health concern, is unknown. This study aimed to examine the association of a history of marijuana use with current e-cigarette use among adults in the United States.

Methods: We used data from the National Health and Nutrition Examination Survey, 2013-2016. We included 6,995 adults aged 18 - 59 years old. Logistic regressions were used to estimate the odds ratio (OR) and 95% conference interval (CI) of the association of ever marijuana use and age of marijuana use initiation with current e-cigarette use.

Results: In this study, the weighted proportion of adults who had ever used marijuana was 57.7%, including 11.5% (standard error [SE] 0.7) of adults reporting that they initiated marijuana use between the age of 12 and 14, 23.0% (SE 0.9) initiated between the age of 15 and 17, and 23.2% (SE 0.7) initiated at 18 or older. After adjustment for age, sex, race/ethnicity, body mass index, socioeconomic factors, and lifestyle factors including cigarette smoking, people who had ever used marijuana had a 3.2-fold increase in current e-cigarette use in adulthood (OR 3.2, 95% CI 1.6-6.4). Individuals who engaged in marijuana use at a younger age had higher odds of e-cigarette use in adulthood. Compared with individuals who never used marijuana, the OR of e-cigarette use was 3.5 (95% CI 1.6-7.9) for those who initiated marijuana use between 12 and 14 years old, 3.2 (95% CI 1.5-7.0) for those who initiated marijuana use between 15-17 years old, and 3.0 (95% CI 1.4-6.5) for those who initiated marijuana use at the age of 18 or older.

Conclusions: In this nationally representative sample of US adults, a history of marijuana use was associated with significantly higher likelihood of current e-cigarette use in adulthood.

Substance Use

An Examination of Relationships between Cannabis Legalization and Fatal Motor Vehicle and Pedestrian-Involved Crashes Collin Calvert* Collin Calvert Darin Erickson

While a fair amount of attention has been given to how legalization of recreational cannabis may affect traffic crash rates, there was been limited research on how cannabis may affect pedestrians involved in traffic crashes. This study examined the association between cannabis legalization (medical, recreational use, and recreational sales) and fatal motor vehicle crash rates (both pedestrian-involved and total fatal crashes). We used crash data from the Fatality Analysis Reporting System (FARS) to calculate monthly rates of fatal motor vehicle crashes per 100,000 residents from 1990 (1991 for pedestrian-involved crashes) to 2017. Changes in monthly crash rates in three states that had legalized both medical and recreational cannabis (Colorado, Washington, and Oregon) were compared to states that have not legalized cannabis in any form. We found no significant differences in fatal pedestrian-involved motor vehicle crashes between legalized cannabis states and control states post-recreational marijuana legalization, nor were there any differences after sales of recreational cannabis began. Overall findings suggest a minor elevated risk of total fatal motor vehicle crashes associated with cannabis legalization. Future studies should seek to incorporate additional states as more post-legalization data becomes available.

Substance Use

Longitudinal associations between single, dual, and polytobacco use and incident respiratory disease among adults: Findings from the Population Assessment of Tobacco & Health Study (2015-2017) Jana Hirschtick* Jana Hirschtick Nancy Fleischer

Significance: Patterns of single, dual (two products), and polyuse (three or more products) are evolving with the introduction of Electronic Nicotine Delivery Systems (ENDS). However, little is known about the health impact of distinct combinations of tobacco product use.

Methods: We used nationally representative data (age 18+) from waves 3 (2015-16) and 4 (2016-17) of the Population Assessment of Tobacco and Health to examine longitudinal associations between tobacco product use patterns and incident respiratory disease. We classified tobacco users into seven categories: single product users of 1) cigarettes 2) ENDS 3) other combustibles (e.g., cigars, pipes); dual users of 4) cigarettes plus ENDS 5) cigarettes plus other combustibles 6) ENDS plus other combustibles; or 7) polyusers of cigarettes, ENDS, and other combustibles. We used logistic regression, accounting for the complex survey design, to assess longitudinal associations between the seven product use patterns at wave 3 and incident diagnosed respiratory disease at wave 4, adjusting for age, sex, race/ethnicity, education, and a prior diagnosis of asthma.

Results: Among the 14,623 respondents who had visited a doctor in the past year, 2.8% were newly diagnosed with respiratory disease. Exclusive cigarette use was the most common use pattern (11.3%). In the adjusted model, exclusive cigarette smokers (OR 1.97, 95% CI 1.50, 2.57), cigarette plus ENDS dual users (OR 2.02, 95% CI 1.10, 3.71), and cigarette plus other combustible dual users (OR 2.21, 95% CI 1.15, 4.24) had increased odds of incident respiratory disease compared to non-tobacco users. There was no association between exclusive ENDS use and incident respiratory disease compared to non-tobacco users (OR 0.40 95% CI 0.12, 1.29).

Conclusion: Cigarette smoking exclusively or in combination with either ENDS or other combustibles increased the odds of incident respiratory disease, while exclusive ENDS use did not.

Substance Use

Association between type of opioid misuse and perceived barriers to accessing treatment for substance use disorders Mirinda Gormley* Mirinda Gormley Elizabeth Prom-Wormley Andrew Barnes Robert Perera Juan Lu

Background: Little is known about the relationship between type of opioid misuse and access to treatment for substance use disorders (TSUD). We investigated the association between type of opioid misuse and perceived readiness, financial, structural, and stigma-related barriers to accessing TSUD among insured individuals reporting past year opioid misuse. Methods: Participants from the 2015-2018 National Survey on Drug Use and Health included insured individuals reporting past year misuse of prescription pain relievers (PPR), heroin, or both. Chi-square analyses determined the association between participant's predisposing, enabling, and need characteristics and type of opioid misuse. Multivariate logistic regression assessed the relationship between type of opioid misuse and all four perceived barriers to accessing TSUD. Results: Of the 6,095 individuals reporting past year opioid misuse, 244 (3.7%) perceived at least one barrier to accessing TSUD. Whereas heroin only users most often perceived financial (50.5%) and stigma-related (39.8%) barriers, readiness (45.5%, 50.9%) and structural (41.2%, 44.9%) barriers were most cited by those reporting misuse of PPR or both. Misuse of both PPR and heroin (vs. PPR only) significantly increased the odds of perceiving readiness (OR=2.80, 95%CI=1.08-7.27), structural (OR=3.27, 95%CI=1.26-8.46), and stigma-related (OR=3.98, 95%CI=1.42-11.21) barriers. Severe mental health symptoms and increased number of substance use disorders (SUD) significantly increased the odds of perceiving all four barriers. Conclusions: Type of opioid use, mental health severity, and number of SUD are significantly associated with perceived barriers to accessing TSUD. Targeted strategies that address individual-level factors (e.g., severe mental health problems, multiple SUD, type of opioid use) alongside population-level changes that increase availability of services may increase the likelihood of enrollment into treatment for substance use disorders.

US trends in binge drinking by gender, work status, work prestige, and work structure among adults in midlife, 2006–2018

Sarah McKetta* Sarah McKetta Seth J. Prins Lisa M. Bates Jonathan M Platt Katherine M. Keyes

Binge drinking causes injury and illness. Rates have increased dramatically among women ages 30-49, while men's trends have been stabilizing. The US labor force is now ~50% women. Employment confers health benefits and risks, which may vary by distinct work characteristics, including the prestige and structure (e.g., authority, autonomy, expertise) of one's job. It is unknown how work characteristics relate to gendered drinking trends.

We examined trends in binge drinking among men and women ages 30-49 in the 2006-2018 National Health Interview Survey who have ever worked (N=195,695) by work status (unemployed vs employed), work prestige (General Social Survey's occupational prestige score), and work structure (occupational authority, autonomy, automation, expertise) and their interactions. We estimated the odds of binge drinking by year with survey-weighted logistic models controlled for sociodemographics, smoking, and disability.

In 2018, 33% of women and 36% of men reported binge drinking; drinking increased annually from 2006 to 2018 (OR for women=1.04, OR for men=1.03). Work status, prestige, and work structure modified the association. Women in high (OR=1.07, 95% CI 1.06–1.08) vs. low prestige (OR=1.03, 95% CI 1.02–1.04) jobs had higher increases, as did men (OR=1.05, 95% CI 1.04–1.06). Unemployed respondents with prestigious work history increased drinking (women's OR=1.06, 95% CI 1.03–1.08; men's OR=1.04, 95% CI 1.01–1.06). Respondents in higher authority, autonomy, and expertise jobs increased binge drinking; those in lower automation jobs increased binge drinking.

Increases in mid-life drinking in the US are greater among working adults, especially those in high-prestige jobs, which correspond to higher authority, autonomy, and expertise. Gender differences in drinking attenuated with stratification by prestige and work structure. Labor may be a key component for understanding and addressing national increases in binge drinking.

Past-year binge drinking by occupational prestige, gender, and work status, adjusted averages

Aging
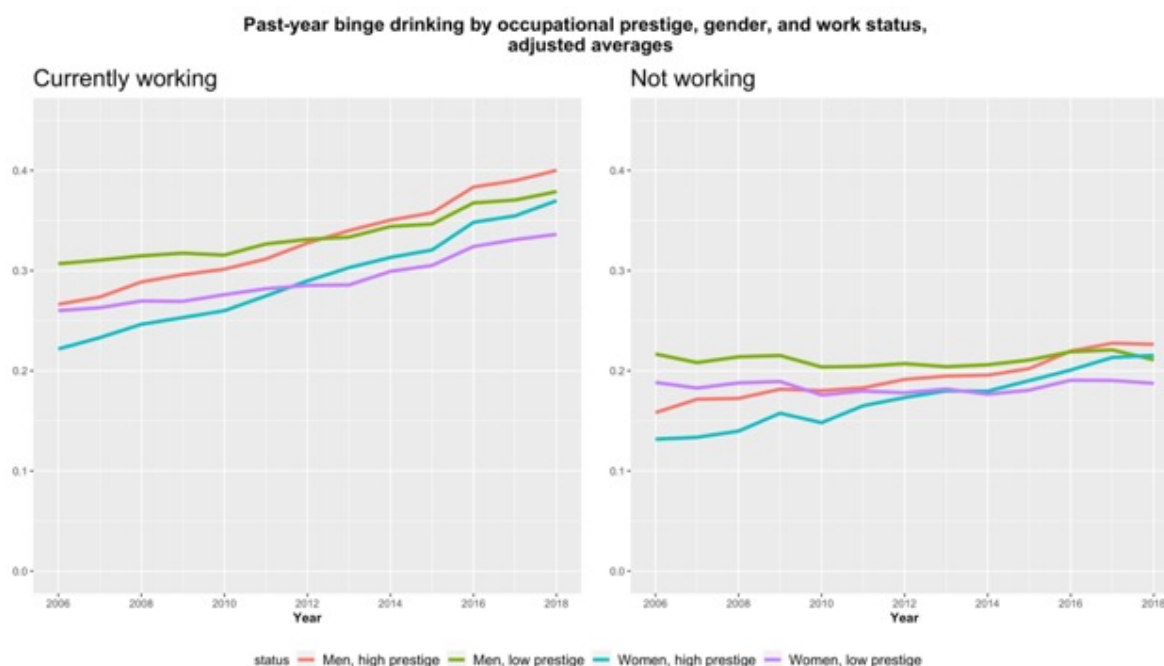
Physical frailty and cognitive impairment among older U.S. nursing homes residents Yiyang Yuan* Yiyang Yuan Kate L. Lapane Jennifer Tjia Jonggyu Baek Shao-Hsien Liu Christine M. Ulbricht

Physical frailty and cognitive impairment often co-occur and are highly prevalent in U.S. community-dwelling older adults. Data is limited for older adults receiving long-term care (LTC) in nursing homes (NHs). Using the database of all Medicare-/Medicaid-certified NHs, Minimum Data Set (MDS) 3.0 (2014-16), this study aimed to estimate the prevalence of and examine the characteristics associated with physical frailty and cognitive impairment at NH admission and in the first 6 months of stay. MDS 3.0 is conducted at admission and quarterly during the NH stay to assess cognitive functioning, mood, behavioral status, physical functioning and diagnoses. Residents who were >=65 years old, not comatose, newly-admitted with life expectancy at admission over 6 months and stayed in NH >100 days were included in this study (n=573,742). Physical frailty was measured by FRAIL-NH (robust/pre-frail/frail) and cognitive impairment by the Cognitive Function Scale (intact/mild/moderate/severe impairment). At admission, 64% of older adults were physically frail; 36% had moderate and 6% severe cognitive impairment. The prevalence of both conditions was consistent in the first 6 months but 30% of pre-frail residents and 23% of those with mild cognitive impairment at admission became frail and moderately/severely impaired, respectively, after 3 months. Similar patterns were observed from 3 to 6 months. The prevalence of physical frailty was higher in residents with worse cognitive impairment, of non-Hispanic black race, admitted from acute or LTC hospitals, and who had a diagnosis of stroke, seizure, multiple sclerosis or fracture. Other common comorbidities of physical frailty, such as depression and arthritis, did not differ by frailty levels. These preliminary results lay the groundwork for understanding the trajectories of physical frailty and cognitive impairment in older NH residents to guide the development of timely intervention in care planning for this vulnerable population.

Aging

Peripheral Immune System Markers and Cognitive Decline and Incident Dementia in the Sacramento Area Latino Study of Ageing
Rebecca C Stebbins* Rebecca Stebbins Allison E. Aiello

The etiology of dementias and cognitive decline remain largely unknown. It is widely accepted that inflammation in the central nervous system plays a critical role in the pathogenesis of dementia. However, less is known about the role of the peripheral immune system, though a growing body of literature suggests that it too may play a role in cognitive decline and incidence of dementia. Using the data of over 900 participants 60+ years old from the Sacramento Area Latino Study of Aging, we investigated variation in age trajectories of cognitive decline by cytokine levels. Linear mixed effects models were used to examine the association between baseline levels of Interleukin (IL)-6, C-reactive protein, and tumor necrosis factor (TNF)-α, and trajectories of log(Modified Mini Mental State Examination (3MSE) scores) over 10 years, and to examine interactions between cytokines and cortisol. Inverse probability weights were used to account for loss-to-follow-up and confounding by sex, educational attainment, depression, and self-rated health. All cytokines, modeled as both continuous and dichotomized-at-the-median variables, were statistically significantly associated with rate of decline (for IL-6, for example, $\beta=0.0027$ (95% CI: 0.0017, 0.0038) and $\beta=0.025$ (95% CI: 0.015, 0.035) per year, respectively), and IL-6 was also associated with average cognitive level ($\beta=0.013$ (95% CI: 0.0069, 0.019 and $\beta=0.085$ (95%CI: 0.032, 0.14), respectively) over the study period. Furthermore, among those with low cortisol levels, each unit increase of TNF-α was associated with 2.18 (95% CI: 1.03, 4.62) more errors on the 3MSE than those with high cortisol levels. These findings support the theory that the peripheral immune system may play an important role in cognitive decline. Furthermore, they identify specific markers in that process and suggest points of intervention for slowing decline and delaying dementia onset.

Aging

The association between gait speed and falls in older adults and the impact of mild cognitive impairment on findings Claire Adam* Claire Adam Erin Semmens Annette Fitzpatrick Cindy Leary

Background. Falls in older adults are common with 20-30% of adults over 65 falling each year. Screening programs are designed to minimize falls by identifying individuals at risk so that prevention measures can be implemented. However, screening for fall risk in older adults in the primary care setting does not occur consistently. Gait speed has been promoted as a reliable and efficient way to screen for fall risk in a clinical setting, but its relevance in individuals with mild cognitive impairment (MCI) is unclear. Methods. We evaluated the relationship between gait speed and falls in 3,069 participants in the Ginkgo Evaluation of Memory Study, a randomized controlled trial conducted in four U.S. communities between 2000-2008 designed to determine efficacy of G. biloba supplements in decreasing risk of dementia. Gait speed was assessed annually with a timed 15 foot walk test. Falls were ascertained every 6 months by questionnaire. We investigated the association between gait speed and odds of falling for all participants in analyses adjusted for age, gender, and treatment assignment. We also evaluated these associations in analyses restricted to those with MCI. Results. We included 2,660 study participants with complete data for the variables of interest in the analysis. A one meter per second (m/s) increase in gait speed was associated with a 55% decrease in odds of a fall (95% CI: 26%, 73%). Although MCI was a significant predictor of falls (OR: 1.42; 95%CI: 1.10 to 1.85), in analyses restricted to participants with MCI (n=379), gait speed was not a significant predictor of fall risk (OR: 0.33; 95% CI: 0.10 to 1.05). Conclusions. We observed an association between slower gait speed and increased odds of a fall. However, gait speed was not a significantly associated with odds of falling in people with MCI. These findings have direct application to how gait speed can be used as a screening tool for fall risk in clinical practice.

Racial/ethnic differences in health-related quality of life among older adults with and without dementia in a nationally-representative sample Eleanor Hayes-Larson* Eleanor Hayes-Larson Taylor M Mobley Andrea Gilmore-Bykovskyi Jennifer J. Manly Elizabeth Rose Mayeda

Given the lack of effective preventive or disease-modifying treatments for dementia, maximizing quality of life is a major priority for persons with dementia. Despite well-documented racial/ethnic disparities in dementia incidence and prevalence, quality of life comparisons across race/ethnicity among persons with dementia in population-representative samples are lacking. We estimated racial/ethnic differences in health-related quality of life (HRQOL) among people with and without dementia in Wave 5 of the National Health and Aging Trends Study (2015). We examined indicators of 5 domains of HRQOL (depression, anxiety, overall health, pain, and functional limitations) reported by the participant or a proxy. We used sample-weighted relative risk regression models adjusted for sex and age and stratified by dementia (unweighted n=1550 with reported diagnosis, proxy-reported cognitive changes, or cognitive test score <1.5 standard deviations below mean in ≥1 domain) vs. no dementia (unweighted n=5632). The weighted dementia sample was 68% White, 14% Black, and 13% Latino. Screen-positive depression and anxiety were 26% and 22% prevalent, respectively; 41% reported fair/poor health, 40% had ≥1 functional limitation, and 57% were bothered by pain. After sex-and age-adjustment, Latinos with dementia had higher prevalence of screen-positive depression (prevalence ratio (PR) 1.42, 95% CI 1.09-1.85), screen-positive anxiety (PR 1.51, 95% CI 1.11-2.06), and ≥1 functional limitation (PR 1.20, 95% CI 0.98-1.48) than Whites with dementia. Both Blacks and Latinos with dementia were more likely to report fair/poor health than Whites with dementia (PR 1.28, 95% CI 1.08-1.52 and 1.48, 95% CI 1.21-1.81, respectively). Prevalence of reported pain was similar by race/ethnicity among those with dementia. Those without dementia reported lower prevalence of the other outcomes, but racial/ethnic differences tended to be larger. More work is needed to explain the drivers of these findings.
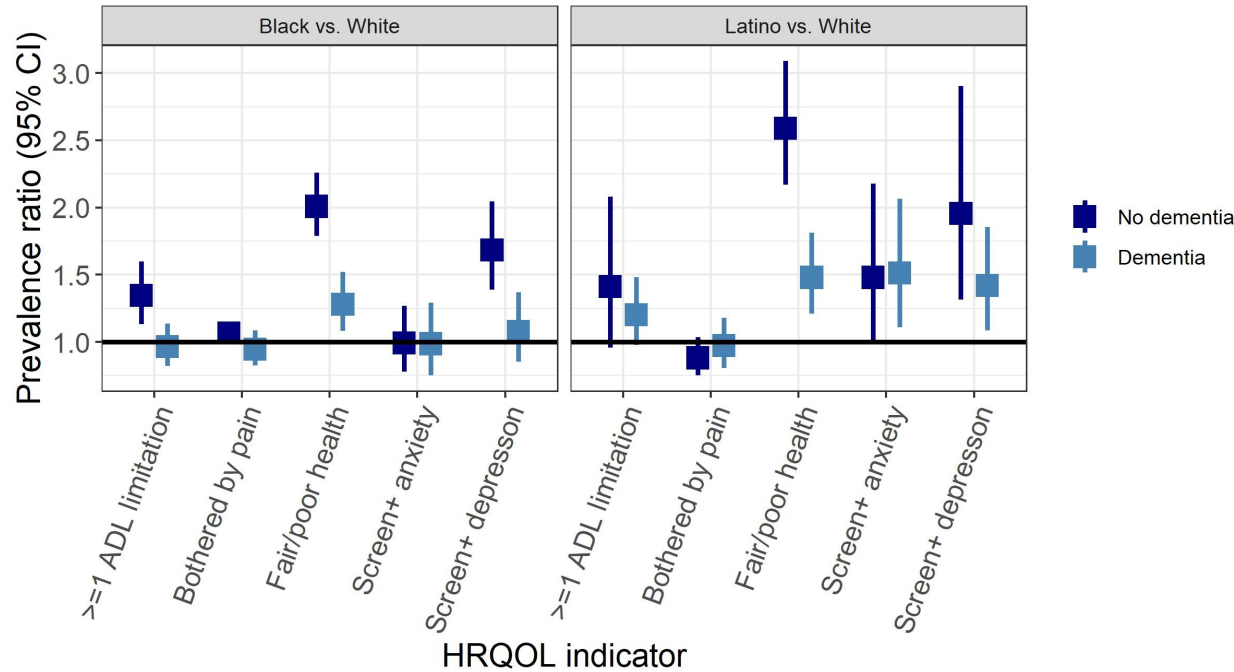
Figure: Prevalence ratios for HRQOL indicators among NHATS Wave 5 participants with and without dementia

Effect of cumulative exposure to psychosocial stressors at work on global cognitive function: A 25-year longitudinal study Caroline S. Duchaine* Caroline S. Duchaine Chantal Brisson Denis Talbot Michel Vézina Ruth Ndjaboué Caroline Diorio Yves Giguère Alain Milot Danielle Laurin

By 2050, an estimated 152 million people will be living with dementia. Prospective studies suggest that exposure to psychosocial stressors at work could be associated with a higher risk of mild cognitive impairment or dementia, but the evidence is still not clear. This study aimed to evaluate the effect of cumulative exposure to psychosocial stressors at work on global cognitive function in a cohort study followed for over 25 years. At baseline in 1991-1993 (T1), 9,188 white-collar workers were recruited. Two follow-ups were carried out in 1999-2001 (T2) and 2015-2019 (T3). This analysis was done among 5,728 participants working in T2, which participated in T3. Global cognitive function was evaluated with the validated Montreal Cognitive Assessment test and categorized in three groups according to standardized cut-offs. Psychosocial stressors at work were evaluated with validated questionnaires at each time. The effect of cumulative exposure to psychosocial stressors at work at T1 and T2 on cognitive function categories at T3 was estimated with marginal structural models using inverse probability of treatment and censoring weights. Each observation was weighted for the inverse of the probability of 1) death and lost to follow-up, 2) exposure at T1 according to potential confounders (age, sex, education, number of years in the same job) and 3) exposure at T2 according to exposure at T1 and potential confounders (same as those at T1 plus comorbidities, and lifestyle habits in T1). Multiple imputation of missing data was performed. Men or women, exposed to low psychological demand and men exposed to low job control at work at both T1 and T2 were at higher risk of moderate to severe cognitive impairment than non-exposed workers. (RR and 95% CI: 1.34 (1.09;1.64) and 1.34 (1.01;1.77) respectively). Primary prevention of cognitive impairment could be possible with the reduction of these modifiable stressors at work.

Aging

Modelling of dementia risk and health behaviour burden at the population-level Stacey Fisher* Stacey Fisher Douglas G Manuel Carol Bennett Yulric Sequeira Meltem Tuna Anan Bader Eddeen Mahsa Jessri Amy Hsu Laura Rosella Monica Taljaard Geoffrey Anderson Peter Tanuseputro

Background: Population-level primary prevention strategies for dementia are informed by population risk distribution and estimates of the burden of risk from modifiable risk factors. Population-based cohort data with follow-up for health outcomes allows for the use of a multivariable approach for risk assessment and risk factor burden estimation that has significant advantages over the more widely-used population attributable fraction approach. Methods: Five-year population risk and the number of incident dementia cases in Canada was estimated by applying a validated dementia risk algorithm to respondents of the 2013/14 Canadian Community Health Survey who were 55+ years of age (N = 62,528, representing 10 million Canadians). The burden of smoking, poor diet and physical inactivity in the presence of sociodemographic and other risk factors was evaluated by comparing the predicted risk in the current population with that from a population where poor health behaviours were eliminated. Results: The five-year estimated dementia risk was 3.8% for men and 5.2% for women, corresponding to an estimated 452,000 incident cases of dementia in Canada between 2013/14 and 2018/19. An estimated 31% (56,500 out of 181,000 incident cases) of dementia risk among males and 47% (127,000 out of 271,000 incident cases) of risk among females may be attributed to smoking, poor diet and physical inactivity. The leading risk factor among males was physical inactivity (13.3% attributable risk and 24,000 cases), while smoking was the leading risk factor among females (19.9% attributable risk and 54,000 cases). Conclusion: To our knowledge, this is the first time a multivariable approach has been used to evaluate population dementia risk and the burden of unhealthy lifestyle behaviours on this risk. These results will support implementation of Canada's recently-released dementia strategy by informing resource allocation decisions and the development of primary prevention strategies.

Aging

Health Correlates of Self-Reported Energy Levels in a Population-Based Cohort of High-Functioning Community-Dwelling Older Adults Rebecca Ehrenkranz* Rebecca Ehrenkranz
Andrea Rosso Teresa Tian Nancy Glynn Caterina Rosano

Introduction:
While fatigue in older age has been well studied in relation to negative health outcomes, the clinical relevance of maintaining higher energy late in life is less known. We explored associations of self-reported energy levels with health characteristics, physical function, and mood.
Methods:
The Health, Aging and Body Composition study collected data on high functioning older adults(N=2,529, mean age 75.7, 58.3% white, 51.5% women, median Modified Mini Mental State Exam score: 92.0). Self-report of energy level over the past month was recorded on a scale of 0-10, from least to most energy. Health characteristics included presence/ absence of diabetes, cancer, hypertension, peripheral artery disease, and arthritis (per self-report and medication history); physical function metrics of fitness (measured via 400 meter walk), strength (via Kin-Com dynamometer), physical activity (by self-report); and mood (Center for Epidemiologic Studies Depression scale). Variables bivariately associated with energy entered a multivariate linear regression model, adjusted for age, race, sex, education, and body mass index.
Results:
Self-reported energy score was normally distributed and greater for women, blacks, and those with less education (p<0.05). In the multivariable model, higher self-reported energy was associated with lower prevalence of peripheral artery disease (β = -0.48 [-0.83, -0.13]) and hypertension (β= -0.18 [-0.34, -0.03]), better fitness (indicated by faster 400 meter walk time (β = -0.004 [-0.005, -0.002]), greater physical activity (β=0.0005 [0.0002, 0.0009]), and lower depressive symptoms (β = -0.14 [-0.16, -0.12]).
Conclusion:
In this cohort of high-functioning older adults, self-report of higher energy indicates overall better function, independent of demographics. Future studies should validate self-reported energy against objective energy metrics, and evaluate if longitudinal changes in energy protect against clinical and functional outcomes.

Aging

Feasibility of Community-Delivered Baduanjin (八段錦) Training to Improve Functional Performance of Frail Older Adults Xiao Liu (Alisa)* Xiao Liu Jean Seah Benedict Pang Mary Ann Tsao Ng Wai Chong Gu Falong Junie Tay

Background:
Studies have explored the health benefits of Baduanjin (BDJ) among different populations but not frail older adults. This study aimed to investigate the feasibility and effects of a community-delivered BDJ training program among pre-frail/frail community-dwelling older people.

Methods:
In this single-arm feasibility study, twelve prefrail/frail older residents participated in a group-based, 16-week BDJ training. Frailty status was determined using Frailty Phenotype. Attendance and adverse events were recorded throughout the training. Effects of the intervention on physical and functional outcomes (hand grip strength, knee extension strength, Time Up and Go (TUG), Physiological Profile Assessment (PPA), 30-second Sit-to-Stand test, 6-meter fast gait speed test), frailty outcomes (frailty score and status), and other outcomes (Maastricht Questionnaire (MQ), Fall Efficacy Scale (FES), Montreal Cognitive Assessment (MoCA), Geriatric Depression Scale (GDS), and EQ-5D-5L) were examined before and after the program.

Results:
Eleven participants (aged 77±6 years; 2 frail, 9 prefrail at baseline) completed the program with an average overall attendance of 89%. There were significant improvements in hand grip strength (p=0.013), knee extension strength (p=0.048), TUG (p=0.018), MQ (p=0.001), FES (p=0.022), MoCA (p=0.014), GDS (p=0.028), EQ-5D-5L index score (p=0.029). The reduction of frailty score and PPA fall risk score showed moderate-to-large effect size. Participants either reversed (n=2) or maintained (n=9) their frailty statuses. The program received positive feedback with no training-related adverse events.

Discussion and Conclusion:
Community-delivered BDJ training program was safe and feasible for prefrail/frail older adults with the potential to improve physical and cognitive function, reduce fall risk, improve psychological well-being, and reverse frailty status.

Childhood Infectious Disease Burden, Adult Height, and Incident Late Life Cognitive Impairment Rindcy Davis* Rindcy Davis Sarah Tom Amelia Boheme Cheyanne Barba Michael Crowe

Background: Childhood infectious disease burden (CIDB) may divert energy resources from cognitive and physical development. It is unclear if CIDB is associated with cognition in older adulthood. We test the hypotheses that 1) greater CIDB is associated with increased risk of incident cognitive impairment and 2) this relationship will be stronger among those of short stature, an indicator of poor nutritional availability. Methods: Data were obtained from 2,585 men and women ($\geq$60 years) of the Puerto Rican Elderly: Health Conditions study. Cognition was based on Mini-Mental Caban scores regressed on age, female gender, years of education, and self-reported reading ability and was measured at baseline(2002-2003) and at follow-up(2006-2007). The CIDB variable was a sum of reported dengue fever, malaria, typhus fever, rheumatic fever, hepatitis, tuberculosis, and polio, categorized as 0,1,$\geq$2 infections. Models were adjusted for childhood socioeconomic status, number of siblings, rural residence during childhood, mother's reading ability, baseline vascular risk factors, and adult socioeconomic status. Results: The majority of participants were female (62%), completed less than high school education (64%), could read (93%), had mothers who could read (66%), and had no difficulty paying for health/living expenses (83%). Participants who reported $\geq$2 infections during childhood had increased odds (Adjusted OR (AOR):2.26; 95%CI:1.10,4.65) of incident cognitive impairment, compared to those with no history of childhood infections. Each inch of height was associated with a 9% decrease in the odds of incident cognitive impairment (AOR:0.91; 95%CI:0.88,0.95). The relationship between CIDB and incident cognition did not vary by height. Discussion: Greater CIDB and shorter height were associated with greater odds of incident cognitive impairment. Future studies should examine potential adult life mediators.

Aging

Development of a 20-year dementia risk score calculator: cross-validation prevented elimination of variables compared to a p-value approach S. Rae Wannier* S. Rae Wannier Irene Yen

To estimate future dementia risk in the US, we develop a twenty-year cumulative dementia risk calculator. Data come from the Health and Retirement Study, 1992 cohort (aged 50-65 at first cognitive assessment), with cognitive assessments through 2016 (N=7,780). We predicted a previously developed dementia probability score (range:0-1), with estimates at each wave to create 20-year cumulative dementia risk models. Candidate variables (and interactions) were: baseline cognitive assessment (immediate and delayed word recall (WR), serial 7 subtractions, and backwards counting from 20 and 86), childhood socioeconomic variables, comorbid conditions, health behaviors and demographics. To optimize model fit we compared [1] linear regression without cross-validation (retained variables $p<0.05$), [2] linear regression with k-fold cross-validation, and [3] LASSO with k-fold cross-validation. Cross-validation models had k=5 folds and variables were retained to minimize mean-squared error (MSE). Model fit was compared using MSE. In linear regression without cross-validation, retained variables were: age, race, immediate WR (with age, race interactions), delayed WR, serial 7 subtractions, backwards counting from 20 and 86, sex, maternal education, occupation, employment status, home ownership, Southern birth, smoking status, hypertension, and diabetes (MSE=0.01770; fig 1). Compared to linear regression without cross validation, performing cross-validation retained: foreign-birth, interactions for delayed and immediate WR with age and race, and age with backwards counting from 86 and serial 7's (MSE=0.01764). Compared to linear regression without cross validation, LASSO retained: foreign-birth and interactions for immediate WR with age and race, but excluded occupation (MSE=0.01767). All models meaningfully predicted dementia; the three approaches retained similar variables, though cross-validation retained more variables than the conservative p-value threshold approach.
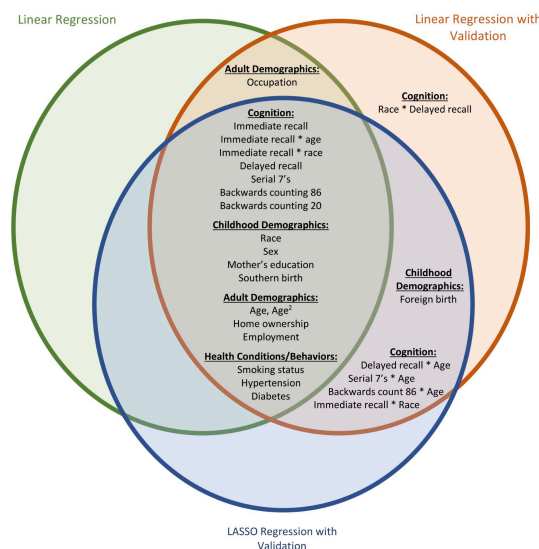
Figure 1. Venn diagram showing the retention and elimination of variables in the risk score calculator across the three model building approaches [1] linear regression without cross-validation (retained variables p<0.05), [2] linear regression with k-fold cross-validation, and [3] LASSO with k-fold cross-validation. MSE was used to compare model fit during cross-validation.

Aging

Anticholinergic and Sedative Drug Load Among Medicare Beneficiaries Shahar Shmuel*
Shahar Shmuel Virginia Pate Marc J. Pepin Janine C. Bailey Laura C. Hanson Til Stürmer Rebecca B. Naumann Yvonne M. Golightly Danijela Gnjidic Jennifer L. Lund

Background: Medications with anticholinergic and sedating properties are widely used among older adults despite strong evidence of their harm. The Drug Burden Index (DBI), a clinical screening tool that incorporates dose and cumulatively measures these properties across drug classes, may identify patients at high risk of physical and cognitive function-related adverse events. However, the DBI has been studied mainly outside the US, and not using US Medicare claims.

Methods: We screened medications for DBI properties and operationalized the DBI for Medicare claims. We then conducted a retrospective cohort study of a 20% random, nationwide sample of 4,137,385 fee-for-service Medicare beneficiaries aged 66+ years (134,757,062 person-months) from 2013 to 2016. We measured the monthly distribution based on mean daily DBI, categorized as (1) >0 vs. 0 (any use) and (2) 0, 0<DBI≤1, 12, and examined temporal trends. We described patient-level factors (e.g., demographics, healthcare use, and health status) associated with high (>2) versus low (0<DBI≤1) DBI exposure.

Results: The person-month distribution of the mean daily DBI was: 58.1% DBI=0, 29.0% 0<DBI≤1, 9.3% 12. The estimated annual period prevalence of any (>0) DBI exposure decreased slightly over the study period, while the monthly point prevalence was stable. Predictors of high monthly DBI exposure (>2) included certain indicators of increased healthcare use (e.g., high number of drug claims), white race, younger age, low-income subsidy, frailty, and a psychosis diagnosis code.

Conclusions: This study operationalized the DBI in Medicare claims and described patterns of DBI exposure over time. The predictors of high monthly DBI exposure can be used to inform discussions between patients and providers about medication appropriateness and potential de-prescribing. Future studies should assess the association between the DBI and adverse events among Medicare patients.

Aging

The Role of Sleep Apnea in APOE-Alzheimer's Disease Pathway Krupa Hegde* Krupa Hegde
Xiuhua Ding Marylin Gardner

Background: Previous studies have shown contradictory findings on if the APOE gene is associated with sleep apnea. Thus, the goal of this study is to examine the relationship between the APOE gene and sleep apnea and investigate whether levels of amyloid beta in cerebrospinal fluid (CSF) depend on sleep apnea and/or APOE gene. Methods: Data was obtained from the National Alzheimer's Coordinating Center (NACC). We restricted participants to those who were enrolled at or after 2015 due to availabilities of sleep apnea measurements and with normal cognition status at enrollment. CSF sample data for a subset of these participants were merged to initial visit data by subject ID and year of visit. Logistic regression was used to investigate the association between sleep apnea and APOE and backward elimination was used to identify a final model. T-tests were used to compare the mean levels of CSF amyloid beta between APOE gene groups and between sleep apnea groups, respectively. Results: Of a total of 1630 subjects identified to meet criteria, 3.83% participants had sleep apnea and are APOE ε4 carriers, 26.87% did not have sleep apnea and are APOE ε4 carriers, 9.88% had sleep apnea and are APOE ε4 non-carriers, 59.45% did not have sleep apnea and are APOE ε4 non-carriers. Logistic regression showed that sleep apnea was not significantly associated with APOE gene after adjusting age, gender and BMI. The mean levels of CSF amyloid beta among APOE ε4 carriers (mean± SD: 414.7±241.7) were lower than APOE ε4 non-carriers (mean± SD: 500.9±150.5), and the mean levels of CSF amyloid beta among sleep apnea subjects (mean± SD: 434.6±90.1) were lower than subjects without sleep apnea (mean± SD: 504.9±194.3). However, the differences were not statistically significant. Conclusion: In this study, sleep apnea was not significantly associated with APOE in the NACC sample and the mean levels of CSF amyloid beta did not depend on sleep apnea or APOE gene in cognitively normal subjects.

Aging

Distinct Plasma MicroRNA Signature at Advanced Age Predicts Lifespan but not Health-span

Julia W Wu* Julia Wu Michelle Mens Jaap Goudsmit Jaco Klap Yuan Ma Albert Hofman Alfan M Ikram Mohsen Ghanbari

MicroRNAs (miRNAs) are small noncoding RNAs that regulate protein-coding gene expression. Evidences from small sample-sized studies have shown differentially expressed miRNAs in relation to age. We hypothesized that a plasma-based miRNA signature of age is predictive of chronological age and can be used as a biomarker of risk for all-cause mortality. We determined 2083 miRNAs expression by HTG EdgeSeq miRNA Whole TranscriptomeAssay in plasma of 1,930 participants in the Rotterdam Study Cohorts with a mean age of 72 years, followed from 2000-2012. After normalization 591 miRNAs were available for analysis. We used elastic net regression and cross-validation to build an age prediction model while adjusting for gender. We used Cox proportional hazard models to assess the association between miRNA DeltaAge (miRNA predicted age minus chronological age) and risk of mortality as well as first major morbidity, with adjustment for chronological age, APOE status and gender. Of 1,930 participants, 696 had mortality over 12 years of follow-up. Of the 591 miRNAs remained after normalization, we identified 291 miRNAs that were differentially expressed in relation to age, at $p < 8.5 \times 10^{-5}$ (Bonferroni-corrected). The top three significant miRNAs were: miR_19b_3p, miR_3141 and miR_197_5p. The predicted miRNA Age was highly correlated with chronological age (r=0.58). Each additional year increase in miRNA DeltaAge was associated with 9% elevated risk (HR= 1.09, 95%CI 1.05-1.13) of mortality, after adjusting for age, APOE status and gender. When we assessed the association of miRNA Delta Age and risk of developing first major morbidity, no evidence was found (HR=1.007, 95%CI 0.96-1.05). To our knowledge we have first systematically described a distinct plasma miRNA age signature in an advanced-age cohort. The plasma-based miRNA age predictor was associated with lifespan but not health-span, shedding lights on the complicated process of human aging and aging-related outcomes.

Figure 1. Relationship between miRNA Age and chronological age, in the validation set (n=720), the Rotterdam Study, 2000–2012. (a) miRNA Age was highly correlated with chronological age (r=0.58). (b) miRNA Delta Age was normally distributed.
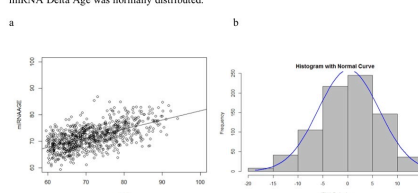
Association Between Neighborhood Characteristics and Neuropsychiatric Symptoms Among Community-Dwelling Older Adults with Alzheimer's Disease Dana AlHasan* Dana AlHasan Matthew Lohman Jana Hirsch Maggi Miller Bo Cai

Neuropsychiatric symptoms, NPS, are among the most complex, stressful, and costly aspects of care and lead to a myriad of poor health outcomes among those experiencing dementia. Little work has investigated the role of neighborhood characteristics on dementia and dementia symptomology, including NPS. This study 1) examined the geographic distribution of dementia incidence from 2010-2014 in South Carolina (SC); and 2) estimated cross-sectional associations between neighborhood characteristics and NPS among community-dwelling older adults with dementia living with a caregiver in 2010 in SC. Diagnosed dementia cases and data on NPS among those with dementia were obtained from the SC Alzheimer's Disease Registry and a subset of data collected from the Registry, respectively. Neighborhood measures (within ½-mile of residence) came from the Decennial Census, American Community Survey, and Rural Urban Commuting Area Code. Standardized dementia cases were mapped across SC census tracts. To estimate the associations between neighborhood social characteristics and NPS (n=212), we conducted a negative binomial regression. The overall standardized dementia incidence rate was 4.43% (95% CI= 4.34-4.47). In an adjusted model, neighborhood characteristics had a significant association with NPS. We estimated those who live in low income neighborhoods (defined as <$30,500) had 1.53 (95%CI = 1.06-2.23) times higher NPS score as those who live in high income neighborhoods (defined as $40,000) after adjusting for individual level age, sex, race/ethnicity, caregiver education, rurality, and residential instability. The results from this study show people with AD experience greater symptomology when living in greater socioeconomic disadvantaged areas. Future research should explore potential mechanisms for this relationship. Independent of mechanisms, identifying neighborhood characteristics associated with high NPS is important for resource allocation and in the management of dementia symptoms.

Age-Sex Standardized Dementia Incidence Rate per 100,000

- 0
- 0.1 - 1000.0
- 1000.1 - 5000.0
- 5000.1 - 10000.0
- 10000.1 - 34514.0

0   15   30   60 Miles

N

Aging
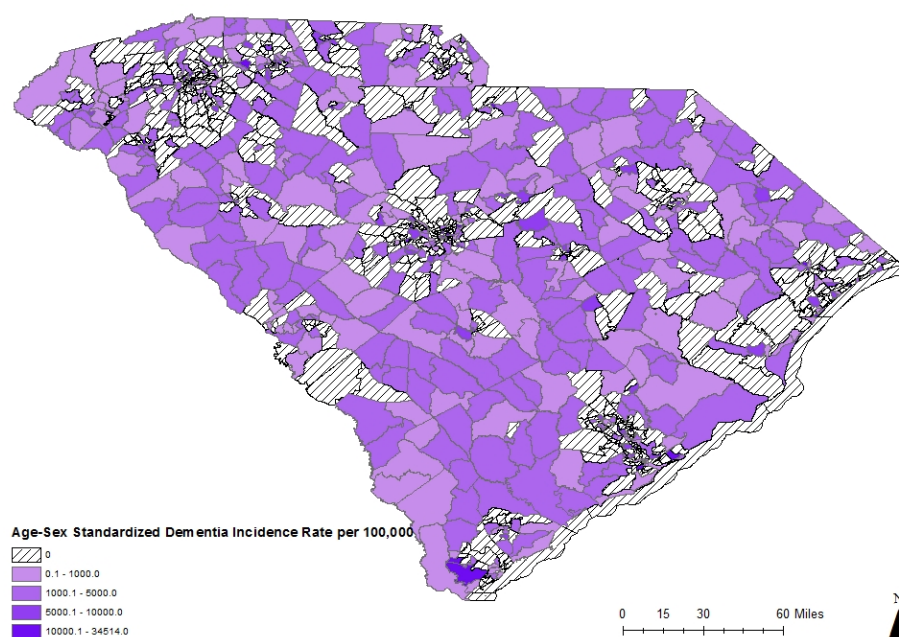
Poor oral health and incidence of disability: results from studies of older people in the uk and usa Eftychia Kotronia* Eftychia Kotronia S. Goya Wannamethee A. Olia Papacosta Peter H. Whincup Lucy T. Lennon Marjolein Visser Robert J. Weyant Sheena E. Ramsay

Background: To examine the association between oral health markers and disability 4 years later in two population-based studies of older people in the UK and USA.

Methods: Analyses were conducted in the British Regional Heart Study (BRHS) comprising older men (n=2147) and the Health, Aging and Body Composition (HABC) Study comprising American older men and women (n=3075). Data from a 4-year follow up period were used. Oral health measures included tooth loss, periodontal disease, dry mouth, and self-rated oral health. Mobility limitations and Activities of Daily Living (ADL) were markers of disability. Logistic regression was performed and analyses were adjusted for confounders (age, socioeconomic position, lifestyle factors, and chronic diseases).

Results: Over a 4 year follow-up, 15% of subjects in the BRHS and 19% in the HABC Study developed mobility limitations. In both studies, 12% of participants developed ADL problems. In the BRHS, tooth loss (complete and partial), periodontal disease, dry mouth, difficulty eating and accumulation of oral health problems were associated with an increased risk of developing mobility limitations after adjustment for confounders (partial tooth loss, OR=1.86, 95% CI 1.18-2.94, ≥3 dry mouth symptoms, OR=1.97, 95%CI 1.25-3.09). Similar results were observed for the risk of developing ADL problems. In the HABC Study, complete tooth loss and accumulation of oral health problems were associated with greater risk of incident mobility limitations (OR=1.77, 95%CI 1.13-2.76; OR=1.18, 95% CI 1.02-1.37, respectively). Moreover, self-rated oral health and difficulty eating were associated with increased risk of ADL problems, after adjustment for confounders.

Conclusion: Poor oral health was associated with increased risk of developing disability in community-dwelling older people. Underlying pathways, such as inflammation and nutrition, should be examined in future studies.

Helicobacter pylori, periodontal pathogens and their interactive association with incident all-cause and Alzheimer's Disease dementia in a large national survey MAY A. BEYDOUN* MAY BEYDOUN HIND A. BEYDOUN JORDAN WEISS ZIAD W. EL-HAJJ ALAN ZONDERMAN SHARMIN HOSSAIN

Co-infection between Helicobacter pylori (Hp) and groups of periodontal pathogens may alter the onset of Alzheimer's Disease (AD) and all-cause dementia. We examined the interactive associations among Hp sero-positivity, periodontal disease (Pd) and infections with incident AD and all-cause dementia, among older adults (≥65y at baseline). Up to 1,431 participants from phase 1 of the National Health and Nutrition Survey III (1988-1991) had complete data till January 1st, 2014 on Hp sero-positivity with a mean follow-up of 10-11years for AD and all-cause dementia incidence. Exposures consisted of 19 periodontal pathogens, constructed factors and clusters, and two Pd markers- probing depth and clinical attachment loss (CAL). Cox proportional hazards models were performed. Around 55% of the selected sample was Hp+. We found that Prevotella intermedia, Campylobacter Rectus, Factor 2 (Pi/Prevotella nigrescens/Prevotella melaninogenica), and the Orange-Red cluster interacted synergistically with Hp sero-positivity, particularly with respect to AD incidence. The presence of higher levels of Actinomyces Naeslundii (An) enhanced the effect of being Hp+ on both AD and all-cause dementia incidence. In contrast, Fusobacterim nucleatum (Fn), and Factor 1 (which included Fn), exhibited an antagonistic interaction with Hp in relation to all-cause dementia. Both probing depth and CAL had direct associations with all-cause dementia among Hp+ individuals, despite non-significant interaction. Selected periodontal pathogen titers, factors and clusters interacted mostly synergistically, with Hp sero-positivity, to alter the risk of AD and all-cause dementia. Ultimately, a randomized controlled trial is needed, examining effects of co-eradication of Hp and select periodontal pathogens on neurodegenerative disease.

Aging

School quality and later life self-rated cognitive impairment – considering study enrollment and selective survival Dominika Seblova* Dominika Seblova Kelly Peters Susan Lapham Laura Zahodne Ben Chapman Carol Arlene Prescott Tara Gruenewald Thalida Em Arpawong Margaret Gatz Jennifer J. Manly

Background: Longer education predicts better cognitive health, but less is known about other aspects of education such as school quality. We examined the association of high school quality with self-reported cognitive complaints in later life and considered selective enrollment and survival.

Methods: In 1960, about 5% of all US high schools participated in Project Talent (PT). PT measured demographic and aptitude data in students in selected schools and gathered objective information about school characteristics. In 2018-2019, 22,600 participants were sampled for follow-up, yielding 6,465 respondents (mean age=74.6), 10,638 were not found or did not respond, and 5,497 deceased prior to 2018. A latent school quality factor, capturing term length, class size, and teacher qualifications, was used as a predictor of the odds of subjective cognitive impairment (a score of 2 or greater on the AD8 Dementia Screener). Logistic regression models controlled for cognitive aptitude in 1960, sex, age, race, and a composite measure of parental socioeconomic status (SES). The role of selective enrollment and survival was examined using inverse probability weighting (IPW).

Results: Compared to non-respondents and those who died, respondents had higher adolescent cognitive aptitude, parental SES, and school quality and were more likely to be White. About 17.7% (n=1,141) of respondents met criteria for cognitive impairment in 2018. Unweighted models indicated that higher school quality in 1960 predicted lower risk of cognitive impairment 58 years later (OR=0.93 95% CI: 0.86-0.99). IPW showed that the unweighted models underestimated the magnitude of the association by about 4%. The magnitude of underestimation was similar when considering selective enrollment versus survival.

Discussion: Lower high school quality was associated with later life cognitive impairment. Failing to take selective study enrollment and survival into account underestimates the magnitude of the association.

Aging

Influence of school starting age and preschool on late-life cognition: does timing and type of entry into schooling matter? Chloe W. Eng* Chloe W. Eng Anusha Vable Paola Gilsanz Jennifer Manly Rachel Whitmer Maria Glymour

Introduction: Higher levels of completed education are known to benefit later-life cognition. However, the relationship with cognitive decline remains poorly understood and research to-date has focused on attained education but not characteristics of how and when people enter into schooling, despite evidence that the early childhood environment impacts brain development.

Methods: We characterized effects of entrance into education on memory scores for a subset of 5,493 Health and Retirement Study participants completing the 2015 or 2017 Life History Mail Surveys. Average memory performance and decline across all available biennial survey waves from 1998 to 2016 (average follow-up: 4.8 visits) were estimated for independent and joint effects of preschool attendance and elementary school entry age (as 5 or less verses 6+) using sociodemographic-adjusted [quadratic interview age, gender, race, birthplace region (South, West, Northeast, Midwest), parental education, memory practice effect] mixed linear regression models with random age slopes, with subsequent adjustment for own years of attained education.

Results: Average entry age was 5.49 ± 0.93; 14.0% of participants reported preschool attendance. Elementary school entry after age 5 was associated with cognitive scores that were -0.02 (95% CI: -0.02, -0.02) points lower than those entering age 5 or earlier and a 5-year memory decline that was 0.01 (95% CI: -0.02, -0.01) points faster than those who entered school earlier, unchanged after adjustment for attained education. Preschool was not associated with performance (B: 0.00, 95% CI: -0.01, 0.01) or decline (B: 0.00, 95% CI: -0.00, 0.00); no joint effect of entry age and preschool for cognitive performance (p= 0.56) or decline observed (p=0.38).

Conclusion: Earlier entry into schooling showed small but significant benefits for late-life cognitive performance and decline; effects persisted independently of own attained education and preschool attendance.

Aging
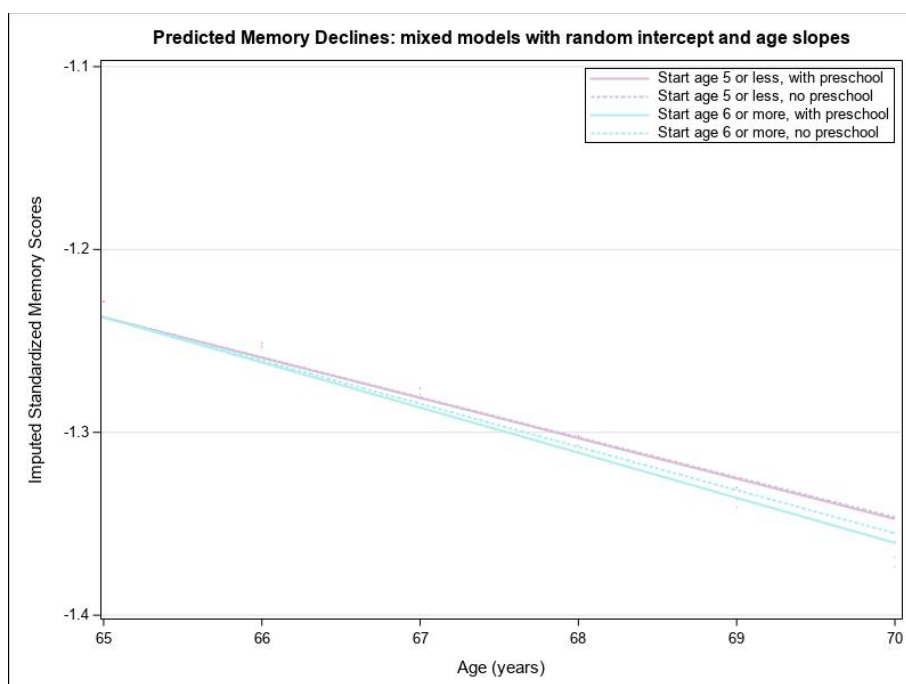
Estimating the cognitive effects of migration to the US and Mexico for older Mexicans: a comparison of migrants, return migrants, and non-migrants Audrey Rose Murchland* Audrey Murchland Adina Zeki Al Hazzouri Scott C. Zimmerman Alicia Riley Rebeca Wong Mary Haan Jacqueline M.Torres Richard N. Jones M. Maria Glymour

Background: To evaluate the effects of migration from Mexico to the US, it is important to include non-migrants, migrants, and return migrants and to account for lifecourse selection.
Methods: We merged data for Mexicans living in Mexico who participated in the Mexican Health and Aging Study (N=17,260; N=15,763 non-migrants and N=1,497 return migrants) with data for Mexican-born migrants living in the US participating in the Health and Retirement Study (n=854). We examined a harmonized global measure of cognition (calibrated to the US population aged about 70 in 1998) assessed in 2000/2001, 2002/2003, and 2012 (HRS/MHAS, respectively) for Mexican migrants, return migrants, and non-migrants, before and after accounting for sociodemographic factors that predict migration, return migration, and late life cognition. Linear mixed effects models (linear splines with a knot at age 70 to account for nonlinearities) were adjusted for sex, birth year, and parental education with inverse probability weights for migration and return migration; weights were estimated based on time-constant variables, years of education and age at life events (marriage, divorce or widowhood, labor force entry, and smoking initiation).
Results: Mean baseline age was 61 years (9 SD). Global memory score at age 50 was 0.66 (95% CI: 0.57, 0.75) higher among US-residing migrants compared to non-migrants. Rate of memory decline per decade before age 70 was slower among US-residing migrants compared non-migrants (b=0.02; 95% CI: -0.054, 0.094). Level and rate of change in global cognition did not differ between non-migrants and return migrants (Figure 1).
Conclusions: US residing migrants averaged higher levels of global cognition compared to non-migrants and return-migrants residing in Mexico. Selective migration partially explains differences in rates of cognitive decline between these groups. Comparing internal migrants in Mexico to stayers may help further address selection bias.

Figure 1. Predicted memory trajectories by migration group from adjusted linear mixed effects models, shown for females.
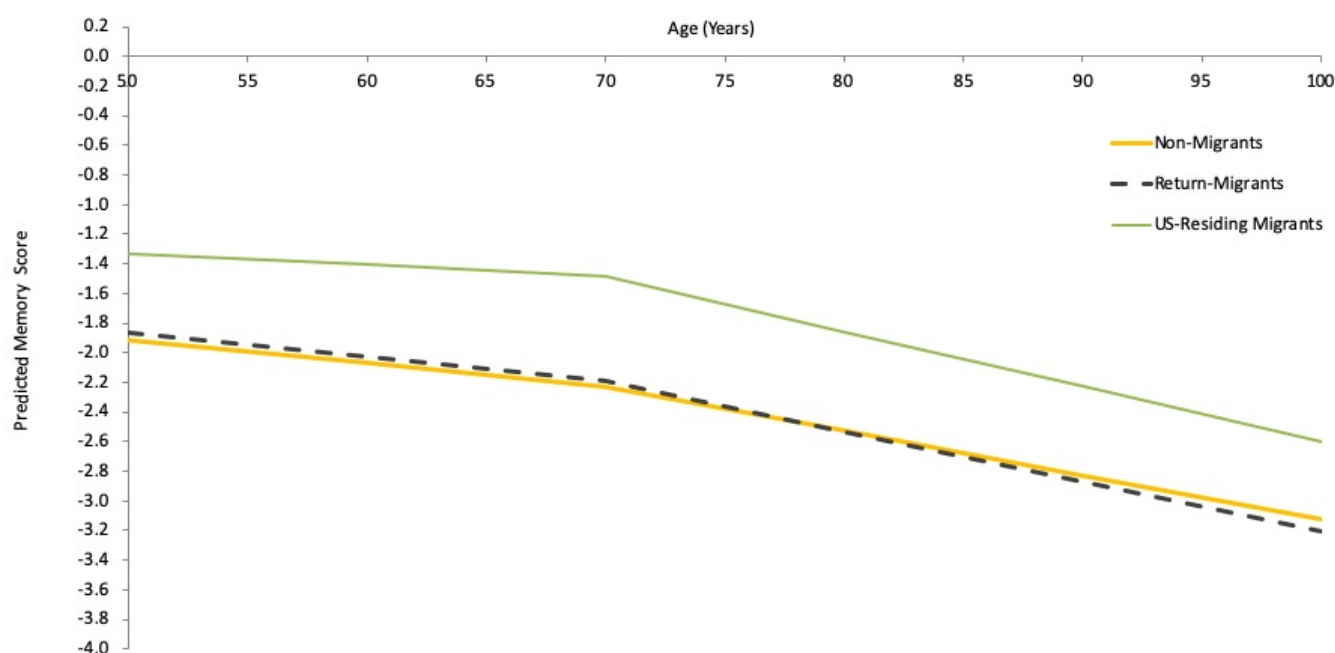
Long term impact of 9/11 disaster related chronic disease on physical and mental health functional status Robert Brackbill* Robert Brackbill Sean Locke Erin Takemoto Howard Alper James Cone

The World Trade Center (WTC) disaster was an unprecedented exposure of up to 400 thousand persons to airborne toxins, psychological trauma, and potential injury. WTC exposure related health outcomes include asthma, heart disease, diabetes and other chronic diseases. We examined the long-term impact of chronic conditions, including multi-morbidity, on physical and mental health functional status 16 years after the event.

Since 2003, the World Trade Center Health Registry has followed 71,000 persons exposed to the 9/11 disaster. Four waves of interviews have provided self-reported diagnosed chronic conditions and mental health symptom screening. A fifth focused survey (N=4994) in 2017 measured physical and mental health status using the Short Form-12. Among participants without a history of post-traumatic stress disorder, we assessed the prevalence of different combinations of conditions (multi-morbidity). We also used linear regression to model the physical and mental component summary scores (PCS-12; MCS-12; range 0-100, higher scores indicate better health status) with the number of chronic physical and mental health conditions.

The prevalence of diagnosed chronic conditions ranged from hypertension (47%) to stroke (2%). The most prevalent multi-morbidity was hypertension and cancer (5.2%) (Figure). There was a direct relationship between number of chronic physical health conditions diagnosed since 2005 and difference in PCS-12 mean score relative to no condition of -3.5 (95% CI, -4.0, -2.9) for one condition and -9.2 (95% CI, -10.9, -7.4) for 3 conditions. There was also a significant association between number of physical health conditions and MCS-12 with a difference of -5.6 (95% CI, -7.1, -4.2) for 3 physical health conditions.

These results indicate that 9/11 exposed populations may be vulnerable to reduced functional status for nearly two decades after the event with implications for increasing burden on societal and family resources and capacity.
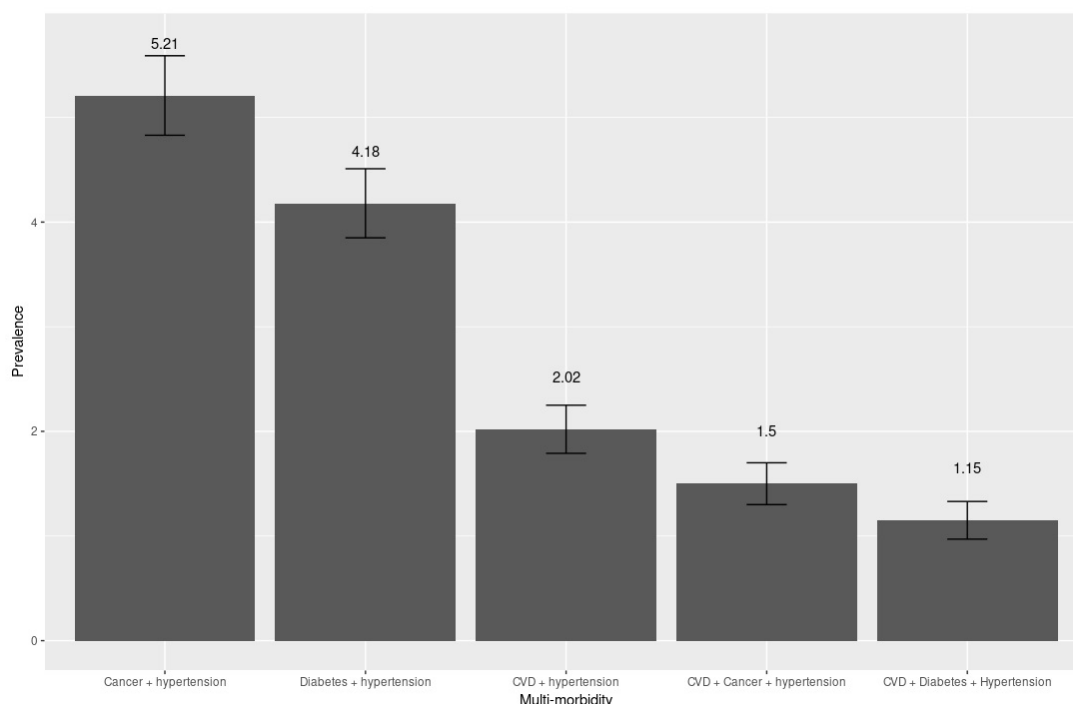
LATEBREAKER

Aging

The Association Between Cumulative Stressors Across the Life Course and Cognitive Function In Late life Ruijia Chen* 3647] Chen David Williams Laura Kubzansky Jennifer Weuve

Background: Cumulative stressors across the life course have been linked to various health outcomes, but their relationships with late-life cognitive function remain unclear. One methodological challenge related to the understanding of life course stressors and late-life cognitive function is accounting for treatment-confounder feedback, where the confounders affect the exposures and prior exposures affect the confounders. As standard statistical adjustment approaches tend to introduce bias in estimates in the presence of treatment-confounder feedback, g-methods such as marginal structural models are required. This study aims to use marginal structural models to quantify the associations of cumulative stressors across the life course with executive function and episodic memory in late life.

Method: Data came from the Midlife Development in the United States Study (MIDUS) (N=3,819). Cumulative stressors were operationalized using ten domains of acute and chronic stressors in childhood and adulthood. To estimate the differences in cognitive performance across levels of stressors, we conducted weighted generalized estimating equations (GEE) analyses with an identity link and normal distribution, accounting for twin and sibling clusters. We fitted separate models for different types of exposures, starting with counts of cumulative stressors and progressing to continuous cumulative stressors. Additionally, we conducted GEE models to assess the relationship between life course stressor profiles (no high stressors during childhood and adulthood, childhood-only high stressor, adulthood-only high stressor, or persistent high stressors during childhood and adulthood) and cognitive performance at MIDUS2, with the "no high stressors during childhood and adulthood" category serving as the reference group. Lastly, we performed weighted GEE models to quantify the differences in rates of changes in cognitive performance over time across levels of stressors.

Conclusion: Our findings reinforce the importance of using rigorous methods to account for the bias induced by treatment-confounder feedback in life-course epidemiology. As cumulative stressors are strongly associated with levels of executive function and episodic memory, interventions and programs should target structural factors that shape exposure to stressors at the population level.

Life-course Cumulative Stressors and Cognitive Function in MIDUS2 (N=3,954)

	Weighted, adjusted for pre-childhood confounders β (95% CI)		Unweighted, adjusted for pre-childhood confounders β (95% CI)		Unweighted, adjusted for pre- and post-childhood confounders β (95% CI)	
	Executive Function	Episodic Memory	Executive Function	Episodic Memory	Executive Function	Episodic Memory
Continuous Stress, per one SD	-0.10 (-0.14, -0.05) c	-0.09 (-0.15, -0.03) c	-0.11 (-0.14, -0.08) c	-0.07 (-0.11, -0.04) c	-0.08 (-0.11, -0.05) c	-0.07 (-0.10, -0.03) c
Count stress						
0 high stressor	ref	ref	ref	ref	ref	ref
- 1-2 high stressors	-0.19(-0.31, -0.06) b	-0.15 (-0.29, -0.004) a	-0.08 (-0.16, -0.005) a	-0.04 (-0.13,0.04)	-0.05 (-0.13,0.02)	-0.03 (-0.12,0.05)
- 3-4 high stressors	-0.32 (-0.48, -0.17) c	-0.23 (-0.39, -0.06) b	-0.21 (-0.30, -0.12) c	-0.13 (-0.22, -0.04) b	-0.14 (-0.22, -0.05) b	-0.09 (-0.19,0.0001)
- ≥5 high stressors	-0.43 (-0.62, -0.24) c	-0.34 (-0.59, -0.08) c	-0.30 (-0.41, -0.20) c	-0.23 (-0.35, -0.12) c	-0.17 (-0.27, -0.07) c	-0.18 (-0.29, -0.06) b

Note:
- CI: confidence interval
- Generalized estimating equations (with normal distribution and identity link) were used to estimate the mean scores in cumulative stressors with cognitive function, adjusting for clustering by sibling status.
- Pre-childhood confounders included age, sex, race/ethnicity status, and parent's education levels.
- Post-childhood confounders included annual household income, education, whether had chronic conditions or not, marital status, current working status, whether had a child or not
- Multiple imputation results are from 50 imputed data sets.

Transient and chronic loneliness on risk of incident stroke in middle and late adulthood

Yenee Soh* 3647] Soh

Background

Loneliness has been implicated to be a risk factor for cardiovascular disease, yet no study has examined how patterns of loneliness are associated with risk for incident stroke.

Methods

We analyzed individuals from the Health and Retirement Study (HRS) who were aged >50 years and stroke-free at study baseline (2006/2008 - 2010/2012), over which loneliness was assessed (N=8,936). Loneliness was measured at 2 consecutive time points for rotating 50% subsamples of the HRS every 4 years (high defined as score ≥6 ; low as score <6). Individuals were assigned to groups based on their dichotomized loneliness scores across the two time points (consistently low, decreasing, fluctuating, increasing and consistently high). Incident stroke was assessed over a subsequent 6-year period, based on self-reported doctors' diagnoses. Analyses were conducted with Cox proportional hazards models adjusted for demographics, health behaviors and health conditions.

Results

During follow-up, 375 incident strokes occurred. Individuals with consistently high loneliness scores had a significantly higher hazard ratio (fully adjusted HR: 1.67, 95% CI: 1.10-2.52) than the consistently low group (reference). Individuals in the decreasing and increasing groups did not show increased stroke risk relative to those with consistently low symptoms. Sensitivity analyses adjusting for depressive symptoms and social isolation minimally attenuated the results.

Conclusions

Among middle-aged and older U.S. adults, chronic loneliness was associated with increased hazard of stroke. This study emphasizes the public health significance of loneliness for risk of stroke, and suggests those who are chronically lonely might be an important target for clinical care.

Adult child educational attainment and cognitive aging among older parents: new directions in intergenerational epidemiology

Jacqueline.Torres@ucsf.edu* Jacqueline Torres Sirena Gutierrez, Erika Meza, Stefanie Piña Escudero, Joseph Saenz, Adina Zeki Al Hazzouri, M. Maria Glymour, Jacqueline M. Torres Erika Meza Stefanie Piña Escudero Joseph Saenz

Background: Emerging research has documented the effects of intergenerational socio-economic status (SES) on late-life health and aging. To our knowledge, none has evaluated the effects of adult children's SES on older parents' cognitive decline. Methods: We used data from Mexican Health and Aging Study, a national study of adults > 50 years in Mexico (baseline, 2001; follow-up, 2003, 2012, and 2015). We evaluated the effect of adult child education on parents' immediate and delayed verbal memory scores (each with range 0 – 8) using linear mixed models with inverse probability of attrition weights. We evaluated educational attainment across all children; our primary exposure was whether at least one adult child had completed secondary education vs. having no adult children who had completed secondary education. Confounders included respondents' early and mid-life socio-economic status and demographic characteristics. We evaluated heterogeneity by respondents' age and own educational attainment. Results: At baseline, respondents (4650 women and 5540 men) were an average of 62 years old, two-thirds co-resided with an adult child, and 52% had at least one child who had completed secondary education. Having at least one adult child with at least secondary educational attainment was associated with higher baseline immediate (ß: 0.27, SE: 0.001, women; ß: 0.18, SE: 0.001, men) and delayed (ß: 0.27, SE: 0.05, women; ß: 0.24, SE: 0.05, men) verbal memory scores compared to having no children with secondary educational attainment. There was no evidence of association between adult child education and decline in verbal memory, including in models stratified by respondent characteristics and using alternative exposure specifications. Discussion: Using national-level data from Mexico, we found associations between highest level of adult child education and level of verbal memory among older parents, but no association with parents' memory decline over a 14-year period.

Aging

Direct and Environmental Adverse Childhood Experiences and Subjective Cognitive Decline in Adulthood Monique J. Brown* Monique Brown Amandeep Kaur Carlos Avalos Nikki L. Hill

Background: One in four children will undergo at least one adverse childhood experience (ACE) in their lifetime. Direct (occurring towards the child) and environmental (contextual) ACEs have been linked to poorer objective cognition. However, research on the relationship between direct and environmental ACEs and subjective cognitive decline (SCD; the perception of worsening memory or thinking) is lacking. Therefore, the aim of this study was to examine the association between direct ACEs, environmental ACEs and SCD among adults.

Methods: Data for this cross-sectional study were obtained from the 2011 Behavioral Risk Factor Surveillance System Survey (n=4,514; age = 45+ years). Multivariable logistic regression models were used to determine the associations between direct ACEs (sexual and physical/psychological abuse), environmental ACEs (for e.g., witnessing domestic violence and living with someone with a mental illness) and SCD.

Results: After adjusting for sex, age, and race/ethnicity, respondents who reported sexual abuse, physical/psychological abuse and environmental ACEs, were more likely (OR: 5.46; 95% CI: 3.51 – 8.49; OR: 3.35; 95% CI: 2.37 – 4.73; and OR: 3.44; 95% CI: 2.39 – 4.95, respectively) to report SCD compared to respondents who were not exposed to ACEs. Similarly, respondents who reported one ACE were seven times as likely (OR: 6.58; 95% CI: 2.41 – 18.0) and those who reported three or more ACEs were three times as likely (OR: 3.00; 95% CI: 2.15 – 4.18) to report SCD.

Discussion: Direct and environmental ACEs were associated with SCD in adulthood. Studies examining the mechanisms between ACEs and SCD are needed since SCD is associated with many poor aging-related outcomes such as depressive symptoms and lower quality of life. Cognition intervention programs addressing childhood histories of sexual abuse, physical/psychological abuse and environmental ACEs may support improved cognitive aging among individuals at risk for SCD.

Variation in the association between the ε4 allele and cognitive decline by birth year cohort V. Eloesa McSorley* V. Eloesa McSorley Don Hedeker Brandon Pierce Patricia Boyle Diane Lauderdale

The ApoE ε4 allele is a well-established genetic risk factor for Alzheimer's disease (AD). There is less consistent evidence as to whether the ε4 allele is associated with cognitive decline prior to, or in the absence of, AD. Heterogeneity between studies could be due to differences in study methods, such as type of cognitive assessment, or to the modification of the effect of the ε4 by other factors that vary between cohorts, such as socioeconomic background or ancestry. Gene by environment studies have tested for effect modification of the ε4 allele by environmental factors measured contemporaneous to cognitive assessment and by educational attainment. Using Health and Retirement Study (HRS), we evaluate whether birthyear cohort (an indicator of early life environment) is an effect modifier of the relationship between the ε4 allele and cognitive decline. HRS resurveys every two years and has enrolled six birthyear cohorts, which we combine into two: those born before (b. 1894-1941) and after (b. 1942-59) the start of WWII. We use mixed-effects change-point models with interactions to assess whether cognitive decline due to the ε4 allele varies between birthyear cohorts for individuals of the same age. We also evaluate whether cohort differences are due to education distribution. We use likelihood ratio tests to compare model fit. A model with three-way interaction terms for cohort by ε4 by age significantly improves model fit over a saturated two-way interaction model (LR chi2=9.12, df=2, p=0.01). Interactions terms are positive; evidence suggesting that the impact of the ε4 allele on cognitive decline is weaker in the postwar cohort. Model fit is still improved with education in the comparison models (chi2=6.67, df=2, p=0.04), and the magnitude of the three-way interaction is unchanged. Cohort differences in genetic penetrance speak to broad changes in the environment that could be protective against genetic risk for cognitive decline.

Epidemiology of multimorbidity and associated factors in patients hospitalized for ambulatory care sensitive conditions Ana Carolina CN Mafra* Ana Carolina Mafra Gabriel Barreiros Machado Fernanda Amendola Mario Maia Bracco

Background: Multimorbidity is an important public health problem in terms of prevalence, severity, and monitoring possibilities. It negatively affects patient's health-related quality of life and increases the use of health services. It consists of having two or more chronic diseases simultaneously in an person and tends to increase with aging. Objective: To describe multimorbidity profiles among patients hospitalized for Ambulatory Care Sensitive Conditions (ACSC) who took part of a prospective cohort study in a large public hospital. Methods: This is a cross-sectional study which analyzed the patients selected for the baseline of the study "Healthcare integration strategy implementation based on distance education and communication for health professionals in São Paulo City, Brazil". Patients with or without multimorbidity were compared by Chi-square or Fisher's exact hypothesis tests when the categories were nominal, or by Mann-Whitney tests when the categories were ordinal. Results: From 559 patients admitted with some ACSC between March, 2014 to March 2016, 357 (63.9%) had multimorbidity, 80.1% among patients over 60 years old. Of these, the most prevalent chronic diseases were Hypertension (88.0%), Diabetes Mellitus (56.5%) and Congestive Heart Failure (37.9%). Patients with multimorbidity are generally older ($p < 0.001$), with more difficult to see ($p < 0.001$), greater difficulty walking or climbing stairs ($p < 0.001$), with less education ($p < 0.001$). They have, to a greater extent, a network of relatives or friends who support their illness (76.6%) and are not working (63.3%). In greater proportion have smoked, but quitted (48.0%) and do not currently drink alcohol (79.5%). Conclusions: The study allowed us to find factors that reinforce the importance of monitoring and controlling chronic diseases in primary care and thereby avoiding complications and consequent hospitalizations of these patients.
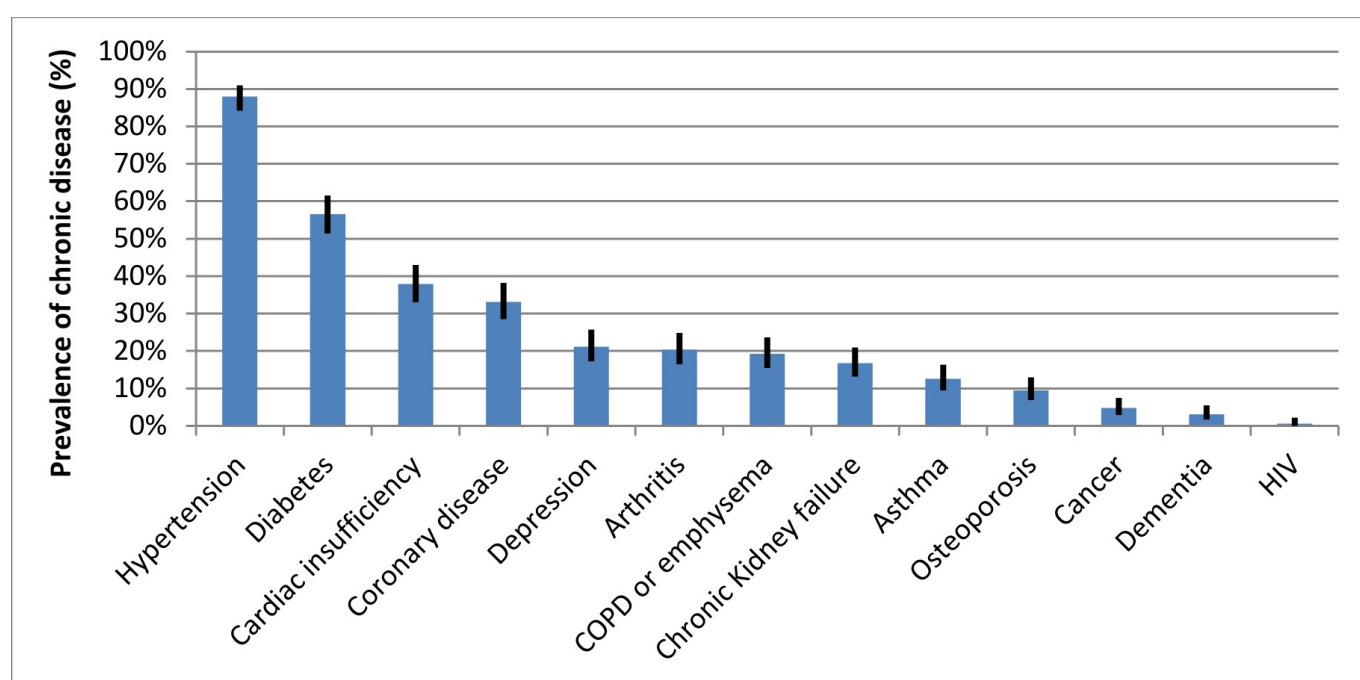
Figure 1: Distribution of prevalence of chronic diseases in patients with multimorbidity - with 95% confidence interval. N = 359.

Behavior

Prospective Associations Between Optimism and Physical Activity Across Midlife Farah Qureshi* Farah Qureshi Ying Chen Laura D. Kubzansky Jackie Soo Eric S. Kim Donald Lloyd-Jones Julia K. Boehm

Background: Prior work finds that optimism is linked with better cardiovascular health over time, but less research has explored behavioral pathways that might underlie this relationship. Our study tests whether higher baseline optimism is associated with higher levels of physical activity (PA) over 15 years among middle-aged adults.

Methods: Data are from 3,278 participants (mean age=40.2) in the Coronary Artery Risk Development in Young Adults (CARDIA) Study. Optimism was assessed in year 15 via the Life Orientation Test-Revised. PA was assessed every 5 years from year 10 to 30 using the CARDIA Physical Activity Questionnaire. Linear mixed models evaluated the relationship between optimism and PA from years 15 to 30, controlling for year 10 PA and relevant covariates. To mitigate possible confounding by pre-baseline PA, sensitivity analyses tested associations only among participants who met recommended levels of PA in year 10. Effect modification by gender and race was examined via stratification and interaction terms.

Results: PA decreased by 1.8 units per year (β=-1.8; 95% CI=-2.4, -1.2; p<0.001). In fully adjusted models, each standard deviation higher optimism was associated with a 19.0-unit higher PA score pooled over the follow-up (95% CI=11.9, 26.1; p<0.001): an association 10.6 times greater than annual PA declines related to aging. Higher optimism was also associated with a slower decline in PA over time (time*optimism interaction β=0.8; 95% CI=0.2, 1.4; p=0.01). Results were robust to stratification by pre-baseline PA. Tests for interaction found subgroup differences in the impact of optimism on PA pooled over time (p=0.03), with the strongest association noted in black men (Figure 1). There was no evidence of a 3-way interaction with the rate of PA change (p=0.1).

Conclusion: Higher baseline optimism is associated with both higher levels of PA over 15 years and a slower decline in PA over time, but the magnitude of associations vary by race and gender.

Figure 1: PA trajectories by level of baseline optimism, stratified by race and gender.
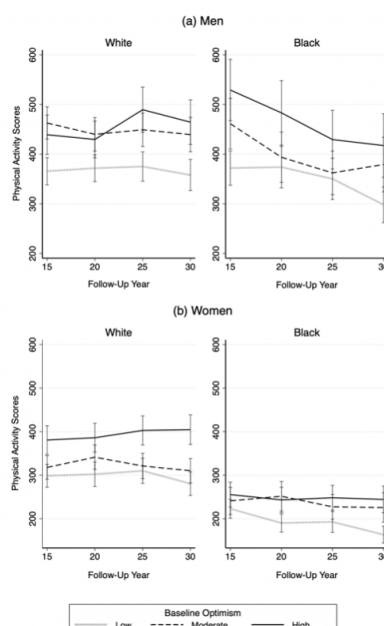
Factors associated with longitudinal behavior change based on transtheoretical model: Aichi Health Promotion Study Kohta Suzuki* Kohta Suzuki Rei Wakayama Keiki Ueda Akihiko Narisada

In Japan, 40 years or older people have to take an annual medical check-up based on the Japanese Law. In the check-up, the stage of behavior change based on transtheoretical model (TTM) was determined by questionnaire. Moreover, their objective health status and lifestyle habits such as smoking habits and physical activity were collected. Thus, this study aimed to explore the factors associated with behavior change during 5 years by using the huge longitudinal medical check-up data. This study included 5131 people aged 40-70 who were determined their stage of behavior change as precontemplation in 2013 (baseline) and followed them up during 5 years. Three outcomes of the study were gradually determined. Then, factors associated each outcome were explored by logistic regression models. Study factors were sex, age, weight status, smoking status, alcohol consumption, weight change since 20 years of age, physical activity, breakfast consumption, medication for hypertension, diabetes, and dyslipidemia and request to health guidance. First, 2920 (56.9%) people changed their stage during 5 years. At baseline, female, obese, more than 10kg weight gain since 20 years of age, breakfast consumption, non-alcohol consumption, medication of diabetes and request to health guidance were associated with this change. Second, of these, people who did not return their stage to precontemplation during this period was 1785 (61.1%). Female, non-smoking and request to health guidance were associated with this outcome. Finally, of these, people who were maintenance stage in 2017 were 467 (26.2%). Male, younger age, non-smoking, regular exercise, breakfast consumption and request to health guidance were related to this achievement. It was suggested that these results could help to perform effective health guidance for health promotion and non-communicable disease prevention.

Behavior

Prevalence of LGBT students in schools is associated with unhealthy weight-control behaviors in LGBT youth: A multilevel analysis. Carolina Franca Bandeira F Santos* Carolina Santos Fabiana Godoy Valdenice Aparecida de Menezes Viviane Colares Patrícia Maria Pereira de Araújo Zarzar Raquel C. Ferreira Ichiro Kawachi

Background: Previous studies found that a school climate of more heteronormativity is associated with adverse effects on the mental health of LGB students.
Aim: To assess the association between low LGB visibility in schools and unhealthy weight-control behaviors among LGB youth.
Methods: Cross-sectional, multilevel study based in public high schools from Olinda, a city in Northeast Brazil. A multilevel logistic regression was performed, including 2,501 adolescents enrolled in 27 schools. The contextual variable was the prevalence of LGB youth in each school (as a proxy for LGB visibility) while the outcome was unhealthy weight-control behaviors (fasting, purging, and taking diet pills) among students identifying themselves as LGB. We controlled for socioeconomic characteristics (age, gender, receiving a family allowance), obesity, and self-reported happiness.
Results: Low LGB visibility in schools associated with higher odds of engaging in unhealthy weight-control behaviors (OR: 1.51, 95%CI:1.02, 2.23) among all youth as well as the following individual characteristics: girls (OR: 1.70, 95%CI:1.17, 2.46), LGB (OR: 1.88, 95%CI:1.12, 3.17) , obese (OR: 2.06, 95%CI:1.22, 3.48), trying to lose weight (OR: 2.43, 95%CI:1.59, 3.71), suffering victimization (OR: 1.61, 95%CI:1.09, 2.38), and self-perception of unhappiness (OR: 1.76, 95%CI:1.14, 2.71).
Conclusion: A school environment of low LGB visibility was associated with unhealthy weight-control behaviors in youth.

Adolescent sleep across 24 countries and and age, gender and socioeconomic differences

Genevieve Gariepy* 3647] Gariepy

Background: Insufficient and poor sleep patterns are common among adolescents and a growing public health concern in many countries. Up to now, the evidence on adolescent sleep has been mostly informed by country-specific studies that used different sleep measures and age groups, making direct comparisons difficult. Cross-national data on adolescent sleep that could inform nations and international discussions are lacking. We examined the sleep patterns of adolescents across 24 countries and by gender, age and affluence groups.

Methods: We obtained sleep data on 165,793 adolescents (ages 10-16) in 24 countries from the recent cross-sectional Health Behaviour in School-Aged Children surveys (2013-14 and 2017-18). For each country, we calculated the age-standardized mean in sleep duration, timing, and consistency, and the proportions meeting sleep recommendations on school and non-school days from self-reported bedtimes and wake times. We conducted stratified analyses by gender, age, and family affluence group.

Results: Adolescent sleep patterns varied cross-nationally. Notably, the average sleep duration ranged between 7:47-9:07 h on school days and 9:31-10:22 h on non-school days, and the proportion of adolescents meeting sleep recommendations ranged between 32-86% on school days and 79-92% on non-school days. Sleep patterns by gender and affluence groups were largely similar, but older adolescents slept less and went to bed later on school days than younger adolescents in all countries.

Conclusions: The sleep patterns of adolescents vary across countries and sociodemographic groups. Insufficient sleep on school days is common in many countries. Public health and policy efforts to promote healthy adolescent sleep are encouraged.

7:47 h	7:53 h	7:54 h	7:55 h	8:01 h	8:07 h
Poland	Latvia	Greece	Estonia	Slovenia	Slovakia
8:13 h	8:16 h	8:18 h	8:21 h	8:23 h	8:24 h
Czech Republic	Hungary	Ukraine	Portugal	Switzerland	Finland
8:24 h	8:26 h	8:28 h	8:29 h	8:29 h	8:30 h
Iceland	Republic of Moldova	Spain	Scotland	Sweden	Netherlands
8:33 h	8:33 h	8:37 h	8:40 h	8:41 h	9:07 h
Denmark	Wales	French Belgium	Norway	Canada	Flemish Belgium

Big Data

Longitudinal metabolomic profile trajectories in healthy pregnancy and variation by BMI and fetal sex Susanna Mitro* Susanna Mitro Jing Wu Mohammad L. Rahman Mengying Li Stefanie N. Hinkle Andrew A. Bremer Natalie L. Weir Michael Y. Tsai Bizu Gelaye Cuilin Zhang

Background: Maternal plasma metabolites have been linked with pregnancy outcomes, and two studies reported that metabolite levels differ by trimester. However, dynamic metabolite trajectories in normal pregnancy have not been characterized. We examined metabolite trajectories and tested whether trajectories differed by maternal body mass index (BMI) or fetal sex.

Methods: We quantified 3 panels of targeted metabolites—37 amino acids, 37 phospholipid fatty acids and 28 acylcarnitines— in blood samples collected longitudinally from 214 pregnant women (at 10-14, 15-26, 26-31, and 33-39 weeks, staggered to sample most weeks of pregnancy). Participants were healthy controls in a nested case-control study in the Fetal Growth Studies—Singletons. We used linear mixed models to estimate metabolite trajectories and evaluate if trajectories varied by maternal BMI (<25, 25-29.9, ≥30) or fetal sex. We used novel methods such as hierarchical clustering to group metabolite trajectories.

Results: Concentrations of most carnitines, 57% of fatty acids, and 24% of amino acids (e.g., branched chain amino acids) significantly decreased over pregnancy; 22% of fatty acids and 24% of amino acids (e.g., threonine, histidine) significantly increased. Trajectories of 2 carnitines (propionylcarnitine and stearoylcarnitine) and 3 fatty acids (15:0, 17:0, 22:0) significantly differed by sex. Trajectories of dodecenoylcarnitine, 2 fatty acids and 2 fatty acid ratios (17:0, 20:3n6, AA/DHA, AA/(DHA+ EPA)) significantly differed by BMI: specifically, 17:0, AA/DHA, and AA/(DHA+ EPA) decreased less over pregnancy for women with high BMI.

Conclusions: Concentrations of most metabolites significantly changed during pregnancy, and trajectories of some carnitines and fatty acids differed significantly by maternal BMI and fetal sex. Future pregnancy metabolomics studies should consider BMI, fetal sex, and multiple samples across pregnancy.

Big Data

The use of "phecodes" for electronic phenotyping of primary immune deficiencies in a large electronic health record database Emily Ricotta* Emily Ricotta Chris Shin D. Rebecca Prevots

International Classification of Diseases (ICD) codes are often used to study diseases in electronic health record (EHR) data sets. These codes provide a global standard for recording health events for ease of data sharing and analysis. The most recent revisions (9 and 10), comprise over 150,000 unique codes. However, ICD analysis is limited in that it is difficult to capture all codes associated with a disease state. Thus, researchers have categorized phenotypically related ICD codes into "phecodes". We aimed to use phecodes to describe patients with primary immune deficiencies (PID) in a large EHR data set.

All diagnosis codes from all encounters for patients with an ICD9/10 code for selected PIDs were enumerated from the Cerner HealthFacts EHR dataset. Phecodes were joined to ICD codes using the Phecode Map (available from phewascatalog.org), and both phecode phenotype and category were summarized to describe clinical manifestations of each PID. Phenotype summaries were further assessed by age (over/under 16 years old).

Overall, 11,126 patients had a selected PID ICD code; 16,876 (77%) unique ICD codes for comorbidities joined to ≥1 phecode, totaling 1770 phecodes in 17 distinct categories. The most common phecode category was endocrine/metabolic (92% of patients had ≥1 code), however most PID ICD codes are included in this category. The next most common were respiratory (73%), circulatory (67%), symptoms (63%), hematopoietic (62%), and digestive (61%). The distribution of phecodes varied by PID (Fig 1) and within PID by age.

This preliminary analysis demonstrates the utility of phecodes for analysis of EHR data and would be useful for feature selection and reduction in preparation for machine learning. Future research includes classifying unmatched ICD codes, validation of matching codes, and more extensive interrogation of the differences in phecode distribution between and within PIDs.

Distribution of Phecode Categories for Patients with PIDs
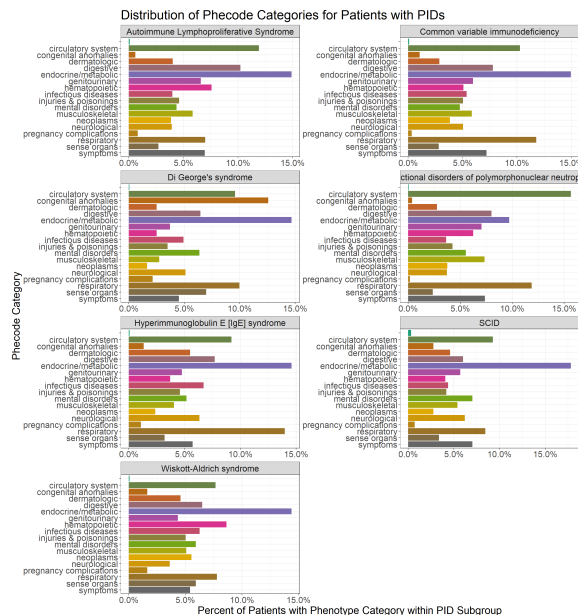
The Premature Mortality Population Risk Tool (PreMPoRT): a population-based risk tool for assessing premature mortality risk in the community setting Meghan O'Neill* Meghan O'Neill Laura C. Rosella Mackenzie Hurst Lori Diemert Kathy Kornas Stacey Fisher Douglas G. Manuel

Introduction: Premature mortality, defined as death between the ages of 18 and 74, is an important population health indicator used to assess health system functioning and to identify areas in need of health system intervention. Predicting the future incidence of premature mortality in the population can assist in informing prevention efforts and equitable delivery of public health services.

Objective: To develop and validate a population-based risk prediction tool for premature mortality using routinely collected national survey data.

Methods: We developed the Premature Mortality Population Risk Tool (PreMPoRT) using a cohort of respondents from six cycles of the Canadian Community Health Survey linked to the Canadian Vital Statistics Database with follow-up to December 2017. Sex-stratified logistic models were used to estimate the 5-year odds of premature mortality for people $\geq$ 18 years of age among females (N=267,475) and males (N=233,415), respectively. Predictor variables included self-reported sociodemographic characteristics, modifiable lifestyle risk factors, and chronic conditions.

Results: There were 5,090 premature deaths among females and 6,790 premature deaths among males over the study period. Age, self-rated health, body mass index, smoking status, heavy alcohol consumption and cancer were the strongest predictors associated with an increased odds of premature mortality. Among men, marital status was additionally strongly associated with premature mortality. PreMPoRT demonstrated excellent discrimination among females (C statistic= 0.85) and males (C statistic= 0.84), respectively. Temporal validation results will be reported at the meeting.

Conclusion: Using routinely collected risk factor information, PreMPoRT produces population-based estimates of premature mortality and will be used to identify subgroups at elevated risk to help inform targeted interventions.

Big Data

Using national de-identified electronic health records to evaluate American Diabetes Association screen guideline Knag Lin Hsieh* Kanglin Hsieh Xiaoqian Jiang Angela Ross

Purpose:

Diabetes is a prevalent chronic condition. American diabetes association proposed an annual screen guideline for early identification. This research applied the guideline to national de-identified electronic health records for evaluation.
Methods:

Cerner Health Facts encompassed seventy million patients' data from 2004 to 2017. The research examined the HbA1c screening rate of the two study populations. The first population is patients whose age above or equal forty-five years old. We sampled patients whose ages between forty-five and fifty for study and examined whether those patients were receiving the first HbA1c within 2017. Patients whose age below forty-five must have both BMI is over 25 and at least one risk factor in ADA screen guideline between 2014 and 2016. The risk factors included records of hypertension, gestational diabetes, cardiovascular disease, and polycystic ovaries, abnormal results of HDL, triglyceride, and unusual reading of systolic blood pressure and diastolic blood pressure. We also examined the second population received the first HbA1c within 2017.

Results:
3,732,720 sampled patients were in the first population, and only 0.65% of them received HbA1c screen. 20,843,358 patients whose ages were below forty-five in 2017 and 65,152 of them were at risk. In those patients at risk, only 4,278 had records of the HbA1c Test. For those receiving HbA1c in both populations, we further examine gender, race, hospital bed size, the region of U.S., and urban/rural areas. The results showed in figure.
Conclusions:
The screen rate of diabetes still be very low in the U.S. according to the results. The limitation of this conclusion is this national database still cannot cover all U.S. patients.

Results of American Diabetes Association Screen guideline (2017) for Diabetes

Big Data
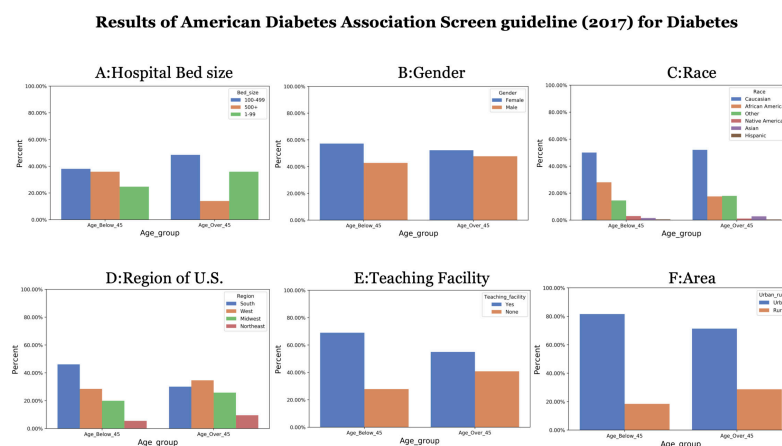
Maximizing research value and use through enhanced data documentation Julie* John Obrycki Goldman

Introduction:

Long-term cohorts provide a valuable scientific resource. Cohort datasets can be analyzed for numerous questions that go beyond the initial study's aims. However, this potential is achieved only if thorough data documentation and accessibility strategies are implemented. As cohort studies can span several decades, proper documentation is essential because data may have multiple file types that are not always stable over time. The National Institutes of Health continues to develop data management initiatives and guidelines to ensure research results are Findable, Accessible, Interoperable, and Re-usable (FAIR). Recent funding from NIH provides opportunities to incorporate new expertise into research projects to enhance overall data management.

Methods:

A new collaboration between Boston Children's Hospital and Harvard University Library is directly linking researchers and data science librarians to implement recommended data management practices for research studies. The combination of these two perspectives provides a comprehensive approach on all aspects of the data lifecycle. Some examples of the data management methods used in this study include: preparing data documentation in long-term stable file formats with associated readme files, documenting research analysis code with markdown and Jupyter Notebook, applying biomedical ontologies to ensure data are findable and operable, and depositing all data into stable repositories, such as the Harvard Dataverse.

Results:

Examples of the project's data management framework and documentation will be shown to the session attendees. Additional information will be shared on ways to enhance data documentation efforts whi

Big Data

Is current trial data sharing status conducive for evidence generation for personalized medicine: a failed attempt to conduct an individual patient trial data network meta-analysis Lin Wang* Lin Wang Hwanhee Hong Channing Paller Otis Brawley Tianjing Li

Background: Meta-analysis of individual patient data (IPD) can address patient characteristics that modify treatment effect and inform personalized medicine. Considering the increasing trend of trial data sharing. We attempted an IPD network meta-analysis to compare multiple chemohormonal therapies for advanced prostate cancer.
Methods: Bibliographic databases, trial registries, and regulatory documents were searched. And thirteen eligible clinical trials were identified. IPD were requested from several trial data sharing platforms including Vivli, ClinicalStudyDataRequest, YODA, and projectdatasphere.
Results: IPD were available for only four (31%) of the thirteen eligible trials. IPD were not available for various reasons. 1) The trial was ongoing or was completed within 18 months . This could be a completed trial with full results published or an ongoing trial with interim results published. 2) The product and relevant indications had not been approved by regulators in the United States and/or European Union. This could be a product-indication combination that has been approved by one regulator but not the other. 3) The trial sponsor was not a data contributor for the platform; was a data contributor but the trial of interest was not yet listed on the platform; or refused the request because of similar study interest, "trial data monopoly." For the available IPD sourced from different platforms, an integrated analysis was not feasible. Because neither IPD downloading nor cross-platform transmission was allowed.
Conclusions: Current trial data sharing status is not conducive for evidence generation for personalized medicine. Issues disclosed above need to be addressed to enhance secondary use of IPD. Cross-platform data transmission are of the utmost importance. Efforts need be made to reduce the delay from trial completion to data sharing. Finally, data access decisions should be made transparent to ensure equity for all researchers.

Electronic Medical Records for Population Health: A Case Study Estimating Obesity Prevalence in King County, Washington Census Tracts Stephen J Mooney* 3647] Mooney Lin Song David E Arterburn Sean D Mooney Nicholas Dobbins Brian E Saelens

In light of declining funding for surveillance and declining response rates, electronic medical records hold considerable potential as an alternate 'big data' source for population health research and practice. However, care provider record systems contain information only about a systematically selected sample of a region's population. To assess how much sampling affects population estimates, we compared three estimates of the prevalence of obesity by census tract in King County, Washington: one using Kaiser Permanente Washington (KP) health records, another using UWMedicine (UW) health records, and a third using Behaviorial Risk Factor Surveillance System (BRFSS) results.

Data were available from KP primary care visits among healthy adults between January 1, 2005 and December 31, 2006. We identified primary care visits in UW records in the same timeframe. Next, we computed home census tract from billing addresses, classified each patient's obesity status, and used an empirical Bayes approach to correct obesity prevalence by tract for differential population inclusion in the care system. Finally, we compared these to population obesity estimates from the 2012-2016.

Estimates of obesity by tract ranged from 6% to 51% using UW, 11% to 57% for KP, and 10% to 37% using BRFSS. BRFSS estimates were highly correlated with both UW estimates (r=0.68) and KP (r=0.79), which were themselves intercorrelated (r=0.63). Visual inspection of maps showed similar distributions of obesity across the county from all systems.

Using care delivery records to assess population obesity prevalence holds promise. Future work, to be completed before SER 2020, will explore using clinical visit data temporally matched to BRFSS data, using demographic sample weights rather than empirical Bayes estimation, and comparing within-tract trends over time.

The Association of Sibling Fracture History with Major Osteoporotic Fractures in Individuals from a Population-Based Cohort Amani Hamad* 3647] Hamad Lin Yan William D. Leslie Suzanne N Morin Shuman Yang Randy Walld Leslie L. Roos Lisa Lix

Background: Major osteoporotic fractures (MOF) are associated with significant morbidity and healthcare system burden. We aimed to determine whether sibling fracture history is associated with MOF risk amongst individuals from a population-based cohort using objectively-ascertained measures of fracture history.

Methods: This retrospective cohort study used administrative databases from the province of Manitoba, Canada, which has a universal healthcare system. The cohort included individuals aged 40 years and older between 1997 and 2015 with linkage to at least one sibling. The exposure was MOF diagnosis occurring at age 40 years or older in a randomly selected sibling. The outcome was incident clinically-diagnosed MOF (hip, wrist, humerus or spine) identified in hospital and physician records using established case definitions. A multivariable Cox proportional hazards regression was used to test the association of sibling fracture history with the risk of MOF in individuals after adjustment for known fracture risk factors.

Results: The cohort included 217,519 individuals; 92% were linked to full siblings (i.e., same mother/father) and 49% were females. During a median follow-up of 11 years (IQR 5 -15), 7274 (3.3%) incident MOF cases were identified. Sibling MOF history was associated with an increased risk of MOF (HR 1.71, 95% CI 1.48–1.97). The risk was elevated in both men (HR 1.63, 95% CI 1.29-2.06) and women (HR 1.78, 95% CI 1.48-2.13) but was higher among sisters (HR 2.08, 95% CI 1.65-2.61) compared to brothers (HR 1.67, 95% CI 1.20-2.32). In a secondary analysis of sibling fracture site, the highest risk was observed with a diagnosis of wrist followed by spine fractures (HR 1.86, 95% CI 1.57-2.21 and HR 1.46, 95% CI 1.08-1.98, respectively).

Conclusion: Sibling fracture history is associated with increased MOF risk in individuals and should be considered as a candidate risk factor for improving fracture risk prediction.

Cancer

Validation of an Electronic Algorithm for Hodgkin and non-Hodgkin Lymphoma in ICD-10-CM Mara M. Epstein* Mara Epstein Sarah K. Dutcher Judith Maro Cassandra Saphirak Sandra DeLuccia Muthalagu Ramanathan Tejaswini Dhawale Sonali Harchandani Christopher Delude Laura Hou Autumn Gertz Nina DiNunzio Cheryl N. McMahill-Walraven Mano S. Selvan Justin Vigeant David V. Cole Kira Leishear Jerry H. Gurwitz Susan Andrade Noelle M. Cocoros

Background: Non-Hodgkin lymphoma is the seventh most commonly diagnosed cancer among both US men and women, and a health outcome of interest for drug safety studies. Large-scale studies using administrative health data would benefit from the rapid and accurate identification of lymphoma cases. We developed and validated an ICD-10-CM-based algorithm to identify lymphoma within the Sentinel Distributed Database.
Methods: We developed a three-step algorithm to identify patients aged 15 years and older who were newly diagnosed with Hodgkin (HL) or non-Hodgkin (NHL) lymphoma from January 2016 to July 2018 among members of four Data Partners (three national insurers and one integrated healthcare delivery system) within the Sentinel Distributed Database.
The algorithm defined potential cases as patients with at least two ICD-10-CM lymphoma diagnosis codes on different dates within 183 days; and at least one procedure code for a diagnostic procedure (e.g. biopsy or flow cytometry) and at least one procedure code for a relevant imaging study within 90 days of the first lymphoma diagnosis code. Cases identified by the algorithm were adjudicated via chart review, and positive predictive value (PPV) was calculated.

Results: We identified 8,723 potential lymphoma cases via the algorithm and randomly sampled 213 for validation; 138 charts (65%) were retrieved, and 134 (63%) were abstracted and adjudicated. The overall PPV for the algorithm was 77% (95% Confidence Interval: 69-84%). Most validated cases also had subtype information available, with 88% of cases identified as NHL and 11% as HL.

Discussion: This novel algorithm based on ICD-10-CM diagnosis and procedure codes and applied to administrative claims data was able to identify lymphoma cases with good accuracy. This tool could represent an efficient and cost-effective way to target this important health outcome of interest for large-scale studies of drug safety and public health surveillance.

Sexual risk behavior and sexually transmitted infections in gay and bisexual men after prostate cancer: Findings from the Restore II study Elizabeth Polter* Elizabeth Polter Christopher Wheldon Morgan Wright Nidhi Kohli Christopher Hoefer B.R. Simon Rosser

Gay and bisexual men experience unique challenges in sexual rehabilitation after prostate cancer treatment. Long-term erectile dysfunction is a common side effect of prostate cancer treatment that can hinder anal intercourse. Anal penetration requires a firmer erection than vaginal intercourse, and some gay and bisexual men may forgo condom use in an attempt to maintain firmer erections during insertive anal sex. This may result in increased sexually transmitted infections (STIs) including human immunodeficiency virus (HIV) given the higher population prevalence of these infections among gay and bisexual men. In this cross-sectional, online survey (Restore II) of 401 gay and bisexual men treated for prostate cancer, we describe incidence of HIV and other STIs before and after cancer treatment, as well as self-reported risk behavior. Overall, 245 participants (61%) reported an STI diagnosis in their lifetime, including 67 (17%) diagnosed with HIV. 45 (11%) reported at least one STI diagnosis after prostate cancer treatment, including 5 (1%) diagnosed with HIV. Participants with a post-cancer STI diagnosis were less likely to be partnered (40%, N=18) than other participants (50%, N=181) and had a longer average time since prostate cancer diagnosis (8.2 vs 4.9 years). Twenty-five (61%) participants with a post-cancer STI diagnosis and 178 (55%) of those without reported that not using a condom because of erectile concerns had been a problem in the four weeks preceding the survey. Nine (20%) participants with a post-cancer STI diagnosis and 32 (9%) of those without reported unprotected insertive anal sex with more than one partner in the past four weeks. These exploratory findings, if confirmed in longitudinal analyses, further underscore the importance of prostate cancer rehabilitation treatment for gay and bisexual men and may indicate a need for STI prevention in prostate cancer survivors.

Cancer

Estrogen bioassay concentrations and risk of invasive breast cancer among postmenopausal women in the Nurses' Health Study Etienne Holder* Etienne Holder Serena Houghton Susan Hankinson Jing Qian Shelley Tworoger Martyn Smith Sylvia Sanchez Heather Eliassen

Estrogens (E) increase breast cancer risk through E receptor (ER) mediated pathway activation. Classic endogenous E (estradiol (E2), estrone, estrone sulfate) have been consistently positively associated with breast cancer risk. Whether a broader assessment of plasma-mediated ER activation is more strongly related to increased risk is unclear. To test this hypothesis, we evaluated the association between an E cell line bioassay and invasive breast cancer in the Nurses' Health Study cohort.

A nested case-control study was conducted among 371 cases and 731 controls identified over 8 years of follow-up (1994-04). Women were postmenopausal and not using hormone therapy at blood collection in 1989-90, had provided questionnaire data, and had plasma classic endogenous E measurements available. Case status was confirmed via medical records. E pathway activation was assessed via a luciferase reporter bioassay using the T47D-Kbluc cell line. Multivariable RR and 95% CI were calculated using conditional logistic regression. To define bioassay variables independent of classic E, an E2 subtraction method and E2- and 3 E-adjusted bioassay residuals from linear regressions were used.

Compared to women in the lowest quartile of measured bioassay, women in the highest quartile had an 81% increased risk of invasive breast cancer (RR 1.81, 95% CI 1.10-2.98, P-trend=0.01). A non-significant association was observed among women with measured E2-adjusted bioassay (RRQ4vsQ1 1.18, 95% CI 0.68-2.04, P-trend=0.47) and E2 subtracted bioassay (RRQ4vsQ1 1.10, 95% CI 0.66-1.83, P-trend=0.37). No association was observed between the 3 E-adjusted bioassay and invasive breast cancer (RRQ4vsQ1 0.99, 95% CI 0.54-1.81, P-trend=0.86).

Postmenopausal E concentrations measured via bioassay were significantly positively associated with invasive breast cancer risk. However, after accounting for several classic endogenous E, the association was substantially attenuated and not statistically significant.

Cancer

Association between socio-demographic factors and risk of depression among Localized Prostate Cancer Patients of Louisiana of 6 months follow up of CEASAR study Pratibha Shrestha* Pratibha Shrestha Edward Peters Xiao Cheng Wu

Men diagnosed with prostate cancer often face physical and psychological challenges that may lead to depression. The objective of this study was to examine the association of socio-demographic factors on the risk of depression among men with localized prostate cancer.

Louisiana data from the six-month follow-up Comparative effectiveness Analysis of Surgery and Radiation for Localized Prostate cancer (CEASAR) study was used. Participants were identified and recruited through the Louisiana Tumor Registry. Depression was assessed using 9-items of CES-D with scores ranging from 9-36. A median score of 13 was considered as a cut-off point for having depressive symptoms. Log binomial regression was used to estimate the relative risk for the association between socio-demographic factors (age, race, marital status, income, and education) and depression among 722 participants out of 950 total Louisiana CEASAR participants after excluding missing values.

Of the 722 participants,19.1% were black, mean age=64.7years, 70% were married, 43% had less than a college degree, 52% had low income, 60% (n=563), of participants, had probable depression. In the adjusted model, lower income men were1.4 times more likely to exhibit depressive symptoms compared to higher-income men [RR: 1.4; 95% CI: 1.1– 1.6]. We observed no associations with respect to marital status, race, age and education, see Table 1.

Among the socio-demographic factors, age, race, marital status, income and education, only income was observed to be associated with early depression among Louisiana men with prostate cancer. As follow-up is ongoing, future analysis plans will examine the interplay among social, environmental and clinical factors, with their association on the depression trajectory among longer term prostate cancer survivors.

Table 1: Association of socio-demographic factors and risk of depression among participants using log-binomial model

Model	Unadjusted model		Adjusted model	
	Relative risk (RR)	Confidence interval (CI)	Relative risk (RR)	Confidence interval (CI)
Single vs married	1.31	1.11– 1.54	1.16	0.98 -1.38
Black vs White	1.26	1.06- 1.50	1.08	0.90- 1.29
Low income (below or equal $50,000) vs High income (above $50,000)	1.48	1.25 -1.74	1.36	1.12-1.64
Low education (grade school or less or high school) vs High education (Some college or graduate)	1.27	1.09 -1.49	1.11	0.94 -1.31
41-60 years vs 61-80 years at baseline study	1.07	0.90 – 1.26	1.11	0.94 – 1.31

Cancer

Predicted vitamin D status and incidence of colorectal cancer in the Black Women's Health Study Lauren E. Barber* Lauren Barber Hanna Gerlovin Kimberly A. Bertrand Lucile L. Adams-Campbell Lynn Rosenberg Julie R. Palmer

Observational studies, mostly among white populations, suggest that low vitamin D levels increase risk of colorectal cancer. African Americans, who are disproportionately burdened by colorectal cancer, tend to have lower vitamin D levels compared to other populations. We assessed predicted vitamin D score in relation to colorectal cancer incidence among 49,534 participants in the Black Women's Health Study, an ongoing prospective cohort study of African American women who were followed from 1995 to 2017 through biennial questionnaires. We used a previously validated prediction model, derived using 25-hydroxyvitamin D levels measured in plasma samples collected from 2,856 participants in 2013-2015, to estimate predicted vitamin D scores at baseline and at each questionnaire period. We calculated the cumulative average of predicted vitamin D score at every 2-year questionnaire cycle by averaging predicted scores from current and previous time points. Using Cox proportional hazards regression, we estimated hazard ratios (HR) and 95% confidence intervals (CI) for overall and site-specific colorectal cancer incidence according to quartiles of average predicted vitamin D score, adjusting for established colorectal cancer risk factors. During follow-up, 488 colorectal (370 colon; 105 rectal) cancer cases were diagnosed. Women in the lowest quartile of predicted vitamin D score had a 42% (HR 1.42, 95% CI 1.05-1.91) higher risk of colorectal cancer compared to those in the highest quartile. Results were similar among women currently taking vitamin D supplements and women not currently taking supplements. HRs for lowest vs. highest quartile of predicted vitamin D score were 1.55 (95% CI 1.12-2.14) for colon cancer and 1.26 (95% CI 0.67-2.36) for rectal cancer. The results suggest that low vitamin D status may contribute to the disproportionately high incidence of colorectal cancer experienced by African Americans.

Cancer

Association between serum iron biomarkers and breast cancer incidence Ann Von Holle* Ann Von Holle Katie M. O'Brien Dale P. Sandler Clarice R. Weinberg

Iron is both a growth factor that is essential to life and potentially toxic. Extremely high iron stores are associated with increased risk of some cancers. Epidemiologic studies of associations between iron levels and breast cancer are both sparse and inconsistent. A recent meta-analysis found positive associations between serum iron biomarkers and breast cancer, but heterogeneity among studies. Our aim was to assess breast cancer incidence in relation to three serum iron biomarkers: iron, ferritin, and transferrin saturation in a prospective cohort study.

We sampled participants in the Sister Study, a cohort of 50,884 women aged 35-74 who had never had breast cancer themselves but had an affected sister. The case-cohort sample of 5,982 women, including 2,995 incident cases, had been followed for a median of 7.9 years. Serum iron biomarkers were measured in baseline samples. We used Cox proportional hazards models to estimate the hazard ratios (HR) for the biomarkers, which we analyzed both as categorical (quartiles) and continuous. We adjusted for baseline smoking, alcohol, education, HRT, parity, oral contraceptive use, early menopause (<=45 years), time since last menstrual period, BMI, menopause status and a product term between the last two variables.

Median (IQR) serum iron, ferritin, and transferrin saturation was 93 (74, 115) ug/dL, 68 (37, 114) ug/L, and 29% (22, 36), respectively. Adjusted HRs for the highest versus lowest quartiles (95% CI) were 1.06 (0.90, 1.24) for iron, 1.01 (0.86, 1.20) for ferritin, and 0.94 (0.79, 1.10) for transferrin saturation. A sensitivity analysis restricting to the first four years of follow-up indicated similarly near-null hazard ratios.

In a study with a large sample size and with all three measures of circulating iron, ferritin, and transferrin saturation, we found no evidence to support an association between iron status and breast cancer risk.

Cancer

Adult lifetime antibiotic use and the risk of invasive breast cancer: results from the Nurses' Health Studies Serena Houghton* Serena Houghton Heather Eliassen Michelle D Holmes Rulla M Tamimi Bernard Rosner Susan E Hankinson

Antibiotic use has been hypothesized to Increase breast cancer risk; however, most past studies of this association have had a number of potential limitations (e.g., residual confounding, detection bias). We examined this hypothesis within the two large prospective Nurses' Health Studies (NHS) with comprehensive information on breast cancer risk factors and mammography use. Women (n=135,329) self-reported antibiotic use duration (none to 5+ years) throughout adulthood and reasons for use (e.g., respiratory infection, acne/rosacea) in 2004 (NHS)/ 2005 (NHS2) and again four years later. We additionally summed the midpoint of the response categories across all ages for total adult lifetime use. Self-reported incident invasive breast cancer was confirmed by medical record review until 2016 (NHS)/ 2015 (NHS2). We used multivariable Cox proportional hazards models to estimate the HR and 95% CI and inverse probability weighting to account for variations in mammographic screening. Over 10+ years of follow-up, 3,661 incident invasive cases were documented. Over 98% of women reported antibiotic use, most commonly for respiratory infections (65%). Antibiotic use in adulthood was not associated with breast cancer (HR for 1001+ vs 1-50 days=0.95, 95% CI=0.79-1.13). Results did not change when accounting for mammography (HR=0.91, 95% CI=0.74-1.13). No significant associations were observed in a specific period of adulthood; the HR for 2+ years vs <15 days (95% CI) for early, middle and late adulthood were 1.16 (0.80-1.70), 0.92 (0.58-1.46) and 0.76 (0.45-1.29) respectively in the NHS, and 0.96 (0.73-1.26), 1.27 (0.90-1.79) and 1.18 (0.75-1.84) respectively in NHS2. Additionally, associations did not vary by age, menopausal status or tumor hormone receptor status. In conclusion, antibiotic use in adulthood was not associated with breast cancer risk in two large prospective cohorts with comprehensive information on breast cancer risk factors.

Smoking, alcohol, and breast cancer recurrence across four molecular subtypes Nicole C. Lorona* Nicole Lorona Linda S. Cook Mei-Tzu C. Tang Deirdre A. Hill Charles L. Wiggins Christopher I. Li

Background
The association between alcohol consumption and smoking and breast cancer recurrence is unclear, and few studies have explored these associations across molecular subtypes.
Methods
A population-based prospective cohort study was conducted, including women aged 20-69 diagnosed with a first primary invasive breast cancer between 2004 and 2015. Based on estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) patients were categorized as: luminal A (ER+/HER2-), luminal B (ER+/HER2+), HER2-overexpressing (H2E) (ER-/HER2+), or triple-negative (TN) (ER-/PR-/HER2-). Recurrences were ascertained by medical record review. Alcohol consumption and smoking status were assessed through medical record reviews and structured interviewer-administered questionnaires. Cox proportional hazards models were fit for each subtype to calculate hazard ratios (HR) and 95% confidence intervals (CI).
Results
After adjustment for covariates, current alcohol consumption at breast cancer diagnosis was associated with a 37% reduced risk of breast cancer recurrence for luminal A cases (HR: 0.63; 95% CI: 0.43, 0.93). There was no statistically significant association between alcohol consumption and recurrence among any other subtype. Being a current smoker of ≥10 pack years was associated with a 51% increased risk of recurrence for TN cases (HR: 1.51; 95% CI: 1.02, 2.25). Other observed positive associations between smoking and recurrence were not statistically significant.
Conclusions
We found evidence of a reduced risk of recurrence associated with alcohol among luminal A cases, as well as an increased risk of recurrence associated with smoking among TN cases. Understanding the role of modifiable risk factors of breast cancer recurrence may improve care and recommendations for patients after their diagnosis.

Cancer

Assessing causal associations between periodontal disease and risk of lung and pancreatic cancers using a two-sample Mendelian randomization analysis Laura Corlin* Laura Corlin Mengyuan Ruan Kostas Tsilidis Yau-Hua Yu Elizabeth Platz Rachael Stolzenberg-Solomon Chris Amos Karl T. Kelsey Dominique S. Michaud

Background: Large prospective cohort studies have reported strong positive associations for periodontal disease and lung and pancreatic cancer risk. However, the causal role of periodontal disease is unclear; bias due to confounding may explain the observational results. Our objective was to assess whether single nucleotide polymorphisms (SNPs) associated with periodontal disease in genome-wide association studies (GWAS) could predict pancreatic or lung cancer using a two-sample Mendelian randomization (MR) analysis.

Methods: We identified 6 SNPs associated with aggressive and/or severe periodontal disease in GWAS studies with replication in independent populations. Separately, we estimated the associations between the 6 SNPs and cancer risk among 5105 cases and 8738 controls in the Pancreatic Cancer Cohort Consortium (PanScan I, II and III) and 18,082 cases and 13,780 controls in the International Lung Cancer Consortium (ILCCO). We obtained Mendelian randomization estimates using inverse variance weighting (IVW); sensitivity analyses were conducted using weighted median, weighted mode, and MR-Egger.

Results: Genetically predicted periodontal disease was not associated with log odds of lung cancer overall or by different tumor subtypes in our consortium dataset. We observed positive associations for predicted periodontal disease and pancreatic cancer risk in PanScan III cohort dataset (IVW estimate = 0.18, p-value = 0.043, simple median estimate = 0.25, p-value =0.033); however, no associations were observed in the PanScan I and II datasets.

Conclusions: Our preliminary results do not support the hypothesis that genetically predicted periodontal disease is causally linked to lung cancer risk. There is some indication that it may play a causal role in pancreatic cancer. Discrepancies among datasets are being examined. Our 6 SNP genetic score was derived mostly from GWAS on aggressive periodontitis, thus limiting our ability to generalize to all periodontal diseases.

A prospective investigation of serum bile acids and risk of colon and liver cancer Erikka Loftfield* Erikka Loftfield Roni Falk Joshua Sampson Demetrius Albanes Stephanie Weinstein Neal D. Freedman Rashmi Sinha

Background. Experimental studies indicate an important role of bile acids (BAs) and the microbiome in bidirectional communication between the gut and liver (i.e., gut-liver axis). Primary BAs are synthesized and conjugated with glycine or taurine in the liver before being released into the gut. There, BAs can be deconjugated and metabolized by bacteria to form secondary and tertiary BAs, which travel via the portal vein to the liver. BAs are key mediators of lipid absorption, the colonic microbiome, the immune system, and perhaps disease, but there are few epidemiologic studies of BAs and cancer.

Methods. In separate 1:1 matched nested case-control studies of colon (n=327 cases) and liver (n=247 cases) cancer within the Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study (ATBC) cohort, we measured serum concentrations of 14 BAs using a targeted, fully quantitative, liquid chromatography, tandem-mass-spectrometry platform. Serum was collected up to 27 years before cancer diagnosis. We used multivariable conditional logistic regression models to estimate odds ratios (ORs) for cancer outcomes and BA concentrations (ng/mL, 90th v 10th percentile), adjusting for potential confounders.

Results. Higher systemic concentrations of glycine and taurine conjugated primary BAs were associated with greater risk of colon and liver cancer. Additionally, lithocholic acid, which is a secondary BA, as well as glycine and taurine conjugates of secondary and tertiary BAs were associated with greater risk of liver cancer (Figure).

Conclusion. Pre-diagnostic concentrations of BAs, particularly glycine-conjugated BAs, are positively associated with colon and liver cancer risk.
Impact/Significance: Our strong findings extend results from animal studies and suggest a potentially important role for BAs and other byproducts of host-microbial interactions in colon and liver cancer.

Associations of bile acids with colon cancer (327 cases; 327 controls) and liver cancer (247 cases:247 controls) in the ATBC cohort
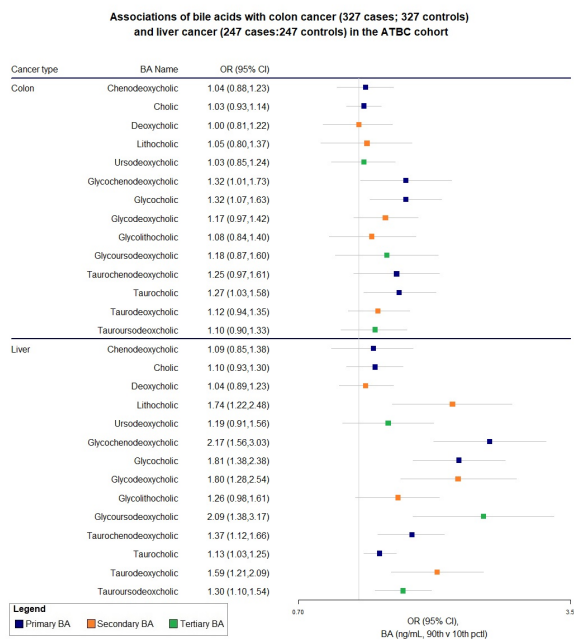
Cancer

A Prospective Analysis of Intake of Red and Processed Meat in Relation to Pancreatic Cancer among African American Women Jessica L Petrick* Jessica Petrick Nelsy Castro-Webb Hanna Gerlovin Traci N. Bethea Shanshan Li Edward A. Ruiz-Narváez Lynn Rosenberg Julie R. Palmer

African Americans have the highest incidence of pancreatic cancer of any racial/ethnic group in the US. There is evidence that consumption of red or processed meat and foods containing saturated fat may increase the risk of pancreatic cancer, but there is limited evidence in African Americans. Utilizing the Black Women's Health study (1995-2018), we prospectively investigated the associations of red and processed meat and saturated fat with the incidence of pancreatic adenocarcinoma (n=168). A food frequency questionnaire used to assess diet was completed by 52,706 participants in 1995 and 2001. Multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression. We observed an interaction with age (p-interaction=0.01). Thus, results were stratified at age 50 (<50, ≥50). Based on 148 pancreatic cancer cases among women aged ≥50 years, the highest quartile of red meat intake, relative to the lowest, was associated with a 65% increased risk of pancreatic cancer (HR=1.65, 95% CI: 0.98–2.78, p-trend=0.05). For every 50 gram increase in red meat intake, risk of pancreatic cancer increased by 22% (HR=1.22, 95% CI: 0.94–1.59). Red meat intake was not associated with pancreatic cancer risk in women <50 years of age. Further, there was a non-significant association between saturated fat and pancreatic cancer among women ≥50 years (HR Q4 vs. Q1=1.85, 95% CI: 0.92–3.72, p-trend=0.08), but there was no association with processed meat in either age group. Our results indicate that red meat—and possibly saturated fat—intake is associated with an increased risk of pancreatic cancer in African American women aged 50 and older.

Cancer

Residential history-based point and cumulative measures of socioeconomic status as predictors of obesity and breast density: two established risk factors for breast cancer.

Carola Sanchez-Diaz* Carola Sanchez-Diaz Garth H Alpana Shannon

Introduction: In the United States, obesity and higher breast density are established risk factors for breast cancer (BC) in general and for Hispanic women specifically. We examined census tract based measures of socioeconomic status (SES) and acculturation as risk factors for obesity and breast density. Because breast cancer can have a long latency period, a patent's residential history (RH) prior to diagnosis may be more clinically meaningful than at diagnosis. Therefore, we defined cumulative historical measures of tract % Hispanic.
Methods: We linked 2749 Latina women with a diagnosis or breast imaging exam (2001-2017) with LexisNexis to obtain RHs. RHs were merged with established measures of interpolated, census-based tract disadvantage and affluence, and proportion Hispanic ("Hispanicity"), scaled in standard deviation (SD) units. We defined both point and cumulative measures at 10 and 20 years prior to diagnosis/last exam. Logistic regression was followed by X-standardization of coefficients in order to compare the relative magnitude of associations.
Results: Spearman correlations between tract SES measures ranged from 0.45-0.65. In age-adjusted models of Hispanic women, greater tract Hispanicity and disadvantage and lower affluence were associated with obesity for all point and cumulative measures. Lower Hispanicity and disadvantage and higher affluence were associated with greater breast density for all measures. For obesity, disadvantage (range of X-standardized coefficients: 0.11, 0.15) and affluence (range: 0.13, 0.15) were generally stronger predictors of obesity than Hispanicity (range: 0.07, 0.10). For breast density, however, tract proportion Hispanic was the only meaningful predictor in mutually adjusted models of breast density.
Conclusion: Established measures of tract-level socioeconomic status predict obesity and BMI-adjusted breast density among Hispanic women. RH-based point and cumulative measures produced associations of similar magnitude.

Oral health and risk of upper gastrointestinal cancers in a large prospective study from a high-risk region: Golestan Cohort Study
Yukiko Yano* Yukiko Yano Christian C. Abnet Sanford M. Dawsey Akram Pourshams Emily Vogtmann Reza Malekzadeh Arash Etemadi

Tooth loss and periodontal disease have previously been associated with several cancers, and poor oral health may be an important risk factor for upper gastrointestinal (i.e. esophageal and gastric) cancers in high-risk areas. In this study, we assessed the relationship between oral health and upper gastrointestinal cancers using a large prospective study of more than 50,000 adults (40-75 years old) living in Golestan Province in northeast of Iran, a high-incidence area for these cancers. Participants in Golestan Cohort Study were recruited from January 2004 to June 2008, and oral health was assessed in detail by trained interviewers. We used Cox proportional hazards regression models to estimate hazard ratios (HRs) and 95% confidence intervals (95% CIs) for the association between three different measures of oral health (the number of missing teeth, the sum of decayed, missing, and filled teeth (DMFT), and the frequency of tooth brushing) and incident esophageal and gastric cancers. During a median follow-up duration of 12 years until January 31, 2019, there were 342 and 354 incident cases of esophageal and gastric cancer, respectively. Excess tooth loss was significantly associated with the risk of esophageal cancer (HR = 1.61; 95% CI: 1.10, 2.37) but not gastric cancer (HR = 1.25; 95% CI: 0.85, 1.85). Daily tooth brushing was associated with decreased risk of developing both esophageal (HR = 0.75; 95% CI: 0.53, 1.05) and gastric (HR = 0.64; 95% CI: 0.45, 0.90) cancers. There was no significant association between DMFT and either upper gastrointestinal cancer. These results suggest increased risk of developing esophageal and gastric cancers among individuals with poor oral health, and those who do not have regular oral hygiene practices.

Esophageal cancer

		HR	95% CI	p-value
Tooth brushing	Never	Reference		
	Non-daily	0.769	(0.535, 1.10)	0.154
	Daily	0.749	(0.533, 1.05)	0.0960
Tooth loss group	Expected or less	Reference		
	Q1	1.02	(0.739, 1.42)	0.889
	Q2	1.01	(0.724, 1.41)	0.950
	Q3	1.20	(0.891, 1.63)	0.226
	Q4	1.61	(1.10, 2.37)	0.0145
	Linear trend			0.0294
	Global trend			0.139
DMFT group	Expected or less	Reference		
	Q1	0.870	(0.653, 1.16)	0.341
	Q2	1.04	(0.751, 1.43)	0.833
	Q3	1.22	(0.868, 1.73)	0.248
	Q4	1.11	(0.659, 1.89)	0.685
	Linear trend			0.368
	Global trend			0.553

Gastric cancer

		HR	95% CI	p-value
Tooth brushing	Never	Reference		
	Non-daily	0.739	(0.519, 1.05)	0.0933
	Daily	0.636	(0.450, 0.899)	0.0103
Tooth loss group	Expected or less	Reference		
	Q1	0.863	(0.623, 1.20)	0.378
	Q2	0.865	(0.609, 1.23)	0.415
	Q3	1.03	(0.763, 1.39)	0.855
	Q4	1.25	(0.849, 1.85)	0.256
	Linear trend			0.498
	Global trend			0.514
DMFT group	Expected or less	Reference		
	Q1	0.859	(0.646, 1.14)	0.295
	Q2	0.914	(0.660, 1.27)	0.590
	Q3	1.21	(0.869, 1.68)	0.261
	Q4	1.16	(0.712, 1.89)	0.551
	Linear trend			0.447
	Global trend			0.482

Cancer

Glucosamine and chondroitin supplements and risk of colorectal adenoma in US adults

Elizabeth Kantor* Dong Hoon Lee Dong Hoon Lee Chao Cao Xuehong Zhang Kelli O'Connell Mingyang Song Kana Wu Mengmeng Du Edward L. Giovannucci Yin Cao Elizabeth D. Kantor

Background: Several studies have shown use of glucosamine and chondroitin supplements to be associated with reduced colorectal cancer (CRC) risk. However, the association with colorectal adenoma, a colorectal cancer precursor lesion, has not been examined. We therefore evaluated the association between use of glucosamine and chondroitin supplements and risk of adenoma, with a focus on those high-risk adenomas most likely to develop into CRC.

Methods: Analyses include 43,163 persons from the Nurses' Health Study (NHS), Health Professionals Follow-up Study (HPFS), and NHS2. Our study was restricted to persons who reported on use of glucosamine and chondroitin in 2002 and who subsequently underwent at least one lower bowel endoscopy prior to 2012. 5,715 conventional adenomas were detected, including 2,016 high-risk adenomas and 4,953 serrated polyps. Multivariable logistic regression models for clustered data were used to calculate odds ratios (ORs) and 95% confidence intervals (CIs).

Results: Use of glucosamine and chondroitin was inversely associated with high-risk adenoma in NHS and HPFS: in the pooled multivariable-adjusted model, use of combined glucosamine + chondroitin at baseline was associated with a 26% (OR=0.74, 95% CI=0.58-0.95) lower risk of high-risk adenoma. However, no association was observed among younger women (NHS2), and the pooled effect estimate across all three studies was null (OR: 0.84; 95% CI: 0.63-1.11). No significant associations were observed between baseline glucosamine/chondroitin use and risk of any conventional adenoma or serrated polyps.

Conclusion: We found baseline use of glucosamine and chondroitin to be associated with a lower risk of high-risk adenoma in older adults; however, this association did not hold in NHS2, a study of younger women, or for overall conventional adenoma or serrated polyps. Our study provides first evidence that glucosamine and chondroitin may act on early colorectal carcinogenesis in older adults.

Cancer

Effect of insulin on insulin-like growth factor 1: a two-sample Mendelian randomization study Jack C M Ng* Jack C M Ng C Mary Schooling

Context: Insulin-like growth factor 1 (IGF-1) is hormone produced predominantly by the liver and is downstream to the growth hormone. IGF-1 has been linked to development of cancers due to its ability in promoting cell growth. Notably, release of growth hormone is affected by blood glucose, which is regulated by insulin. We investigated the effect of genetically predicted insulin on IGF-1. Methods: We performed a two-sample Mendelian randomization (MR) analysis by applying single-nucleotide polymorphism (SNPs) strongly (p-value $<5 \times 10^{-6}$) and independently ($r2 < 0.05$) associated with insulin protein (effect size) from a genome-wide association study of proteins (n=3,301) to IGF-1 (nmol/L) in a genome-wide association study from the UK Biobank (n$\leq$361,194). SNP-specific Wald estimates were meta-analyzed using inverse-variance weighting with multiplicative random effects. As sensitivity analyses, we discarded proxy SNPs with low r2 (<0.7) and potential confounders of the insulin-IGF-1 association, and used other estimators. Results: We obtained 13 SNPs independently predicting insulin protein with mean F-statistic of 23.12. Insulin was positively associated with IGF-1 (inverse-variance weighted beta, 0.07; 95% CI, 0.01 to 0.13). Sensitivity analyses yielded similar estimates, with no statistical evidence of heterogeneity in SNP-specific Wald estimates or directional pleiotropy. Conclusions: Genetically predicted higher insulin was associated with a higher IGF-1, suggesting insulin is a valid target of intervention for IGF-1. The underlying mechanism and its relevance to reduction in the burden of cancer require further investigation.

Neurocognitive Effects of Chemotherapy in Colorectal Cancer: A Systematic Review and Meta-Analysis of Eight Studies

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Objectives: This study aims to quantify the effects of chemotherapy on neurocognitive functions among colorectal cancer patients by systematic review and a meta-analysis.

Methods: PubMed/MEDLINE, Embase and CENTRAL/Cochrane Database of Systemic Reviews were searched at January 2019 with keywords related to cancer, chemotherapy, and cognition. Eight studies which met the inclusion criteria provided 706 colorectal cancer patients who received chemotherapy. Standardized mean differences (SMDs) of each neuropsychological test were calculated and were merged to estimate pooled effect size. Random effect model was used to calculate pooled effect sizes. Publication bias was estimated by funnel plot and Egger's test. Subgroup analysis by measurements of neurocognitive functions (objective vs. subjective) was performed, and meta-regression was conducted to investigate the association between the mean age of each study participants and the neuropsychological test results. Additionally, for studies with objective neurocognitive function assessment tests, results from each tests were pooled by neurocognitive function domain.

Results: We could not find significant association between chemotherapy and subsequent neurocognitive decline (SMD=0.003, p=0.939). Egger's test and funnel plot showed no significant evidence of publication bias (p for asymmetry=0.277). Results from both studies with 'objective neurocognitive tests' (SMD==0.0000,, p=0.998) and studies with 'subjective reports' (SMD=0.015, p=0.601) showed no clear evidences of neurocognitive decline. A result from meta-regression showed that SMDs were more likely to be negative in studies with older participants (β=-0.016, p<0.001).

Conclusion: We found no significant evidence suggesting neurocognitive decline after chemotherapy in colorectal cancer patients. However, our results from subgroup analysis suggest that older patients might be more vulnerable to neurocognitive decline after chemotherapy.
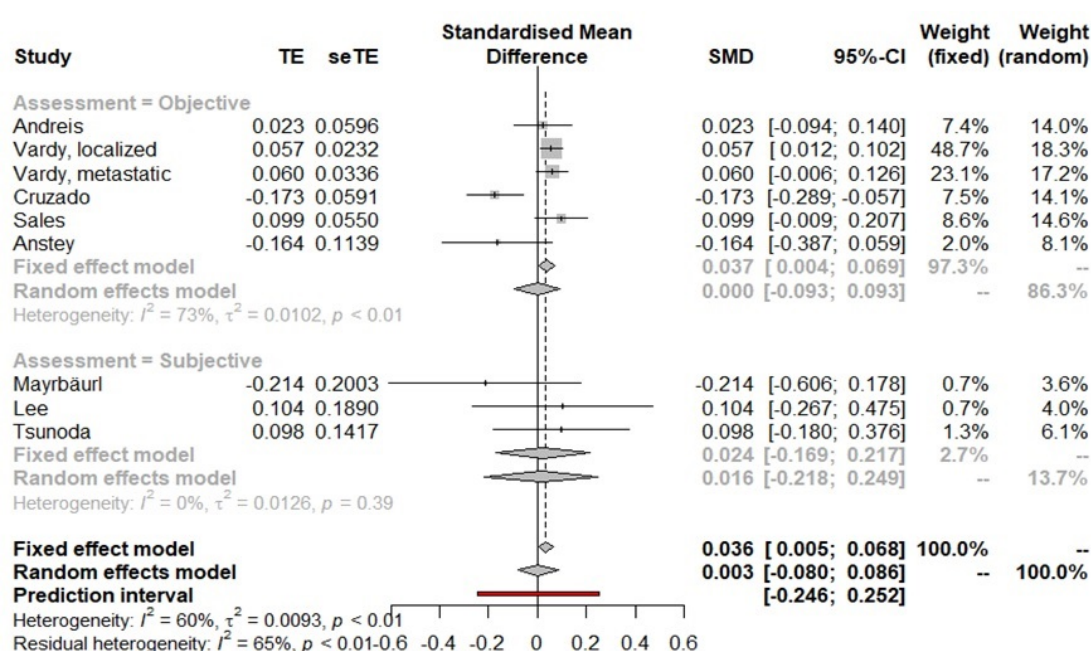
Cancer

Impact of adherence to the 2010 Alternative Healthy Eating Index on overall survival and bladder cancer disease-specific survival in a population-based study Reno C. Leeming* Reno Leeming Margaret R. Karagas Diane Gilbert-Diamond Jennifer A. Emond Michael S. Zens Brock C. Christensen John D. Seigne Michael N. Passarelli

Background: Preclinical studies have shown that specific foods and nutrients have antitumor effects on urothelial carcinoma, yet little is known about diet quality and bladder cancer death. We examined overall diet quality in association with overall survival (OS) and disease-specific survival (DSS) among those with non-muscle invasive bladder cancer (NMIBC). Methods: Men and women diagnosed with NMIBC between 1998-2004 and who participated in a population-based case-control study were followed for mortality outcomes using the National Death Index through 2017. A total of 527 participants who were asked about their pre-diagnostic diet were eligible for this study (242 participants completed the Harvard Food Frequency Questionnaire and 285 completed the National Cancer Institute Diet History Questionnaire). Diet quality was measured using the 2010 Alternative Healthy Eating Index (AHEI-2010). Cox proportional hazards regression was used to calculate HRs and 95% CIs per 1-unit increase in AHEI-2010 score for OS and DSS, accounting for competing risks of death. HRs were adjusted for sex, diagnosis age, smoking status, education, tumor grade, first-course treatment, energy intake, and dietary instrument. Results: Over a median follow-up of 14.2 years after diagnosis, 253 deaths occurred, including 54 deaths due to bladder cancer. AHEI-2010 diet quality score was not associated with OS (HR: 1:00; 95% CI: 0.98-1.01) or DSS (HR: 1.00; 95% CI: 0.97-1.03). Greater adherence to AHEI-2010 sugar-sweetened beverage (SSB) guidelines was associated with poorer OS (HR: 1.04; 95% CI: 1.01-1.08) but not DSS (HR: 1.02; 95% CI: 0.95-1.10). Greater adherence to sodium guidelines was associated both with better OS (HR: 0.92; 95% CI: 0.85-1.00) and DSS (HR: 0.83; 95% CI: 0.68-0.99). Conclusions: Diet quality at diagnosis as defined by AHEI-2010 was not associated with survival. Our results suggest that SSB and sodium intake and survival after NMIBC diagnosis warrants further study.

Renal cell carcinoma and metabolomics in the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial Kathleen M. McClain* Kathleen McClain Joshua N. Sampson Jessica L. Petrick Kaitlyn M. Mazzilli Robert E. Gerszten Clary B. Clish Mark P. Purdue Loren Lipworth Steven C. Moore

Background: In the US in 2019, 73820 kidney cancers are expected and >80% are renal cell carcinomas (RCCs). Along with excess fat, laboratory and epidemiologic evidence implicates metabolic dysfunction in RCC etiology. To identify metabolites associated with RCC, we conducted a 1:1 matched case-control study nested within the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.

Methods: We measured 522 serum metabolites in n=267 cases/controls within PLCO. Cases were followed for a median 7.1 years from blood draw to diagnosis. Covariates, including RCC risk factors, were assessed at baseline. Conditional logistic regression estimated ORs and 95% CIs comparing risk at the 90th percentile to the 10th of log metabolite intensity, with the significance threshold defined as a false discovery rate <0.20.

Results: Four metabolites were inversely associated with RCC risk—C38:4 PI (OR=0.33, 95%CI:0.19-0.58), C34:0 PC (OR=0.42, 95%CI:0.25-0.70), C14:0 SM (OR=0.44, 95%CI:0.26-0.73), and C16:1 SM (OR=0.40, 95%CI:0.23-0.70). Two were positively associated with RCC risk—C3-DC-CH3 carnitine (OR=2.84, 95%CI:1.72-4.68) and C5 carnitine (OR=2.83, 95%CI:1.70-4.72). Adjustment for metabolic risk factors (BMI, physical activity, diabetes/hypertension history) did not attenuate ORs (attenuation |ln(OR)<0.2|), except modestly for C5 carnitine (ORnew=2.31) and C16:1 SM (ORnew=0.34). Metabolites associated with RCC had only weak correlations (|r|<0.2) with risk factors of BMI, physical activity, smoking, alcohol, and diabetes/hypertension history. In mutually adjusted models, 3 metabolites (C38:4 PI, C14:0 SM, and C3-DC-CH3 carnitine) were independently associated with RCC risk.

Conclusions: Serum concentrations of 6 metabolites were associated with RCC risk. These metabolites may point toward new biological pathways of relevance to RCC risk, including carnitines, which are known to be transporters of acyl groups and have been linked with metabolic plasticity.

Cancer

Douching, genital talc use, and prevalent and incident cervical cancer Katie O'Brien* Katie O'Brien Aimee A. D'Aloisio Kristen R. Moore Clarice R. Weinberg Dale P. Sandler

Background: While human papillomavirus is the primary cause of cervical cancer, other factors may play a role by influencing individuals' susceptibility and response to the virus. Candidate risk factors include use of personal care products, particularly those applied near the cervix. Previous case-control studies have reported positive associations between douching and cervical cancer, but no prospective studies have been done. No prior studies have examined the association between genital talc use and cervical cancer.

Methods: We evaluated the association between history of douching and genital talc use and self-reported cervical cancer using data from the Sister Study (2003-2009), a US-wide cohort study of women ages 35-74 at enrollment. We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs), adjusted for measured confounders. We considered prevalent (n=523) and incident (n=31) cervical cancer separately.

Results: At ages 10-13, 3% of participants douched and 19% used genital talc. As adults, in the 12-months prior to study enrollment, 14% douched and 15% used genital talc. Adolescent douching was positively associated with prevalent cervical cancer (HR=1.32, 95% CI: 0.85-2.03), but the association between adolescent talc use and prevalent cervical cancer was near-null (HR=0.94, 95% CI: 0.75-1.18). Douching in the year before enrollment was positively associated with incident cervical cancer (HR=2.54, 95% CI: 1.09-5.94), but we observed no clear association between recent genital talc use and incident disease (HR=1.81, 95% CI: 0.79-4.15).

Discussion: Douching was positively associated with cervical cancer. These results are consistent with the previous literature and further demonstrate that the association remains when exposure is assessed prior to disease development. In the first study to examine genital talc use and cervical cancer, we did not see strong evidence of an association.

Cancer

Personal use of permanent hair dyes and cancer risk and mortality in US women: prospective cohort study Yin Zhang* Yin Zhang Brenda M. Birmann Jiali Han Edward L. Giovannucci Frank E. Speizer Meir J. Stampfer Bernard A. Rosner Eva S. Schernhammer

Background
Personal use of permanent hair dyes has been examined as a potential risk factor for numerous cancers, but epidemiological evidence remains inconclusive.
Methods
The Nurses' Health Study is an ongoing prospective cohort study of US female nurses. A total of 117200 women free of cancer at baseline and who reported information on personal use of permanent hair dyes, were included and followed for 36 years. Hazard ratios (HRs) and 95% confidence intervals (95%CIs) for associations of personal use of permanent hair dyes with risk of overall and specific cancers and cancer-related death were estimated by using Cox models. The exposures included status, duration, frequency, cumulative dose, age at first use, and time since first use of permanent hair dyes.
Results
Compared with non-users of permanent hair dyes, ever-users had no significant increases in risk of solid (n=20805 cases; excluding non-melanoma skin cancers) (HR, 95%CI =0.98, 0.96-1.01), or hematopoietic cancer risk overall (n=1807 cases) (1.00, 0.91-1.10), or of risk of most specific cancers, and cancer-related death (n=4860 cases) (0.96, 0.91-1.02). Basal cell carcinoma risk was slightly increased for ever-users (n=22560 cases) (1.05, 1.02-1.08). Further, cumulative dose was positively associated with basal cell carcinoma, breast cancer and ovarian cancer risk. Some findings varied by natural hair color, including an increased risk of Hodgkin lymphoma observed only for women with naturally dark hair, and higher risks of basal cell carcinoma and breast cancer observed for women with naturally light hair.
Conclusion
There was no positive association between personal permanent hair dye use and risk of most cancers and cancer-related mortality. The increased risk for basal cell carcinoma, breast cancer and ovarian cancer, and the mixed findings for basal cell carcinoma, breast cancer and Hodgkin lymphoma in analyses stratified by natural hair color should be noted and warrant further confirmation.

Cancer Survival among WTC Rescue and Recovery Workers: A Collaborative Cohort Study

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Background: Increased cancer incidence has been reported among World Trade Center (WTC)-exposed responders. Until now, the survival of WTC-responders who developed cancer has not been investigated. The WTC Health Program (WTCHP) provides medical monitoring/treatment for health conditions, including cancer, to WTC-exposed responders.

Objectives: To estimate the relative survival of WTC-exposed responder cancer patients enrolled in a NYC-based WTCHP compared to 1)New York State(NYS) non-WTC-exposed cancer patients;2)WTC-exposed responder cancer patients NOT enrolled in a NYC-based WTCHP.

Methods: We combined 3 WTC-exposed cohorts: Fire Department of the City of New York (FDNY), General Responder Cohort (GRC) and other responders followed by the WTC Health Registry (WTCHR). FDNY and GRC participants are enrolled in the WTCHP, but WTCHR participants who are not also enrolled in either the FDNY or GRC cohort are not. The 3 level exposure variable was: WTC-exposed and enrolled in a NYC-based WTCHP; WTC-exposed and NOT enrolled in a NYC-based WTCHP; all other cancer cases in the 11 southernmost NYS counties but NOT exposed to the WTC disaster. Analyses restricted cases to these counties since most responders resided in these areas, yielding similar proximity to large cancer centers and environmental exposures. Parametric survival models estimated all-cause mortality and cancer-specific mortality. Follow-up started at first primary cancer diagnosis after 1/1/05 since the majority of the combined cohort enrolled by that point. Follow-up ended at death or were censored at 12/31/16.

Results: All-cause mortality and cancer-specific mortality were reduced in members who were enrolled in a NYC-based WTCHP (Figure).

Conclusions: WTC-exposed responder cancer patients enrolled in a WTCHP had longer survival compared with references after accounting for demographic factors and temporal trends, possibly reflecting the effect of medical monitoring and access to free WTC-covered cancer treatments.

Figure: All-cause and Cancer-Specific Mortality for All Cancers[a,b,c]

All-cause mortality — HR (95% CI)

	HR (95% CI)
Responders enrolled in a NYC-based WTCHP vs New York State	0.53 (0.48, 0.58)
Responders NOT enrolled in a NYC-based WTCHP vs New York State	0.91 (0.78, 1.05)
Responders enrolled in a NYC-based WTCHP vs Responders NOT enrolled in a NYC-based WTCHP	0.58 (0.49, 0.69)

Cancer-specific mortality — HR (95% CI)

	HR (95% CI)
Responders enrolled in a NYC-based WTCHP vs New York State	0.58 (0.53, 0.65)
Responders NOT enrolled in a NYC-based WTCHP vs New York State	0.94 (0.79, 1.12)
Responders enrolled in a NYC-based WTCHP vs Responders NOT enrolled in a NYC-based WTCHP	0.62 (0.51, 0.76)

Abbreviations: WTCHP: World Trade Center Health Program; HR: hazard ratio of mortality; CI: confidence interval

a: Responders enrolled in a NYC-based WTCHP include 2,815 cancer cases; 445 overall deaths; and 361 cancer deaths

b: Responders NOT enrolled in a NYC-based WTCHP 574 cancer cases; 175 overall deaths; and 131 cancer deaths

c: adjusted for calendar year, age, race/ethnicity, sex, stage and cancer site (all analyses restricted to cancer cases from 11 southernmost New York State counties)

Cancer

Integrative Analyses of Tumor Molecular Pathology, Microbiota, and Immunity in Relation to Exposures in Tansdisciplinary Epidemiologic Research Shuji Ogino* Shuji Ogino Tomotaka Ugai Molin Wang Rong Zhong Kota Arima Melissa Zhao Mai Chan Lau Koichiro Haruki Kenji Fujiyoshi Naohiko Akimoto Andrew T. Chan Jeffrey A Meyerhardt Edward L. Giovannucci Marios Giannakis Mingyang Song Jonathan A. Nowak

Cancer immunology has been rapidly advancing, and immunoprevention and immunotherapy strategies have a great potential to reduce cancer burden. As tumors represent heterogeneous pathological processes due to interactive influences of the exposome (including the microbiome), the immune system, and tumor cells (Figure), we need to investigate influences of exposures on tumor molecular pathology and immunity. Using archival tumor tissue of 1,620 incident colorectal cancer cases in the Nurses' Health Study and the Health Professionals Follow-up Study (with 173,229 participants), we have conducted proof-of-principle studies to provide evidence for influences of smoking (Hamada et al. J Natl Cancer Inst 2019), aspirin (Cao et al. Gastroenterology 2016), vitamin D (Song et al. Gut 2016), inflammatory diet (Liu et al. Gastroenterology 2018), marine omega-3 fatty acids (Song et al. JAMA Oncol 2016), calcium (Wang et al. Cancer Prev Res 2019), and germline genetic variation (Khalili et al. Carcinogenesis 2015) on incidence of colorectal cancer subtypes classified by local immune response to tumor, assessed by routine histopathologic examination and immunohistochemistry. We have recently conducted whole exome sequencing on tumor/normal DNA pairs, tumor RNA-sequencing, validated multiplex immunofluorescence assays to spatially characterize various immune cells (e.g., T cell subtypes, M1 and M2 tumor-associated macrophages), and microbial assays to detect putative cancer pathogens. To adjust for selection bias due to tissue data availability, we developed methods of applying inverse probability weighting (IPW) (Liu et al. Eur J Epidemiol 2018), utilizing covariate data from 4,420 incident colorectal cancer cases. Our unique research framework to integrate microbial and immune assays on archival tumor tissue into epidemiological cohort studies can provide novel etiological insights and possible paths for precision prevention and public health.
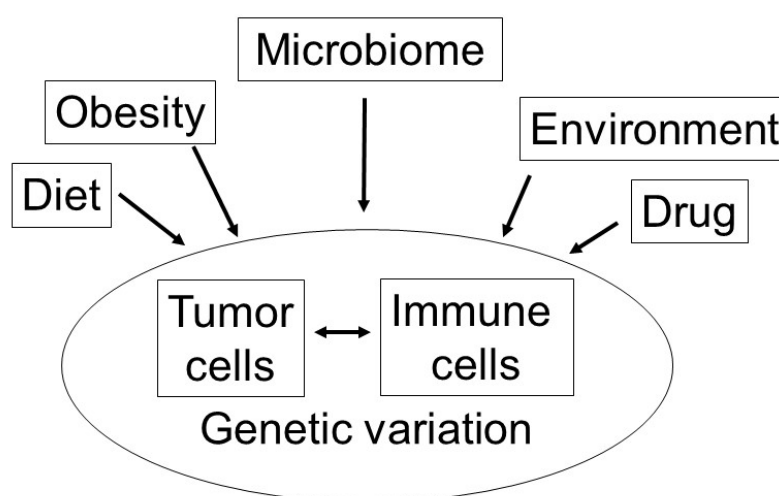
Idea modified from
Ogino et al. Lancet 2018

Cancer

Dietary Polyunsaturated Fat Intake in Relation to Liver Cancer Incidence in the NIH-AARP Diet and Health Study Shawn A. Zamani* Shawn Zamani Barry I. Graubard Linda M. Liao Xuehong Zhang Katherine A. McGlynn Jessica L. Petrick

Polyunsaturated fatty acids (PUFAs) are fatty acids containing more than one double bond. Fish and marine meats are rich sources of PUFAs—specifically long-chain n-3 PUFAs, which express anti-inflammatory properties and prevent liver tumor progression in laboratory models. Conversely, n-6 PUFAs, mainly found in non-marine oil-rich diets, exhibit carcinogenic properties. In epidemiologic studies, there is consistent—albeit limited—evidence that higher fish intake is associated with decreased liver cancer risk, but the associations between n-3 and n-6 PUFA subtypes and risk of liver cancer remain unclear. Utilizing the NIH-AARP Diet and Health Study (1995-2011), we prospectively investigated the associations of PUFA subtypes, their ratio, and fish consumption with the incidence of the two primary subtypes of liver cancer—hepatocellular carcinoma (HCC, n=575) and intrahepatic cholangiocarcinoma (ICC, n=157)—among 468,952 participants with a median follow-up of 15.5 years. A validated food frequency questionnaire was used to assess diet at study baseline. Multivariable-adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards regression with years of follow-up as the underlying time metric. Long-chain n-3 PUFAs (eicosapentaenoic, docosapentaenoic, and docosahexaenoic acids) were associated with a 36% decreased HCC risk (quintile 5 vs. 1 HR=0.64, 95% CI: 0.49–0.84, P-trend=0.007). Similar associations were observed for intake of non-fried fish (excluding tuna; HR=0.71, 95% CI: 0.53–0.96, P-trend=0.02) and tuna (HR=0.59, 95% CI: 0.45–0.78, P-trend=0.0003). Additionally, the ratio of long-chain n-3 to n-6 PUFAs was associated with decreased HCC risk (HR=0.62, 95% CI: 0.48–0.81, P-trend=0.0004). No associations were observed between PUFA or fish intake and ICC risk. Our results indicate that dietary long-chain n-3 PUFAs, non-fried fish, and tuna intake is associated with lower HCC risk.

Cancer

Relationship between Religious Participation and Survival Time among Elderly Cancer Patients in Mainland China: A Retrospective Cohort Study Stephen W. Pan* Zihan Dong Qikai Wang Stephen W Pan

Background: In China, cancer is one of the largest contributors of disability-adjusted life years among the elderly. Timely hospital diagnosis and treatment can improve the survival time of cancer patients, and may be influenced by individual religious practices. However, there is a paucity of research on the relationship between religion and cancer outcomes in China. In response, this study investigates the potential associations between religious participation and survival time after cancer diagnosis among elderly cancer patients in China. Methods: This study uses data from the Chinese Longitudinal Healthy Longevity Survey (CLHLS). The participants of this study were individuals between 65 and 108 years old who enrolled into the CLHLS between 1998 and 2002. Study inclusion criteria: free of cancer at baseline, diagnosed with cancer during follow-up and reported death or censoring by the 2005 interview wave. Statistical analyses were conducted using Cox proportional hazard regression models. Multivariable models controlled for sex, age, ethnicity, residency, marital status, co-residence and health behaviors. Results: Analyses indicated that the direction and magnitude of association between religious activity and cancer survival time changed over time (n=385). Between cancer diagnosis and 11.6 months post-diagnosis, religious activity was associated with markedly poorer survival time ($1.00 < HR < 3.57$, $p=0.059$). However, the magnitude of association diminished over time, and after 11.6 months post-diagnosis, religious activity was associated with superior survival time ($0.54 < HR < 1$, $p=0.059$). Conclusion: Findings indicated that religious participation may be associated with cancer survival time and that effects may change over time. Additional studies are needed to elucidate the mechanisms by which religion may impact cancer survival time among elderly population in China.

Metabolic syndrome and all-cause mortality among endometrial cancer survivors Renee Kokts-Porietis* Renee Kokts-Porietis Jessica McNeil Linda Cook Gregg Nelson Kerry S. Courneya Christine M. Friedenreich

Background: Endometrial cancer is one of the few cancers with both increasing incidence and mortality rates. While central adiposity, diabetes and hypertension have been identified as major risk factors for endometrial cancer incidence, the combined effect of these risk factors on endometrial cancer survivorship remains unclear.

Aim: To determine the associations between Metabolic Syndrome and all-cause mortality among endometrial cancer survivors.

Methods: Cases from a population-based case-control study who were diagnosed with primary, histologically confirmed endometrial cancer between 2002 and 2006 in Alberta, Canada were followed until death or March 20, 2019, whichever occurred first. Baseline in-person interviews, direct anthropometric measurements and a minimum eight-hour fasting blood samples were used to assess Metabolic Syndrome with the Harmonized criteria. Individuals with three or more of the following conditions were considered to have Metabolic Syndrome: elevated waist circumference (≥88 cm), high blood pressure (systolic ≥130 mmHg or diastolic ≥85 mmHg), elevated fasting blood glucose levels (≥100 mg/dL), elevated triglycerides (≥150 mg/dL) and low high-density lipoprotein cholesterol (<50 mg/dL). A Cox proportional hazards regression model was used to estimate multivariate-adjusted HR (95%CI) and the proportional hazard assumption was assessed with Schoenfeld residuals.

Results: Of 501 women with endometrial cancer, 321 had Metabolic Syndrome and 96 died during the median 14.2 years of follow-up (range 0.4-16.4 years). Women with Metabolic Syndrome had an increased hazard of all-cause mortality (HR=1.68; 95% CI=1.02, 2.75) after adjusting for endometrial cancer type (I/II), age, treatment (adjuvant and primary hysterectomy), education level, smoker type, and Body Mass Index (kg/m2) (Figure 1).

Conclusion: These findings suggest that Metabolic Syndrome is associated with increased all-cause mortality among women living with endometrial cancer.

Metabolic Syndrome and All-Cause Mortality among Endometrial Cancer Survivors: Cox Proportional Hazards Regression
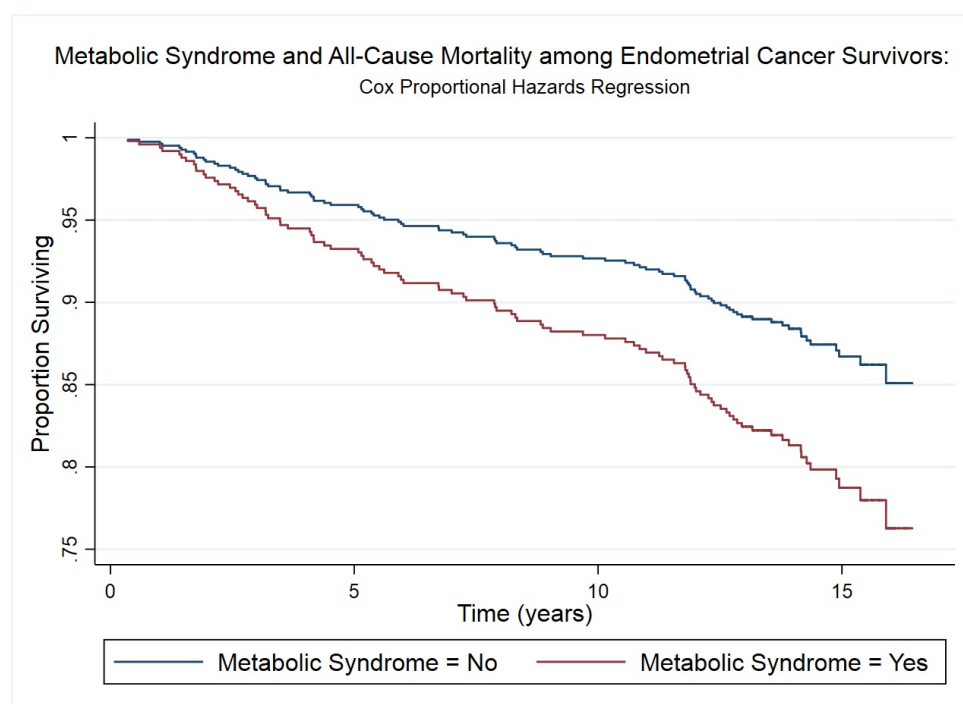
Cancer

Post-diagnostic dairy products intake and colorectal cancer survival in US population Xing Liu* Xing Liu Wanshui Yang Kana Wu Shuji Ogino Weibing Wang Na He Andrew T. Chan Jefferey A. Meyerhardt Edward Giovannucci Xuehong Zhang

The association between dairy products intake and survival among colorectal cancer patients remains unclear. This study analyzed follow-up data from the Nurses' Health Study (NHS) and the Health Professionals Follow-up Study (HPFS). Information on dairy product intake and other dietary and life-style factors were updated from the self-reported questionnaire every 2 or 4 years. Individual dairy items including milk, cheese, yogurt, etc. were reported and total dairy product intake and high-fat and low-fat dairy intake were derived. After a median follow-up time of 8.2 year, 1,753 eligible CRC cases were identified until 2012, from which 703 deaths were documented, and 242 were due to CRC. Overall, post-diagnostic total dairy intake did not show significant association with CRC-specific mortality (HR: 1.35, 95% CI: 0.85-2.13, 21+ vs. <7 servings/week) or overall mortality (HR: 1.28, 95% CI: 0.98-1.67, 21+ vs. <7 servings/week). However, high-fat dairy, including whole fat milk, cheese, etc., was positively associated with overall mortality (HR: 1.33, 95% CI: 1.08-1.65, 10.5+ vs. <3.5 servings/week), but not CRC-specific mortality (HR: 1.31, 95% CI: 0.91-1.90, 10.5+ vs. <3.5 servings/week). Low-fat dairy, including those skim or non-fat milk, cottage or ricotta cheese, etc., was inversely associated with both CRC-mortality (HR: 0.66, 0.45-0.97, 7-<10.5 vs. <3.5 servings/week) and overall mortality (HR: 0.74, 95% CI: 0.59-0.92, 10.5+ vs. <3.5 servings/week). For CRC-specific survival, positive associations were found for American or cheddar cheese and regular ice cream, and inverse associations for cottage or ricotta cheese. For overall survival, positive associations were found for whole milk, and inverse associations for milk, skim or low-fat milk, cottage or ricotta cheese and sherbet, frozen yogurt or non-fat ice cream. High intakes of high-fat dairy products were associated with increased mortality, while low-fat dairy was associated with lower risk.

Risk factors for young-onset breast cancer in the Canadian Partnership for Tomorrow Project: updated analyses Robert Basmadjian* Robert Basmadjian Darren Brenner Joy Pader Nicole Mealey Dylan O'Sullivan Yibing Ruan Edwin Wang May Lynn Quan Christine Friedenreich Rachel Murphy

Background: Young-onset breast cancer (YOBC) remains the most common cancer in Canadian women under the age of 50 and incidence has increased over the past 25 years. Mutations in the BRCA1 and BRAC2 genes increase breast cancer risk; however, they only account for 5-10% of cases under age 50. This suggests that other intrinsic and extrinsic factors may contribute to the development of YOBC. Aim: This ongoing study investigates the relationship between lifestyle factors and YOBC in three prospective Canadian cohorts. Methods: A matched-case control study is ongoing from three cohorts from the Canadian Partnership for Tomorrow Project including, the Alberta Tomorrow Project (ATP), BC Generation (BCGen), and Ontario Health Study (OHS). Participants diagnosed with breast cancer under 50 years were identified through linkage with provincial cancer registries. Cases were matched to three control participants of similar age, sex, follow-up, and without a history of breast cancer from the same cohort. Lifestyle data were obtained from questionnaires completed by participants. Conditional logistic regression was used to estimate ORs (with 95% CIs) for associations between lifestyle factors and YOBC. Here, we present results from the ATP cohort. Results: From the ATP, 90 cases were matched to 270 controls. ORs were estimated for lifestyle exposures, including physical activity (OR=0.82; 95% CI: 0.32-2.07), use of hormonal contraceptive (OR=2.03; 95% CI: 0.48-8.58), smoking status (OR=0.97; 95% CI: 0.63-1.50), and alcohol intake (OR=0.95; 95% CI: 0.10-1.97). Next steps: Matched case-control analyses will be conducted in the OHS (484 cases, 1452 controls) and BCGen (36 cases, 108 controls) cohorts then estimates will be pooled using random effects models to account for variation between cohorts. Additionally, tumour samples are being collected from the Alberta Cancer Research Biorepository for a set of cases from the ATP for mutational signatures related to exposures.

Cancer

Examining the effect of exemestane metabolism on physical health-related quality of life in postmenopausal women participating in the MAP.3 trial Robert Basmadjian* Robert Basmadjian Harriet Richardson Philip Lazarus Paul Goss Dongsheng Tu

Background: In the Mammary Prevention.3 (MAP.3) trial of exemestane (EXE) for breast cancer prevention, postmenopausal women commonly reported physical symptoms, such as joint pain and fatigue. The aim of this study was to determine whether the UGT2B17 homozygous deletion, which impairs elimination (via glucuronidation) of the active EXE metabolite 17-DHE, was detrimental to physical health-related quality of life (HRQL) in participants randomized to EXE. Objectives: To characterize the relationship of 1) the UGT2B17 deletion and 2) glucuronidation of 17-DHE, with clinically meaningful decline in physical HRQL. Methods: UGT2B17 genotype and EXE metabolite concentrations were determined from blood draws at baseline using allelic discrimination and LC/MS/MS, respectively. Glucuronidation of 17-DHE was quantified as a ratio between the concentrations of the glucuronidated product of 17-DHE (17-DHE-Gluc) and 17-DHE. Physical HRQL data in MAP.3 was collected using the Menopause-Specific Quality of Life Questionnaire (MENQOL) at baseline and 12-month follow-up. An increase in MENQOL score of ≤1 of 8 points during this period was defined as decline in physical HRQL. Log-binomial regression was used to assess the effect of the UGT2B17 deletion on decline physical HRQL and the effect of glucuronidation of 17-DHE on decline in physical HRQL. Results: The UGT2B17 deletion was associated with meaningful decline in physical HRQL among women in the EXE arm. (RR=1.30, 95% CI: 1.02-1.67). Higher glucuronidation of 17-DHE exhibited a protective (RR=0.84, 95% CI:0.74-0.94) and moderately linear (Slope=-0.18, R=0.57) effect on meaningful decline in physical HRQL. Conclusions: Postmenopausal women with the UGT2B17 deletion were more likely to develop worsened physical HRQL in the EXE arm, presumably due to increased concentration of circulating active EXE metabolites (17-DHE). Further research is needed to support the utility of UGT2B17 screening for breast cancer prevention with EXE.
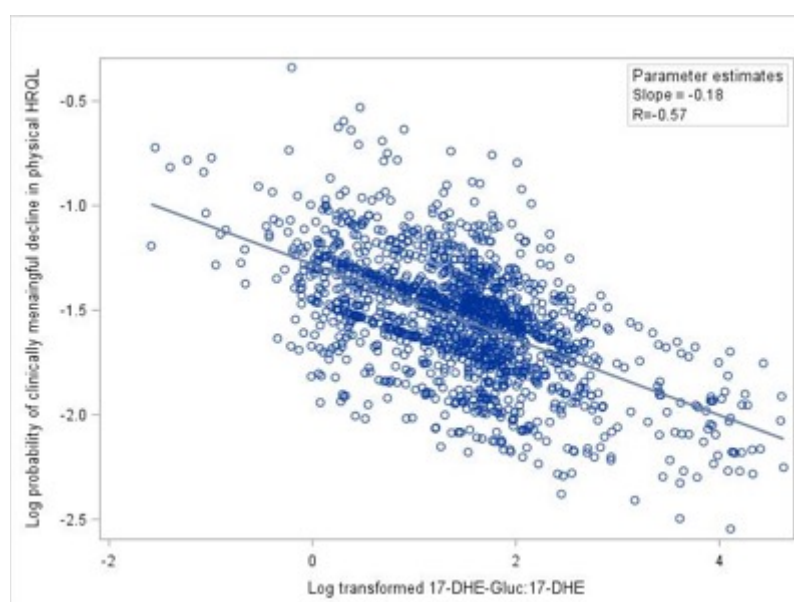
The relationship between human papillomavirus (HPV) beliefs and perceived ambiguity regarding cancer prevention recommendations among young adults Miraides Brown*

Miraides Brown Lynette Phillips

Objective

The purpose of this study is to determine if perceived ambiguity regarding cancer prevention recommendations is related to perceived cancer preventability and HPV beliefs among young adults aged 18-26 years.

Methods

From the National Cancer Institute 2017 Health Information National Trends Survey 5 (HINTS5) Cycle 1, and 2018 HINTS 5 Cycle 2, logistic regression analyses were used to evaluate the relationship between perceived ambiguity about cancer prevention recommendations and two outcomes: perceived cancer preventability overall, and belief that HPV causes four HPV-related cancers.

Results

A total of 266 participants aged 18-26 years were included. Over 32% reported not having ever heard of HPV. Of those who had, 78.9%, 23.8%, 20.3%, and 27.2% believed that HPV can cause cervical, penile, anal, and oral cancers. Sixty-nine percent had high perceived ambiguity, but only 22.2% had low perceived preventability. Belief that HPV causes cervical cancer was significantly associated with non-Caucasian race and having ever smoked (Table 1). A non-significant association was found between perceived ambiguity and perceived preventability after adjusting for demographics and cancer protective behaviors (OR=2.62, 95% CI: 0.52-13.33). The effect of perceived ambiguity on HPV-related cancer beliefs was not significant in the multivariate analyses.

Conclusion

Young adults had high perceived ambiguity, high perceived preventability, but only 1/3 had heard of HPV. Contrary to other studies, perceived ambiguity and perceived preventability were not associated. Perceived ambiguity levels were high, but not associated with HPV beliefs, which may indicate educational interventions are needed for promoting HPV knowledge and that HPV can cause cancers other than cervical, hoping to increase the sense of vulnerability to HPV-related cancers among young adults.

Brown M, Phillips L

The relationship between human papillomavirus (HPV) beliefs and perceived ambiguity regarding cancer prevention recommendations among young adults

TABLE 1. Multivariable logistic regression models: relationships between outcomes and perceived ambiguity

Effect	Model 1 Perception of cancer preventability OR	95% CI		Model 2 HPV can cause cervical cancer OR	95% CI		Model 3 HPV can cause oral cancer OR	95% CI		Model 4 HPV can cause penile cancer OR	95% CI		Model 5 HPV can cause anal cancer OR	95% CI	
Self-age (years)	1.10	0.81	1.51	1.09	0.68	1.76	1.06	0.83	1.36	0.95	0.72	1.24	0.99	0.82	1.20
Self-gender F vs M	1.52	0.53	4.36	0.75	0.18	3.25	0.94	0.28	3.17	1.29	0.34	4.89	1.69	0.51	5.54
Education Some College vs HS or less	0.12	0.02	0.73	1.04	0.12	8.87	2.58	0.44	15.03	3.36	0.47	24.00	1.16	0.20	6.83
Education College grad or more vs HS or less	0.15	0.03	0.68	0.47	0.04	5.19	1.40	0.27	7.40	2.46	0.52	11.67	1.12	0.27	4.71
Caucasian yes vs no	0.60	0.14	2.54	0.15	0.03	0.76	0.91	0.25	3.34	1.20	0.35	4.14	1.06	0.31	3.57
marital status married/living as married vs other	2.73	1.01	7.34	1.62	0.23	11.44	1.44	0.41	5.06	1.46	0.46	4.57	1.47	0.38	5.69
Weekly exercise (min)	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
Ever smoke no vs yes	0.40	0.05	3.00	0.09	0.01	0.91	0.76	0.16	3.50	0.52	0.07	4.02	0.61	0.17	2.13
Have Regular HCP yes vs no	1.59	0.50	5.03	0.87	0.30	2.53	0.95	0.31	2.92	1.01	0.26	3.88	0.95	0.27	3.38
Perceived Ambiguity high vs low	2.62	0.52	13.33	0.68	0.12	3.94	0.84	0.21	3.35	1.39	0.26	7.42	0.93	0.21	4.15

Cancer

Disaggregating thyroid cancer incidence by Asian ethnic subgroup shows clear differences
Alice Lee* Alice Lee Roy Mendoza Lihua Liu

Background: Thyroid cancer is the fastest growing cancer in the United States. Important disparities in thyroid cancer incidence by major racial group and sex have been observed with rates being highest among Asian/Pacific Islander (API) females. However, most thyroid cancer research aggregates APIs into a single group despite their heterogeneity, hence it is unclear whether thyroid cancer incidence remains high when API ethnic subgroups are considered.

Methods: Thyroid cancer age-adjusted incidence rates (AAIRs) for each racial/ethnic group by sex was determined using 2000-2014 population-based registry data from the Surveillance, Epidemiology, and End Results Program. We calculated incidence rate ratios (IRRs) and 95% confidence intervals (CIs) to compare each API ethnic subgroup to non-Hispanic Whites (NHWs) by sex. We also calculated annual percent change (APC) in AAIRs for each group to quantify trends over time.

Results: In comparison to NHW females, all API ethnic subgroups had a lower incidence of thyroid cancer except Filipinos who showed a 34% increased incidence (IRR=1.34, 95 CI 1.30-1.38). This was also seen among males, with Filipino males having the highest incidence albeit lower than all females regardless of racial/ethnic group (e.g. AAIR for Filipino males=7.06 per 100,000 versus AAIR for Japanese females=8.36 per 100,000). Interestingly, while most racial/ethnic groups showed increasing thyroid cancer incidence, the largest growing trends were observed among NHW males (APC 5.09, 95% CI 4.71-5.46) and NHW females (APC 5.82 95% CI 5.38-6.25).

Conclusions: Among API ethnic subgroups, only Filipino females showed a higher incidence of thyroid cancer than NHW females. This was also observed for males, which underscores the importance of disaggregating APIs in cancer research. Such information can help improve future prevention strategies and shed light on the etiology of thyroid cancer.

Obstructive sleep apnea severity and risk of cancer incidence and mortality in the Cardiovascular Health Study Arthur Sillah* Arthur Sillah Mary L Biggs Nathaniel Watson David Gozal Javier Nieto Christopher Li Amanda Phipps

Introduction: Obstructive sleep apnea (OSA) afflicts an estimated 25 million Americans. In vitro and animal models suggest that OSA-related intermittent hypoxia and fragmented sleep contribute to increased cancer risk and poorer prognosis. Therefore, it is expected that individuals with more severe OSA should be at greater cancer risk than those with no OSA or mild OSA. However, human studies of OSA in relation to overall cancer risk have been inconsistent and studies of cancer mortality have been scarce.

Methods: We assessed the association of OSA severity according to hypoxemic burden (% of sleep spent with oxygen <90% saturation) with incident cancer (N=982) and cancer mortality (N=1,248) among the participants of the Cardiovascular Health Study who also participated in the Sleep Heart Health Study. Cancer incidence was ascertained through linkage with state cancer registries through 2005; cancer specific death was adjudicated through 2015. We used Cox proportional hazards regression to calculate hazard ratios (HR) and 95% confidence intervals (CI) for associations of OSA severity with cancer incidence and cancer mortality, adjusting for baseline sociodemographics, lifestyle factors, and medical history.

Results: The mean age of the overall study population was 78 years, 57% were female, and 81% were white. Overall, 154 first incident cancers and 179 cancer deaths were identified over median follow-up of 9 and 11 years, respectively. Compared with individuals in the lowest OSA category (12%) OSA was 1.15 (0.78, 1.68) and 1.20 (0.66, 2.19) respectively. Cancer mortality HR (95% CI) estimates were 0.98 (0.69, 1.39) and 1.10 (0.62, 1.93) for moderate and severe OSA respectively.

Conclusions: We found no evidence for statistically significant associations between OSA severity, and increased cancer incidence or cancer mortality.

Geospatial modeling of residential radon exposure and lung cancer risk in western Pennsylvania Shaina L. Stacy* Shaina Stacy Mary G. Krauland Raanan S. Gurewitsch David O. Wilson Saumyadipta Pyne Mark S. Roberts Jian-Min Yuan

Residential exposure to radon-222 and its decay products is the second leading cause of lung cancer overall and the leading cause among non-smokers. The objective of this study was to construct a novel geospatial modeling system to examine associations between radon exposure and lung cancer risk using large, state-collected data registries. Lung cancer incidence and mortality from 2010 to 2017 in five western Pennsylvania counties was obtained from the state cancer registry through an IRB-approved application process. We also obtained a database of professional radon testing results conducted at households and reported to the Pennsylvania Department of Environmental Protection. We used A Framework for Reconstructing Epidemiological Dynamics (FRED), an agent-based modeling system, to construct a model of lung cancer risk, radon concentration, cigarette smoking, and other risk factors at the census tract block level. In the five-county study area, mean radon levels exceeded the federal action level of 4 pCi/L in 60% of census block groups. More rural counties, including Beaver and Butler, had pockets of high mean radon levels (>4 pCi/L), while average levels were lower in Allegheny County, which includes the city of Pittsburgh. Preliminary analysis revealed that census block group-level radon and lung cancer mortality were not well correlated; however, this correlation did not account for smoking or other risk factors (Figure 1). Using FRED, we are building a more sophisticated model of lung cancer risk that includes age, duration of smoking, smoking intensity, and smoking status, in addition to radon exposure. Ultimately, we will extend this model to examine associations with other relevant cancers, such as thyroid and stomach, which may be related to radon exposure but have not been as extensively studied.

Lung Cancer Mortality (Age 55+) and Radon Levels, by Census Block Group 2010 - 2017
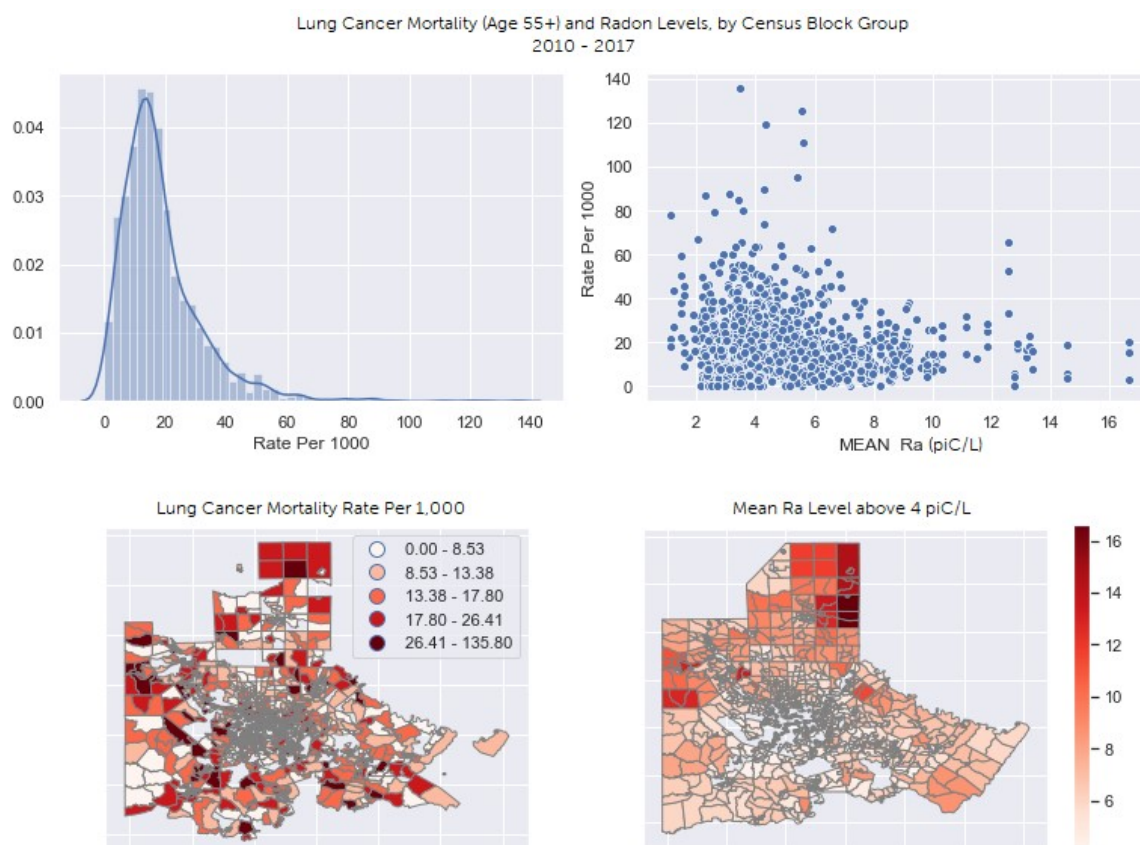
Cancer

Periodontal Disease and Breast Cancer Risk: Results from the Nurses' Health Study Zeinab Farhat* Zeinab Farhat Claire Cadeau Heather Eliassen Jo Freudenheim

Background: Periodontal disease is a multifactorial inflammatory disease that has been identified as a potential risk factor for breast cancer. While there is some evidence for periodontal disease and increased risk of oral, esophageal, head and neck, pancreatic, and lung cancers, limited evidence exists for breast cancer. Methods: In the Nurses' Health Study, a total of 77,544 women without previous breast cancer were prospectively followed since 1998. Incident, primary, invasive and in situ breast tumors were verified by physician adjudication. Ever diagnosis of periodontal disease was self-reported in 1998 and updated in 2000. We used Cox proportional hazard models to calculate multivariable hazard ratios (HRs) and 95% confidence intervals (95% CIs) after adjustment for age, smoking and other known breast cancer risk factors. Person-years were calculated from the baseline questionnaire return date (1998 or 2000, depending on when the participant first had information on periodontal disease) to the date of breast cancer diagnosis, death, or end of follow-up (June 2014). Results: 14.39% of women reported having periodontal disease over the study period. 5,100 incident breast cancer cases were identified through 2014. At baseline, those with periodontal disease were more likely to be ever oral contraceptive users, current smokers, ever post-menopausal hormone users, and have higher alcohol consumption compared to those with no history of periodontal disease. We did not observe any association between periodontal disease and overall breast cancer risk (HR 1.03, 95% CI: 0.97-1.15). Results were not modified by smoking status. Conclusion: We did not observe any association between periodontal disease and breast cancer risk. Further research is warranted with repeated and standardized measures of periodontal disease.

Assessing the relationship between self-rated health status and access to care on risks of depressive symptoms among women with breast cancer Tasha L. Gill* 3647] Gill Oluwaseun Adeyemi Rajib Paul Larissa R. Brunner Huber

Background: Women with breast cancer may experience depression. Barriers to accessing care may contribute to the occurrence of depressive symptoms. **Purpose:** The purpose of this study was to conduct a population-based analysis to assess the relationship of self-rated health and access to care on the risk of depressive symptoms among women with breast cancer, and to determine if time since diagnosis modified these relationships. **Methods:** This study used pooled data (1998-2017) from the National Health Interview Survey (NHIS). Women ≥30 years who were diagnosed with breast cancer as an adult (≥18 years) were included (n=8,979). The outcome variable was presence of depressive symptoms. Predictor variables were available place for care, delayed appointments, affordable care, and self-rated health. Sociodemographic variables were included as potential confounders. Weighted logistic regression was used to obtain odds ratios (ORs) and 95% confidence intervals (CIs). We also stratified by time since diagnosis. **Results:** Nearly 60% of women had depressive symptoms. Women with delayed appointments had four-fold increased odds of depressive symptoms (AOR=4.24, 95% CI: 2.17-8.27). Among women who were diagnosed ≤2 years from interview, risk factors for depressive symptoms were no available place for care (AOR=2.53; 95% CI: 1.61-3.99), unaffordable care (AOR=1.91; 95% CI: 1.14-3.22), and poor self-rated health (AOR=6.48; 95% CI: 3.-5-13.77). Among women who were diagnosed ≥5 years from interview, risk factors for depressive symptoms were delayed appointment (AOR=10.07; 95% CI: 3.25-31.21), poor (AOR=3.79; 95% CI: 2.20-6.52) and fair self-rated health (AOR=1.94; 95% CI: 1.45-2.59). **Conclusions:** Self-rated health is a risk factor for depressive symptoms among women with breast cancer. Factors related to accessing care differ by time since cancer diagnosis. These findings suggest that mental health screening and treatment may improve quality of life among women with breast cancer.

Simplified breast risk tool integrating lifestyle, mammographic density, and polygenic risk score: development and validation Graham Colditz* 3647] Colditz Bernard Rosner

Growing emphasis on the clinical use of breast cancer risk prediction requires simplified models. We evaluate such a model of lifecourse variables reduced from the validated Rosner-Colditz model. We add mammographic density (MD) and polygenic risk scores (PRS), to assess performance from ages 45 to 74. We use 10-year risk as the prediction outcome. We validate using prospective data from the Mayo Mammography Health Study.

We derived the simplified model in the Nurses' Health Study (NHS). During 10 years of follow-up from 1990, 2799 cases of invasive breast cancer were diagnosed, 770,679 person years. MD was assessed in a nested case control study using Cumulus software as was a PRS. We assess performance using the nested case-control data set. The prospective Mayo Mammography Health Study collaborate for validation of the model with 434 incident cases identified during 10 years of follow-up.

In the NHS, percent density has the strongest odds ratio of the 3 components of risk for 10-year risk prediction The odds ratio for the 90th vs 10th percentile, $OR_{90\% - 10\%} = 2.80$ (95% CI 2.03 – 3.86). This is followed by the PRS, $OR_{90\% - 10\%} = 2.25$ (95% CI 1.64 – 3.10) and then the lifestyle score, $OR_{90\% - 10\%} = 1.74$ (95% CI 1.28 – 2.37). The age-adjusted AUC is 0.655. In the prospective Mayo Clinic data preliminary analyses show similar performance, overall age-adjusted C-statistic = 0.660.

A simplified lifestyle assessment of risk factors for breast cancer, combined with MD and a PRS, performs consistently to discriminate those at high risk of subsequent breast cancer over a 10-year interval. This combination of three established predictors is robust and after controlling for age, identifies more than 23.7% of cases coming from the top 10.4% of the distribution of risk in the total population. Stratification of risk using a model that integrates lifestyle, PRS and MD could usefully be adapted to clinical practice to modify frequency and intensity of screening programs.

Figure. 10 year Overall Risk Score by case/control status
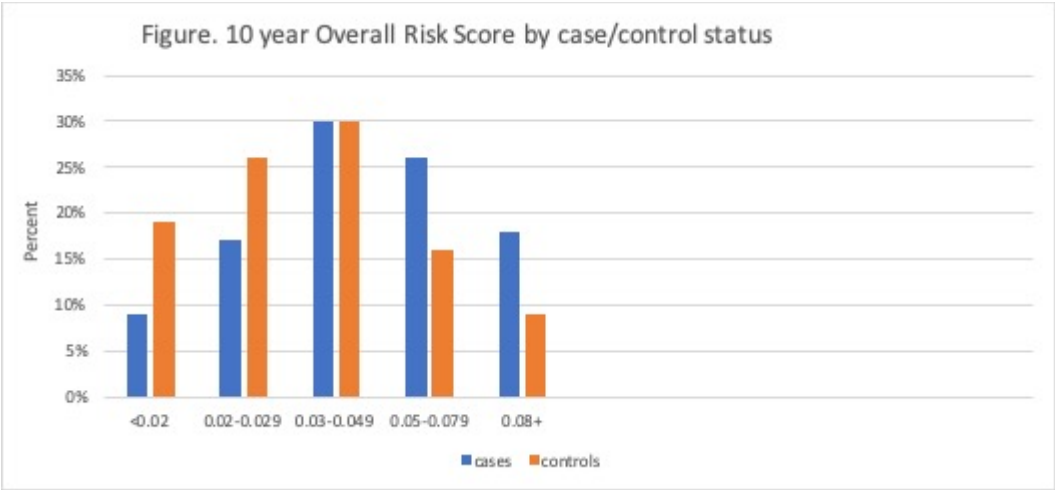
The effect of prenatal Diethylstilbestrol (DES) exposure on prostate cancer risk Bill
Strohsnitter* 3647] Strohsnitter

Introduction Animal and human observational studies have suggested that prostate cancer (PCa) has
a prenatal etiologic component. Animal studies have also lent evidence that prenatal xenoestrogenic
exposure conveys a PCa susceptibility to later estrogenic insults. Aging and obesity are believed to
increase the estradiol to testosterone ratio in men. Prenatally DES exposed men may then have
increased PCa risk due to this later increase.

Methods A cohort of 3,400 men who were and were not prenatally exposed to DES was assembled
between 1953 and 1994 and were uniformly followed for PCa development via survey response and
outcome registry review from 1994 through 2016. PCa rates were modeled using Poisson regression
considering obesity and prenatal DES exposure. The Relative Excess Risk due to Interaction was
used to estimate departure from additivity.

Results There was no association between prenatal DES exposure and overall PCa rates ($RR_{age\text{-}adjusted}$
= 0.95; 95% CI: 0.68, 1.33). Overall obesity-specific effect estimates of DES' effects on PCa rates
differed slightly. Among the obese:($RR_{age\text{-}adjusted}$ = 1.14; 95% CI: 0.59, 2.22). Among the non-
obese:($RR_{age\text{-}adjusted}$ = 0.79; 95% CI: 0.51, 1.22). For more aggressive tumors, obesity-specific effect
estimates differed to a greater extent. Among the obese:($RR_{age\text{-}adjusted}$ = 1.71; 95% CI: 0.48, 6.1).
Among the non-obese:($RR_{age\text{-}adjusted}$ = 0.63; 95% CI: 0.25, 1.64). The measures of departure from
additivity of all the obesity-specific estimates, however, were considerably imprecise.

Conclusions Prenatal DES exposure alone does not appear to influence PCa rates. Also, these study
results do not lend strong support to the hypothesis that later estrogen exposure after prenatal DES
exposure confers an increased risk in overall PCa. When restricting the outcome to more aggressive
PCa, the difference in obesity-specific DES' effect estimates gets larger. The imprecision of these
estimates, however, make their biologic interpretation difficult.

Aspirin use and ovarian cancer risk using extended follow-up of the PLCO Cancer Screening Trial Lauren Hurwitz* 3647] Hurwitz Paul Pinsky Wen-Yi Huang Neal Freedman Britton Trabert

Introduction: Regular use of aspirin has been associated with an approximately 10% reduced risk of ovarian cancer in observational studies. However, it is unclear if only low-dose aspirin confers a protective benefit. We examined associations between dose of aspirin use and ovarian cancer risk in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial.

Methods: PLCO is a multicenter, randomized controlled trial designed to test whether certain cancer screening modalities reduce cancer mortality. Participants were enrolled between 1993-2001 and followed for cancer outcomes through 2014. Detailed data on aspirin use (e.g., dose, frequency of use) were ascertained via a supplemental questionnaire administered in 2006-2007. For this study, we restricted to women without a history of cancer or bilateral oophorectomy and who were less than 70 years old at the time of the supplemental questionnaire. We used Cox proportional hazards regression to calculate hazard ratios (HRs) and 95% confidence intervals (CIs) for associations between regular aspirin use (≥once/week) and incident ovarian cancer, overall and by aspirin dose.

Results: There were 18,579 women included in this analysis, of whom 105 developed incident ovarian cancer. Forty-eight percent of women reported regular aspirin use (72% low-dose, 28% adult-strength). Overall, regular aspirin use was not significantly associated with ovarian cancer risk (HR: 0.85, 95% CI: 0.58-1.25). An inverse association was suggested for regular use of low-dose aspirin (HR: 0.77, 95% CI: 0.49-1.20) but not for adult-strength aspirin (HR: 0.98, 95% CI: 0.55-1.76).

Conclusions: For low-dose aspirin, the direction of the association was consistent with prior studies, suggesting a potential modest effect of low-dose aspirin in reducing ovarian cancer risk. However, effect estimates were imprecise given the small number of events, and further research will be needed to confirm and extend our findings.

Cancer

Multimorbidity and health-related quality of life in older adults with gastric cancer Bomi Park* Bomi Park Keun-Young Yoo Seonhwa Lee

Cancer patients may have a higher risk of development or progression of other chronic diseases or secondary cancer which can lead to limiting health-related quality of life (HRQoL). The current study assessed the prevalence of multimorbidity and estimated the impact of multimorbidity on HRQoL in patients with gastric cancer which is the most common cancer in Korea. The analysis is based on data for adults aged 50 and older derived from the cross-sectional nationally representative Korean National Health and Nutrition Examination Survey (KNHANES) conducted in 2007-2017. Multimorbidity in gastric cancer patients was defined as having one or more of 23 diseases pre-specified in KNHANES (hypertension, dyslipidemia, stroke, myocardial infarction, angina, osteoarthritis, rheumatic arthritis, tuberculosis, asthma, depression, kidney failure, atopic dermatitis, diabetes mellitus, thyroid disease, hepatitis B, hepatitis C, liver cirrhosis, liver cancer, colon cancer, breast cancer, cervical cancer, lung cancer, thyroid cancer) in addition to gastric cancer. HRQoL was assessed using the EuroQol 5 Dimensions. All estimates were weighted to account for the complex survey design, and so the results can represent the entire Korean population. The weighted frequency of gastric cancer patient aged 50 years and older was 190,656, with males comprising 47%. Multimorbidity was present in 66% of the participants with gastric cancer, and the mean number of co-morbid diseases was 2.9. The quality of life was lower in patients with gastric cancer and other diseases (geometric mean: 0.85) than in patients with gastric cancer alone (geometric mean: 0.91). In conclusion, this study demonstrated that multimorbidity in older adults with gastric cancer are highly prevalent and associated with impaired HRQoL. Further research in the pattern of multimorbidity in the gastric cancer patients is needed to develop cancer treatment plans and survivorship package accounting for multimorbidity.

Cancer

Association between smoking status and late-stage diagnosis of breast cancer Yu-Hsiang Kao* Yu-Hsiang Kao Mei-Chin Hsieh Xiao-Cheng Wu Tung-Sung Tseng

Background: Breast cancer patients with late-stage diagnosis have been proved to be associated with worse survival. Smoking is one of the risk factors of breast cancer but research on the association of smoking with late-stage diagnosis is scarce.
Objective: To investigate the association of smoking status with late-stage diagnosis of breast cancer.
Methods: Data were collected by the Louisiana Tumor Registry, including women aged 18 years and older who are non-Hispanic white and black as well as newly diagnosed with invasive breast cancer in 2011 -2013 were selected. Smoking status at diagnosis classified into never smokers, former smokers, current smokers, and unknown. The AJCC stage III and IV was classified as late-stage. Multiple logistic regression models were used.
Results: Of 7,564 patients, 14.6% of them were current smokers. Among the current smokers, 24.5% were late-stage, higher than former smokers (19.7%), never smokers (19.7%), and unknown (17.7%). After adjusting for age, race, poverty, insurance, comorbidity, and Bloom-Richardson grade, current smokers were still significantly associated with increased odds of late-stage as compared with never smokers (adjusted OR=1.23; 95%CI, 1.04-1.46). Former smokers had a tendency to have a higher likelihood of late-stage diagnosis than never smokers (adjusted OR=1.05; 95%CI, 0.89-1.25).
Conclusions Breast cancer patients who are current smokers were more likely to have late-stage diagnosis than never smokers. Breast cancer screening programs should target this population to help them detect cancer earlier and also reduce cancer mortality.

Cardiovascular

Contribution of migraine to cardiovascular disease risk prediction Pamela M. Rist* Pamela Rist Julie E. Buring Nancy R. Cook Tobias Kurth

Background: Migraine with aura (MA) is associated with cardiovascular disease (CVD) independent of traditional vascular risk factors. However, the importance of MA on CVD occurrence relative to existing CVD prediction tools remains unclear.
Methods: Participants in the Women's Health Study self-reported MA status at baseline and were followed for incident CVD events. We determined whether adding MA status to two cardiovascular disease risk prediction models, the Reynolds Risk Score and the AHA/ACC pooled cohort equation, improved risk prediction by assessing discrimination (Harrell c-index), integrated discrimination improvement (IDI), and the categorical net reclassification improvement (NRI),
Results: MA status predicted CVD risk after including covariables in the Reynolds Risk Score (HR=2.09; 95% CI: 1.54, 2.84) and the AHA/ACC score (HR=2.10; 95% CI: 1.55, 2.85). Adding MA status significantly improved discrimination of both the Reynolds Risk Score (c-index=0.792 (95% CI: 0.773-0.813) to c-index=0.797 (95% CI: 0.778-0.816), p-value=0.02) and the AHA/ACC score models (c-index=0.793 (95% CI: 0.774-0.814) to c-index=0.798 (95% CI: 0.778-0.818), p-value=0.01). We observed a statistically significant improvement in overall model fit as reflected in the IDI when we added information on MA status. However, the magnitude of these improvements was small and may not be clinically meaningful. Similarly, we did not find an improvement in risk stratification into clinically important categories as reflected by the categorical NRI.
Conclusion: In this large prospective study of women, adding information on migraine aura status to commonly used CVD risk prediction algorithms enhanced discrimination and model fit but did not substantially improve risk stratification. Despite the strong association with CVD risk, the relatively low prevalence of MA inhibits its usefulness in improving risk classification at the population level.

Cardiovascular

Patterns of causes of death in European countries 2000-2913: Do mortality rates for coronary heart disease reflect morbidity?
Susanne Stolpe* Susanne Stolpe Bernd Kowall Andreas Stang

Mortality from ischemic heart disease (IHD) is an important indicator for populations' health. Risk factor control and better treatment have been equally claimed responsible for its worldwide longstanding decline. However, potential national particularities in diagnosing underlying causes of death that might impact IHD mortality rates have not been investigated so far.

Using the WHO Detailed European Mortality Database we investigated the patterns of causes of death in the population ≥35 years for 25 countries of the WHO European Region in 2000 and 2013. Among all deaths, we calculated the proportion of deaths from competing causes for IHD as ill-defined causes ('garbage codes'), dementia, and other specific cardiovascular diseases.

Decline of IHD mortality rates between 2000 and 2013 varied between 10% (Lithuania, Czech Republic) and >55% (Estonia, the Netherlands, Georgia). Moreover, IHD mortality rates differed strongly between countries reporting similar cardiovascular mortality. It is questionable if these disparities result from morbidity differences alone.

The countries' mortality patterns comprised disparate proportions of deaths from IHD, ill-defined causes and dementia, among others. In 2013, the proportion of deaths attributed to IHD was 6% in France, 20% in Finland, and 37% in Lithuania. Among all deaths, the proportion of ill-defined causes was <4% in Lithuania, UK and Finland, 15% in France, and 28% in Poland – with disparate trends since 2000. Dementia accounted for 15% of all deaths in Finland, but for only <1% in eastern European countries.

Larger proportions of competing causes of death lead to lower proportions of deaths potentially diagnosed with IHD as cause of death, and, consequently, to lower IHD mortality rates. National particularities in diagnosing causes of death strongly influence IHD mortality rates, not necessarily reflecting underlying morbidity. This has to be taken into account in analyzing causes of decreasing IHD mortality rates.

Cardiovascular

Frailty and Risk of Cardiovascular Disease: Findings from Singapore Longitudinal Ageing Studies Xiao Liu (Alisa)* Xiao Liu Gao,Qi Gwee Xinyi Ng Tze Pin Wee Shiou Liang

Background and objective
Frailty is reported to be associated with cardiovascular disease (CVD), but longitudinal studies of time-to-event are few. This study aimed to determine whether frailty status at baseline predicted the onset of CVD in Singapore community-dwelling older adults.
Methods
A total of 5,015 participants (age mean= 65.8, SD=7.6) without CVD at baseline in the Singapore Longitudinal Ageing Study (SLAS) were followed up for an average of 10.2 (SD=3.6) years. Frailty status was defined by Fried criteria (unintentional weight loss, low physical activity level, weakness, exhaustion, and slow gait speed), and the onset of incident CVD events (stroke, acute myocardial infarction, or CVD-related mortality) from the National Disease Registry. Hazard ratio (HR) was estimated from hierarchical Cox regression model, with sensitivity analyses for sub-cohorts (SLAS-1 and SLAS-2) and lag periods of 1 year.
Results
CVD incidence rate was 8.3 per 1000 person-years. 46.2% were prefrail, and 3.7% were frail. 18.1% of the participants were positive in weakness dimension. Frailty increased the risk of CVD (prefrail: HR=1.24, 95% confidence interval [CI]: 1.00,1.54; frail: [HR]=1.60, 95% CI: 1.08, 2.37). By frailty dimension, weakness increased the risk of CVD (HR=1.36, 95% CI: 1.09, 1.70). Similar results were shown in separate model by SLAS-1 and SLAS-2 sub-cohorts, and by excluding CVD cases within 1 year from baseline.
Conclusion
Our findings suggest the physical frailty phenotype is independently associated with future elevated risks of developing CVD. As frailty is reversible, these findings open up new avenues of predicting, monitoring and preventing future risks of CVD.

Cardiovascular

Incident CVD and change in workforce participation: A longitudinal study of older working-age Australians Muhammad Shahdaat Bin Sayeed* Muhammad Shahdaat Bin Sayeed Grace Joshy Emily Banks Rosemary Korda

Background
People who develop cardiovascular disease (CVD) often have difficulty continuing their usual work. However, large-scale evidence from Australia on this relationship is limited. We quantified change in workforce participation in relation to incident CVD in Australia, overall and according to CVD subtypes.
Methods
Baseline and follow-up questionnaire data from 66,043 CVD-free cohort study participants from Australia (the 45 and Up Study, n=267,153) in the workforce at baseline and aged 45-<65 at follow-up were linked through CHeReL to hospitalisations to identify incident CVD. Modified Poisson regression estimated risk ratios (RRs) for non-participation in paid work and retirement due to ill health at follow-up in those who did and did not develop CVD, adjusting for relevant factors. Generalised linear models compared average change in paid hours of work per week between surveys.
Results
Over a median 5 years follow-up, 2983 (4.5%) participants developed CVD and, compared to those not developing CVD, they were more likely to leave the workforce during follow-up (26.1% vs 16.9%; RR=1.28, 95%CI 1.20-1.36). RRs were elevated for all CVD subtypes investigated: ischaemic heart disease, myocardial infarction, stroke, heart failure and peripheral arterial disease. Compared to people with neither CVD nor physical functional limitations, RRs for workforce non-participation were 1.16(95%CI 0.98-1.39) for those with CVD and no limitations and 2.78(95%CI 2.48-3.11) for those with both CVD and severe limitations. Among those working at follow up, participants with incident CVD had a greater decrease in work-hours/week [mean difference of change -0.63(95%CI: -0.82,-0.43)]; among retirees, those with incident CVD were more likely to have retired due to ill-health (40.4% vs 17.0%; RR=1.90, 95%CI 1.70-2.13).
Conclusions
Lower workforce participation was observed in those with versus without incident CVD for all CVD subtypes, especially in those with CVD and physical disability.

Cardiovascular

Measures of exercise capacity as predictors of metabolic outcomes in moderate to severe chronic kidney disease Sofija Zagarins* Sofija Zagarins Emily Miele Michael Germain Jyovani Joubert Elizabeth Evans Charles Milch Samuel Headley

Chronic kidney disease (CKD) is associated with progressive cardiovascular dysfunction, such that cardiovascular outcomes are key indicators of health in CKD patients. Peak oxygen consumption (VO2peak) is a widely-used measure of cardiorespiratory fitness (CRF), but exercise training interventions with CKD patients often report only modest improvements in VO2peak. Rather than suggesting a failure of exercise training, these smaller-than-expected improvements may suggest that the VO2peak measure is not sensitive to the modest but potentially impactful changes in CRF observed in CKD patients, and that other exercise capacity variables, such as the time to exhaustion on a treadmill during the peak exercise test (TT), may be more appropriate for measuring CRF in this population. The purpose of the current analysis is to examine the relationships between VO2peak, TT, and metabolic outcomes in order to identify whether TT better predicts changes in metabolic parameters in CKD as compared to VO2peak. We used data from a 4-month randomized controlled study of an aerobic exercise intervention in n=46 CKD patients. While VO2peak and TT decreased slightly in the control group, VO2peak increased by 8.2% (P=0.07) in the aerobic exercise group and TT increased by 22.8% (P<0.01). In multivariable linear regression models adjusted for baseline values, the observed improvements in VO2peak and TT in the aerobic exercise group were associated with higher blood pressure values at follow-up, such that a 1-minute increase in TT was associated with an increase of 1.8 mmHg in DBP at follow-up (P=0.02), while a 1 mL/kg/min increase in VO2peak was associated with an increase of 0.7 mmHg in BDP at follow-up (P=0.05). Results were similar for SBP. Neither VO2peak nor TT were associated with changes in body fat percentage, cholesterol measures, or arterial stiffness. The observed positive association between exercise capacity and blood pressure was unexpected and warrants further investigation.

Potential Explanations for Within State Differences in Death rates for Coronary Heart Disease and Stroke

Brandi Vollmer* Brandi Vollmer Mitchell S. Elkind Amelia Boehme

Background: Coronary heart disease (CHD) and stroke share numerous risk factors, however, standardized stroke and CHD death rates vary drastically from one another in some states. Methods: Age-adjusted stroke and CHD death rates by state obtained from National Center for Health Statistics for 2014-2016 were standardized. Standardized differences were calculated, with positive values indicating stroke death rates to be less than CHD death rates. Pearson's correlation coefficients were calculated for standardized differences with variables of interest obtained. Results: New York, Rhode Island, Oklahoma, Michigan and Vermont had the greatest differences in standardized rates favoring low stroke mortality, but high CHD mortality. Alabama, Georgia, Utah, South Carolina and Oregon had the greatest differences favoring low CHD mortality, but high stroke mortality. For all 50 states, primary or comprehensive stroke centers per km2 were positively correlated with standardized differences, however the correlation was weak with a coefficient of 0.297 (p=0.036). Shared risk factors of obesity, smoking, high cholesterol and hypertension, were not correlated with difference of standardized rates. When investigating differences for the Northeast and South census regions separately, the correlation with stroke centers was attenuated and no longer significant for both regions. However, for the Northeast census region, healthcare cost burden was strongly positively correlated (R=0.704, p=0.034) with standardized differences. Conclusion: Preliminary results suggest shared risk factors for stroke and CHD cannot explain differences seen between their standardized mortality rates. Access to certified primary and comprehensive stroke centers likely contribute to improved stroke death rates, while CHD mortality remains high within states. However, differences within regions may further inform why discrepancies in rates are seen.

Table 1. Correlation Coefficients for differences in standardized death rates (CHD rate - Stroke rate = standardized difference)

	All 50 states		Northeast states (n=9)		South States (n=16)	
	Correlation	P value	Correlation	P value	Correlation	P value
PSC/km²	0.283	0.046	0.205	0.597	0.205	0.446
CSC/km²	0.329	0.018	0.176	0.651	0.280	0.293
PSC+CSC/km²	0.297	0.036	0.207	0.593	0.219	0.415
% Rural	-0.074	0.601	-0.360	0.342	-0.216	0.422
% White	0.293	0.039	-0.500	0.170	0.537	0.032
% Hispanic	0.131	0.363	0.598	0.089	0172	0.525
Median Age	0.351	0.013	-0.613	0.079	0.314	0.236
Median Income (household)	0.071	0.625	-0.089	0.820	0.027	0.920
Obese	-0.130	0.370	-0.127	0.745	-0.180	0.505
Binge drinkers	0.129	0.373	-0.243	0.529	-0.044	0.872
Current Smokers	0.011	0.937	-0.635	0.066	0.123	0.650
High Cholesterol (2015)	-0.136	0.346	0.242	0.530	-0.176	0.515
Hypertension (2015)	0.003	0.984	-0.157	0.686	0.128	0.637
Diabetes	-0.147	0.307	0.124	0.751	-0.241	0.369
Eats vegetables at least once per day	-0.107	0.460	0.054	0.664	-0.097	0.721
Alzheimer's Death Rate	-0.254	0.075	-0.269	0.484	-0.468	0.067
Healthcare Coverage	0.091	0.530	-0.167	0.668	0.395	0.130
Healthcare Cost Burden	0.103	0.475	0.704	0.034	-0.048	0.861
Had a health visit within the past year	0.056	0.699	0.299	0.434	-0.019	0.943
Had teeth removed	0.185	0.198	0.042	0.915	0.228	0.396

District of Columbia excluded due to exceedingly high stroke centers per km2 (>2000), Puerto Rico excluded due to missing data.
PSC: primary stroke center (Joint commission certified); CSC: comprehensive stroke center (Joint commission certified);
Northeastern states: Connecticut, Maine, Massachusetts, New Hampshire, New jersey, New York, Pennsylvania, Rhode Island, Vermont
Southern states: Alabama, Arkansas, Delaware, Florida, Georgia, Kentucky, Louisiana, Maryland, Mississippi, North Carolina, Oklahoma, South Carolina, Tennessee, Texas, Virginia, West Virginia

Cardiovascular

Dietary inflammatory index and blood pressure among adolescent females in Mexico City, Mexico Miatta Buxton* Miatta Buxton Karen Peterson Yun Liu Yanelli Rodríguez-Carmona1 Martha María Tellez-Rojo Margaret Banker Erica C. Jansen Nitin Shivappa James R. Hebert Alejandra Cantoral

Background: A pro-inflammatory diet may increase systemic inflammation, which is associated with hypertension. Increases in blood pressure during adolescence may lead to the development of adult hypertension, and in women, hypertension during pregnancy (HDP). Females transition to the childbearing period after adolescence and may be at risk for HDP; thus, understanding the relationship between diet quality and blood pressure during adolescence could inform HDP prevention strategies. Therefore, we investigated the associations between diet quality (using energy-adjusted Children's Dietary Inflammatory Index (C-DII)TM [E-CDII]) and systolic (SBP), and diastolic blood pressure (DBP) at two time points among adolescent females (ages 10-18) in Mexico City, Mexico.
Methods: E-CDII scores were generated from food frequency questionnaires (FFQ) for 109 adolescent females in the Early Life Exposures in Mexico to Environmental Toxicants study at two time points. The reference period for the FFQ was the last month. Blood pressure was assessed at both time points using a digital automatic blood pressure monitor. Mean follow-up time between the first and second visits was 22 months. Adjusted general linear models were used to evaluate the associations between E-CDII score and SBP and DBP at time 1 and 2.
Results: Mean age at visits 1 and 2 were 13.1 and 15 years, respectively. In adjusted models, E-CDII (time1) was associated with increases in SBP (1.76 mmHg, p=0.0008) and DBP (1.15 mmHg, p=0.01) at time2. However, E-CDII was not associated with SBP or DBP for measures from the same visit (i.e. E-CDII and BP at time1 or E-CDII and BP at time2).
Conclusion: Pro-inflammatory E-CDII scores were associated with increases in both SBP and DBP. Temporal differences in the association between E-CDII and blood pressure suggest that the effects may develop gradually over time. These results appear to support the hypothesized mechanisms by which inflammation influence hypertension.

Cardiovascular

The impact of lung function on cardiovascular diseases and cardiovascular risk factors: a two sample Mendelian randomization study Shiu Lun Au Yeung* Shiu Lun Au Yeung C Mary Schooling

Background: Observational studies suggested lung function is inversely associated cardiovascular disease (CVD) although these studies could be susceptible to residual confounding. We conducted a 2 sample Mendelian randomization study using summary statistics from genome wide association studies (GWAS) and UK Biobank to clarify the role of lung function in CVD.

Methods: We constructed genetic instruments for forced expiratory volume in 1 second (FEV1, 209 instruments) and forced vital capacity (FVC, 249 instruments) from the UK Biobank (n=361,194), and applied them to GWAS of coronary artery disease (CAD) (60,801 cases and 123,504 non cases), stroke (40,585 cases and 406,111 non-cases), atrial fibrillation (60,620 cases and 970,216 non cases), and heart failure (47,306 cases and 930,014 non cases), blood pressure (n=361,194) and lipids (n=188,577). Inverse variance weighting was used to derive the causal estimate of lung function in these outcomes. Sensitivity analyses included MR-Egger, weighted median, and exclusion of instruments related to height.

Results: FEV1 was inversely associated with CAD (OR: 0.67 per L increase, 95%CI 0.57 to 0.79), overall stroke (OR: 0.86 per L increase, 95%CI 0.74 to 0.99) and positively associated with atrial fibrillation (OR: 1.47 per L increase, 95%CI 1.27 to 1.70), but not heart failure. FVC was similarly associated with CAD (OR: 0.72 per L increase, 95%CI 0.64 to 0.81) and atrial fibrillation (OR: 1.48 per L increase, 95%CI 1.34 to 1.64) but relations were less clear for other cardiovascular diseases. The relations of FEV1, FVC with CAD were consistently observed in sensitivity analyses whilst other observed associations were attenuated to null when we excluded height related instruments. For CVD risk factors, we only observed consistent inverse relation of FEV1 with systolic blood pressure.

Conclusion: Increased FEV1 and FVC likely protects against CAD. Blood pressure may have a role in the cardioprotective effect of FEV1.

Cardiovascular

Fat and muscle mass phenotyping by dual x-ray absorptiometry is not superior to body mass index in prediction of cardiometabolic risk Lisa Kakinami* Prince Kevin Danieles Kehinde Ajibade Sylvia Santosa Jessica Murphy Lisa Kakinami

Background: Although commonly used to assess adiposity, body mass index (BMI) cannot distinguish between muscle and fat mass. As an alternative, classifying adiposity based on muscle and fat mass phenotypes has been proposed. Whether these phenotypes are more accurate in predicting cardiometabolic risk than BMI-classified weight status (WS) is unknown and is explored in this study.

Methods: Data were from representative samples of the general US population (NHANES: 1999-2006 cycles). WS was determined by the World Health Organization cut-offs of BMI (weight/height^2). Dual X-ray absorptiometry (DXA) data was used to create a phenotype classification of adiposity based on permutations of fat (high/low) and muscle (high/low) mass. High was defined as ≥50th percentile of sex, age, and WS-specific population curves. The area under the curves (AUCs) of logistic regression models predicting the presence of abnormal lipids (total cholesterol [TC], high- and low-density lipoproteins [HDL, LDL], and triglycerides), glucose, and insulin resistance (HOMA-IR) were calculated. AUCs between WS and phenotypes were compared by computing standard errors and CIs through bootstrap samples. All analyses were stratified by sex and incorporated the complex survey design and weighting of NHANES.

Results: Among females (N=2682), WS performed significantly better than phenotypes for TC (AUCs: 0.58 vs 0.55, p=0.05), triglycerides (0.67 vs 0.62, p<0.01), and HOMA-IR (0.80 vs 0.77, p<0.01). The same was true for males (N=2996) regarding TC (0.59 vs 0.53, p<0.05), glucose (0.67 vs 0.60, p<0.01), and HOMA-IR (0.80 vs 0.77, p<0.01). No statistically significant differences were observed for the other outcomes.

Discussion: Despite DXA's high cost and detailed output regarding body composition, its phenotype classification failed to be superior to WS in predicting cardiometabolic risk. Further studies exploring whether these findings are consistent across other populations and outcomes are needed.

Do Changes in Fitness Predict Adiposity in Youth? The Longitudinal Relationship between Fitness and Body Mass Index in New York City Public School Students, 2006-2017 Emily M. D'Agostino* Emily D'Agostino Sophia Day Kevin Konty

Just one in four US youth meet national physical activity guidelines. Low youth physical activity corresponds to low physical fitness, including near failing grades on criterion-referenced health-related fitness standards nationally. Reduced fitness is also strongly correlated with noncommunicable chronic conditions in childhood and adulthood, including cardiovascular disease, type 2 diabetes, metabolic syndrome, dementia and Alzheimer disease, breast and colon cancer, and disability later in life. Recent research debates whether fitness is an "important" predictor of youth adiposity. No prior studies examine at a population-level the relationship between youth fitness and lagged body mass index (BMI) drawing from individual-level longitudinal data. Eleven cohorts of New York City public school students were followed from grades 4-12 (2006/7-2016/17; n=575163 youth, n=2168484 observations; 52% female; 35% Hispanic, 28% non-Hispanic black, 18% Asian, 18% non-Hispanic white; 69% qualifying for free/reduced price school meals). Three-level longitudinal generalized linear mixed models were used to test the association between fitness changes and one-year lagged child-specific BMI percentiles. Models adjusted for individual-level sex, race/ethnicity, household poverty, English language learner status, home neighborhood poverty, grade, and time showed that relative to youth with a large improvement in fitness from the prior year (>35%), youth with a 15-35% improvement, 35% reduction in fitness showed increases in BMI percentiles per year (b=0.02 [95%CI: -0.31, 0.27], b=0.18 [95%CI: -0.02, 0.39], b=0.48 [95%CI: 0.22, 0.75], and b=0.45 [95%CI: 0.23, 0.68], respectively). These findings suggest that fitness declines positively predict youth BMI, and may have important implications for supporting physical activity interventions to promote youth health.

Left ventricular ejection fraction acts as a mediator between the effects of myocardial strain and heart failure/mortality Jonathan Weber* Jonathan Weber Niloofar Fouladi Nashta Harsimar Singh J. Jane Cao

Background:
Left ventricular ejection fraction (LVEF) is a standard measure of cardiac function estimating the proportion of blood output by the heart per beat with reference to the heart size. Left ventricular longitudinal strain (LS) directly measures the extent of myocardial movement in the longitudinal direction. LVEF and LS are associated with each other. However, some stages of cardiomyopathies may manifest as reductions in LS but not LVEF. The reduction of LVEF or LS is associated with incident heart failure and mortality risk. We sought to test LVEF as a mediator between LS and heart failure/mortality.

Methods:
The study subjects were clinical patients at a single hospital. The outcome was a composite of all-cause mortality and heart-failure inpatient admission. The exposure was abnormal LS on MRI defined by a 2 standard deviation reduction from normal. Reduced LVEF (<50%) was assessed as a mediator (Figure). Confounders adjusted for include age, gender, body surface area, family history of heart disease, diagnosis of hypertension, diabetes, arrhythmia, coronary artery disease, valvular disease and smoking status. Mediation analysis for time-to-event data was performed on proportional hazard models with interaction testing and CIs using the delta method.

Results:
There were 792 subjects (70% male, 81% white, 55±15 years, 220 (28%) with outcome) included. The total effect (TE) was 1.89 (1.42-2.52). The natural direct effect of LS (HR 1.49 CI 1.08-2.05) was slightly stronger than the natural indirect effect (HR 1.27 CI 1.07-1.52) mediated through LVEF. Nearly half (48%) the effect of abnormal LS on our outcome was mediated. There was no exposure-mediator interaction and the TE was robust to sensitivity testing, but CIs of the direct and indirect effects were susceptible to plausible bias.

Conclusion:
These results indicate that only half of effect of LS on heart failure and mortality risk is mediated by LVEF supporting the independent role of LS in outcome risk.

Figure: Directed acyclic graph

Cardiovascular
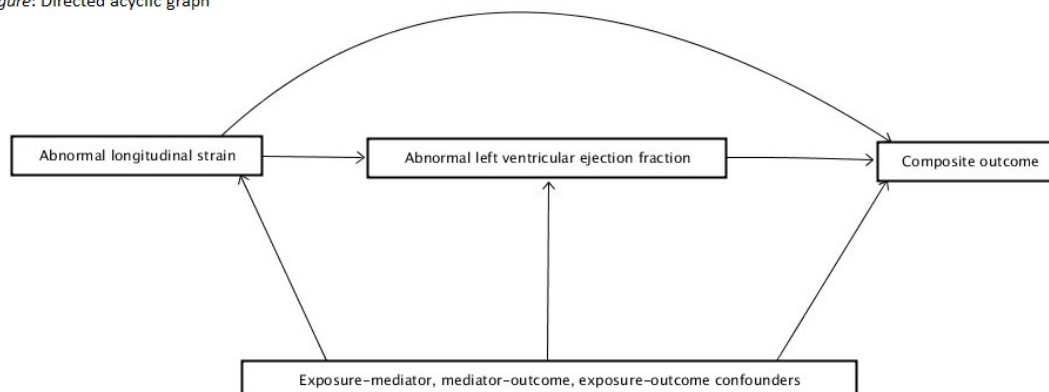
Association between Organic Food Consumption and Metabolic Syndrome: A Longitudinal Study in Older Adults Abeer Aljahdali* Abeer Aljahdali Ana Baylin Elizabeth Ludwig-Borycz Heidi Guyer

Objective: An inverse association between organic food consumption and metabolic syndrome (MetS) has been reported in cross-sectional studies, but the association has not been investigated in prospective studies Our study aimed to examine the association between organic food consumption and MetS among adults aged ≥ 51 years in the Health and Retirement Study (HRS).

Research design and methods: We used 2012–2016 data from the HRS, a nationally representative sample of older adults in the U.S. Our analysis included 1594 participants free of MetS at baseline (mean age, 63.7 years; 55% women) with measurements of blood pressure, fasting blood glucose, high-density lipoprotein cholesterol (HDL-C) , triglycerides, and waist circumference. At baseline, participants completed a food frequency questionnaire. The 2009 interim consensus statement was applied to ascertain the presence of MetS at the follow-up visit. Logistic and linear regressions, accounting for the complex survey design, were used to model the occurrence of Mets and its components, respectively.

Results: 48.8% of participants reported organic food consumption. Organic food consumers were younger, less likely to be smokers and have chronic diseases, and had higher education and level of physical activity compared to non-organic food consumers (all p values 0.05). We found significant associations of organic food consumption with triglycerides and HDL-C in the crude models only (All p values < 0.05).

Conclusion: Organic food consumption was not associated with lower odds of developing MetS . The association of organic food consumption and MetS has not been investigated in longitudinal or controlled studies. Replication of these findings with validated assessment tools for organic food consumption and analysis of the role of different types of organic food are warranted.

Short-term exposure to air pollution and novel markers of cardiovascular effect: a repeated measures study in the Multi-Ethnic Study of Atherosclerosis (MESA) Yu Ni* 3647] Ni Russell Tracy Elaine Cornell Joel Kaufman Adam Szpiro Sverre Vedal

Background: Several pathophysiologic mechanisms have been proposed to underlie the associations between ambient air pollutants and cardiovascular disease. We employed a repeated measures design to investigate the short-term associations of four outdoor air pollutants – particulate matter smaller than 2.5 micrometers in diameter ($PM_{2.5}$), nitrogen dioxide (NO_2), ozone (O_3) and sulfur dioxide (SO_2) – with two blood markers involved in vascular effects of oxidative stress, soluble lectin-like oxidized LDL receptor-1 (sLOX-1) and nitrite, using data from the MESA study. **Methods:** 740 participants with plasma nitrite and sLOX-1 measurements at three MESA exams between 2002 and 2007 were included. Daily concentrations of $PM_{2.5}$, NO_2, O_3 and SO_2 0-7 days prior to blood draw at each exam were estimated from central monitors in the six MESA regions, pre-adjusted using splines of meteorology, indicators for day of the week, and splines of site-specific time trend. Unconstrained distributed lag linear mixed effect models and generalized estimating equations were used to estimate net effects over several days with adjustment for demographic, socioeconomic and behavioral factors. **Results:** Median detectable nitrite and sLOX-1 concentrations were 24.7 umol/L and 94.5 pg/ml, respectively. Higher short-term $PM_{2.5}$, but not other pollutants, were associated with elevated sLOX-1 level analyzed both as a continuous outcome (% change per interquartile (IQR) increase: 18.5%, 95%CI: 2.4-37.2%) and dichotomized at the median (odds ratio per IQR increase: 1.21, 95%CI: 1.01-1.44); the finding was not meaningfully changed after adjustment for additional covariates or in several sensitivity analyses. Pollutant concentrations were not associated with nitrite levels. **Conclusion:** This study supports the mechanistic hypothesis that oxidative modification of endogenous phospholipids in the lung by $PM_{2.5}$ drives vascular endothelial cell activation via cell surface pattern recognition receptors.

Cardiovascular

Assessment of cardiovascular outcomes up to one year postpartum in women with congenital heart defects
Jessica H Knight* Jessica Knight Karrie F Downing Elizabeth C Ailes Michelle Gurvitz Matthew E Oster Naomi Tepper Sherry L Farr

Background: Congenital heart defects (CHD) are the most prevalent type of birth defect and are an important heart condition in pregnant women. Clinical guidelines suggest that women with CHD may have long-term decreases in cardiac health after pregnancy; however, little data exist to confirm this. Therefore, our objective was to understand changes in cardiovascular health in women with CHD up to 1 year post-partum.

Methods: In the IBM MarketScan Commercial Claims Database we identified acute cardiovascular events in privately insured women ages 15-45 with ≥1 inpatient or ≥2 outpatient CHD diagnosis codes separated by ≥30 days. Women with a pregnancy ending in a live birth 2009- 2012 were matched on age at baseline, CHD severity, calendar year, and region to women without a pregnancy 2008-2013. The risk difference (RD) for each outcome, identified using ICD-9 diagnosis and procedure codes, was calculated comparing the risk 1 year to 3 months before the estimated last menstrual period with risk 3 months to 1 year after pregnancy (or risk in the same calendar months for matched non-pregnant women). To account for changes in cardiac health with age, the risk difference was compared between pregnant and non-pregnant women.

Results: Among 614 women with CHD and a recent pregnancy, risk of hospitalization for any reason (RD=3.3% [95% confidence interval=0.3, 6.2]) increased after pregnancy, but did not change for the 614 women without a recent pregnancy (RD = 0.2% [-2.8, 3.1]. However, the difference between these risk differences? was not statistically significant, 3.1 [-1.1, 7.3]. Risk differences for other health events did not differ between groups (Figure).

Conclusion: Women with CHD experienced increased hospitalizations beyond 3 months postpartum, but this change in risk did not differ statistically from non-pregnant women with CHD. Further investigation is needed to assess if this increase represents delayed medical procedures or postpartum changes in cardiac health.

Figure. Risk of cardiovascular health events in a matched sample of 614 pregnant and 614 non-pregnant women with congenital heart defects (CHD) in the one year before and one year after pregnancy[1]
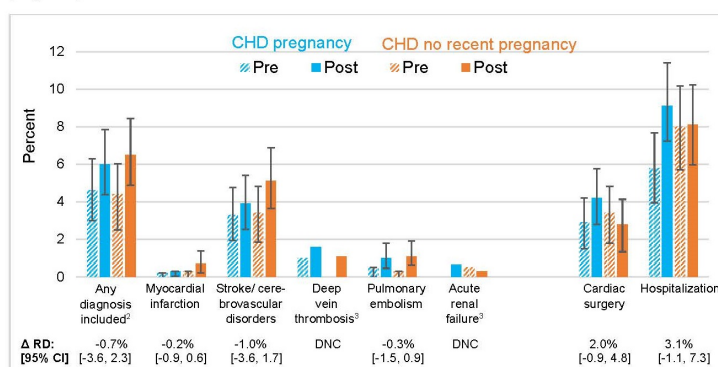
CHD=congenital heart defect

Δ RD = Represents the difference in risk differences for women with CHD and a pregnancy vs CHD no recent pregnancy

DNC = did not converge

[1]Matched on age, CHD severity, enrollment year, and region; risk in the pre-pregnancy period was calculated for the nine months spanning one year to three months before estimated last menstrual period (or the equivalent time period for the non-pregnant woman). Risk in the post-pregnancy period was calculated for the nine months spanning three months to one year after birth

[2]Any diagnosis included represents the presence of any of the following: myocardial infarction, stroke/cerebrovascular disorders, deep vein thrombosis, pulmonary embolism and acute renal failure

[3]The generalized estimating equation model did not converge so standard errors and the difference between risk differences (or interaction term) could not be estimated

Diabetes

Endocrine-disrupting chemical concentrations and diabetes among adults in the United States, NHANES 2005-2014 Julia Ward* Julia Ward Catherine Cowie Sarah Casagrande

Phenols and parabens are ubiquitous and have been associated with various markers of cardiovascular disease. However, the literature lacks population-based studies examining the link between these endocrine disruptors and diabetes. We examined the association between paraben/phenol concentrations and diabetes among a nationally representative sample of US adults. We utilized data from the 2005-2014 National Health and Nutrition Examination Surveys (N=8,498). Total urinary concentrations of bisphenol A, triclosan, benzophenone-3, and propyl-, butyl-, ethyl-, and methyl parabens were measured from urine specimens collected during the examination session. Diabetes status was based on self-report of a previous diagnosis or hemoglobin A1c $\geq$ 6.5%. We used logistic regression to estimate odds ratios and 95% confidence intervals associated with the difference in log-transformed values of the 75th and 25th percentiles for each phenol and paraben. Final models were adjusted for the potential confounders of urinary creatinine, time of venipuncture, age, sex, race/ethnicity, education, income, smoking status, and alcohol use. The adjusted odds ratios of diabetes comparing the 75th to 25th percentiles of each paraben/phenol were 1.09 (95% CI: 0.96, 1.23) for bisphenol A, 0.84 (95% CI: 0.72, 0.98) for triclosan, 0.69 (95% CI: 0.61, 0.79) for benzophenone-3, 0.71 (95% CI: 0.61, 0.83) for propyl paraben, 0.66 (95% CI: 0.54, 0.80) for butyl paraben, 0.60 (95% CI: 0.51, 0.71) for ethyl paraben, and 0.79 (95% CI: 0.68, 0.91) for methyl paraben. To conclude, higher concentrations of triclosan, benzophenone-3, and propyl, butyl, ethyl, and methyl parabens were associated with lower odds of diabetes. These findings warrant further investigation into the potential mechanism behind these associations and the temporal direction given that we cannot rule out reverse causation. Future studies of these endocrine disruptors may improve the understanding of their relationship with diabetes.
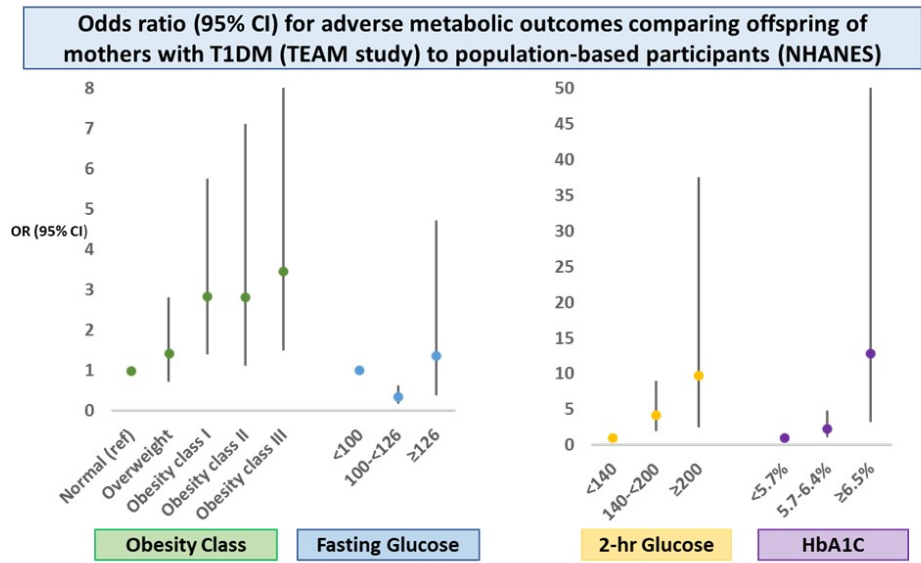
Elevated anthropometric and metabolic indicators among offspring of mothers with type 1 diabetes—early results from the Transgenerational Effect of Adult Morbidity Study (The TEAM Study) Katherine Bowers* Katherine Bowers Shelley Ehrlich Larry Dolan Resmi Gupta Mekibib Altaye Nicholas Ollberding Rhonda Szczesniak Jane Khoury

Exposure to maternal diabetes in utero increases the risk for offspring metabolic disturbances including obesity, insulin resistance, and type 2 DM. However, the timing of hyperglycemic exposure across pregnancy as well as level and variability of exposure necessary to cause impairment has not been elucidated. In response to this data gap, the TEAM Study was initiated to evaluate young adult offspring, 24 to 42 years-old, of mothers with type 1 diabetes (T1DM) to determine the association between the timing and variability of glucose exposure in pregnancy and risk of obesity, diabetes, and renal and cardiovascular compromise in these adult offspring.

The TEAM Study is currently enrolling, with the goal of 250 offspring of women who participated in a Program Project Grant (PPG) 1978 - 1995. For the mothers, comprehensive medical and obstetric data were collected at regular clinic visits including 4-6 daily glucose measures across pregnancy. TEAM Study participants (offspring of the original PPG mothers) undergo one clinic visit for evaluation of metabolic, renal, cardiovascular, and neurocognitive function. For the current analyses, the first 100 offspring of women with T1DM were compared to a population sample of ~1:2 age-, sex- and race-matched participants from the National Health and Nutrition Examination Survey (NHANES) 2015-2016. Descriptive and regression analyses were employed to compare TEAM to NHANES participants.

Participants exposed to T1DM in utero had significantly higher mean BMI (32.1 versus 28.5 kg/m2), glycohemoglobin A1c (5.6 versus 5.3%), and two-hour glucose (138 versus 108 mg/dL). Increasing BMI, glycohemoglobin and two-hour glucose were also associated with in utero exposure to T1DM in analyses (Figure).

Exposure to T1DM in utero may be associated with an increased risk of anthropometric and metabolic dysfunction in adult offspring. Results could have important clinical implications and will be replicated on the full TEAM cohort.

Odds ratio (95% CI) for adverse metabolic outcomes comparing offspring of mothers with T1DM (TEAM study) to population-based participants (NHANES)

Diabetes

Association of maternal pre-pregnancy diabetes and gestational diabetes with congenital anomalies of the newborn: a nationwide population-based study in 29 million mother-infant pairs

Yuxiao Wu* Yuxiao Wu Buyun Liu Yangbo Sun Yang Du Mark K. Santillan Donna A. Santillan Linda G. Snetselaar Wei Bao

Background: Intrauterine hyperglycemic environment may cause oxidative stress and increase the risk of congenital anomalies in developing fetuses. However, the association between maternal diabetes and different subtypes of congenital anomalies remains unclear.

Objective: To examine the association of maternal pre-pregnancy diabetes, gestational diabetes mellitus (GDM), and 12 subtypes of congenital anomalies of the newborn in a large and multi-racial/multi-ethnic population.

Methods: We included 29,211,974 live births with maternal age ranged from 18 to 49 years old documented in the National Vital Statistics System in the United States, 2011-2018. Information on maternal history of pre-pregnancy diabetes and GDM, congenital anomalies, and maternal-infant sociodemographic characteristics and medical history was retrieved from birth certificates. Log-binomial regression was used to estimate risk ratios (RRs) and 95% confidence intervals (CIs) for congenital anomalies overall and by subtypes.

Results: Of the 29,211,974 births, there were 90,061 infants with congenital anomalies identified at birth. The adjusted RRs of congenital anomalies at birth were 2.44 (95% CI, 2.33-2.55) for pre-pregnancy diabetes and 1.28 (95% CI, 1.24-1.31) for GDM. The association was generally consistent across subgroups by maternal age, race/ethnicity, pre-pregnancy obesity status, and infant sex. For specific subtypes of congenital anomalies, maternal pre-pregnancy diabetes or GDM was associated with an increased risk of most subtypes.

Conclusion: Both pre-pregnancy diabetes and GDM were significantly associated with several subtypes of congenital anomalies. These findings underscore the importance of diabetes prevention before and during pregnancy for the prevention of congenital anomalies.

Diabetes

Early childhood glucose metabolism and adiposity in association with mid-to late-pregnancy maternal glycemia and prepregnancy obesity: findings from the prospective Health Start study Ellen Francis* Ellen Francis Brandy Ringham Dana Dabelea Wei Perng

Maternal diabetes in utero is associated with risk for obesity and type 2 diabetes in the offspring. However, whether maternal glycemia during pregnancy is associated with markers of glucose metabolism in offspring independent of adiposity, is unknown. We explored this question among 535 mother-child pairs participating in the prospective Healthy Start Study in Colorado. Maternal HbA1c was measured at a gestational age (GA) of 20-34 weeks, and offspring fasting glucose and insulin levels were measured at age 4.79 years (SD 0.70). We calculated child % fat mass (%FM) using air displacement plethysmography. We used multivariable linear regression to estimate the total effect of maternal HbA1c tertiles on childhood glucose, insulin, HOMA2-IR, and HOMA2-β. We assessed the extent to which these associations were independent of maternal prepregnancy BMI, and mediated by offspring %FM by estimating the direct effects in models adjusted for maternal race, age, education, GA at HbA1c measure, weight gain and smoking during pregnancy, and offspring sex and age. The median (range) of maternal HbA1c was 5.99 (3.70, 6.10). There was a significant positive total effect of maternal HbA1c on childhood glucose, insulin, and HOMA-IR. After accounting for prepregnancy BMI and offspring %FM the estimated direct effects of HbA1c on offspring glucose and HOMA-IR remained significant. For example, the direct effect on HOMA-IR was 0.03 (-0.06, 0.13) units for T2 vs. T1, and 0.11 (0.00, 0.21) units for T3 vs. T1 (Ptrend=0.10). Excluding women with gestational diabetes mellitus (n=8) did not impact the results. Offspring adiposity and maternal prepregnancy BMI only partially explain the effect of maternal glycemia on offspring glucose metabolism. Our findings add to our understanding of the relative contribution of maternal glycemia, even within normal levels, on childhood glucose metabolism, with implications for targeted intervention/prevention approaches.

Table 2. Total and direct effects of maternal HbA1c exposure and early childhood glucose metabolism markers. Data are presented as the estimated β and 95% confidence intervals

	Model 1	Ptrend	Model 2	Ptrend	Model 3	Ptrend	Model 4	Ptrend	Model 5
	n=443		n=424		n=423		n=383		n=382
T3	0.20 (0.11, 0.30)	<.001	0.19 (0.09, 0.28)	<.001	0.18 (0.09, 0.28)	<.001	0.19 (0.10, 0.28)	<.001	0.18 (0.09, 0.28)
T2	0.06 (-0.02, 0.14)		0.04 (-0.04, 0.12)		0.04 (-0.04, 0.12)		0.04 (-0.04, 0.12)		0.04 (-0.05, 0.12)
T1	ref		ref		ref		ref		ref
	n=467		n=448		n=447		n=405		n=404
T3	6.93 (1.44, 12.4)	0.01	5.86 (0.32, 11.4)	0.03	5.28 (-0.28, 10.8)	0.05	4.85 (-0.69, 10.4)	0.09	4.46 (-1.10, 10.0)
T2	3.93 (-1.02, 8.89)		3.09 (-1.93, 8.11)		2.98 (-2.06, 8.02)		2.13 (-2.86, 7.11)		2.12 (-2.86, 7.11)
T1	ref		ref		ref		ref		ref
	n=412		n=403		n=402		n=363		n=362
T3	0.15 (0.04, 0.25)	0.01	0.13 (0.02, 0.23)	0.03	0.12 (0.01, 0.23)	0.04	0.11 (0.01, 0.22)	0.08	0.11 (0.00, 0.21)
T2	0.07 (-0.03, 0.16)		0.05 (-0.05, 0.14)		0.05 (-0.05, 0.14)		0.03 (-0.06, 0.13)		0.03 (-0.06, 0.13)
T1	ref		ref		ref		ref		ref
	n=412		n=403		n=402		n=363		n=362
T3	3.91 (-3.64, 11.45)	0.52	3.11 (-4.57, 10.79)	0.64	2.89 (-4.84, 10.63)	0.72	1.96 (-5.75, 9.68)	1.00	1.87 (-5.89, 9.62)
T2	2.41 (-4.37, 9.19)		2.11 (-4.71, 8.92)		2.00 (-4.85, 8.86)		1.01 (-5.71, 7.73)		1.05 (-5.70, 7.80)
T1	ref		ref		ref		ref		ref

Abbreviations: T1, tertile 1; T2, tertile 2; T3, tertile; BMI, body mass index
Model 1: Adjusted for maternal age, race, gestational week at HbA1c measurement, offspring sex, offspring age at assessment (4-7 yrs.)
Model 2: Model 1 + education, gestational weight gain status (inadequate, adequate, excessive) up until HbA1c measurement, smoking during pregnancy
Model 3: Model 2 + prepregnancy BMI
Model 4: Model 2 + offspring fat mass %
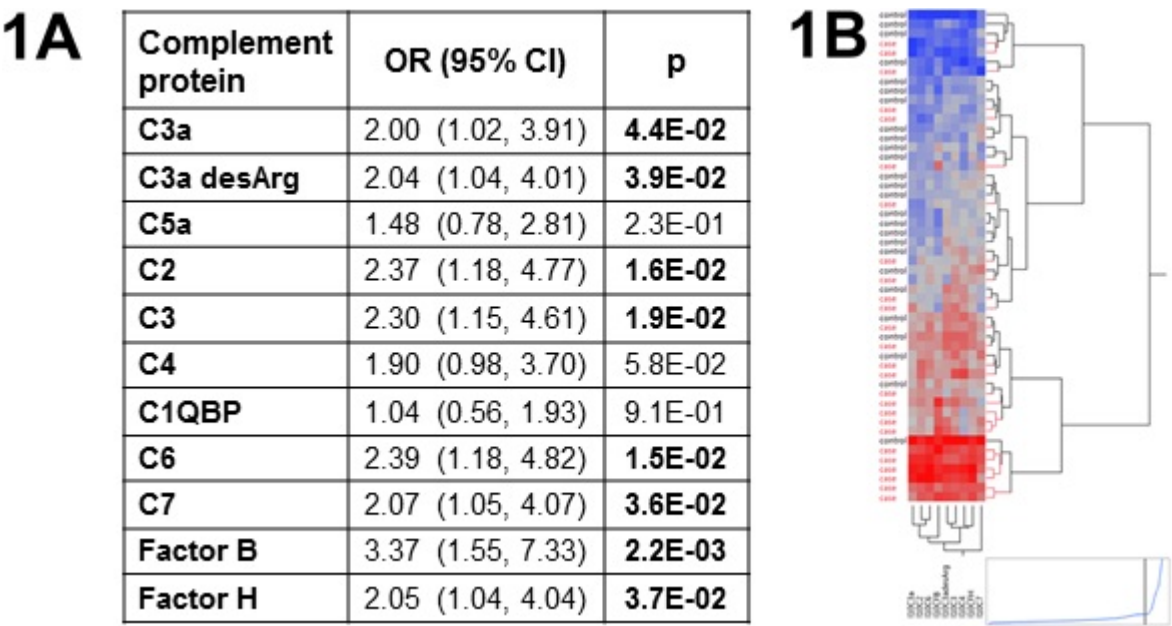Model 5: Model 3 + offspring fat mass %

Diabetes

Complement Pathway and Risk of Early Progressive Renal Function Decline in Type 1 Diabetes (T1D)

Salina Moon* Salina Moon Heather L. Donsky Ling Chen Karen Fernandez Simon T. Dillon Monika A. Niewczas

Our recent untargeted proteomic study of subjects with advanced diabetic kidney disease (DKD) identified the activation of the Complement pathway associated with progressive renal function decline. However, the role of Complement in earlier stages of the disease has not been studied before.

In a nested case-control study in Type 1 Diabetes (T1D) and early DKD (n=52) within the Joslin Kidney Study cohort, we compared profiles of Complement proteins in baseline urines between subjects who developed renal function decline and those who maintained stable renal function over 5-year follow-up. Our primary outcome was binary: cases were defined as subjects with a prospective eGFR loss >40%. Our secondary outcome was continuous and represented by individual linear regression-based eGFR trajectories. At baseline, all subjects had normal renal function (eGFR: 94±18 mL/min/1.73m2) and moderate albuminuria (ACR: 656 (390, 1301) µg/mg creatinine).

Eight of the Complement proteins were significant in the univariable logistic regression models at α=0.05, and five of them remained significant in the multivariable models (Fig.1A: effects sizes are shown per tertile change of the urinary creatinine adjusted proteins on the monotonic scale; 1 degree of freedom). Complement proteins correlated among each other with Spearman non-parametric correlation coefficients from r=0.48 to r=0.94. Principal component analysis identified one relevant component (Prin1; Eigenvalue >1). Odds ratios (95%CI) of renal function loss per one tertile change of the Prin1 were 2.19 (1.10, 4.34); p=0.02. Hierarchical cluster analysis revealed sample heterogeneity, neither explained by the baseline clinical covariates nor by the prospective caseness (Fig.1B, dendrogram; distances are shown).

Our study revealed significant associations of Complement proteins with renal function decline. Our study suggests that the Complement pathway may play a role earlier than formerly assumed.

1A

Complement protein	OR (95% CI)	p
C3a	2.00 (1.02, 3.91)	**4.4E-02**
C3a desArg	2.04 (1.04, 4.01)	**3.9E-02**
C5a	1.48 (0.78, 2.81)	2.3E-01
C2	2.37 (1.18, 4.77)	**1.6E-02**
C3	2.30 (1.15, 4.61)	**1.9E-02**
C4	1.90 (0.98, 3.70)	5.8E-02
C1QBP	1.04 (0.56, 1.93)	9.1E-01
C6	2.39 (1.18, 4.82)	**1.5E-02**
C7	2.07 (1.05, 4.07)	**3.6E-02**
Factor B	3.37 (1.55, 7.33)	**2.2E-03**
Factor H	2.05 (1.04, 4.04)	**3.7E-02**

1B

Hidden Markov Models for Identifying High Risk Type 2 Diabetes in Japanese Akihiko Narisada* Akihiko Narisada Kohta Suzuki

Background: Diabetes prevention is effective when targeting high risk. However, the definition for high risk using fasting blood glucose (FBG) is not uniformed between WHO (110 mg/dL) and ADA (100 mg/dL). Hidden Markov models (HMMs), in which the distribution that generates an observation depends on the state of undelaying and unobserved Markov process, are used to characterize the statistical properties of the sequencing in areas such as human speech processing and the analysis of DNA sequence. HMMs could provide new insights concerning high risk type 2 diabetes. The aim of this study is, using 2 independent Japanese cohort data, to develop type 2 diabetes model based on HMMs and to identify high risk type 2 diabetes.

Methods: Using longitudinal FBG data in Japanese (The Collab-Health Study: n = 51,808）, we developed type 2 diabetes model based on HMMs. The model had three-states (normal, high risk and diabetes), and was assumed that each latent state (normal and high risk) had each observed data which was Gaussian distribution (see Figure). On the basis of the developed model, the distributions of normal and high risk states, and transition probabilities among each state were estimated. Replication was done in other independent dataset (AHP Study: n = 23,205).

Results: Fitting 3 states HMM to 179,933 person-year data, the model estimated that normal state was 90.3±7.6 mg/dL and that high risk state was 104.6±7.1 mg/dL. The estimated transition probabilities after 1 year from normal to high risk, that from high risk to normal or that from high risk to diabetes were 7.9%, 0.01% and 6.0%, respectively (see Figure). HMM fitting to other dataset (AHP Study) indicated similar results.

Conclusion: The estimated distribution of high risk indicated that the cut-off point for high risk in WHO definition is too high. In addition, from the estimated transition probability from high risk to normal state, individuals with high risk state might rarely return to normal state.

Figure: The Hidden Markov Model for the onset of type 2 diabetes in the Collab-Health Study
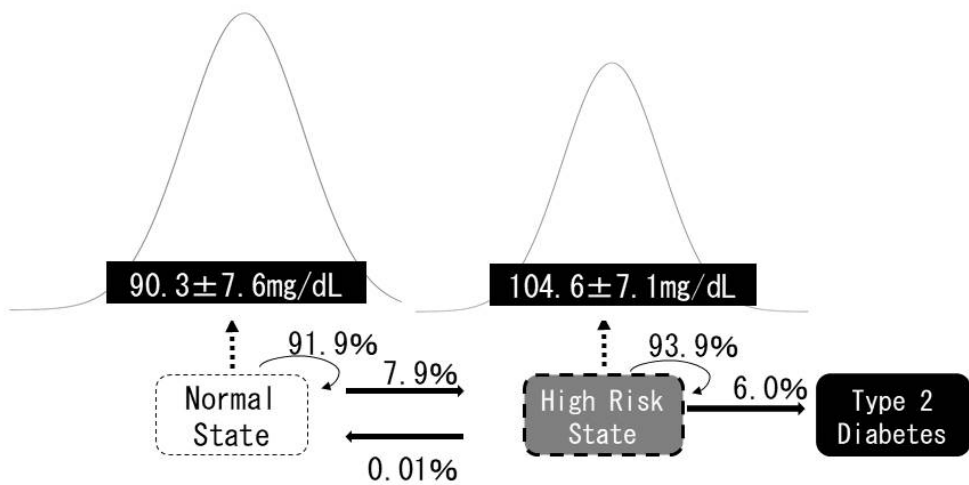
Maternal pre-pregnancy BMI and physical activity and type 1 diabetes in the offspring

Catarina Machado Azeredo* 3647] Azeredo Marianna Cortese Kassandra L Munger Alberto Ascherio

Objective: Our aim was to assess the relationship of maternal pre-pregnancy BMI and physical activity with type 1 diabetes in their offspring. **Methods**: Prospective study among parous women in the Nurses' Health Study II with information on pre-pregnancy (n=43,072) or early life (n=51,611) BMI and physical activity. We identified 276 cases of type 1 diabetes among offspring (n=70,168) with maternal pre-pregnancy information and 448 cases among offspring (n=111,692) with maternal early life information. We estimated risk ratios (RR) and 95% confidence intervals (95%CI) for the association of maternal BMI and physical activity with risk of type 1 diabetes in their offspring using generalized estimating equations to account for family clusters and adjusted the models for infant and maternal covariates, including maternal diabetes (gestational, type 1, and type 2). **Results:** Pre-pregnancy maternal BMI and physical activity were not associated with offspring type 1 diabetes. The estimates were similar in separate and in mutually adjusted multivariable models. In the mutually adjusted model, the RR comparing overweight to normal weight mothers was 1.08 (95% CI: 0.73-1.58), while the RR comparing obese to normal weight mothers was 0.94 (95% CI: 0.49-1.79, p-trend across categories: 0.98). For the comparison of highest to lowest quartile of maternal physical activity the RR was 0.90 (95% CI: 0.61-1.32; p-trend across quartiles: 0.72). Early life maternal BMI and physical activity were also not related to an increased risk of type 1 diabetes in the offspring. Maternal type 2 diabetes was associated with an increased risk of type 1 diabetes in the offspring, independent of BMI and physical activity (RR=1.87; 95%CI: 1.25-2.80). **Conclusions:** Our findings suggest that there is no relationship between maternal pre-pregnancy BMI or physical activity and the risk of type 1 diabetes in the offspring.

Differences in Quality Monitoring Practices Among Adult Diabetics in the United States

Isaiah Brown* 3647] Brown Sharon Jackson

Despite recent expansions in access to care, health disparities in chronic disease persists in the United States. A possible mechanism for this persistence is the disparity in access to quality care across populations. We examined pooled data from 3 cohorts of the National Health and Nutrition Examination Survey, each with over 9700 respondents providing biological and survey data. Weighted, linear regression analyses were used to assess differences in quality of care among adult, self-reported diabetics who reported having seen a doctor within the previous year. Estimates were adjusted for glycemic control (HA1c<7%), race/ethnicity, age, sex, education, and poverty status. Physician-monitoring for diabetes-related microvascular and skin complications included foot exams, HA1c monitoring and pupil dilation in the past year. Self-monitoring was assessed using self-report of foot exams. Diabetics with poorer glycemic control (1.920, 95%CI 1.259-2.929) were more likely than diabetics with adequate glycemic control to have reported checking their own feet for sores. Other Hispanics (0.513, 95%CI 0.316,0.833) and non-Hispanic Asians (0.499, 95%CI 0.312,0.798) were less likely than non-Hispanic whites to report that a doctor checked their feet for sores. Additionally, non-Hispanic Blacks (.423 ,95%CI 0.258 ,0.696) and other Hispanics (0.454, 95%CI 0.249,0.829) were less likely than non-Hispanic Whites to report having had their HA1c monitored at least once in the past year. Income also had an effect as we found that wealthier diabetics (1.62, 95% CI 1.031-3.399) were more likely to have had their pupils dilated for an eye exam in the past year than poor diabetics. Collectively, these findings indicate that differences in health monitoring may be a driving factor of disparities among diabetics of different race/ethnicity and income levels. Further research in the quality of care among diabetics needs to be done to fully understand the implications of this study.

Quantifying systemic inflammation and its association with sagittal abdominal diameter in US adults Koya Ferrell* 3647] Ferrell Dr. Sharon Jackson

Expending adiposity has been linked to chronic inflammation, which plays a central role in the progression of metabolic diseases such as diabetes. Using a novel cumulative inflammation index (CII) compiled from clinical laboratory test (race-specific quartiles for white blood cell ratios and gender-adjusted uric acid), we examined the association between systemic inflammation and sagittal abdominal diameter (SAD), an anthropologic measure of visceral obesity. We examined data from the 2013-14 and 2015-16 National Health and Nutrition Examination Survey (n=10,175 and 9,971 respectively). Demographics, self-reported diabetic status and medication use, hemoglobin A1C, 3 measures of metabolic risk (triglyceride, cholesterol, and blood pressure), physical activity, binge drinking and smoking status were measured. Weighted multivariable regression models were used to assess the association between SAD and CII, stratified by diabetes status. Overall, 13.9%, 18.3% and 67.8% of the sample were diabetic, prediabetic and non-diabetic, with mean CII of 5.1±0.10, 4.8±0.10, 4.3±0.10. We found that for each unit (cm) increase in SAD, CII was 0.11 higher (95% CI 0.08, 0.15) in diabetics, 0.09 higher (95% CI 0.07, 0.12) in prediabetics and 0.12 higher (95% CI 0.10, 0.14) in non-diabetics. These estimates were adjusted for covariates measured; age, gender, poverty status, education, race/ethnicity, physical activity, binge drinking and smoking status. Collectively, these findings suggest an independent association between adiposity and inflammation, that indicates that increased visceral fat can trigger an increase in inflammation. Future longitudinal studies are needed to confirm our findings.

History of gestational diabetes mellitus and risk of Type 2 Diabetes Mary V Diaz-Santana*
3647] Diaz-Santana Katie M. O'Brien Yong-Moon Mark Park Dale P. Sandler Clarice Weinberg

Background: As of 2019, over 31 million individuals in the United States (US) had Type 2 Diabetes
Mellitus (T2D). T2D causes serious disability and almost 2.7% of all deaths among women in the US.
It is important to identify people at high risk of T2D so they can be screened for early detection.
Gestational diabetes mellitus (GDM) complicates 4.6% to 9.2% of pregnancies in the US and is
strongly predictive of T2D. But it is not known to what extent the relative risk changes with time
since a GDM pregnancy.

Methods: We assessed the association between GDM and T2D using nationwide data from the
Sister Study (2003-2009), a prospective cohort study of 50,884 women ages 35-74 at enrollment. We
modeled the change in diabetes risk according to the time elapsed since the most recent GDM
pregnancy. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) using Cox
proportional hazards models, with age as the primary time scale, adjusting for body mass index and
ethnicity.

Results: Three percent of participants reported having had at least one GDM pregnancy. Women
who had just completed a GDM pregnancy had a markedly elevated estimated hazard ratio (adjusted
HR=4.34, 95%CI: 2.80-6.71) for T2D as compared to women without GDM. Additionally, we
estimated an 18% (HR=0.82 95%CI: 0.66-0.90) attenuation of that elevated T2D hazard per decade
of time elapsed since the most recent GDM diagnosis. Compared to women without GDM, the risk of
T2D was higher among participants with multiple GDM pregnancies (after the 3rd with GDM the
peak HR was 8.38, 95%CI: 4.22-16.63 vs. after the 1st with GDM the peak HR was 3.88, 95%CI:
2.47-6.11).

Conclusions: Women with GDM had markedly increased estimated risk of T2D, which was
substantially higher among women with multiple GDM pregnancies. The estimated relative hazard
then slowly declined over time, but remained elevated for decades. Women with a history of GDM
need to be screened regularly for T2D, even late in life.

Environment/Climate Change

Assessing the Effectiveness of Vehicle Emission Regulations on Improving Perinatal Health: A Population-Based Accountability Study Mary D. Willis* Mary Willis Elaine L. Hill Molly L. Kile Susan Carozza Perry Hystad

Background: Over the last 3 decades extensive regulations were implemented to reduce traffic-related air pollution (TRAP), costing billions of dollars, yet the cumulative effectiveness of these regulations has not been assessed with respect to infant health, a subpopulation that is highly susceptible to TRAP. We hypothesize that the series of emissions regulations yielded improved infant health outcomes among mothers most exposed to TRAP. In this analysis, we conduct an accountability study to test this hypothesis.

Methods: We assessed changes in outdoor NO2 concentrations (a marker for TRAP) across Texas. Then, we created a population-based retrospective birth cohort with geocoded residential addresses in Texas metropolitan areas from 1996 through 2009 (n=1,458,021). We compared term birth weight (TBW) (37-42 weeks gestation) among maternal residences within 300m of a highway (high TRAP exposure) (n=394,346) and 500-1,500m of a highway (low TRAP exposure) (n=1,063,675). We implemented linear regression models to evaluate interactions between high TRAP exposure and birth year, adjusting for demographics, socioeconomic status, and neighborhood context. In addition, we used propensity score matching (PSM) to further reduce potential residual confounding among our groups.

Results: From 1996 to 2009, outdoor NO2 decreased by 51.3% based on regulatory monitoring data in Texas. Time-stratified models show decreasing impacts of living in high TRAP areas on TBW when comparing infants born in 1996-1997 to 2008-2009 (Figure 1). Among mothers who resided in the high TRAP zone during pregnancy, interaction terms between TRAP exposure and birth year show an increase in birth weight of 0.8g (95% CI: 0.4, 1.3) in unadjusted models and 0.3g (95% CI: 0.0, 0.5) in PSM models per year.

Conclusion: Infant health risks associated with exposure to TRAP have reduced over time, paralleling regulations that have reduced tailpipe emissions.

Figure 1: Mean Term Birth Weight by Distance from a Major Highway in 1996-1997 vs. 2008-2009
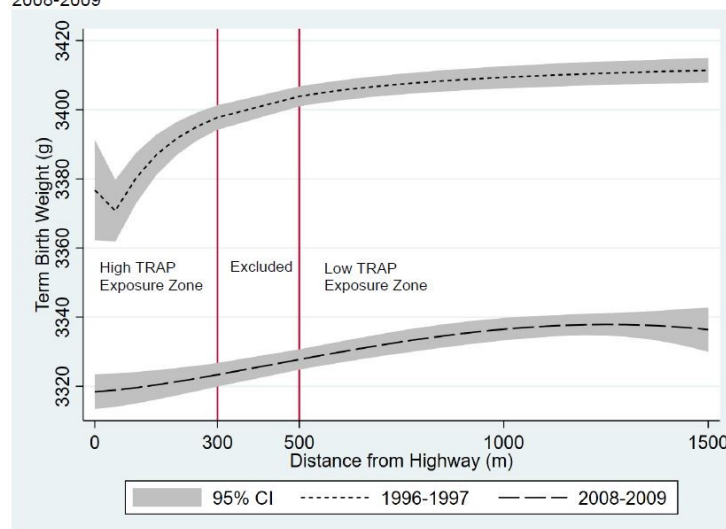
TRAP = Traffic Related Air Pollution. Results are unadjusted mean term birth weights for maternal residences at each 50m interval between 0 and 1,500m from a major highway with a fractionated polynomial regression to create smoothed lines. For this analysis, births to mothers between 0-300m are the high TRAP exposure zone while births to mothers between 500-1,500m are the low TRAP exposure zone.

Environment/Climate Change

Correcting urinary biomarkers for hydration status using specific gravity: A comparison of methods using NHANES 2007-2008 Jordan R. Kuiper* Jordan Kuiper Kelly K. Ferguson Katie M. O'Brien Jessie P. Buckley

Epidemiologic studies using urinary biomarkers must account for urine dilution. Specific gravity is commonly believed to be less influenced than creatinine by sociodemographic factors and health conditions. However, this assumption has not been formally evaluated. We aimed to identify predictors of specific gravity in a nationally representative sample and compare methods for using specific gravity to correct urinary biomarkers for urine dilution in an applied analysis. We conducted a cross-sectional analysis of 6781 individuals aged six years or older participating in the 2007-2008 cycle of the United States National Health and Nutrition Examination Survey (NHANES). We identified predictors of specific gravity, separately for children/adolescents and adults, using weighted linear regression. We compared four approaches to correct for urine dilution: "uncorrected" (no correction), "covariate-adjusted" (specific gravity as covariate), "Boeniger" (multiplying exposure by a ratio of the population mean to individual specific gravity concentration, the most common method), and "O'Brien" (covariate-adjusted specific gravity standardization based on a method proposed for creatinine). Using these methods, we evaluated associations of molar sum di-2-ethylhexyl phthalate ($\sum$DEHP) concentrations with serum total 25-hydroxyvitamin D [25(OH)D] using weighted linear regression. Specific gravity was associated with age, sex, race/ethnicity, body mass index, time of sample collection, diabetes, hyperthyroidism, and hypertension. Associations of $\sum$DEHP with 25(OH)D corrected using "Boeniger" and "O'Brien" methods were comparable. We observed that specific gravity is influenced by a number of factors and has similar limitations as creatinine when used to account for urine dilution in analysis of urinary biomarkers. We recommend employing correction methods that explicitly account for such factors.

The impact of multiple toxic metal exposures on self-rated health in Detroit, Michigan

Evans K. Lodge* Evans K. Lodge Allison E. Aiello

Introduction: Toxic metals like lead (Pb), chromium (Cr), mercury (Hg), and manganese (Mn) have been linked to cardiovascular and endocrine disease, reproductive complications, neurological damage, and cancer. Associations between toxic metal exposures and poor self-rated health (SRH), an accurate predictor of all-cause mortality, have been previously identified in small cross-sectional studies. Using survey and biomarker data from the Detroit Neighborhood Health Study (DNHS), we estimated the longitudinal effects of elevated serum Pb, Cr, Hg, and Mn on SRH.

Methods: Survey data and blood serum samples were collected annually in the DNHS from 2008-2013. Annual serum concentrations of Pb, Cr, Hg, and Mn were measured by inductively-coupled plasma mass spectrometry. We used multivariate logistic regression to model the longitudinal effect of individual metals on SRH, and Bayesian kernel machine regression to flexibly model the effect of simultaneous exposure to multiple metals on SRH.

Results: Pb, Cr, Hg, and Mn were collected at least once in 779 participants, and twice or more in 546 participants. The average participant was 53 years of age, female (58%), and non-Hispanic African American (82%) at enrollment. 38% rated their health as "Excellent" or "Very Good." Longitudinal logistic regression models controlling for gender, race, ethnicity, age, and income showed no associations between repeated measures of serum Pb, Cr, Hg, or Mn and self-rated health. Using Bayesian kernel machine regression to assess non-linear and potentially interactive effects of multiple metal exposures yielded similarly null results.

Conclusions: Previous studies of toxic metals have demonstrated positive associations between metal exposure and poor self-rated health. Using a longitudinal data set and novel mixture-methods approaches, we provide evidence that exposure to Pb, Cr, Hg, and Mn are not associated with poor self-rated health in Detroit, Michigan.

Figure 1. Distribution of Pb, Cr, Hg, and Mn by DNHS Wave
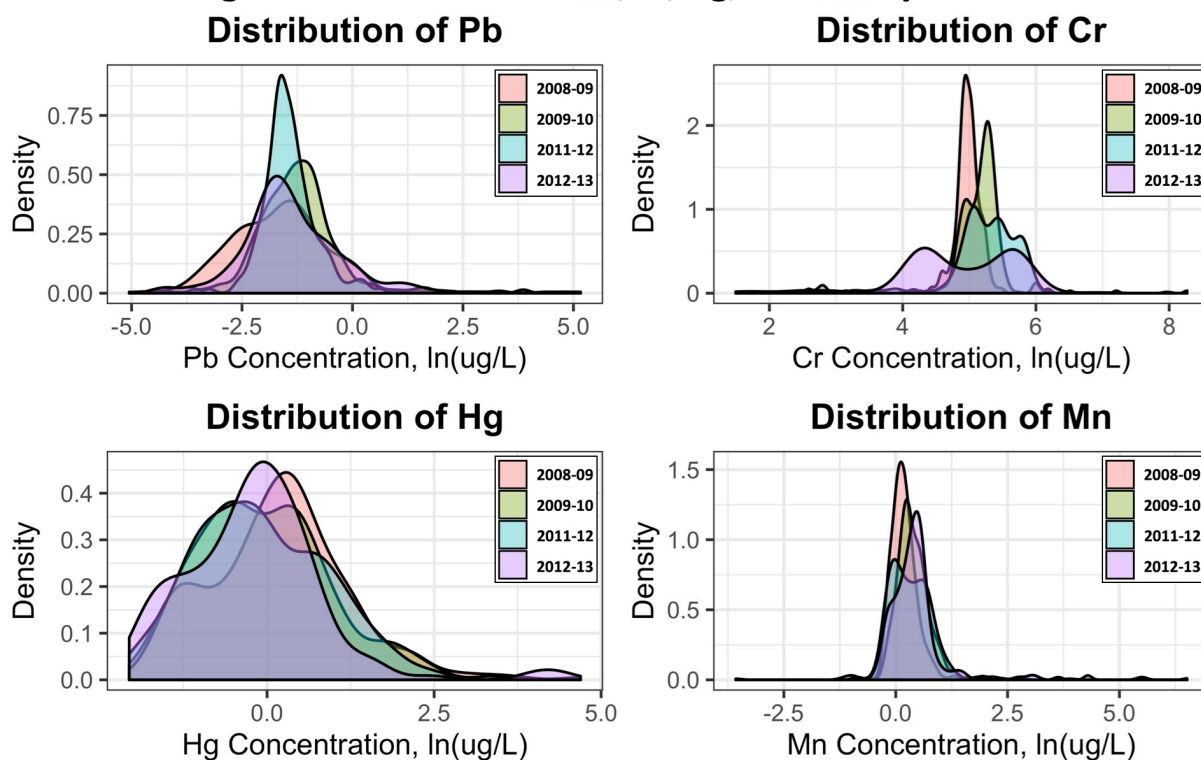
Perception of Worry of Harm from Air Pollution: Results from the 2012 Health Information National Trends Survey Samantha Ammons* Samantha Ammons Gabriel Lai Armen Ghazarian Gary Ellison

Background: Air pollution exposure has been associated with a multitude of diseases and poses a significant concern to public health. For targeted environmental risk communication and interventions to be effective, it is important to correctly identify characteristics associated with worry of harm from air pollution.

Objectives: We sought to identify sociodemographic and cancer-related characteristics associated with worry of harm from air pollution exposure in the United States.

Methods: Using responses from 3,630 participants of the 2012 Health Information National Trends Survey 4 Cycle 2, we assessed worry of harm from exposure to indoor (IAP) and outdoor (OAP) air pollution. Multinomial logistic regression was used to calculate odds ratios (OR) and 95% confidence intervals (CIs) to examine the relationship between selected sociodemographic and cancer-related characteristics and worry of harm from IAP and OAP.

Results: Hispanics were more likely to worry about harm from IAP [OR:2.44, 95% CI: 1.34 – 4.43] and OAP [OR: 3.02, 95% CI: 1.78 – 5.15] compared to non-Hispanic whites. Participants that lived in urban counties were more likely to worry about harm from IAP [OR: 1.64, 95% CI: 1.27 – 2.11] and OAP [OR: 1.88, 95% CI: 1.08 – 3.28] compared to those who lived in rural counties. Finally, those who believed their chances of getting cancer was high were more likely to worry about harm from IAP [OR: 2.15, 95% CI: 1.50-3.08] and OAP [OR: 2.30, 95% CI: 1.52 – 3.48] compared to those who thought their likelihood of getting cancer was low.

Discussion: Worry of harm from IAP and OAP varied across sociodemographic and cancer-related characteristics. Public health professionals should consider these characteristics when developing targeted environmental risk communication and interventions.

Weekly gestational exposure to fine particulate matter and ozone are associated with preterm birth in a state-wide North Carolina cohort from 2006 – 2015 Kristen M Rappazzo*
Kristen Rappazzo Joshua L Warren Thomas J Luben

Adverse pregnancy outcomes, including preterm birth, are associated with exposure to criteria air pollutants. In this analysis, we examine associations between gestational exposure to particulate matter less than 2.5 micrometers in diameter (PM2.5) and ozone with preterm birth (less than 37 weeks completed gestation) in a North Carolina (NC) birth cohort from 2006 through 2015 (n=904,909). Residential locations from birth records were geocoded and linked to daily air pollutant concentration estimates provided at the census tract centroids by the EPA's CMAQ downscaler model and averaged for each week of each individual's specific pregnancy period. Risk differences (RD) and 95% confidence intervals were estimated for exposures at each week of gestation. RDs for PM2.5 exposure were elevated from the null throughout pregnancy (e.g., RD (95%CI) per 10,000 births for a 5 ug/m3 increase in week 8: 49 (42, 57), in week 33: 22 (16, 29)), while RDs for ozone were elevated in early pregnancy and below the null in later pregnancy weeks (e.g., RD for a 10 ppb increase in week 3: 30 (25, 35), in week 31: -4 (-9, 1)). Results of copollutant models were similar to the single pollutant results. Air pollutant exposure is associated with increased risk of preterm birth, however, critical windows of exposure varied by pollutant.

The views expressed in this abstract are those of the authors and do not necessarily reflect the views or policies of the United States Environmental Protection Agency. Mention of trade names or commercial products does not constitute endorsement or recommendation for use.
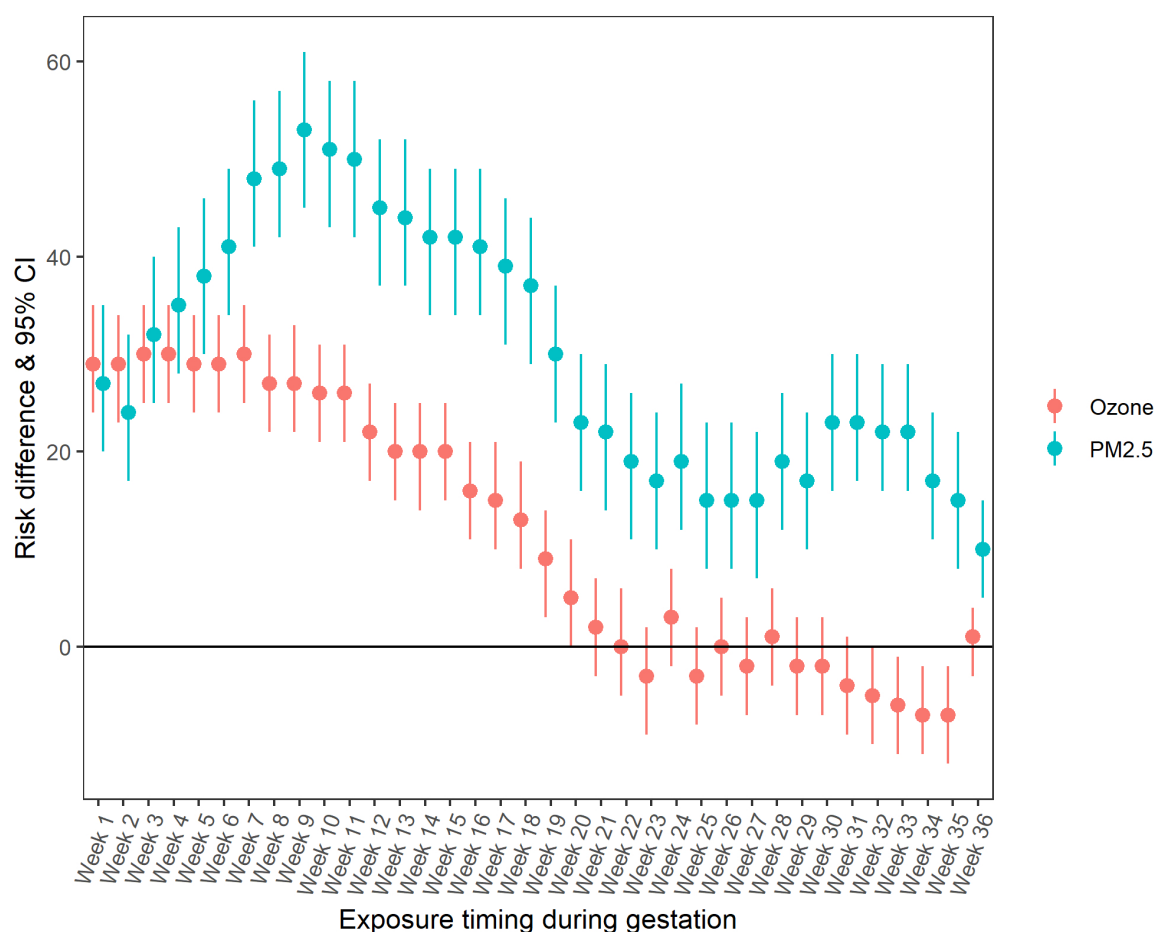
Early Life Exposure to Green Space and Childhood Cognition Marcia Pescador Jimenez*
Marcia Pescador Jimenez Jessica Shoaff Marie-France Hivert Sheryl L. Rifas-Shiman Emily Oken
Peter James

Objectives: Green space (GS) may be important for cognitive function through mitigation of air
pollution, but the influences of early life exposure to GS on cognitive development are not well
understood. We examined associations of residential proximity to GS at birth and early childhood
with mid-childhood cognition.

Methods: We studied 754 mother–child pairs in Project Viva, a pre-birth cohort study in
Massachusetts. We estimated GS surrounding each participant's address at birth and early
childhood (median age 3.2 y), using 30m resolution Landsat satellite imagery [Normalized
Difference Vegetation Index]. In mid-childhood (median age, 7.7 y), we administered standardized
assessments of verbal and nonverbal intelligence, visual motor abilities (VMA), and visual memory
(VM). We used linear regression to examine prospective associations of GS at birth and early
childhood with cognition at mid childhood, adjusted for children's age, sex, race/ethnicity, household
income, neighborhood socioeconomic status, maternal intelligence, and parental education. Early
childhood models further adjusted for GS at birth. We also evaluated non-linear relationships using
cubic regression splines.

Results: GS at birth was positively associated with mid-childhood verbal IQ and VM in minimally
adjusted models; but after adjustment for confounders, associations were attenuated. At early
childhood, compared with children in the lowest quartile of GS exposure, those in the highest
quartile had higher mid-childhood non-verbal IQ [4.5 points; 95% CI: 0.1, 8.8], and higher VM [1.5
points; 95% CI: 0.4, 2.7], but no difference in verbal IQ. In addition, compared with children in the
lowest quartile of GS exposure at early childhood, those in the second quartile had lower mid-
childhood VMA [-4.5 points; 95% CI: -8.5, -0.5]. Spline analyses provided evidence of non-linear
associations between GS and cognition (Figure 1).

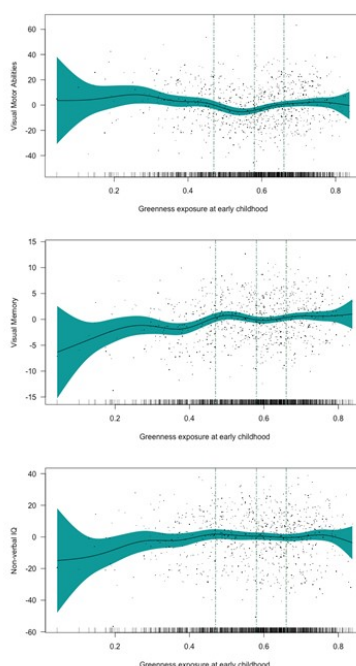Conclusions: Early childhood exposure to GS may affect cognitive development.

Restricted

Figure 1. Cubic regression splines for (a) Non-verbal IQ, (b) Visual Memory, and (c) Visual Motor Abilities

Environment/Climate Change

Concentrations of multiple between persistent organic pollutants and measures of kidney health in adults: Cross-sectional findings from the 1999-2004 National Health and Nutrition Examination Survey Jessica M. Madrigal* Jessica Madrigal Victoria Persky Mary Turyk Sally Freels Robert Sargis Martha Daviglus James Lash

Background: Persistent organic pollutants (POPs) may be risk factors for chronic kidney disease (CKD). Our aim was to investigate the associations between multiple POPs and measures of kidney function in a representative sample of adults. Methods: We evaluated cross-sectional associations of serum concentrations of 42 polychlorinated biphenyls (PCBs) and nine organochlorine pesticides with estimated glomerular filtration rate (eGFR) and albumin to creatinine ratio (ACR) in two samples from the 1999-2004 National Health and Nutrition Examination Survey (NHANES). Dichotomous endpoints included low eGFR (30). We summed total PCBs, toxic equivalencies, estrogenic, and anti-estrogenic PCBs. Multivariable adjusted survey-weighted linear and logistic regression models were used to estimate beta coefficients or odds ratios and their 95% confidence intervals for exposure quartiles. Effect modification by sex was evaluated with interaction terms. Results: In the PCB sample (n=3,851), the average age was 46.2 years (SD 0.37) and 50.3% were female. Most measures of PCBs were positively associated with eGFR. Sex-stratified estimates indicated a positive association between PCBs and eGFR among males, and no association among females. Participant characteristics in the pesticide sample (n=3,134) were similar to the PCB sample. p,p' DDE was positively associated with eGFR (p-trend 0.05) but the difference in eGFR by quartile of p,p' DDE was small. Heptachlor epoxide (p-trend 0.006) and oxychlordane (p-trend 0.10) were positively associated with odds of low eGFR. No other associations were observed. Conclusions: Our findings suggest that PCB concentrations may be associated with small increases in eGFR, particularly among males, but it is unclear if these associations are due to bias in GFR estimation. Heptachlor epoxide may be associated with increased odds of low eGFR. Investigation into these exposures with longitudinal data is warranted to fully understand health impacts.

Active living environments and hospitalization in adults with and without type 2 diabetes

Sarah M Mah* Sarah M Mah Claudia Sanmartin Mylène Riva Kaberi Dasgupta Nancy Ross

Background: The extent to which one's neighborhood is conducive to active living ('walkability') could reduce hospitalization through enabling physical activity and may be of particular importance to those with type 2 diabetes (T2D).

Methods: The linked dataset is a combination of survey data from Canadian respondents aged 45+, records from a national census of acute hospitalizations, and the Canadian Active Living Environment (Can-ALE) database - which is a 5-class measure based on street connectivity, points of interest, and population density. T2D patients were identified using an algorithm as well as diabetes-related hospitalizations prior to survey response. We modeled the risk of all-cause and cardiometabolic hospitalizations for respondents living in more versus less favorable environments using logistic regression and assessed for differences by T2D status. Models were adjusted for individual-level factors and proximity to a hospital. An offset variable was included to account for different follow-up times.

Results: 232 000 respondents were included with a mean follow-up time of 5.37 years. 26 225 respondents had T2D at baseline (11.30%). Those living in progressively more favorable neighborhoods (classes 2, 3, 4, and 5) exhibited incrementally lower risk of hospitalization compared to those living in the least favorable (class 1). Relative to respondents living in the least favorable environments (class 1), odds ratios were 0.84 (95% CI 0.76-0.93) for all-cause hospitalization and 0.80 (95% CI 0.68-0.93) for cardiometabolic hospitalization for respondents living in the most favorable environments (class 5). Although hospitalization risk was higher for T2D patients, there was little evidence of interaction between the active living environment and T2D status.

Conclusions: Living in neighborhoods that are conducive to active living are associated with lower risk of all-cause and cardiometabolic hospitalization. Associations are similar in adults with and without T2D.

Environment/Climate Change

Development and validation of a directed acyclic graph relating coexposure to multiple metals and cardiometabolic outcomes

Emily Riseberg* Emily Riseberg Rachel Melamed Kathy James Tanya L. Alderete Laura Corlin

Background: Individual metals and metalloids [e.g., cadmium (Cd), inorganic arsenic (iAs), manganese (Mn), and tungsten (W)] are associated with cardiometabolic outcomes. Few studies examined associations between coexposure to multiple metals and cardiometabolic outcomes. Theoretically-grounded analytical models probing the relationships among time-varying metal mixture exposures and cardiometabolic outcomes requires an understanding of the (assumed) causal structure.

Methods: We conducted a literature review using PubMed, ProQuest, and Embase to determine the established relationships among metals and cardiometabolic outcomes. We developed an evidenced-based directed acyclic graph (DAG) in Daggity to represent the causal structure. We tested the conditional independencies suggested by this DAG using data from 1440 participants in the San Luis Valley Diabetes Study (mean age = 54 years, 54% women, 48% Hispanic). We used the DAG to specify Bayesian kernel machine regression (BKMR) models testing the associations between urinary concentrations of metals and development of cardiometabolic outcomes over 5 years.

Results: We included 28 articles in the literature review: 7 meta-analyses, 16 literature or systematic reviews, 3 multi-centric cross-sectional studies, 1 multi-centric cohort study, and 1 multi-centric case-cohort study. Most included iAs and Cd (13 studies each), while 4 each included Mn and U and 1 included W. Of the testable conditional independencies suggested by the DAG, 67% were supported. Correlation coefficients among metal concentrations were <0.35. BKMR analyses indicated that the strongest individual relationship was between Mn and Type 2 diabetes. No single metal had a strong relationship with CHD though the mixture of metals had a weak association with greater risk of CHD.

Conclusion: Evidenced-based DAGs can be developed and applied to specify appropriate analytical models prospectively relating environmental mixture exposures to health outcomes.

Environment/Climate Change
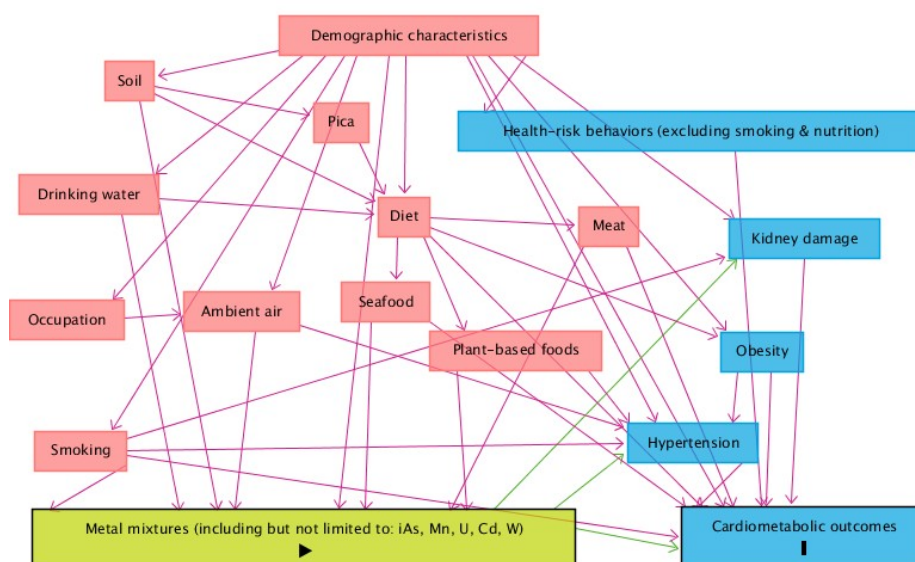
**Environmental and psychological distress related to oil and gas development in West Texas' Permian Basin** Holly Elser* Joan Casey Holly Elser Sidra Goldman-Mellor Nicole Deziel Rachel Morello-Froschh

Introduction: The Permian Basin in West Texas hosted the most oil drilling rigs of any US formation in 2019. Simultaneously, flaring (burning of unused natural gas at the drilling site) has reached an all-time high. In some cases, underground injection of produced wastewater has induced earthquakes, which could accelerate as drilling expands in the future. Limited public health studies have taken place in the Permian.

Methods: We conducted an online survey of Texas residents using the validated Environmental Distress Scale, which measures the bio-psychosocial costs of ecosystem disturbance. Three subscales capture (1) threat of environmental issues; (2) possible impact of environmental change; and (3) solastalgia, the mental or existential stress associated with environmental change. We used generalized linear models to estimate the change in each distress subscale score in relation to residence in a county overlaying the Permian basin, residence in a county with any oil wells, residence in a county with any earthquake ≥ magnitude 3.

Results: After adjusting for sex, age, and employment, we find that reported threat of environmental issues is 4.4% higher among those residing in the Permian Basin versus elsewhere (95% CI: 0.3 to 8.4%). Solastalgia was also higher among Permian residents (3.9%, 95% CI: -0.8 to 8.5%). Differences in reported impact of environmental change were less pronounced (2.1%, 95% CI: -1.6 to 5.8%). Among residents in counties with oil wells, reported impact of environmental change appeared higher (4.0%, 95% CI: -1.9 to 9.9%) as was reported solastalgia (6.0%, 95% CI: -1.4 to 13.4%). We find minimal differences in subscale scores for residents living in counties with earthquakes versus without.

Conclusions: These preliminary findings suggest that residents are attuned to industrial activities in their communities that may pose environmental threats.
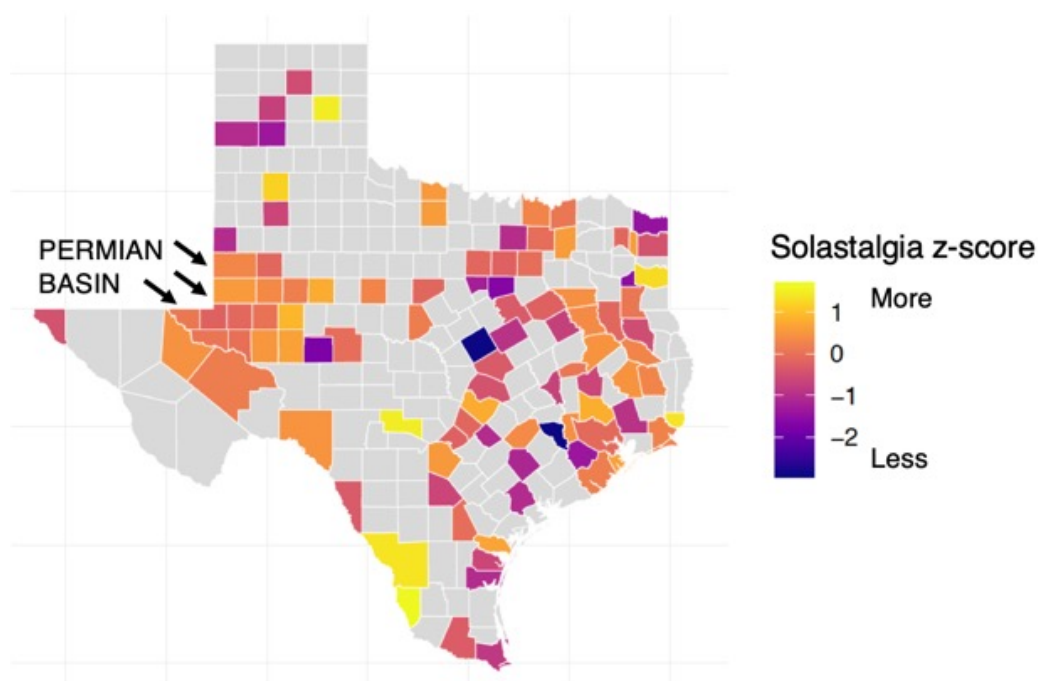
Neighborhood Green Space is Associated with Objectively-Measured Adolescent Sleep Patterns Stephanie L. Mayne* Stephanie Mayne Knashawn Morales Ariel A. Williamson Struan F.A. Grant Alexander G. Fiks David F. Dinges Babette S. Zemel Jonathan A. Mitchell

Background: Neighborhood green space has been linked to improved physical and mental health. One potential mechanism is through supporting healthier sleep. However, the association of green space with sleep among adolescents, a population at high risk for poor sleep outcomes, has not been examined. This study examined associations of neighborhood green space with objectively-measured adolescent sleep duration and timing. Methods: In a prospective cohort study, longitudinal data on sleep duration (hours/night), onset (hours from 00:00), and offset (hours from 00:00) were assessed from 108 adolescents for 14 days during the fall or spring school terms in both 8th grade and 9th grade using actigraphy. Participants' home addresses were geocoded and linked to neighborhood green space data from the US National Park Service's National Land Cover Database, operationalized as percent tree canopy cover within a half-mile buffer. Multivariable mixed-effects linear regression estimated associations of tree canopy cover with sleep outcomes, adjusting for sex, race, parent education, household income, grade, and school night status. Interactions by school night status were tested. Results: A total of 2,388 nights of sleep data were provided by 108 adolescents (53% female, 25% black). A 1-standard deviation increase in neighborhood tree canopy cover was associated with 11 minutes earlier sleep onset (beta= -0.19, 95% CI: -0.35, -0.03) and 7 minutes earlier sleep offset (beta= -0.12, 95% CI: -0.23, -0.02). Associations of tree canopy cover with sleep timing were stronger on non-school nights compared to school nights (p-interaction: 0.026, Figure). No associations were observed for sleep duration. Conclusion: Higher neighborhood tree canopy cover was associated with earlier sleep timing among adolescents. Earlier sleep timing may benefit adolescents who face earlier school start times. Results suggest neighborhood green space may aid in circadian alignment.

Figure. Associations of green space with sleep timing by school night status
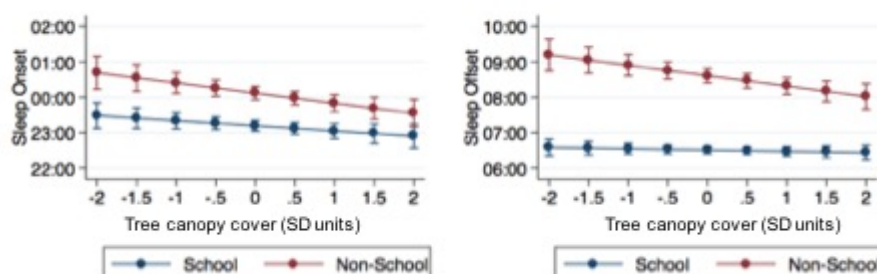
Multiple imputation of non-detects and calibration to improve measurement of low-level inorganic arsenic exposure Catherine Bulka* Catherine Bulka Paige Bommarito Rebecca Fry

Background: The toxicity of inorganic arsenic is well-established and adverse health outcomes are increasingly being linked to chronic low-level exposures. ΣAs, calculated as the sum of inorganic arsenic (As+3, As+5) and methylated metabolites (monomethylarsonic acid [MMA], dimethylarsinic acid [DMA]) in urine, is used as the main biomarker of exposure. However, accurate measurement at low concentrations is challenging for two reasons. For one, instrumental limits of detection (LODs) result in incomplete left-censored data. Second, because organic arsenic – which is non-toxic and primarily derived from seafood – is metabolized to DMA, it is difficult to isolate the toxic inorganic species (Figure).

Methods: We analyzed urinary biomarker data from 19,227 National Health and Nutrition Examination Survey (NHANES) 2003-2016 participants. We performed 10 multiple imputations by chained equations of As+3, As+5, MMA, and DMA as well as the organic arsenic species arsenocholine and arsenobetaine using interval regression. Imputation models included sociodemographic characteristics, urinary creatinine (a measure of hydration status), and intakes of potentially contaminated dietary constituents (e.g., water, rice, seafood). We then calculated ΣAs and calibrated this measure by expanding a residual-based method to remove the contribution of organic arsenic.

Results: The percent below the LOD ranged from 21.6% (DMA) to 96.5% (As+5). Using the standard approach of replacing non-detectable values with the LOD/√2, the median ΣAs was 5.8 µg/L (interquartile range, IQR: 3.4-8.0). After imputation and calibration, we estimated a median of 0.8 µg/L (IQR: 0.6-1.2).

Discussion: In populations with seafood consumers and low-level exposures to inorganic arsenic, standard approaches appear to substantially overestimate the amount of toxic inorganic species in urine. Our approach of combining imputation and regression-based calibration should be considered to reduce measurement error.

Environment/Climate Change
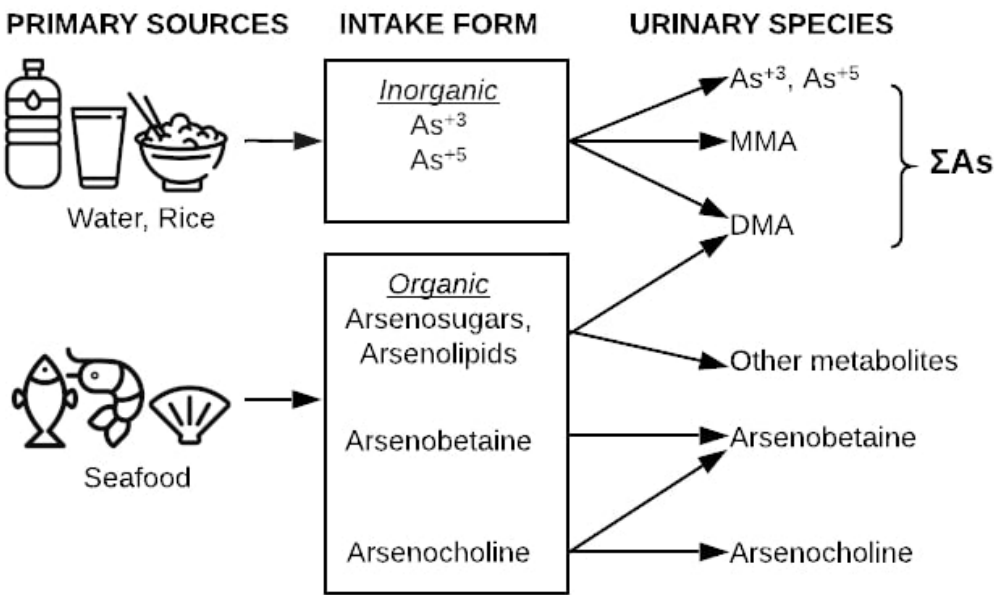
The association between ozone and emergency room visits for depression, self-harm, and suicide in California, 2005-2013 Angela-Maithy Nguyen* Angela-Maithy Nguyen Rupa Basu Brian Malig

Depression, self-harm, and suicide are all leading causes of morbidity and mortality in the US. Recent studies have suggested that exposure to gaseous pollutants, such as ozone, may increase the incidence of these mental health outcomes, however research is limited. We examined the association between short-term exposure to ozone and daily emergency room visits from depression, self-harm, and suicide (ICD-9 codes: 311, E95-E959) from 2005 through 2013. Air monitoring data were provided by the US EPA's Air Quality System Data Mart and data on emergency room visits were provided by the California's Office of Statewide Health Planning and Development. Our study population included 162,451 cases of depression and 198,509 cases of self-harm and suicide in California. We conducted a two-stage analysis with a quasi-Poisson regression, controlling for mean apparent temperature, day of the week, and holidays. We first used a time-series approach to calculate effect estimates for each air monitor zone, followed by a meta-analysis to produce a combined estimate. After testing several lag models, we observed significant 7-day lag associations between ozone for either depression or self-harm and suicide. Weekly mean levels of ozone were associated with a 1.87% increase in depression (95% CI: 0.62, 3.15) and a 1.43% increase in self-harm and suicide (95% CI: 0.35, 2.51). In sub-group analyses, we found increased risks for depression, self-harm, and suicide among females, those up to 35 years of age, Asians, and Hispanics. We did not observe any consistent seasonal variation. Our results suggest that exposure to ambient ozone may increase the risk of depression, self-harm, and suicide, though underlying biological mechanisms remain to be explored. Our study's findings underscore the importance for further research to better understand the health impacts of air pollution on mental health conditions.

Exposure to ambient fine particulate matter and preterm birth: evidence from Temuco, Chile, a city heavily impacted by residential wood-burning Estela Blanco* Estela Blanco Maria Elisa Quinteros Ximana Ossa Juana Maria Delgado-Saborit Juan Pablo Cárdenas-Ramírez Carola Blázquez Suzanne Bartington Roy Harrison Pablo Ruiz-Rudolph

Background: Exposure to fine ambient particulate matter (PM2.5) during pregnancy has been related to increased risk preterm birth (PTB), with evidence primarily from cities impacted by traffic and industry. As different compositions of PM2.5 may relate to different health impacts, we evaluated the relationship between PM2.5 and PTB in Temuco, a city in southern Chile heavily impacted by residential wood-burning for heating.

Methods: Between 2009-2015, information on all live births from the single regional public hospital in the Temuco urban area was collected (n=15510). Gestational age was calculated based on ultrasound. PTB was classified as gestational age <37 weeks, while moderate PTB (mPTB) was defined as gestational age between 33 and 36, and very PTB (vPTB) between 28 and 32 weeks. Exposure to PM2.5 in each trimester of pregnancy was estimated using a land-use regression model specifically developed for this study. Survival analysis was used to estimate the effects of exposure to air pollution in each trimester for risk of PTB, mPTB, and vPTB per 10 µg/m3 adjusting for potential confounders.
Results: Women had a median age of 24 years (IQR 20-30), had completed secondary school (66%) and had public insurance (90%). Median (IQR) of PM2.5 exposure was 32.3 (14.3-59.9) in the first trimester, 34.5 (15.5-59.6) in the second and 33.6 (13.9-59.9) in the third. PTB, mPTB, and vPTB was observed in 10.1%, 7.2% and 2.0% of the sample, respectively. In adjusted models, a 10 µg/m3 increase in PM2.5 exposure in the first and third trimesters related to increased risk of PTB: HR=1.13 (1.07-1.20) and HR=1.14 (1.07-1.22), respectively. Results were similar for mPTB. We did not observe a difference for vPTB, nor differences for any PTB category associated with PM2.5 exposure in the second trimester.

Conclusions: We confirmed that maternal PM2.5 exposure in a city dominated by wood-burning increased risks of PTB with a magnitude in the upper range reported in other cities.

Long-term aircraft noise exposure and risk of hypertension in the Women's Health Initiative

Daniel Nguyen* Daniel Nguyen Eric A. Whitsel Gregory A. Wellenius Jonathan I. Levy James D. Stewart Melissa N. Eliot Matthew P. Fox Andrew Malwitz JoAnn E. Manson L. Adrienne Cupples Junenette L. Peters

Background: Aircraft noise is a persistent concern for communities surrounding airports. Some studies report associations with hypertension, yet establishing causation is difficult as few were longitudinal. We evaluate the association between long-term aircraft noise exposure and hypertension risk among postmenopausal women in the Clinical Trial and Observational Study cohorts of the Women's Health Initiative, an ongoing prospective US study. Methods: Noise metrics, including day-night average (DNL) and night equivalent sound levels (LAeqN), were modeled for 90 US airports from 1995-2015 in 5-year intervals using the Aviation Environmental Design Tool and linked to participant geocoded addresses from 1993-2012. Hypertension was defined as systolic/diastolic blood pressure measurements ≥140/90 mmHg or inventoried/self-reported anti-hypertensive medication use. Using time-varying Cox proportional hazards models, we estimated hazard ratios (HR) for incident hypertension per 10 decibel (dB) increase and dichotomized at 45 and 55 dB, controlling for sociodemographic, behavioral, and environmental/contextual factors. Results: Of the 45,504 women free of hypertension at baseline, 21.9% were exposed to ≥DNL 45 dB, 3.8% to ≥DNL 55 dB, 2.8% to ≥LAeqN 45 dB, and 0.1% to ≥LAeqN 55 dB. Median follow-up time was 6.7 years and 26,718 developed hypertension. We observed adjusted HRs (95% CI) of: 0.99 (0.95-1.02) per DNL 10 dB; 0.98 (0.96-1.01) at DNL 45 dB; 0.99 (0.93-1.05) at DNL 55 dB; 0.98 (0.85-1.13) per LAeqN 10 dB; 1.02 (0.95-1.09) at LAeqN 45 dB; and 0.89 (0.63-1.26) at LAeqN 55 dB. Adjustment for NO2 and PM2.5 concentrations did not alter estimates. Conclusions: Preliminary analyses indicate no increased risk of hypertension for postmenopausal women exposed to aircraft noise after adjustment for potential confounders. Further research is needed to elucidate the effects of aircraft noise exposure, particularly using different noise metrics, to inform national noise policies.

Associations of exposure to traffic and particulate matter in mid-adulthood with age at natural menopause in the Nurses' Health Study II cohort
Huichu Li* Huichu Li Jaime Hart Shruthi Mahalingaiah Rachel Nethery Rulla Tamimi Elizabeth Bertone-Johnson Francine Laden

Background: Exposures to particulate matter (PM) and traffic have been associated with reproductive health outcomes in women. However, their relationships with age at natural menopause, a critical indicator of women's health in the course of aging, is understudied.
Methods: The Nurses' Health Study II (NHSII) is an ongoing prospective cohort study with follow-up every two years since 1989. In this analysis, premenopausal participants were included at age 40, and those who reported hysterectomy, oophorectomy, death, or cancer diagnosis were excluded at baseline or censored in the follow-up through 2015. Validated spatiotemporal models were used to estimate annual mean PM less than 10 μm in diameter (PM10), 2.5 μm (PM2.5) and PM2.5-10 at each participants' residential addresses. Distance to major roadway was also calculated. Time-varying Cox proportional hazard models with age as the time scale were used to model hazard ratios (HRs) and 95% CIs of natural menopause at any age. Models were adjusted for calendar year, geographic region, and anthropometric, reproductive, lifestyle and socioeconomic factors.
Results: A total of 105,938 NHS II participants were eligible for the analysis. We observed 64,379 reports of natural menopause during 1,058,554 person years of follow-up. In adjusted models, each 10 μg/m3 increase of the average PM10, PM10-2.5, and PM2.5 from age 40 to 1 year before menopause was associated with higher risk of earlier menopause (HR: 1.02, 95%CI: 1.01, 1.04; HR: 1.03, 95%CI: 1.00, 1.05, and HR: 1.03, 95%CI: 1.00, 1.06, respectively). Women living within 49 m of major roadways showed higher risk of earlier menopause (HR: 1.03, 95%CI: 1.00, 1.07) compared to those who lived further away (> 500 m). Similar associations were found when restricting to exposures in age 40-45.
Conclusion: Exposure to particulate matter and traffic in mid adulthood may be modestly associated with earlier natural menopause, which may indicate accelerated reproductive aging.

Long-term exposure to coarse particulate matter, physical activity, and risk of cardiovascular disease and overall mortality in U.S. women

Elise G. Elliott* Elise Elliott Francine Laden Peter James Eric B. Rimm Kathryn M. Rexrode Jaime E. Hart

Background: Long-term air pollution exposure has been linked to increased rates of cardiovascular disease (CVD) and overall mortality, while higher physical activity has been linked to decreased rates. However, increased respiration during physical activity may increase exposure to air pollutants, attenuating the benefits of physical activity.

Objectives: We examined the interaction between long-term residential exposure to particulate matter 2.5-10 microns (PM2.5-10) and physical activity on rates of incident CVD and overall mortality.

Methods: Exposure to PM2.5-10 was assigned to each residential address using a spatio-temporal model and physical activity and CVD were reported on biennial questionnaires in the Nurses' Health Study, a nationwide prospective cohort. We determined nonaccidental death through searching the National Death Index. We followed 104,985 women between 1988 and 2008. We used Cox proportional hazards models to assess associations with each factor separately and jointly, adjusted for demographics, CVD risk factors, diet, and individual- and area-level socioeconomic status.

Results: In fully adjusted models, 24-month average residential PM2.5-10 exposure was associated with modest increased risk of CVD (Hazard ratio [HR] for each 10 μg/m3 increase: 1.04, 95% confidence interval [CI]: 0.98-1.11) and overall mortality (HR: 1.04, 95% CI: 0.99-1.09). Increasing overall physical activity was associated with decreased risk of CVD (HR for each 9 metabolic equivalent of task-hours/week increase: 0.94, 95% CI: 0.93-0.95) and decreased risk of overall mortality (HR: 0.84, 95% CI: 0.83-0.85). We observed no interactions between PM2.5-10 exposure and physical activity in association with CVD risk and overall mortality (Figure).

Conclusions: Higher levels of physical activity and lower levels of PM2.5-10 were associated with decreased CVD risk and overall mortality in this study of U.S. women. There was little evidence of interaction between these exposures.

Environment/Climate Change
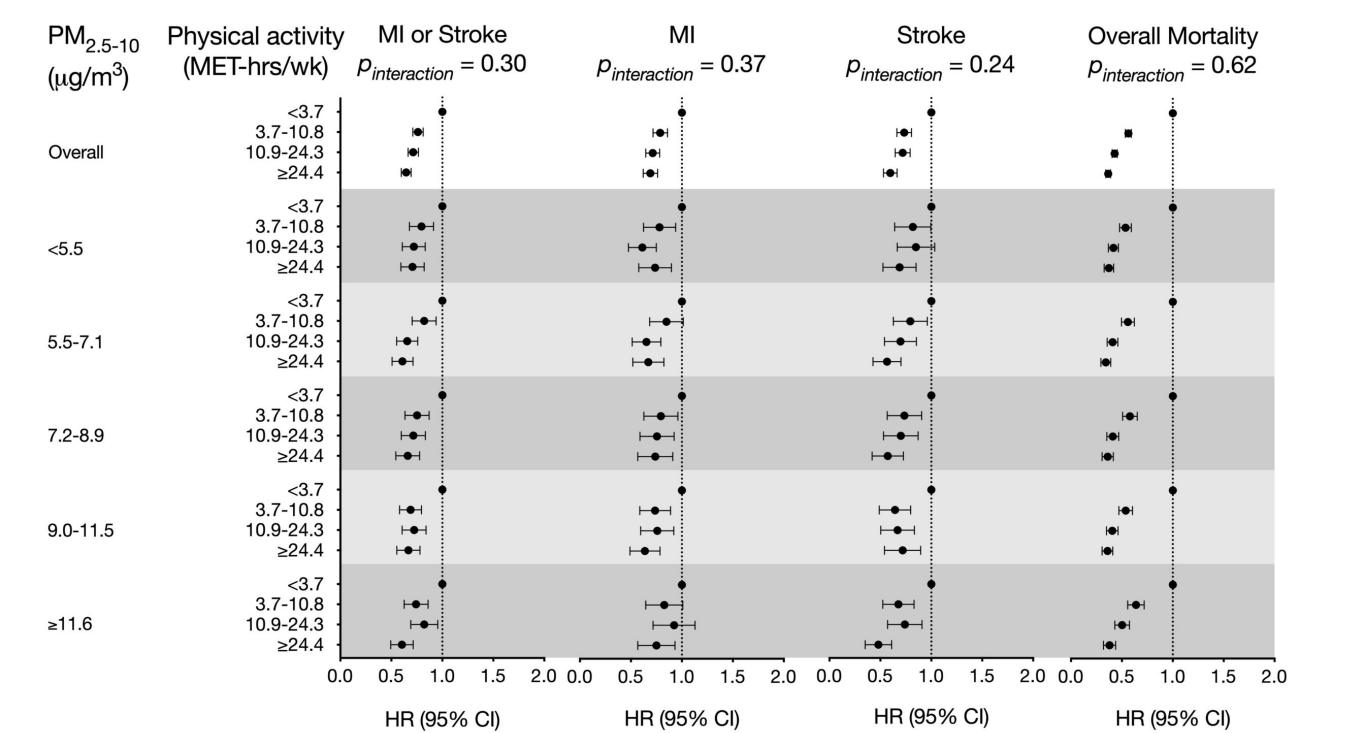
Sensitive windows of manganese exposure and cortex function in adolescents Julia Bauer*
Julia Bauer Roberta White Christine Austin Qiong Yang David C. Bellinger Thomas F. Webster
Stefano Guazzetti Brent Coull Silvia Zoni Chiara Fedrighi Chiara Benedetti Donatella Placidi
Manuela Oppini Giuseppa Cagna Robert Wright Manish Arora Donald Smith Roberto Lucchini Birgit
Claus Henn

Introduction: Studies have observed Mn-associated decrements in IQ composite scores. We
examined patterns of IQ subtest scores to create hypotheses about the underlying structural
changes in the brain that may be produced by Mn exposure among adolescents living near
ferromanganese industry.
Methods: We analyzed deciduous teeth from 190 Italian children ages 10-14 years. Mn levels were
measured in the tooth matrix to represent prenatal, early life (0-1 year) and childhood (1~6 years)
exposure periods. Neuropsychologists administered the Wechsler Intelligence Scale for Children,
3rd edition. We focused on seven subtests: Arithmetic, Comprehension, Information, Similarities,
Vocabulary, Digits forward and Digits backward. Linear regression and generalized additive models
were used to estimate adjusted associations between ln-tooth Mn and subtest scores.
Results: Adjusting for age, sex, socioeconomic status, blood lead, and tooth attrition, we observed
varied patterns of associations between tooth Mn and subtest performance, depending on the
window of exposure. Overall, subtests associated with Mn across exposure windows measure
memory, problem solving and attention, suggesting frontal system and hippocampal involvement.
Childhood Mn was non-linearly associated with Digits forward (pgam=0.06), and lower Information
scores (β=-0.35 (95%CI=-1.11, 0.41)). Early life Mn was associated with better performance on
Arithmetic (β=0.27 (95%CI=-0.63, 1.17)), Information (β=0.35 (95%CI=-0.42, 1.13)), and Digits
forward (β=0.51 (95%CI=0.21, 0.81)). We found inverted U-shaped associations between prenatal
Mn and Arithmetic, Comprehension, Information and Digits forward (pgam=0.18-0.39). These
results support that the shape of the Mn-subtest relationship is dependent on exposure timing.
Conclusion: Our results suggest that frontal cortex function may be sensitive to Mn exposure. Higher
Mn may be toxic in childhood, potentially identifying a window for intervention implementation.

Comparing spatial exposure surrogates with detections and concentrations of unconventional oil and gas-related carcinogens in residential drinking water Cassandra J. Clark* Cassandra Clark Boya Xiong Kristina M. Gutchess Emma C. Ryan Kelsie Cassell Mario A. Soriano, Jr. Elise G. Elliott Yunpo Li Rebecca J. Brenneis Desiree L. Plata James E. Saiers Nicole C. Deziel

Approximately 30 epidemiologic studies of unconventional oil and gas development (UOG) have identified associations with adverse health outcomes, such as birth outcomes, asthma, and cancer. These studies used spatial surrogates of exposure, such as distance to nearest UOG well, which are feasible approaches for assessing aggregate exposures in large-scale studies. However, the exposure pathways captured by these surrogates are poorly understood. We used logistic and linear regression to assess whether commonly-used spatial surrogates are correlated with detection frequencies and concentrations of UOG-related chemicals in residential drinking water, an exposure pathway of public health concern. We compared detections and concentrations of 30 UOG-related known or suspected carcinogens from 94 private water wells in Bradford County, Pennsylvania with count of UOG wells within a buffer around the home, distance to nearest UOG well, inverse distance weighted (IDW), and inverse distance-squared weighted (IDW2) well counts. A total of 10 known or suspected carcinogens or carcinogen mixtures were detected in ☐20% of water samples, albeit at low concentrations. Of those, only benzene was associated with spatial surrogates. The odds of detecting benzene decreased by 55% with each increasing kilometer between the drinking water source and nearest UOG well (OR 0.45, 95% CI 0.24, 0.87); there were no associations with any other metric. While benzene concentration was significantly correlated with well count within 2km, distance to well, IDW 2km, and IDW2 2km (all rspearman<0.30), associations were not significant in regression models. Preliminary results indicate that spatial surrogates are poorly associated with the detection and concentrations of UOG-related carcinogens except benzene. More complex models incorporating groundwater flow and contaminant fate and transport may be needed to accurately capture drinking water exposure for future health studies.

Solar ultraviolet radiation and circulating markers of systemic immunity and inflammation in the United States

Zhi-Ming Mai* Zhi-Ming Mai Scott N. Byrne Michael R. Sargen Eric A. Engels Elizabeth K. Cahoon

Background: A comprehensive characterization of the effects of solar ultraviolet radiation (UVR) on circulating markers in systemic immunity and inflammation may provide insight into the mechanisms through which UVR induces immunosuppression, a key risk factor for common skin cancers and potentially protective factor in some autoimmune and inflammatory illnesses.

Methods: Serum levels of 78 markers were measured using multiplex immune assays in 1817 non-Hispanic whites, ages 55-74 years, who participated in the Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO) and were cancer-free at the time of blood draw. Solar UVR exposure was derived by linking the geocoded locations of 10 screening centers and the date of blood draw (same day, and averaging 1-2, 1-3, 1-7, 1-14, 1-30, or 1-60 days before, respectively) to the modeled irradiance available through the Environmental Health Tracking Program of the U.S. Centers for Disease Control and Prevention. Propensity-score sampling weights were used to make the present data representative of the entire PLCO screening arm (155,000 participants from the general U.S. population). We examined the association between continuous ambient UVR (per 1000 watt-hour/meter2) for eight markers (dichotomized highest versus lowest group) with ptrend < 0.05 above by calculating ORs and 95% CIs across seven different periods above.

Results: In analysis of continuous UVR by different periods of exposure (Figure 1), UVR exposure was significantly negatively associated with CTACK/CCL27 and IFN-γ, while significantly positive for TARC/CCL17. The latter positive association became non-significant after 1-3 days, and waned with the prolong periods of UVR exposure.

Discussion: This is the first study to show that solar UVR exposure is associated with lower circulating levels of two inflammatory/immunomodulatory markers (CTACK/CCL27, IFN-γ) and higher levels of TARC/CCL17, a marker previously associated with skin autoimmune disease.

Figure 1. ORs and 95% CIs of the associations between ambient UVR (1000 watt-hours/meter^2) averaged from 1 to 60 days and eight statistically significant markers
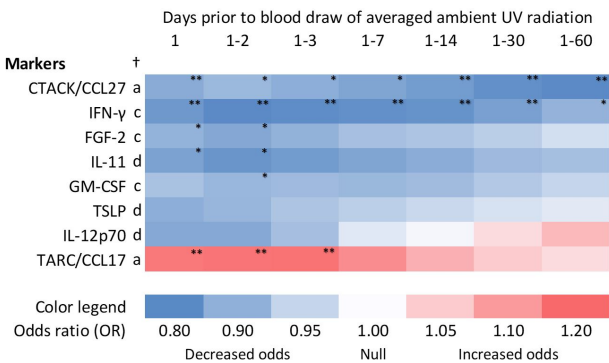
Abbreviation: UVR, ultraviolet radiation; CTACK/CCL27, cutaneous T-cell-attracting chemokine (chemokine (C-C motif) ligand 27); IFN-γ, interferon gamma; FGF-2, fibroblast growth factor-2; IL, interleukin; GM-CSF, granulocyte macrophage-colony stimulating factor; TSLP, thymic stromal lymphopoietin; TARC/CCL17, thymus and activation-regulated chemokine.

Estimated with weighted logistic regression that yielded ORs of eight markers († a: comparing highest quartile vs lowest quartile, b: comparing highest tertile vs undetectable, c: comparing above median for detected vs undetectable, and d: comparing detectable vs undetectable; according to the proportion below the lowest limit of detection) with exposure to ambient UVR per 1000 watt-hours/meter2. All models adjusted for 5-year age group, sex, case-control study origin (non-Hogdkin's lymphoma and ovarian cancer vs lung cancer study), smoking status (former and current vs never smokers), body mass index (<18.5, ≥25-<30 and ≥30 vs ≥18.5-<25 kg/m^2), coffee consumption (<2.5 and ≥2.5 cups/day vs nondrinkers), and the time of blood draw (post meridiem vs ante meridiem).

* P <0.05; ** Statistically significant after applied 5% false discover rate correction.

Characterizing multi-pollutant exposure profiles among a cohort of pregnant women via self-organizing maps Brett Doherty* Brett Doherty Megan Romano John Pearce Margaret Karagas

Exposure to pollutants during pregnancy can adversely impact development during the sensitive prenatal period. Pregnant women are exposed to multi-pollutant mixtures, which complicates the identification of common exposure patterns and investigation of health effects of multi-pollutant exposures. One approach to the investigation of chemical mixtures is to derive exposure profiles from multi-pollutant exposure data, obviating the challenging parameterization of multi-pollutant exposures in regression models and enabling contrasts across profiles. A promising method for profile discovery and characterization is the self-organizing map (SOM). SOMs are similar to the k-means clustering algorithm, with the added utility of providing topology among clusters that enhances understanding of between-cluster relationships. We used SOMs to characterize multi-pollutant exposure profiles among pregnant women from the New Hampshire Birth Cohort Study. Multi-pollutant exposures were assessed via silicone wristband passive monitors, worn by 111 women for 7±2 days at 13±2 gestational weeks. Wristbands were analyzed for concentrations of 1530 organic pollutants via gas chromatography – mass spectrometry. Of 140 chemicals detected in at least one wristband, 21 were detected in ≥50% of wristbands. These 21 chemicals included six phthalates, four pesticides, and several chemicals used in consumer products and personal care products. We determined that a 2-dimensional rectangular 3x3 SOM satisfactorily fit these multi-pollutant data. The 9 profiles reflected unique combinations of these chemicals and ranged in size from 34 to 6 participants per profile. These SOMs may be used to assess characteristics related to profile membership. We believe that this work demonstrates the utility of SOMs for characterizing exposure profiles from multi-faceted exposure data and that this method may be constructively applied to a variety of epidemiologic investigations.
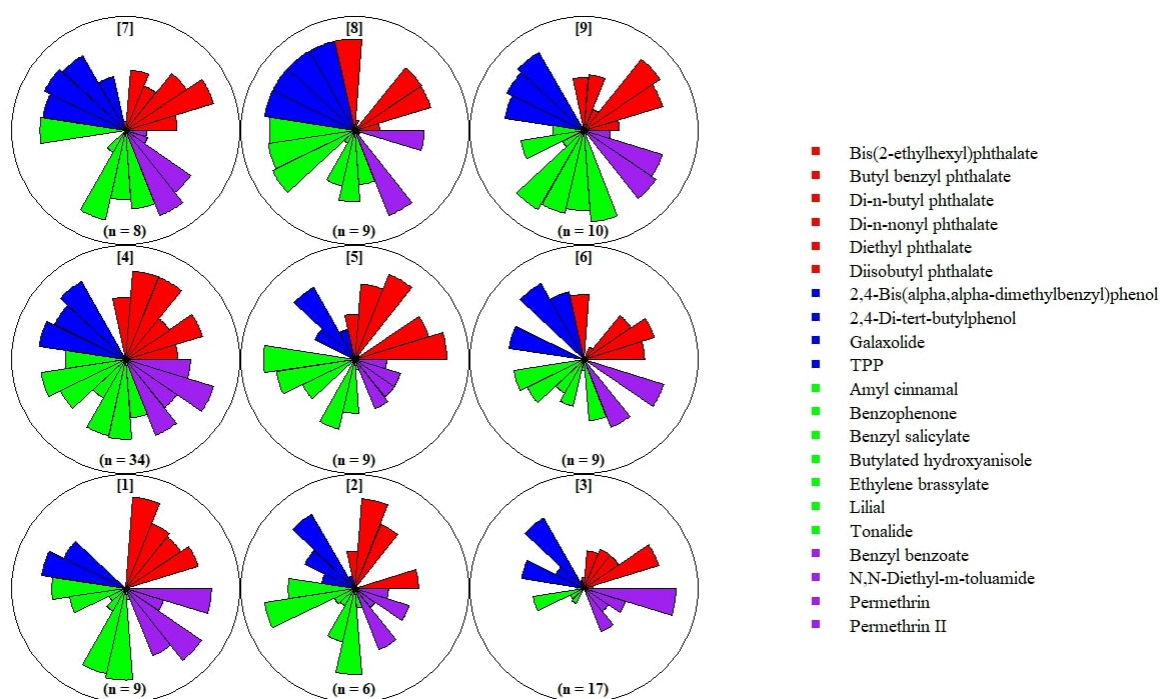
Figure. A 3x3 rectangular Self-Organizing Map (SOM) depicting multi-pollutant exposure profiles among pregnant women participating in the New Hampshire Birth Cohort Study (n=111). Each circle contains a profile [1-9], and each segment within the circle reflects the relative concentration of each chemical in that profile.

Perinatal nutrient-toxic exposure mixtures and the infant gut microbiome: a prospective analysis in the New Hampshire Birth Cohort Study Hannah E. Laue* Hannah Laue Hilary G. Morrison Emily R. Baker Juliette C. Madan Margaret R. Karagas

Background: Perinatal exposure to environmental exposures, including nutrient and toxic elements, are known to influence infant health including the early-life microbiome. Whether microbial alterations persist through infancy is not yet known.

Objective: Prospectively characterize the association between perinatal exposure to a nutrient-toxic mixture and the gut microbiome at ~1 year of age in a longitudinal pregnancy cohort.

Methods: Arsenic, cadmium, copper, iron, mercury, manganese, nickel, lead, selenium, and zinc (As, Cd, Cu, Fe, Hg, Mn, Ni, Pb, Se, Sn, Zn) were measured in infant toenail clippings at ~6 weeks of age (n=108). DNA from infant stools (~1 year) underwent metagenomic sequencing to quantify microbial diversity, taxa, and functional pathways. Taxa and functions were inferred via the BioBakery pipeline. Models included all elements concurrently and confounders. BioBakery methods (MaAsLin2) identified taxa and functions associated with exposures and linear regression was used for diversity. Bayesian kernel machine regression (BKMR) was implemented to examine interactions between exposures.

Results: Perinatal Ni and Sn exposures were associated with increased diversity at 1 year of age with a 0.3 95% CI (0.06, 0.54) and 0.22 95% CI (0, 0.45) point increase in Shannon Index per SD increase in Ni and Sn, respectively. As, Cd, Cu, Fe, Pb, Se, Sn, and Zn each correlated with the relative abundance of at least 1 species, including a positive relation between Zn and Bifidobacterium bifidum. BKMR supported this linear relationship and revealed a Ni-dependent curvilinear negative association between Se and Bacteroides vulgatus (Figure). As exposure was negatively associated with abundance of the glutamate metabolism pathway.

Conclusions: Our findings suggest that perinatal nutrient and toxic elements may have lasting consequences for infant gut microbial diversity, and the relative abundance of species and functional pathways.

Relative abundance of *Bacteroides vulgatus*
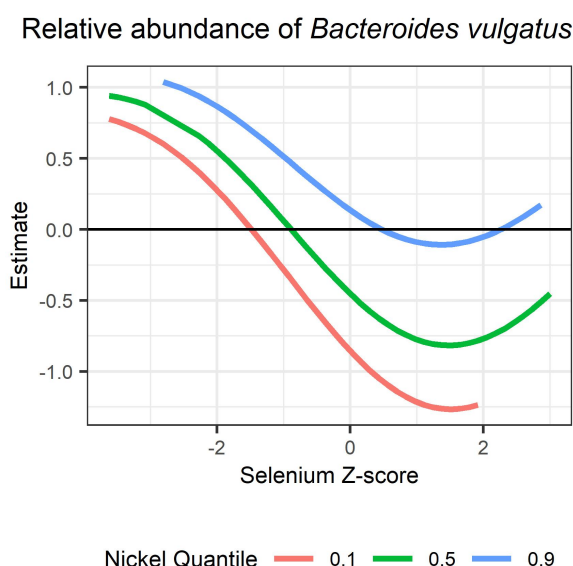
Vitamin D supplementation during pregnancy and maternal and cord blood metal concentrations at delivery: results from a randomized controlled trial in Bangladesh Anne Marie Jukic* Anne Marie Jukic Anna Zuchniak Huma Qamar Abdullah Al Mahmud Tahmeed Ahmed Daniel Roth

In animal and in vitro studies suggest that vitamin D may increase the intestinal absorption of toxic metals such as lead and cadmium, but evidence from human trials is lacking. We hypothesized that vitamin D supplementation increases circulating lead, cadmium, manganese and mercury concentrations in pregnant women. The Maternal Vitamin D for Infant Growth (MDIG) trial was a placebo-controlled, multi-arm study of maternal vitamin D supplementation during pregnancy in Dhaka, Bangladesh. Women were randomized in their second trimester to blinded weekly doses of placebo or 4200 (low), 16800 (mid), or 28000IU (high) of vitamin D3 throughout pregnancy. Metals were measured by inductively-coupled plasma mass spectrometry in whole blood samples from women at delivery (N=619) and cord blood (N=516). Percent differences between each vitamin D group versus placebo were estimated using unadjusted linear regression models. Cadmium was undetectable in 76% of infant cord blood samples and thus was dichotomized and analyzed with log-binomial regression. Maternal blood metal concentrations did not differ between treatment and placebo group (Table). However, compared with placebo, the low and high dose vitamin D supplementation groups had higher cord blood lead levels and the mid and high dose vitamin D groups also had a higher risk of detectable infant cord blood cadmium (Table). Inferences were unchanged in sensitivity analyses in which we excluded women with sufficient 25OHD at baseline or excluded women who completed less than 95% of their treatment visits. Adjustment for season or fish consumption did not alter inferences. Cord concentrations of the other metals did not differ across treatment groups. In conclusion, maternal blood metal levels did not differ across treatment groups, yet vitamin D supplementation resulted in higher lead and cadmium levels in cord blood. As there are no safe levels of metal exposures in infants, these increases require further exploration.

Intent-to-treat analysis of the effect of vitamin D supplementation on relative metal levels in maternal (N=619) and infant venous cord (N=516) blood samples, compared with placebo.

	Treatment group (IU/week)		
	4,200 % difference (95% CI)	16,800 % difference (95% CI)	28,000 % difference (95% CI)
N (maternal, infant)[a]	141, 104	121, 111	239, 201
Lead			
Maternal[b]	6.3 (-4.1, 18)	7.4 (-3.5, 20)	6.0 (-3.4, 16)
Cord	8.5 (-3.5, 22)	16 (3.3, 30)	11 (0.4, 23)
Cadmium			
Maternal	6.6 (-5.0, 20)	4.9 (-7.0, 18)	1.6 (-8.4, 13)
Maternal[c]	6.1 (-5.4, 19)	5.2 (-6.6, 18)	1.8 (-8.2, 13)
	Relative Risk (95% CI) of detectable cadmium[d]		
Cord[d]	2.2 (1.3, 3.7)	1.4 (0.8, 2.5)	1.7 (1.0, 2.9)
Cord[c]	1.9 (1.1, 3.2)	1.4 (0.8, 2.5)	1.6 (0.96, 2.7)

[a] Placebo group: 118, 100
[b] Overall likelihood ratio p-value = 0.08
[c] Adjusted for season; overall likelihood ratio p-value = 0.08
[d] Overall likelihood ratio p-value = 0.02

Disparities in ambient fine particulate matter exposure and health burden between immigrants and native-born in the United States Kelvin Fong* Kelvin Fong Michelle Bell

Background: Immigrants to the United States (US) experience different health risks compared to those born in the US. It is unknown if different levels of environmental exposures such as ambient fine particulate matter (PM2.5) contribute to immigrant health disparities.

Methods: We compiled counts of immigrants (i.e., foreign-born) and US-born living in each Census tract in 2000 and 2010 from the Census Bureau. With ground-level ambient PM2.5 exposure surfaces from a validated spatiotemporal model, we then calculated the average annual PM2.5 exposure for the US-born, immigrants, and immigrant subgroups by country of origin. Among these population subgroups, we estimated disparities in PM2.5 exposure and mortality attributable to PM2.5 exposure.

Results: In 2000, the total number of immigrants living in the US was 30.86 million compared to 248.72 million US-born while in 2010, there were 38.39 million immigrants and 263.55 million US-born. On average, in 2000 immigrants were exposed to PM2.5 levels 1.25 µg/m3 higher than those of the US-born and 0.36 µg/m3 higher PM2.5 in 2010. The disparity of mortality attributable to PM2.5 exposure in immigrants compared to the US-born was +19,518 (95% CI: +19,270, +19,765) deaths/100,000 people in 2000 and +6,058 (95% CI: +5,933, +6,182) deaths/100,000 people in 2010. We found heterogeneity in exposure and mortality attributable to PM2.5 disparities compared to the US-born depending on immigrants' country of origin, with higher mortality attributable to PM2.5 among immigrants from Africa, Asia, and Latin America (see Figure).

Conclusions: Overall, immigrants had a higher mortality burden from PM2.5 exposure compared to the US-born. The heterogeneity in effect estimates depending on country of origin suggest that environmental exposures may contribute to health disparities among immigrants. From 2000 to 2010, disparities in mortality attributable to PM2.5 exposure between the immigrants and the US-born decreased.

Excess Mortality Attributable to PM$_{2.5}$ Compared to US-Born in 2010
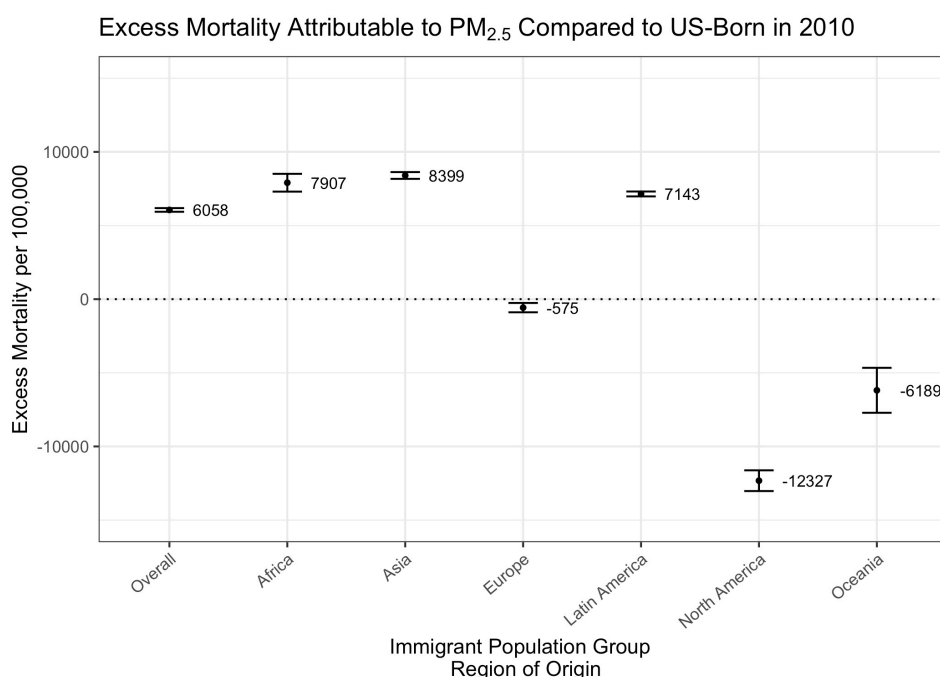
Assessing the spatial variation in joint-effects of heat waves and ozone impacts on respiratory hospitalizations in California Lara Schwarz* Lara Schwarz Kristen Hansen Sindana D. Ilango Anna Alari Nelson Bernal Rupa Basu Tarik Benmarhnia

Extreme heat and ozone are co-occurring exposures that have been shown to independently and synergistically increase risk of respiratory disease. While some studies have quantified the joint effects of temperature and ozone, none assessed its fine spatial variation. We propose the use of a spatial analysis to examine the potential heterogeneity (on the additive scale) in joint effects between heat and ozone at a small geographical scale. Temperature data was downloaded from the National Ocean and Atmosphere Administration Cooperative Observer stations across the United States and ozone data was estimated at the daily level using 24-hour daily means sampled and analyzed by the US EPA Air Quality System. A spatial extension of the case-crossover design was applied to study this association at the zip code level; spatially varying relative risk due to interaction (RERI) was quantified to consider joint effects. A total of 3,858,196 unscheduled respiratory hospitalizations occurred in California from 2004 to 2013 in the May-September period, and mean thresholds for heat waves ranged from 37.75ºC to 39.57ºC. For ozone, average concentrations ranged from 61.66 ppb to 79.90 for the different thresholds considered. When considering the overall joint effect in all of California, the RERIs revealed no additive interaction. However, when considering the joint-effects at the zip code level, some areas show a strong joint-effect and other areas indicate negative interaction. Results indicate unspecific patterns of heterogeneity, but by considering spatial differences in these impacts variation in the effect of ozone, heat waves and joint-effects is apparent throughout California. Results indicate the importance of going beyond average measures to consider spatial variation in the health effects of ozone and heat. This information can be used to inform hybrid early warning systems to protect populations from the deleterious effects of both ozone and heat.

Nighttime light pollution in urban residential area and sleep insufficiency Jong Cheol Shin*
3647] Shin Diana S. Grigsby-Toussaint

Introduction: Nighttime light exposure has been shown to influence circadian rhythm and may affect
sleep patterns and quality. Less well understood is whether this association holds at various levels of
geography. Using a geo-spatial approach, we examine the association between nighttime light
pollution and insufficient sleep of urban residents in major US cities. Methods: A cross-sectional
analysis of 26,435 census tracts from the 2016 Centers for Disease Control and Prevention 500
Cities project was conducted. The census tracts represent 498 of the 500 most populated cities in
the US. Sleep insufficiency (defined as <7 hours of sleep during a 24-hour period) and health
behavior data (e.g., physical activity) were derived from the 500 Cities dataset. The 2012-2016
American Community Survey and the 2016 Tiger/Line shapefiles were used to provide socio-
economic characteristics for each census tract. Nighttime light data was derived from the 2016
Visible Infrared Imaging Radiometer Suite (VIIIS) satellite data. Spatial boundaries of urban
residential areas included the census place and urban area in addition to census block groups.
Simple and multiple linear regression models were used to examine the association between light
pollution and insufficient sleep. Results: We found a positive association between nighttime light
pollution and insufficient sleep (B=0.002; 95% CI=0.001-0.003) after adjustment for risk factors
such as the absence of physical activity (B=0.108.; 95% CI=0.098-0.117) and poor mental health
(B=0.683; 95% CI=0.660-0.707). Conclusion: Nighttime urban light pollution influences the
prevalence of insufficient sleep. Further analysis of daily nighttime and daytime light exposure is
still needed to disentangle this relationship.

Nightttime Light Pollution in Residential Area for Major 498 cities
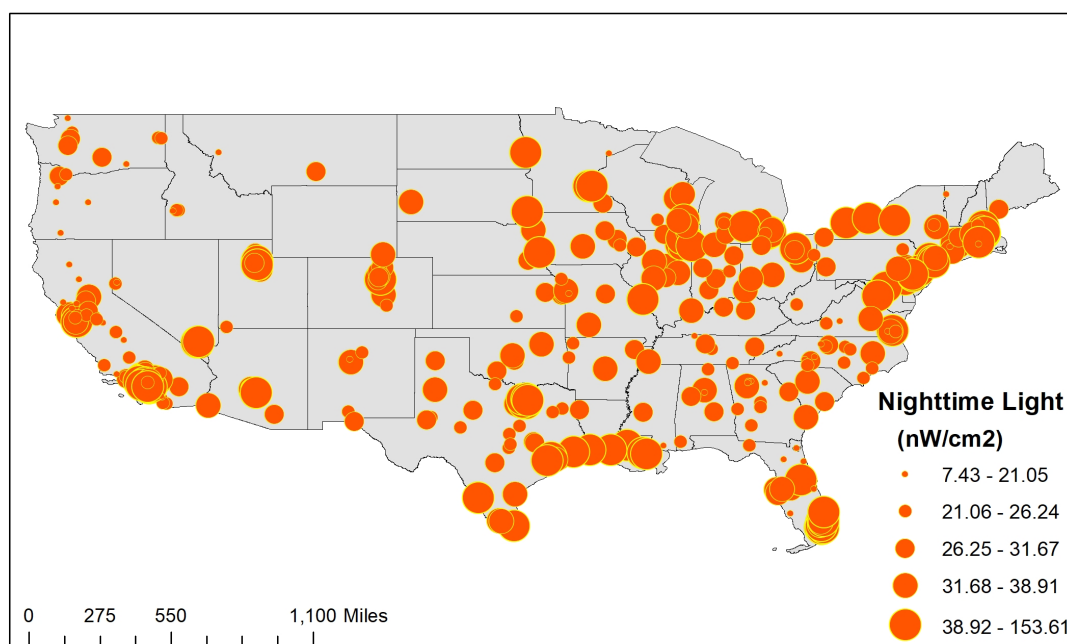
Associations between gestational exposure to perfluoroalkyl substances in early pregnancy and child body composition Michael Bloom* 3647] Bloom ECHO-FGS Study Group

Objective: To examine associations between gestational exposure to perfluoroalkyl substances (PFAS), persistent developmental toxicants, and body composition in a racial/ethnically diverse cohort of children.

Study Design: We used ultrahigh performance liquid chromatography coupled to tandem mass spectrometry to determine concentrations of 10 PFAS in 1st trimester (8-13 gestational weeks) plasma collected from women participating in the NICHD Fetal Growth Studies (n=803). Children's body mass index (BMI) and waist circumference were ascertained (ages 4-8) by study staff and fat mass, fat-free mass, and % body fat were quantified using body impedance analysis. Multivariable regression was used to assess individual maternal PFAS as predictors of children's body composition, adjusted for maternal age at the time of specimen collection, prepregnancy BMI, education, race, and plasma cotinine, and child's gender and age at the time of the examination.

Results: Nearly all (>96%) mothers had measurable PFAS. Maternal plasma perfluorooctane sulfonate (PFOS; 5.3ng/mL), perfluorooctanoic acid (PFOA; 2.0ng/mL), perfluorohexane sulfonate (PFHxS; 0.9ng/mL), perfluorononanoic acid (PFNA; 0.8ng/mL), and perfuoroundecanoic acid (PFUnDA; 0.3ng/mL) had the highest median levels. We found positive differences in children's mean waist circumference z-score per standard deviation greater gestational PFOA (β [95%CI]: 0.06 [-0.01, 0.14]) and PFUnDA (β [95%CI]: 0.07 [-0.004, 0.14]). Greater gestational PFUnDA levels were also associated with children's % body fat (β [95%CI]: 0.01 [-0.001, 0.01]). Additionally, greater gestational PFNA (OR [95%CI]: 1.21 [0.99, 1.49]) and PFUnDA (OR [95%CI]: 1.14 [0.93, 1.38]) were associated with greater odds for overweight children (30 kg/m^2> BMI ≥25 kg/m^2).

Conclusions: Greater 1st trimester maternal gestational PFOA, PFNA, and PFUnDA exposure may be associated with greater central adiposity and odds for overweight in their offspring at 4-8 years of age.

idiopathic erythrocytosis): a case for pfcs Ogbebor Omoike* 3647] Omoike Liang Wang

Background
Exposure to Perfluoroalkyl chemicals (PFCs) has been associated with adverse health outcomes in epidemiological studies. Few studies have looked at the effect of these exposures on human red blood cells. Idiopathic erythrocytosis is a term used to define, broadly, a group of persons with elevated hematocrit whom no known cause of erythrocytosis has been identified.

Objectives
We investigated the association of PFCs with erythrocytosis.

Methods
Data (n=6652) was obtained from non-institutionalized civilians in the United States. The response variables were serum hematocrit, red blood cell folate, serum alkaline phosphatase, serum aminotransferase, serum uric acid, serum vit b12. Exposure variable was PFCs compounds including PFHS, PFNA, PFOA, PFOS and PFDE which were detected in greater than 98 percent of the study population. Sex, educational status and ethnicity were included as factors in the model. Age, poverty income level, body mass index (BMI) and cotinine levels were included as covariates. Independent variables included in the adjusted model had significant associations with the outcome variables on univariate analysis. Models were built with type III main effects and parameter estimation was by maximum likelihood. The covariance matrix was built with a model-based estimator. Wald and likelihood ratio chi-square statistics were used to test the null hypothesis. Tolerance was placed at 1E-012 and change in parameter estimates at 1E-006. Generalized linear models and logistic regression models were used to test for associations between PFCs and our outcome variables which were initially modeled as continuous and then PFCs and hematocrit categories and then red blood cell folate categories. Hematocrit categorized as high if >=50 % and not high (=628ng/ml or 1422nmol/l and not high if < 628ng/ml while adjusting for the same set of independent variables. PFCs were also modeled as continuous variables and then categorized as quintiles while adjusting for the same set of covariates. Variables were selected using stepwise method with entry level of 0.05, removal at 0.10, a maximum iteration of 20 and classification cut-off of 0.5. Confidence interval for exponentiated beta was 95%.

Results
PFOA was associated with elevated hematocrit OR: 1.04(CI: 1.01, 1.08). PFOA, PFNA, PFOS, PFDE were associated with reduced RBC folate OR: 0.668(CI: 0.62, 0.72), OR: 0.5(CI: 0.4, 0.6), OR: 0.92(0.9, 0.93), 0.08(0.04, 0.17). Categorical quintile analysis for PFOA did show significant increase (p for trend <0.001) for hematocrit but non-significant trend for red blood cell folate levels (p=0.161). In models including PFCs and our dependent variables modeled as continuous, all outcome variables were associated with PFCs exposure (P<0.05).

Conclusion.
Our findings are in keeping with erythrocytosis (polycythemia). This indicates that PFCs are associated with (idiopathic) erythrocytosis.

Probabilistic modeling of carbon dioxide equivalents generated from serving animal-based foods.

Hayden Smith* Hayden Smith

Background: The substitution of food entrées based on carbon dioxide equivalents (CO2e) is considered a simple change towards lessening greenhouse gas (GHG) emissions. The use of catered, buffet-style, lectures in graduate medical education results in an associated CO2e footprint regardless of the actual conference attendance and food consumed. Substitution of beef entrées can provide a large return on investment in decreasing GHGs. Objective: To provide a simulation framework for quantifying interventional impacts on the environment.

Methods: Monte Carlo-based simulations were used to quantify the impact of switching from beef entrée options. Model inputs included CO2e values for common animal-based proteins, food portion sizes, planned conference attendance, and fuel economy for vehicles. Outputted results were CO2e values converted to the unit of an annual average U.S. passenger vehicle. Also calculated was a Number Needed to Eat (NNE) estimate, representing the number of lectures with a non-beef substitution needed to remove a single US passenger vehicle from the roads.

Results: Probabilistic estimates based on one million simulations revealed substituting beef entrées (serving: 3-4 ounces) at a weekly Internal Medicine conference (attendance: 40-48) and monthly Pediatric conference (attendance: 60-70) across a year with a comparable amount of pork, farm-raised salmon, turkey, chicken, egg, or assorted entrées would result in removing 1.8, 1.8, 1.8, 2.1 or 2.2 or 1.9 vehicles from the road, respectively (Figure). Associated estimates for NNE calculations were 44, 44, 42, 37 35, and 40 for the number of pork, farm salmon, turkey, chicken, eggs, and assorted option catered lectures needed to remove a passenger vehicle from the roads, respectively.

Conclusion: Results from these analyses showed how the use of food substitution across time can result in a substantial elimination of GHGs. Alternating foods with plant-based options could remove additional CO2e gases.
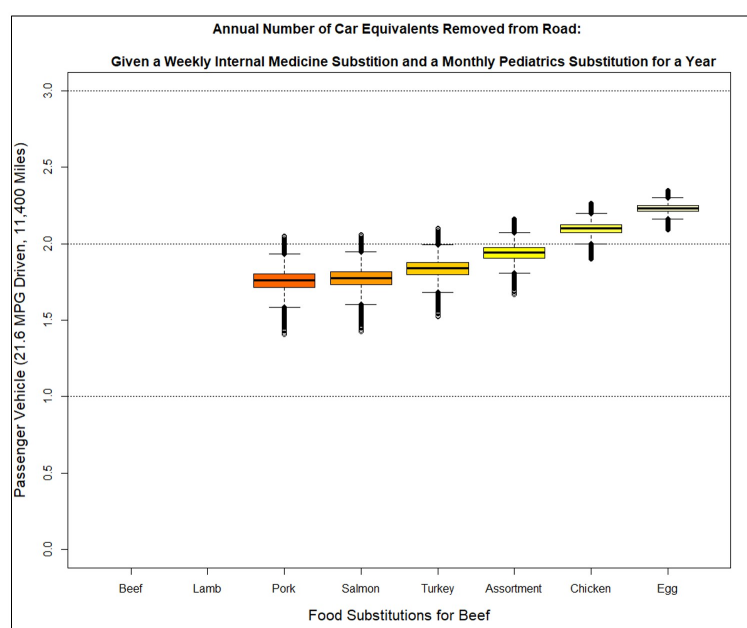
Figure. Boxplot of probabilistic modeling of the potential removal of US passenger car equivalents from the road given the substitution of beef options with non-beef options during a weekly Internal Medicine and a monthly Pediatric lecture across an academic year.

Is neighborhood traffic exposure associated with lower peak flow measurements among a multi-racial cohort of children from the ECHO-FGS study? Pam Ferguson* JacKetta Cobbs Pamela Ferguson John Pearce John Vena Kelly Hunt

Adverse respiratory symptoms in children pose a significant clinical and public health burden. We aimed to examine exposures to environmental air pollution in relationship to peak flow measurements in a multi-racial cohort of children. A cross-sectional analysis of the association between environmental air pollution and lung function was conducted on 685 children aged 4 to 8 years old in the Environmental Influences on Child Health Outcomes Fetal Growth Studies (ECHO-FGS). Peak flow measurements in liters per minute, were obtained from children using the TrueZone peak flow meter (Monaghan Medical Corp, NY, USA). Logistic regression was used to examine traffic exposure in relationship to peak flow. Normal peak flow was defined as 80% or greater predicted normal peak flow after adjusting for child's race-ethnicity, age, gender and height. For 16% of children, parents responded "Agree" or "Strongly Agree" to the question, "There is so much traffic along the streets that it makes it difficult or dangerous to walk with my child in my neighborhood". Mean peak flow (95% Cl) values by age were: 123 (115, 132), 134 (130, 140), 151 (147, 155), 173 (169, 178) and 184 (177, 192) L/min for 4, 5, 6, 7 and 8 year olds, respectively. Among race-ethnic groups, mean peak flow values (95% Cl) were 143 (139, 147), 148 (141, 156), 164 (159, 170), and 174 (169, 180) L/min for Black, Asian, Hispanic, and White children, respectively. Children exposed to traffic had a higher odds of having lower than 80% predicted normal peak flow than children without neighborhood traffic [OR=1.97 (95% CI: 1.04, 3.74)] after controlling for race-ethnicity, age, gender, maternal education level, maternal marital status, socioeconomic status and obesity. Neighborhood traffic appears to be associated with lower peak flow measurements. Better characterization of neighborhood traffic is needed since many high risk children may live in close proximity to this source of environmental air pollution.

The influence of spatial resolution of Normalized Difference Vegetation Index (NDVI) data on greenness exposure misclassification Raquel Jimenez Celsi* Raquel Jimenez Celsi Patricia Fabian Kevin Lane

Epidemiologic studies analyzing the associations between vegetation and health increasingly rely on Normalized Difference Vegetation Index (NDVI) to assess exposure. Most epidemiology studies use 250m NDVI in spite of the availability of data at higher spatial resolution, and few studies have considered the potential impact of resolution on exposure misclassification.

We estimated greenness exposure for 31,328 children (age 5 to 18) living in the Greater Boston Area in 2016. NDVI for the study area was derived using data from the Moderate Resolution Imaging Spectroradiometer (MODIS, 250m), Landsat 8 (30m), Sentinel-2 (10m), and the National Agricultural Imagery Program (NAIP, 1m) accrued between July 1st and July 31st, 2016. We quantified mean NDVI in buffers of varying radii (50m, 250m, and 1000m) from participant's geocoded addresses using each NDVI dataset and compared the distributions as continuous and categorical variables in order to match exposure assessment methods used in epidemiological studies. Differences in continuous distributions were assessed using descriptive statistics and t-tests, whereas discrepancies in categorical NDVI distributions were evaluated using accuracy metrics.

NDVI estimates from MODIS were consistently higher than those from Landsat 8, Sentinel 2, and NAIP, regardless of buffer size (Mean NDVI in 250m buffer: 0.48, 0.45, 0.34, and 0.11, respectively). We observed significant differences in categorical exposure assessment across spatial resolution and buffer size, with the largest discrepancies in participant's greenness quantiles observed between MODIS and NAIP NDVI.

Spatial resolution, aggregation area, and categorical variable classification are critical parameters in the estimation of greenness exposure, and can contribute to exposure misclassification. NDVI at higher resolution should be used when exposure is aggregated over smaller buffers in order to reduce the risk of greenness exposure misclassification.
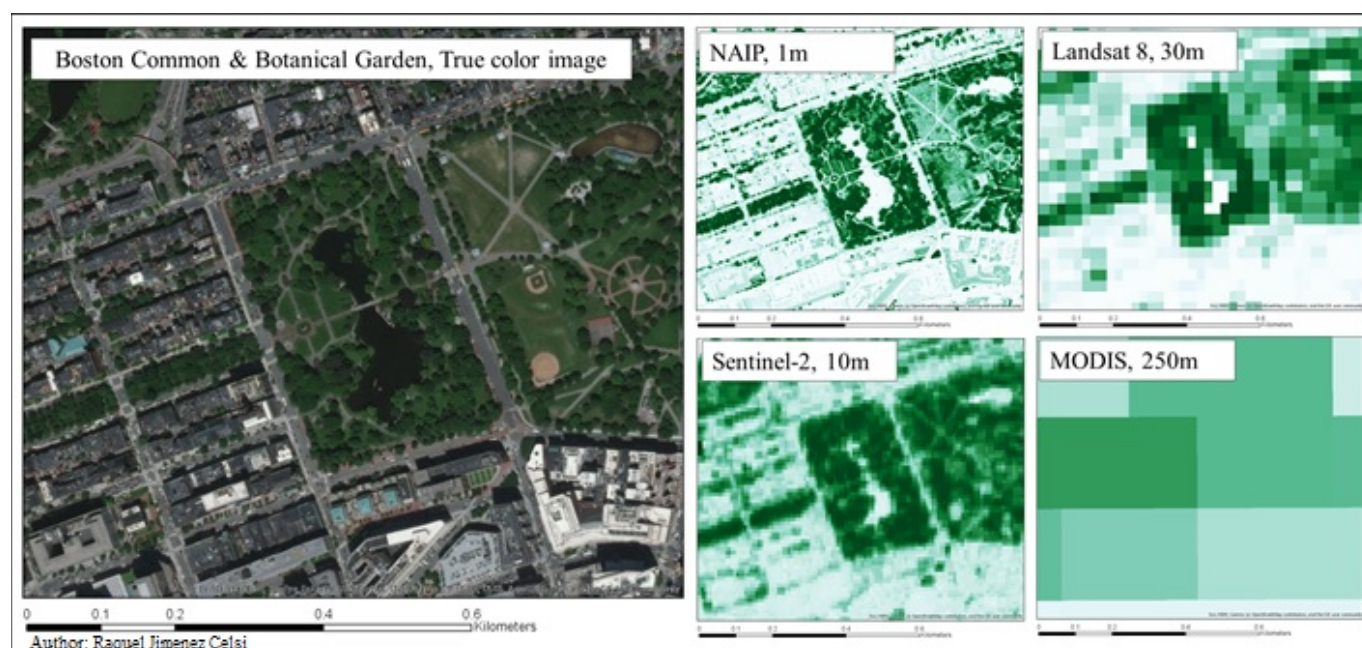
Genetics

Genetic risk scores and hallucinations in Parkinson's disease patients Cynthia Kusters*
Cynthia Kusters Kimberly Paul Aline Duarte Folle Adrienne Keener Jeff Bronstein Christina Lill Ole-Bjorn Tysnes Guido Alves Jodi Maple-Grodem Janet Sinsheimer Beate Ritz

Objective: Non-motor symptoms among Parkinson's disease (PD) patients are common. As genetic risk factors for hallucinations remain elusive, here we examine the overlap of genetic architecture for Alzheimer's disease (AD), schizophrenia (SZ), and Parkinson's disease (PD) with the occurrence of hallucinations in PD.

Methods: We assessed the associations between four polygenic risk scores (PRS) and hallucinations after five years of mean disease duration in two population-based studies (ParkWEST, Norway, and PEG, USA) providing us with 399 subjects with European ancestry and PD diagnosis after age 55. Four PRS were created based on existing GWAS: one for AD, SZ, and PD each; a PRS for height served as a negative control.

Results: A positive association between the AD-PRS (adjusted OR (aOR): 1.34 (95%CI: 1.01-1.80); p-value 0.05) and hallucinations was identified. This effect was mainly driven by APOE (aOR: 1.94 (95%CI: 1.14-3.28); p-value 0.01) and there was an interaction between the AD-PRS and age at diagnosis. In addition, a suggestive negative association between the SZ-PRS and hallucinations (aOR: 0.77 (95%CI: 0.59-1.01); p-value 0.05) was identified.

Conclusions: With increasing age at diagnosis, hallucinations are influenced by the genetic architecture that contributes to cognitive decline in AD, while the genetic risk factors for SZ were negatively associated with the development of hallucinations independent of age at diagnosis. These results suggest that genetic mechanisms for hallucinations in PD may differ by and depend on age at diagnosis.

Genetics

The associations of perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) with DNA methylation in newborn dried blood spots Sonia Robinson* Sonia Robinson Xuehuo Zeng Weihua Guan Rajeshwari Sundaram Pauline Mendola Kurunthachalam Kannan Diane Putnick Erin M. Bell Edwina H. Yeung

Perfluorooctane sulfonate (PFOS) and perfluorooctanoic acid (PFOA) are persistent organic pollutants which can cross the placental barrier and have been related to adverse neonatal outcomes such as low birth weight. Epigenetic alterations represent one potential pathway through which PFOS/PFOA may impact fetal development. Prior studies examining the relation of PFOS/PFOA to DNA methylation are small (n<200) and few associations replicate across studies. Therefore, evaluation in a larger cohort is necessary.

We examined the relations of PFOS and PFOA with DNA methylation among 616 neonates in the Upstate KIDS study. PFOS and PFOA were quantified in newborn dried blood spots (DBS). DNA methylation was measured with the Infinium MethylationEPIC BeadChip in DBS. We used robust linear regression with a false discovery rate (FDR) correction to examine the associations of log-transformed PFOS and PFOA with 837,933 individual CpG sites. Covariates included sample plate, estimated cell counts (cord blood reference), infant sex, plurality and epigenetically derived ancestry, and mother's age, race/ethnicity, education, marital status, pre-pregnancy BMI and smoking status.

Median concentrations of PFOS and PFOA were 1.74 and 1.12 ng/ml, respectively. Neither PFOS nor PFOA was related to DNA methylation at individual CpG sites. CpGs with the strongest associations for PFOS included cg03694660 (near SRGAP3-AS4), cg13387994 (MATK) and cg19133973 (LINC00423) with FDR-corrected P-values from 0.19 to 0.39. For PFOA, top hits were cg04590119 (CHRM2), cg08276497 (HMCN1) and cg17898252 (FDR P-value: 0.77). None of the top ten CpG hits found in our study had been previously reported to relate to maternal PFOS or PFOA concentrations. Models comparing the top decile of PFOS or PFOA with the lowest decile were similar.

Neonatal PFOS and PFOA concentrations were not associated with DNA methylation in the Upstate KIDS study, potentially due to the low concentrations of PFOS.

Genetics

A healthy childhood environment helps to combat inherited susceptibility to obesity Anke Huels* Anke Huels Marvin N Wright Leonie H Bogl Jaakko Kaprio Lauren Lissner Denes Molnár Luis Moreno Stefaan De Henauw Alfonso Siani Toomas Veidebaum Wolfgang Ahrens Iris Pigeot Ronja Foraita

Background & Aims: Although obesity is highly polygenic, previous gene-environment interaction analyses mainly focused on <100 genetic variants that account for only <3% of BMI variation. Since most studies were conducted in adults, it is unknown by which degree inherited susceptibility to obesity is modified by environmental factors early in life. Here, 1) we show the prediction capacity of an obesity-related genome-wide polygenic risk score (PRS) for BMI and waist circumference (WC) in European children and adolescents and 2) analyze its interaction with sociodemographic and lifestyle factors.

Methods: The analyses are based on 8,609 repeated observations from 3,098 participants aged 2 to 16 years from the IDEFICS/I.Family cohort. A genome-wide polygenic risk score (PRS) was calculated using summary statistics from independent genome-wide association studies of BMI. Associations were estimated using generalized linear mixed models adjusted for potential confounders.

Results: The PRS was strongly associated with BMI ($r2=0.11$, p-value=7.9×10^{-81}) and WC ($r2=0.09$, p-value=1.8×10^{-71}). The associations with BMI increased from $r2=0.03$ in 3-year olds to $r2=0.18$ in 14-year olds and associations with WC from $r2=0.03$ to $r2=0.14$. We observed significant interactions with demographic and lifestyle factors for BMI as well as WC. The risk of becoming obese among those with higher genetic susceptibility was ~38% higher in children from Southern Europe (BMI: p-interaction = 0.0066, Central vs. Southern Europe) and ~61% higher in children with a low parental education (BMI: p-interaction = 0.0012, low vs. high). Furthermore, the risk was attenuated by a higher intake of dietary fiber (BMI: p-interaction=0.0082) and shorter screen times (BMI: p-interaction=0.018).

Conclusions: Our results highlight that a healthy childhood environment might partly offset a genetic predisposition to obesity during childhood and adolescence.

Genetics

Biological and genetic underpinnings of polygenic psychiatric disorders Hannah Olson-Williams* Hannah Olson-Williams Kenneth Nieser Amy Cochran

Psychiatric disorders such as major depressive disorder (MDD), schizophrenia (SCZ), and bipolar disorder (BD) contribute to significant disability, distress, and comorbidity. These disorders are likely polygenic, however genetic determinants of these disorders are not well understood. While current approaches exist to identify a set of genes that is associated with a disorder, these techniques do not fully capture the differential biological contributions from each gene. Using a model-based approach to gene-set analysis driven by biophysical principles, we quantify the association of genes related to abnormal intracellular calcium ion concentrations and neuronal firing rate with three psychiatric disorders. We leveraged two math biology models of neuron activity and summary genetic data publicly available through the Psychiatric Genetics Consortium (MDD: n=500,199; SCZ: n=65,967; and BP: n=41,653). We found that genes related to intracellular calcium ion concentration are significantly related to BP (p=0.0002) but not SCZ (p=0.09) or MDD (p=0.30). Meanwhile, genes related to neuronal firing rate was found to contribute significantly to SCZ (p=0.005) and BP (p=0.02) but not MDD (p=0.15). These findings are important for understanding biological and genetic underpinnings of these polygenic psychiatric disorders.

Genetics

Experience of childhood abuse is associated with polygenic risk for autism, schizophrenia, major depressive disorder, and neuroticism Andrew Ratanatharathorn* Andrew Ratanatharathorn Karestan C. Koenen Lori Chibnik Marc Weisskopf Peter Kraft Janet Rich-Edwards Natalie Slopen Andrea L. Roberts

Offspring of women who experienced childhood abuse are at increased risk for mental illness. Twin studies suggest that inherited genetic risk for mental illness may account for some of these associations. Yet, the hypothesis that women who have experienced childhood abuse may carry genetic loading for mental illness has never been tested with genetic data. Using polygenic risk scores for six psychiatric disorders - attention-deficit hyperactivity disorder (ADHD), autism spectrum disorder (ASD), bipolar disorder (BPD), major depressive disorder (MDD), neuroticism, and schizophrenia – we tested whether genetic risk for mental illness was associated with increased risk of experiencing three types of childhood abuse: physical/emotional abuse, physical assault, and sexual abuse in a cohort of white non-Hispanic women (N=11,315). ADHD and MDD were associated with moderately higher risk of experiencing each type of childhood abuse, while neuroticism, schizophrenia, BPD, and ASD were associated with higher risk of experiencing physical/emotional abuse and physical assault, but not sexual abuse. Sensitivity analyses examining potential bias from differential recall of childhood trauma, parental socioeconomic status, and population stratification were consistent with the main findings. We found that genetic risk for mental illness was associated with modestly elevated risk of experiencing childhood abuse. Therefore, inherited genetic risk may partly account the increased risk for offspring mental illness in women who have experienced childhood abuse. In addition, future treatments for mental illness will benefit from taking into consideration the co-occurrence of childhood trauma and genetic loading.

Genetics

Lipidomics heritability and quantitative trait loci from a genetically isolated founder population

Randi K. Johnson* Randi Johnson Tonya Brunetti Kevin Quinn Katrina Doenges Monica Campbell Nichole Reisdorph Rasika A. Mathias Kathleen C. Barnes Michelle Daya

Isolated populations, such as Tangier Island, Virginia in Chesapeake Bay, have been effectively used to discover genetic risk factors for complex traits. Integration of metabolomics with genetics further enhances the ability to understand disease pathogenesis. However, previous studies cataloguing genetically-driven metabotypes have focused on a limited set of known compounds (m<500) and have not covered the lipidome. Using samples collected from Tangier Island residents (n=349), we identified heritability and quantitative trait loci (mtQTL) for 1,810 lipids. DNA extracted from blood samples were genotyped on Illumina's MEGA array, and imputed to the TOPMed reference panel. Untargeted lipidomics was generated by QTOF-MS on fasting serum samples. We used the Tangier Island 12-generation pedigree to estimate heritability using linear mixed effects models adjusted for age, sex, and technical batch effects. Metabolite heritability ranged from 0.008% to 52.4% (median=12.4%, IQR=4.9% to 20.6%). Candidate metabolites with the highest heritability (m=10, ≥46.4%) included 2 identified, 5 putatively annotated, and 3 unknown compounds. These were carried forward for genome-wide association study using adjusted linear mixed effects models. Strong association peaks (p≤2e-9) were observed for phosphatidylcholine(18:3/20:1) and sphingomyelin (d18:1/24:1) (see Figure). Both peaks contain genes known to play key roles in lipid metabolism (FADS1-FADS2 and ABCA1, respectively). Despite small effective sample size, we catalogued heritability of 1,810 lipids and identified novel, biologically plausible mtQTLs. These genetically-driven metabotypes may help elucidate genetic risk factors for numerous complex traits characterized by dysregulation of lipid metabolism, including asthma, allergic disease, and diabetes.
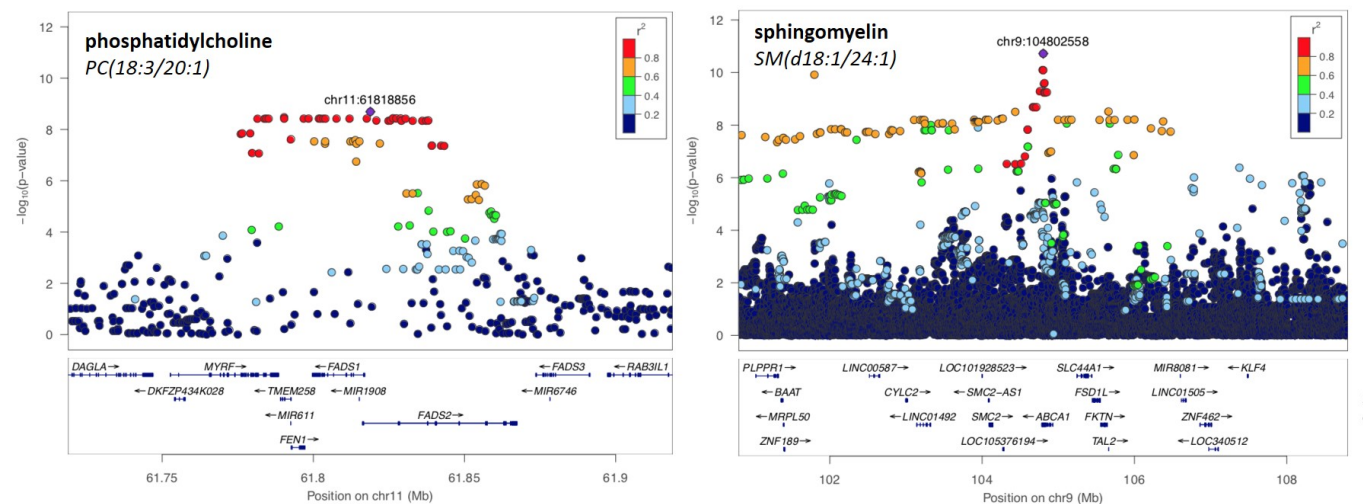
Propensity Scores as a Novel Method for Guiding Sample Allocation to Minimize Batch Effects During the Design of High Throughput Experiments

Patrick Carry* Patrick Carry Lauren Vanderlinden Fran Dong Teresa Buckner Liz Litkowski Tim Vigers Katerina Kechris Jill Norris

Batch effects can bias high throughput experiments if batches are differentially distributed across levels of the covariates. Propensity scores are used to assess balance in covariates. We developed a novel algorithm that selects the allocation of samples to batches, among all possible allocations, that minimizes the difference in average propensity score between batches. Effectiveness of the optimal allocation method was compared to randomization and stratified randomization allocation methods in a case-control study (30 per group) with two confounding variables. Differences between cases and controls were compared in a simulated gene expression set (10,000 features, log2 scale) where the difference in expression levels between cases and controls was simulated to be null. Batch effect variability was twice the median biological variability in the expression set. The max mean differences in parameter estimates relative to truth, ie, no batch effect, were evaluated before and after correction for batch effects using Combat (sva R package). Average max bias and range of bias were minimized in the optimal condition (mean: 5.89E-02, range: 2.79E-02) compared to randomization (mean: 1.18E-01, range: 3.67E-01) and stratified randomization (mean: 8.69E-02, range: 2.37E-01, Figure 1). After Combat batch correction, max bias was lower in the optimal condition (mean: 5.92E-02, range: 2.65E-02) compared to randomization (mean: 6.18E-02, range: 3.97E-02) and stratified randomization (mean: 5.99E-02, range: 2.88E-02). Adjustment for batch effects using Combat had more of an impact on the randomization and stratified randomization conditions. However, after Combat adjustment, average and to a greater extent, range of max bias remained lower in the optimal condition. Our algorithm provides a more effective method for assigning samples to batches by exploiting knowledge of covariates prior to sample allocation to ensure these variables are evenly distributed across batches.
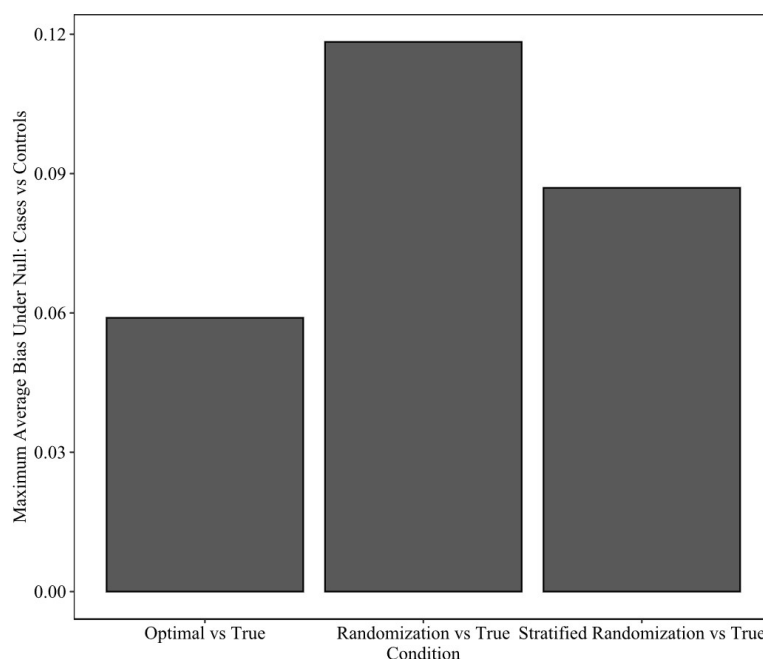
Figure 1. Average Maximum Bias by Condition
Figure Description: Average (across simulations) of maximum difference in log2 gene expression values between cases and controls under each batch selection conditions compared to no batch selection.

Genetics

Genomic Inflation is a Potential Concern in High Throughput Omics Analyses Using Inverse Probability Weighting

Patrick Carry* Patrick Carry Lauren Vanderlinden Fran Dong Teresa Buckner Liz Litkowski Tim Vigers Katerina Kechris Jill Norris

Omics studies often use existing samples from cohort studies. Conditioning on sample availability has the potential to induce selection bias in a case-control study if sample availability is non-random. Inverse probability weighting (IPW) is one method to reduce this bias. However, an increase in the observed test statistics relative to the expected, empirical distribution (genomic inflation) is a potential concern when applying IPW generalized estimating equation (GEE) models to a genome wide analysis. We conducted a simulation study (1000 iterations) to evaluate linear IPW models in an epigenome wide analysis. DNA methylation was measured using the Illumina 450K chip in unaffected, healthy subjects (n=114). Assuming the subjects represented the 'target' population we randomly assigned subjects to the case vs control group to simulate the null hypothesis. Probability of selection was simulated to be correlated to case and age. We tested 321,251 probes under 3 conditions: full (all subjects), naïve (subjects dropped but selection not accounted for), and IPW (subjects dropped but selection accounted for using IPW). The average proportion of subjects dropped from the full model for the naïve and IPW conditions was 28%. The IPW average beta was closer to full (average difference in M value: -7.60E-05) than the naïve model (average difference: -7.64E-05). Maximum average bias was also lower in the IPW (2.20E-02) than the naïve (2.23E-02) model. Average genomic inflation was underinflated in the full, 0.233, and the naïve, 0.224, but slightly inflated in the IPW model,1.01. The proportion of probes significant (FDR adjusted $p<0.05$) was <0.01% in the full, <0.01% in the naïve and 0.04% in the IPW model. After adjusting for genomic inflation (Bacon R package), 0.01% of probes were significant in the IPW model. IPW methods reduce average bias in genome-wide analyses. Genomic inflation is a potential concern that can be minimized using methods that adjust for inflation.

Epigenome Wide Association Study in Monozygotic Twin Pairs with Idiopathic Scoliosis Reveals Differential or Variable Methylation at Chromosomes 2, 7, and 17 Patrick Carry*

Patrick Carry Liz Terhune Ken Jones Lauren Vanderlinden Nancy

Idiopathic scoliosis (IS) is a complex musculoskeletal disease characterized by a lateral curvature of the spine. The disease has a strong familial component. However, genetic factors only explain a proportion of variability, suggesting a potential environmental influence. Methylation is a mechanism that may provide a link between genes, environment, and disease. DNA was extracted from peripheral blood samples collected from 8 monozygotic twin pairs with IS. Six of the twins differed on the basis of curve severity (discordant pairs, pairwise difference in cobb angle >10°). Two pairs presented with similar curves (concordant pairs, pairwise difference in cobb angle <10°). Methylation was measured with the Infinium HumanMethylation EPIC Beadchip. We tested for differences in methylation levels and variability between discordant twins. We also tested the association between methylation and curve severity in all twins (curve severity analysis). Significance was assessed at a false discovery rate (FDR) adjusted p-value of 0.10. In the discordant analysis, variability at cg02477677 (DPY19L1), an open sea probe on chromosome (chr), 7 was significantly less variable in cases (FDR=0.0791). In the curve severity analysis, increasing curve severity was associated with hypomethylation at four open sea probes (FDR<0.10). One probe was associated with chr 17 (cg02477677, RARA), two probes with chr 2 (cg12922161, LOC150622, and cg08826461), and one probe with chr 7 (cg16382077). Top hits from the differentially methylated region analysis of promoter regions included NNAT on chr 14 for the curve severity analysis (FDR=0.0237) and the BCL2L2 (FDR=0.0113) on chr 14 for the discordant analysis. These preliminary results highlight several promising methylation sites and regions. Differential methylation near RARA is of particular interest based on the role of retinoic acid signaling in embryonic body axis extension, left-right somite synchronization, and limb development.
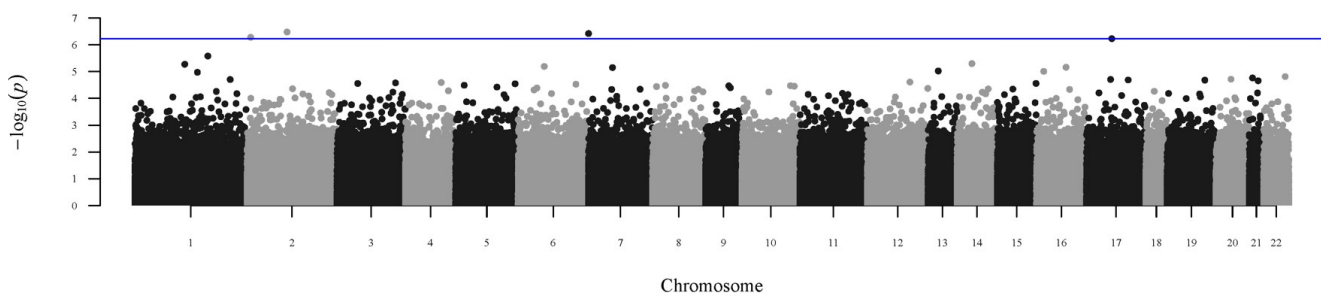
Figure 1. Manhattan Plot: Curve Severity Analysis

Figure Description: *The Manhattan plot provides p values for each methylation probe evaluated in the curve severity analysis. The Y axis represents the -log10(pvalues) and the X axis represents the location of the probes within each chromosome. Points above the blue line represent probes that were significant at the FDR adjusted level of 0.10.*

LATEBREAKER

Genetics

Development and Validation of Polygenic Risk Score for Lipoprotein (a): Potential Utility of Aggregate Genetic Information in Approximating a Biomarker Moa Lee* 3647] Lee Misa Graff Shannon Rhodes Keri L. Monda Armando L. Pineda Paul S. de Vries Christie Ballantyne Kari E. North Christy L. Avery

Lipoprotein(a) [Lpa] is an atherogenic low density lipoprotein-like particle that has emerged as a therapeutic target for cardiovascular disease. However, Lpa has been inconsistently measured in large-scale studies, limiting characterization. Given the highly heritable nature of Lpa, we assessed the ability of genetic variants as summarized in polygenic risk scores (PRS) to approximate Lpa levels and identify populations with levels above the threshold for clinical interventions. Restricting to European ancestral populations, we developed a PRS for Lpa in the UK Biobank (n=342,749; 54% female; mean age=57 years), which was validated in the Atherosclerosis Risk in Communities (ARIC) Study using Lpa measured at visit 4 (n=7,515; 53% female; mean age=63 years). The PRS was constructed in the UK Biobank using the PRSice software, restricting to well-imputed (quality>0.4), independent (r=0.01) with suggestive or significant (P<5×10^{-5}) associations with Lpa. Predictive and discriminative abilities were assessed using the coefficient of determination R^2 and the area under the receiver-operator curve (AUC, Lpa threshold=50mg/dL), respectively. The Lpa PRS, constructed using 572 SNPs at 10 loci, explained 32% of the variation in measured Lpa in ARIC. Performance of the Lpa PRS was inversely associated with age (R^2=0.33 [age < 65] vs. 0.29 [age ≥ 65]) and estimated coronary heart disease risk (R^2=0.34 and 0.31 in the lowest and highest quartiles of 10-year predicted CHD risk, respectively). Finally, the Lpa PRS discriminated ARIC participants with measured Lpa above 50 mg/dL (n=1,229) with an AUC of 0.83 (95% CI: 0.81, 0.84). In conclusion, Lpa PRS may provide a useful tool in classifying individuals with clinically elevated Lpa in settings where GWAS data are available, but Lpa is unmeasured. Further efforts are needed to evaluate the performance of Lpa PRS in other settings, particularly in diverse populations.

Gene-Acculturation Interactions on BMI in a Hispanic/Latino population using a Polygenic Risk Score Cristin McArdle* 3647] McArdle Lindsay Fernández-Rhodes Victoria Buchanan Carmen R. Isasi Mariaelisa Graff Kari E North

Abstract

Background: Hispanic/Latino adults and children living in the US face a disparate obesity burden and comprise an understudied ethnic minority in genetic epidemiology. We examined if US acculturation modifies one's innate genetic susceptibility as measured by a polygenic risk score (PRS) for Body Mass Index (BMI).

Methods: The Hispanic Community Health Study/Study of Latinos (HCHS/SOL) includes 6,832 unrelated self-identified Hispanic/Latino adults with genome-wide genetic and BMI data (age: 20-76; BMI 18.5-70 kg/m^2; collected 2008-2011). Generalized linear models were adjusted for age, gender, study site, top five PRS principal components, and sampling weights. We estimated interactions between PRS and BMI across nativity/age at immigration categories—a proxy of acculturation to the US—and described how these interactions varied by gender.

Results: Each quartile-change in PRS was associated with a 1.06 kg/m^2 (95% CI: 0.97-1.15) increase in BMI and was greatest in the most acculturated. The largest increase was for US-born individuals (0.50 kg/m^2; 95% CI: 0.20-0.80) or those who immigrated to the US at <8 years of age (0.63 kg/m^2; 95% CI: 0.20-1.05), compared to immigrants arriving in their 40s. Gender stratified models showed evidence of differential PRS-acculturation interactions, as each quartile-change in PRS was associated with a significant increase for US-born females born in the US (0.57 kg/m^2; 95% CI: 0.15-0.98) or who immigrated at <8 years (0.94 kg/m^2; 95% CI: 0.34-1.55), as compared to females who immigrated during their 40s. The PRS-acculturation interaction was similar for US-born men (0.47 kg/m^2; 95% CI: 0.05-0.88), but attenuated for men who had immigrated at <8 years (0.20 kg/m^2; 95% CI: -0.37-0.76).

Conclusions: This study reveals that nativity/immigration history may pattern their polygenic risk of elevated BMI, and that this gene-environment interaction may place US-born Hispanic/Latinos or female-child immigrants at greatest risk for obesity.
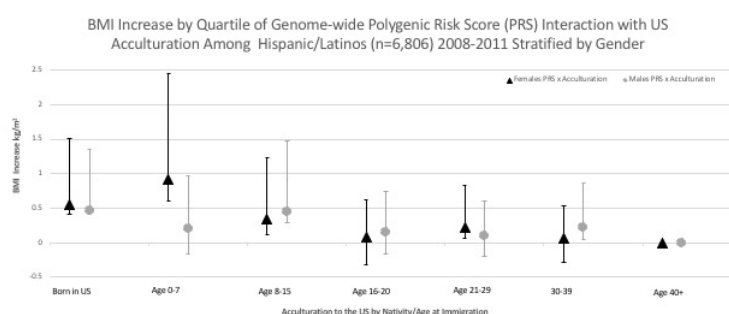
LATEBREAKER

Genetics

The time-dependent association between socioeconomic position and DNA methylation during childhood: findings from a prospective, longitudinal British cohort Jiaxuan Liu* 3647]

Liu Janine Cerutti Yiwen Zhu Alexandre A. Lussier Erin C. Dunn

Background: Low childhood socioeconomic position (SEP) is strongly associated with socioeconomic wellbeing in adulthood as well as lifelong physical and mental health. Growing evidence suggests DNA methylation (DNAm) is a potential biological mechanism explaining how socioeconomic disadvantage "gets under the skin." However, few studies have examined how the timing, duration, and upwards/downwards mobility of SEP associate with epigenome-wide DNAm profiles. **Methods**: Using data from a subsample of mother-child pairs from the Avon Longitudinal Study of Parents and Children (ALSPAC; N=676-779), we assessed the effect of both household- and neighborhood-level SEP domains on DNAm at age 7. SEP measures included: financial hardship, major financial problem, job loss, family income, income reduction, and neighborhood quality. These domains were measured repeatedly, in very-early childhood (age 0-2), early childhood (age 3-5), and middle childhood (age 6-7). We used a two-stage structured life course modeling approach (SLCMA) to test three sets of life-course models to determine which model explains the most variability in age 7 DNAm: 1) *sensitive period* models, in which the effect of low-SEP depends on the developmental period of the exposure; 2) an *accumulation* model, in which the effect of low-SEP increases with the number of occasions exposed, regardless of timing; 3) *mobility* models, in which DNAm is associated with an upward or downward change in SEP across development. **Results:** Preliminary analysis showed that DNAm was associated with SEP at both household- and neighborhood-levels. Strongest associations were found in neighborhood quality, job loss, and major financial problem. Different life-course models were selected across SEP domains, while *sensitive period* and *mobility* models were most selected. Gene set analysis suggested that top DNAm loci were enriched for genes involved in metabolism, early child development, and neurological diseases. **Conclusion:** Our early results suggest an important role for the developmental timing of socioeconomic disadvantage as well as mobility (e.g., worsening SEP) during childhood in its effect on DNAm. Findings from this study may help optimize the timing of interventions or programs aimed at reducing socioeconomic disadvantage throughout childhood.
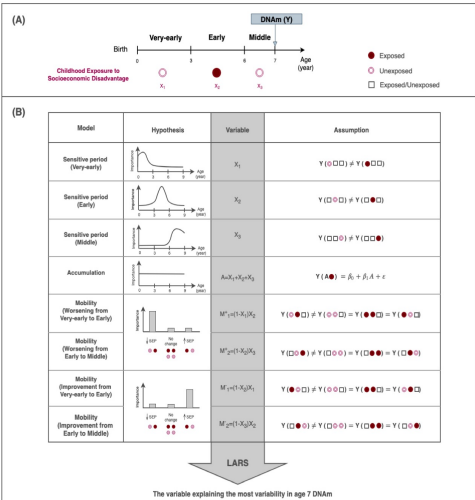
Figure 1. Study design and SLCMA models. (A) The timeline of SEP and DNAm measurement; (B) Illustration of the hypothesis, variable coding, and modeling assumptions for the eight models tested in the analysis.

Global Health

The association between oral hygiene and current depression among adults residing in Brazil
Sanda Cristina Oancea* S. Cristina Oancea Zachary Hoggarth Luciana B. Nucci

Purpose: There is very limited literature about the association between oral hygiene (OH) and current depression (CD) in South American countries such as Brazil. The purpose of this study is to investigate this association among adult individuals residing in Brazil.

Methods: The sample for this cross-sectional study was obtained from the 2013 Brazilian National Health Survey (N=58,234). CD was identified using the Personal Health Questionnaire (PHQ-8). OH was self-reported and defined as poor OH if the individual brushes their teeth less than once per day. Multivariable weighted and adjusted logistic regression models were used to investigate the above-mentioned association. Adjustment was made for age, gender, heavy drinking, smoking status, education, race, and obesity. The effect modifying role of education (non-high school graduate vs. high school graduate or further education) was also investigated.

Results: In the final study sample, the overall prevalence of CD was 7.90%, poor OH was 1.11%, and non-high school graduates was 54.68%. The prevalence of CD among poor OH was 15.10% compared to 7.82% for adults who brush their teeth at a minimum of once per day. There was a marginally significant interaction effect of education and OH on CD (p-value = 0.13). There is no significant weighted and adjusted association between poor OH and CD among adult Brazilians who completed high school or further education (p-value = 0.79). Among non-high school graduates there is a significant weighted and adjusted association between poor OH and CD (WAOR = 2.78, 95% CI 1.94 to 3.99).

Conclusion: The association between poor OH and CD among adult non-high school graduates in Brazil illuminates a key population of individuals with high odds for CD. Raising awareness for performing daily OH among less educated residents of Brazil may also provide protection against CD.

The association between cataract diagnosis and current depression among Brazilian elderly Sanda Cristina Oancea* S. Cristina Oancea Kshipra Sharma Luciana B. Nucci

Objectives – Cataract is one of major causes of blindness around the world among people age 60 years and older. This study aims to evaluate the association between cataract diagnosis (CATD) in one or both eyes and current depression (CD) among elderly Brazilians.

Methods – The study sample for this cross-sectional study was based on Brazilian National Health Survey 2013 (N= 9,904). The outcome of interest, the presence of CD, was measured using the Personal Health Questionnaire-8 (PHQ-8). The exposure of interest CATD was self-reported. Multivariable logistic regression was used to calculate weighted and adjusted odds ratios (WAOR) with 95% confidence intervals (CI) to investigate the association between CATD and CD after adjusting for age, gender, race, obesity, diabetes, hypertension, current smoking status, heavy drinking and health insurance. Association of cataract surgery with current depression was also evaluated.

Results – After adjusting for the confounders of interest, CATD among elderly Brazilians was significantly associated with CD (WAOR 1.51, 95% CI, 1.19-1.92). The weighted and adjusted odds of depression were significantly greater in females (WAOR 1.68, 95% CI: 1.30-2.17), individuals with diabetes (WAOR 1.39, 95% CI: 1.06-1.82), hypertension (WAOR 1.58, 95% CI: 1.22-2.06) and current smokers (WAOR 1.66, 95% CI: 1.14-2.41). Among elderly with CD, after adjusting for potential confounders, cataract surgery was not found to be significantly associated with CD among elderly with CATD (p-value=0.61).

Conclusions – While CATD and CD are significantly associated in elderly Brazilians, cataract surgery does not associate with CD. These results indicate the importance of assessing the mental health status of elderly Brazilians with CATD, independent of their receiving cataract surgery.

Chronic intimate partner violence and its effects on child development outcomes in a low-income setting Precious Esie* Precious Esie Joanna Maselko Lisa M. Bates

Background. Marital intimate partner violence against women is highly prevalent in low-income settings and associated with an array of poor physical and mental health outcomes. Yet, the effects of chronic maternal IPV exposure on child developmental outcomes in these settings is less understood.

Methods. Data were derived from a cluster randomized controlled trial study originally intended to evaluate the effects of a perinatal depression intervention on child development outcomes over a 36-month period in rural Pakistan. Chronic IPV exposure was defined as experiencing past-year physical, sexual, or psychological IPV at baseline and each follow-up period at 12, 24, and 36 months. Child developmental outcomes were measures of growth (i.e. stunting and underweight), socio-emotional (SDQ), language, and motor skills, evaluated at 36 months.

Results. There were 800 women with non-missing values included in the analysis. The prevalence of chronic IPV exposure was 10.9%. Approximately 18% of index children were stunted and 12.8% were underweight. After adjusting for sociodemographic confounders, chronic IPV was associated with a 45.7% increased prevalence of stunting (95% CI: 1.01, 2.11), and an 18.4% increased risk of the index child being underweight (95% CI: 0.73, 1.93). Socio-emotional scores were slightly worse for children whose mothers were exposed to chronic IPV compared to those whose mothers were not. There were no marked differences in language and motor development.

Conclusion. The prevalence of poor child growth and development outcomes is high in low- and lower-middle-income countries, yet the contribution of highly prevalent social factors such as intimate partner violence to these outcomes is relatively understudied. This analysis suggests chronic maternal IPV contributes to detrimental child outcomes, particularly stunting, and adds to the dearth of literature examining this association in these settings.

Effect of chronic IPV exposure on child development outcomes

Adjusted for treatment group, household asset index score, education, and age
SDQ = Strengths and Difficulties Questionnaire (socio-emotional development)
Motor and language scores were derived from Bayley Scales of Infant and Toddler Development
Stunting and underweight are binary (yes/no) outcomes; all others are continuous

Global Health
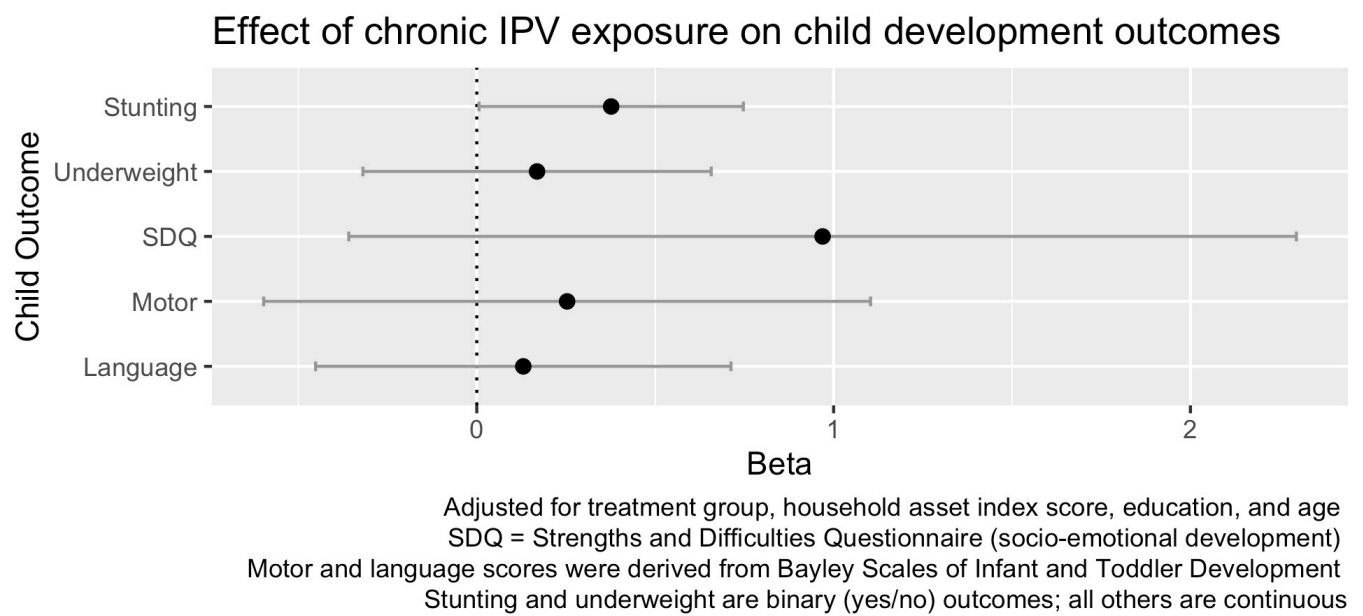
The association between arthritis and current depression among adult Brazilians Sanda Cristina Oancea* S. Cristina Oancea Kshipra Sharma Luciana B. Nucci

Objectives –Arthritis is a chronic inflammatory disease which affects joints and surrounding tissues, leading to painful movement. This study aims to evaluate the association between arthritis and current depression (CD) among adult Brazilians.

Methods – The study sample for this cross-sectional study was based on Brazilian National Health Survey 2013 (N= 59,399). The outcome of interest, CD, was measured using the Personal Health Questionnaire-8 (PHQ-8). Arthritis diagnosis, the exposure of interest, was self-reported. Multivariable logistic regression was used to calculate weighted and adjusted odds ratios (WAOR) with 95% confidence intervals (CI) to investigate the association between arthritis and CD after adjusting for age, gender, race, obesity, diabetes, hypertension, physical activity, current smoking status, heavy drinking and health insurance. Age group (18-39, 40-59, 60+ years old) was tested for effect modification.

Results – After adjusting for the confounders of interest, arthritis was significantly associated with CD (WAOR 2.32, 95% CI: 1.98-2.71). Age group was found to be an effect modifier of the association between arthritis and current depression (p=0.02). Therefore, among individuals of age group 18-39 years with arthritis, the weighted and adjusted odds of current depression were highest among all age groups (WAOR 3.07,95% CI: 2.03-4.64), followed by age group 40-59 years (WAOR 2.74, 95% CI 2.17-3.48) and age group 60 years and older (WAOR 1.93, 95% CI: 1.52-2.46).

Conclusions – Arthritis is associated with current depression. Management of arthritis by using clinical approach may improve current depression in adults. These analyses suggest that young individuals (ages 18-39 years) with arthritis are more prone to depression as compared to elderly individuals (ages 60+ years) with arthritis. Therefore, young adults need more frequent mental health assessments, especially when presenting with arthritis.

Global Health

Biological and demographic factors influencing stage at diagnosis of cervical cancer in Botswana Tara Friebel* Tara Friebel Douglas Wiebe Nandita Mitra Timothy Rebbeck Anne Marie McCarthy Surbhi Grover

Background. In Botswana, cervical cancer is the leading cancer diagnosis and foremost cause of cancer death in women. Few studies have assessed factors driving late stage of cervical cancer diagnosis in this country. Methods. Between January 2015 and January 2020, 957 women were diagnosed with cervical cancer at the Princess Marina Hospital in Gaborone. 838 (88%) women with complete information were included in this cross sectional study. Factors evaluated included age at diagnosis, cervical cancer screening, HIV status, gynecological symptoms, sexual history, smoking history, alcohol use, and marital status. To determine the association of stage of disease at diagnosis and biological and demographic factors, univariate and multivariable logistic regression analyses were performed. Results. 402 (46%) of women were diagnosed with late stage tumors (stage III/IV). Median age at diagnosis was 47.9 years (22.4-95.2). 59% of women reported previous cervical screening, 70% were HIV-infected, and 45% reported having sexual intercourse within the previous 12 months. Of the patients, 3% of women smoked, reported using alcohol (8%) and 23% were married. Commonly reported gynecological symptoms were abnormal vaginal bleeding (59%), pelvic/lower back pain (55%), and vaginal discharge (48%). Factors associated with diagnosis of a late stage tumor included prior cervical cancer screening (OR 0.61, 95%CI: 0.46-0.81), positive sexual history (OR 0.66, 95%CI: 0.50-0.88) and gynecological symptoms (OR 5.93, 95%CI: 3.08-11.44). Conclusion. Women with cervical cancer screening and recent sexual activity were significantly less likely to present with late stage tumors, thus decreasing the risk of death. Women reporting previous symptoms had increased odds of having a late stage tumor. These results highlight the need for enhanced efforts to expand screening and ensure timely response to gynecologic symptoms in order to reduce morbidity and mortality from cervical cancer in Botswana.

Scaling up an integrated child development intervention in Chatmohar, Bangladesh Helen O. Pitchik* Helen O. Pitchik Mahbubur Rahman Fahmida Tofail Fahmida Akter Jesmin Sultana Abul Kasham Shoab Tarique Md. Nurul Huda Tania Jahir Md. Ruhul Amin Md. Khobair Hossain Jyoti B. Das Md. Rezaul Hasan Farzana Yeasmin Jenna E. Forsyth Malay K. Mridha Peter J. Winch Lia C.H. Fernald Stephen P. Luby

Background: Millions of children in Bangladesh experience developmental delays. Delivery of an integrated early-child development intervention through the government health system may be a feasible way to improve child development at scale. We assess the prevalence of risk factors for poor development, and the feasibility of delivering an integrated early-child development intervention through the government health system in Chatmohar, Bangladesh.

Methods: To assess the prevalence of risk factors for poor development we used probability proportional to size sampling followed by age-stratified random sampling to select primary caregivers of children 6-24 months within villages of Chatmohar. We then implemented a group-based, integrated, child development, nutrition, water, sanitation, hygiene, and lead exposure prevention intervention through the government health system throughout Chatmohar. To assess feasibility of this intervention, we will collect data on session completion, quality and attendance, and conduct qualitative interviews and focus group discussions.

Results: Caregivers interviewed (n=1635) in May and June 2019 were on average 26 years old (SD 5.6). Caregivers participated in an average of 3.3 (SD 1.4) stimulation activities (out of 6) with their child, and 7% of households had one or more children's book. Minimum dietary diversity was achieved by 21% of children, and 35% had access to a handwashing station with soap and water. As of January 2020, 71 health workers have been trained, and 72% of planned sessions have been implemented. Results include the prevalence of risk factors for poor child development, and implementation metrics up to June 2020.

Conclusion: Children in Chatmohar, Bangladesh experience multiple risk factors for poor child development. It is feasible for government health workers to deliver an integrated early child development curriculum in this region. Experiences to date, and implications for further scale up will be discussed.

Table 1: Risk factors for poor child development in Chatmohar, Bangladesh

Indicator	% (n) or mean (SD)
Caregiver received <6 years of formal education	37% (609)
FCI: Play activities[1]	3.2 (SD 1.4)
FCI: Play materials[2]	2.1 (SD 1.4)
Children's books in the home (1+)	7% (109)
CES-D[3]	14 (SD 9.1)
Child Minimum dietary diversity[4]	21% (338)
Maternal Minimum dietary diversity[5]	74% (1210)
Access to handwashing with soap & water	35% (579)
Access to functional, clean & hygienic latrine[6]	21% (344)

[1] Play activities subscale of the Family Care Indicators (0-6)
[2] Play materials subscale of the Family Care Indicators (0-6)
[3] Center for Epidemiologic Studies 20 Question Depression questionnaire (0-60), with higher scores indicating more depressive symptoms reported
[4] Children >6 months reported eating 5 or more food groups in the last 24 hours
[5] Mothers reported eating 5 or more food groups in the last 24 hours
[6] Clean toilet: No visible feces in the pan or slab; Hygienic latrine: Flush or pour-flush toilet/latrine to (i) Piped sewer system, (ii) Septic tank; Pit latrine with slab and water seal, Pit latrine with slab and lid, no water seal, Pit latrine with slab and flap, no water seal, Ventilated Improved Pit (VIP) latrine, Composting latrine

Muslim females and avoidance of health care services in China: a nationally representative cross-sectional study Stephen W. Pan* Stephen Pan Wanqi Wang Zihan Dong

Background: Evidence suggests that Muslim minority females in the US have lower rates of healthcare utilization than the overall population, partly due to religious-based values of privacy and modesty, and healthcare services that lack Islamic cultural sensitivities. However, the relation between minority Muslim identity, sex, and healthcare utilization is poorly understood in China, despite a population of >20 million Muslims. This study tested the hypothesis that healthcare avoidance is significantly more likely among Muslim females compared to non-religiously affiliated males and females in China. Methods: This study was a secondary analysis of the 2010 East Asian Social Survey (EASS) China component. The EASS is a survey that includes nationally representative probability samples of residents > 18 years old. Health care avoidance was defined as refraining from seeing a doctor in the past 12 months, despite an illness or injury. Multiple logistic regression with probability sampling weights was used to examine associations between a) religious affiliation and gender and b) health care avoidance. Control variables included age, marital status, educational attainment, relative household income, urbanicity, province of residency, health insurance status, chronic disease status, alcohol use, physical activity, and tobacco use. Standardized predicted probabilities were calculated using the Margins command in Stata 15. Results: The analytic sample size was 3461. Consistent with our hypothesis, the standardized predicted probability of refraining from seeing a doctor was significantly higher for Muslim females (64.4%, 95% CI: 45.0-83.8%) compared with non-religiously affiliated males (40.7%, 95% CI: 37.3-44.2%) (Figure). Conclusion: Healthcare avoidance is very prevalent among Muslim minority females in China. Research is needed to augment health care service uptake and elucidate how healthcare avoidance may be impacting health outcomes among Muslim females in China.

Figure: Standardized and weighted predicted probabilities and 95% confidence intervals of refraining from seeing doctor in past 12 months despite illness or injury in China, by religious affiliation and sex (n=3461)
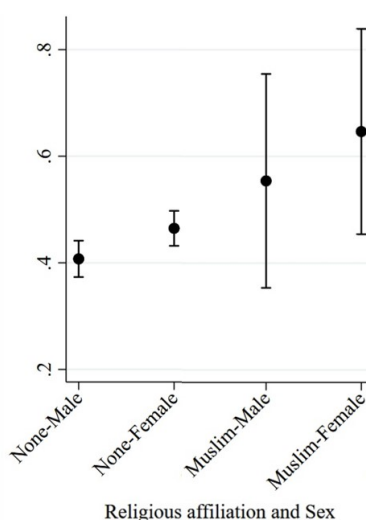
Predicted probabilities controlling for age, marital status, relative income, educational attainment, urbanicity, province of residency, health insurance status, chronic disease or longstanding health problem, smoking, alcohol, and physical activity.

Global Health

Extreme heat, preterm birth, and stillbirth: a global analysis across 21 low-to-middle-income countries Sara McElroy* Sara McElroy

Stillbirths and complications from preterm birth (PTB) are two of the leading causes of neonatal deaths across the globe. Low-to-middle-income countries (LMICs) are experiencing some of the highest rates of these adverse birth outcomes. In addition to high PTB and stillbirth rates, LMICs face many additional burdens like poverty, civil war, and lack of accessible health care, making women living in LMICs especially vulnerable to adverse birth outcomes. Research has suggested that environmental determinants, such as extreme heat events can increase the risk of PTB and stillbirth. In the context of climate change, changes in precipitation regimes around the globe have contributed to the increasing severity, duration, and frequency of heatwaves. Thus, it is imperative to examine how exposure to extreme heat affects adverse birth outcomes, as this trend is likely to continue in the future. Most of the evidence tying extreme heat and adverse birth outcomes has been generated from developed countries because measuring extreme heat in LMICs has proven challenging due to the scarcity of ground monitors. This study will rely on modern techniques such as remote sensing data to overcome this challenge in exposure measurement. Remote sensing data was linked with Demographic Health Surveys data on adverse birth outcomes. A global analysis of 21 LMICs was conducted by exploiting each country's relative extreme heat events via a time-stratified case-crossover design. Conditional multi-level regression with sampling weights was employed to ascertain the relationship between acute exposure to extreme heat and PTB and stillbirths. Heatwaves were found to increase the risk of PTB and stillbirth in 14 of the 21 countries. Results from this study could be used to inform early warning systems (EWS) to target pregnant women by introducing preventative actions that can reduce exposure to extreme heat and ultimately help mitigate the rates of PTB and stillbirth in LMICs.

LATEBREAKER

Global Health

The effect of vaccination on children's learning achievements: findings from the India Human Development Survey Catherine Arsenault* 3647] Arsenault Sam Harper Arijit Nandi

Background

Beyond the prevention of illness and death, vaccination may provide additional benefits such as improved educational outcomes. However, there is currently little evidence on this question. Our objective was to estimate the effect of childhood vaccination on learning achievements among primary school children in India.

Methods

We used cohort data from the India Human Development Survey (IHDS). Vaccination status and confounders were measured among children who were at least 12 months old at baseline in 2004-05. In 2011-12, the same children completed basic reading, writing and math tests. We estimated the effect of full vaccination during childhood on learning achievements using inverse probability of treatment weighted logistic regression models and results reported on the risk difference scale. The propensity score included 33 potential community, household, mother and child-level confounders and state fixed effects.

Results

Among the 4,877 children included in our analysis, 54% were fully vaccinated at baseline, and 54% could read by the age of 8-11. The estimated effect of full vaccination on learning achievements ranged from 4 to 6 percentage points, representing relative increases ranging from 6% to 12%. Bias analysis suggested that our observed effects could be explained by unmeasured confounding, but only in the case of strong associations with the treatment and outcome.

Conclusion

These results support the hypothesis that vaccination has lasting effects on children's learning achievements. Further work is needed to confirm findings and elucidate the potential mechanisms linking vaccines to educational outcomes.

Health Disparities

Using additive and relative hazards to quantify colorectal survival inequalities for patients with a severe psychiatric illness: comparing Aalen and Cox-Proportional Hazards regression models

Alyson Mahar* Laura Davis Alyson Mahar Paul Kurdyak Timothy Hanna Natalie Coburn Patti Groome

Introduction: Reporting both absolute and relative measures is important when examining health equity. Differing methods can generate diverging evidence and conclusions, resulting in increased disparities among already vulnerable populations. We demonstrate the use of both measures by examining colorectal cancer (CRC) survival for patients with severe psychiatric illness (SPI).

Methods: Retrospective cohort study of CRC patients diagnosed between 01/04/2007 and 31/12/2012, using linked administrative databases. SPI was defined as diagnoses of major depression, bipolar disorder, schizophrenia, and other psychotic illnesses six months to five years preceding cancer diagnosis and categorized as inpatient, outpatient or none. The association between SPI history and the risk of death from any cause was examined using Cox Proportional Hazards regression to obtain a relative measure of hazard ratio of death and Aalen's semi-parametric additive hazards regression to obtain absolute differences. Both models controlled for age, sex, primary tumour location, and rurality.

Results: The final cohort included 24,507 CRC patients. 58.1% of those with inpatient SPI history died (n=150), 47.1% of those with outpatient SPI history died (n=227). Risk of death was 40% in patients with an outpatient SPI history (HR 1.40, 95% CI: 1.22-1.59) and 91% in patients with an inpatient SPI history (HR 1.91, 95% CI: 1.63-2.25), relative to no history of a mental illness. An outpatient SPI history was associated with an additional 33 deaths per 1000 person years, and an inpatient SPI was associated with an additional 82 deaths per 1000 person years after controlling for confounders.

Conclusion: Reporting of both relative and absolute effects is possible and calculating risk difference with time-to-event data is relatively simple using Aalen models. We encourage future studies examining inequalities with time-to-event data to use this method and report both relative and absolute effect measures.

Tract socioeconomic status and breast cancer survival using residential histories in the Metro Chicago Breast Cancer Registry Garth H Rauscher* Garth Rauscher Alpana Kaushiva David Stinchcomb Shannon Zenk

Introduction: Census tract socioeconomic status (SES) at diagnosis predicts breast cancer (BC) survival, but SES measured at other time points could add information. We used residential histories (RH) to examine associations of census-based measures of tract disadvantage, affluence, and segregation with BC-specific survival for 15,302 patients diagnosed with BC between 2001 and 2017. Methods: Identifiers were linked with LexisNexis and geocoded addresses were merged with established measures of interpolated, census-based tract disadvantage, affluence and segregation. We created 6 definitions for each measure: (1) cumulative from diagnosis to death or censoring, (2) at diagnosis, (3) cumulative from diagnosis to 10 years prior, (4) at 10 years prior, (5) cumulative from diagnosis to 20 years prior, and (6) at 20 years prior. Hazards ratios (HR) for a one standard deviation (SD) increase in tract SES were estimated from Cox regression. Results: Associations with BC survival did not appear to depend much on which version of each measure was employed, and with no consistent pattern. For example, a 1 SD increase in disadvantage was associated with HR of 1.09, 1.12, 1.08, 1.15, 1.12, and 1.09 for definitions 1-6 respectively. Likelihood ratio tests from nested models, however, suggested that pre-diagnostic measures added predictive value alongside post-diagnostic measures. Associations also varied by race/ethnicity: HRs for post-diagnosis segregation, disadvantage and affluence were 3.94 (95% CI: 2.0, 7.7), 1.31 (95% CI: 1.1, 1.5), and 0.82 (95% CI: 0.74, 0.93) for non-Latina (nL) White patients, as compared to HRs of 1.11 (95% CI: 0.69, 1.77), 1.00 (95% CI: 0.88, 1.13), and 0.92 (95% CI: 0.76, 1.09) for nL Black patients. Conclusion: Measures of tract SES defined at different time points appear to be capturing additional information and not solely serving as proxies for each other, and linking to residential histories can add value to studies of BC survival.

Health Disparities

Injuries caused by law enforcement among young people: Disparities and trends among California emergency department and hospital patients, 2005-2014 Kriszta Farkas* Kriszta Farkas Jennifer Ahern Catherine Duarte

Police violence is a critical public health issue. Though research on police violence has substantially grown, few studies have examined its burden among young people. Given a broader literature that documents lasting adverse effects of early-life exposure to trauma and disproportionate policing of Black youth linked to racialized constructions of their being older and dangerous, further inquiry is warranted. This study examined the demographic and temporal distributions of injuries caused by law enforcement, severe enough to require hospital care, among young people. Using statewide data on all hospitalizations and emergency department visits in California, 2005-2014, we identified patients, ages 19 years or younger, with ICD-9-CM external cause of injury codes for legal intervention (LI) injury, and calculated rates using Census population denominators. From 2005-2014, 13,855 young people in California were treated for LI injury. Non-Hispanic Black males, ages 15-19 years, had the highest rate overall (217.5 per 100,000 person-years [PYs]) – over three times that among same aged non-Hispanic White males (64.1 per 100,000 PYs). Among 10-14-year-olds, Black boys had five times the LI injury rate of White boys (22.2 vs. 4.3 per 100,000 PYs). Notably, the rate among Black girls (8.9 per 100,000 PYs) was twice and six times the rates, respectively, among White boys and White girls (1.5 per 100,000 PYs). Trends in annual rates also varied by race. Rates among White youth increased by 29.3%, peaking in 2009, but returned below the 2005 rate by 2014, whereas rates among Black youth increased 63.6% by 2009, and did not return to the 2005 level. Results suggest that the burden of LI injuries among young people substantially varies by minoritized identity. Specifically, Black boys and girls experience dramatically greater rates of LI injury, and relative inequities are even greater at younger ages.

Health Disparities

Prevalence of health risk behaviors among adolescents experiencing food insecurity

KATHRYN KRUPSKY* Kathryn Krupsky Ellen Barnidge Sarah Sliwa Hilary Seligman

Roughly 6.8 million US youth (10-17 years) live in food insecure households, lacking reliable access to affordable and nutritious food. Food insecurity (FI) is associated with poorer health, which is likely due to multiple complex pathways. One pathway may be increased health risk behaviors and adverse experiences resulting from efforts to manage basic needs and cope with material deprivation. We describe the prevalence of substance use, sexual risk behaviors and experiences, and violence relative to FI among adolescents. Data are from the 11 states that administered the high school Youth Risk Behavior Survey in 2017, included 1 item to assess household FI and openly shared weighted data. Descriptive statistics detail demographic characteristics (e.g. age, sex and race) and health risk behaviors and experiences overall and by FI. Crude and covariate-adjusted prevalence ratios were generated using Poisson regression models with robust standard errors and account for survey design. Estimates are generalizable to high school students from participating states. Of the 28,702 adolescents in our sample, 11% experienced FI. The prevalence of health risk behaviors and experiences ranged from 2% (injecting illegal drugs) to 44% (no condom use during last sexual intercourse). FI was associated with a higher prevalence of all health risk behaviors and adverse experiences, even after controlling for race/ethnicity and sexual identity. FI was associated with a $\geq$ 2-fold greater prevalence of ever using illicit drugs, having sexual intercourse before age 13 years, ever being forced to have sexual intercourse and ever experiencing sexual violence ($p<0.05$ for all comparisons). The prevalence of health risk behaviors and adverse experiences is substantially higher among adolescents with FI. Efforts to decrease FI may help alleviate adolescents' daily struggles to meet basic needs, and possibly reduce priority health risk behaviors with potential long-term public health implications.

Health Disparities

Eating disorder disparities at the intersection of sexual orientation, gender expression, and weight status: An intersectional MAIHDA analysis of the Growing Up Today Study cohorts
Ariel Beccia* Ariel Beccia Jonggyu Baek William Jesdale S. Bryn Austin Kate Lapane

The objective of this study was to quantify the intersectional effect of sexual orientation, gender expression, and weight status on eating disorder and disordered eating behavior risk among young people in the U.S. Using data from 11,071 participants aged 14-30 years in the Growing Up Today Study 2010-11, we estimated intersectional effects with the Multilevel Analysis of Individual Heterogeneity and Discriminatory Accuracy (MAIHDA) method. Participants were nested in 32 intersectional strata defined by combining 4 sexual orientation (heterosexual, mostly heterosexual, bisexual, gay/lesbian), 4 gender expression (gender conforming (GC) males, GC females, gender nonconforming (GNC) males, GNC females), and 2 weight status categories (overweight/obese, non-overweight obese, based on body mass index) in random intercepts multilevel logistic models. For each outcome (past-year binge eating, fasting, purging, and self-reported eating disorder diagnosis), we estimated age-adjusted stratum-specific risks and calculated the variance partition coefficient (VPC) to measure the strata's discriminatory accuracy. We then adjusted for sexual orientation, gender expression, and weight status to identify strata experiencing elevated risks above and beyond the additive effects of these identities (i.e., intersectional interactions). Overall, binge eating was the most prevalent outcome (23%) and eating disorder diagnosis the least prevalent (3%). There were large disparities between groups, with certain strata (e.g., GNC bisexual women) consistently experiencing higher than average risks. Although VPCs indicated meaningful clustering by strata (range 5-33%), there were no intersectional interactions for any outcome; all between-group variation was explained by the additive effects. Our findings highlight the importance of addressing diversity within sexual orientation groups to inform targeted interventions and the utility of MAIHDA to document intersectional health disparities.

Early Life and Midlife Socioeconomic Status Association with Multiple Lifestyle Risk Factors and Multiple Chronic Conditions in Ethnically Diverse Women Autumn Clemons*
Autumn Clemons Parisa Tehranifar Jasmine A. McDonald

Background
Early life socioeconomic status (SES) is associated with lifestyle risk factors (LRFs) and chronic conditions in adulthood. Research is limited to the influence of early life SES on developing multiple LRFs and multiple chronic conditions in midlife.

Purpose
Using the New York National Collaborative Perinatal Project, we examined the association of early- and mid-life SES with co-occurrence of multiple LRFs and multiple chronic conditions.

Methods
We included 261 female offspring (African American 36%, Hispanic 38%) enrolled at birth (born 1959-1963) with prospectively collected SES data (maternal education, parental occupation, income at the time of participants' birth). We used self-reported data collected in midlife such as adult SES (education, occupation, income), LRFs (current smoking status, low physical activity, being overweight or obese), and chronic conditions (e.g., hypertension). We measured SES across 3 variables: SES at birth, cumulative SES score (summed early- and mid-life SES), and social mobility (change in early- and mid-life SES). We conducted relative risk (RR) regression analyses to examine the relationship between SES and the reported number of LRFs (0-3) and separately, the number of chronic conditions (0, 1, or 2 or more). We tested for confounding by maternal smoking, maternal pre-pregnancy body mass index, and participants' race/ethnicity.

Results
The cohort had a mean (standard deviation) age of 41.8 (1.8) years, 33% had multiple LRFs, and 34% had multiple chronic conditions. A lower cumulative SES score and the lack of upward social mobility was associated with reporting multiple LRFs in midlife (RR 1.2, 95% CI 1.0-1.3 and RR 2.0, 95% CI 1.1-3.8, respectively). We observed no association between SES and multiple chronic conditions.

Conclusion
Persistently low SES in both early- and mid-life increased the risk of reporting multiple LRFs, but not multiple chronic conditions, in this multiethnic cohort of relatively young women.

Health Disparities

Neighborhood Socioeconomic Status and Tooth Loss in US Black Women Yvonne Robles*
Yvette Cozier Yvonne Robles Brenda Heaton Hanna Gerlovin Patricia Coogan Julie R Palmer Lynn
Rosenberg Yvette C Cozier

In the U.S., blacks experience higher rates of tooth loss compared to whites and other racial/ethnic groups. Neighborhoods affect health by shaping community norms, health-related information and behaviors. Evidence suggests a link between neighborhood socioeconomic status (NSES) and oral health. Yet little data are available on blacks who are more likely to live in disadvantaged neighborhoods than are whites of similar education and income. We assessed the relationship between NSES and tooth loss in the Black Women's Health Study, a biennial follow-up study of US black women begun in 1995 when participants were aged 21-69 years. In 2007, participants reported the total number of teeth lost as an adult "to tooth decay or gum disease"; in 2011 and 2015, they reported tooth loss "in the past 4 years". Residential addresses were geocoded to US Census block group data for the domains of household income, family assets, education, and poverty. We combined these data into a summary NSES score and divided into quintiles. The analytic sample consisted of the 20,763 women who in 2007 (baseline) reported no (0) adult tooth loss. On average, they were aged 47 years, had completed 16+ years of education, and lost one tooth during up to eight years of follow-up. We used Cox proportional hazards models to approximate IRRs and 95% CIs adjusted for age, body mass index, geographic region, education, smoking, diabetes, and parity. The IRR for the association of lowest versus highest quintile of NSES in relation to any tooth loss was 1.33 (95% CI: 1.19-1.50) (P trend= 0003). Dental cleaning (DC) within the past 2 years modified the association: the IRRs for lowest NSES quintile relative to highest among those with no recent DC was 1.38 (95% CI: 1.08-1.77), while the IRR among those with recent DC was 1.26 (95% CI: 1.10-1.44) (P interaction= <0.01). These results suggest that the neighborhood socioeconomic environment influences oral health in middle-class black women.

Severe maternal morbidity among asylum seekers in Ontario, Canada: a population-based study Susitha Wanigaratne* Susitha Wanigaratne Vanessa Redditt Astrid Guttmann Marcelo L Urquia

Background – In Canada, asylum seekers differ from sponsored refugees, since they arrive on their own, claim asylum and wait for a hearing to determine the veracity of their claim. Asylum seekers are eligible for temporary federal health care and transition to provincial care if asylum is granted. Little is known about the health of those eligible for the federal program; but research suggests that practitioners lack awareness and understanding of the program, potentially affecting care. We aimed to compare severe maternal morbidity (SMM – an indicator of the quality of obstetric care) among asylum seekers who delivered while eligible for federal care to those eligible for provincial care.

Methods – This retrospective population-based study used the Longitudinal Immigration Database, linked to hospital deliveries in the province of Ontario (2002-2014). Analyses included asylum seekers with a temporary resident refugee permit who were eventually granted asylum and permanent residency (PR). Since hearing dates were unknown, we approximated the transition to provincial care by comparing SMM risk at deliveries occurring before 30, 60, 180 days and 1 year prior to the PR date to deliveries occurring after the same date. Log-binomial regression with generalized estimating equations were used to estimate unadjusted (RR) and adjusted risk ratios (ARR) with 95% CI. Models were adjusted for age, education and landing year.

Results – Among asylum seekers who delivered before 180 days prior to the PR date, 50 of 3,200 deliveries had at least one SMM (15.6 per 1000) vs. 200 of 21,300 among those who delivered after (9.4 per 1000) – an RR of 1.41 (1.00-1.99) and ARR of 1.44 (0.98-2.12). ARRs were significant and strengthened with shorter time prior to the PR date.

Conclusion – Findings suggest that the obstetric care of asylum seekers under the federal program may not be ideal and may also reflect the complexity of accessing health care before and around the time of gaining PR.

Assets, race, and depression in U.S. adults: understanding the relation between race and mental health
Catherine K. Ettman* Catherine Ettman Gregory H. Cohen Sandro Galea

Racial disparities in physical health are well documented. The relation between race and mental health, however, remains unclear. Between-group racial differences in assets—with minorities having access to fewer health-generating assets than majority groups—may contribute to racial differences in mental health. We aimed to better understand the relation between race and depression by assessing the role assets play in shaping their association. We conducted a serial cross-sectional study using nationally representative data from the National Health and Nutrition Examination Survey spanning 2007-2016. Our final sample included 26,382 U.S. adults over age 18. We measured depression using the Patient Health Questionnaire (PHQ-9) and a cut-point of 10 or above. We considered three types of assets: liquid assets (income), physical assets (housing), and social assets (marital status and education). We calculated weighted prevalence estimates, odds ratios (with 95% confidence intervals) comparing odds of depression among non-Hispanic blacks and Hispanics to those of non-Hispanic whites, and predicted probabilities of depression across assets and race, controlling for gender and age. In the unadjusted model, non-Hispanic blacks and Hispanics had 1.34 (p<0.05) and 1.27-times greater odds of having depression than whites (p <0.001). When we adjusted for assets and demographic variables, being non-white was associated with reduced odds of depression: 0.84 times the odds for non-Hispanic blacks (p<0.05) and 0.77 times the odds for Hispanics (p<0.01), relative to whites. The figure shows that household income more clearly determines the prevalence of depression than does race. Racial minorities have a higher risk of depression relative to whites in unadjusted models. However, when assets are controlled for, racial minorities have a lower risk of depression than whites. Assets may, in part, explain the association between race and depression.

Weighted depression prevalence by race
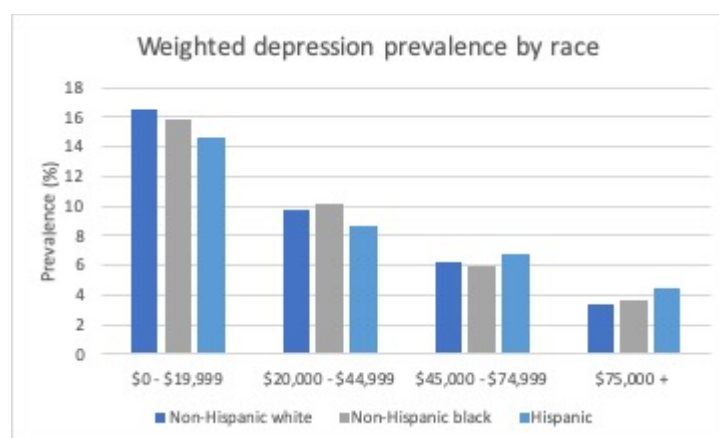
Racial/ethnic disparities in exposures to air pollution during pregnancy Sandie Ha* Sandie
Ha Yueqi Yan Valerie Martinez

Background: Socially disadvantaged populations have disproportionately higher risk of adverse
pregnancy outcomes, many of which are linked to air pollution. We aim to investigate whether
groups defined by maternal race/ethnicity are exposed to differential levels of air pollution
throughout pregnancy in a highly polluted area, and to quantify these differences.

Methods: We identified 278,048 singleton pregnancies with gestation ages 15-42 weeks from the
San Joaquin Valley, California (2007-2015) and spatiotemporally linked them to zip-code level daily
fine particulate (PM2.5) and ozone (O3) estimated by modified Community Multi-scale Air Quality
Models. Maternal characteristics including race/ethnicity [non-Hispanic White (25.1%), non-Hispanic
Black (4.3%), Hispanic (58.5%), American Indians/Alaskan Natives (AI/AN, 0.7%), Asian (7.1%),
Hawaiian/Pacific Islanders (0.2%), Other (0.7%), Multi-race (2.4%)] were assessed using birth
certificates. Generalized linear models quantified the relationship between air pollution exposures
across pregnancy and maternal race/ethnicity after adjusting for seasonality, and other maternal
characteristics. Pollutants were log-transformed due to right skewness and statistical significance
was set at 0.05.

Results. Average PM2.5 exposure decreased through pregnancy while O3 exposure increased (trend
p-values <0.001). Compared to Whites, first-trimester PM2.5 exposure was higher for Black [1.8%
(95% CI: 0.9%-2.7%)], Hispanics [6.3% (5.9%-6.7%)] and AI/AN [5.2% (3.1%-7.3%)]. Similarly, third-
trimester O3 exposure was higher for Black [5.1% (4.4%-5.8%)], Hispanic [5.9% (4.0%-7.8%)],
Hawaiian/Pacific Islander [5.2% (3.3%-7.1%)], Other [5.8% (4.2%-7.4%)], and Multi-race [3.7%
(3.0%-4.4%)] women.

Conclusions. Maternal race/ethnicity is a major risk factors for exposures to air pollution. While
awaiting studies with personal air pollution monitoring, it is important to raise awareness and target
public health messages among highly-exposed groups.

Health Disparities

Whiteness, Blackness, and Otherness among Arab mothers in Massachusetts and their impact on infant health outcomes Nadia N. Abuelezam* Nadia Abuelezam Adolfo Cuevas Abdul M. El-Sayed Sandro Galea Summer S. Hawkins

Background: Growing attention has been placed on the role of racism on maternal and infant health in the US. While there is some evidence that Arab ethnicity is protective for infant health, little attention has been given to the impact of race on infant health outcomes among Arab Americans. We aim to examine differences in infant outcomes by mother's self-identified race among Arab Americans as well as quantify differences in infant outcomes by self-identified race for Arabs and non-Arabs.

Methods: This study used data from the Standard Certificate of Live Birth on 8,204 infants born to Arab mothers and 325,354 infants born to non-Arab mothers between January 1, 2012 and December 31, 2016 in Massachusetts. Mothers' race was categorized as White, Black, or Other and, separately, mothers' ethnicity was categorized as Arab or non-Arab. Outcomes of interest included birth weight (grams), preterm birth (<37 weeks), LBW (<2500 grams), small-for-gestational age (SGA, 90th percentile for gestational age and sex).

Results: After adjustment, Black Arab mothers had increased odds of preterm birth (AOR: 1.36, 95% CI: 1.06, 1.74) and LBW (AOR: 1.41, 95% CI: 1.04, 1.91) than White Arab mothers. White Arab mothers had increased odds of LBW (AOR: 1.13, 95% CI: 1.01, 1.26) and SGA (AOR: 1.23, 95% CI: 1.12, 1.35) when compared to White non-Arab mothers. Arab mothers who self-identified as Black or Other had babies that were 41.5 and 56.9 grams lighter than babies born to White Arab mothers, respectively.

Conclusions: Both ethnicity and race are important determinants of the health of Arab American infants. Our findings suggest that Arab ethnicity may play a seemingly protective role in the maternal and infant health of Arab Americans, particularly among those who identify as Black. Understanding the lived experiences of Arab American mothers, may help better inform public health and medical practice.

Lifestyle Behavioral Risk Factors among Native Americans of the United States: Findings from the 2017 Behavioral Risk Factor Surveillance System Guixiang Zhao* Guixiang Zhao Jason Hsia William S. Garvin Machell Town

Purpose: To examine lifestyle behavioral risk factors among American Indians and Alaska Natives (AI/ANs) across Indian Health Service (IHS) Administrative Areas and in comparison with non-Hispanic (NH) whites.

Methods: The 2017 Behavioral Risk Factor Surveillance System collected data of participants (n=8,196) in 50 states and DC on lifestyle behaviors. We examined 5 behavioral risk factors: current smoking, heavy drinking, binge drinking, physical inactivity, and obesity. We conducted log-linear regression analyses to assess disparities in these behaviors among AI/ANs by IHS areas and between AI/ANs and NH whites while controlling for potential confounders including age, sex, education, marital status, employment, and federal poverty level.

Results: Among AI/ANs, prevalences of having 5 lifestyle risk behaviors differed significantly across IHS areas. After adjustment for sociodemographic variables, compared with AI/ANs living in the United South and Eastern Tribes area, those in Great Lakes, Great Plains, and Rocky Mountain areas were 52%, 40%, and 29% more likely to report current smoking, respectively; whereas AI/ANs in Albuquerque Area Southwest, California, Inter-Tribal Council of Arizona, and Navajo areas were 39%, 55%, 49%, and 62% less likely to report current smoking, respectively. AI/ANs in Great Lakes area were 94% more likely to report heavy drinking, and AI/ANs in Great Lakes and Great Plains areas were 55% more likely to report binge drinking. Additionally, AI/ANs in Navajo area were 30% less likely to report physical inactivity, and AI/ANs in Inter-Tribal Council of Arizona and Oklahoma areas were 28% and 19% more likely to report obesity, respectively. Nationwide, AI/ANs were 11% more likely to report current smoking and 21% more likely to report obesity than NH whites.

Conclusions: Significant disparities in lifestyle risk behaviors of AI/ANs existed across 11 IHS Administrative areas, and the disparities existed between AI/ANs and NH whites as well.

Health Disparities

Bias Analysis of Depression Rate Comparisons between Racial/Ethnic Groups Kenneth Nieser* Kenneth Nieser

Previous epidemiologic surveys have reported that non-Hispanic blacks experience lower or equal rates of major depressive disorder compared to non-Hispanic whites. This finding is significant given that non-Hispanic blacks tend to experience greater disease rates than non-Hispanic whites for many other health conditions, such as heart disease, diabetes and asthma. However, there are potential sources of bias—differential survey participation rates and depression measurement error—that could affect the validity of this result. In this study, a Monte Carlo sensitivity analysis was conducted to estimate bias-adjusted depression prevalence odds ratios for non-Hispanic blacks relative to non-Hispanic whites. Similar analyses were conducted to compare depression rates among non-Hispanic Asians and Hispanics to non-Hispanic whites. The study combined data from two survey cycles (2013-2014 and 2015-2016) of the National Health and Nutrition Examination Survey (NHANES) and included adults aged 20-80 (n=10,390). Depression status was measured using the Patient Health Questionnaire-9. Choice of probability distributions for bias parameters was informed by NHANES 2013-2016 data and several external sources. For each of the three comparisons, measurement bias adjustment greatly increased the width of interval estimates and selection bias adjustment shifted interval estimates in the direction of positive association. For example, non-Hispanic blacks had comparable odds of depression relative to non-Hispanic whites prior to adjustment (95% interval: 0.95–1.43) but significantly greater odds of depression after adjustment for selection bias (95% interval: 1.37–2.13). Adjustments for non-Hispanic Asians and Hispanics also resulted in increased depression odds ratios. These analyses suggest that measurement error and selection bias might be masking the true relationship between race/ethnicity and depression.

Associations between Household Water Fluoridation Status and Drinking Tap or Bottled Water among US Youth Aged 2-19 Years

Mei Lin* Mei Lin Susan O. Griffin Sohyun Park Chien-Hsun Li Valerie Robison Lorena Espinoza

Background: Fluoridation of public water systems (PWS) is the most cost-effective measure to prevent dental caries in the U.S. Its effectiveness may be attenuated if people do not drink tap water. We examined associations of PWS fluoridation status and sociodemographic characteristics with drinking tap water.

Methods: We used data from the 2013–2016 National Health and Nutrition Examination Survey for 5,193 youth aged 2–19 years, whose household tap water had low (<0.6 mg/L) or optimal (0.6–1.2 mg/L) fluoride content. Plain water consumption (none, any tap, bottled only) was obtained from a 24-hour dietary recall. We used 2 binomial regressions to estimate the adjusted prevalence ratios (APR) for drinking any tap vs. bottled only or none and drinking bottled only vs. any tap or none. Independent variables included household water fluoride content (low or optimal) and sociodemographic characteristics.

Results: Overall, 19.4% of youth did not drink plain water, 52.6% drank tap water (43.8% exclusively and 8.8% both tap and bottled) and 28%, bottled water only on a given day. Neither drinking any tap water (APR: 0.96, 95% CI: 0.84–1.10) nor bottled water only (APR: 1.03, 95% CI: 0.86–1.22) were associated with tap water fluoride content. Compared to non-Hispanic (NH) white youth, NH black and Hispanic youth were about 30% less likely to drink tap water and about 60%–80% more likely to drink bottled water only. Youth from families with low income and low education and youth with no past-year dental visit were about 10%–20% less likely to drink tap water than their counterparts.

Conclusions: Our findings suggest that fluoridating water may extend its caries preventive benefits to at least 50% of youth served by the water system. Youth who are likely to be at higher risk for caries (poor, minority, low parental education, and low dental utilization) may be less likely to receive the preventive benefits than their counterparts.

Adjusted Prevalence Ratios and 95% CI for Drinking Tap Water Related to Household Water Fluoridation Status and Sociodemographic Factors Among Children Aged 2-19 Years, National Health and Nutrition Examination Survey 2013-2016

Note. Adjusted prevalence ratios were generated from the binomial regression model including the following covariates: household tap water fluoride level, age, sex, race and ethnicity, family income, household education, being US-born or not, and past-year dental visit status.

The intersectional effect of poverty, home ownership, and racial/ethnic composition on average childhood blood lead levels in Milwaukee County neighborhoods Emily E. Lynch*

Emily Lynch Helen C.S. Meier

Background: Environmental conditions that contribute to childhood lead exposure are spatially patterned. While socioeconomic and racial inequities in childhood lead exposure at the neighborhood level have been documented, research evaluating the intersectional effect of home ownership, poverty, and racial/ethnic composition is limited.

Methods: Using surveillance data from the Wisconsin Department of Health Services, Division of Public Health and the US Census Bureau, this cross-sectional study determined the intersectional effect of poverty, home ownership, and racial/ethnic composition on childhood lead exposure in Milwaukee County neighborhoods using linear regression adjusting for average census tract educational attainment, number of children, and housing age. The final analytical sample consisted of 48,726 individual childhood blood lead levels aggregated to 215 Milwaukee County census tracts.

Results: Census tracts with average childhood blood lead levels greater than or equal to 5 µg/dL were predominantly tracts with low home ownership, high poverty, and majority non-White residents (Figure 1). In examining the intersectional effect, low home ownership, high poverty, and majority non-White tracts had a 1.43 (95% CI: 1.00, 1.86) µg/dL higher average childhood blood lead level than high home ownership, low poverty, and majority White tracts. Race/ethnic differences in the joint effect of low home ownership and high poverty on average childhood blood lead levels were observed (majority non-White tracts 0.76 µg/dL, 95% CI: 0.29, 1.23 vs. majority White tracts 0.63 µg/dL, 95% CI: -0.13, 1.38).

Conclusion: Social determinants at the neighborhood level co-occur and interact to produce inequities in childhood lead exposure. Lead prevention efforts should align with equity-focused housing and economic policies that target primary prevention in neighborhoods disproportionately burdened by childhood lead exposure.

Figure 1. Milwaukee County Census Tract Maps of (A) Average Childhood Blood Lead Levels (B) Percent Non-White Residents (C) Percent Renter Occupied Housing Units and (D) Percent of Families Living Below the Poverty Level
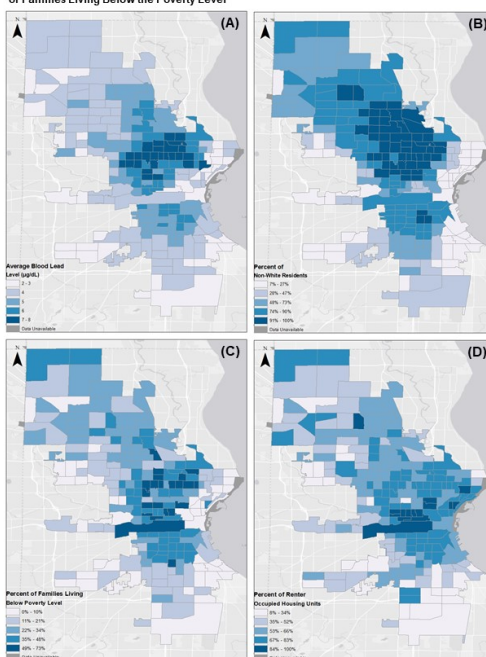
Sources: 2014 – 2016 Lead Surveillance Data from the Wisconsin Department of Health Services, Division of Public Health and U.S. Census Bureau, 2012-2016 American Community Survey 5-Year Estimates. Service Layer Credits: Esri, HERE, Garmin, (c) OpenStreetMap contributors, and the GIS user community. Classification Method: Jenks Natural Breaks (5 classes) based on the geographic distribution of the data at the census tract level.

Fatal police violence in pregnant women's communities and hazard of preterm birth in California Dana Goin* Dana Goin Anu Manchikanti Gomez Kriszta Farkas Deborah Karasek Brittany Chambers Catherine Duarte Andrea Jackson Jennifer Ahern

Background: Exposure to fatal police violence during pregnancy may play a role in population-level inequities in risk for preterm delivery.

Methods: We used California birth and death records and the Fatal Encounters database, which consists of media accounts and public records of fatal police violence, from 2007-2015 to assess whether occurrence of fatal police violence in a woman's Census tract during pregnancy was associated with increased hazard of early (20-31 weeks) and late (32-36 weeks) preterm delivery. We compared women within Census tracts over time, and modeled the exposure as cumulative over the course of gestation. Cox proportional hazard models were used to estimate hazard ratios (HR), and inference was clustered at the Census tract level.

Results: We found fatal police violence was associated with a small increase in the hazard of late preterm birth using both the death records (HR=1.05, 95% CI=1.00, 1.09) and the Fatal Encounters data (HR = 1.03, 95% CI = 1.00, 1.06) to identify incidents of fatal police violence. We did not observe an association for early preterm birth for either the death records (HR = 0.92, 95% CI = 0.80, 1.06) or the Fatal Encounters data (HR = 1.01, 95% CI = 0.94, 1.09).

Conclusion: Exposure to fatal police violence in a woman's Census tract during pregnancy was associated with small increased hazard of late, but not early, preterm delivery. Efforts to reduce police use of lethal force may improve birth outcomes in communities where police violence occurs.

Disparities in urinary tract infection among older American Indian and Alaskan Native adults: Findings from the Urologic Diseases in America project Erline E. Martinez-Miller*

Erline Martinez-Miller Julia B. Ward Kevin C. Abbott Tamara Bavendam Ziya Kirkali John Lim Brian Matlaga Casey Pierce Lydia B. Feinstein

Urinary tract infections (UTIs) are highly prevalent among older adults and are becoming increasingly difficult to treat with multidrug resistance on the rise. In the United States, aging American Indians/Alaskan Natives (AI/ANs) experience disparities in many health conditions, life expectancy, and access to quality healthcare. While the prevalence of UTI has been shown to vary by race/ethnicity, little is known about the burden of UTIs among AI/ANs. We used the 2007-2016 Medicare 5% Sample to assess trends in UTI prevalence, management, and 12-month recurrence among beneficiaries aged ≥65 years. Analyses were conducted both overall (N=582,517) and specifically among AI/ANs (N=2,355). UTI was defined as an outpatient claim with a relevant diagnosis code followed by a pharmacy claim for an anti-infectious agent within 72 hours. From 2007-2016, the annual UTI prevalence averaged 13% among AI/ANs compared to 10% in the overall population, a trend that persisted over time (Figure 1a). AI/ANs were slightly more likely to be prescribed medications for a duration longer than the 3-7 days recommended in guidelines (42% vs. 38% overall). Quinolones were the most commonly prescribed medication overall (42%), but were least likely to be prescribed to AI/ANs (39%) compared to other race/ethnic groups. In contrast, AI/ANs were more likely to be prescribed cephalosporins (15% vs. 11% overall). AI/ANs had the highest 12-month cumulative probability of recurrent UTI following their initial infection (46% vs. 42% overall; Figure 1b). Comorbid conditions were common among AI/ANs with a UTI, with 51% having diabetes and 44% having benign prostatic hyperplasia. Our findings suggest a disparity in UTI burden among older AI/ANs in the United States that persisted over the 10-year study period. The higher frequency of recurrence also increases concerns of drug resistance in this population, which may have contributed to a higher use of cephalosporins.

Figure 1. The prevalence (A) and cumulative probability of 12-month recurrence (B) of urinary tract infection (UTI) among Medicare beneficiaries[a], overall and by race/ethnicity, 2007-2016.
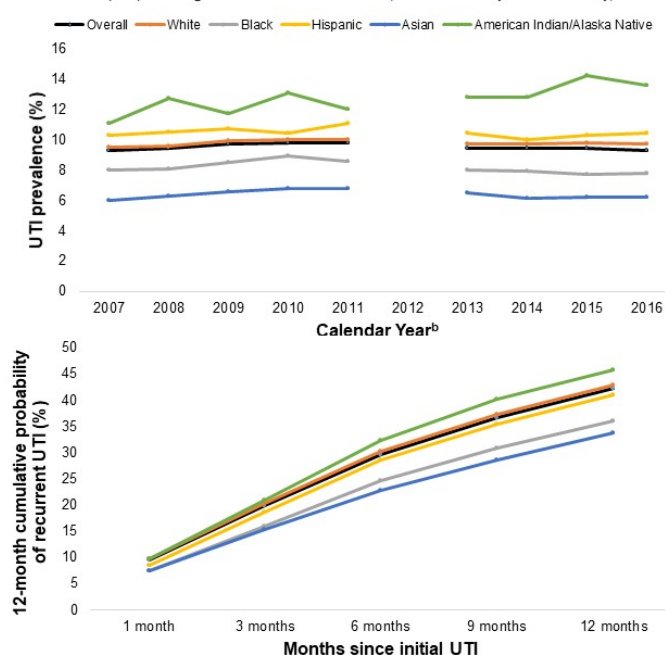
[a]Aged ≥65 years with continuous and full Part A and B enrollment and no HMO enrollment in a given year.
[b]Data for 2012 not included due to a one-time shift in the sources of the 5% which led to poor matching of Part A/B enrollment with Part D enrollment and resulted in biased, low estimates of pharmaceutical use.

Health Disparities

Notable mortality disparities among sexual minorities in Veterans Health Administration, fiscal years 2000-2017 Kristine E Lynch* Kristine Lynch Benjamin Viernes Elise Gatsby Sara Knight Scott L DuVall John R Blosnich

Introduction: Lesbian, gay, and bisexual (LGB) Veterans represent a unique group of the LGB community with distinct characteristics compared to their non-Veteran sexual minority counterparts. Research suggests LGB individuals have greater mortality than heterosexuals, but the extent to which this disparity exists among Veterans is unclear. This study investigated all-cause mortality among a cohort of Veterans with LGB sexual orientation documented within the Veterans Health Administration (VHA) electronic health record (EHR).

Methods: We identified LGB documentation within clinical notes from fiscal year (FY) 2000-2017 using natural language processing. A cohort of patients without LGB documentation was randomly matched 1:1 to the LGB cohort FY of visit, age group, and gender. The index date was date of first LGB documentation for LGB Veterans and the first visit in the matching FY for non-LGB Veterans. Follow-up time accrued from index date to death or October 1, 2017. Kaplan-Meier curves and Cox proportional hazards were used to compare the survival distributions between groups. Sex differences were also assessed.

Results: There were 96,411 Veterans with at least one LGB documentation in the EHR (32% women, 68% men) and 7.7 million Veterans without LGB documentation (7% women, 93% men) for potential matching. Overall, 12,277 LGB Veterans (12.7%) and 8,010 (8.3%) of the 96,411 matched non-LGB Veterans died. The median follow-up time was 4.5 years. After matching on FY, age, and gender, LGB Veterans had significantly higher mortality risk compared to non-LGB Veterans (hazard ratio:1.66 (95% confidence interval: 1.62,1.71)). Although women had better survival than men overall, sex differences between LGB Veterans and non-LGB Veterans were similar.

Conclusions: Similar to what has been reported outside VHA, we observed notable mortality disparities in LGB Veterans compared to non-LGB Veterans after accounting for differences in age and gender distributions

Figure 1. Survival curves of LGB and non-LGB Veterans. The dashed red line is the curve for non-LGB Veterans prior to age and gender matching (FY match only). Solid lines are survival curves for LGB (black line) and non-LGB (red line) after age, gender, and FY matching.
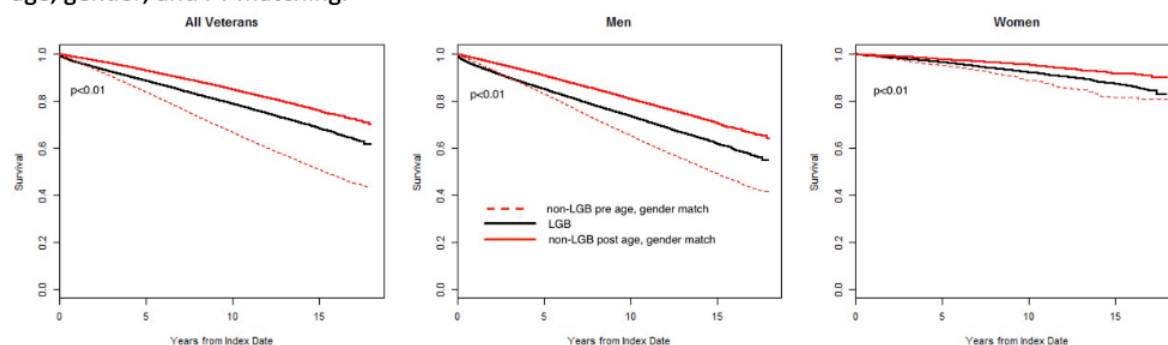
Examination of the allostatic load construct and its longitudinal association with health outcomes in the Boston Puerto Rican Health Study
Andrea Lopez Cepero* Andrea Lopez-Cepero Amanda McClain Milagros C. Rosal Katherine L. Tucker Josiemer Mattei

Introduction: Despite evidence on allostatic load (AL) as a model explaining associations between stress and disease, there is no consensus on how to measure it. This study aimed to contrast various AL constructs and their longitudinal associations with disease and disability.

Methods: Baseline and 5-year follow-up data from 738 adults participating in the Boston Puerto Rican Health Study were used. Five AL scores were created by summing presence of 21 dysregulated multi-system physiological parameters using: (1) z-scores, (2) population-based quartile cutoffs, (3) clinical-based cutoffs, (4) ten pre-selected clinical-based cutoffs (AL-reduced); and (5) twelve clinical-based cutoffs selected a posteriori based on association with disease (AL-select). Multivariable-adjusted logistic regression models were used to examine associations between each AL score at baseline and 5-year incident type 2 diabetes (T2D), cardiovascular disease (CVD), activities (or instrumental activities) of daily living (ADL; IADL) for physical impairment, and cognitive impairment.

Results: AL z-score was associated with higher odds of IADL. AL-quartile was associated with greater odds of T2D, CVD, and IADL. AL-clinical and AL-reduced were each similarly associated with higher odds of T2D, CVD, IADL, and ADL. AL-select showed stronger associations than other AL constructs with T2D, CVD, IADL, and ADL, and with higher odds of cognitive impairment.

Conclusion: AL scores computed with clinical-based cutoffs performed robustly. A select AL clinical construct comprising 12 multi-system parameters was the strongest predictor of disease and disability, providing a practical operationalization of AL and supporting its use as a disease-predicting model.

Figure 1. Association between baseline categories of AL-select and health outcomes at 5 years.
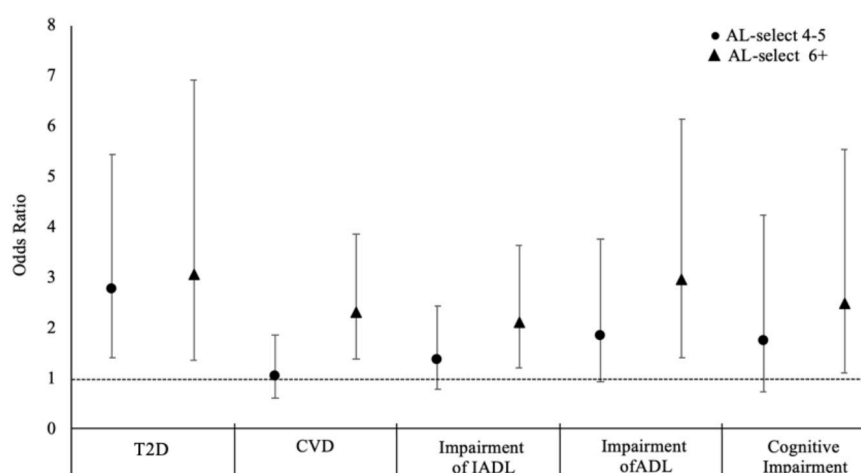
AL=allostatic load. T2D=type 2 diabetes; CVD=cardiovascular disease; ADL=activities of daily living IADL= instrumental activities of daily living. All models adjusted for baseline covariates . All models adjusted for baseline covariates. Reference group includes sums of 0-3 parameters. Excluded individuals with disease at baseline. For T2D, none of the AL constructs contain fasting glucose, HOMA-IR, glycosylated hemoglobin or diabetes medications. Diabetes: n=450; CVD: n=580; IADL: n=385; ADL: n=217; cognitive impairment: n=288.

Social inequalities and regional disparities in edentulism among Brazilian adults Raquel Ferreira* Raquel Ferreira Lorrany Gabriela Rodrigues Fernanda Lamounier Campos Anna Rachel Soares Santos Ichiro Kawachi

We evaluated the magnitude of socioeconomic inequalities in edentulism among Brazilian regions as well as the effect of the use of dental services. Data from the National Oral Health Survey (SB Brazil, 2010) of adults (35-45 years, n = 9779) and seniors (65-75 years, n = 7619) were analyzed. Edentulism was defined by the absence of 32 teeth. Socioeconomic position was measured by years of schooling (0-3, 4-7, 8-11, >12 years). Regular use of dental services was defined as a dental visit within the past year. The prevalence of age and sex-adjusted edentulism was estimated for each level of education and region of Brazil. The magnitude of inequalities was estimated by the Relative Inequality Index (RII) and Slope Inequality Index (SII). Across all regions of Brazil, the highest prevalence of edentulism was observed in the less educated groups. Meta-analysis suggested homogeneity in RII and SII among regions. The pooled RII were 0.06 and 0.53 and the SII was -0.05 and -0.35 for adults and seniors, respectively. The RII values were attenuated by 55.4% and 12.6% for adults and seniors who regularly used dental services, respectively. The attenuation was 54.0% (adults) and 34.9% (seniors) in the SII. There is a social gradient in edentulism across all regions of Brazil, and this gradient is attenuated among those who use dental services regularly.

Health Disparities

Disparities by Skin Color among Young African-American Women Kristen Moore* Kristen Moore Donna Baird David Williams

Within-group disparities associated with differences in skin color is a globally important but scarcely studied dimension of inequality. Among African-Americans, light-skin disadvantage (hypothesized to result from intra-racial colorism due to resentment by darker-skinned individuals) has been described in majority African-American populations but is less studied than dark-skinned disadvantage. We investigated whether light-skin disadvantage is seen in a contemporary African-American study population, most of whom have resided throughout their lives in an area with mostly African-Americans. Secondly, we investigated dark-skin disadvantage in this same group. Utilizing a broad range of data we examined outcomes in three domains: socioeconomic, health, and psychosocial. We used skin reflectance and questionnaire data from 1,693, young African-American women in Detroit, Michigan, and dichotomized each outcome as advantaged/disadvantaged. We tested for evidence of light-skin disadvantage by comparing women with light vs. medium skin color with prevalence differences and 95% CIs. For outcomes not exhibiting light-skin disadvantage, we evaluated dark-skin disadvantage with prevalence ratios and 95% CIs for a 10-unit increase in skin color. There was little evidence for light-skin disadvantage, but darker skin was associated with disadvantage across socioeconomic, health, and psychosocial domains. The strongest associations were for socioeconomic status, but even after controlling for the strongest of these, other associations were seen; e.g., higher body mass index (PR: 1.14 95% CI: 1.08-1.20) and higher financial stress (PR: 1.18 95% CI: 1.06-1.31). Dark-skin disadvantage was the predominant form of colorism. Utilizing skin color metrics in public health research may capture more useful information than simple racial/ethnic categories, and such research could bring awareness to the deep-rooted colorism in society today.

LATEBREAKER

Health Disparities

Socioeconomic trajectories of early adulthood and their contribution to later life cardiometabolic health, 1970 British Cohort Study (BCS70) Eleanor Winpenny* 3647]
Winpenny Jane Maddock Rebecca Hardy

Background

There is limited understanding of how inequalities in cardiovascular health are generated across the life course. In this study we assess the contribution of early adulthood socioeconomic trajectories (SETs) to cardiovascular health in mid-adulthood.

Methods

Participants are from BCS70 (n=7,061) with data on economic activity during early adulthood (age 16-24y) and cardiometabolic outcomes at age 46y. Longitudinal latent class analysis was used to identify classes following different SETs, based on participation in education, employment by occupational class, unemployment or inactivity from age 16y to 24y. Cardiometabolic outcomes (waist circumference, systolic blood pressure (SBP), HDL cholesterol, triglycerides, HbA1c) at age 46 were regressed on early adulthood SET class, with and without adjustment for adult socioeconomic position (SEP) (age 46). Models were adjusted for sex, childhood SEP, adolescent health and early adulthood partnership and parenthood.

Results

Six classes of early adulthood SET were identified: (1) Continued education, (2) Managerial employment, (3) Skilled non-manual employment, (4) Skilled manual employment, (5) Partly skilled employment, (6) Inactive. Compared to class 1 'Continued education', waist circumference showed an increase across the classes to +3.94cm (95%CI 2.35,5.52) in class 6, and triglycerides an increase to +14.27% (95%CI 3.88,25.7) in class 6. Compared to class 1, SBP was higher across classes 2-5, and HDL cholesterol lower across classes 2-6. No difference was seen in HbA1c levels across classes. Adjustment for SEP at age 46 resulted in only a small attenuation of these coefficients.

Conclusion

These findings support the hypothesis that the exposures of early adulthood may contribute to development of behaviors or psycho-social factors which persist through adult life; further research is needed to understand these pathways, and the extent to which early adulthood SETs are mediated by SEP in later life.

Maternal vulnerabilities as a risk factor for severe, early life respiratory syncytial virus (RSV)-related illness: a birth cohort study in Ontario (Canada), 2012-2018 Tiffany Fitzpatrick* 3647] Fitzpatrick J Dayre McNally Jeffrey Kwong Hong lu David Fisman Astrid Guttmann

Background: Respiratory syncytial virus (RSV) is the leading cause of hospitalization among infants globally. Several RSV vaccine candidates are currently in trial and the severity of RSV-related illness can be reduced with prophylaxis. To optimize delivery of these programs and reduce inequities, a detailed understanding of risk factors for severe RSV-related illness is required.

Objectives: To quantify the risks of severe, early life RSV-related illness in terms of medical conditions, birth characteristics and novel socio-economic factors.

Methods: We used linked population-based health and socio-demographic administrative data for all children born in Ontario (Apr 1st,2012-March 31st,2018) to identify all RSV-related hospitalizations and Emergency Department (ED) visits occurring before a child's third birthday or end of follow-up (March 31st, 2019). We calculated the relative risk of RSV-related admission or ED visit (separately), adjusted for factors related to medical complexity (e.g. congenital disease) and RSV transmission (e.g. seasonality).

Results: 11,279 RSV-related hospitalizations and 3,146 ED visits were identified among 789,484 children; 57% of admissions and 49% of ED visits occurred before 6 months of age. We identified several socio-economic factors independently associated with increased risk of severe RSV-related illness, including several maternal factors: young age at first delivery (RR <20 vs 40+ years: 2.27, 95% CI: (1.89, 2.73)), involvement with the criminal justice system [1.34 (1.16, 1.55)], social assistance use (varied by program; e.g. Ontario Works vs no use: 1.53 (1.45, 1.62)), homelessness [1.69 (1.01, 2.83)], mental health/addictions concerns [1.51 (1.36, 1.67)] and child apprehension [1.59 (1.29, 1.96)].

Conclusions: Maternal vulnerabilities are independently associated with increased risk of severe, early life RSV-related illness, which could inform the selection of high-risk groups for RSV prophylaxis or immunization programs.

Differences in Tinnitus Characteristics and Management Needs Between Urban and Rural VA-using Veterans
Elizabeth R. Hooker, MS MPH* 3647] Hooker Tess A. Gilbert Kelly Reavis Kathleen F. Carlson

Background: Tinnitus, or ringing in the ears, is prevalent among military Veterans and can adversely impact quality of life. The Veterans Health Administration (VHA) offers evidence-based tinnitus management that can significantly reduce tinnitus associated distress, yet few Veterans access this service. To better understand access barriers, we examined differences in characteristics and tinnitus management needs between urban and rural Veterans enrolled in the VHA.

Methods: We conducted random stratified sampling of 1,800 VHA health care using Veterans with a tinnitus diagnosis. Veterans were invited to participate in an online or mailed survey asking about their tinnitus symptoms, knowledge about tinnitus management, and demographics; 891 participated. Veterans were categorized as urban versus rural based on their census tract RUCA score. We examined associations between Veterans' rurality and their tinnitus characteristics and management needs using modified Poisson regression models. Inverse probability weights were used to account for sample stratification and potential non-response bias, and multiple imputation was used to address missing data.

Results: Among Veterans with a tinnitus diagnosis, we estimated 44.1% (95% confidence interval [CI]: 38.7, 49.4) were rural; these Veterans were generally older, white, and with lower health care utilization compared to urban Veterans. Nearly half of rural Veterans, 48.2% (95% CI: 39.8, 56.6), had severe or very severe tinnitus, and 23.1% (95% CI: 16.0, 30.3) expressed strong interest in tinnitus management. Compared to urban Veterans, rural Veterans with tinnitus may be more likely to have very severe tinnitus (prevalence ratio [PR]=1.3; 95% CI: 0.9, 2.0), yet no more likely to be interested in tinnitus management (PR=0.9; 95% CI: 0.6, 1.3).

Conclusions: Our results suggest that nearly half of Veterans with tinnitus live rurally but the perceived need for tinnitus management is low. Future work should examine methods to create awareness of evidence-based tinnitus services and examine mechanisms to improve awareness of and access to these services among rural Veterans.

Disparity among state-specific prevalence of current e-cigarette use by disability status and type – United States, BRFSS 2016-2018 Q. Cathy. Zhang* 3647] Zhang Elizabeth A. Courtney-Long Lisa B. Sinclair Sierra Reese Brian S. Armour Stuart K. Shapira

Monitoring changes in tobacco use can help inform tobacco control policies and public health practices. The objective of this study was to assess the US overall and state-specific prevalence of e-cigarette use among adults by disability status, disability type, sex, and age group. People with disabilities are those who have serious difficulty with vision, hearing, mobility, cognition, or any difficulty with self-care or independent living; adults with disabilities represent nearly 25% (61 million) of the US population. Aggregated data from the 2016-2018 Behavioral Risk Factor Surveillance System (BRFSS), a state-based telephone survey of US adults aged ≥18 years (n=1,150,775), were used to estimate overall and state-specific prevalence of current e-cigarette use (reporting using an e-cigarette every day or some days at the time of the survey) among adults with and without disabilities, overall and stratified by sex and age group. 2018 BRFSS consists of data for 36 states only since e-cigarettes questions were in the optional module that year. Therefore estimates for 14 states plus DC will consist of 2016 and 2017 2 years of data. Current e-cigarette use was significantly higher among adults with disabilities than those without disabilities (6.5% vs 4.3%), and use among adults with disabilities varied by state, ranging from 2.5% in the District of Columbia to 10.0% in Colorado. For adults with a disability, the prevalence of e-cigarette use also varied by disability type, sex, and age group, with the highest median prevalence among those with cognitive disabilities (10.0%), those aged 18–24 years (18.7%), and males (7.3%). The study findings underscore differences by disability status that are not fully understood but can be addressed in public health programmatic efforts.

Life-course effects of childhood adversity and adult socio-economic status on depression among older people in Japan: Four-way decomposition analysis Aki Yazawa* Aki Yazawa Ichiro Kawachi

Adverse childhood experiences (ACE) such as maltreatment, neglect, and poverty have been linked to diminished health achievement across the life course. Several potential mechanisms have been proposed – e.g., critical period hypothesis, social trajectory hypothesis, stress sensitization hypothesis. In reality, multiple pathways are believed to coexist simultaneously – e.g., the direct effect of ACE on health, and mediation and/or interaction between ACE and adult socioeconomic status on health. Less well understood is the quantitative contributions of each pathway on adult health. We used a four-way decomposition analysis to explain how mediation and/or interaction between ACE and adult socioeconomic status (SES) determine depression among older people. Data came from two waves (2013 and 2016) of the Japan Gerontological Evaluation Study, a nationwide cohort of people aged 65 years or older in Japan. Participants were asked whether they had experienced the following adversities before the age of 18: parental loss, parental divorce, parental mental illness, domestic violence, physical abuse, psychological neglect, psychological abuse, and economic disadvantage. Low adult SES was defined as earning less than 2 million yen of equivalized income and fewer than 10 years of schooling. Depressive symptoms in 2016 were assessed using the Geriatrics Depression Scale (19.9%). Results showed that ACE was associated with a direct effect on depression in later life, largely irrespective of adult SES. Nonetheless, a pure indirect effect through low adult SES was observed accounting for approximately 6% of the total effect. Considering the limited magnitude of mediation, we conclude that ACE is a strong and independent determinant of depression in later life, and this supports the critical period hypothesis.

Health Disparities

Maternal socioeconomic status and risk of congenital heart diseases Qun (Grace) Miao* Qun (Grace) Miao Sandra Dunn Shi Wu Wen Jane Lougheed Mark Walker

Background/purpose: Congenital heart disease (CHD) is a leading cause of infant morbidity and mortality in Canada. Although numerous studies have been published regarding socioeconomic status (SES) disparities and the risk of CHD, findings remain unclear and inconsistent. The purpose of this study is to examine the relationships between maternal SES indicators and risk of CHD. Methods: This was a population-based retrospective cohort study, including all singleton stillbirths and live births in Ontario hospitals from April 1, 2012 to March 31, 2017. The data sources were the BORN Information System and the Canadian Institute for Health Information databases. Multivariate logistic regression models were performed to examine the relationship between the maternal neighbourhood after-tax income and the risk of CHD. Income was categorized by quintiles (Q1 – lowest income to Q5 – highest income). Adjustments were made for maternal age at birth, parity, assisted reproductive technology, obesity, previous caesarean section, pre-existing health conditions, folic acid intake, substance use during pregnancy, rural or urban residence, and infant's sex. Results: Among the cohort of 670,102 singletons, 7,971 (1.19%) infants with CHD were identified; 2,585 (0.39%) cases were severe CHD. Compared to infants whose mothers lived in Q5 neighbourhoods (highest income), infants whose mothers lived in Q1 neighbourhoods (lowest income) had a higher risk of CHD (adjusted OR: 1.17, 95% CI: 1.08-1.27). There was no significant difference in the risk of CHD for infants with maternal residences in Q2, Q3, or Q4 neighbourhoods. Compared to those in urban areas, infants with rural maternal residences had a higher risk of CHD (adjusted OR: 1.11, 95% CI: 1.03-1.19). Compared to males, female infants had a 10% increased risk of CHD (adjusted OR: 1.10, 95% CI: 1.04-1.15). Conclusion: Low maternal SES increases risk of CHD, highlighting a significant social inequity in Ontario, Canada.

Identifying the extent that sex, age, and BMI impact are associated with medical and pharmacy costs in a large school district in the United States Ray Martell Merrill* Ray Merrill Rylan Fowers

Objective To identify the extent that sex, age, and body mass index (BMI) is associated with medical and pharmacy costs.
Design Retrospective cohort.
Setting A school district in the Western United States involving 2531 workers continuously employed during 2011-2014.
Main outcome measures Medical and pharmacy costs and BMI.
Results Approximately 84% of employees participated in wellness screening. Participants were 1.03 (95% CI 1.01- 1.06) times more likely to be women and younger (M = 47.8 vs. 49.8, p < 0.001). Median medical and pharmacy costs were higher for women than men, increased with age, and were greater in morbidly obese individuals (p < 0.001). Annual pharmacy claims were 18% more likely to be filed by women than men, 23% more likely filed by those aged ≥60 versus <40 years, and 6% more likely filed by morbidly obese individuals than of normal weight (p < 0.001) individuals. Greater medical and pharmacy costs in older age were most pronounced in underweight and morbidly obese groups. Higher use of medication among women than men was primarily because of drugs involving birth control, osteoporosis, thyroid disease, and urinary tract infection. Higher medication use in older age was primarily related to medications used to treat gastrointestinal problems. Medication use was positively associated with BMI weight classifications for most of the 33 drug types considered, with exceptions involving birth control, herpes, and osteoporosis. A J-shape relationship was observed between BMI and medication use for acne, antibiotic, cold/influenza/allergy, eye infection, edema, muscle spasms, pain, and ulcers.
Conclusions Medications associated with higher medical and pharmacy costs among women, older age, and underweight or obese individuals are identified. Lowering medical and pharmacy costs requires weight management in older ages, particularly for underweight and obese. Higher pharmacy costs for certain drugs among underweight individuals may be associated with poorer nutrition.

Assessing the validity of health administrative data compared to population health survey data for the ascertainment of low back pain Jessica J. Wong* Jessica Wong Pierre Côté Andrea C. Tricco Laura C. Rosella

Background: Low back pain (LBP) is a high burden condition that lacks routine surveillance data. Health administrative data may be used for surveillance, but its validity for ascertaining LBP has not been established. We aimed to 1) assess the validity of health administrative data compared to self-reported data for ascertaining LBP in a population-based cohort of adults in Ontario; 2) describe the characteristics of LBP cases based on the data source.

Methods: Adult respondents (≥18 years) of 5 cycles of the Canadian Community Health Survey (CCHS) from 2003 to 2012 were included (N=150,695). CCHS data were individually linked to health administrative data, including Ontario Health Insurance Plan and hospitalization data. As the reference standard, LBP ascertainment from CCHS was based on self-report of a back problem diagnosed by a health professional. LBP ascertainment from billing records was identified as ≥1 physician billing or procedural code for LBP within 2 years before CCHS interview date. Prevalence (weighted with CCHS sampling weights), Kappa coefficient, percent agreement, sensitivity, specificity, positive and negative predictive values (PV) were calculated.

Results: LBP prevalence was 13.1% in health administrative data and 21.2% using self-reported data. Kappa was 0.23 (95% CI 0.22-0.24). Sensitivity of using health administrative data was 0.30, specificity was 0.90, positive PV was 0.49, and negative PV was 0.80. Positive and negative agreement were 0.37 and 0.85 respectively. When assessing cases identified by health administrative data that did not self-report LBP, a higher proportion was female or in the lowest income quintile, and a lower proportion consulted a chiropractor.

Conclusions: Health administrative data may underestimate LBP prevalence in adults and lead to misclassification bias that is likely non-differential. There was a higher probability that adults defined as having no LBP based on health administrative data truly did not have LBP.

Figure 1. Canadian Community Health Survey (CCHS) respondents from Ontario individually linked to provincial health administrative data from 2003 to 2012
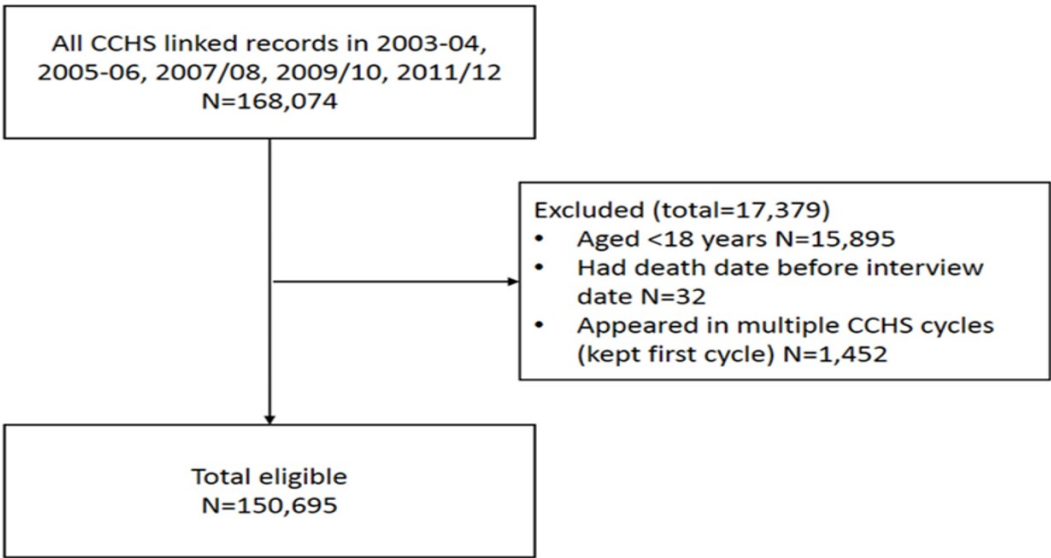
CCHS – Canadian Community Health Survey

Health service quality as a driver of HIV testing and retention in rural South Africa Hannah Leslie* Hannah Leslie Rebecca West Rhian Twine Audrey Pettifor Kathleen Kahn Sheri A. Lippman

Background: Early and sustained engagement with health care is essential to ending the HIV epidemic. Poor quality of care may deter individuals from using HIV services. We conducted a facility assessment and population survey to test effects of facility quality on HIV service use in a high HIV-prevalence area of Mpumalanga, South Africa.

Methods: We assessed care and patient experience at 3 24-hour community health centres (CHC) and 6 basic primary clinics in a demographic surveillance area using multiple methods (Figure). A simultaneous household survey of 2089 adults aged 18-49 assessed HIV testing in the past 12 months and lapses in care ($\geq$6 months with no clinic visits) among those on treatment. We use log-binomial models with survey weights and clustering to model the effect of quality of the closest facility on testing and lapses among 907 respondents in 12 villages served by a single facility.

Results: Facilities showed gaps in inputs to care, modest provider stigma, and wait times from 1.5 to 2 hours on average. Most patients were confident of receiving effective care. 79% of women and 44% of men not previously positive reported an HIV test and 36 of 114 of those on treatment reported $\geq$1 lapse. Testing among women was negatively associated with nearest facility being a CHC (adjusted RR 0.84, 95% CI 0.82, 0.86) and provider stigma (ARR 0.13, 95% CI 0.05, 0.35), and positively with patient confidence in care (ARR 6.11, 95% CI 3.82, 9.77). Testing among men was higher near CHCs (ARR 1.25, 95% CI 1.16, 1.35). Wait time was positively associated with testing and negatively associated with lapses in care.

Conclusion: Health facility characteristics are associated with population-based HIV service use, though associations differed by gender. Patient trust was particularly important for women while men living near 24-hour CHCs reported more HIV testing. Patient-reported quality of care may shape utilization decisions and can guide health system strengthening to improve population outcomes.

Clinic Quality Assessment methods

Facility Audits (n=9)	Provider Interviews (n=86)	Patient Exit Interviews (n=226)	Mystery Clients (n=90)	Time-Motion Observations (n=225)
• Service availability and readiness • Inputs to care (workforce, infrastructure, tools)	• Provider experience • Job satisfaction • Stigmatizing views related to HIV • Knowledge of HIV treatment as prevention (TasP)	• Patient experience with care • Overall confidence in health system	• Volunteers sought HIV counseling and testing (HCT) • Assessed care competence, user experience, confidence in the clinic	• Followed patients throughout visit to record wait time and time spent with providers

Impact of trauma center accreditation on mortality and complications in a Canadian trauma system: An interrupted time series analysis.

Brice Batomen* Brice Batomen Lynne Moore Erin Strumpf Arijit Nandi

Background: Trauma systems have led to important reductions in injury mortality in many high-income countries. Periodic external accreditation visits aiming to determine whether trauma centers are fulfilling the criteria for optimal care are part of most trauma systems. However, despite the growing trend towards accreditation of trauma centers, its impact remains unclear. In addition, a recent systematic review found inconsistent results on the association between accreditation and patient outcomes, mostly due to the lack of robust controls. We aim to address these gaps by assessing the impact of accreditation on patient outcomes using a quasi-experimental design.

Methods: Data are from admissions to all level I and II trauma centers in Quebec, Canada between 2008 and 2017. We first obtained monthly estimates of the proportions of in-hospital mortality and complications adjusted for change in patient case-mix using prognostic scores. We then used piecewise regressions with autocorrelated errors to estimates change in levels and trends in both outcomes due to accreditation.

Results: Globally, we did not observe an association between accreditation and studied outcomes. However, the impact of accreditation was heterogenous across centers, and those experiencing an increase in mortality or complications during the pre-accreditation period, had a decrease in levels and trends following accreditation.

Conclusion: Using a quasi-experimental design while accounting for changes in patient case-mix, our results indicate that accreditation was mostly beneficial for centers that were experiencing a decrease in performance in the months preceding the accreditation.

Center 2 : Adjusted
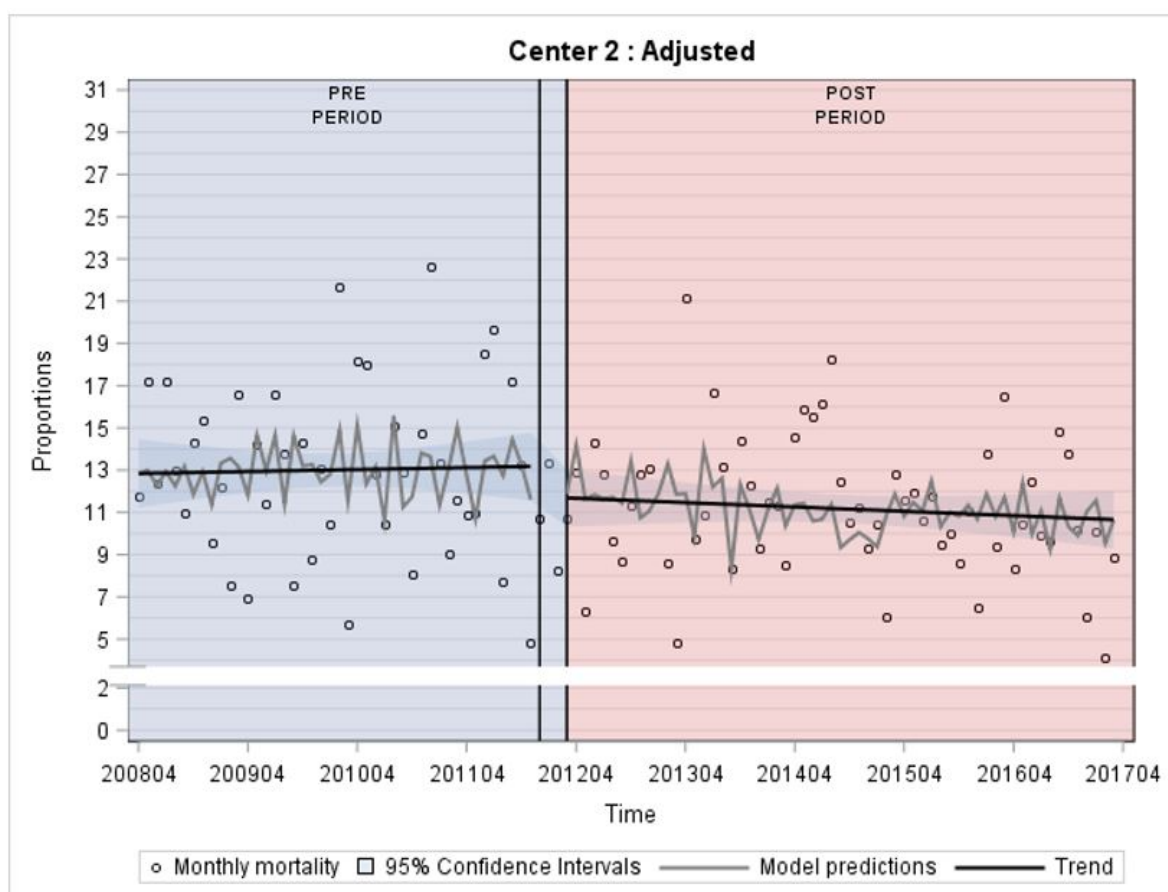
Influenza vaccinated patients have a higher hospitalization risk, but lower follow-up mortality: cohort study of 2014/15 flu season in Switzerland
Agne Ulyte* Agne Ulyte Wenjia Wei Oliver Gruebner Caroline Bähler Beat Brüngger Eva Blozik Holger Dressel Matthias Schwenkglenks Viktor von Wyl

Real-world effectiveness of influenza vaccination (IV) is debated, especially for the elderly. IV is hypothesized to attenuate health outcomes, need for hospitalization and mortality after flu.

This study aimed to estimate the attenuating effect of IV on severe health outcomes. We analyzed mandatory Swiss health insurance claims of a cohort of 343505 patients >18 years old and with chronic illnesses for whom IV was recommended in 2014/15. Information on sex, age, health status, comorbidities (by medication use and inpatient diagnoses), health care use and IV was extracted. IV effect was analyzed in multi-state multivariate Cox model (MSM) for all-cause mortality, hospitalization with a respiratory infection or its potential complications, and mortality after such a hospitalization. We compared the hazard ratios (HR) during and after season, as well as for the joint period. We additionally analyzed the subgroup of ≥65 years old patients (177107). We did not analyze before-season period, because patients with high short-term mortality risk are expected not to be vaccinated, introducing potential bias.

The table shows the number of events (N) and HR estimates of MSM. Paradoxically, during flu season, vaccinated patients had increased HR of hospitalization (1.25; 1.21 for ≥65), and decreased HR of overall mortality before (0.79; 0.80 for ≥65) and after hospitalization (0.80; 0.86 for ≥65). CIs of the latter overlapped no effect, potentially due to smaller N. HRs of all outcomes were larger during than after flu season.

Therefore, while overall mortality estimates may still be affected by residual confounding, the mortality risk reduction after hospitalization in persons with IV is consistent with a previously hypothesized, specific attenuating effect of IV to prevent severe health outcomes after flu. Analyzing multiple outcomes may provide a key to reconcile inconsistent findings regarding IV effectiveness in other observational studies.

Table N of events of the outcomes and HR estimates of multi-state Cox models for patients with chronic illnesses: hospitalization and death before, during and after flu season 2014/15. HR [95% CI]

	During season (Dec 16 – May 3)			After season (May 3 – Aug 31)		
	D	H	H→D	D	H	H→D
All ages >18						
N	3764	1655	255	2662	861	109
HR [95% CI]	0.79 [0.74-0.85]	1.25 [1.13-1.39]	0.80 [0.60-1.05]	0.91 [0.84-0.99]	1.12 [0.97-1.30]	0.79 [0.51-1.23]
≥65 subgroup						
N	3407	1307	220	2341	659	88
HR [95% CI]	0.80 [0.75-0.86]	1.21 [1.08-1.35]	0.86 [0.64-1.15]	0.87 [0.80-0.95]	1.05 [0.90-1.23]	0.65 [0.41-1.05]

	During and after season (Dec 16 – Aug 31)					
	D	H	H→D			
All ages >18						
N	6357	2440	433			
HR [95% CI]	0.84 [0.79-0.88]	1.21 [1.11-1.32]	0.77 [0.62-0.95]			
≥65 subgroup						
N	5785	1307	286			
HR [95% CI]	0.83 [0.78-0.88]	1.15 [1.05-1.27]	0.79 [0.62-0.99]			

D – death, H – first hospitalization, H→D – death after hospitalization during specified period, HR – hazard ratio, >18 – patients older than 18 years, ≥65 – 65 years old or older. Each time period was modelled separately. CI of HR in grey overlap 1.00.

Personal health record utilization patterns among a national cohort of Veterans living with HIV: a longitudinal multi-channel sequence analysis Tigran Avoundjian* Tigran Avoundjian Lara Troszak Shayna Cave Stephanie Shimada Keith McInnes Amanda Midboe

Personal health records (PHR) may facilitate health management for patients with chronic diseases, such as HIV. In a national cohort of Veterans living with HIV, we longitudinally characterized utilization patterns and associated patient characteristics of the Veteran's Health Administration's (VHA) PHR, MyHealtheVet (MHV).

We used VHA administrative data to identify all Veterans living with HIV who used MHV between fiscal year (FY) 2013 and FY 2018. We used multichannel sequence analysis to compare patient trajectories of MHV tool use over a two-year period, starting at the earlier of MHV registration or 10/01/12. MHV tools of interest included Rx Refill, Blue Button (downloads medical records), Secure Messaging, View Appointments and View Labs. We created separate quarterly trajectories of tool use for each patient and MHV tool. Using multichannel optimal matching, we summarized differences in tool use as a dissimilarity matrix of overall differences in MHV use. We used hierarchical clustering to organize Veterans into specific MHV use typologies.

Among 11843 Veterans living with HIV who used MHV between FY13 and FY18, we identified 5 profiles of MHV users (Figure): primarily Rx Refill use (24% of total sample); low tool use (50%); appointment-driven use (8%); high tool use (12%); and medication and monitoring use (7%). The low tool use profile had the highest proportion of Black Veterans (46%), Veterans who were unstably housed (18%), and Veterans with a substance use disorder (18%) or alcohol use disorder (14%). The high tool use profile had the highest proportion of White Veterans (67%), Veterans living in rural areas (19%), and Veterans with depression (43%), bipolar (7%), or PTSD (19%).

Our findings highlight the diversity in PHR use patterns among Veterans living with HIV and potential disparities in PHR use by race, housing status, and substance use. Further research is needed to uncover barriers to PHR use for patients in the low tool use profile.

MHV Tool Use Across Quarters (by Cluster)
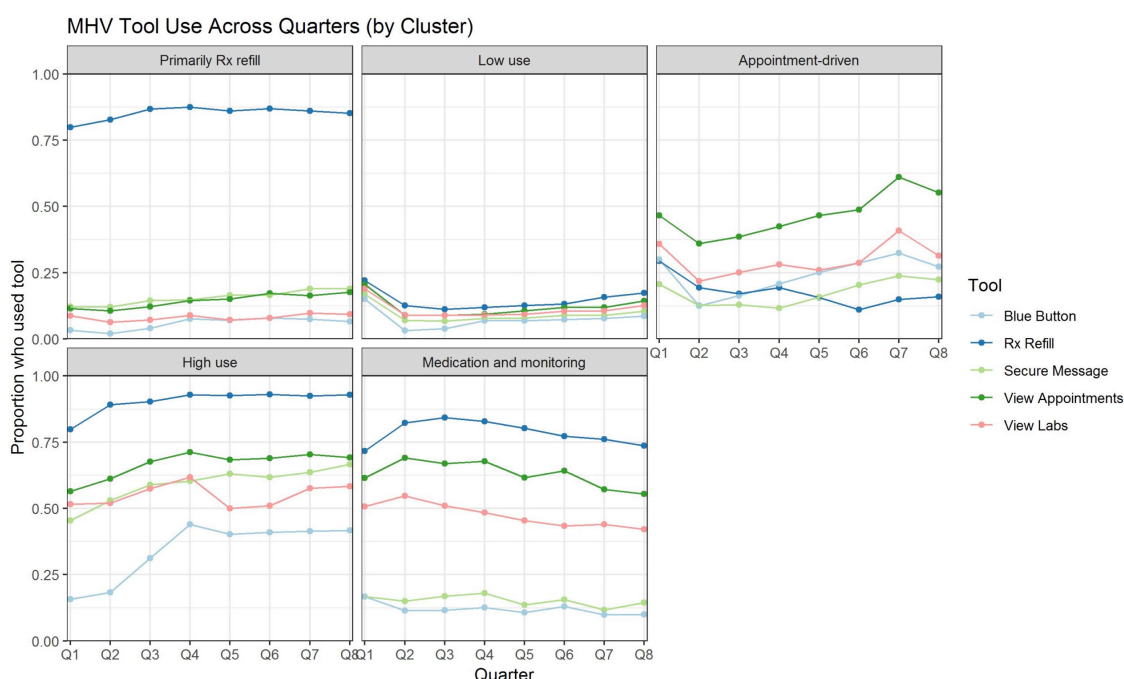
The impact of abortion law reforms on women's health services and outcomes in low- and middle-income countries: a systematic review Foluso Ishola* Foluso Ishola Vivian Ukah Babatunde Alli Arijit Nandi

A number of countries are revisiting their abortion legislation and making considerable changes in constitutions and penal codes. However, the implications of these legislative reforms on women's health services and outcomes in most LMICs is uncertain. First, there are methodological challenges to the evaluation of abortion laws, since these changes are not exogenous. Second, extant evaluations may be limited in terms of their generalizability. This systematic review aimed to synthesize empirical research evidence concerning the impact of abortion law reforms on women's health services and outcomes in LMICs. Methods: We searched Medline, Embase, CINAHL, and Web of Science databases. As our goal is to draw inference on the impact of abortion law reforms, we included quasi-experimental studies examining the impact of change in abortion laws on use and access to abortion services, fertility rates, contraceptives and maternal and neonatal morbidity and mortality. We assessed the methodological quality of studies using the quasi-experimental study designs series checklist. Result: Of the 2796 records identified, 1956 titles and abstracts were screened, and 32 articles assessed for full-text review, which resulted in 14 eligible articles. The studies were conducted in Uruguay, Ethiopia, Portugal, Mexico, Nepal, Chile, Romania, India, and Ghana. Reform year ranged from 1972 to 2012. Legislative reforms focused on increasing restrictions in 2 studies and decriminalization in 12 studies. Designs used included pretest-posttest, difference-in-difference, synthetic control, and interrupted time series. Abortion reforms reduced rates of birth among women in their prime reproductive ages particularly teenagers and single mothers, increased the use of the contraceptives when there was post abortion contraceptive counselling, reduced low birth weight and maternal morbidity. The suboptimal study designs and lack of studies evaluating use of and access to abortion services shows further research is needed.

Socioeconomic inequalities in healthcare utilization in Paraguay: description of trends from 1999 to 2018 Diego A. Capurro* Diego Capurro Sam Harper

Background. Provision of healthcare is critical to improve population health and reduce health inequalities. Paraguay's healthcare system is characterized by segmented sub-systems and low public spending, which translates into limited coverage and asymmetries in terms of access and quality of care. Currently, there is no rigorous assessment of the magnitude and change of socioeconomic inequalities in healthcare use in the country.

Methods. We used data from the Paraguayan Permanent Household Surveys (EPH), for the period 1999-2018. EPH are cross-sectional surveys conducted annually, designed to generate national estimates on relevant social indicators. Healthcare use was defined as having reported a health problem and subsequent healthcare use in the last 90 days before interview. We used poverty-to-income ratio as the socioeconomic stratifier. Income-related inequality was summarized by the concentration index, in its relative and absolute versions, corrected to account for the binary nature of the outcome. To explore potential heterogeneities, analyses were also conducted by area, sex, and among the elderly.

Findings. Inequalities were present in all years assessed, although their magnitude varied over the period. Relative inequality ranged from 0.21 (95%CI 0.17; 0.25) in 1999 to 0.04 (95%CI -0.01; 0.08) in 2018. Absolute inequality ranged from 0.22 (95%CI 0.17; 0.26) in 2001 to 0.03 (95%CI -0.01; 0.08) in 2018. Trends in both scales were generally stable from 1999 to 2009, with a noticeable decrease in 2010. The sharpest decreases relative to the 1999 baseline were observed in the period 2010-2018, reflecting changes in healthcare use and income distribution. In general, trends were similar in sub-group analyses. Decreases coincide temporally with increments in public health expenditure, the removal of user fees in public healthcare facilities, and the expansion of conditional cash-transfer programs. Future research should disentangle their roles in explaining the trends described.

Trends of income-related inequality in health care use
Paraguay, EPH 1999 to 2018
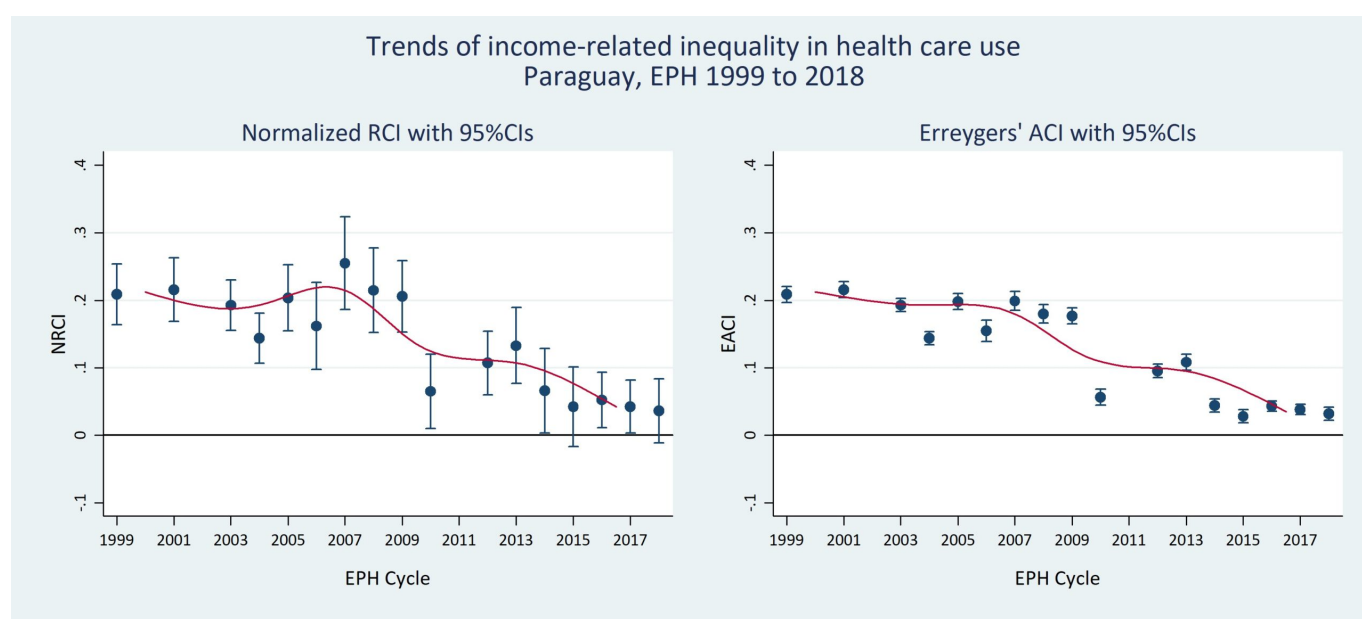
Recent Depressive Episodes and Health Care Use Before and After a Diagnosis of Diabetes

Eva Graham* Eva Graham Laura Rosella Tristan Watson Norbert Schmitz

Background: Adults with depression and diabetes use health services more frequently than adults with diabetes alone, suggesting that depression may exacerbate health care utilization in those with diabetes. It is not clear whether adults with depression and diabetes also have a history of higher health care use prior to diagnosis of diabetes. This study examined health care visits among adults with diabetes before and after diabetes diagnosis, comparing those with and without recent depressive episodes.

Methods: Participants were from the Canadian National Population Health Survey (1996/1997) and the Canadian Community Health Survey (2000/2001; 2003). We included survey participants with new diagnoses of diabetes within 7 years of their interview, identified using administrative data (n=3553). Recent depressive episodes were measured at the time of survey using the Composite International Diagnostic Interview–Short Form. The outcome of number of health care visits to physicians was calculated annually from 3 years prior to 3 years after a diagnosis of diabetes using administrative data. Negative binomial regression models estimated associations between recent depressive episodes and health care visits before and after a diagnosis of diabetes. Random intercepts accounted for repeated annual measures of health care visits in individuals.

Results: Recent depressive episodes were associated with increased visits to physicians both before and after a diagnosis of diabetes (RR before diagnosis 1.52, 95% CI 1.37-1.70; RR after diagnosis 1.30, 95% CI 1.19-1.42). Interaction analyses show that depressive episodes had weaker relative associations with health care visits after a diagnosis of diabetes (interaction RR 0.85, 95% CI 0.77-0.94; RERI -0.12, 95% CI -1.88-1.64).

Conclusions: Increased health care use among adults with diabetes and depression, compared to those with diabetes alone, may be partially attributable to higher health care use prior to diabetes diagnosis.

The Impact of the Medicaid Expansion on Coverage and Access to Oral Health Services: a Quasi Experimental Study Hawazin Elani* Hawazin Elani Benjamin Sommers Ichiro Kawachi

Objectives:To estimate the impact of Medicaid expansion under the Affordable Care Act (ACA) on changes in dental coverage and utilization of oral health services five years after the expansion.

Methods:We used data from the National Health Interview Survey from 2010 to 2018. We used a differences-in-differences linear regression analysis to compare changes in dental coverage and access to dental care in expansion states relative to control states before and after the expansion. Our study sample was limited to low-income adults (n=75,162).

Results:Medicaid expansion was associated with a significant increase in having any dental coverage (19.1 percentage points,95%CI 4.6, 33.5). As expected, expansion states that provide dental benefits showed the greatest gains in Medicaid dental coverage after the expansion(from 21.2% to 48.1%) and greatest reduction in the share of adults with no dental coverage(from 63.9% to 34.6%). Meanwhile, the net change in private dental insurance was non-significant after the expansion in both states with and without dental benefits. In terms of utilization, expansion states that provide dental benefits showed the greatest increase in reporting a dental visit in the past year, though this change was only significant among white adults(4.1 percentage points,95%CI,0.8,7.5). For oral health outcomes, the expansion was significantly associated with an increase in complete teeth loss, which is both a marker of poor oral health and potentially a marker of gaining access to dental services(1.4 percentage points,95%CI,0.0, 2.9).

Conclusions:Our findings demonstrate that after five years of coverage expansion there was no significant increase in utilization of dental services among low-income adults, though there were significant increases among white adults. As future policies consider whether states choose to provide adults with dental benefits, additional measures to improve dental care utilization among vulnerable populations must be considered.

Referral trajectories in patients with vertigo, dizziness and balance disorders and their association with functioning and health-related quality of life – Results from the MobilE-TRA cohort study Benedict Katzenberger* 3647] Katzenberger Daniela Koller Linda Sanftenberg Karen Voigt Eva Grill

Heterogeneous and non-rational referral patterns in primary care seem to delay effective therapy of vertigo, dizziness and balance problems (VDB). We therefore examined current trajectories of referral in a cohort of older adults, their predictors, and their potential impact on patient-reported outcomes of functioning and health-related quality of life (HRQoL).

MobilE-TRA is a primary care based cohort study among adults aged 65 or older in two German federal states (Bavaria and Saxony) conducted from 2017 to 2019 with a baseline examination and two follow-ups after 6 and 12 months. Referral trajectories were clustered using state sequence analysis. Predictors for cluster membership were identified using multinomial logistic regression. The effect of cluster membership on HRQoL and vertigo-specific functioning (Vestibular Activities and Participation Measure) at 12 months was examined using linear regression models.

116 patients (69.6% women, mean age at baseline = 77.1 years) were included. We identified four distinct clusters of similar referral trajectories. Cluster size decreased with increasing number of referrals. Participants most frequently remained at the primary care physician (PCP) without further referral (cluster 1), followed by a combination of PCP and additional referral to one specialist (clusters 2 and 3). Simultaneous referrals to more than one specialist (cluster 4) were rare. Cluster membership was significantly predicted by federal state. Referral trajectories mostly predicted vertigo-specific functioning. Patients having simultaneously visited both PCP and neurologist over several assessment periods (cluster 3) were significantly more disabled by vertigo than patients without further referral (cluster 1). Cluster membership did not predict HRQoL.

This study implies inefficiency of current referral patterns in primary care. Referral patterns showed significant regional differences. Measures to standardize care pathways are urgently needed.

Patient-reported opioid analgesic use after surgical procedures: systematic literature review Celeste Mallama* 3647] Mallama Christina Greene Apostolos Alexandridis Jana McAninch Gerald Dal Pan Tamra Meyer

Importance: Many patients report having unused opioid analgesic (OA) tablets after recovery from surgery, which can contribute to nonmedical use and poisonings. OA prescribing guidelines can help minimize unused tablets. In December 2019, the National Academies of Science, Engineering, and Medicine published a framework for developing evidence-based OA prescribing guidelines. The report stresses the need for observational studies to understand the link between intermediate outcomes (e.g., quantity OA tablets used) and health outcomes (e.g., pain). As a step toward this goal, we systematically reviewed observational studies of OA use post-surgery by procedure and quality metrics for these studies.

Objective: To synthesize the available evidence on patient-reported OA use in the outpatient setting post-surgery.

Methods: We searched Pubmed, Web of Science, and Embase for U.S. studies published since 2013 that contained patient-reported OA use.

Findings: Ninety-six studies met eligibility criteria. We provide the range of patient-reported use of 5mg oxycodone tablets, by surgical procedure, for 56 studies with sufficient information for standardization. Patient-reported OA use varied by procedure: a median of zero tablets used after vasectomy was reported in one study, while a mean of 147 tablets use was reported in a study of knee arthroplasty. The quantity used for similar surgical procedures varied within and between studies. Within-study variation was attributed to differences in patient factors (e.g., prior opioid exposure). Variability between studies for the same procedure may be explained by differences in patient populations, data collection, and surgical techniques.

Conclusions: There is variation both within specific surgical procedures and across a variety of surgical procedures in the number of OA tablets used after surgery. Understanding these variations can inform guideline development and clinical decisions to "right-size" outpatient OA prescriptions.
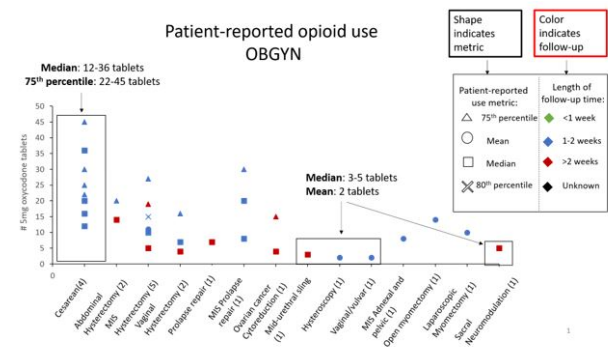
*Abbreviations: OBGYN: Obstetrics and Gynecology; MIS: Minimally invasive surgery

Graph presents standardized results on the number of 5mg oxycodone tablets patients reported using after select OBGYN procedures in our systematic literature review. The number of articles that met standardization criteria and reported on the specified procedure type is indicated in parentheses on the x-axis. A single study could have contributed multiple distribution metrics (median, mean, 75th percentile, or 80th percentile) in a single column.

Does regional location mediate GES and influence cervical cancer mortality outcomes?
Doris Durán* Doris Durán María Jose Monsalves

Introduction: The Explicit Health Guarantees policy (GES in spanish) consider four points of protection in health: opportunity, access, financial protection and quality. Opportunity's guarantee sets times for health actions to be done. The law sets these times for the delivery of cancer care across the country equally, but with fifteen regions and a highly centralized system, this standard is hard to accomplish. We hypothesized a mediation role of the region in the effect of the policy for cervix cancer.

Aim: To estimate the mediation role of the region of residence, on the effect of a timely Opportunity coverage of GES, on cervical cancer mortality in Chile between 2010 and 2017.

Methods: Ecological study carried out to analyze mortality data and timely opportunity coverage of GES for cervical cancer. Mortality data was obtained from the Department of Statistics and Health Information (DSHI) of the Ministry of Health, and the information about the opportunity GES enforcement from the National Fund of Health (FONASA). We assessed the role of the region as a mediator in the relationship opportunity- cervical cancer mortality (See figure for DAG and variables). We established up to a 5% of regional untimely GES delivered as acceptable (treatment=0) and a 6% or more as the exposure (treatment=1). We included an interaction term for the exposure and mediator and used bootstrap for standard errors.

Results:

We observed a Controlled Direct Effect (CDE) of 0.009 (CI95% -0.153;0.064), a Natural Direct Effect (NDE) of 0.008 (CI95% -0.012; 0.027), and a Natural Indirect Effect (NIE) of 0.003 (CI95% -0.000; 0.008). Little mediation for the region was observed.

Conclusions:

Region of residence`s mediation role was less strong than expected. This can be because the mediator was analyzed as a binary variable, not considering differences between regions.
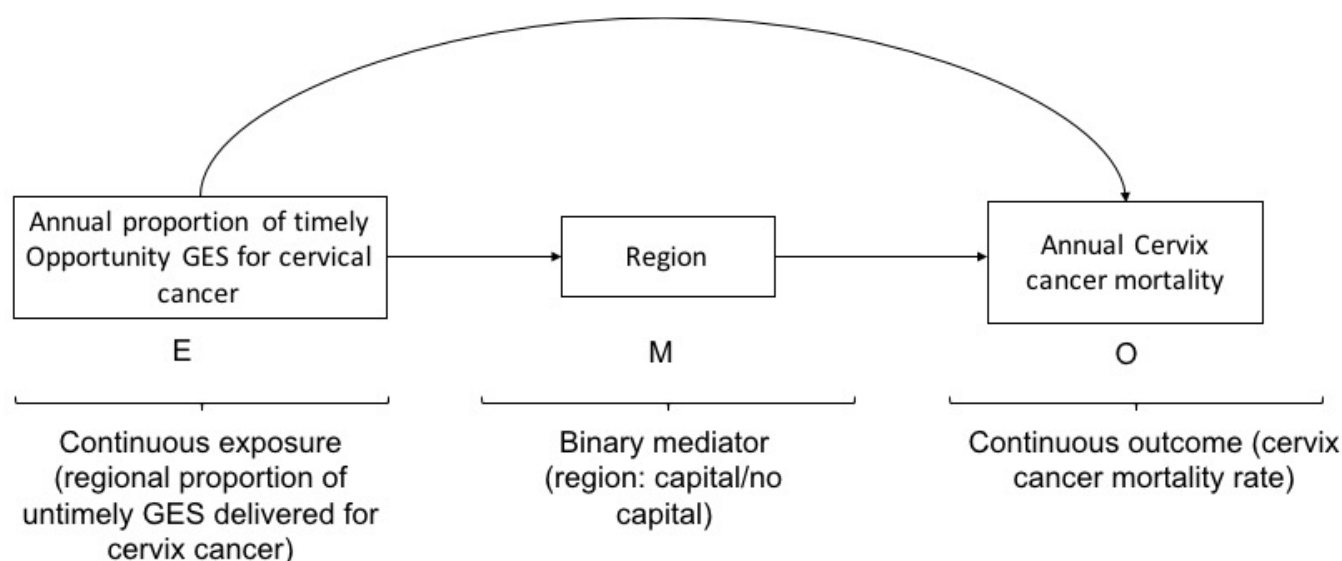
Assessing the reliability of self-reported sexual behavior among male couples Alison Walsh*
Alison Walsh Rob Stephenson

Assessing the reliability of self-reported sexual behavior among male couples
Coupled men who have sex with men (MSM) are at particularly high risk for HIV transmission and a clear understanding of risk behaviors is key to designing effective interventions and reducing incidence. Accurate self-reports of sexual activity is a crucial component of valid sexual and reproductive health research, yet this data's reliability remains understudied. The goal of this study was to quantify and identify predictors of dyadic discordance in reported 3-month anal intercourse (AI) occurrence and frequency. Using cross-sectional data collected from 407 male couples in the United States (2016-2017), we explored the reliability of self-reported sexual activity. We used dyad-level logistic models and multiple linear regression to identify dyadic demographic, behavioral, and relationship traits associated with the odds of discordant frequency reporting and the magnitude of disagreement. Results: Couples had high levels of concordant binary reports of 3-month anal AI (97%) but low levels of agreement in reported frequency (37%). Among couples with discordant frequency reports, the mean disagreement magnitude was 52.80% ± 35.91%. After adjusting for covariates, the odds of discordance was significantly associated with dyadic employment, age difference, differences on the Communal Coping to Reduce HIV Threat Scale (CCS), and overall volume of sexual activity between partners (all p<0.05). In the multiple regression model, the magnitude of disagreement was positively associated with CCS (p<0.05). These results indicate that among MSM couples in long-term, committed partnerships, self-reported of sexual behavior data may be impacted by data granularity, individual recall, and relationship characteristics. Further research in this area is warranted to identify ways to detect and correct for measurement error in self-reported sexual activity data.

Examining sustained HIV viral suppression in women: A gender comparison of psychosocial and demographic factors in Miami-Dade County Melissa Ward-Peterson* Melissa Ward-Peterson Sofia B. Fernandez Diana M. Sheehan Kristopher P. Fennie Mary Jo Trepka

Introduction: Women living with HIV often delay entry into care and experience poor outcomes. The purpose of this study was to identify factors unique to women associated with sustained viral suppression.

Methods: Descriptive and bivariate analysis provided an initial profile of the sample, which included 6,486 individuals enrolled in the Ryan White Program in Miami-Dade County in 2017. The outcome of interest was failure to achieve sustained viral suppression. Sustained viral suppression was defined as having all viral load tests below 200 copies/ml in 2017; the outcome variable was derived from twice yearly laboratory tests. To account for possible clustering by case management site (n=11), multilevel logistic regression treating case management site as a random effect was used to estimate ORs with 95% CIs. Independent variables included psychosocial and demographic factors. Analysis was stratified by gender; tolerance was examined to assess multicollinearity.

Results: The intraclass correlation coefficient for case management site was 0.032. For women (n=1,503), not disclosing HIV status to a partner/adult in the household (OR=1.37, CI: 1.03-1.83) and perinatal exposure (OR=3.75, CI: 1.20-11.78) were associated with higher odds of not achieving sustained viral suppression. For men (n=4,983), being Haitian (OR=2.37, CI: 1.53-3.67) or non-Hispanic black (OR=1.89, CI: 1.32-2.70), depression (OR=1.37, CI: 1.08-1.74), and lacking access to food (OR=2.08, CI: 1.25-3.49) were associated with not achieving sustained viral suppression. In both groups, age, poverty level, experiencing HIV symptoms, ever having an AIDS diagnosis, problematic drug use, and homelessness were associated.

Conclusion: Factors unique among women are associated with sustained viral suppression. While programs along the HIV Care Continuum benefit both genders, including a women-centered care approach to disclosure support may improve outcomes for women living with HIV.

Latent Class Analysis of Syndemic Factors Associated with Consistent Viral Suppression among Ryan White HIV/AIDS Program Clients in Miami, 2017 Rahel Dawit* Rahel Dawit Diana M. Sheehan Semiu O. Gbadamosi Sikeade Caleb-Adepoju Mary Jo Trepka

Consistent viral suppression is critical to ensure reduced risk of HIV transmission and disease progression. The interaction of multiple adverse factors affects health outcomes for people living with HIV (PWH). The objective was to identify the association between classes of patterns of mental illness, substance misuse, sexual risk behavior, and adverse social conditions, and consistent viral suppression for PWH.

Latent class analysis was used to identify patterns of classes based on seven dichotomous variables for clients in the Miami-Dade County Ryan White Part A Program in 2017. These included alcohol use, drug use, depression, difficulty sleeping, domestic violence, homelessness, and >1 sexual partner in last 12 months. Multivariable logistic regression was conducted to examine the association between latent classes and consistent viral suppression (all viral load tests <200 copies/ml within a year) controlling for sociodemographic characteristics.

Data for 6,554 PWH were analyzed, and a five-class model was selected. Class 1 members (75.9%) had no co-occurring conditions. Class 2 (8.4%) had one condition of mental illness. Class 3 (6.4%) had two co-occurring conditions of substance misuse and multiple sexual partners. Class 4 (5.5%) had three co-occurring conditions of mental illness, domestic violence, and multiple sexual partners. Class 5 (3.6%) had all co-occurring conditions (substance misuse, mental illness, multiple sexual partners, and homelessness). Compared to Class 1 and after controlling for sociodemographic factors, the odds of achieving consistent viral suppression was significantly lower for members in Class 2 (aOR: 0.67; 95% CI: 0.54-0.83), Class 3 (0.60; 0.47-0.76), Class 4 (0.71; 0.55-0.93), and Class 5 (0.26; 0.19-0.35).

PWH with multiple adverse conditions are at lower odds of achieving consistent viral suppression. Findings underlie the need for targeted interventions that address syndemic factors that contribute to poor health outcomes.

Barriers to Implementing HIV Pre-Exposure Prophylaxis among Primary Care Providers in a Safety-Net Health System

Afiba Manza-A. Agovi* Ifedioranma Anikpo Afiba Manza-A. Agovi Matthew Cvitanovich Rohit P. Ojha

Background: Safety-net health systems are a primary source of care for socioeconomically disadvantaged populations, which have a high risk of HIV infection and could benefit from HIV pre-exposure prophylaxis (PrEP). Primary care providers (PCP's) in safety-net health systems are thus uniquely positioned to help meet national targets for PrEP use for eligible individuals, but little is known about potential barriers to scaling up PrEP implementation in this setting. We aimed to examine barriers to implementing and expanding PrEP services among safety-net PCP's.
Methods: We conducted a cross-sectional survey at JPS Health Network (JPS), which is a safety-net health system in Tarrant County, Texas, to assess barriers to implementing PrEP including self-reported knowledge, attitudes, practices, and training needs. Individuals eligible for our survey were PCPs (physicians, nurse practitioners, clinical pharmacists, and physician assistants) at primary care medical homes within JPS. Eligible providers were recruited by direct email over a one-month period in 2019. Descriptive statistics were used to summarize data from the survey.
Results: Our eligible population included 283 providers, of whom 62 (22%) completed the survey. Evaluable providers were predominantly female (64%), non-Hispanic White (61%), and included mostly PCPs (46%) with either <5 or ≥ 20 years of practice experience (53%). Self-rated knowledge of PrEP was endorsed as medium or high by 53% of respondents, but 55% reported inadequate knowledge of PrEP to have an informed discussion with patients. The majority (87%) of respondents endorsed additional training on PrEP.
Conclusion: Our results suggest that barriers to PrEP implementation include limited provider knowledge and uncertainty about prescribing PrEP, which may be amenable to educational intervention. Our findings are useful for the local setting and may also be useful for similar settings to facilitate meeting national targets for PrEP uptake.

Caregiver during childhood is associated with HIV test uptake among Chinese college students: A cross-sectional study in Suzhou, China Wanqi Wang* Wanqi Wang Zihan Dong Hanrui Zhao Stephen W. Pan

INTRODUCTION: Due in part to growing acceptance of casual sex and limited sex education, many college students in China are increasingly vulnerable to HIV infection. Unfortunately, HIV testing rates among college students in China remain suboptimal. Previous studies indicate that caregiver during childhood may be associated with healthcare avoidance. This study examined the association between childhood caregiver and HIV test uptake among college students in Suzhou, China.
METHOD:
Data were collected from a cross-sectional online survey. Links to the survey were distributed via email to enrolled students at an English language university in East China. Eligibility criteria: current university student between 18 and 30 years old in the study city, ever had anal, oral or vaginal sex. Caregiver during childhood and HIV testing history was based on participants' self report. Logistic regression was used to assess the association between caregiver during childhood and HIV test uptake. Age, sex, income, and household registry were entered as control variables.
RESULTS:
A total of 265 participants were included in the study. 8.3% of participants had ever tested for HIV, 63.4% were raised by two parents, 24.5% were raised by single parents, 7.17% were raised by one or more grandparents, and 4.9% were raised by other people. The odds of HIV testing were 3.7 times greater for students raised by other people, compared with students raised by two parents (OR=4.70, CI=1.110~19.916, $p<0.05$). No significant differences in HIV testing were observed between students raised by two parents, a single parent and grandparents.
CONCLUSION
Students who are not raised by parents or grandparents may be more likely to test for HIV, which may due to their perceived risk, or their more responsibility to health. To improve the HIV testing among college students, further studies are needed to understand the mechanisms of association between childhood caregivers and HIV testing.

Years of life lost due to cancer among people with HIV Qianlai Luo* Qianlai Luo Eric Engels Marie-Josephe Horner Ruth Pfeiffer Noone, Anne-Michelle Shiels, Meredith

Background

In the US, declines in mortality have resulted in the growth and aging of the HIV-infected population and an increase in the number of incident cancers, particularly non-AIDS-defining cancers. Years of life lost (YLL) is an important mortality metric that more heavily weighs deaths that occur at younger ages. We estimated YLL due to malignant cancers (overall and by cancer sites) in the HIV/AIDS Cancer Match Study.

Methods

We used data from 593,862 people with HIV (PWH) alive at 2001 in a linkage of population-based HIV and cancer registries in 11 U.S. regions. Cox proportional hazard regression models were used to estimate the survival distribution starting from HIV diagnosis of the overall cohort and of a hypothetical cancer-free cohort (by censoring at cancer diagnosis), adjusting for sex, race/ethnicity, transmission categories, and registry. Individual survival curves were estimated using the baseline hazards and covariate values, then these survival curves were averaged at each event time. The mean YLL of the overall cohort due to cancer in PWH was estimated by comparing the areas under the averaged curves of the two cohorts.

Results

During 2001–2015, there were 121,360 total deaths (21,211 deaths occurred after a cancer diagnosis). The total YLL to cancer was 525,877 years, representing 3.1% of all life years during the time period. The largest number of YLL were due to non-Hodgkin Lymphoma (23.5%), followed by lung cancer (13.6%), Kaposi sarcoma (KS) (12.0%), anal cancer (5.9%), liver cancer (5.7%) and Hodgkin lymphoma (3.4%). AIDS-defining cancers accounted for 37.3% of the total YLL due to cancer among PWH. On average, there were 17.7 YLL per cancer case.

Conclusions

Cancer remains an important comorbidity among PWH. In a cohort of nearly 600,000 PWH, 3.1% of potential life years were lost due to cancer with an average of 17.7 years lost per cancer case. Public health interventions should continue to focus on cancer prevention in this aging population.

The role of poly substance use and depression on adherence to antiretroviral treatment in the Miami Adult Studies on HIV (MASH) Cohort Abraham Mengist* Abraham Mengist Karl Krupp Marianna Baum

Background
This study examined poly substance use and adherence to ART and assess whether depression moderates this relationship.
Methods
Data for 391 HIV patients from the Miami Adult Studies on HIV (MASH) cohort was analyzed for this study. Participants were asked if they failed to take any of their anti-HIV drugs over the past three or more months, and in the past four days. Harmful alcohol drinking behavior was evaluated using the Alcohol Use Disorders Identification Test. Depression symptomology was evaluated using The Center for Epidemiologic Studies Depression Scale. Substance use was assessed using self-report and/or urine test.
Results
Out of 391 HIV patients, 45.3% missed at least one anti-HIV drug dose over the past three or more months. Cocaine/crack use (adjusted odds ratio [aOR] 2.00) and harmful alcohol drinking behavior (aOR 2.01) were significantly associated with missing at least one anti-HIV drug over the past three or more months. Opiate use was associated with an increased numbers of anti-HIV drugs missed over the past four days (regression coefficient [β] 0.83). The odds of missing ART drug was particularly significantly greater among patients who were using two or more substances – alcohol and marijuana (aOR 2.98); alcohol and cocaine/crack (aOR 5.04); alcohol and tobacco (aOR 2.35); marijuana and cocaine (aOR 2.72); cocaine and tobacco (aOR 3.03); alcohol, marijuana and cocaine (aOR 5.52); alcohol, cocaine and tobacco (aOR 5.72). An increase in the depression status of the patients was also associated with an increase in the odds of missing anti-HIV drugs (aOR 1.04). Depression significantly moderated the relationship between cocaine/crack use and the mean numbers of anti-HIV drugs missed (β -1.14).
Conclusions
These findings suggest that poly substance use, particularly cocaine/crack, opiates and harmful alcohol may increase the risk of poor adherence to ART among HIV patients. Depression was also associated with poor adherence.

Summing it all up: the impact of missing data in analyses using cumulative viremia

Xianming Zhu* 3647] Zhu Alison G Abraham Benjamin Barrett Frank J Palella Joseph B Margolick Bernard JC Macatangay Roger Detels

Background Cumulative exposures are of great interest in health research, since they represent long-term factors that often play a larger role in comorbid disease and mortality risk than single time-point exposures. Prospective long-term studies often collect repeated measures of exposures such as viral load (VL) that can be used to construct cumulative measures. Viral copy years (VCY), a metric used to express accumulated exposure to HIV viremia, has been found more strongly linked to AIDS and death than single time-point VL measures. However, missed visits and lower limits of detection (LLD) result in gaps and uncertainties of within-person VL history that could impact study inferences. Here we examined the impact of missing data on associations between VCY and mortality. **Methods** Data were included from HIV seroconverters enrolled in the Multicenter AIDS Cohort Study (MACS) who had complete VL data and no VL under LLD for the first 6 visits after seroconversion. To simulate missingness due to missed visits or missed tests, 1000 datasets were generated with 15%, 30% and 50%missing VL data under a missing completely at random (MCAR) mechanism. Two common strategies for handling missing data were used: multiple imputation (MI) and interpolation (INT). MI were used longitudinally (in long form data) and horizontally (in wide form data). For uncertainty due to LLD, we created new LLDs set at 10 times, 50 times and 100 times the true LLD and set all VLs to missing below these limits. We used MI, truncated normal imputation (TN), set to limit of detection (LDI) and set to midpoint of the interval (midI) as strategies for addressing uncertainty due to LLD. Observed VCY estimates (using the complete observed data) were compared with results from simulated missingness and correction. Additionally, hazard ratios (HR) for the association between VCY and mortality using observed VCY estimates (using the complete observed data) were compared to those obtained from each scenario. All analyses were performed using SAS and R. **Results** There were 110 male seroconverters included, with a median age of 36.3 years (IQR: 30.5, 45.8) at seroconversion; 77.9% of the VL data were from the pre-HAART era (before 1996). 82.1% of the VLs were tested through Roche 2nd gen assay (LLD=400 copies/ml). When the prevalence of missing was 15%, 30% and 50%, the median percent relative bias for INT was -3.0% (IQR: -6.7%, 1.0%), -6.5% (IQR: -12.3%, -0.4%) and -10.9% (IQR: -20.4%, -0.2%; INT) respectively. MI in long form data resulted in a median percent relative bias of -6.4% (IQR: -12.4%, 0.3%), -14.5% (IQR: -21.6%, -7.0%) and -28.4% (IQR: -35.3%, -20.9%; MI) respectively. MI in wide form data had similar bias with MI in long dataset. For uncertainty resulted from LLD, 73 (11.1%), 226 (34.2%) and 338 (51.2%) VLs were set to missing when LLD was 10, 50, and 100 times the true LLD, respectively. MidI consistently resulted in the lowest bias for the HR estimate (4.3%, 11.7% and 27.6% for each simulation), while LDI resulted in the largest bias (9.3%, 34.2% and 88.3%). **Conclusions** When the prevalence of missing VL is low, both INT and MI performed well but INT outperforms MI when the missing prevalence is higher. For uncertainty due to LLD, midI performed the best even with substantial uncertainty.
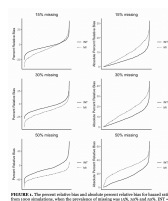
FIGURE 1. The percent relative bias and absolute present relative bias for hazard ratios from cross simulations, when the prevalence of missing was 15%, 30% and 50%. INT = Interpolation; MI = Multiple imputation.

Sexual identity, sexual behavior and current PrEP use in Black sexual minority men: The N2 cohort study in Chicago Liadh Timmins* 3647] Timmins John A. Schneider Denton Callander Yen-Tyng Chen William C. Goedel Rebecca Eavou Dustin T. Duncan

Pre-Exposure Prophylaxis (PrEP) is an effective means of HIV prevention, including for marginalized populations. Despite particularly high vulnerability to HIV, Black sexual minority men (SMM) are less likely to than Latino or White SMM to be on PrEP. However, relatively little is known about which sexual identity and behavior subgroups of Black SMM are the most susceptible and not engaged in PrEP care. This study investigated current sexual identity and sex with women in the past six months as potential predictors of current PrEP use in Black SMM. Data were from the interim baseline (n=324) of the Neighborhoods and Networks (N2) Study, an ongoing cohort study of young Black SMM in Chicago IL, Jackson MS, and New Orleans and Baton Rouge, LA. Three groups of HIV-negative black cisgender men from the Chicago were included: gay men who have sex with men only (n=76), bisexual men who have sex with men only (n=21), and bisexual men who have sex with men and women (n=29). Logistic regression analyses with self-reported current PrEP use as the dependent variable and subgroup as the independent variable were performed. Age, education, employment, income and housing stability were controlled for. In total, 50.0% of gay and 59.1% of bisexual men who only have sex with men were on PrEP, compared with 11.3% of bisexual men who have sex with men and women. Multivariate results confirmed that bisexual men who have sex with men and women were significantly least likely to be on PrEP than gay (OR=.11, 95% CI [.02, .63]) or bisexual men who have sex with men only (OR=.07, 95% CI [.01, .37]). No significant differences were found between gay and bisexual men who have sex with men only. Black bisexual-identified men who have sex with men and women may be particularly unlikely to use PrEP. Relying solely on whether black men have sex with men and ignoring sex with women may mischaracterize PrEP rates and miss uniquely vulnerable individuals.

LATEBREAKER

HIV / STI

Data Movies of Demographic Trends in US HIV Diagnoses, 2008-2017 Lauren Zalla* 3647]
Zalla Jessie K. Edwards Stephen R. Cole Tiffany Breger Jacqueline Rudolph Arti Virkud Anna Satcher Johnson H. Irene Hall

Introduction: Rich surveillance data can be difficult to summarize in a way that is both efficient and informative. In this setting, dynamic visual displays or "data movies" can be valuable tools for investigating and communicating underlying patterns. Using the example of HIV in the US, we illustrate how data movies can help us discern trends in the distribution of disease. **Methods:** Using data from the National HIV Surveillance System, we created data movies to study the evolving epidemiology of HIV from 2008-17. We explored trends in diagnoses by age group, sex, race/ethnicity and region. We do not present confidence intervals because these surveillance data represent a census of diagnoses. **Results:** Overall, the number of HIV diagnoses decreased from 2008-13, remained stable from 2013-16, and decreased from 2016-17. In the latter half of the period, diagnoses decreased in the Northeast and Midwest but remained stable in the South. A rising number of diagnoses among Hispanic Americans accounted for a 3% increase in the West. We observed a dramatic shift in the age distribution of diagnoses among men from 2008-17, with a 19% increase among men ages 20-30 paired with a 52% decrease among men ages 40-50. Diagnoses among women initially decreased and then leveled off in all age groups except women 60+, among whom diagnoses increased by 16% from 2008-17. Rate ratios (RRs) comparing diagnoses among African Americans and Hispanics to Whites failed to decline over the ten-year period. Among men, RRs ranged from a low of 7.0 to a high of 7.5 for African Americans, and from 2.9 to 3.4 for Hispanics. Among women, RRs range from a low of 14.1 to a high of 21.6 for African Americans, and from 2.7 to 4.3 for Hispanics. RRs for both African Americans and Hispanics relative to Whites were greatest among those younger than 24 and over 60. **Conclusion:** Data movies are an efficient way to summarize rich surveillance data and uncover trends in the population distribution of disease.

Evolving Demographics of US HIV Diagnoses
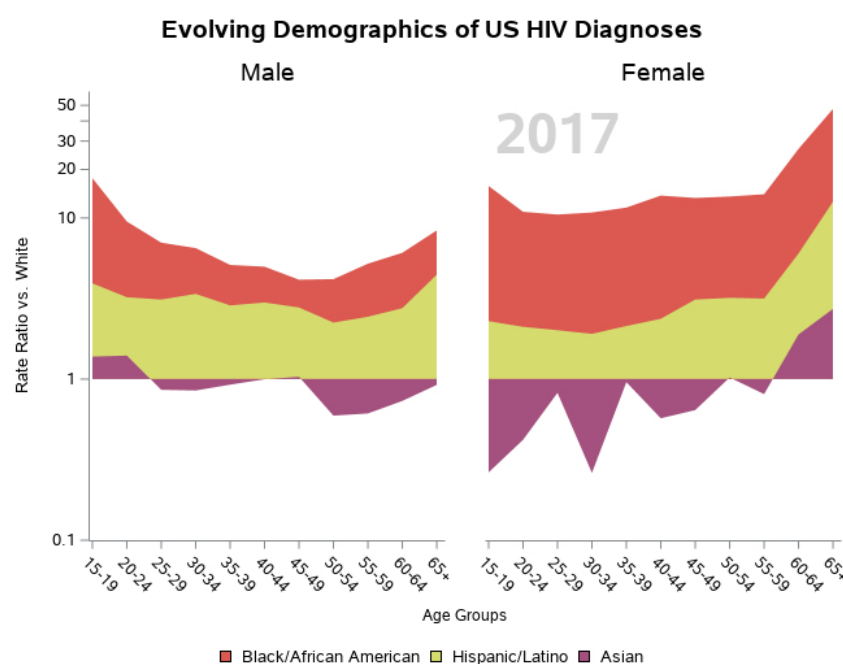
Data Provided by the US Centers for Disease Control and Prevention and US Census Bureau
Animation Produced by the UNC Causal Inference Research Lab

Infectious Disease

Hepatitis C virus (HCV) community viral load: novel metrics to enhance HCV surveillance and control Ashly E Jordan* Ashly E Jordan David C Perlman Charles M Cleland Bruce R Schackman Katarzyna Wyka Denis Nash

Introduction
Hepatitis C virus (HCV) incidence is increasing in the US in the recent opioid epidemic. There are gaps in HCV prevention and in HCV surveillance metrics. The community viral load (CVL) construct has been productively applied to HIV epidemiology but not yet to HCV. We construct and empirically evaluate a CVL metric, examine geographic and demographic variation in CVL, and examine the association of area-level CVL with area-level HCV incidence in ecologic analysis.

Methods
HCV viral load (VL) data from a retrospective observational cohort of patients in an opioid treatment program in 1/2013-12/2016 contributed to the engaged-in-care CVL metric. HCV CVLs reflect the mean of the sum of each individual's most recent HCV VL (in copies/mL). CVLs were calculated, log transformed for analyses, and compared among demographic subgroups and areas of residence. Associations of area-level CVLs and area-level HCV incidence were examined in negative binomial regression analysis.

Results
The overall engaged-in-care HCV CVL was 3.5 million copies/mL. Higher area-level HCV CVL was associated with higher area-level HCV incidence: for each 1 log10 increase in HCV CVL, the HCV incidence rate was expected to be multiplied by about 2.7 (incidence rate ratio (IRR): 2.72, 95% CI: 0.77-11.13). Engaged-in-care HCV CVLs varied by patient zip code area of residence (Spearman's R: -0.44, p-value: 0.008).

Discussion
HCV CVLs can be constructed and be applied to empiric data. HCV CVL varied significantly among patient zip code area of residence; monitoring HCV CVLs be valuable in geographically focusing prevention and treatment services. In the first examination of the association of HCV CVL and HCV incidence, we identified an association in the hypothesized direction suggesting that further studies of HCV CVL measures as potential predictors of HCV incidence are warranted. CVL measures are promising HCV surveillance metrics.

Infectious Disease

Prediction models for pulmonary tuberculosis treatment outcomes: a systematic review
Lauren Saag Peetluk* Lauren Peetluk Felipe Ridolfi Valeria Rolla Timothy Sterling

Objective: We aim to identify and synthesize existing prediction models for TB treatment outcomes, including bias and applicability assessment.
Design: Systematic review
Methods: Our review will adhere to methods that developed specifically for systematic reviews of prediction model studies. PubMed, Embase, Web of Science, and Google Scholar (first 200 citations) were searched from January 1, 1995 to December 1, 2019. Inclusion criteria: studies that internally and/or externally validate a model for TB treatment outcomes (defined as one or multiple of cure, treatment completion, death, treatment failure, relapse, default, and lost to follow-up) among pulmonary, drug-susceptible, TB patients. We will exclude studies that include only extra-pulmonary or multi-drug resistant TB cases. Study screening, data extraction, and bias assessment will be conducted independently by two reviewers with a third party to resolve disputes. Study quality will be assessed using the Prediction model Risk Of Bias Assessment Tool (PROBAST).
Results: The initial search yielded 27,538 articles, and after de-duplication, 14,029 remain. After screening titles, abstracts, and full-text, we will extract data from relevant studies, including publication details, study characteristics, methods, and results. Data will be summarized with narrative review and in detailed tables with descriptive statistics. We anticipate finding disparate outcome definitions, contrasting predictors across models, and high risk of bias in methods. Meta-analysis of performance measures for model validation studies will be performed if possible.
Discussion: TB outcome prediction models are important but existing ones have not been rigorously evaluated. This systematic review will synthesize TB outcome prediction models and serve as guidance to future studies that aim to use or develop TB outcome prediction models.

Randomised controlled trials for the identification and establishment of new correlates of protection for influenza vaccines Wey Wen Lim* Wey Wen Lim Benjamin J Cowling

Correlates of protection (CoPs) are important to evaluate and develop next-generation influenza vaccines. The three CoPs that are currently used for inactivated influenza vaccines (IIVs) do not fully explain IIV-induced protection and do not predict effectiveness of live-attenuated influenza vaccines, driving the need for additional CoPs for next-generation influenza vaccines. Here we assess study design considerations, including sample size requirements for epidemiological studies to assess the independent associations of two or more CoPs with clinical endpoints and their causal contributions to vaccine-induced protection. We simulated randomized controlled vaccine trials of different sample sizes to estimate their statistical power to establish independent associations of two CoPs with influenza virus infection and detect the causal contribution of each CoP towards vaccine-induced protection with causal mediation analysis. The hemagglutination inhibition antibody (HAI) and neuraminidase inhibition antibody (NAI) titers were used as examples in these analyses. In simulations where unit increases in HAI titer reduces the risk of infection by 20%, consistent with 50% protection for a titer of 40, sample sizes of approximately 4,000 participants are estimated to have 80% power to identify the HAI titer as a CoP if the baseline risk of infection is 10%. When unit increases in HAI and NAI titers reduces risk by 20% and 15% respectively, our study suggests that a sample size of above 5,000 may be needed for a study to have 80% power to detect independent associations between both HAI and NAI titers with influenza virus infections and their individual causal contribution towards protection. Large sample sizes may be required to assess the association of a new CoP with clinical endpoints and its causal contribution to protection. This indicates the need for independent studies that are specifically designed and adequately powered to achieve this objective.

Infectious Disease

Disparities in individual and neighborhood level education are associated with the risk of acute respiratory illness in the Detroit Neighborhood Health Study Helen CS Meier* Ryan Malosh Helen CS Meier Regina Manansala Allison Aiello Ryan E Malosh

Introduction: Acute respiratory infections (ARI) are the most frequent cause of illness in children and cause substantial morbidity in adults. Social determinants are not routinely considered important drivers of ARI transmission, though health care utilization due to ARI is socially patterned.

Methods: We used data from the second and third waves of the Detroit Neighborhood Health Study (DNHS) collected during and after the 2009 influenza pandemic to examine associations between individual and neighborhood level educational attainment and the risk of ARI. ARI was defined as self-reported cold, cough, runny nose or flu. Individual educational attainment was categorized as high school graduate, some college or technical training, or college graduate (referent). Individual education levels were aggregated to generate average neighborhood education level. We used generalized linear mixed-effects model with a random effect for neighborhood to model the association between average individual educational attainment and ARI risk, controlling for age, sex, race, children in household, health status, and homeownership status for wave 2.

Results: ARI risk among high school graduates was 67% higher than those with a college degree (p=0.003). ARI risk and educational attainment clustered by neighborhood. Neighborhoods with a higher proportion of less educated residents had greater risk of ARI (Figure 1). In mixed-effect models, lower educational attainment was associated with higher risk of ARI during the second wave (2009-2010) (aOR 1.53 95% CI: 1.08, 2.16) of DNHS.

Discussion: The risk of ARI is socially patterned in this population-representative study. With the development of new vaccines for influenza and Respiratory Syncytial Virus on the horizon, it is important to understand drivers of infection and develop policies to ensure equitable distribution and access by socioeconomic status to these preventive measures.

Figure 1. Neighborhoods with a greater proportion of lower educated residents had higher risk of acute respiratory infection (ARI) in the Detroit Neighborhood Health Study, 2009-2010

Infectious Disease
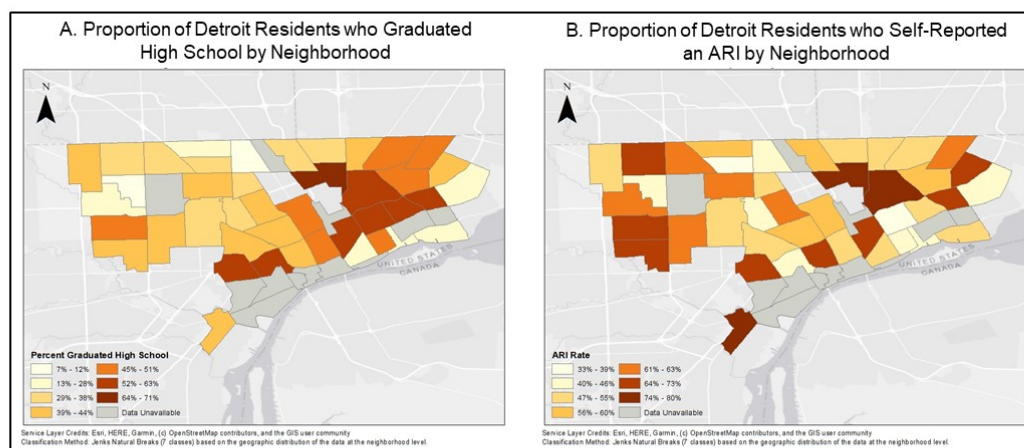
Community-based antibiotic prescribing attributable to respiratory syncytial virus and other common respiratory viruses: a population-based study of Scottish children, 2009-2017 Tiffany Fitzpatrick* Tiffany Fitzpatrick William Malcolm Jim McMenamin Arlene Reynolds Pia Hardelid

Background: Recent research suggests inappropriate antibiotic prescribing, such as that for viral illness, is common in primary care. This is of growing interest given concerns around antimicrobial resistance and harms associated with unnecessary treatment. The objective of this study was to estimate the proportion of antibiotics prescribed in the community to young children attributable to common respiratory viruses, including respiratory syncytial virus (RSV), influenza, human metapneumovirus (HuMPV) and parainfluenza.

Methods: We fit time series negative binomial models to predict weekly antibiotic prescribing rates from positive viral pathogen tests rates for the period April 1, 2009 through Dec 27, 2017 using comprehensive, population-based administrative health data for all Scottish children (<5 years). We used these models to estimate the proportion of antibiotics prescriptions explained by the circulation of common viruses. We further stratified our analysis to investigate potential differences according to age, presence of high-risk chronic medical conditions, and antibiotic class.

Results: We included data on over 6 million antibiotic prescriptions among nearly 800,000 children. An estimated 6.9% (95% CI: 5.6, 8.3), 2.4% (1.7, 3.1), and 2.3% (0.8, 3.9) of prescribed antibiotics were attributable to RSV, influenza and HuMPV, respectively. RSV was consistently associated with the highest proportion of antibiotics prescribed across all analyses but particularly among children without chronic conditions and for amoxicillin and macrolide prescriptions.

Conclusions: Nearly 14% of antibiotics prescribed to Scottish children in this study were estimated to be attributable to common viral pathogens for which antibiotics are not recommended, such as RSV. This highlights clear targets for antibiotic stewardship programs and further suggests antibiotic prescribing could be considerably reduced among children once an RSV vaccine is introduced in the coming years.
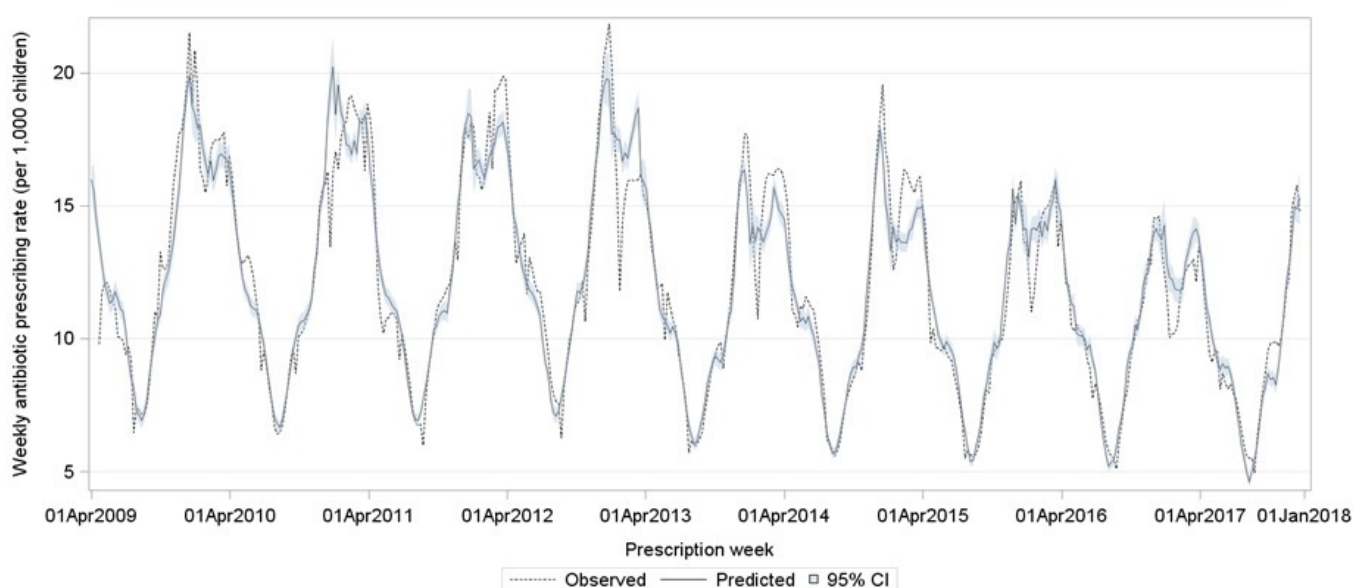
Figure 1. Observed and predicted (95% CI) rates of weekly antibiotic prescribing (smoothed four-week moving average), among Scottish children under 5 years of age

Infectious Disease

Machine learning to predict yellow fever mortality in Brazil's urban outbreak Andre Filipe de Moraes Batista* Andre Filipe de Moraes Batista Andre AN Gonçalves Luiz Gonzaga F. A. B. D'Elia Zanella Carlos Henrique V. Moreira Renata Buccheri Gabriela B. F. Diniz Anna Carla P. Castiñeiras Alice T. W. Song Igor C. Borges Daniel Joelsons Natalia B. Cerqueira Vivian I. Avelino-Silva Yeh-Li Ho Esper Kallas Helder I Nakaya Alexandre Dias Porto Chiavegatto Filho

After a long period without reported cases of yellow fever, outbreaks have been documented in Brazil since 2018, despite the existence of a safe and efficacious vaccine. In 2018, a total of 504 autochthonous cases were confirmed in different regions of the São Paulo state, and 176 died (35% mortality). Due to the complexity of the disease and its increasing presence in new urban areas, new decision-making algorithms may help the medical team to improve clinical assistance. The objective of the study was to test the performance of popular machine learning algorithms to predict 60-day mortality among patients diagnosed with yellow fever, using as predictions variables collected upon hospital admission. We analyzed data from a cohort of patients in two large hospitals in São Paulo during the 2018 outbreak (n = 197 with 49 deaths, i.e. 24.87% mortality). We tested the 10-fold cross-validated predictive performance of popular machine learning algorithms such as random forests, gradient boosted trees and artificial neural networks. The highest predictive performance was obtained by the gradient boosted trees algorithm, with an Area Under the Curve of the Receiver Operating Characteristic (AUC ROC) of 0.958. All other algorithms also obtained an AUC ROC higher than 0.9. The top 20% patients with the highest predicted risk provided by the best model included 79.59% of total deaths of the cohort. In conclusion, it is possible to predict with high performance the 60-day mortality risk among patients with yellow fever. Interactions between clinical professionals and data analysis technologies are a fertile ground for the development of predictive machine learning models, which may help to assign accurate risk scores to patients and to improve decisions about the necessity and intensity of medical care.

Infectious Disease

Mortality following medically-attended norovirus infection in a national cohort of US Veterans, 2010–2018 Jordan Cates* Jordan Cates Cynthia Lucero-Obusan Ben Lopman Mark Holodniy Aron J. Hall Cristina Cardemil

Background: Norovirus gastroenteritis causes an estimated 1,000 deaths in the United States every year, primarily in older adults. However, prior studies have relied on indirect attribution from all-cause gastroenteritis mortality, and laboratory confirmed results are needed to strengthen these data. We aimed to estimate the effect of laboratory-confirmed norovirus infection on mortality among a national cohort of >6.3 million US Veterans who seek care within the Veterans Affairs (VA) healthcare system.
Methods: Electronic laboratory testing results for norovirus were obtained from VA's Praedico Public Health Surveillance System (Jan 2010-Dec 2018); indeterminate test results were excluded. We estimated age-adjusted ORs for the odds of mortality within 7, 14, 21, and 90 days after a norovirus diagnostic test using a logistic regression model, comparing patients with positive and negative norovirus test results. We also conducted a case-crossover analysis in which patients who died after a norovirus diagnostic test served as their own controls, comparing test results in the 0–6, 7–13, and 14–20 days preceding death to a control period.
Results: During 2010–2018, 23,196 Veterans from 110 VA Medical Centers had 25,762 stool sample tested for norovirus infection, of which 2,160 (8.4%) tested positive. The age-adjusted ORs of mortality within 7, 14, 21, and 90 days were 1.28 (95% CI: 0.82, 2.02), 0.96 (95% CI: 0.66, 1.40), 0.98 (95% CI: 0.72, 1.34), and 0.81 (95% CI: 0.65, 1.00). The case-crossover matched ORs of a norovirus-positive test within 0–6, 7–13, and 14–20 days preceding death compared to 31–37 days was 3.5 (95% CI: 1.41, 8.67), 1.67 (95% CI: 0.61, 4.59), and 2.17 (95% CI: 0.77, 6.95), respectively.
Conclusions: These results suggest a trend towards increased odds of mortality in the first 7 days after a norovirus-positive test. Veterans with a laboratory-confirmed diagnosis of norovirus may benefit from timely management and implementation of interventions.

Infectious Disease

Impact of Household Characteristics on Aedes aegypti Presence in Rural Ecuador Rachel Sippy* Rachel Sippy Froilan Heras Heras Sadie Ryan Anna Stewart-Ibarra Erin Mordecai

Aedes aegypti is the principal vector for dengue, chikungunya and Zika. Human cases and mosquitoes are linked to the environment but the impact of housing is unclear. Using surveys, housing assessments and entomological data captured across the dengue transmission season in two cities (Zaruma and Portovelo) in Ecuador, we compare the effect of housing on Ae. aegypti presence. We used binomial generalized linear mixed models (houses within clusters as random effects), adjusting for potential confounders. Across seasons, 65 houses from Portovelo and 73 houses from Zaruma participated.

In Portovelo, patios affected Ae. aegypti risk. Compared to homes with no patio, those with messy patios had a risk increase (RR: 2.30, 95% CI: 1.38—3.84) as did homes with clean patios (RR: 2.78, 95% CI: 1.44—5.36). In Zaruma, patio presence, patio cleanliness, and frequency of trash pickup affected risk. Compared to homes with no patio, those with messy patios had a risk increase (RR: 2.52, 95% CI: 1.07—5.94) and no effect among homes with a clean patio (RR: 1.39, 95% CI: 0.58—3.34). Compared to homes with trash pickup of 3 times a week or less, homes with daily pickup had increased risk (RR: 3.10, 95% CI: 1.14—8.41).

Each location had different built environment risk, which could be explained by mosquito adaptation to local environments or differential effects of climate on the built environment in each city. Mosquitoes may have unmeasured preference for specific housing characteristics present in each location (e.g. homes with patios in Portovelo have some unmeasured additional breeding habitats), or there are unmeasured confounders. This work demonstrates that built environment impacts on Ae. aegypti presence may vary according to location, meaning public health communication and control efforts should be place-specific. Additional research must assess the mediating effects of climate and the built environment or potential interactions in the creation of suitable Ae. aegypti habitats.

Modeling the Impact of Staff to Patient Ratios on MRSA Acquisition in an Intensive Care Unit Stephanie Johnson* Eric Lofgren Matthew Mietchen

Background: Hospital staff-to-patient ratios impact patient care. Increasing the staff in an intensive care unit (ICU) should impact rates of healthcare-associated infections (HAIs) by reducing the number of patient contacts per provider. However, a change in staffing rates is difficult to study empirically. An RCT would be logistically difficult and observational studies would have to contend with extensive confounding.

Methods: We use a mathematical model of Methicillin-resistant S. aureus (MRSA) to study the impact of changes in staffing on HAIs. For a 15-bed ICU, we vary the number of intensivists on staff from 1 to 3, and within those scenarios, set the Nurse:Patient ratio at 1:1, 1:2.5, 1:3 and 1:5. The outcome of each scenario was the mean number of hospital-associated MRSA acquisitions in one year.

Results: Treating the 1-intensivist, 1:3 Nurse:Patient ratio as the baseline with 44.7 MRSA acquisitions per year, increasing the number of intensivists had a modest impact on rates, with 2- and 3-intensivists having a rate ratio (RR) of 0.91 and 0.74. Increasing the number of nurses from 5 to 6 (moving from a 1:3 to 1:2.5 Nurse:Patient Ratio) had a RR of 0.90, suggesting a small change in nurse staffing levels has a large impact on rates, due to the high volume of contacts nurses have with patients. More dramatic changes had larger shifts in MRSA acquisition rates, with 1:1 Nurse:Patient ratio scenarios having an RR = 0.36 and at the other extreme a 1:5 Nurse:Patient ratio having an RR of 1.21. Confidence intervals are not presented here, as for modeling studies they can appear deceptively precise.

Conclusion: High staffing levels impact HAI rates. The cost of staffing be weighed against its impact on HAIs as well as other axes of patient care. This study considers only the impact from changes in contact patterns emerging from different staffing levels – further gains may exist from improved patient care, reduced errors, increased time for hand hygiene, etc.

Infectious Disease

flu@home - Self-Testing for Influenza Virus in the United States Monica Zigman Suchsland*

Monica Zigman Suchsland Barry Lutz Ivan Rahmatullah Victoria Lyon Enos Kline Helen Chu Shawna Cooper Chelsey Graham Mark Rieder Philip Su Matthew Thompson

Background: Each year, influenza virus (flu) produces a substantial health burden around the world. Detecting flu early in symptom presentation for an individual can potentially reduce the risks of virus spread and illness severity due to early treatment. This can potentially be achieved through the use of rapid diagnostic self-testing.

Methods: We conducted a prospective observational study with a convenience sample of adults reporting flu like symptoms (ILI) across the US from March 2019-May 2019. Recruitment was conducted through targeted advertising on websites. Participants completed an app-guided rapid diagnostic lateral flow test using an unsupervised self-collected foam-tipped low nasal swab, compared to a reference test of a second self-collected nasal swab transported to a central lab in universal viral transport media tested by molecular assay. The primary outcomes were accuracy and user success of completing the self-test.

Results: A total of 1146 self-test kits were mailed to participants with ILI. There were 737 participants who successfully completed the study, of whom 77% reported ≥4 flu-like symptoms. The majority of participants tested themselves ≥4 days after symptom onset. The flu positivity rate confirmed by molecular assay was 6.1%. The sensitivity of the self-test was 14% (95% CI 5-28%) and specificity was 90% (95% CI 87-92%).

Conclusions: There was a drop in participation between consent and study completion. Potential reasons contributing to this are symptom resolution or effort required to mail samples back. While specificity was high, sensitivity is lower than existing literature on this type of assay. Potential reasons for the high false negatives include late presentation of illness, late testing, and user errors in testing. Providing self-tests for influenza to the general public has the potential to be a powerful tool with value in the community, particularly during seasons of high flu prevalence, providing sensitivity can be increased.

Infectious Disease

Examining patterns of pediatric vaccination in the United States: a latent class analysis of vaccine uptake and timeliness among a nationally-representative sample of children 19 months of age Margaret K. Doll* Margaret K. Doll Aman Verma Kathryn T. Morrison

Background: Pediatric vaccine hesitancy is a growing trend in the United States (U.S.) and elsewhere. Some vaccine-hesitant parents delay or refuse select vaccines, adopting an alternative vaccine schedule that differs from one endorsed by an immunization technical advisory group. Given the high number of pediatric immunizations, the use of an individualized vaccine schedule can yield thousands of vaccination patterns that are difficult to characterize using traditional descriptive methods.

Methods: We implemented a latent class analysis to identify distinct patterns of U.S. pediatric vaccination by 19 months of age using data from the 2012-2017 National Immunization Survey-Child (NIS-Child). NIS-Child is a representative sample of U.S. children that estimates vaccine coverage using healthcare provider records. Participant receipt of each vaccine antigen and age were compared with the U.S. recommended vaccine schedule and used in latent class analyses. We selected the number of classes based on interpretability, and weighted the likelihood function to adjust for sampling weights.

Results: Between 2012-2017, NIS-Child included 90,679 participants with adequate provider data and survey weights, representing 34,471,357 children. In preliminary analyses, we selected a five class model with the following assigned descriptions and membership probabilities: 1) all vaccines, occasionally late (37%), 2) all vaccines except rotavirus, often late (12%), 3) few or no vaccines, always late (5%), 4) all vaccine antigens but missing doses, mostly late (12%), 5) all vaccines, never late (34%) (Figure 1). Analyses to characterize temporal and demographic patterns in class membership are forthcoming.

Conclusions: Despite considerable variation, there are common patterns in uptake and timeliness of pediatric vaccination. Understanding these patterns is important to inform the population-level risks of vaccine-preventable diseases, and develop interventions to address undervaccination.

Figure 1. Probability of latent class membership by the number of vaccine doses received and timeliness of vaccine administration for each vaccine antigen[+].
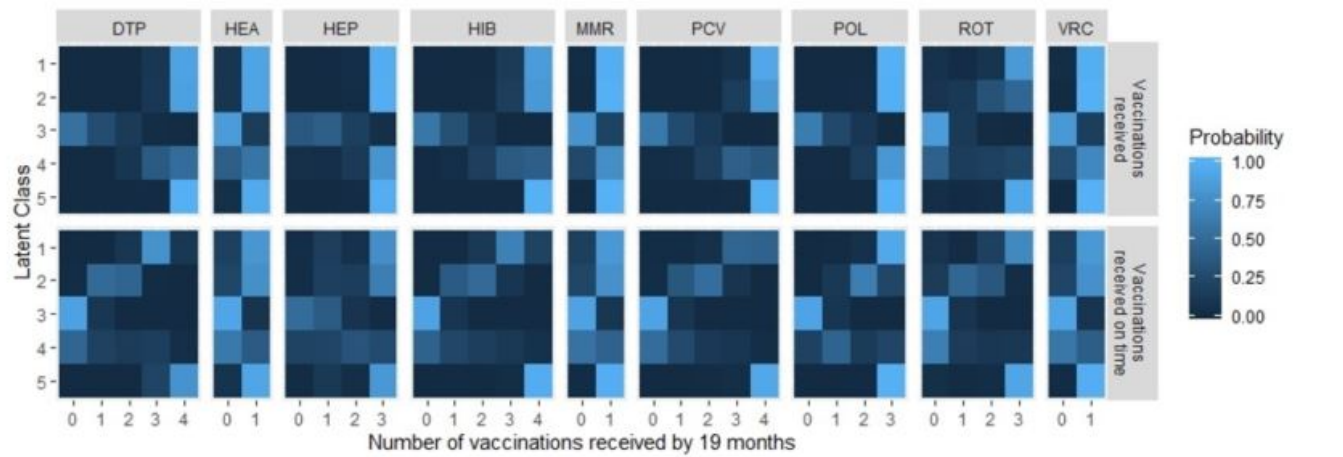
[+]*Abbreviations*: DTP: diphtheria, tetanus, pertussis; HEA: hepatitis A; HEP: hepatitis B; HIB: *Haemophilus influenzae* type B; MMR: measles, mumps, rubella; PCV: pneumococcal; POL: polio; ROT: rotavirus; VRC: varicella.

Trends in genital human papillomavirus by age group among males and females in a national survey, United States, 2013-2016 Rayleen Lewis* Rayleen Lewis Julia Gargano Elizabeth Unger Troy Querec Lauri Markowitz

Introduction: In the United States, patterns of human papillomavirus (HPV) prevalence by age have been described qualitatively as increasing from teens to early-20s among males and females, decreasing through middle age among females, but remaining stable among males. We quantitively assessed relations between vaccine-type (VT) and non-vaccine-type (nVT) HPV prevalences and age by sex.

Methods: Penile and cervicovaginal swabs were self-collected from 15-59 year-olds and tested for 37 HPV types in the 2013-2016 National Health and Nutrition Examination Surveys, nationally representative, complex surveys. Weighted VT (6/11/16/18) and nVT (any of 33 other types) prevalences were estimated by sex in 3-year age groups. Segmented linear regression was used to model prevalence by age group, determine number of segments, their slopes (β [95% CI]), and placement of joinpoints.

Results: Among males, there was a positive relation with nVT prevalence and age from 15-17 to 21-23 years (β: 15.7 [9.5, 22.0]); a smaller positive slope was noted through older ages (Figure). Among females, there was a positive relation through age 21-23 (β: 18.1 [9.0, 27.1]), followed by a negative relation through 30-32 years (β: -6.5 [-15.0, 2.1]); thereafter, prevalence was not related to age. VT prevalence in males showed a similar pattern to nVT prevalence but with an older age joinpoint (30-32 years). VT prevalence was positively related to age among females through 24-26 years (β: 1.9 [0.6, 3.2]) and negatively related from 24-26 to 57-59 years (β: -0.4 [-0.6, -0.1]).

Conclusion: Using segmented linear regression, the relation between HPV prevalence and age varied over the lifespan and differed by sex. Patterns may reflect sex differences in natural history of HPV and sexual behavior. Older ages of joinpoints in VT than nVT models suggest vaccine impact. Due to VT declines in vaccine-targeted age groups, the highest VT prevalences are no longer among persons in their early 20s.

Figure: Non-vaccine-type and vaccine-type prevalences by age group among males and females, NHANES, 2013-2016
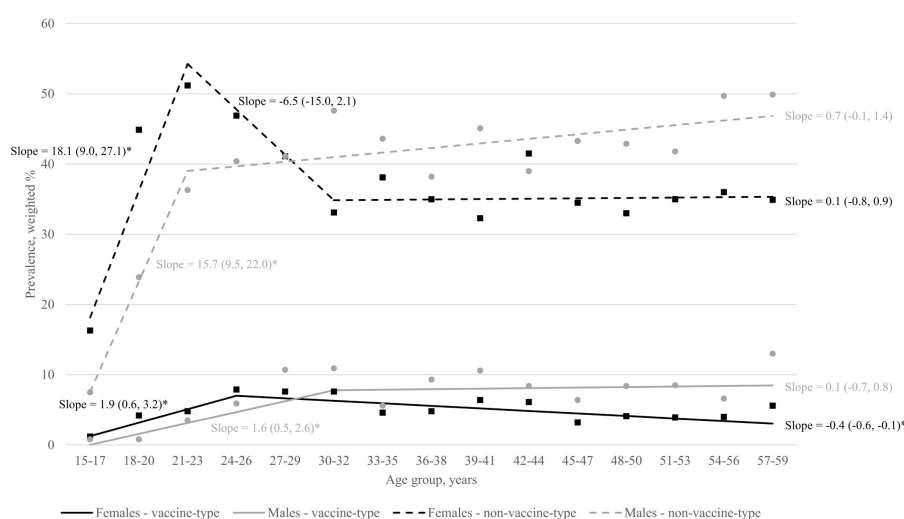
Infectious Disease

Estimating excess sepsis mortality and hospitalization burden associated with influenza in Hong Kong, 1998 to 2015 Jessica Y. Wong* Jessica Y. Wong Chung-mei M. Cheung Vicky J. Fang Benjamin J. Cowling Peng Wu

Background: Influenza infection is associated with high morbidity and mortality, and a significant proportion of this results from associated sepsis. However, severe influenza is frequently underdiagnosed and there is currently limited data on the importance of sepsis as a clinical outcome of influenza virus infection. As a result, there is a need for statistical modelling in the estimation of morbidity and mortality burden of influenza.

Methods: We applied linear regression models to mortality and hospital admission data coded for septicaemia from 1998 to 2015 in Hong Kong, and included proxy measures for influenza virus activity in the community for each influenza type/subtype as covariates, and also adjusted for covariates including RSV activity, mean temperature and absolute humidity. A covariate was included to account for change in sentinel surveillance practice in Hong Kong during and after the 2009 influenza A(H1N1)pdm09 pandemic.

Results: Our study estimates an annual influenza-related excess sepsis mortality rate of 0.28 (95% CI: 0.05, 0.48) and an excess respiratory hospitalization rate of 1.95 (95% CI: 0.94, 2.80) per 100,000 persons per year. The mortality and hospitalization burden were highest in influenza B and influenza A(H3N2) subtype respectively. Influenza-related sepsis disease contributed to a significant hospitalization burden across all age groups, in particular the extremes of age.

Conclusion: Our study applied statistical model to estimate excess hospitalization and mortality rates resulting from influenza-associated sepsis. Estimates were in line with current literature and demonstrated the highest morbidity and mortality in the older adults and young children, and in cases associated with influenza A(H3N2). These are potential areas where public health interventions could be targeted. Our model could allow more accurate estimation of disease activity and facilitate public health interventions and policy planning.

Infectious Disease

Population-level effects of household income and maternal education interventions on acute respiratory disease in children under-5 in Bangladesh Sharia M Ahmed* Sharia Ahmed Michelle C Odden Barrett Welch Sakila Afroz Joya M. Omar Sharif Ibn Hasan Mohammad L Rahman Mostofa Golam Quazi Quamruzzaman Mahmudar Rahman David C Christiani Molly L Kile

Bangladesh has made phenomenal progress in reducing under-5 mortality. Yet, childhood mortality remains high with respiratory infections being responsible for a fifth of under-5 deaths. Poverty and maternal education influence numerous risk factors of childhood respiratory infection, including nutrition, water treatment, handwashing behaviors, and indoor air pollution. We aimed to estimate the real-world population effects of hypothetical interventions to increase household income and maternal education on acute respiratory infection (ARI) incidence in children in Bangladesh.
In a cohort of pregnant women (recruited 2008-2011) and their children (N=950) in Bangladesh, we collected information on demographic, reproductive, environmental, and behavioral exposure risk factors using structured questionnaires. We actively surveyed mothers every 2 weeks regarding their children's ARI symptoms from age 4-5 years, and used targeted maximum likelihood estimation (TMLE) to estimate the real-world population-level effect of intervening on current poverty and maternal education levels.
We observed an incidence rate of 1.3 cases of respiratory illness per 100-person days. We estimated that interventions to lift all household incomes to a minimum of 3,000Taka/month would reduce ARI by 20% (incident rate ratio IRR=0.80, 95% CI: 0.69, 0.92). Similarly, we estimated a 10% reduction in ARI if all mothers completed at least primary education (IRR=0.90, 95% CI: 0.78, 1.03). These estimated impacts were attenuated at higher income thresholds.
We show that household income and maternal education interventions could have a substantial impact on reducing childhood disease burden from respiratory infections in rural Bangladesh. This impact is likely through the myriad of pathways by which income influences other infectious disease risk factors. Our results also suggest interventions targeting the poorest households and least educated mothers would have the greatest impact.

Infectious Disease

Estimating the case fatality rate of Yellow Fever infections Joseph L Servadio* Joseph Servadio Mark Fiecas Matteo Convertino Claudia Muñoz-Zanzi

Background: Yellow Fever (YF) is a flavivirus spread by multiple mosquito genera. The virus is endemic in sub-Saharan Africa and South America, where monkey species are a reservoir. A widely cited estimate states that half of severe cases are fatal, but this figure has not been updated or validated empirically. This study aims to generate an updated estimate of the case fatality rate of YF by collecting data from published literature. Methods: Data pertaining to YF fatalities were collected through a comprehensive literature review. A total of 842 articles were found through a search in PubMed and Ovid MEDLINE, 164 of which remained after title and abstract screening. Of these, 30 articles provided 128 counts of reported YF cases and fatalities with associated time and location. Case definitions from the articles were used to identify febrile patients with jaundice, hemorrhaging, or other symptoms of severe YF as well as cases that were laboratory confirmed or suspected. Observed proportions of fatal cases and standard errors were used to estimate an overall case fatality rate with uncertainty through Monte Carlo sampling to produce expected numerators of fatal cases per study, holding denominators constant. Results: Preliminary results show that, among confirmed cases with fever, jaundice, and other YF symptoms, the case fatality rate is 40.8% (95% CI: [37.7%, 45.3%]). When including confirmed cases without explicit mention of symptoms, the fatality rate is 31.2% (95% CI: [29.2, 33.4]). The estimated case fatality rate for suspected YF cases with symptoms is 35.1% (95% CI: [31.8, 37.9]), and the estimated rate for suspected YF cases without requiring symptoms is 30.7% (95% CI: [30.0, 31.4]). These estimates are lower than the WHO estimate, but differences in case definition for severe cases may impact results. Conclusions: The case fatality rate for confirmed YF with severe symptoms is estimated to be 40%, less than the commonly cited fatality rate for severe cases.

Identifying foods most commonly associated with Listeria monocytogenes infection in Minnesota

Joseph L Servadio* Joseph Servadio Craig W Hedberg

Background: Listeriosis is a foodborne disease caused by Listeria monocytogenes (Lm) bacteria, and nearly all cases require hospitalization. Elderly, immunocompromised, and pregnant people have greatest infection risk. FDA warns those at risk to avoid deli meats and unpasteurized dairy, among others. These recommendations are based mainly on older outbreak data, not accounting for novel outbreak vehicles. Most cases also are sporadic rather than outbreak-associated. This study aims to identify "risky" foods for listeriosis by seeking foods eaten more by listeriosis cases compared to non-cases. Methods: Data for 94 non-outbreak listeriosis cases in 2004-2016 were provided by the Minnesota (MN) Department of Health and include 28-day food histories for 43 food items. Proportions of cases consuming food items in 28 days were used to estimate two-day proportions using relationships between weeklong and monthlong consumption from MN FoodNET surveys. Population diet patterns were available from the 2015-2016 National Health and Nutrition Examination Survey (NHANES), providing two recall days for 205 food categories. Estimated two-day proportions of consumption for Lm cases were compared to those for NHANES respondents by matching 10 respondents to each Lm case by age, sex, race, and pregnancy status. Proportions were tested using chi-squared tests for proportion differences (PD). Results: Compared to the matched NHANES population, a higher proportion ($p<0.05$) of Lm cases consumed hot dogs (PD=0.087), precooked shrimp (PD=0.068), and cantaloupe (PD=0.073). Similar results were seen using the national NHANES population for reference. Conclusions: A selection of foods from the Listeria questionnaire were eaten in greater frequency by Lm cases in MN compared to both the nationally representative and demographically matched NHANES populations. These indicate potential for increased risk due to different dietary patterns, informing food recommendations and surveillance.

Infectious Disease

Reducing Carbapenem-resistant Enterobacterales infections in a densely connected healthcare facility network Dana K Pasquale* Dana K Pasquale Courtney Luterbach James Moody Heather Henderson Eric Cober Robert A Salata Robert C Kalayjian Richard R Watkins Yohei Doi Keith S Kaye Scott Evans Vance G. Fowler, Jr Robert A Bonomo David van Duin

BACKGROUND
Carbapenem-resistant Enterobacterales (CRE) infections have a >20% mortality rate and are often healthcare-associated. Acute care hospitals (ACH) with more connections to other facilities via patient transfers have higher CRE burdens. The Consortium on Resistance Against Carbapenems in Klebsiella and other Enterobacteriaceae (CRACKLE-1) collected a prospective clinical cohort of patients with a positive CRE culture from a set of Midwestern ACH during a 4 ½-year period.
METHODS
We created a facility-based network of patient transfers between the ACH of CRE diagnosis and facilities prior to admission and upon discharge (skilled nursing facility (SNF), long term acute care (LTAC), outside hospital (OSH), or hospice). We used admission and discharge dates to create another network of probabilistic CRE transmission potential based on facility co-residence and pathogen similarity (combination of susceptibility testing and clonal bacterial typing). Using the putative transmission network, we simulated an agent-based system to model the effect of a 50% transmission reduction intervention at ACH in different network positions on total nosocomial CRE transmissions across the network.
RESULTS
The observed facility network comprised 16 ACH, 173 SNF, 28 LTAC, 51 OSH, and 8 hospices. The analysis set included 859 patients who had 1,169 admissions with CRE diagnosis. We observed 1,010 transfers; most ACH transfers (84%) were to/from a SNF. Across the entire network, intervening at ACH with the highest transfers in or out (degree) had the greatest reduction in total network nosocomial infections, nearly reaching the level of intervening at all ACH, vs. intervening at ACH with the highest observed transmission probabilities or ACH with moderate degree and betweenness centrality.
CONCLUSIONS
Patient transfers affected total network-wide nosocomial CRE infections. The number of nosocomial infections was efficiently reduced by intervening at ACH with the highest patient transfers.

Infectious Disease
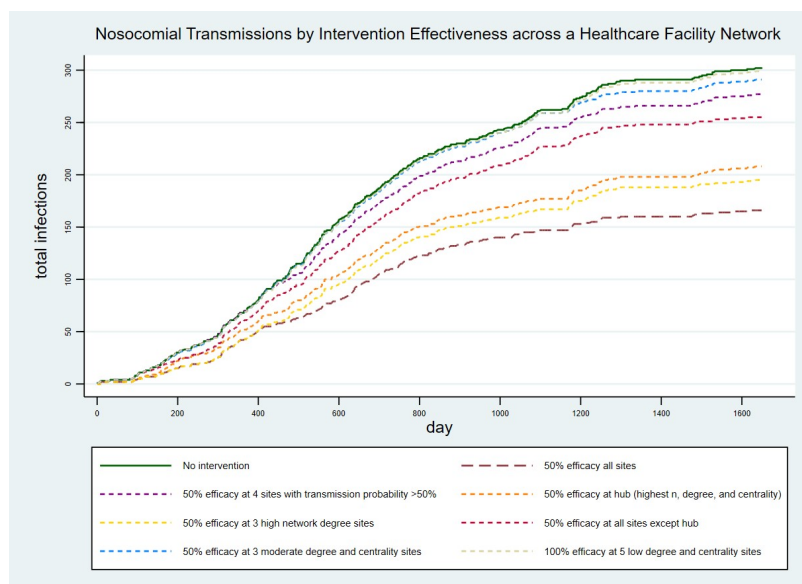
Prior Inpatient Antibiotic Use among Hospitalized Patients with Community-Onset Extended-Spectrum β-lactamase (ESBL)-producing and non-ESBL producing Enterobacteriaceae
Hannah Wolford* Hannah Wolforod Kelly Hatfield James Baggs Babatunde Olubajo Sujan Reddy Isaac See Anthony Fiore John Jernigan

Background: The burden of extended-spectrum β-lactamase (ESBL)-producing Enterobacteriaceae has increased 50% since 2012. We assessed the association between inpatient antibiotics and community-onset (CO) ESBL infection.

Methods: We examined extended-spectrum cephalosporin resistance for the first clinical CO Escherichia coli or Klebsiella spp. culture (obtained prior to day 4 of hospital admission) per inpatient in the Premier Healthcare Database from 2013-2017. Extended-spectrum cephalosporin resistance was used as a surrogate for ESBL-production. We assessed antibiotic use during any hospitalizations at the same hospital within 30 days prior to an incident clinical culture and compared receipt of inpatient antibiotics (overall, 3rd and 4th generation cephalosporins, vancomycin, fluoroquinolones) among ESBL and non-ESBL-producing Enterobacteriaceae (non-ESBLs) using chi-square tests.

Results: We identified 31,939 patients with CO-ESBLs and 276,222 CO-non-ESBLs from 256 hospitals. A hospitalization within 30 days prior was more common among patients with ESBLs (18.0% vs 9.8% for non-ESBLs; p-value<0.0001). Among patients with a recent hospitalization, those with ESBLs were significantly more likely to have received inpatient antibiotics (86.0% vs 66.1% for non-ESBLs respectively; p-value < .0001). By class, the largest difference occurred in the use of 3rd and 4th generation cephalosporins ≤30 days before positive culture (41.2% for ESBL patients and 14.8% for non-ESBL patients; p-value <.0001; Figure 1).

Conclusions: Hospitalized patients with CO-ESBLs were more likely than hospitalized patients with CO-non-ESBLs to have had recent inpatient antibiotic use in the same hospital, particularly for 3rd and 4th generation cephalosporins. If these patterns are reflective of overall antibiotic use in this population, reducing inappropriate use of 3rd and 4th generation cephalosporins may be a measure for preventing CO-ESBL infections.

Figure 1. Proportion of community-onset extended-spectrum β-lactamase (ESBL)-producing and non-ESBL producing *Enterobacteriaceae* with a hospitalization in the prior 30 days receiving an inpatient antibiotic
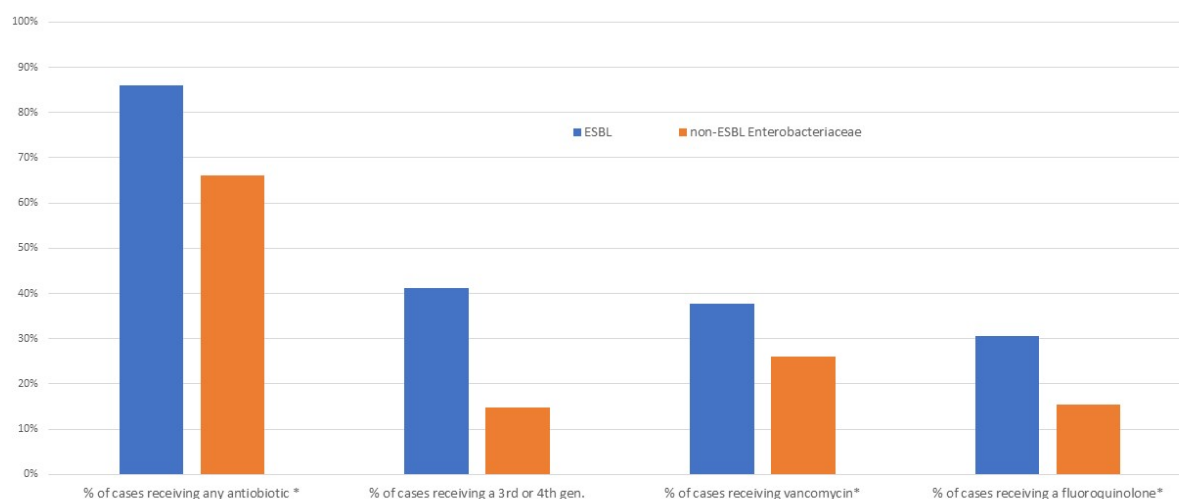
*significant difference was found between ESBLs and non-ESBL *Enterobacteriaceae*
Note: Antibiotic categories are not mutually exclusive.

LATEBREAKER

Infectious Disease

Characterizing mobility and TB treatment in East Africa using enriched clinical cohort and outcome tracing data Grace Mulholland* 3647] Mulholland Jess Edwards Milissa Markiewicz

Between March and December of 2019, TB treatment records were abstracted for all adults who enrolled in tuberculosis (TB) treatment in the six months preceding study initiation at 12 facilities on the shores of Lake Victoria. Patients in the study population initiated TB treatment between October 2018 and December 2019. Among these patients, 297 were interviewed about engagement in care and mobility during TB treatment. In the survey, 30% reported any overnight trips outside their district of residence following TB treatment initiation, and 21% reported spending 7 or more nights away from home in the 30 days preceding the survey. The most common reason for mobility among TB patients was employment; 60% of trips reported were to find employment or work. Among patients reporting suboptimal TB treatment adherence, low adherence was most commonly attributed to being busy with work (32% of reasons reported for suboptimal adherence) or traveling away from home (11% of reasons). TB treatment outcomes were ascertained by records abstraction at the conclusion of the study period and a tracing study among patients who were lost to follow-up or not evaluated. At the time of follow-up, 23% of patients had no outcome and were presumed still on treatment. Of those with recorded or traced outcomes, 53% were cured or completed treatment, treatment failed for less than 1%, 11% were deceased, 6% were recorded as losses to follow-up, and 29% had transferred out or had an unknown outcome. Mobility was not associated with successful TB treatment. Among patients who took any overnight trips outside the district since treatment initiation, 89% of those with recorded or traced outcomes were cured or completed TB treatment, as compared to 78% of those who did not take such trips. Among those who spent 7 or more of the prior 30 nights away from home, 73% were cured or completed treatment, whereas 85% of those who spent more nights at home were cured or completed treatment.

LATEBREAKER

Infectious Disease

Can we improve sepsis prediction by parameterizing clinical criteria within immunocompromised hosts? Margaret L Lind* 3647] Lind Amanda Phipps Steven A Pergam Stephen J Mooney Marco Carone Benjamin Althouse

Title: Can we improve sepsis prediction by parameterizing clinical criteria within immunocompromised hosts?

Background: Current clinical sepsis criteria were developed in general population studies that excluded allogeneic hematopoietic stem cell transplant (HCT) recipients and have low predictive value among this population. Here, we examine if population specific parameterization of the Systemic Inflammatory Response Syndrome (SIRS) leads to improved predictive performance in relation to bacterial sepsis (gram-negative, *Staphylococcus aureus*, or *Streptococcus* sp. bacteremia).

Methods: All distinct potential infections (PIs) from the first 100 days following adult HCTs that occurred between June 2010-2019 at a single center were retrospectively collected and randomly assigned to a model or validation dataset (ratio: 7/3). Using the model dataset, a weighted integer-scoring logistic regression method, and decision tree selected biological thresholds; we generated a population specific SIRS score (PS3). In the validation dataset, we compared the predictive performance of SIRS (threshold: 2) and PS3 (Youden Index selected threshold) in relation to bacterial sepsis.

Results: Between June 2010-2019, 1737 HCT recipients were transplanted and experience ≥1 PIs. In total, they contributed 14,263 PIs and 517 sepsis events. Patients were similar between the modeling and validation datasets and the proportion of sepsis to PIs was similar (3.8% & 3.1%, respectively). In comparison to the PS3 (threshold 7), SIRS (threshold 2) had lower sensitivity (SIRS 43.8%, 95% CI: 36.4-51.4%, PS3 51.9% CI: 43.1-60.5%) and similar specificity (SIRS 64.3% CI: 62.9-65.8%, PS3 64.2% CI: 62.7-65.6%).

Conclusion: We were able to increase the sensitivity of the SIRS model through population specific parameterization. However, the developed tool had limited predictive value and future work should identify clinical factors predictive of bacterial sepsis among this and similar high-risk populations.

Figure: Receiver Operating Characteristic Curves for SIRS and a Population Specific SIRS (PS3) in Relation to Bacterial Sepsis Among Allogeneic HCT Recipients

Biological Thresholds and Scores By Criteria

	SIRS		PS3	
	Threshold	Score	Thresholds	Score
Temperature	> 38 C	< 36 C	1	> 38 C	1
Heart Rate	> 90 bpm	1	> 101 bpm	2
Respiratory Rate	> 20 bpm	1	> 14 bpm	4
White Blood Cell Count	>12,000/mm³	< 4,000/mm³	1	> 100/mm³	4

The Effect of Blight Abatement on Domestic Crime by Alcohol Availability: A Triple-Difference Analysis
Sandhya Kajeepeta* Sandhya Kajeepeta Christopher Morrison Katherine Theall

There is increasing evidence that place-based interventions, including blighted property abatement and vacant lot remediation, reduce crime and interpersonal violence in urban settings. However, evidence concerning the impacts of these neighborhood interventions on domestic crime is inconclusive. We tested the hypothesis that a place-based intervention in New Orleans, LA, was associated with decreased incidence of domestic crime. Because alcohol availability and consumption are strongly related to domestic crime incidence, we also assessed whether these associations were moderated by alcohol outlet density. We used data from a City of New Orleans blighted property abatement initiative and assessed associations using a triple-difference approach. The analytic sample was 204 remediated lots and 612 matched control lots over 84 months (2011-2017), comprising a total of 68,544 lot-months. In difference-in-difference analyses, the intervention was associated with additional domestic crime incidence (β = 0.352, 95%CI: 0.055, 0.650; p = 0.020). In triple-difference analyses, bar density moderated this association (β = -0.117, 95%CI: -0.144, -0.090; p < 0.001), such that in areas with higher bar density, the increases in domestic crime density over time were lower in remediated lots compared with control lots. Findings suggest that a place-based intervention to reduce blighted property may have contributed to fewer domestic crime incidents in areas with more bars, or conversely, may have led to increased call volume for domestic events in areas with fewer bars potentially through increased social control in these areas.

Child abuse and sleep quality among adult women: The role of child socioeconomic status

Erin Higa* Cheryl L Currie Erin Higa Lisa-Marie

Background: A recent systematic review highlighted associations between child abuse and adult sleep quality, and the need for research focused on women and moderating variables. The objective of the present study was to examine the role that child socioeconomic status (SES) might play in associations between child abuse and adult sleep quality among women. Methods: In-person data were collected from women living in a mid-sized city in western Canada in 2019 (N = 120; M age = 40 years). Sleep quality was measured using the Pittsburgh Sleep Quality Index and reverse-coded for analysis. Child physical and verbal abuse were assessed using single items (yes or no). Childhood SES was assessed by a single item and dichotomized at the mean (low-middle income and upper-middle/upper income). Separate linear regression models examined associations between each form of child abuse and continuous adult sleep quality score, adjusted for age and adult SES, and stratified by childhood SES. Results: Among women who grew up in low and middle-income homes (n = 61), child physical and verbal abuse were associated with a 2.6 and 3.0-point decrease in adult sleep quality; respectively, on a 20-point scale (95% CIs 0.24-5.0 and 1.0-5.0). Among women who grew up in upper middle- and upper-income homes (n = 59), child physical and verbal abuse had no impact on adult sleep quality. Conclusion: Growing up in a home with higher socioeconomic status may serve as a buffer against the adverse impacts of child physical and verbal abuse on sleep quality among adult women.

Injuries/Violence

A prediction model for potential dental casualties in the Canadian Armed Forces Randall Boyes* Randall Boyes Alyson Mahar Constantine Batsos

The mission of the Royal Canadian Dental Corps is to maintain a high state of dental readiness in the Canadian Armed Forces. Dental Fitness Classification is used to assess a member's risk of becoming a dental casualty. This classification is based on perceived 12-month risk of dental emergency; Class 3 indicates high risk (not deployable). We have developed a model that incorporates demographic, medical, and dental history to better predict dental readiness.

The model was developed using data from 2,545 new recruits and a cross-section of 2,312 additional Canadian Armed Forces members who were deployable at baseline dental examination and had at least one year of active service following the exam between 2014 and 2017. An extensive selection of demographic, dental, and social predictor variables were extracted from electronic records.

Separate models were developed for the new recruits and the mature cross-section. The models are L1/2 penalized logistic regression models which predict a Class 3 designation within 12 or 18 months. Internal model validation used optimism-corrected bootstrapping.

Class 3 was assigned to 5.8% of recruits within 12 months and 11.0% within 18 months. Mature cohort members had event rates of 5.1% and 9.6%. Models were evaluated using the area under the receiver operating curve (AUC) and the f1 score. The recruit models have an AUC of 0.76 and f1 score of 0.25 at 12 months and an AUC of 0.76 and f1 score of 0.36 at 18 months. Our mature models have an AUC of 0.67 and f1 score of 0.20 at 12 months and an AUC of 0.68 and f1 score of 0.28 at 18 months.

The final risk prediction models will permit the Royal Canadian Dental Corps to more effectively determine dental visit frequency and target dental resources to Canadian Forces Bases. The models will enable military commanders to gauge the dental readiness of their personnel. Future research could externally validate this model and calibrate it for use in other military populations.

Injuries/Violence

Latent Class Analysis of Diagnostic and Treatment Procedures among Patients Diagnosed with Traumatic Brain Injury: 2004-2014 Nationwide Inpatient Sample Hind Beydoun* Hind Beydoun Catherine Butt May A. Beydoun Shaker M. Eid Alan B. Zonderman Brick Johnstone

Objectives: To characterize latent classes of diagnostic and/or treatment procedures among hospitalized U.S. adults, 18 to 64 years of age, with a primary diagnosis of TBI from the 2004-2014 Nationwide Inpatient Sample.

Methods: A total of 10 procedure groups were generated using ICD-9-CM procedure codes. Latent class analysis (LCA) was applied to these procedure groups and disparities by injury, patient and hospital characteristics as well as healthcare utilization outcomes were examined using multivariable regression modeling.

Results: A total of 200,637 records included one or more procedure groups. LCA resulted in two classes of hospitalizations, namely class I (n=155,559) labeled as "mostly rehabilitative" and class II (n=45,078) labeled as "mostly non-rehabilitative". Whereas orthopedic procedures were equally likely among latent classes I and II, skin-related, physical medicine and rehabilitation procedures, as well as behavioral health procedures were more likely among latent class I, and other types of procedures were more likely among latent class II. Compared to class I records, class II records were more likely to belong to patients with moderate-to-severe TBI who were admitted on weekends, to urban, medium-to-large hospitals located in the Midwestern, Southern or Western regions, and less likely to belong to female, non-White patients, who were > 30 years of age. Class II patients were less likely than class I patients to be discharged home and necessitated longer hospital stays and greater hospitalization charges.

Conclusions: Rehabilitation appears to distinguish two groups of hospitalized patients with TBI. Further research is required to confirm these preliminary findings.

Injuries/Violence

Type of abuse victimization and relationship between victim and perpetrator: Associations with binge eating impairment in Project EAT 2018 Cynthia Yoon* Cynthia Yoon Rebecca Emery Susan Mason Dianne Neumark-Sztainer

Background: Abuse is a public health concern, as it occurs over the life course, affects all genders and ethnic/racial groups, and is a risk factor for binge eating.
Objective: Assess whether the risk of binge eating differs by (1) the type of abuse (2) the cumulative victimization experience over a lifetime, and (3) the relationship between victim and perpetrator.
Methods: Childhood sexual abuse, sexual intimate partner violence, childhood physical abuse, physical intimate partner violence, and binge eating impairment were assessed in 2018 among participants in a longitudinal study of weight-related health (EAT 2010-2018; (N=1459; ages 18-30). For sexual abuse only, participants were asked about both familial and non-familial perpetration. Multinomial logistic regression examined the association between victimization of abuse and binge eating impairment.
Results: The prevalence of childhood sexual abuse, sexual intimate partner violence, childhood physical abuse, and physical intimate partner violence was 13.9%, 6.2%, 16.7%, and 8.1% respectively. Childhood abuse and adulthood abuse were each risk factors for binge eating, with greater risk when victimized at both time points. The number of lifetime cumulative victimization experiences was associated with increasing risk of binge eating (OR: 2.15, 2.60, 2.51, and 4.35, for 1, 2, 3, and $\geq$ 4 victimizations, respectively). Sexual abuse by a non-family member was associated with overeating (OR: 2.64, 95% CI: 1.27-5.51) and binge eating (OR: 2.33, 95% CI: 1.15-4.72), whereas sexual abuse by a family member was not. Victimization from a dating partner or spouse was associated with binge eating (OR: 3.59, 95% CI: 1.65-7.81). Findings were attenuated after adjustment for demographic variables.
Conclusion: Childhood sexual abuse and physical abuse are prevalent and are associated with binge eating in adulthood. Screening for history of abuse may inform prevention of risky eating behaviors among emerging young adults.

Injuries/Violence

Prescription opioid availability and the evolving epidemiology of suicide in California Julia P. Schleimer* Julia Schleimer Christopher D. McCort Aaron B. Shev Veronica A. Pear Garen J. Wintemute Aimee K. Moulin

Background: The concurrent crises of suicide and opioid use are likely related, but their association is understudied. Opioid availability may be both an underlying driver of increases in suicidality and a source of lethal means. Aim: To determine whether county-level opioid prescribing rates are associated with changing trends in method-specific suicide from 2006-2017 in California. Methods: Data on suicides and opioid prescribing rates were obtained from the California Department of Public Health and Centers for Disease Control and Prevention. We used Bayesian spatio-temporal negative binomial regression models to estimate the association between rates of opioid prescribing and suicide, overall and by method. Analyses were stratified by time before and after the peak in prescribing. Results: On average, opioid prescribing rates increased by 2.6% per year from 2006-2011 and decreased by 5.9% per year from 2012-2017. In adjusted models, a standard deviation increase in opioid prescribing rates from 2006-2011 within counties was associated with an increase in overall suicide ([ARR], 1.24; 95% credible interval [CI], 1.05-1.47), and suicides by poisoning (1.40; 1.05-1.87) and hanging (1.74; 1.32-2.29). In 2012-2017, increases in prescribing within counties were associated with decreases in overall suicide and suicides by hanging, firearm, and other methods (ARR ranging from 0.72-0.89), but not by poisoning. Though prescribing did not explain cross-sectional differences in suicide rates between counties, poisoning suicide and poisonings of undetermined intent increased 5% faster (95% CI, 1-10%) in counties with faster vs. slower increases in prescription rates from 2006-2011. Conclusions: Findings suggest early increases and later decreases in opioid prescribing contributed to rising rates of suicide in California. Suicide prevention efforts should consider the links between opioid prescribing, suicide risk, and population-level shifts in choice of lethal means.

Injuries/Violence

Effects of Building Demolitions on Firearm Violence in Cleveland, Ohio and Detroit, Michigan

Rose Kagawa* Rose Kagawa Benjamin Calnin Tsui Chan Magdalena Cerda Claudia Coulton Nigel Griswold Michael Henderson Melissa Mason Francisca Richter Michael Schramm 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, firearm violence 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, though results from this research are mixed.

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 home values- cannot be controlled for without blocking causal pathways between demolitions and crime, our outcome of interest.

This study estimates the effects of building demolition in Cleveland, Ohio and Detroit, Michigan on the incidence of violent crime using detailed property-level data from 2010-2017 and longitudinal targeted maximum likelihood estimation. Primary outcomes include violent crimes (homicide, rape, robbery, and aggravated assault) with and without firearms, nonfatal shootings, and property crimes. We compare the incidence of violent crimes following building demolition in areas approximately the size of a square city block to an estimate of what would have happened had there been no demolition in the two years prior in each city.

Efforts to alter the context in which violence takes place, such as through the demolition of vacant and decaying properties, may have greater probability of achieving broad and sustained impact than individual-level interventions. The results of this study may help local officials make city planning decisions that will maximize the potential to drive down rates of firearm violence, and violence more generally.

Injuries/Violence

Financial strain and intimate partner violence between parents at different stages of childhood and adolescence Melissa Tracy* Melissa Tracy Laura Hunter Jessica Phillips Jennifer Amoh Shannon Kilburn

Chronic financial hardship and acute financial stressors may increase the risk of intimate partner violence (IPV), creating a hazardous environment for both children and adults in the household. Few studies have investigated how relations between financial strain and IPV may vary at different stages of the relationship between parents with young children. We used prospectively collected data from 11,319 households in the Avon Longitudinal Study of Parents and Children (ALSPAC) to examine the longitudinal relations between financial strain and maternal physical or emotional abuse during their offspring's childhood and early adolescence (from birth through age 12), and whether these relations varied across time period. We used generalized estimating equations to account for repeated measures within participating households. Financial hardships like difficulty affording basic necessities (e.g., food, clothing, heat, rent) were reported by about 60% and acute financial stressors like losing a job or becoming homeless were reported by about 20% of the participating households at each of eight assessments. About 10% of participating mothers reported physical and/or emotional abuse by their partners at each assessment. Both financial hardship (adjusted OR [aOR]=1.40, 95% CI=1.29-1.66) and acute financial stressors (aOR=2.43, 95% CI=2.18-2.71) were strongly associated with maternal reports of IPV throughout the study period, when adjusting for parent education, income, race/ethnicity, marital status, and time of assessment. We did not find evidence of certain time periods (e.g., the postpartum period) when either financial hardship or acute financial stressors were more strongly associated with IPV. These results illustrate the consistent association between household financial strain and risk of IPV, suggesting that interventions to address economic insecurity could benefit all couples with children and adolescents to reduce the risk of IPV and its harmful consequences.

Logging off isn't enough: the role of sexual identity in the connection between cyberbullying and victimization-related behaviors Noah T. Kreski* Noah Kreski Katherine M. Keyes

Adolescents who are bullied online are more likely to be bullied offline, but little is known about the extent to which these associations vary on the basis of sexual identity, even as sexual minority students experience more bullying overall. We examined heterogeneity of online-offline bullying associations using Youth Risk Behavior Survey national data (2015 and 2017, N = 30,389), testing interactions across sexual identity (heterosexual, gay/lesbian, bisexual, "not sure") in logistic regressions. Interactions were significant across sexual identity for the associations between being cyberbullied and carrying a weapon, both in general and at school, and physical fighting, both in general and at school (see attached figure). Heterosexual students exhibit a weaker association between being cyberbullied and weapon carrying in school (OR:1.46, 95% CI:1.18, 1.80) compared to sexual minority peers (gay/lesbian OR:2.20, CI:0.88, 5.48; bisexual OR:2.87, CI:1.61, 5.13; "not sure" OR:2.98, CI:1.57, 5.63). In school, the association between being cyberbullied and physical fighting significantly varied across sexual identity, strongest among gay/lesbian students (OR:5.06, CI:2.08, 12.32), followed by those who list their sexual identity as "not sure" (OR:4.77, CI:2.77, 8.23), heterosexual students (OR:2.23, CI:1.88, 2.64), and lastly bisexual students (OR:1.90, CI:1.28, 2.84). Some sexual minority students who are cyberbullied may be more vulnerable to offline violence and exhibit self-defense behaviors. However, the association between being cyberbullied and being bullied in person was stronger among heterosexual students (OR:14.96 vs gay/lesbian OR:10.57, bisexual OR: 9.18, "Not Sure" OR:11.47). Still, sexual minority students experience more bullying in general, including far more students getting either cyberbullied or bullied in person, underscoring the potential health and psychological sequalae of violence that minority students experience in the US.

Victimization–Related Behaviors by Sexual Identity and Experience of Being Cyberbullied, YRBS 2015–2017
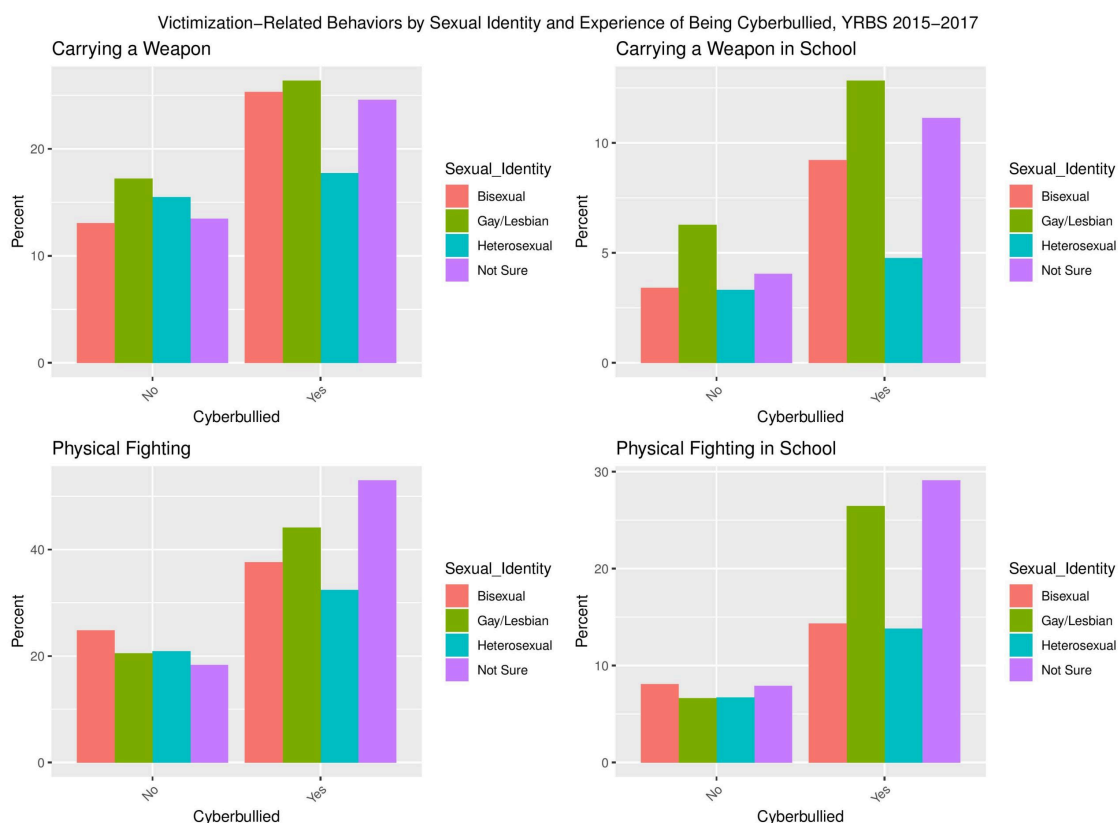
Estimating the dose-response relationship between vacant building removal and crime in Cleveland Colette Smirniotis* Colette Smirniotis Michael Schramm Claudia J. Coulton Rose M.C. Kagawa

Like many cities in the United States, Cleveland, Ohio experienced increasing rates of urban decay and depopulation following the 2007-2009 Great Recession. As a result, many neighborhoods experienced a rising number of vacant, abandoned, and dilapidated buildings, along with localized increases in crime. In an effort to stabilize Cleveland's housing market, local agencies implemented demolition programs to remediate these decaying buildings. In this study, we estimated the concentration of demolitions needed to produce the greatest change in the occurrence of firearm violence, non-firearm violence, and property crime.

The study used property-level housing data aggregated to a uniform grid of 2000-foot hexagon areal units. Counts of drug, disorder, property, and violent (firearm and non-firearm) crimes were geolocated to the hexagonal grid. Both the property data set and the crime data set covered the years 2010 through 2017. Preliminary results confirmed strong spatial clustering of both demolition and crime, as demonstrated by the attached figure mapping Cleveland's demolition and violent crime counts in 2013. Using a Bayesian hierarchical spatio-temporal framework featuring conditional autoregressive priors, we modeled crime counts with demolition and property-condition covariates. The model and Markov chain Monte Carlo simulations were implemented in R via the CARBayesST package. Demonstrating a relationship between crime and the removal of blighted structures could provide cities like Cleveland with an effective strategy to combat crime—changing the physical space through a targeted dose of demolitions.

Cleveland Demolition and Violent Crime Counts, 2013

Injuries/Violence
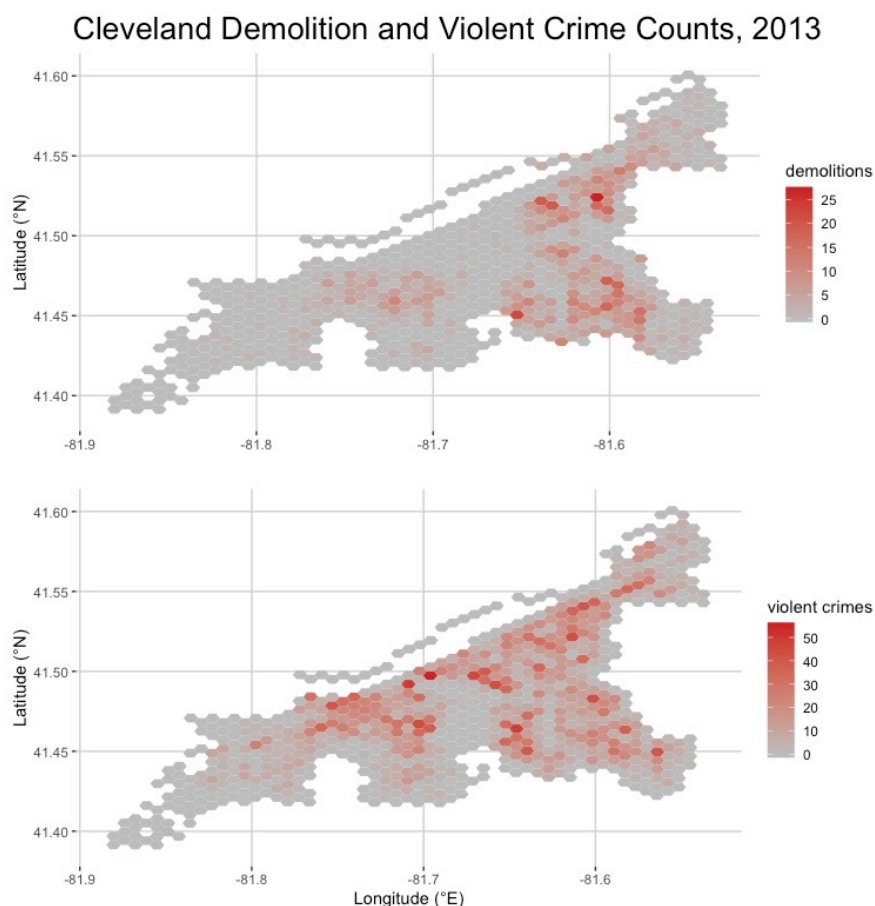
Threat assessment: Using firearm transaction records to identify suicide risk factors

Colette Smirniotis* Colette Smirniotis Christopher McCort Julia Schleimer Aaron Shev Rose Kagawa Garen Wintemute Hannah Laqueur

The public health crisis of firearm violence in the United States extends beyond what the headlines show. While homicides and mass shootings occur at much higher rates than in other developed countries, the majority of gun deaths are less visible; firearm suicides account for more than 60% of the firearm deaths in the United States. Previous research has established a link between firearm purchases and the risk of firearm homicide and suicide. This study aims to build on those findings by using the population of all legal firearm transaction records in California since 1996 to determine risk factors for suicide by firearm.

California law requires that every firearm transaction, including those between private parties, be conducted through a licensed dealer and recorded as a Dealer Record of Sale transaction. The resulting database, known as the Automated Firearms System (AFS), contains information on more than 5 million transactions and over 2 million individuals. It details handgun transfers from 1985 through 2015 and long gun transfers from 2014 through 2015, with information such as firearm type and purchaser demographic information. By linking AFS with the California Comprehensive Death file, we compare the firearm transactional behavior of several thousand victims of firearm suicide to that of the general population of California firearm purchasers. We begin with traditional descriptive statistics and hypothesis testing to determine if suicide victims differ from their counterparts in significant ways. Next, we employ supervised machine learning methods like random forest and random survival forest to further help us identify factors associated with an elevated risk of firearm suicide. As suicide attempts involving a firearm are more likely to result in a fatality than other methods, determining risk factors for firearm suicide could provide an opportunity to intervene and save lives.

Injuries/Violence

Racial/ethnic differences in the correlates of gun carrying among male US high school students
Marie-Claude Couture* Marie-Claude Couture Jee eun Kang David Hemenway Erin Grinshteyn

Background: Gun carrying is an important public health issue in the U.S., particularly among adolescents. We examine factors associated with gun carrying among male high school students, by race/ethnicity.

Methods: The 2017 Youth Risk Behavior Survey (YRBS) was used to determine correlates of gun carrying in White, Black, and Hispanic male students. Chi-square tests and multiple logistic regression models using complex survey weights were conducted. Analyses were stratified by race/ethnicity.

Results: Gun carrying in the past year was 7.0% for Whites, 9.8% for Blacks and 7.7% for Hispanics. After controlling for covariates, White students who had been previously been threatened/injured had 3.51 times the odds (p<0.0001), Blacks 3.95 the odds (p=0.06) and Hispanics 5.68 the odds (p<0.0001) of carrying a gun compared with those who had not. Among Whites, students reporting alcohol binge drinking (AOR=2.76; 95% CI: 1.44-5.30) and prescription pain medication misuse (AOR=2.58; 95% CI: 1.54-4.33) were more likely to carry guns. Among Black students, marijuana use (AOR=4.56; 95% CI: 2.47-8.44), binge drinking (AOR=3.04; 95% CI: 1.13-8.15), and previous victimization from dating violence (AOR=3.97; 95% CI: 1.46-10.74) were associated with gun carrying. Hispanic students who reported binge drinking (AOR=3.87; 95% CI: 3.14-7.01), pain medication misuse (AOR=5.14; 95% CI: 2.18-12/15), and dating violence victimization (AOR=2.77; 95% CI: 1.07-7.24) were more likely to carry a gun. Sexual orientation, bullying victimization, and mental health were not associated with gun carrying.

Conclusions: Carrying a gun is a dangerous behavior that can result in devastating consequences among adolescents. We find alcohol/drug use and violent victimization were common correlates of gun carrying. The public health community needs to better understand predictors of gun carrying and the differences in predictors across diverse adolescent subgroups in an effort to prevent it among adolescents.

Economic Shocks and Violence: a comparison of economic measures in the prediction of county-level rates of violence-related injury Jeanie Santaularia* Jeanie Santaularia Susan Mason Marizen Ramirez Micheal Oakes Paul Glewwe

Background
Economic shocks are associated with violence perpetration, but which dimensions are most strongly associated are not known. The goal of this study was to measure the association of unemployment, mass layoffs, and foreclosure rates, and county-level violence-related injury.
Methods
This study used Minnesota Hospital Discharge data linked by county to Bureau of Labor Statistics, Bureau of Economic Analysis and Minnesota Housing Link data. Violence was defined using explicit diagnostic codes (injures were the cause is identified as intentional) and proxy codes (injuries likely due to violence were the cause is identified as unknown) across counties from 2004 to 2014 in Minnesota. Rate ratio were estimated using negative binomial regression models with generalized estimating equations to account for county-level clustering. Both crude and adjusted models were run with explicit violence and proxy codes regressed separately on each economic indicator.
Results
In the adjusted models, counties with equal to or more than the average foreclosure and unemployment rates had a 1.39 (95% CI: 1.19-1.62) and 1.21 (95% CI: 1.09-1.35) times the rate, respectively, of violent-related injuries compared to counties with less than average foreclosure or unemployment rates. Mass layoff rates were not associated with explicit violence rates. The proxy codes had a more subtle association with unemployment, mass layoffs, and foreclosure rates. In counties with equal to or more than the average unemployment, mass layoffs, and foreclosure rates, proxy violence rates were 1.09 (95% CI: 1.01-1.17), 1.02 (95% CI: 0.93-1.12), and 1.07 (95% CI: 0.96-1.20) times the rate, respectively, compared to counties with less than average rates of economic hardship.
Discussion
Results indicate that foreclosure and unemployment rates are more strongly correlated with violence than mass layoffs; these factors were more strongly correlated with explicit violence diagnoses than proxy measures of violence.

Impact of the Enhanced Fatality Analysis Reporting System on Drugs Detected in Fatally Injured Drivers Stanford Chihuri* 3647] Li Stanford Chihuri

The prevalence of drugged driving has been increasing in the United States in the past two decades, with over 45% of fatally injured drivers testing positive for at least one nonalcohol drug and about 20% positive for two or more nonalcohol drugs. The Fatality Analysis Reporting System (FARS) is a census of fatal motor vehicle crashes occurring on US public roads and serves as the premier data source for monitoring drugged driving. Up to 2017, the FARS recorded up to three nonalcohol drugs using a hierarchy to decide which drug testing results to include. To improve data quality and capacity, the National Highway Traffic Safety Administration made extensive changes to the FARS starting in 2018, including a toxicological testing data file that captures all drug test results and specimens used for drug testing. In this study, we assessed the impact of the enhanced FARS on drugs detected in fatally injured drivers by comparing alcohol and drug testing data between 2017 (n=15,017) and 2018 (n=13,299). Overall, the prevalence rates of alcohol and drugs detected in fatally injured drivers were similar between 2017 and 2018. Approximately, 36% of fatally injured drivers tested positive for alcohol and 47% tested positive for at least one non-alcohol drug. The most commonly detected drug was marijuana (19% in 2017 and 21% in 2018), followed by stimulants (14.2% in 2017 and 15.3% in 2018), narcotics (8.9% in 2017 and 8.9% in 2018), and prescription opioids (7.9% in 2017 and 7.7% in 2018). Concurrent use of alcohol and marijuana was the most frequently detected polysubstance combination, found in 9.4% and 9.6% of fatally injured drivers in 2017 and 2018, respectively. The proportion of fatally injured drivers testing positive for three or more nonalcohol drugs increased from 6.7% in 2017 to 8.3% in 2018. Results of this study indicate that recent changes to the FARS have not made a substantial impact on drugs detected in fatally injured drivers.

The effects of laws expanding the public's right to use lethal force: a systematic review

Alexa Yakubovich* 3647] Yakubovich Brittany Lange Michelle Degli Esposti G.J. Melendez-Torres Alpa Parmer Douglas Wiebe David Humphreys

Background: Since 2005, states across the USA have implemented or expanded laws that broaden when civilians can use lethal force in self-defense, including Stand Your Ground laws.

Objectives: To systematically synthesize the available evidence on the impact of altering restrictions on public use of lethal force on health and criminal justice outcomes.

Methods: We registered our protocol on Open Science Framework (https://osf.io/uz68e/). We systematically searched for published and unpublished studies using 13 electronic databases, reference harvesting, and expert consultation up until December 2019. We evaluated study risk of bias using ROBINS-I. Where data were available, we transformed effect estimates in studies of the same outcome to percent change in rates pre- and post-implementation.

Results: We included 29 studies that quantitatively estimated the health or criminal justice impacts of self-defense laws. Most studies (n=25) investigated Stand Your Ground laws; the most common outcomes analyzed were firearm and total homicide. Studies comparing states with and without Stand Your Ground laws estimated a null to positive effect on firearm homicide (n=6 studies, point estimate ranging from 0-14% increase) and total homicide rates (n=3 studies, 1-14% increase). Studies of Florida estimated considerable increases in homicide rates following Stand Your Ground compared to pre-implementation (see Figure). Distributional studies of Florida demonstrated that homicide cases involving non-white (versus white) victims were more often ruled justifiable (versus unlawful), even when adjusting for situational characteristics (e.g., victim firearm use).

Conclusion: The evidence suggests that, particularly in Florida, Stand Your Ground laws have led to an increase in homicide rates. In addition, there are racial inequities in the outcomes of Stand Your Ground homicide cases, with those involving non-white victims ruled justifiable more often.
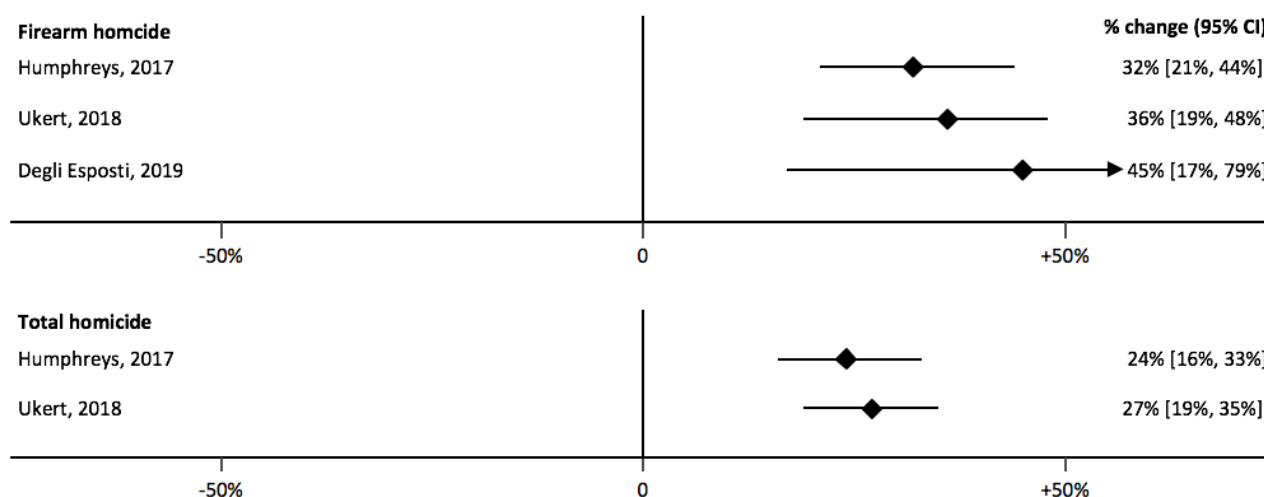
Figure: Percent change in violent outcomes pre versus post-implementation of Stand Your Ground in Florida-specific interrupted time series studies, based on incidence rate ratios.

Suicide and Job Loss in the Diesel Exhaust in Miners Study II (DEMS II) Jacqueline Ferguson* 3647] Ferguson Sadie Costello Sally Picciotto Andreas Neophytou Stella Koutros Debra Silverman Ellen Eisen

Objective: The highest suicide rates in the U.S. have been found among males in construction, mining, and extraction occupations. In recent years, the rate has increased dramatically, which may reflect the lack of economic opportunities for miners. We examined the impact of job loss, both permanent and temporary, on risk of suicide and overdose among a cohort of 11,304 male miners in Wyoming, Missouri, and New Mexico from the Diesel Exhaust in Miners Study II (DEMS II).

Methods: We fit Cox models to estimate hazard ratios (HRs) for suicide and overdose in relation to leaving work, age at leaving work, and intermittent time-off work. Separate models were fit for job loss pre- and post-1980 to examine effect modification by time period as the industry curtailed its workforce in the early 1980s.

Results: Based on 261 suicides and overdoses, miners who left work were more likely to die by suicide compared to those remained at work (HR 3.12 (95% CI: 2.18, 4.45)). Miners with 1-2 years of cumulative time-off had a modestly increased risk of suicide and overdose (1.15 (0.95, 2.53)) compared to those with no intermittent time-off work. Leaving work at a younger age was associated with a higher risk of overdose (left work before age 30 compared with 40 or older (1.83 (1.04, 3.23)) but not suicide. Evidence of effect modification by time period was present as the HRs for suicide/overdose and age at leaving work differed significantly between the stratified analyses (job loss pre-1980 vs. post-1980). HRs for job loss pre-1980 were null, yet, among miners with post-1980 job loss, leaving work before age 30 increased the risk of suicide and overdose compared with leaving work after age 55 (1.78 (1.00, 3.17)).

Conclusions: Our results suggest that leaving work, both permanently and temporarily, may increase risk of suicide and overdose among miners.

A North American prospective study of depressive symptoms and semen parameters Jennifer Yland* Jennifer Yland Michael L Eisenberg Elizabeth E Hatch Craig J McKinnon Yael I Nillni Greg J Sommer Tanran R Wang Kenneth J Rothman Lauren A Wise

Background: Major depression is a leading cause of disability worldwide. Studies of the association between depressive symptoms and semen quality have yielded inconsistent results.

Objective: We prospectively evaluated the associations between major depression inventory (MDI) score and selected semen parameters.

Methods: We analyzed data from 290 men (500 semen samples) aged ≥21 years participating in a semen testing substudy of Pregnancy Online Study (PRESTO), a preconception cohort of North American couples. At baseline, participants filled out the MDI, a validated 12-item tool that assesses depressive symptoms during the past 2 weeks (range of scores: 0-50), with a higher MDI score indicating more severe symptoms. Immediately after enrollment, male participants were invited to perform semen testing using the Trak system. We estimated the percent difference (%D) in mean log-transformed semen parameter values for associations between MDI score and semen volume (mL), total sperm count in ejaculate (million), sperm concentration (million/mL), motility (%), and total motile sperm count (million). We also fit restricted cubic splines to allow for a smoothed nonparametric fit of the relation between MDI score and semen parameters. Models were adjusted for abstinence time, age, BMI, multivitamin or folate supplement use, and sleep duration.

Results: The %D (95% CI) associated with a 5-unit increase in MDI score was -2.7% for semen volume (-6.0%, 0.7%), -3.5% for total sperm count (-11.8%, 5.5%), -0.9% for sperm concentration (-8.8%, 7.7%), -4.1% for motility (-8.3%, 0.3%), and -9.6% for total motile sperm count (-18.2%, 0.0%). The restricted cubic spline results also indicated an inverse association between MDI score and total motile sperm count (Figure 1).

Conclusion: Preliminary results indicated inverse associations between MDI score and sperm motility and total motile sperm count, and more modest inverse associations with semen volume and total sperm count.

Figure 1. Restricted cubic spline for the association between MDI score and total motile sperm count.
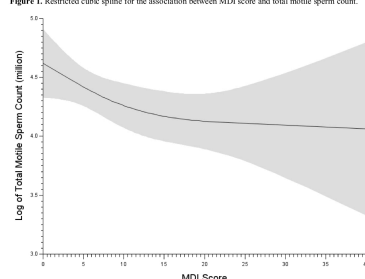
Abbreviations: MDI, major depression inventory.
Notes: Total motile sperm count (million) was log-transformed and the model was adjusted for abstinence time, age, BMI, multivitamin or folate supplement use, and sleep duration. The spline was modeled with three knots at 2, 8, and 25.

Sex-specific associations of insulin resistance with chronic kidney disease and kidney function: a bi-directional Mendelian randomization study Jie V Zhao* Jie V Zhao C Mary Schooling

Background: To provide insight to the sexual disparity in chronic kidney disease (CKD) we contextualized within evolutionary biology. We explored sex-specific effects of insulin because it may have sex-specific effect on the reproductive axis. Impaired kidney function may also cause insulin resistance.

Methods: We used a bi-directional, sex-specific, two-sample Mendelian randomization (MR). Given insulin, fasting glucose and HbA1c are related, we used MR-Bayesian model averaging (MR-BMA) to identify the best fit model, and then used univariable or multivariable MR, as appropriate. Genetic associations with glycemic traits were obtained from genome-wide association studies (GWAS) in Europeans without diabetes (n=108,557 for fasting insulin, as a proxy for insulin resistance, and for fasting glucose, n=123,665 for HbA1c in MAGIC), applied to 480,698 Europeans for overall associations with CKD (41,395 cases) and estimated glomerular filtration rate (eGFR). We also used sex-specific individual information (179,918 men, 5,959 CKD cases; 212,080 women, 5,935 CKD cases) from the UK Biobank.

Results: Insulin resistance, proxied by fasting insulin, was selected as the most likely exposure by both overall and sex-specific MR-BMA. It increased CKD in men (odds ratio (OR) 7.72 per pmol/L higher insulin, 95% confidence interval (CI) 2.91 to 20.5) but not women (OR 1.04, 95% CI 0.26, 4.10), reduced eGFR in men (-0.22, 95% CI -0.39, -0.05) but not women (0.05, 95% CI -0.12, 0.21). Genetically predicted eGFR was unrelated to insulin.

Conclusions: Genetically predicted insulin resistance was sex-specifically associated with CKD and unfavorable kidney function but was not affected by kidney function.

Mental Health

Examining the Association between Psychological Distress and Alcohol Dependence among Adult Individuals Residing in the United States Sanda Cristina Oancea* S. Cristina Oancea Taylor Strand Arielle Selya

Aims: The relationship between mental health and alcohol abuse is well-known; however, previous literature has not distinguished alcohol dependence from alcohol consumption. This study examines the association between psychological distress and alcohol dependence after controlling for the quantity of alcohol consumed in the past 30-day period and other confounding factors.
Methods: Data were drawn from the 2015 National Survey on Drug Use and Health (n=41,838). Weighted and adjusted logistic regression was run to assess the relationship between having psychological distress symptoms and alcohol dependence, after confounding adjustment.
Results: The weighted and adjusted odds (WAO) of alcohol dependence among psychologically distressed U.S. residents were nearly 3.5 times significantly higher when compared to their counterparts who were not psychologically distressed (OR=3.47; 95% CI: 2.88 – 4.18). Females had significantly lower WAO of alcohol dependence than males (OR=.64; CI: 0.52 – 0.80). Non-Hispanic black (OR=.71; CI: 0.57 – 0.88) and Non-Hispanic Asian individuals (OR=.58; CI: 0.36 – 0.92) had significantly lower WAO of alcohol dependence than Non-Hispanic whites. In addition, individuals 35 years of age and older have significantly lower WAO of alcohol dependence (OR=.74; CI: 0.59 – 0.91) than those 18-25 years old. Finally, for every additional alcoholic drink consumed per day within a 30-day period, the WAO of alcohol dependence significantly increased by 21% (OR=1.21; CI: 1.17 – 1.25).
Conclusions: Experiencing psychological distress was found to be significantly associated with alcohol dependence among U.S. adults, even after adjusting for the number of alcoholic drinks consumed per day within a 30-day period.

Savings, home ownership, and depression in low-income US adults Catherine K. Ettman*
Catherine Ettman Gregory H. Cohen Patrick M. Vivier Sandro Galea

While the association between income and depression is well established, little is known about the relation between wealth and depression, particularly among low-income adults. We studied the relation between two types of assets—savings and home ownership—and depression in low-income US adults. We used data from the National Health and Nutrition Examination Survey (NHANES) from 2007-2016. Our final sample included 12,019 adults ages 18 years or older in the U.S. at or below 200% of the poverty line. We measured major depressive disorder (MDD) with impairment using the Patient Health Questionnaire (PHQ-9). Low savings was defined as having $5,000 or less in family savings. We calculated weighted prevalence, odds ratios with 95% confidence intervals, and predicted probabilities of MDD across savings and home ownership groups, controlling for gender, age, education, marital status, household size, household income, and NHANES cohort wave. Of low-income US adults, 5.4% had MDD with impairment, 85.9% had $5,000 or less in family savings, and 54.9% rented their home. Persons with low savings had 2.34 (95% CI 1.44-3.79) times the odds of having MDD relative to those with high savings. The association between family savings and MDD was stronger among home renters than home owners: home owners had 2.14 (95% CI 1.20-3.86) and home renters had 3.65 (95% CI 1.45-9.20) times the odds of having MDD if they had low savings relative to high savings. Predicted probabilities of MDD were similarly higher among home renters than home owners across savings groups. Family savings and home ownership are associated with lower burden of depression among low-income adults in the US. Recognizing these associations is an important step in better understanding the relation between wealth and population mental health.

Mental Health
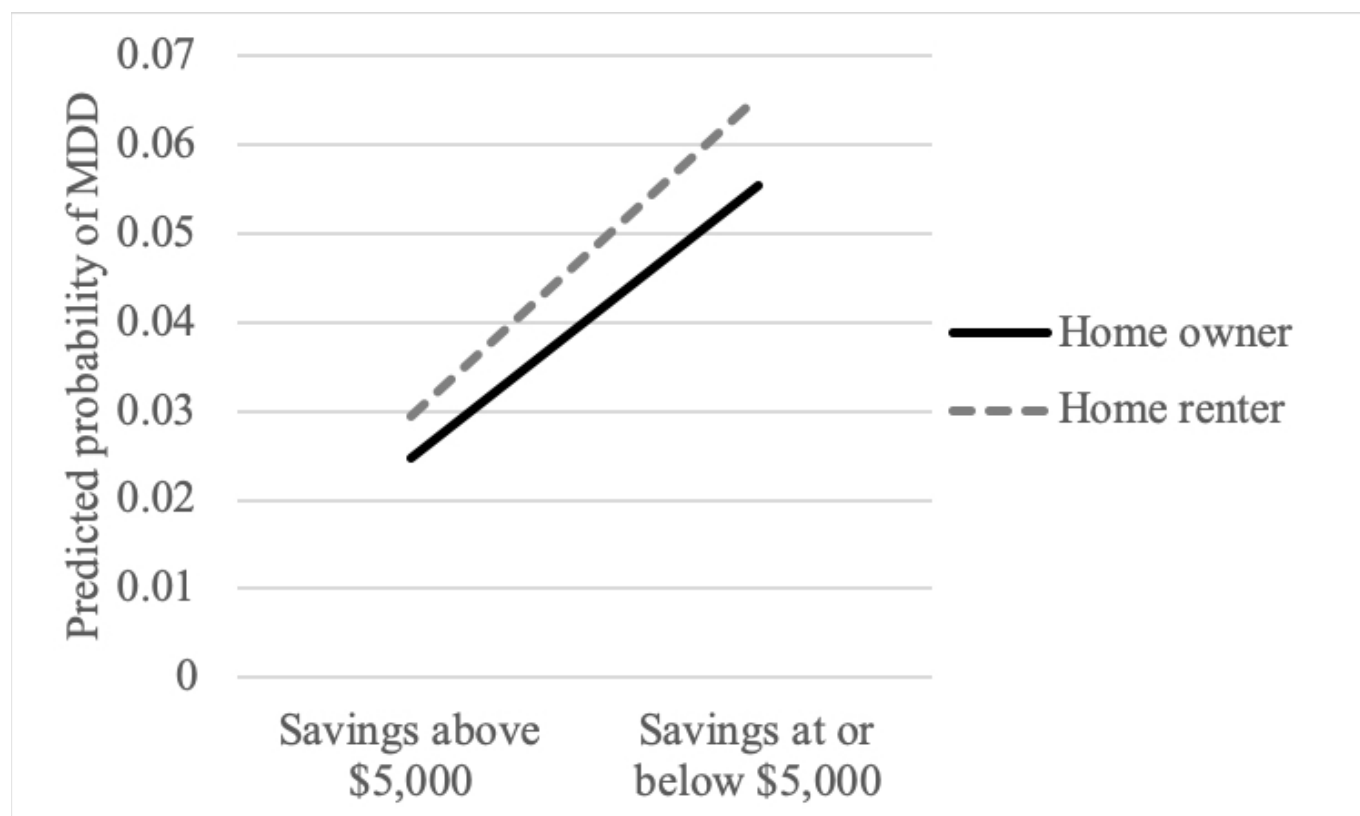
Trajectories of depressive symptoms from four months to three years postpartum: Relations with demographic and perinatal factors Diane L. Putnick* Diane Putnick Rajeshwari Sundaram Erin M. Bell Akhgar Ghassabian Risë B. Goldstein Sonia L. Robinson Yassaman Vafai Stephen E. Gilman Edwina Yeung

Individual trajectories of maternal depressive symptoms vary following childbirth. Identifying risk factors of persistent depressive symptoms is clinically important because over 1 in 10 mothers have a major depressive episode postpartum. The Upstate KIDS study followed mothers (N=4866) of singletons and multiples after delivery. Maternal depressive symptoms were assessed using the abridged Edinburgh Postnatal Depression Scale at 4, 12, 24, and 36 months postpartum. Demographic and perinatal factors were reported at 4 months or abstracted from birth records to identify risk factors for depression. The best-fitting 3-step latent class growth mixture model identified 4 trajectories of depressive symptoms (Figure 1): low-stable (74.7%), low-increasing (8.2%), medium-decreasing (12.6%), and high-persistent (4.5%). Mothers who were older (OR=0.92, CI 0.87-0.97; OR=0.92, CI 0.86-0.97; OR=0.91, CI 0.87-0.96) and had college education (OR=0.44, CI 0.21-0.90; OR=0.40, CI 0.19-0.86; OR=0.40, CI 0.21-0.84) were less likely, and mothers who had a mood disorder (OR=4.19, CI 2.49-7.05; OR=3.73, CI 2.10-6.62; OR=15.38, CI 10.11-23.39) and gestational diabetes diagnosis (OR=2.29, CI 1.18-4.47; OR=4.37, CI 1.48-12.92; OR=2.31, CI 1.36-3.90) were more likely to be in the high-persistent depression class than medium-decreasing, low-increasing, and low-stable classes, respectively. In addition, married (OR=0.46, CI 0.29-0.72), white (OR=0.42, CI 0.27-0.67), and nulliparous women (OR=0.44, CI 0.29-0.68), and women who had babies with higher gestational ages (OR=0.90, CI 0.84-0.97) were less likely to be in the high-persistent class than the low-stable class. Fertility treatment, multiple births, pre-pregnancy BMI, gestational hypertension, and infant sex were not associated with depression trajectories. Mothers with particular demographic and perinatal characteristics may be at increased risk of persistently high symptoms of depression for 3 years after childbirth.

Mental Health
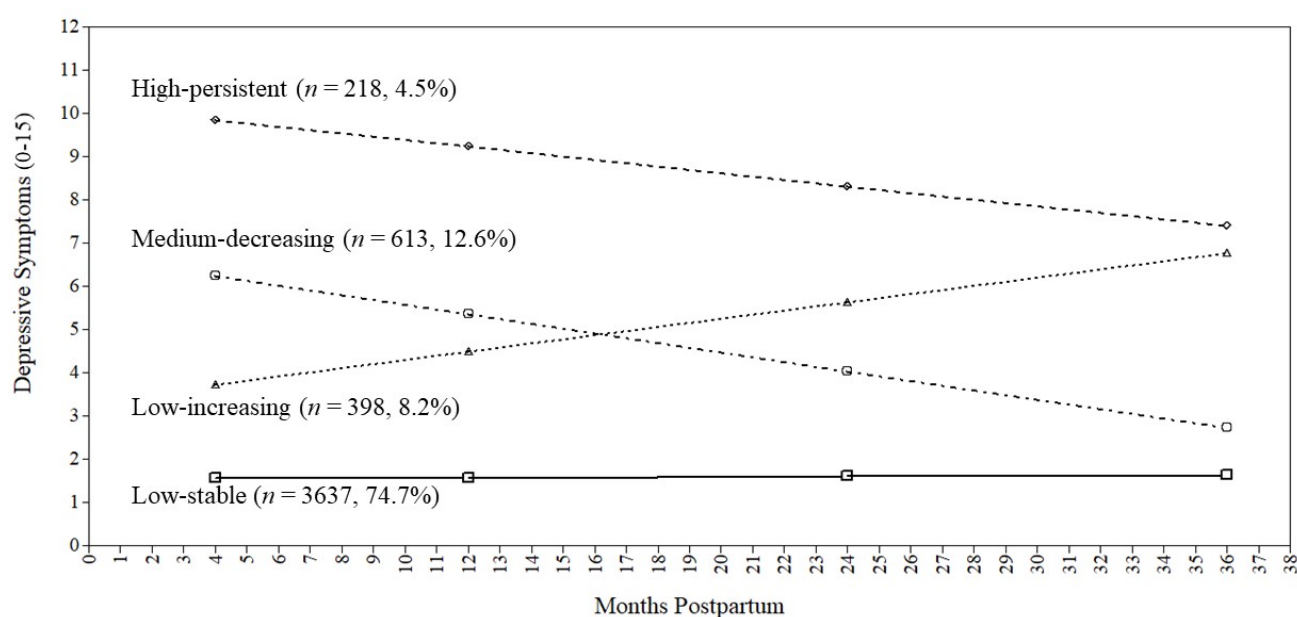
Structure and trends of externalizing and internalizing psychiatric symptoms among adolescents in the US from 1991-2018 Melanie S Askari* Melanie S Askari Caroline G Rutherford Pia M Mauro Noah Kreski Katherine M Keyes

Introduction: Common psychiatric disorders largely structure as two correlated internalizing and externalizing time-invariant dimensions among adults. Among adolescents, the structure and time trends in the occurrence of these symptoms is understudied.

Methods: Data were analyzed from the US nationally-representative cross-sectional Monitoring the Future surveys (1991-2018) among school-attending adolescents (N=320,987). Internalizing symptoms included 8 items (e.g., feel cannot do anything right); externalizing symptoms included 7 conduct-related items (e.g., trespassed). Complete-case exploratory factor analysis was conducted utilizing promax rotation method and maximum likelihood estimation. Trends in mean standardized factor scores over time were assessed using linear regressions with splines, testing a knot at 2012.

Results: The 2-factor solution was a better fit than the 1-factor solution (e.g., AIC for 2-factor solution=325,670 vs AIC for 1-factor solution=875,665) and the 2 factors were correlated (r=0.21). Externalizing items loaded strongly on factor 2 (e.g., hurt another person=0.7038) whereas internalizing items loaded strongly on factor 1 (e.g., not self-satisfied=0.7454). Externalizing factor scores decreased by 0.005 standard deviations (SD) per year (95% CI: -0.010, -0.0004). While internalizing mean scores decreased by 0.001 SD/year (95% CI: -0.002, -0.0004) before 2012, mean internalizing factor scores increased after 2012 by 0.042 SD per year (95% CI: 0.037, 0.047).

Conclusion: Internalizing and externalizing symptoms represent distinct yet correlated psychiatric phenomena in adolescents. Internalizing symptoms significantly increased after 2012 while externalizing symptoms continued to decrease. This suggests that a change in the occurrence or prevalence of shared risk factors for psychiatric symptoms affect these dimensions in opposing directions, raising the importance of considering them together in prevention and intervention efforts.

Mental Health

Prevalence, Treatment, and Control of Depressive Symptoms Before and After Passage of the Affordable Care Act: Evidence from the National Health and Nutrition Examination Survey Daniel Hagen* Daniel Hagen Melody Goodman Emily Goldmann

Background:
The Affordable Care Act (ACA) of 2010 included approaches to improving population mental health such as depression screening in primary care practice. However, it is unclear whether the prevalence, treatment, and control of depressive symptoms has changed since passage of the ACA.

Methods:
Data from the National Health and Nutrition Examination Survey (NHANES) 2013-2014 and 2015-2016 (n=10,506 adults) were used to estimate the prevalence of current depressive symptoms, past-month pharmacological and past-year non-pharmacological mental health treatment, and persisting depressive symptoms among individuals who took antidepressants in the past month, overall and by gender and age. Past-two-week depressive symptom severity was assessed using the Patient Health Questionnaire (PHQ-9) score (minimal: 5-9, moderate: 10-14, moderately severe: 15-19, severe: 20 and above). Percentages and 95% confidence intervals (CI) were compared to results previously reported based on NHANES 2005-2006 and 2007-2008 data.

Results:
In 2013-2016, 24% of respondents reported at least minimal symptoms vs. 22% in 2005-2008, with larger differences between time periods among female and older respondents. Among individuals with more than moderate symptoms, 45% did not receive any mental health treatment, compared to 51% in earlier years. Among respondents taking antidepressants, 49% continued to experience more than minimal symptoms, compared to 45% in earlier years. However, 95% CIs for all estimates overlapped between time periods.

Discussion:
This study found higher prevalence of at least minimal depressive symptoms, increased prevalence of treatment for moderately severe or severe symptoms, and decreased symptom control with antidepressants after passage of the ACA, but estimates were not significantly different between time periods. Continued surveillance of these mental health indicators is critical as the policy landscape continues to evolve.

Associations Between Adjustment Disorder and Hospital-Based Infections in the Danish Population Meghan Smith* Meghan Smith Dora Kormendine Farkas Jennifer A. Sumner Tammy Jiang Timothy L. Lash Sandro Galea Henrik Toft Sorensen Jaimie L. Gradus

Objective: There is some evidence that posttraumatic stress disorder (PTSD) is associated with increased risk of infections, and it is unknown whether adjustment disorder is as well. We assessed the association between adjustment disorder and subsequent infections, and whether they differed by sex.
Methods: The study population included a nationwide cohort of all Danish-born residents of Denmark diagnosed with adjustment disorder between 1995 and 2011, and an age- and sex-matched general population comparison cohort. We compared rates of infections requiring inpatient or outpatient hospitalization in the two cohorts. We fit Cox proportional hazards models to compute adjusted hazard ratios (aHR) for the associations between adjustment disorder and 32 types of infections, and calculated interaction contrasts to assess interaction between adjustment disorder and sex.
Results: Adjustment disorder was associated with increased rates of infections overall (n=19,838 infections, aHR=1.8, 95% confidence interval=1.8, 1.9), and increased rates of each individual infection type (aHRs for 30 infections ranged from 1.5 to 2.3), adjusting for baseline psychiatric and somatic comorbidities and marital status. For many infection types (e.g., skin infections, pneumonia), interaction contrasts indicated rate differences were greater among men than women, while for two (urinary tract infections and sexually transmitted infections), rate differences were greater for women.
Conclusion: These findings are consistent with studies examining the relationship between psychological stress and infections, and between PTSD and infections. Future research should explore whether they are explained by the triggering of unhealthy behaviors, immune responses to stress, or a combination of both. Conducting similar work in different cultural settings, in which behavioral responses may vary, would be informative.

Mental Health

Characterizing acute stress reaction, PTSD, and mTBI diagnoses and their interactions in the US Army Caitlin Haven* Caitlin Haven Kathryn Taylor Kristin Heaton Susan Proctor

An acute stress reaction (ASR) is defined the rapid onset of symptoms immediately (minutes/hours) following a traumatic event. Although this reaction typically resolves within 48 hours of the traumatic incident, the occurrence of ASR can be life-threatening when occurring in a combat situation. For example, one in twelve military service members (SMs) report being unable to function in a combat situation due to severe mental stress. ASR is also a risk factor for subsequent post-traumatic stress disorder (PTSD), however the factors mediating the linkage between ASR and PTSD remain unclear. Some evidence suggests that mild traumatic brain injuries (mTBIs), which occur at higher rates in military SMs compared to the general population and are associated with an increase in anxiety symptoms, may be a contributing factor. Therefore, it is important to investigate the relationship between ASR and PTSD and how these may interact with a co-occurrence of mTBI. Using data from the Soldier Performance and Health Readiness (SPHERE) database, a data repository for all Army personnel, this study documents reported ASR diagnoses, subsequent PTSD diagnoses, and the portion of mTBI diagnoses that precede or follow an ASR diagnosis among active duty Army personnel. Between 2010 and 2018, there were 40,257 instances of ASR with a total of 13,276 SMs affected. Among those with an ASR, 1.18% (n=156) had a subsequent PTSD diagnosis, occurring at any time following the initial ASR diagnosis. Additionally 0.35% (n=47) experienced a mTBI at any time point before or after ASR diagnosis. It has been found that as many as 20% of all Army SMs have been diagnosed with PTSD and that roughly one third of SMs with mTBI also have PTSD. Considering the higher percentage of PTSD cases among those with an ASR and the relationship between mTBI and PTSD, it is imperative to better understand the relationship between these factors to gain a clearer understanding of the progression and mitigating factors.

Mental Health

Money Can't Buy Happiness: Incongruity between subjective and objective socioeconomic status and psychological well-being in rural China Aki Yazawa* Aki Yazawa Ichiro Kawachi

Previous research has shown that subjective socioeconomic status (SES) is associated with psychological well-being even after control for objective SES. However, it remains unclear whether subjective SES simply explains additional variation in psychological well-being or if status incongruity (e.g., having a lower self-assessed social status relative to objective SES) drives this association. In contrast to high-income countries, studies from low- and middle-income countries remain sparse. In this study, we investigated the association between status incongruity and psychological well-being among adults in rural China using a novel diagonal reference model (DRM) approach, which teases out the effect of status incongruity per se from the effects of subjective and objective SES. Cross-sectional data were collected from 797 adults residing in seven rural communities in Fujian, China. Objective SES was obtained by an asset index derived from principal component analysis of 13 consumer durable items (TV, mobile phone, PC, Internet service, rice cooker, motorbike, car, truck, refrigerator, AC, washing machine, microwave, bathroom infrared heater). For subjective SES, participants were asked "Compared to other people in your community, how do you rate your own socioeconomic status?" with responses on a 10-point ladder scale. Psychological well-being was measured by a 10-point happiness scale as well as psychological distress (Kessler 6). Results showed that weights for subjective SES were much bigger than objective SES on both happiness and stress (0.72 vs. 0.28, 0.71 vs. 0.29, respectively), and those who assessed their subjective SES as higher than their objective SES were much happier and reported less distress, regardless of their subjective and objective SES.

Is religious service attendance the active ingredient in protecting against depressive symptoms? The moderating role of religious salience and geographic differences across the US Noah T. Kreski* Noah Kreski Katherine M. Keyes

Depressive symptoms have rapidly increased among adolescents for the past decade, and religious service attendance has shown a slow decline across several decades (see attached figure). Religion is hypothesized to improve mental health through identification with a higher power and community support through religious service attendance. We assessed associations of religious service attendance and personal importance of religion with depressive symptoms in annual cross-sectional surveys of adolescents in Monitoring the Future, years 1989-2019 (N=422,612). Depressive symptoms were measured with a four-item scale based on statements such as "The future often seems hopeless"; total score range: 4 to 20. Without a validated cutscore, we examined several, including >15, the top 5% of scores. Religious service attendance ranged from "never" to "about once a week or more". Personal importance of religion was dichotomized into not important versus important to any extent. Among adolescents who felt that religion was important to any extent, greater service attendance was consistently associated with lower depressive symptoms. However, for adolescents who felt religion was not personally important, the opposite pattern was found. Those attending religious services weekly with no personal importance of religion had the greatest odds for high depressive symptoms of any group, 4.33 (95% CI: 3.82, 4.91) times the odds compared with weekly attendees who felt religion to be important, after adjustment for demographics, substance use, year, and religious denomination. These diverging patterns were even more apparent in the Southern US, where the above adjusted odds ratio for depressive symptoms among those regularly attending services with no personal importance of religion was 4.89 (CI: 3.98, 6.01). Attendance alone does not capture the connection between religion and depressive symptoms, but rather needs the context of personal importance and geography to articulate patterns.

Religious Factors and Depressive Symptom Score over Time
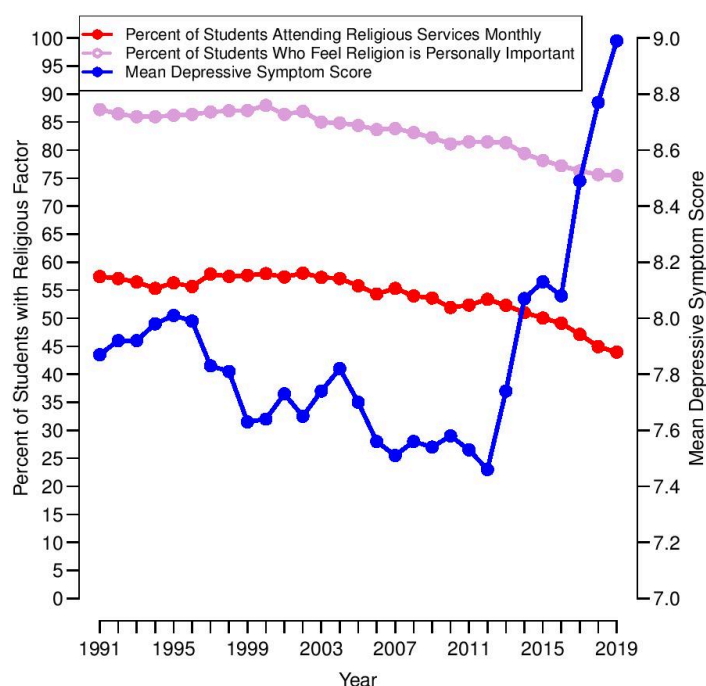
Incident suicidal ideation among long-stay working age residents of nursing homes in the U.S. Julie Hugunin* Julie Hugunin Yiyang Yuan Anthony J. Rothschild Kate L. Lapane Christine M. Ulbricht

The population of working-age adults receiving nursing home (NH) care is increasing. These residents are more likely than older residents to have psychiatric conditions and other risk factors for suicidal ideation but little is known about how their suicide risk changes during the NH stay. We aimed to: measure the incidence of suicidal ideation among long-stay working-age adults newly admitted to a U.S. NH, describe residents' clinical characteristics at admission, and examine their psychotherapeutic care within the first 90 days of their stay. We used the national Minimum Data Set 3.0 (MDS), a comprehensive clinical assessment required for all residents of Medicare-/Medicaid-certified homes that is completed at admission and quarterly thereafter. We identified 71,515 adults aged 22-64 years who: were admitted to U.S. NHs in 2015, remained there for >= 100 days, and completed a resident-reported Patient Health Questionnaire (PHQ-9) at admission and 90 days. We estimated the cumulative incidence of suicidal ideation within the first 90 days of admission as a positive response at 90 days divided by those with a negative response to the PHQ-9 ninth item at admission. Psychotherapeutic care was defined as any receipt of antidepressants, antianxiety medication, antipsychotics, hypnotics, and/or psychological therapy within the 7 days prior to the 90-day MDS. Among the 57,666 working-age residents not reporting suicidal ideation at admission in 2015, 0.8% (95% confidence interval: 0.71-0.85%) had ideation on the 90-day MDS. Of those with incident suicidal ideation, 69.2% had an active diagnosis of depression, 44.3% had an anxiety disorder, and 21.4% had schizophrenia at admission. 88.6% received any psychotherapeutic treatment and <1% received psychological therapy at 90 days. This population may not be receiving the specialty care needed to address their complex healthcare needs. More research is needed to understand suicide risk among long-stay working-age NH residents.

Mental Health

Posttraumatic stress disorder among a cohort of pregnant active duty U.S. military women

Lisa M. Abramovitz* Lisa Abramovitz Monica A. Lutgendorf Anna T. Bukowinski Gia R. Gumbs Ava Marie S. Conlin Clinton Hall

Objectives: To describe demographic and occupational characteristics, comorbidities, and psychotropic medication use associated with diagnoses of posttraumatic stress disorder (PTSD) during pregnancy among a population of active duty military women. Methods: Department of Defense Birth and Infant Health Research program data were used to identify pregnancies among active duty military women from 2007 through 2014. Demographic and occupational data were linked with electronic medical and pharmacy records to capture mental health diagnoses and medication dispensation dates. PTSD cases were identified by ICD-9 diagnostic code 309.81 on maternal records (one inpatient or two outpatient on different days) from one year prior to date of last menstrual period through the end of pregnancy. Results: Among 134,244 identified pregnancies, 2240 (1.7%) were among PTSD cases. Compared with non-cases, PTSD cases were more likely to be non-Hispanic white (51.3% vs. 47.4%), unmarried (33.3% vs. 28.2%), in the Army (49.6% vs. 35.8%), in a service and supply occupation (18.2% vs. 13.6%), in a junior enlisted rank (56.3% vs. 50.1%) and have previously deployed (51.2% vs. 39.6%). Among PTSD cases, the most common mental health comorbidities were adjustment disorder (42.9%), anxiety disorder (38.7%), and depressive disorder (60.2%). During the pregnancy period, psychotropic medications were dispensed among 40.5% of PTSD cases compared with 6.3% of non-cases. Conclusions: Demographic and occupational characteristics, comorbidities, and psychotropic medication use differed substantially among PTSD cases and non-cases in this large record-based study. Future analyses will consider associations between PTSD in pregnancy and adverse pregnancy and infant outcomes.

Does smoking explain the association between depression and lung cancer risk? Claudia Trudel-Fitzgerald* Claudia Trudel-Fitzgerald Emily S. Zevon Ichiro Kawachi Reginald D. Tucker-Seeley Laura D. Kubzansky

Background: Studies evaluating depression's role in lung cancer risk revealed contradictory findings, partly because of small number of cases and failure to account for key covariates including smoking exposure. We investigated the association of depressive symptoms with lung cancer risk in a large prospective cohort over 24 years, while considering the role of smoking.

Methods: Women from the Nurses' Health Study completed measures of depressive symptoms, sociodemographics, and lifestyle factors including smoking in 1992 (N=42,913). Depressive symptoms were also queried in 1996 and 2000, whereas regular antidepressant use and physician-diagnosed depression were collected starting in 1996. Multivariable Cox regression models estimated hazard ratios (HR) and 95% confidence intervals (CI) of lung cancer risk until 2016.

Results: We identified 1,009 cases of lung cancer. Women with the highest versus lowest level of depressive symptoms had an increased lung cancer risk (HRsociodemographics-adjusted=1.62, 95%CI=1.34-1.95; HRfully-adjusted=1.25, 95%CI=1.04-1.51). In a test of mediation, lifetime pack-years of smoking accounted for 38% of the overall association between depressive symptoms and disease risk. When stratifying by smoking status, elevated risk was observed among former smokers but not current or never smokers; however, the interaction term suggested no meaningful differences across groups (p=0.29). Results were similar or stronger when considering time-updated depression status (using depressive symptoms, physician diagnosis, and medication) and chronicity of depressive symptoms.

Conclusion: Although residual confounding remains possible, these findings suggest that higher depressive symptoms may contribute to lung cancer incidence, directly and indirectly via smoking habits, which accounted for over a third of the association.

Mental Health

Prediction of Suicide in People with Depression using Machine Learning and National Danish Registry Data Tammy Jiang* Tammy Jiang Anthony J. Rosellini Erzsébet Horváth-Puhó Sandro Galea Timothy L. Lash Henrik T. Sørensen Jaimie L. Gradus

Depression is one of the most common mental disorders among people who die by suicide. Yet, accurate prediction of suicide among people with depression remains challenging. Knowledge of specific combinations of risk factors across the life course that contribute to suicide risk among people with depression may help identify high risk individuals who should be connected with prevention interventions. The goal of this study is to identify novel time-varying risk factors and interactions that are predictive of suicide among men and women with depression using machine learning. We are conducting a case-control study using data from national Danish health and social registries. The source population is all individuals born or residing in Denmark as of January 1, 1995. Cases are all persons who died by suicide and had a lifetime depression diagnosis between January 1, 1995 and December 31, 2015 (n = 2,820). Suicide cases are obtained from the Danish Cause of Death Registry. We are using risk set sampling to obtain controls who did not die by suicide on the date of death of suicide cases and have a lifetime depression diagnosis. We are using 4:1 matching to obtain 11,280 controls. Demographic characteristics, social variables, psychiatric disorders, physical health diagnoses, surgeries, and medications, as recorded in various registers, are examined as predictors in classification trees and random forests to predict suicide deaths among men and women with depression. The analyses are currently ongoing and we will present our work on the constellations of time-varying risk factors that accurately predict suicide among men and women with depression. This knowledge may have implications for improving identification of high-risk individuals who should be connected with prevention interventions.

Mental Health

Are adults with congenital heart defects at increased risk of depression, anxiety, and post-traumatic stress disorder? Regina Simeone* Regina Simeone Scott Grosse Karrie Downing William Bobo Amber Khanna Sherry Farr

Adults with congenital heart defects (CHD) may be at increased risk for depressive and anxiety disorders, including post-traumatic stress disorder (PTSD), due to their chronic condition. Our objectives were to determine if the one-year prevalence of diagnosed depressive and anxiety disorders among adults ages 18-64 years enrolled in employer-sponsored health insurance differs by presence and severity of CHD. Using MarketScan Commercial claims databases, we identified adults with ≥1 ICD-10-CM code for depressive (F32-F34) or anxiety disorders (F064, F40-F48, F93, F99, R45) in 2017. CHD was defined as ≥2 outpatient ICD-9-CM (745-747) or ICD-10-CM (Q20-Q26) codes separated by ≥30 days or ≥1 inpatient code documented in 2007-2017. Severe CHDs were those requiring surgical/catheter intervention in the first year of life. Eligible adults were continuously enrolled with prescription drug and mental health coverage in 2017 without documented chromosomal anomalies. We used log-binomial regression, including age, sex, and region, to estimate adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) for associations between presence and severity of CHD and depression, anxiety, and PTSD. There were 9,483,936 adults with no CHD diagnosis, and 32,214 with CHD diagnoses. Of adults with CHD, 13% were diagnosed with depressive disorders (7%), anxiety disorders (10%), and/or PTSD (0.7%). Adults with CHD, compared to those without CHD, had higher prevalence of depressive disorders [1.4 (CI: 1.3-1.4)], anxiety disorders [1.4 (CI: 1.4-1.5)], and PTSD [1.5 (CI: 1.3-1.7)]. CHD severity was not associated with the outcomes (aPR range: 0.96-1.05). Based on claims data, over 1 in 7 adults with CHD had diagnosed depressive or anxiety disorders in 2017, 40%-50% higher than adults without CHD. Possible risk factors for these conditions in the CHD population, such as past medical treatments, and best practices for diagnosis and treatment, could be explored in future research.

Prevalence of diagnosed depressive and anxiety disorders, MarketScan Commercial Claims and Encounters, 2017

Mental Health
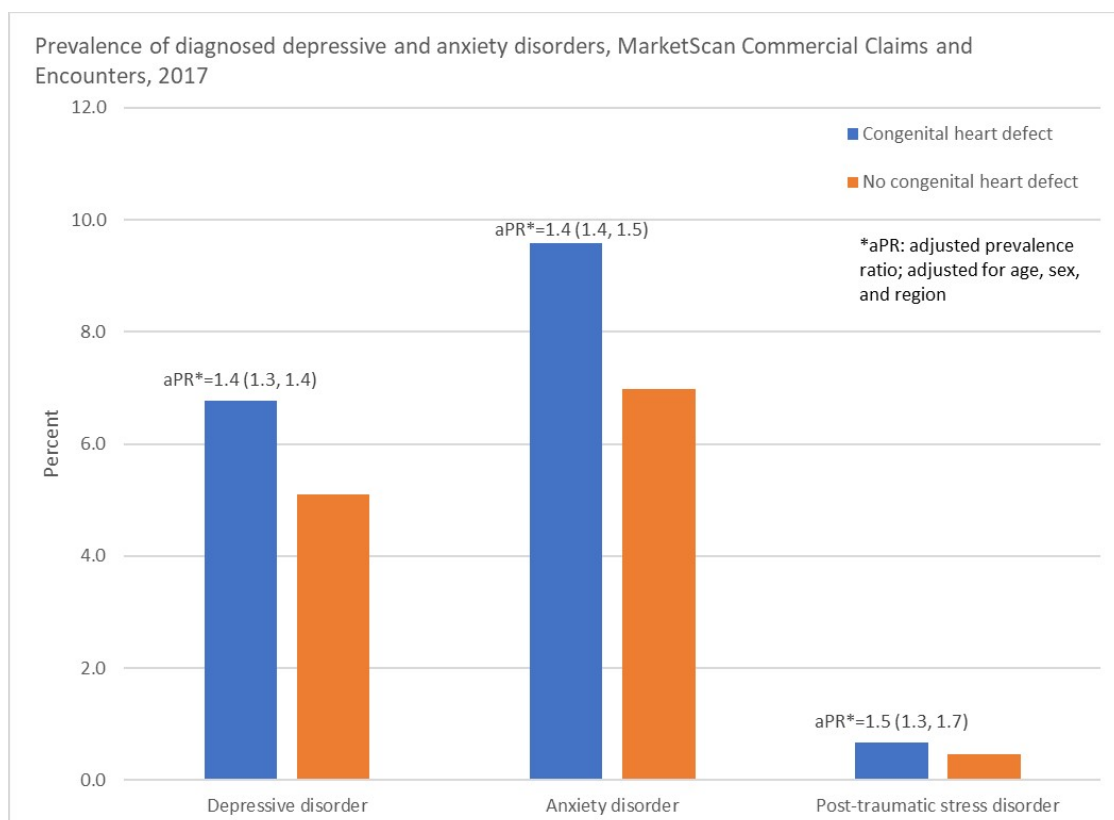
National trends in the prevalence of depression, somatic symptoms and non-somatic symptoms among adolescents in the United States from 2005 to 2017 Shadiya L. Moss*

Shadiya Moss Katherine M. Keyes

In the US, depression has increased over time among adolescents. Assessment of differences in time trends by sex and race can illuminate potential disparities and high-risk groups, and provide recent estimates. This analysis examined time trends in the prevalence of 12-month major depressive episode (MDE), somatic and non-somatic symptoms among adolescents, and differences by race and sex separately and jointly.

Respondents included 12-17 year-olds (N=212,913) from the annual cross-sectional nationally-representative National Survey on Drug Use and Health from 2005 to 2017. Youth-reported 12-month MDE, somatic (i.e., physical) and non-somatic (i.e., psychosocial or behavioral) symptoms were assessed using a structured instrument (DSM-IV criteria). Time trends in prevalence of MDE and symptoms were tested using relative risk regression models, adjusted for age and income.

Across years, there were gender differences in MDE prevalence (girls had 2.38 times the risk of MDE versus boys), and there were limited prevalence differences by race. The prevalence of 12-month MDE (RR for each one-year increase RRyear=1.05), somatic (RRyear=1.03) and non-somatic (RRyear=1.03) symptoms increased from 2005 to 2017. The slope of these increases indicated that increases in MDE prevalence were greater among girls (RRyear=1.05) compared with boys (RRyear=1.03, gender interaction by year, p<.01). Further, the slope of the increase indicate that trends increased over time among non-Hispanic (NH) whites (RRyear=1.05) compared with NH Blacks (RRyear=1.03, race interaction by year, p<.01). There were no differences in trends over time by race and sex jointly.

In the US, the prevalence of MDE and related symptoms are increasing among adolescents, namely among girls and NH whites. These findings indicate that there are a substantial number of adolescents at risk for poor health outcomes. Targeted interventions and mental health care are needed to reduce the burden of depression.

Mental Health

Natural hazard events and mental health Michael Hu* Michael Hu Kaitlyn Lawrence Melanie Gall Dale P. Sandler

Natural disasters pose a risk to the mental health of affected individuals. Studies have shown that a wide range of disasters can negatively affect mental health, but few studies consider multiple disasters or outcomes. We assessed cumulative hazard burden in relation to multiple adverse mental health outcomes, leveraging data from the Gulf Long-term Follow-up Study, a large prospective cohort of oil spill cleanup workers. 11,193 participants living in the Gulf states, a region particularly prone to natural disasters, completed a home visit (2011-2013) that included standardized questionnaires on mental health. 9,935 provided responses to questionnaires for perceived stress (PSS; defined as a score ≥ 9), anxiety (GAD-7; defined as a score ≥ 10), distress (Kessler 6; defined as a score ≥ 13), depression (PHQ-8; defined as a score ≥ 10), and post-traumatic stress disorder (PC-PTSD; defined as a score ≥ 3) and covariates. To characterize exposure to hazard events, we linked participant home addresses to 2005-2010 county-level data from the Spatial Hazard Events and Losses Database for the United States. Exposures included total count and duration of exposure, as well as severity quantified as aggregated property/crop losses per capita from all hazards. We used modified Poisson regression to estimate adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) for associations between each exposure (highest vs. lowest quartile) and outcome. Total count and combined duration, but not cumulative severity was associated with perceived stress (aPR:1.23, 95% CI:1.12-1.36 for total count). Severity defined as property/crop losses per capita but not total count or duration was associated with anxiety (aPR:1.27, 95% CI:1.14-1.43), distress (aPR:1.26, 95% CI:0.99-1.60), depression (aPR:1.14, 95% CI:0.99-1.30) and most notably PTSD (aPR:1.82, 95% CI:1.36-2.43). Higher hazard burden may increase the risk for several mental health outcomes, particularly PTSD.

Mental Health

Artificial light at night and mental disorders among US adolescents Diana Paksarian* Diana Paksarian Kara E Rudolph Daniel Mennitt Joan A Casey Peter James Kathleen R. Merikangas

Disturbances to sleep and circadian rhythms are implicated in the etiology of mental disorder, particularly mood disorders. Light exposure strongly influences circadian rhythms, and experimental evidence from animal studies indicates that artificial light at night (LAN) increases depressive-like behaviors in rodents. However, only one prior epidemiologic study has investigated associations between outdoor artificial LAN and mental health. We linked location data from the National Comorbidity Survey Adolescent Supplement (NCS-A), a nationally-representative cross-sectional survey of US adolescents (age range: 13-18), to block-group-level information on artificial LAN derived from satellite imagery, and to US census data. Classes of past-year mental disorder (mood, anxiety, substance use, and behavior) were obtained via in-person interview using a validated, fully-structured instrument. Adjusting for several individual-level socio-demographic characteristics, each median absolute deviation increase in LAN was associated with higher odds of past-year mood (OR=1.08, 95%CI=1.02-1.15) and anxiety (OR=1.08, 95%CI=1.03-1.13) disorder, but not substance use (OR=1.04, 95%CI=0.93-1.16) or behavior (OR=1.07, 95%CI=0.95-1.21) disorder. Associations with mood and anxiety persisted after adjustment for block-group-level socioeconomic status and population density, both based on census data (mood: OR=1.7, 95%CI=1.00-1.14; anxiety: OR=1.10, 95%CI=1.05-1.16). Limitations include the cross-sectional design, lack of information on individual-level exposure to LAN, and the inability to separate LAN from other co-occurring environmental risk factors such as noise. Nonetheless, results imply that outdoor artificial LAN may be a risk factor for mood and anxiety disorder among adolescents. Population interventions to reduce LAN may mitigate any existing causal effects of LAN on mental health.

Mental Health

Access to mental healthcare services and depression among residents of Washington Heights, New York City Claire Benny* Roman Pabayo Claire Benny Sze Y. Liu Peter Muennig Roman Pabayo

Background: Access to mental health care may be associated with depression. In the US, a third of Latino adults with mental illness receive treatment each year compared with the national average of 43%. This disparity puts Latinos at greater risk for more severe, persistent mental illness. This investigation used data collected from a sample comprised of a majority Latino adults to study the effect of lack of access to mental health services on depression.

Methods: Data are from the 2015 Washington Heights Community Survey, a telephone administered survey among 2489 households in Washington Heights, New York City. We restricted the analytical sample (n=548) to those who reported they had been diagnosed with depression. The outcome was assessed using the PHQ-9, a screening instrument for depression with a sensitivity and specificity of 88%. A PHQ-9 score 10 was used for clinical depression. Scores were also standardized using the z-transformation. Multiple regression models and propensity score matching was used to estimate the association between not having access to mental health care and depressive symptoms and the likelihood of being depressed. Confounders included age, race, sexual orientation, marital status, household income, and diagnosis of depression in the previous 12 months (yes or no).

Results: Among those who were diagnosed with depression, those with no access to mental health services or counseling had significantly higher (=0.36, 95% CI=0.03, 0.70) depressive symptoms and were 1.88 times (95%CI=0.52, 6.86) more likely to be depressed, though the latter was not significant. When propensity score matching was utilized, those with no access to mental health services had =0.80 (95% CI=0.55, 1.05) greater depressive symptoms and were significantly more likely to be depressed (OR=2.38,1.06, 5.35).

Conclusion: Increasing access to mental health services may help those diagnosed with depression reduce their depressive symptoms.

Mental Health

Persistent mental health impacts of disaster. Five-year follow-up after the 2011 Great East Japan earthquake and tsunami Shiho Kino* Shiho Kino Jun Aida Katsunori Kondo Ichiro Kawachi

Background
Posttraumatic stress symptoms (PTSS) and depressive symptoms are common among survivors of major disaster, yet few longitudinal studies have documented their long-term persistence. We examined the trajectories of PTSS and depressive symptoms up to 5.5 years after the Great East Japan earthquake and tsunami in 2011.

Methods
We utilized three waves of the Iwanuma Study, a cohort of community-dwelling older adults. A unique feature of the cohort is that the baseline survey pre-dated the disaster by seven months. PTSS was measured by nine questions (SQD), while depressive symptoms were measured by 15 items (GDS short form). We examined the trajectory of PTSS and depressive symptoms after the disaster.

Results
Overall, we observed a 13.6% incidence of depressive symptoms and a 7.8% incidence of PTSS among people who did not have depression before the disaster.
Experience of housing damage was the strongest predictor of persistent depressive symptoms 5.5 years after the disaster, but only among those without pre-disaster depressive symptoms (RR= 4.38, 95%CI: 1.70, 12.85). On the other hand, among people who had pre-disaster depressive symptoms, disaster trauma did not predict persistent depressive symptoms after the disaster. Traumatic disaster experiences (i.e., housing damage or losing loved ones) were associated with PTSS onset among survivors regardless of pre-disaster depression status. For example, among people without pre-disaster depressive symptoms, loss of relatives/friends & home destruction increased the risk of PTSS by 2.18 times (95%CI: 1.08, 4.37). Among people with depressive symptoms pre-dating the disaster, severe housing damage was associated with 8.04 times (95%CI: 2.50, 25.86) higher risk of PTSS.

Conclusions
The lingering mental health impacts of disaster were apparent nearly six years after the 2011 earthquake & tsunami.

Figure. Trajectory of post-traumatic stress symptoms and experience of housing damage by pre-disaster depressive symptoms (N=2,059)
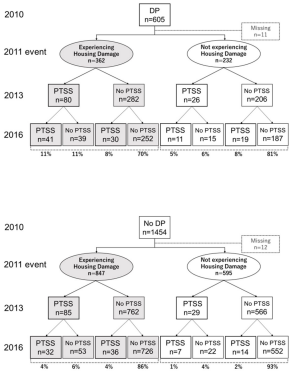
Posttraumatic stress disorder and likelihood of hormone therapy use among women in the Nurses' Health Study II: a 26-year's prospective analysis Rebecca Lawn* 3647] Lawn Kristen Nishimi YongJoo Kim Sun Jae Jung Andrea L. Roberts Jennifer A. Sumner Rebecca C. Thurston Lori B. Chibnik Eric B. Rimm Andrew D. Ratanatharathorn Shaili C. Jha Karestan C. Koenen Shelley S. Tworoger Laura D. Kubzansky

Posttraumatic stress disorder (PTSD) has been linked with higher risk of ovarian cancer, but pathways remain unclear. Despite known relationships between hormone therapy (HT) use and elevated risk of ovarian cancer, there has been little research linking PTSD with likelihood of using HT, which might link PTSD to heightened risk of ovarian cancer. Adding to our prior cross-sectional work, here we investigate if PTSD was prospectively associated with greater likelihood of initiating HT over 26 years. Using data from the Nurses' Health Study II, with trauma exposure and PTSD symptoms assessed by screener in 2008 (including PTSD onset date) and HT assessed via biennial survey, we performed Cox proportional regression models, adjusting for sociodemographic factors, reproductive factors, health conditions and health-related behaviors. We also stratified by timeframe (1989-2002 vs. 2003-2015), age at baseline (> vs. ≤35 years) and race/ethnicity. Over follow-up, more than half of women (24,151 of 46,977) reported initiation of HT. There was a dose-response relationship between trauma/PTSD status and increased likelihood of initiating HT. Over 26 years, compared to women with no trauma exposure, the hazard ratio for initiating HT was 1.33 for those with trauma/4-7 PTSD symptoms (95% CI: 1.27, 1.38), 1.18 for those with trauma/1-3 PTSD symptoms (95% CI: 1.14, 1.23) and 1.10 for those with trauma/no PTSD symptoms (95% CI: 1.07, 1.14), after adjusting for sociodemographic factors (*p* trend <.001). Associations remained significant after adjusting for reproductive factors and health conditions (including depression). Associations of greater magnitude were evident in women below 35 years at baseline and for before 2002, when new clinical guidelines recommended limiting the use of HT. Evidence for a PTSD-HT relationship was strongest for Non-Hispanic White and Black women. Findings suggest HT use may be a biobehavioral pathway linking trauma/PTSD with higher risk of ovarian cancer.

Does cancer treatment cause cognitive impairment? Effect of chemotherapy, targeted therapy, and radiotherapy on cognitive impairment in colorectal cancer patients: a longitudinal analysis from Korea National Health Insurance Service (NHIS) Database.

Kwanghyun Kim* 3647] Kim Sun Jae Jung

Objectives: This study aims to investigate whether chemotherapy, targeted therapy, and radiotherapy could increase risk of cognitive impairment in colorectal cancer patients by analyzing Korean national health insurance database.

Methods: Patients with at least one insurance claim record with ICD-10 'C18-C20' codes from year 2002 to 2018 were defined as colorectal cancer patients. All claims data for randomly selected 40% of colorectal cancer patients were collected (N=247,593). Participants under age of 18 (N=1.173), participants diagnosed with cognitive impairment before cancer (N=11,630), and participants with only one claim with ICD-10 'C18-C20' codes without any claim records for primary cancer treatment (N=35,674) were excluded from the analysis. Time-varying competing risk cox regression were applied to estimate hazard ratio. We investigated for interaction between age and treatment modalities. Landmark analysis with landmark time of 1, 2, and 5 years were applied to compare short-term and long-term effects.

Results: There were 22,965 patients with cognitive impairment (11.56%) among 198,666 colorectal cancer patients. Chemotherapy was positively associated with cognitive impairment in both colon cancer and rectal cancer, while targeted therapy didn't show clear association. Radiotherapy was associated with cognitive impairment in rectal cancer. Age-specific hazard ratios of chemotherapy and radiotherapy were larger in older patients. Landmark time analysis showed that while the effects of chemotherapy became less evident with longer landmark time, unlike the effects of radiotherapy which remained relatively constant.

Conclusion: Chemotherapy and radiotherapy could cause cognitive impairment in colorectal cancer patients, but the association might gradually diminish as time passes by.
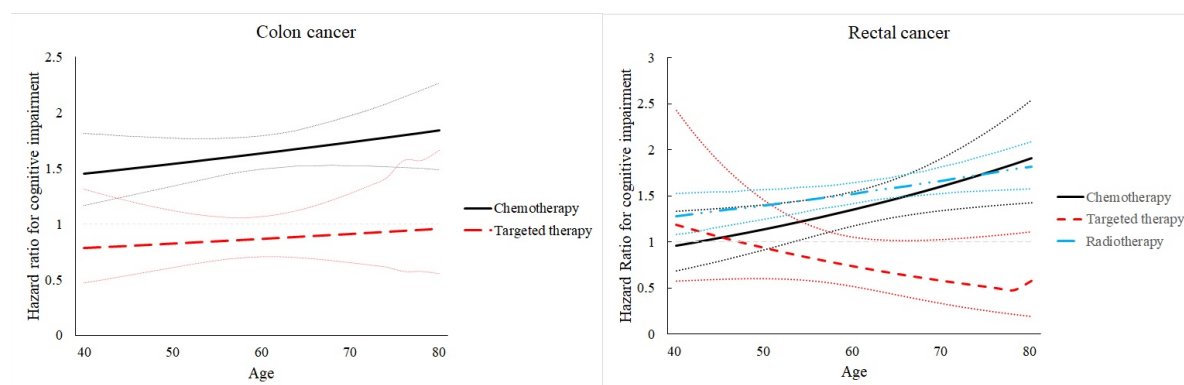
LATEBREAKER

Mental Health

An Exploration of Black Philadelphia Clergy's Perceived Self-Efficacy in the Mental Health Gatekeeper Role Elena Schatell* 3647] Schatell Heather McClintock

Title: AN EXPLORATION OF BLACK PHILADELPHIA CLERGY'S PERCEIVED SELF-EFFICACY IN THE MENTAL HEALTH GATEKEEPER ROLE

Author(s) and affiliations: Elena Schatell, MPH (c), Arcadia University; Heather F. McClintock PhD, MSPH, MSW, Arcadia University

Background: Blacks are more likely to report serious psychological distress compared to Whites but are less likely to utilize formal mental health services. Instead of seeking care from formal services, many seek guidance from clergy. While Black clergy are increasingly playing the role of a mental health gatekeeper, qualitative studies are lacking on Black clergy's perceived self-efficacy in the gatekeeper role. Furthermore, research is lacking in Philadelphia, a historical center of Black religious activity.

Objective: The purpose of this study is to assess Black Philadelphia Protestant clergy's perceived self-efficacy in the gatekeeper role.

Design/Methods: Individual semi-structured interviews are being conducted with Black Philadelphia Protestant clergy. Audio recordings are and will be transcribed and analyzed for themes through the use of NVivo and the Grounded Theory approach. Data collection and analysis will be completed by April 2020.

Results: Currently, all participants recognized a need for mental health support within their communities and discussed the critical role of Black clergy as gatekeepers. However, participants had varying perceptions of clergy's responsibility in regards to serving as a mental health gatekeeper. All clergy described barriers to serving as effective mental health gatekeepers such as limited expertise, limited training, and a lack of community linkages to professional mental health resources. All respondents discussed interest in developing collaborations that may help them provide mental health assistance and connect congregants to mental health professionals in Philadelphia.

Conclusion: Intervention and policy initiatives aimed at collaborating with Black Philadelphia Protestant clergy to address the perceived mental health needs of their congregations could strengthen their self-efficacy in the mental health gatekeeper role.

The impact of experiencing a depressive episode on employment earnings over the following decade: A propensity score matched cohort study Kathleen Dobson* 3647] Dobson Cameron Mustard Simone Vigod Peter Smith

Objective: Experiencing a major depressive episode (MDE) may immediately impact one's productivity at work, employment status, and income. However, the long-term economic consequences of a depressive episode are less clear. This study explored if and how experiencing a MDE impacted employment earnings over the following decade among working-aged Canadian men and women.

Methods: Multiple Canadian Community Health Survey (2003-2014) cycles were linked to national administrative tax records (1997-2016). The sample comprised individuals 18-54 years with information on past year MDEs and earning patterns prior to MDE (n~85,000). MDE presence was assessed with the Composite International Diagnostic Interview Short Form. Annual employment earnings were defined by all paid-employment income (wages, salaries, and commissions before deductions). A 1:1 matched cohort was created for females (n~7,000) and males (n~3,600) based on age, province, survey cycle, and propensity score adjusted for sociodemographic factors and prior earnings. Linear, 3-level random-effect multilevel models quantified the association between MDE and earnings 1-10 years post episode among each gender.

Results: For females experiencing a MDE, earnings were ~$3,000 (95%CI=$-3,700, -$2,300) lower one year and ~$3,900 (95%CI=-$5,000, -$2,800) lower 10 years later compared to females not experiencing a MDE. For males experiencing a MDE, earnings were ~$3,500 (95%CI=$-6,800, $-300) lower one year and ~$4,000 (95%CI=$-6,200, -$1,800) lower 10 years later compared to males not experiencing a MDE.

Conclusions: Employment earnings of a working-aged Canadian experiencing a single MDE are at least ~$3,000 less/year compared to those without depression; this earning gap remains relatively stable among both genders. Although working Canadians are thought to be buffered against the negative effects of mental illness, findings reveal the longstanding economic consequences of depression among this population.

Mental Health

Deconstructing the rising rates of mental health and addictions-related emergency department visits among children and youth in Ontario, Canada Maria Chiu* Maria Chiu Paul Kurdyak Evgenia Gatov Kinwah Fung Astrid Guttmann

Introduction: Rates of mental health-related emergency department (ED) visits for children and youth have been increasing in Canada and other developed nations; whether this relates to access to outpatient care or changes in morbidity is unknown. We examined temporal trends in ED visits and related outpatient care in Ontario, Canada.

Methods: Using multiple linked health administrative databases (2006-2017), we calculated annual age-and sex-standardized rates of mental health ED visits, hospitalizations and outpatient care (primary care, paediatrician, psychiatrist) among the approximate 4 million Ontarians aged 0-24 years. Rates were stratified by age, sex, acuity and diagnosis.

Results: Between 2006 and 2017, ED visit rates increased by 88.6% (from 11.5 to 21.7 visits per 1,000 persons, p<0.001), with the sharpest rise around 2009. The increasing rate was driven by an increase in both the number of unique patients presenting to the ED and the mean number of visits per person. Increasing rates were observed across sex and age groups; and more so for high acuity cases. Anxiety disorders accounted for the highest proportion of ED visits and the greatest increase over time (3.3 to 7.6 per 1,000, p<0.001). Rates of outpatient visits 7 days prior to and following ED visits increased over time, however, the majority of children and youth visiting an ED did not receive outpatient care.

Conclusion: Despite increases in outpatient visits, rates of mental health ED visits among children and youth continue to rise and is largely related to anxiety disorders. Policy needs to address access to timely and appropriate outpatient care before symptoms reach a crisis point. Further work is needed to understand how social media, which gained popularity in 2009, may be influencing the trends we are observing.

Methods/Statistics

Lessons Learned from Use of Inverse Probability Weighting to Adjust for Selection Bias in Molecular Epidemiology Shuji Ogino* Shuji Ogino Tomotaka Ugai Rong Zhong Koichiro Haruki Mai Chan Lau Melissa Zhao Tsuyoshi Hamada Carino Gurjao Edward L. Giovannucci Marios Giannakis Jonathan A. Nowak Mingyang Song Jooyoung Lee Li Liu Daniel Nevo Tyler J. VanderWeele Molin Wang

Molecular pathological epidemiology (MPE) provides integrative methods that can examine associations between exposures and specific pathobiological molecular signatures. MPE research often relies on biospecimen availability, which causes selection bias. To address this limitation, we developed methods of applying inverse probability weighting (IPW) to tissue bio-data-bank within prospective cohort studies. The weight was the inverse of the probability of biomarker data availability estimated by the logistic regression model. In proof-of-principle MPE studies, we utilized IPW-adjusted duplication-method Cox proportional hazards regression models to evaluate etiologic heterogeneity by disease subtypes. In an example study, we assessed smoking status and risk of colorectal cancer (CRC) subtypes by tumor neoantigen loads (high vs. low), using 4,420 CRC incident CRC cases including 571 cases with available tumor neoantigen data, within prospective cohorts of 173,229 participants (followed since 1976). In analyses without IPW, compared with never smokers, 20-39 and ≥40 pack-years of smoking were associated with hazard ratios (HRs) (with 95% CI in parentheses) for neoantigen-low CRC of 0.83 (0.52 to 1.31) and 1.02 (0.65 to 1.60), and HRs for neoantigen-high CRC of 1.86 (1.26 to 2.73) and 2.04 (1.38 to 3.01), respectively (P for subtype heterogeneity = 0.001). In the IPW-adjusted analyses, the corresponding HRs were 0.85 (0.54 to 1.35) and 1.06 (0.68 to 1.66) for neoantigen-low CRC, and 1.97 (1.33 to 2.91) and 2.06 (1.40 to 3.02) for neoantigen-high CRC, respectively (P for subtype heterogeneity = 0.003). Various other MPE studies have confirmed feasibility of our method, and provided a sanity check to ensure a small degree of selection bias in our tissue-available dataset. Our integrative methods of causal inference plus MPE can have a potential to enhance biomarker research for precision medicine and public health.

Quantifying the Robustness of Causal Inferences for Logistic Regression: Switching Cases from Success to Failure Qinyun Lin* Qinyun Lin Kenneth Frank Ran Xu Joshua Rosenberg Spiro Maroulis

Sensitivity analysis is useful for assessing the robustness of inferences to omitted variables or non-random sampling. We propose a new approach to quantify the quality of evidence for causality when the outcome is dichotomous. Specifically, the robustness of inference is interpreted as the number of cases that must be switched from treatment success to treatment failure (or control failure to control success) to alter the inference. A larger number implies more bias would be needed to invalidate the inference, indicating more robust inference. We illustrate this approach with an example regarding whether tobacco smoking can increase the rates of lung cancer (based on Pesch et. al., 2012). The first contingency table for smoking and lung cancer in Figure 1 comes from the study, based on which the t-ratio is 43.20. Assume the threshold for making an inference is based on a t_critical value of 1.96 as is commonly done in practice. To invalidate the inference, we need to reduce the t-ratio below this threshold. If 5,917 (87%) smokers with lung cancers are switched with smokers without lung cancer (the second contingency table), the inference that smoking affects lung cancer would not be sustained (the t-ratio is reduced to 1.956). That is, the robustness of the inference can be quantified by calculating how many smokers with lung cancer would have to be switched to smokers without lung cancer to invalidate the inference. The number of cases to switch can be expressed as a percentage to provide a scale for comparing robustness of inferences across different studies. When covariates are involved, we first generate an implied contingency table based on the odds ratio, standard error and sample information. We created a Shiny app (in-development) for this sensitivity approach, available here: http://konfound-it.com/. We also extend this approach for thresholds based on other significance tests, and compare our approach with other existing approaches, such as the "E-value".

Contingency table implied by the study			
	No Cancer	Cancer	Total
Not smoked	2883	220	3103
Smoked	3829	6784	10613
Total	6712	7004	13716

Contingency table after switches			
	No Cancer	Cancer	Total
Not smoked	2883	220	3103
Smoked	3829+5917=9746	6784-5917=867	10613
Total	6712+5917=12629	7004-5917=1087	13716

Figure 1. Contingency tables for smoking and lung cancer before and after switches.

Exploring the relation between causal inference and causal discovery tools for estimating average treatment effects Yongqi Zhong* Yongqi Zhong Ashley I. Naimi

Causal diagrams are popular tools for articulating conditions in which average treatment effects (ATEs) are identified. However, they can also be used to discover causal relations. Once a causal structure is discovered, a small number of algorithms exist that can be used to generate exposure effects of interest, such as average treatment effects. For example, Bayesian networks are a mathematical representation of causal diagrams, which can be used to discover causal relations with minimal background knowledge. Once the causal diagram is specified, the junction tree algorithm is supposedly able to obtain ATE estimates based on the diagram [Karwa et al. The Annals of Applied Statistics. 2011, 5(2B), 1428-1455.] Here, we compare the performance of standard [i.e. g computation, targeted maximum likelihood estimation (TMLE)] and Bayesian network approaches at estimating ATEs in two simple controlled simulated settings. Data generating mechanisms are depicted in Figure 1. We analyzed these data using g computation, TMLE, and Bayesian network + junction tree algorithm where the causal diagram was correctly specified (i.e. we did not perform any causal discovery). For simulation 1, we observed no bias for standard methods [bias of log(OR) [SD of log(OR)]: g computation= 0.00002(0.0013); TMLE=0.0034(0.027)] but the Bayesian network + junction tree algorithm was extensively more biased [bias of log(OR) [SD of log(OR)]=0.070(0.020]. Similar results were observed for simulation 2. Further exploration revealed that Bayesian networks correctly generated the joint and conditional probabilities that defined the graph. However, the junction tree algorithm quantified only unadjusted marginal associations, and did not adjust for any confounding variables. Our results suggest that, contrary to previous research, the junction tree algorithm cannot estimate ATEs, except in the absence of any confounding bias.

Simulation 1
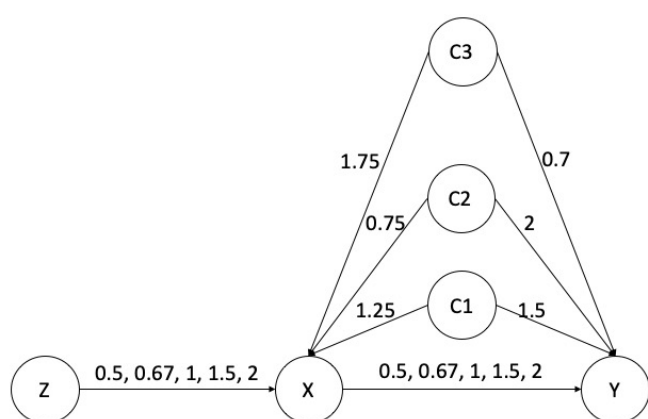
1. Numbers above edges are odds ratios (ORs)
2. Sample sizes are 200, 500, 1000
3. Probabilities (or prevalence): $p_x \cong 0.18, 0.36, 0.58$; $p_y \cong 0.15, 0.32, 0.53$
4. A total of 13,500 simulations were conducted (i.e. 675 different combinations of the parameters with 20 monte carlo simulations per parameter set).

Simulation 2
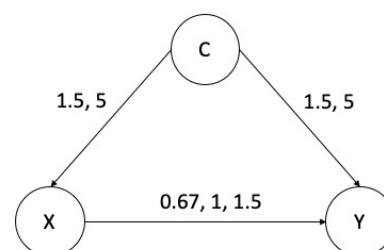
1. Numbers above edges are ORs
2. Sample sizes are 200, 1000
3. Probabilities (or prevalence): $p_x \cong 0.18, 0.58$; $p_y \cong 0.15, 0.53$
4. A total of 1,920 simulations were conducted (i.e. 96 different combinations of the parameters with 20 monte carlo simulations per parameter set).

Methods/Statistics

The meaning of arrows: reflections on the assumption of faithfulness in causal directed acyclic graphs Etsuji Suzuki* Etsuji Suzuki Tomohiro Shinozaki Eiji Yamamoto

In 1999, formal theories of causal directed acyclic graphs (DAGs) was introduced within epidemiology, and causal diagrams have been often used among epidemiologists as a tool to describe what is already known about the relevant causal structure. Simply speaking, a DAG is composed of nodes (or vertices) and arrows (or arcs/edges) connecting them such that the graph is acyclic. Despite the growing popularity of DAGs, however, the meaning of their "arrows" has been less appreciated. In this presentation, we aim to discuss the meaning of the presence or absence of arrow in causal DAGs, by showing its relation to some fundamental rules and assumption. Under the rules of compatibility and weak faithfulness, we can specify the relation between d-separation and statistical independence, and it is consistent with drawing arrows based on the presence or absence of individual causal effect. When we further assume faithfulness (i.e., the converse property of compatibility), however, we can also find the statistical dependencies implied by DAGs. In other words, under the rule of compatibility and the assumption of faithfulness (which are collectively referred to as perfect compatibility), the presence or absence of arrows corresponds to the presence or absence of average causal effect in the target population, instead of individual causal effect. Because faithfulness is controversial as a routine assumption from practical as well as theoretical perspectives, however, some textbooks (including Modern Epidemiology) discuss only uses of graphical models that do not rely on its assumption. From the perspective of causal effect, this study highlights the relevance of the assumption of faithfulness, showing its relation with effect modification. By using a simple numerical example, we emphasize the significance of distinguishing individual causal effect and average causal effect when using causal DAGs.

Using observational data to estimate the short-term effect of interventions: an emulation of a target trial Anthony Matthews* Anthony Matthews Tomas Jernberg Bertil Lindahl Lars Alfredsson Maria Feychting Anita Berglund Miguel Hernan

Large routinely collected healthcare databases facilitate the use of observational analyses to study the comparative effectiveness of clinical interventions. Conflicting results between randomized trials and observational studies are often attributed to unmeasured confounding in observational studies. However, discrepancies may also be due to differences in population characteristics and healthcare settings between the randomized trials and the observational studies. Registry-based randomized trials, in which routinely collected data platforms are used to randomize patients to an intervention, provide a unique opportunity to directly compare the results of trials and observational analyses carried out in the same population.

The VALIDATE randomized trial, conducted within the Swedish national myocardial infarction registry, found no difference between the effect of two anticoagulant interventions, bivalirudin and heparin, on the 180-day risk of death, myocardial infarction, or bleeding, in patients with acute myocardial infarction undergoing percutaneous coronary intervention. Here, we compare the results of the VALIDATE trial to an observational analysis that emulates this trial using pre-trial data from the same registry. 2,154 and 1,950 patients were eligible and administered heparin or bivalirudin respectively between January 2012 and May 2014. Death, myocardial infarction, or bleeding occurred in 183 (8.5%) patients given heparin and 174 (8.9%) given bivalirudin within 180 days.

We show that the observational analysis cannot estimate the short-term effects of treatment due to the inability to replicate the trial's eligibility criteria, resulting in intractable confounding. On the other hand, the observational analysis can correctly estimate long-term effects of treatment in the same setting. We outline the circumstances under which this situation holds and suggest an innovative way to deal with the inability of observational analyses to estimate the short-term effect of treatment.

Methods/Statistics

Connecting multi-stressor epidemiology with public data to estimate birth weight improvements associated with reductions in environmental exposures.

Chad Milando* Chad Milando Maayan Yitshak Sade Antontella Zanobetti Jonathan Levy M. Patricia Fabian

In a multi-stressor exposure context, estimating the public health benefits of exposure reductions requires both multi-stressor epidemiology and corresponding population data that encapsulate variation in demographic, behavioral, clinical, and environmental risk factors. However, these data are often unavailable at the spatial resolutions needed to make meaningful conclusions at a local scale. One approach to generate spatially resolved multi-stressor exposure data is to create synthetic sociodemographic population microdata that can be paired with fine scale exposure measurements and associated multi-stressor epidemiological findings. In this study, public data were used to create synthetic demographic, behavioral, clinical, and environmental data for mothers and newborns in two vulnerable communities in the Boston (MA) area (Chelsea and Dorchester). A multi-stressor epidemiological model for birth weight was then connected to the synthetic microdata. To demonstrate the utility of this model platform, we estimated changes in birth weight following hypothetical Census tract-level improvements in environmental exposures (e.g., increased greenness, reduced ambient temperature, noise, and fine particulate matter). Results highlighted variability in benefits between two low-income communities in close proximity to one another. For example, modeled improvements in birth weight following reduced noise exposures were more than twice as large in Chelsea as in Dorchester, whereas reduced ambient temperatures were associated with larger improvements in Dorchester. This work provides a methodology to estimate the health benefits of interventions or other exposure changes at a local scale (e.g., Census tracts within a city) using public data. It can be applied to any health outcome with multi-stressor epidemiological evidence and may be especially relevant in areas with a high percentage of vulnerable individuals with limited direct exposure data.

Simulation as a tool for teaching and learning epidemiologic methods Jacqueline Rudolph*
Jacqueline Rudolph Ashley Naimi Matthew Fox

As discerning epidemiologists, we must be able to think critically about the fundamental concepts in our field and be able to understand and apply many of the novel methods being developed today. We must also find effective ways to teach basic and advanced topics to graduate students in a short timespan, in a manner that goes beyond simple provision of knowledge. Simulation is an excellent tool for meeting these goals, and it has been our experience that students often think they understand epidemiologic phenomena until they explore them through simulations. Here, we demonstrate how simulation can be used to address two common misconceptions. First, we show how a student could investigate scenarios where non-differential misclassification might bias results away from the null. We walk through simulations of 3 misclassification scenarios: (1) no misclassification, (2) non-differentially misclassified binary exposure, and (3) non-differentially misclassed binary exposure and continuous confounder. We estimate for each scenario the mean difference for a continuous outcome across exposure levels (see Figure). Second, we show how an instructor could provide greater clarity on the correct definition of the p-value, in a relatively intuitive, non-technical manner. Simulation is used to conduct a permutation test. We generate a binary exposure associated with a binary outcome. The exposure is then repeatedly shuffled at random, and its association with the original outcome is estimated within each new data set. The resulting distribution of point estimates can be used to derive the p-value of the original association, and clarifying visualizations can be obtained. Through these examples, we highlight how simulation can be used to clearly and concretely demonstrate theoretical concepts and to experiment with ideas, theories, and methods in a controlled environment. Simulation is useful not only in the classroom but also as a skill for independent self-learning.
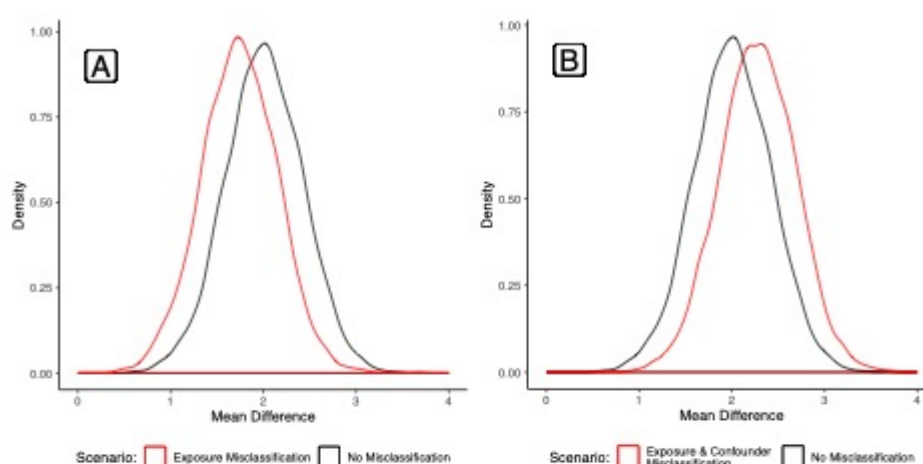
Figure. Distribution of mean difference estimates, comparing the mean difference under no misclassification to the mean difference under (A) non-differential misclassification of only the binary exposure and (B) non-differential misclassification of the exposure and misclassification of a continuous confounder.

Differential characteristics of residential histories by race and socioeconomic status: Linkage with LexisNexis in the Metro Chicago Breast Cancer Registry Garth H Rauscher*
Garth Rauscher Alpana Kaushiva David Stinchcomb Shannon Zenk

Introduction: Breast cancer can have a long latency period, and a patent's residential history (RH) prior to diagnosis may be more clinically meaningful than at diagnosis. However, there is concern that vendors such as LexisNexis might lack reliable and complete RH data for racial/ethnic minority and disadvantaged patients in particular.
Methods: We sampled 40,000 non-Latina (nL) black (Black), nL white (White) and Latina (15302 breast cancer cases and 24,698 controls) with a diagnosis or breast imaging exam (2001-2017). Identifiers were linked with LexisNexis to obtain RH for 39,499 (98.8%) patients, resulting in 272,814 addresses of which 295,829 (92%) were geocoded to the census tract. RHs were merged with established measures of interpolated, census-based tract disadvantage and affluence, in standard deviation (SD) units. We defined both point and cumulative measures at 10 and 20 years prior to diagnosis/last exam. RH data were available at last residence, 10 and 20 years prior for 97%, 93% and 79% of patients.
Results: In multivariable models, Black patients had more distinct addresses (9.1 vs. 7.1 and 7.4, p<0.0001) and a longer RH (31.4 vs. 29.8 and 26.5, p<0.0001) than White or Latina patients, respectively. Disadvantage (Beta=0.23 and 0.46) and affluence (Beta=0.45 and 0.61) were associated with more addresses and longer RH, respectively (p<0.0001 for all). Persons correlations ranged from 0.70 to 0.97 for point and cumulative disadvantage/affluence measures. Established racial/ethnic differences in disadvantage and affluence were consistent in magnitude for point and cumulative measures.
Conclusion: Greater mobility for minority and disadvantaged patients as well as greater credit reporting/mortgage data for more affluent patients, appears to be reflected in observed RH. Disadvantage / affluence at diagnosis/current may be a reasonable proxy for 10-20 year, longer term historical measures.

Comparative Effectiveness of Matching Methods in Improving Covariate Balance between Treatment Groups Vidhya* Vidhya Parameswaran Linda Ficociello

Introduction: Matching methods in epidemiology use extensive manual and iterative searches across various matching solutions to maximize the covariate balance between treatment groups. The aim of the analysis is to compare the effectiveness of propensity score matching (PSM; nearest neighbor method and inverse probability weighting (IPTW)) and coarsened exact matching (CEM) in finding a matching solution for a real-world cohort of hyperphosphatemic dialysis patients prescribed one of two phosphate binder treatments.

Methods: Clinical and demographic data were extracted from the Fresenius Kidney Care Electronic Health Records Database to estimate the effect of prescription of phosphate binders in controlling elevated serum phosphorus levels. All quantities of interest and estimation are presented in Figure1(a). We considered for inclusion 10 pre-treatment covariates (6 continuous, and 4 categorical variables), 6 squared terms, and 10C2= 45 one-way interaction terms, and sampled 500 subsets of these 61 variables. Matching was carried out using (i) 1-to-1 PSM using nearest neighbor method, (ii) 1-to-N PSM using IPTW method, and (iii) 1-to-N CEM. Space graphs were constructed to assess bias-variance tradeoff by plotting L1 and difference in means against number of matched patients (King, 2011).

Results: Data for 1076 hemodialysis patients (256 treatment, 820 control) were matched. The space graphs for the three matching methods are presented in Figure 1(b). Overall, PSM with IPTW presented the best matching solution. CEM-related L1 graph and the difference in means graph displayed the expected tradeoff between imbalance and variance. PSM using the nearest-neighbor method was not an appropriate solution because it pruned several observations thereby increasing the imbalance.

Conclusion: Matching solutions should be extensively compared prior to use to avoid choosing a model which provides inadequate solution for reducing covariate imbalance.

Methods/Statistics

Use of propensity-score calibration in estimating the effect of a primary care reform in Ontario, Canada Nadia Sourial* Nadia Sourial Isabelle Vedel Susan Bronskill Claire Godard-Sebillotte Jacob Etches Tibor Schuster

Rationale
Causal inference methods present an opportunity to improve the evaluation of natural experiments. Propensity score (PS) calibration may be particularly well-suited to leverage additional data sources to minimize residual confounding. This study demonstrated the use of PS calibration in the evaluation of a primary care reform in Ontario, Canada.
Methods
Between 2005 and 2012, an interdisciplinary primary care model was rolled out across the province. Consistency and positivity of the intervention were assessed to be met. The average causal effect (ACE) of interdisciplinary versus traditional primary care on emergency department use in persons with dementia was estimated using inverse-probability weighting. Population-level data were available for a partial set of potential confounders and predictors, creating a so-called "error-prone" PS. Subset data included information on additional covariates from which a "gold-standard" PS was derived. To strengthen the exchangeability assumption, PS calibration was used to estimate the "gold-standard" PS in the population-level data based on a regression calibration model of the error-prone and gold-standard PS in the subset data. A comparison of the PS and weight distributions and estimated ACE with and without PS calibration was conducted.
Results
The regression calibration model using the subset data showed a strong association between the error-prone and gold-standard PS (E[Gold Standard PS] = -0.004 + 0.008*Exposure + 0.998*Error-Prone PS). The PS and weight distributions of the error-prone and estimated gold-standard PS in the population data were nearly identical. The ACE with and without PS calibration was equivalent (relative risk: 1.03; 95% CI: 1.01-1.05).
Conclusion
In this study, the ACE using PS calibration did not differ from the estimate derived using the error-prone PS. Further research is needed to understand the settings in which PS calibration may be effective or not in reducing residual confounding.

Comparing statistical power of machine learning algorithms to identify heterogeneity of treatment effects: a simulation study Nicole Schmidt* Nicole Schmidt Christian Jackson M. Maria Glymour Theresa Osypuk Huiyun Kim David Rehkopf

Increasing interest in precision medicine and targeted social policy highlights the importance of understanding subgroup effects. Yet, efforts to identify subgroup effects have been marked by spurious findings. Applying transparent and replicable machine learning algorithms developed specifically for identifying heterogeneity of treatment effects (HTE) may address current limitations. Yet, the lack of comparison between algorithms makes it unclear for users which is best for a particular type of data structure and scientific question. We simulated data with specific characteristics to evaluate how well five different machine learning algorithms detected interactions: recursive partitioning (Athey); model-based recursive partitioning [MOB] (Zeilis); FindIt (Imai); meta-learner (Kunzel & Sekhon); and ensemble methods (Grimmer). We simulated data for binary treatment, two binary effect modifiers (e.g., health vulnerability and Black race), and a continuous, right-skewed outcome (e.g., psychological distress). We then encoded a 3-way interaction such that a small group (health vulnerable, Black race) did not benefit from treatment, while the other subgroups did benefit (decreased psychological distress relative to controls). We calculated the power for each method to identify this interaction (compared to OLS regression) and the false positive rate under the null, across a sample size ranging from 500 to 3700. With N=3700, power to identify the interaction differed: FindIt = .84; ensemble methods = .71; recursive partitioning = .62; MOB = .50; meta-learner = .44; OLS = .29. FindIt and ensemble methods emerged as promising machine learning methods for identifying HTE with greater power, but the false positive rate for FindIt was .18, possibly indicating overfitting.

Power Curves
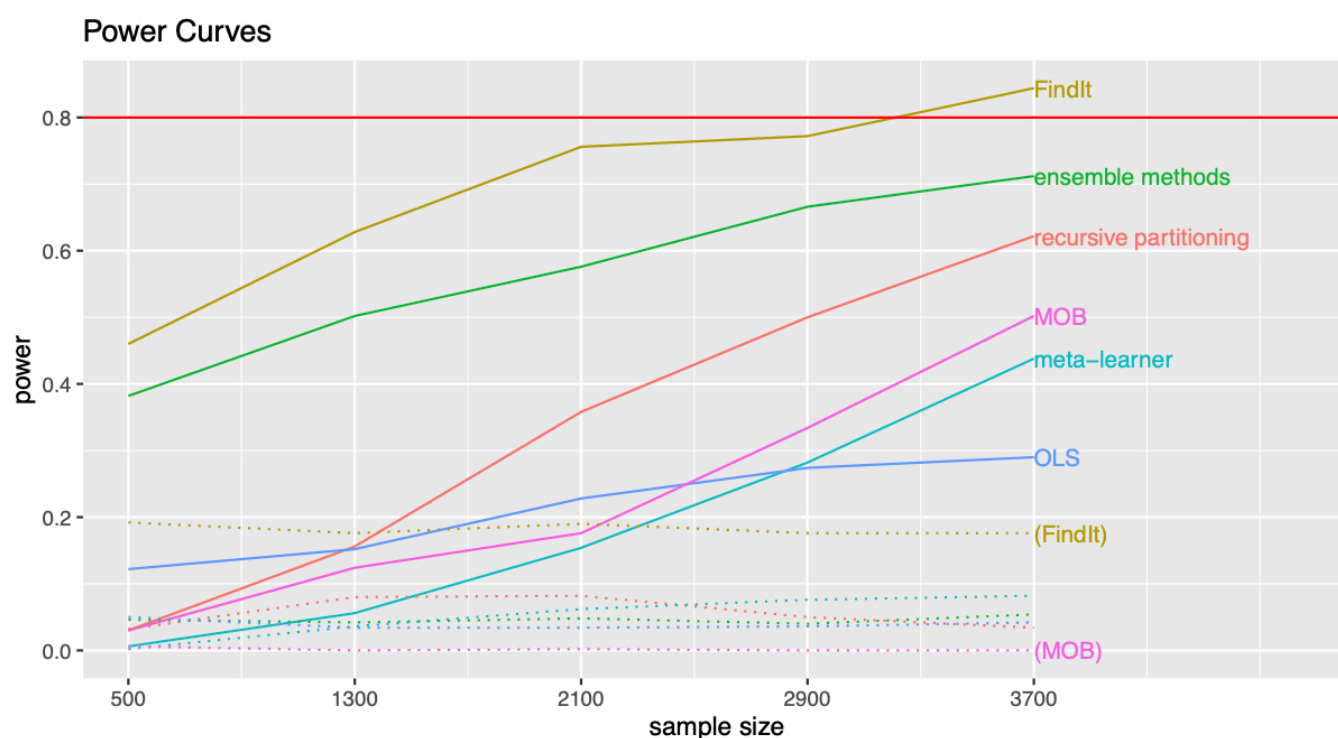
An Empirical Comparison of LASSO and Stepwise Selection Prediction Model Development Strategies with Various Sample Sizes
Sun Young Jeon* Sun Young Jeon Bocheng Jing Alexandra Lee John Boscardin Sei Lee

BACKGROUND: Patients' mortality prediction often involves a large number of predictors. Least Absolute Shrinkage and Selection Operator (LASSO) is a recent method developed to reduce the number of predictors while building a model that is not overfitted in a small sample. However, it is unclear how LASSO compares to conventional regression with backward elimination in large samples. To better understand the difference in prediction model characteristics between these two methods, we compared their discrimination with five different sample sizes. METHODS: We used Veterans Affair (VA) electronic medical records (EMR). Among over 1.2 million outpatient records of Veterans aged 50 or over since 2004, with global 10-year mortality of 48%, we obtained five random samples of various sizes (0.01%, N=1,264; 0.03%, N=3,791; 0.05%, N=12,636; 0.3%, N=37,908; 0.5%, N=63,180) and 924 predictors, including diagnoses, vital signs, labs, drugs, and demographics. To predict 12-year mortality, we fit LASSO and logistic regression with backward elimination in each sample. To test the extent of overfitting, we applied the fitted model to a separate validation sample of the same size and computed C-statistics. RESULTS: The advantage of LASSO stood out when applied to our smallest sample, as logistic regression did not converge. The difference in C-statistics between the two methods on validation data was largest in the 0.03% sample (0.816 vs. 0.808), and smallest in the 0.5% sample (0.844 vs.0.843). The gap in C-statistics between training and validation for both methods narrowed as the sample size increases, from 0.05 to 0.004 with LASSO and 0.04 to 0.005 with backward elimination. CONCLUSION: When the data is large, both methods performed well and there was no significant difference in discrimination. Neither of the two methods is completely free from overfitting, especially on small samples. This problem of overfitting was improved by both methods when applied to the larger samples.

Figure 1. C-statistics of prediction models developed using LASSO and logistic regression with backward selection.
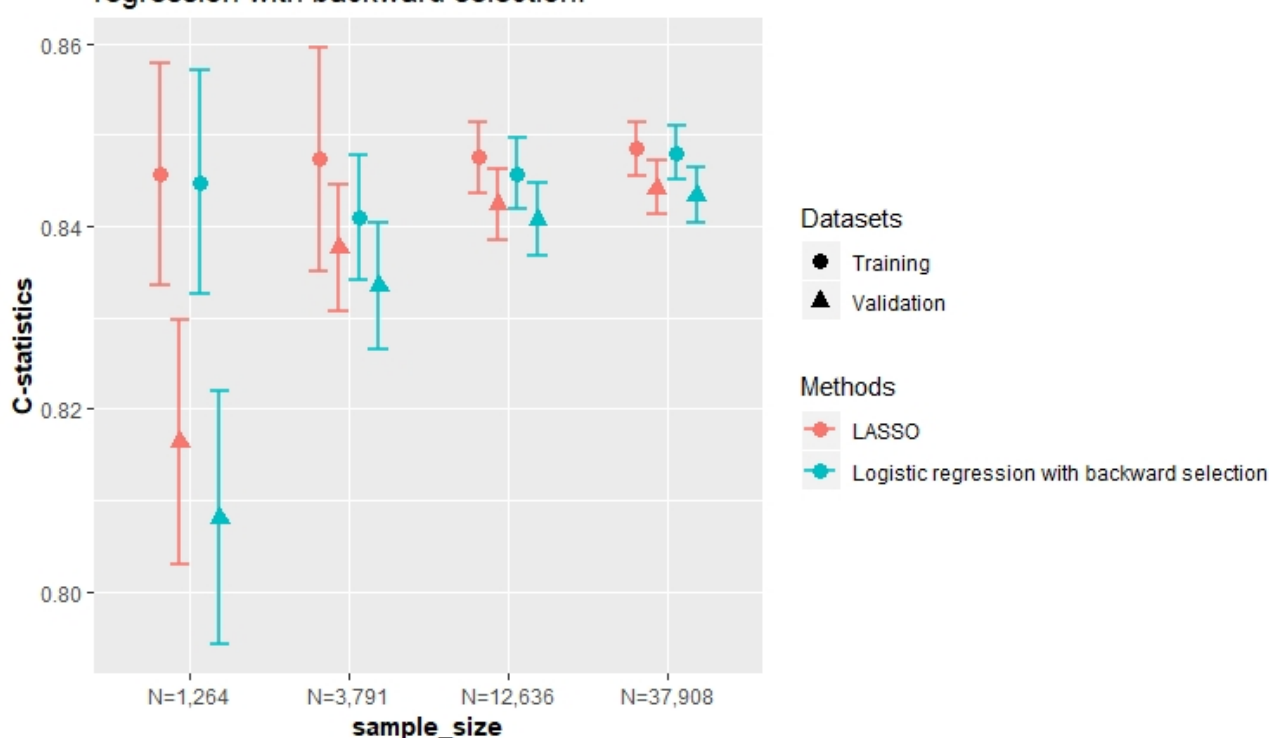
The Unknown Denominator Problem in Population-Level Studies of Disease Frequency

Christopher Morrison* Christopher Morrison Andrew Rundle Charles Branas Guohua Li

Background. Problems related to unknown or imprecisely measured populations at risk have been documented in studies of disease frequency over many decades. In most cases, the size of the population at risk is conceptualized as a denominator to be used in combination with a count of disease cases (a numerator) to calculate incidence or prevalence. However, the size of the population at risk can take other epidemiologic properties in relation to an exposure of interest and the count outcome, including confounding, moderation, and mediation. The goal of this study is to identify the best available approach to this "unknown denominator problem" given a hypothesized association between an exposure, a count outcome, and the size of the population at risk. We use spatial ecological studies of acute disease incidence (specifically injury) as an example because the problem is particularly salient for such studies. Method. Narrative review. Results. Researchers have used five approaches to address the unknown denominator problem in spatial ecological studies of injury incidence: ignoring, controlling for a proxy, approximating, controlling by study design, and measuring the population at risk. No solution is ideal for all scenarios. For example, controlling by study design (e.g. an ecological case-crossover design) is best used when the population at risk is conceptualized as a confounder or a denominator that is unrelated to the exposure of interest. Conclusions. We present recommendations for researchers regarding the best available solution to the unknown denominator problem given the data and the hypothesized association between an exposure of interest, a count outcome, and the size of the population at risk. Researchers should clearly articulate the hypothesized association to justify their chosen approach.
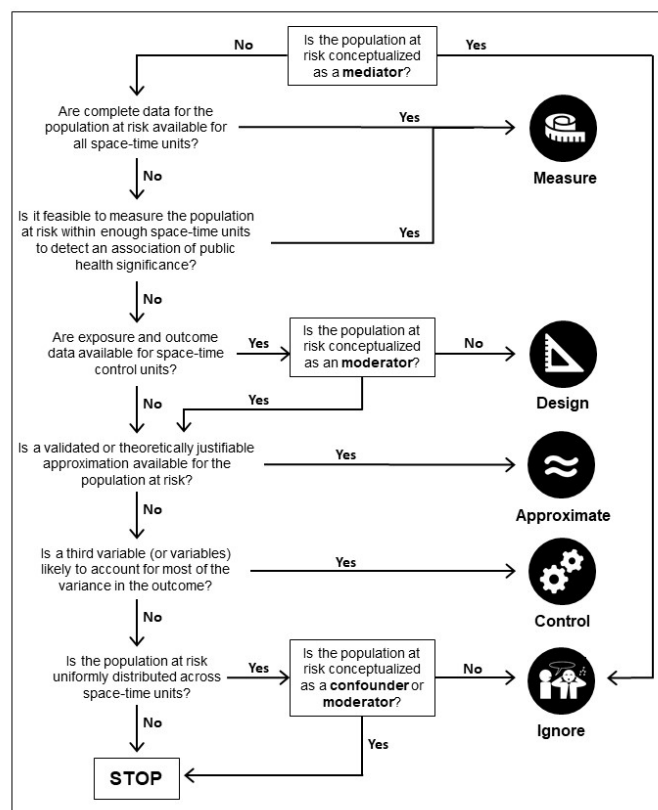
Marginal effect estimates have reduced finite sample bias Rachael K Ross* Rachael Ross
Stephen R. Cole

The parameter representing a covariate-adjusted treatment effect may be marginal or conditional (on covariates). The choice between a marginal or covariate-conditional effect should be driven by the study question, though in some cases they are equivalent. In most observational studies, covariate-conditional effects are reported. Yet we demonstrate here that marginal effect estimates have reduced susceptibility to finite sample bias. Typically, to avoid finite sample bias in logistic and Cox regression, it is recommended that there be 10 or more events per variable in a model.
We simulated 5000 studies each with 500 individuals, a binary exposure, a binary outcome, and independent standard normal covariates that were associated with the exposure and outcome. In two scenarios, we simulated the necessary number of covariates for the logistic outcome model to have 15 events/variable and 2 events/variable. The conditional OR was estimated by maximum likelihood. We used three estimators of the marginal OR: g-computation, inverse probability of treatment weighting (IPTW), and augmented inverse probability of treatment weighting (AIPW). The figure shows the relative bias in 5000 log OR estimates. At 15 events/variable, as expected, all estimates were unbiased. At 2 events/variable, the covariate-conditional estimate was notably biased, but marginal estimates exhibited little bias. Marginal estimates had lower root mean square error than the covariate conditional estimate.
Our experimental results illustrate, to our knowledge for the first time, that marginal estimates of the OR are less susceptible to finite sample bias than are traditional covariate-conditional estimates, at least for the examined scenarios. Reduced susceptibility may mean greater ability to control for bias in scenarios with a large number of confounders and a limited number of events.
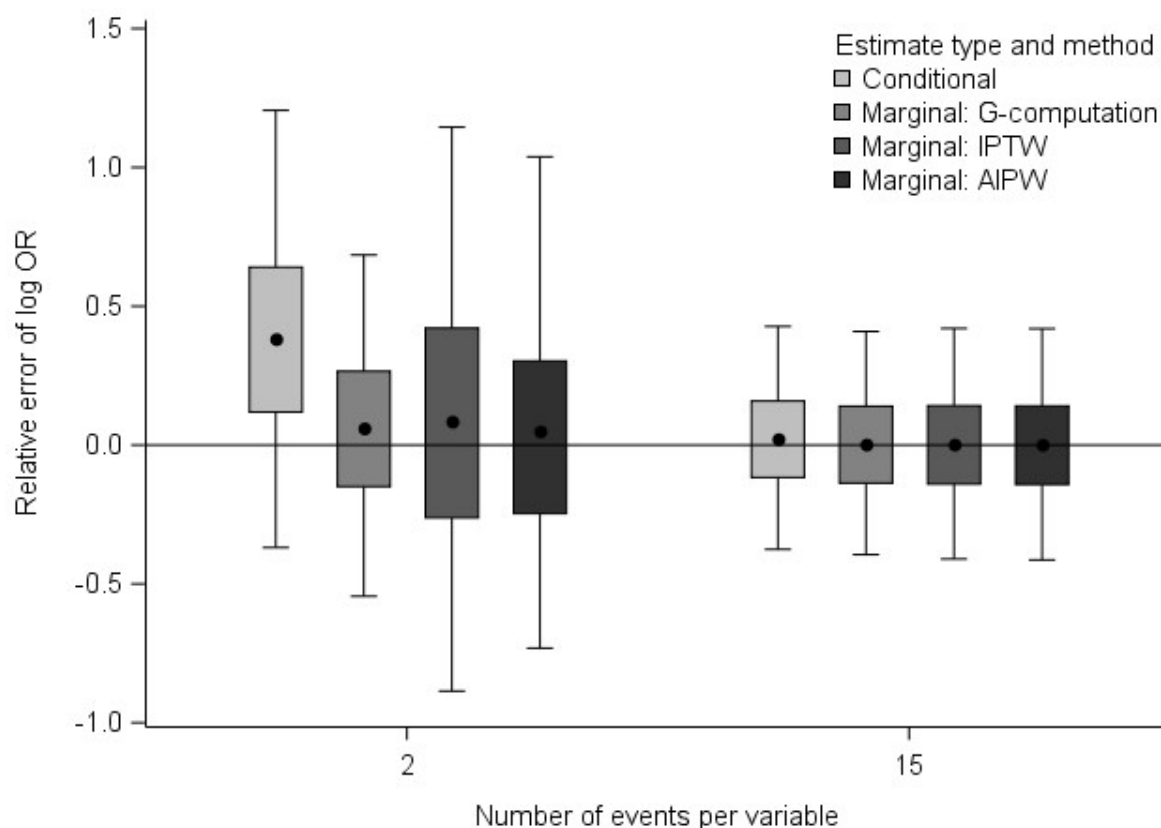
Filled circle marks mean. Whiskers extend from 2.5th to 97.5th percentiles.

Methods for Dynamic Prediction Modeling Erin Schnellinger* Erin Schnellinger Wei Yang
Michael Harhay Stephen Kimmel

Prediction models are used to inform decisions in many areas of medicine. However, these models
are often developed within a single derivation cohort, then applied to individuals outside this cohort,
and only updated periodically, if at all. A new paradigm, dynamic prediction modeling (DPM),
updates models by combining existing information with new data collected from new patients. Yet in
order to employ DPM in practice, one must first determine when model updating is necessary. We
simulated data informed by post-lung transplant mortality data and tested two main approaches for
detecting change: 1) Direct Approach: comparing the coefficients of the current prediction model to
those from the true baseline model; and 2) Calibration Regression approach: testing whether the
intercept and slope of an observed to expected regression line differed from 0 and 1, respectively.
We modeled intercept changes between 0 and 0.1, consistent with the 10% change in post-
transplant survival probability observed between 2007 and 2015. Separately, we examined
coefficient changes corresponding to changes in odds ratios between 0 and 20%, as might be
observed in practice. The Direct Approach isolated which particular coefficient had changed,
although a lower p-value threshold was required to account for multiple testing. Conversely,
Calibration Regression tended to detect changes sooner than the Direct Approach, with a
comparable proportion of false claims before the change, and a greater proportion of true claims
afterward. Adding an offset to the calibration regression line – i.e., fixing the slope at 1 when testing
the intercept, and fixing the intercept at 0 when testing the slope – provided additional power to
detect change, at the expense of the proportion of false claims before the change. Calibration
Regression seems preferable to the Direct Approach, as it can be extended to handle multiple
covariates and employed even when the true data generating model is unknown.

Scenario ii_1: Step change intercept, fixed slope

Scenario iii_1: Step change slope, fixed intercept
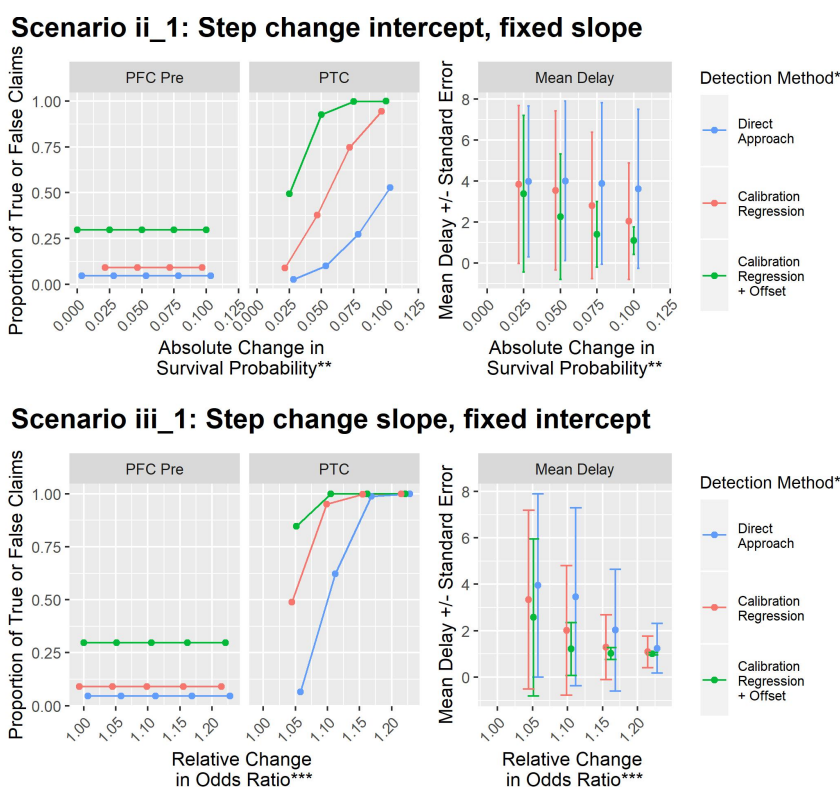
* The acceptance threshold for calibration regression and calibration regression + offset was set to p<0.01, while that for the direct approach was set to p<0.001,
   to account for the fact that the former approach tests the overall (combined) slope, whereas the latter involves testing each coefficient individually.
** Assuming a starting survival probability of 90%. Thus, 0 corresponds to the situation where the survival probability remains fixed at 90%; 0.1 corresponds to
   the situation where the survival probability decreases from 90% to 80%; etc.
*** Assuming a starting odds ratio of 1.2. Thus, 1 corresponds to the situation where the odds ratio remains fixed at 1.2; 1.22 corresponds to the situation where
   the odds ratio increases by 22%, from 1.2 to 1.5; etc.

A simulation study comparing the performance of inverse probability weighting and g-computation Jacqueline Rudolph* Jacqueline Rudolph Ashley Naimi Enrique Schisterman

When estimating the causal effect of a time-varying exposure on an outcome in the presence of time-varying confounding, inverse probability weighting (IPW) and g-computation are two commonly used methods. Theory states that g-computation will be more efficient than IPW, but this theoretical property has not been assessed in complex longitudinal data. Here, we used simulation to compare the performance (in terms of bias and variance) of these methods in the survival setting, both when one does and does not have a competing risk outcome. We generated 200 simulations of 1000 individuals, who were followed for up to 10 time points. Variables included a time-varying, binary exposure and a time-varying, binary confounder, which were predictive of time to outcome. Within each simulation, we estimated log hazard ratios (cause-specific hazard ratios for the competing risk outcomes) using Cox models and pooled logistic regression; confidence intervals were obtained using nonparametric bootstrap (and robust variance for IPW). We compared IPW and g-computation on the basis of their bias, efficiency, 95% confidence interval coverage, and mean squared error. As illustrated by the Figure, we observed little difference between IPW and g-computation; both approaches had limited bias, similar efficiency, and nominal coverage. For the non-competing risk outcome, the approaches had comparable mean squared errors, given the number of simulations: 0.053 for g-computation and 0.041 for IPW with the Cox model. Results for the competing risk outcomes were similar. Going in order for outcomes one to three, the mean squared errors were: 0.064, 0.066, and 0.075 for g-computation and 0.049, 0.055, and 0.060 for IPW, using the Cox model. While theory states that g-computation is more efficient than IPW, this property may not always be observed in practice, especially when working in complex longitudinal data.
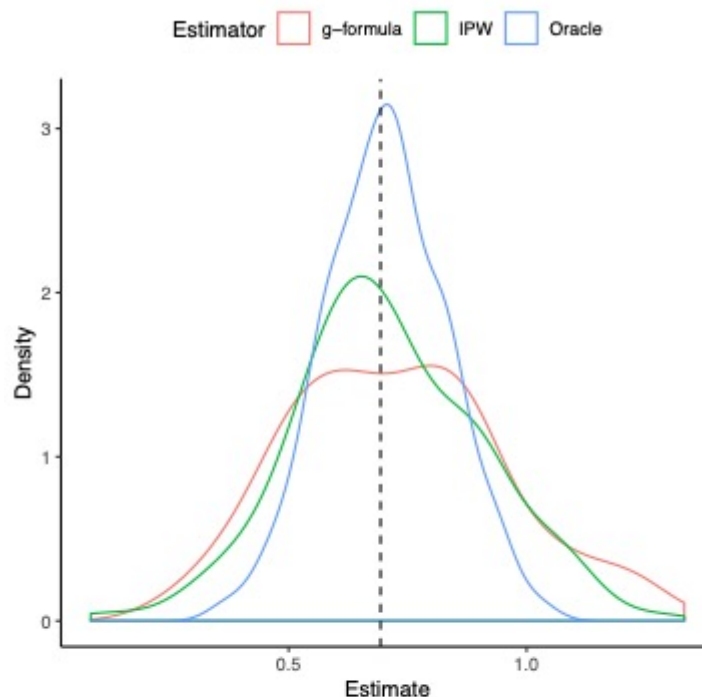
Figure. Distribution of the Cox model log hazard ratios from each simulation for the non-competing risk outcome, using the Oracle, g-computation, and IPW approaches. The dashed line represents the true log HR.

Leveraging long-term follow up time for breast cancer risk model validation: results from the Nurses' Health Study Chi Gao* Chi Gao Sara Lindstrom Rulla Tamimi Liming Liang Peter Kraft

Cohort studies are used to validate risk prediction models, but often only using the first few years of follow-up. For cohorts with long follow up time, information collected outside of the initial time window could also be used for validation. We illustrate this using data from the Nurses' Health Study, which has 22 years of follow up since blood draw(1990). We validated a breast cancer risk prediction model in three non-overlapping temporal cohorts: 1990-1995, 1995-2000, and 2000-2005, as well as in a synthetic cohort formed by concatenating these temporal cohorts. We found that the cohort closest in calendar time to the reference population used in the prediction model had the best calibration.

Analyzing the synthetic cohort as if it was a single cohort assumes that breast cancer incidence is independent across follow-up intervals, conditioned on breast cancer status and measured covariates at the beginning of each time interval. To evaluate the impact of potential violations of this assumption, we conducted a simulation study, in which breast cancer incidence was simulated under a true hazard model incorporating both a known, observed risk factor and an unknown, unobserved risk factor, whereas the predicted incidence was calculated using only the known risk factor. We found that standard estimates of the variance in estimation of the observed incidence rates for deciles of predicted risk performed well, even when the prediction model was mis-specified. This suggests that standard goodness-of-fit tests are valid when combining data across temporal cohorts. Furthermore, the increased sample size in the synthetic cohort, as compared to the individual temporal cohort, resulted in more precise estimates of observed breast cancer incidence, with nearly 50% narrower confidence intervals.

Our study demonstrates the benefits and feasibility of combining cohort subjects from non-overlapping timespans to leverage long follow up time in risk model validation.

Methods/Statistics

A comparison of geographic accessibility measures as predictors of actual travel burden

Jenna Khan-Gates* Jenna Khan-Gates Shannon Zenk Jan Eberth Michael Berbaum Garth Rauscher

Introduction: Studies of geographic accessibility to healthcare services typically measure drive time from patient's residence to the nearest facility without accounting for the capacity of the facility and other nearby facilities to serve the surrounding population. In addition, few to date have examined public transit-based measures. Actual travel burden is often unknown due to lack of data. We compare several accessibility measures as predictors of actual travel burden.

Methods: Analyses were conducted separately for receipt of screening mammography, diagnostic mammography, and biopsy in the population-based Breast Cancer Care in Chicago study (N=989). Actual travel times (drive times and public transit times) were calculated from each patient's address to the actual care facility; similar travel times were calculated to the nearest facility. Geospatial accessibility scores (drive-based and public transit-based) were calculated using the Enhanced 2 Step Floating Catchment Area (E2SFCA) method which considers capacity and demand for all nearby facilities. Fully standardized coefficients (Bxy) were estimated to compare associations of nearest travel times and geospatial accessibility as predictors of actual travel times.

Results: On average, travel times to utilized facilities were 12 (drive) and 45 (public transit) minutes longer than to the nearest facility. Compared to nearest travel times, higher accessibility scores were more strongly associated with reduced actual travel time for both drive time (Bxy=-0.32 vs. 0.04) and public transit time (Bxy=-0.22 vs. 0.12) for screening mammography, with similar results for diagnostic mammography and biopsy. When modeled together, accessibility scores dominated prediction of actual travel times, and nearest travel times were diminished.

Conclusion: The E2SFCA capacity-based measure better predicts actual travel burden than travel time to the nearest and should be used in geospatial access studies when possible.

Model Emulation Using Machine Learning: Applications to Hospital Epidemiology Matthew S. Mietchen* Matthew Mietchen Patrick Keppler Eric Lofgren

Background: Parameter estimation for disease transmission models continue to be computationally expensive. We explore whether machine learning could estimate a model parameter using output of methicillin-resistant Staphylococcus aureus (MRSA) acquisitions within an Intensive Care Unit (ICU). Hospital infection control programs measure driving factors of pathogen transmission well. However, one difficult measurement to obtained is the successful colonization of MRSA on a patient when in contact from a contaminated healthcare worker.

Methods: Stochastic compartmental models represented ICUs of varying bed-size. Random parameter values were selected within specified ranges to produce the outcome, MRSA acquisitions. Using 100,000 model simulations, several methods were implemented to build a prediction model; Exploratory Data Analysis (EDA), Principal Components Analysis (PCA), and linear regression, including Least Absolute Shrinkage and Selection Operator (LASSO) for model evaluation.

Results: A linear model using pair-wise interactions (AIC – 887,554; Adjusted R^2 – 0.8589) was found to be the best fit prediction model, compared to a baseline model (AIC – 951,205; Adjusted R^2 – 0.7241). Root mean squared error (RMSE) was used for having the same units as the output of the model. The LASSO model was comparable to the linear model with RMSE values of 25.893 and 25.885, respectively. Using these models for the parameter prediction, the RMSE for the LASSO and linear models were 0.289 and 0.287, respectively.

Discussion: Detecting a machine learning algorithm to predict a model parameter proved difficult. While linear relationships were found, a useful prediction was not. The RMSE terms were too large and to approximate the parameter from these models, an expected error of 0.29 is too high given it's a probability. Other machine learning techniques would need to be pursued in order to determine if a more efficient method for parameter estimation is possible.

Simulating the probability and impact of random differential outcome misclassification with perfect specificity Talal Alshihayb* Talal Alshihayb Brenda Heaton

Non-differential misclassification of a binary outcome is expected to result in unbiased estimates of the RR when Specificity is 100%. Despite non-differential mechanisms, differential misclassification may be realized by virtue of random errors. To gauge the amount of uncertainty around expectation due to random error only, we estimated the probability of differential outcome misclassification, its extent, and expected impacts via simulation. We simulated datasets with a binary exposure and outcome that varied according to sample size, exposure effects (RR=1.5 or 2), exposure prevalence (0.1 or 0.3), outcome incidence (0.1 or 0.4) and outcome sensitivity (0.6 or 0.8). Using a Bernoulli trial, we introduced misclassification by randomly sampling individuals with the outcome in each exposure group and repeated each scenario 10,000 times. In general, the extent and probability of differential misclassification decreased as the simulation parameter values increased. Across all scenarios, the mean differences in sensitivity (Se) across all repetitions were ≤0.1. Among datasets of 1,000 individuals, differences of ≥0.05 occurred approximately half of the time when Se was set to 0.6 and 41% of the time when Se was 0.8. Across all scenarios, the RR was biased, on average, toward the null when the Se was higher among the exposed, and away from the null when it was higher among the unexposed. The extent of bias (i.e., mean absolute difference between the true and misclassified RR on the natural log scale) for differences ≥0.05 ranged from 0.06 to 0.19 regardless of simulation parameters. However, similar trends were not observed for the OR where the extent and direction of bias was dependent on the outcome incidence, sensitivity of classification and the effect size. The results of this simulation encourage cautious interpretation in situations where non-differential outcome misclassification mechanisms are known to be operational with perfect specificity.

Completeness of reporting of case reports in high impact medical journals Jose Andres Calvache* Jose Andres Calvache Maira Dario Adrian Douglas David

Introduction: Case reports represent a relevant, timely, and important study design in advancing medical scientific knowledge. They allow integration between clinical practice and clinical epidemiology. We aimed to assess the completeness of reporting of case reports published in high impact journals. We assessed the completeness of reporting (COR) of case reports using the CARE guidelines.

Materials and methods: We selected three high-impact journals and one journal specialized in publishing case reports, in which we included all published case reports from July to December 2017. Median COR score was calculated per study, and CORs were compared between journals with and without endorsement of CARE guidelines.

Results: One hundred and fourteen case reports were included. Overall median COR was 81%, IQR [63%-96%]. Sections with the highest COR (84% to 100%) were patient information, clinical findings, therapeutic intervention, follow-up and outcomes, discussion and informed consent. Sections with the lowest COR were title, keywords, timeline and patient perspective (2% to 34%). COR was higher in journals endorsing in comparison to those not endorsing CARE guidelines (77% vs 65%) respectively, median difference = -12% 95%CI [-16% to -7%].

Discussion: Overall completeness of case reports in included journals is high especially for CARE endorsing and dedicated journals but reporting of some items could be improved. Ongoing and future evaluations of endorsement status of reporting guidelines in medical journals should be assessed to improve completeness and reduce waste of clinical research, including case reports.

Methods/Statistics

Characterizing the Causes and Risk Factors for Premature Mortality Supported by NIH Investments in Prevention Research Natasha Oyedele* Natasha Oyedele Luis F. Ganoza

While death is inevitable, extending life expectancy and avoiding premature death is feasible and reducing premature deaths is a major public health focus. The objective of this research is to summarize the main drivers of premature mortality in the US relative to the investments in prevention research supported by the National Institutes of Health. The Office of Disease Prevention (ODP) developed a taxonomy to classify extramural NIH funded research projects under several research foci, creating a database with a representative sample of 11,082 research projects for fiscal year (FY) 2012–2017. Using the 2017 data on risk factors from the Global Burden of Disease (GBD) Study and causes of death from the CDC, we aligned the disease definitions in these projects and estimated the percentage of NIH prevention projects whose study exposures or outcomes address the leading risk factors and causes of premature (<70 years) death in the US. A weighting procedure was applied to this sample to represent the entirety of the extramural NIH prevention research portfolio. We found that 51.4% (95% CI: 49.3% - 53.6%) of FY 2012-2017 NIH-funded prevention research projects measured a leading risk factor or cause of death as an exposure or outcome, where 34.0% (95% CI: 32.2% - 35.9%) of prevention research projects measured a leading risk factor for premature mortality. Similarities were observed between the leading risk factors for all ages and <70 years, however drug and alcohol use had a greater percentage of attributable deaths in people <70 years old than for all age groups combined (16.7% vs 5.6%). These results suggest that the leading risk factors and causes of premature death and the percent of attributable death are comparable to the leading risk factors and causes of death for all ages in the US population. However, the use of drugs and alcohol as a risk factor for premature death better aligns with the percent of prevention research supported by the NIH grants and cooperative agreements.

A different perspective of "cross-world independence assumption" and the utility of natural effects compared to controlled effects. Ian Shrier* Ian Shrier Etsuji Suzuki

Natural effects have been criticized because they require cross-world independence assumption. We present a different perspective that is consistent with recent work on path specific and separable effects. From a potential outcomes framework, we illustrate that both natural and controlled effects are measurable with three interventions, just in different sequences. We also illustrate that if the exposure is a cause of a confounder of the mediator – outcome relationship, controlled and natural effects both require an intervention to block the confounder-mediator path and there are no additional assumptions necessary. Using the sufficient causal framework, we illustrate that natural effects can be envisioned as what would happen if at least one component cause of all sufficient causes for the intervention effect on the mediator were removed. Thus, estimating natural effects can help identify and prioritize which potentially important targets for new interventions should be investigated. Controlled direct effects are meaningful only if one can block all causes of the mediator, which is often unlikely given there are multiple causes for the vast majority of conditions or states.

A Joint Modelling Approach for Greater Efficiency in Analysis of Mixed Outcome Composite Endpoints Martina McMenamin* Martina McMenamin Jessica Barrett Anna Berglind James Wason

Composite responder endpoints combine multiple outcomes to determine the effectiveness of a treatment, with patients labelled as 'responders' if they exceed predetermined thresholds in the individual outcomes and 'non-responders' otherwise. Often these outcomes are a mixture of continuous and discrete measures. By conducting a review of the Core Outcome Measures in Effectiveness Trials (COMET) database, we identified 67 clinical areas out of the 287 core outcome sets which use similar endpoints. In practice, these outcomes are collapsed into a single binary response indicator for the analysis, hence losing information contained in the individual components. To address this methodological shortfall, we propose a latent variable approach for analysing mixed outcome composite endpoints. Employing this framework retains the additional information available by jointly modelling the components, therefore having the potential to greatly improve the efficiency of the analyses performed in these clinical areas. We present the results of a simulation study demonstrating the bias, coverage and precision characteristics of the method and compare this with the standard univariate binary technique. Bias correction based on bootstrapping is demonstrated for when joint normality assumptions are violated. We apply the method to the MUSE study, a trial in systemic lupus erythematosus which uses a four-dimensional endpoint comprised of multiple continuous and discrete measures. We find that our method greatly improves the precision of the reported treatment effect, effectively reducing the required sample size by 60%. We introduce modified Pearson residuals for assessing goodness of fit and use these to illustrate that the model fits the trial data well. We conclude with recommendations for the use of this method in practice.

Methods/Statistics

Evaluating Predictive Validity of a Computerized Battery for Identifying Neurocognitive Impairment among Children Living with HIV in Botswana Amelia E. Van Pelt* Amelia E. Van Pelt Tyler M. Moore Onkemetse Phoi Mogomotsi Matshaba J. Cobb Scott Elizabeth D. Lowenthal

The national prevalence of Human Immunodeficiency Virus (HIV) in Botswana is the third highest in the world. Due to the high rate of HIV among pregnant women, in utero HIV exposures frequently occur, and children living with HIV experience increased risk of neurocognitive deficits. However, standardized cognitive screening does not exist in Botswana. The Penn Computerized Neurocognitive Battery (CNB), which measures both performance accuracy and response speed on major neurocognitive domains, streamlines assessment of neurocognitive performance. The CNB includes 13 tests selected based on the cognitive domains impacted by HIV infection, and it was culturally- and linguistically-adapted for use in Botswana. This research will evaluate the ability of the CNB to distinguish between HIV+ children with and without functionally-significant neurocognitive impairments in Botswana. Participants will include children living with HIV aged 10-17 years receiving care at a large HIV referral center in Gaborone. Based on the best available local tools, the "gold standard" assessment involves the administration of the Montreal Cognitive Assessment, review of school performance, and discussion of classification among four experienced clinicians. Participants will be classified as cases (i.e., with cognitive impairment) or controls (i.e., without cognitive impairment). Sixty-eight children (45 cases and 23 controls) will complete the CNB assessment. Efficiency scores for the CNB tests will be calculated as the sum of the z-standardized accuracy and speed scores. Sensitivity and specificity values will be calculated for predicting the "gold standard" using the CNB, and the area under receiver operating characteristic (ROC) curves will be calculated. Cross-validation will be performed through the leave-one-out approach. Enrollment in this study is ongoing, and results are expected to be complete by June. This analysis will enable the evaluation of the predictive validity of the CNB.

Methods/Statistics

Comparison of WQS, BKMR, BART and Super Learner with G-computation for Estimating Health Effects of Chemical Mixtures in Environmental Epidemiologic Studies Juwel Rana*

Juwel Rana

Background: Environmental epidemiologic studies usually estimate the health effects of each chemical separately, which introduces model misspecification and multicollinearity for multiple correlated exposures. Hence, novel and innovative statistical methods are essential to address model misspecification and multicollinearity. This simulation study, therefore, evaluated a multitude of novel approaches to estimate the health effects of multiple pollutants in relation to child cognitive function.

Materials and Methods: This study evaluated four methods: Weighted quantile sum regression (WQS), Bayesian kernel machine regression (BKMR), Bayesian Additive Regression Trees (BART), G-computation with Super Learner (SLG). We simulated the associations of seven correlated chemicals with four simulated outcomes with increasing complexity in the exposure-response relationships. The performance of WQS, BKMR, BART, and SLG was evaluated by their ability to estimate the independent and cumulative effects of chemicals, detect interactions, and reproduce the true dose-response relationships. We compared these methods with each other and evaluated based on bias, sensitivity, and specificity.

Results: BKMR and SLG predicted the independent and cumulative effects, depicted interactions, and reconstructed dose-response relationships. Overall, the BKMR and SLG were the least biased and most accurate methods for estimating the cumulative, independent effect of chemical mixtures, dose-response relationships, and interaction effects. In other words, BKMR and SLG showed good sensitivity and specificity for the simulated outcomes.

Conclusion: Our simulation results indicated that no single method consistently outperforms over others because each method has strengths and weaknesses. However, these innovative approaches can evaluate multiple aspects and answer different research questions in environmental chemical mixtures research addressing model misspecification and multicollinearity issues.

Logistical and methodologic challenges encountered in the repurposing of an epidemiologic cohort study Rebecca B. McNeil* Rebecca McNeil Corette B. Parker Philip Greenland George R. Saade Victoria L. Pemberton

The NICHD Monitoring Mothers-to-Be (nuMom2b) study enrolled 10,038 nulliparous women in the first trimester of pregnancy during 2010-2013 and prospectively collected diverse data and biospecimens through delivery, including deeply phenotyped pregnancy and maternal outcomes and socioeconomic, behavioral, and clinical risk factors for pregnancy outcomes. The data and biospecimens from this longitudinal cohort have supported an expansion of our understanding of risk factors for pregnancy outcomes. The NHLBI Heart Health Study (HHS; 2014-2020) repurposed this cohort with a new focus on cardiovascular disease risk factors and outcomes in the early years after pregnancy. HHS continued periodic survey follow-ups of subsequent pregnancy outcomes and selected risk factors, including an in-person assessment of clinical risk factors for cardiovascular health outcomes 2-7 years after first pregnancy among 4,508 participants, with stored blood specimens taken during the in-person assessment. A second continuation (2020-2026) will complete semiannual contacts, an in-person study visit and biospecimen collection in 2022, and offer a platform for ancillary studies under external funding mechanisms. Building on the resources of the original cohort has allowed us to explore the complex interplay of cardiovascular disease risk factors, pregnancy outcomes, and later maternal cardiovascular health. However, the expanded scope also presents a number of methodologic challenges. We explore several logistical issues and design and analysis considerations relevant to repurposing an existing research cohort.

Methods/Statistics

Comparing various matching methods with ordinary least squares using a simulation study and empirical tobacco data from the PATH cohort Ruifeng Chen* Ruifeng Chen Tarik Benmarhnia

Matching methods have been widely used in epidemiology to estimate the effect between treated subjects and matched controls. The first matching paper has been published by Rosenbaum and Rubin in the 1980s. The goal of matching is to minimize the difference between treated and untreated groups regarding variables identified as confounders. The well-known matching methods include propensity score matching (PSM), coarsened exact matching (CEM) and Mahalanobis distance matching (MDM). In the last few years, machine learning-based matching techniques have been proposed such as the Matching Frontier algorithm and Genetic matching. Other approaches in conjunction with propensity score estimation such as random forest and boosting have also been recently proposed. Despite all these matching methods, there is no specific guidelines identifying in which circumstances such matching methods provide less biased or more precise estimates as compared to traditional ordinary least square (OLS). We conduct simulation study in different scenarios to compare the performance of different matching methods to OLS, and we provide recommendations regarding the use of different methods in different situations. When the number of covariates is small, OLS performs best with no unmeasured confounder and correct model specification. CEM performs best with no unmeasured confounder but incorrect functional form. In high dimensional settings, we include machine learning based methods for propensity score computation (i.e. random forest and boosting) in addition to other matching methods, and we compare them to OLS. Lastly, we compare these techniques to an empirical example using the longitudinal PATH tobacco data with a large number of covariates and participants.

Adjusting for total energy and other dietary components produces different causal effect estimands in nutrition research Georgia D Tomova* Georgia Tomova Kellyn F Arnold Mark S Gilthorpe Peter WG Tennant

Background:
Estimating the causal effect of individual dietary components on health outcomes is a common aim in nutrition research. Due to clustering in intake of different components, investigators often adjust for total energy intake. But energy intake is compositional, meaning that the total is fully determined by the components thereof. Adjusting for total energy thus changes the estimand to a relative effect – a fact that remains poorly recognised. Adjusting for other components further alters the estimand by changing the reference. This study demonstrates how adjusting for total energy intake in nutrition research (with or without other dietary components) leads to different causal effects being estimated.

Methods:
Data were simulated using dagitty R (0.2-3) according to Figure 1. The total causal effect of sugar-sweetened beverages (SSB) (the exposure) on weight (the outcome) was simulated to be Z=5.0kg/100kcal. Clustering between components was simulated with a common cause ('U'). Coefficients for different adjustment sets were estimated by linear regression.

Results:
With no adjustment, the estimated effect of SSB on weight was confounded by 'U' [Z=5.5 (95% CI: 4.6; 6.5)], but this was eliminated by adjusting for all other dietary components [Z=5.0 (4.0; 6.0)].

In contrast, adjusting for total energy radically changed the estimand, returning a relative effect of apparently smaller magnitude [Z=3.2 (2.2; 4.1)]. Adjusting for total energy, other sugars, and saturated fat changed the estimand again by altering the reference group (to include healthier components), to produce an apparently larger relative effect [Z=3.8 (2.8; 4.7)].

Conclusion:
Adjusting for total energy intake in studies of dietary components changes the estimand to a relative effect, which can be further changed by also adjusting for other components. Interpretational bias is likely if this fact is not recognised. It may also explain some of the apparent heterogeneity between existing studies.

Methods/Statistics
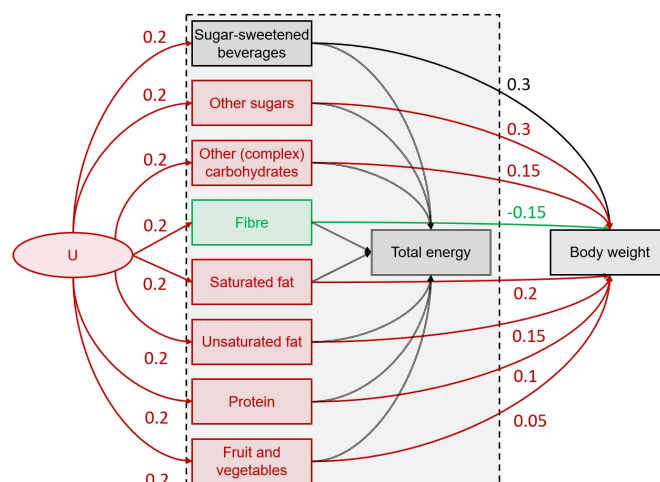
Inverse probability weighted estimation of the effects of proportionally-representative interventions for the setting of limited treatment resources: an application to increased-risk organ transplantation Aaron L. Sarvet* Aaron L Sarvet Kerollos Nashat Wanis Jessica Young Miguel A. Hernán Mats J. Stensrud

Investigators often evaluate treatment effects by considering settings in which all individuals are assigned a treatment of interest, assuming that an unlimited number of treatment units are available. However, many real-life treatments may be constrained and cannot be provided to all individuals in the population. For example, patients on the liver transplant waiting list cannot be assigned a liver transplant immediately at the time they reach highest priority because a suitable organ is not likely to be immediately available. In these cases, investigators may still be interested in the effects of treatment strategies in which a finite number of organs are available at a given time, that is, treatment regimes that satisfy resource constraints. Here, we describe an estimand that can be used to define causal effects of treatment strategies that satisfy resource constraints. We introduce a novel and simple class of inverse probability weighted estimators, and apply one such estimator to evaluate the effect of restricting or expanding utilization of 'increased risk' liver organs to treat patients with end-stage liver disease. Our method is designed to evaluate plausible and policy-relevant interventions in the setting of finite treatment resources.

Methods/Statistics

A logic-based approach for multiple imputation of missing data Chinchin Wang* Chinchin Wang Tyrel Stokes Russell Steele Ian Shrier

Researchers are often advised to use multiple imputation to handle missing at random data to minimize bias while making the best use of all available data. This typically involves selecting a regression model with random variation to predict imputed values, and generating multiple complete datasets for analysis. However, there are contexts where it is very difficult to fit a model due to constraints amongst variables, and using a generic regression imputation model may result in implausible values. We examine the advantages of employing a logic-based resampling with matching (RWM) approach for multiple imputation that differ from generic approaches, but allow for more plausible imputations. We illustrate a resampling approach for multiply imputing missing pain, activity frequency, and sport data using The Childhood Health, Activity, and Motor Performance School Study Denmark. There are multiple constraints between variables in this dataset that cause difficulties for generic regression imputation software: 1) the total activity frequency must be equal to or greater than the number of sports; 2) each sport played must have activity frequency greater than 0; 3) each sport that was not done must have an activity frequency of 0; and 4) the individual activity frequencies for each sport must sum to the total activity frequency. Our approach involves generating probabilities for missing values using the observed data. We match records with missing data to several observed records, and sample from these records based on the probability of each occurring. Because imputed values are generated randomly, multiple complete datasets can be created. They are then analyzed and averaged in the same way as model-based multiple imputation. This approach can be extended to other datasets as an alternative to regression model-based approaches, particularly where there are time-dependent ordered categorical variables or other constraints between variables.

Propensity score calibration extension with beta regression measurement error model

Jessica L. Rohmann* Jessica L. Rohmann Marco Piccininni Maarten van Smeden Tobias Kurth

The propensity score (PS) calibration technique was developed to correct for known but unmeasured confounding in a main (often longitudinal) study using additional information from a second, external (often cross-sectional) study by fusing PS and regression calibration methodology. In PS calibration, a measurement error model uses linear regression to relate the error-prone PS computed using only the confounding variables available in the main study to the 'gold-standard' PS computed using all the confounding variables in the external study. Using this model, the gold-standard PS can be imputed in the main study and used to identify the causal effect of the exposure of interest. However, a linear regression model is not actually suitable to model the PS, which ranges from 0 to 1, and the linear regression assumptions of PS calibration are unrealistic in most applied settings. We propose an extension of PS calibration using a beta regression measurement error model that overcomes these shortcomings and without increasing programming complexity. We showed theoretical and simulation-based justification for the extension under the same assumptions of the classic PS calibration method (see Figure). These assumptions include surrogacy, an often unrealistic but necessary assumption for PS calibration, as well as low variance of the gold-standard PS conditional on the exposure of interest and error-prone PS (i.e. large ϕ parameter for the beta regression) or small coefficient of the true PS in the final causal model (i.e. small $\beta2$). We further empirically compared the performance of this new approach to results obtained using the classic PS calibration with a linear regression model, in terms of bias correction and mean squared error. We performed this comparison in two different scenarios with several constellations of parameters. In all scenarios, the beta regression extension showed better or equal performance compared to the classic PS calibration approach.

Figure
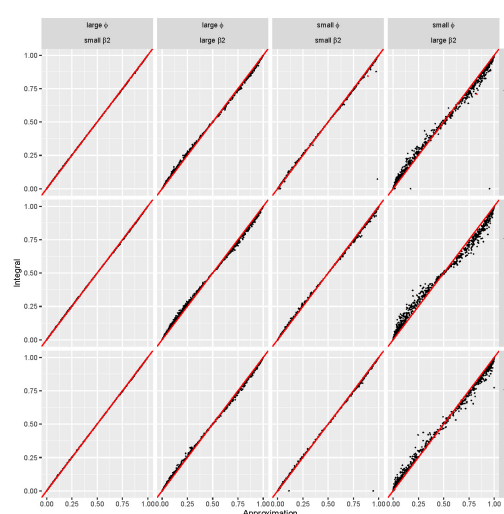
Simulation results showing integral approximation performances. On the y-axis, the solution of the integral corresponding to the probability of being diseased given the exposure status and the error-prone propensity score (PS) computed with adaptive quadrature. On the x-axis, an approximation based on an imputed PS obtained with a beta regression measurement error model. μ represents the mean value of the gold standard PS. 1,000 dots for each quadrant represent 1,000 runs. The regression coefficient for the PS in the final causal model, β2, is considered small if its absolute value is lower than 2. The precision parameter of the beta regression, φ, is considered small if its value is lower than 3. Other quantities were randomly drawn from uniform distributions with suitable ranges.

Methods/Statistics

Is there a place for "preDAGtion" in epidemiology? Marco Piccininni* Marco Piccininni Stefan Konigorski Jessica L Rohmann Tobias Kurth

Historically, causal inference and prediction modeling methodologies in the field of epidemiology have been largely distinct. Directed Acyclic Graphs (DAGs) have become increasingly used to model a priori causal assumptions and inform variable selection strategies for causal questions. In parallel, novel prediction tools with a range of automation are gaining momentum. Machine learning and other prediction strategies are finding applications in causal inference methodology and the field of causal learning is rapidly growing. However, the potential benefit of using causal thinking and graphs to inform modeling strategies and predictor selection in clinical risk prediction modeling has yet to be formally assessed in a structured way. This is the aim of this theoretical and simulation-based study.

Specifically, we investigated whether incorporating knowledge about the underlying causal structure could provide insights on the transportability of diagnostic clinical risk prediction models using two illustrative scenarios. We further probed whether this knowledge can be used to a priori select the optimal set of predictors for a given outcome. We empirically showed that a particular set of variables corresponding to specific nodes in a DAG, is the optimal set of predictors for that outcome in a series of 100,000 simulations with random DAGs.

We found that a logistic regression including this set as covariates showed equal or superior performance with respect to calibration and number of input variables compared with seven other methods including: three logistic regression models using other criteria to select the predictors, lasso, ridge, and elastic net regression models, and a random forest algorithm. These findings support the idea that using causal graphs to identify this set of variables may be a useful, efficient strategy to select predictors if strong knowledge of the underlying causal structure exists.

Methods/Statistics

Introducing Sparse Weighted Sum Regression (SWSR): Variable Selection for Correlated Chemical Exposures Grace R. Lyden* Grace Lyden David M. Vock Shanna H. Swan Emily S. Barrett Sheela Sathyanarayana Ruby H.N. Nguyen

There is a growing demand for methods to determine the effects that chemical mixtures have on human health. One statistical challenge is identifying true so-called "bad actors" from a mixture of highly correlated predictors. Classical regression approaches perform poorly in this situation, assigning coefficient signs at random, and regularization techniques often default to choosing either one or all of the variables from a correlated group. Weighted Quantile Sum (WQS) regression has been proposed to address this problem, but WQS is limited by a lack of sparsity in coefficient estimates and a reliance on data splitting into training and test sets, without which Type I error rates are inflated. We propose a new method called Sparse Weighted Sum Regression that has the ability to set weights to exactly zero, thus performing true variable selection while simultaneously estimating model parameters such as the overall mixture effect. Two options are presented for significance testing of the overall mixture effect, including a permutation test that maintains nominal Type I error rates without data splitting. In extensive simulation studies, we demonstrate our method's minimal bias and improved selection accuracy compared to WQS and standard linear regression, across a range of outcome models and predictor pairwise correlations. We apply our method to The Infant Development and the Environment Study, a multicenter pregnancy cohort study with a focus on prenatal phthalate exposure and child health outcomes. Relative to competing approaches, our method increases power to detect an overall negative relationship between prenatal phthalate metabolite concentrations and anogenital distance in male infants.

Methods/Statistics

Is Epidemiology Appropriate for High School Students? Emily M. D'Agostino* Emily D'Agostino

The methods of epidemiology instruction are critical to ensure students are trained optimally to produce an epidemiology of consequence. How students learn epidemiology, but also when they first receive exposure to the discipline, are topics of debate. While some scholars propose integrating epidemiology into high-school science learning, adolescent students may have unique learning needs and goals making instruction impractical or ineffective. Others have argued that high school students can gain valuable critical thinking skills from epidemiology that can be refined in undergraduate and graduate school epidemiology. This study compared the effectiveness of a semester-long epidemiology course vs. biology, chemistry, geology and statistics in teaching critical thinking skills to high school students (n=110; 63% female, 36% Asian, 30% Hispanic, 22% non-Hispanic White, 12% black; 54% 12th graders, 48% mid- and 24% high-poverty). Student critical thinking skills were assessed based on pre-post performance using the Test of Scientific Literacy Skills (TOSLS), a validated measure of scientific inquiry and interpretation. Multilevel models were fit to examine the association of course subject on student growth in TOSLS performance. Models adjusted for student sex, race/ethnicity, grade, semester, and poverty showed that scientific literacy skills were most improved for physics (b= 1.5 [95%CI: 0.27, 2.72]), biology (b= 1.4 [95%CI: -.54, 3.28]), and epidemiology (b= 0.97 [95%CI:-0.48, 2.43), and less improved for chemistry (b= -.06 [95%CI: -1.55, 1.43]) and geology (b= -0.01 [95%CI:-1.31, 1.29]) relative to the reference group, statistics. These preliminary findings suggest that epidemiology is an appropriate method of supporting youth development of scientific literacy skills. Larger and more nuanced studies are needed to examine the impact of particular epidemiology topics, pedagogical approaches, and grade levels on high school student epidemiology learning.

Methods/Statistics

Mediation Analysis for Spatial Data: An exploration of possible methods for spatially heterogeneous estimates of direct and indirect effects Kristen Hansen* Kristen Hansen Tarik Benmarhnia

Mediation analyses have become a popular approach to disentangle the effect of an exposure on an outcome by a given set of mediators and been applied to a wide range of epidemiologic studies. In recent years, many methodological developments under the counterfactual framework have been proposed. Notably, solutions have been proposed to deal with time varying exposure and mediator-outcome confounders. However, to the best of our knowledge, there was no effort dedicated to spatial confounding. In various epidemiological problems, especially in environmental health, we would expect there to be dependence on spatial location (spatial autocorrelation) and certainly spatial analyses could be used to improve precision in estimates. Take as an empirical example, the relationship between heat and unplanned respiratory disease hospitalizations with the mediator of ozone. This data is inherently spatial so we cannot aggregate measurements across the entire spatial region. Also, we would expect the mediating relationship between ozone and hospitalizations to be different in different locations based on various confounding factors from number of cars to population demographics. Conducting separate models for each spatial unit would be imprecise as hospitalization data is too sparse at the desired spatial scale. There is no combination of spatial modeling and mediation analysis currently developed and we see this as a pertinent issue for many problems involving spatial data types in epidemiology. To solve this problem, we explore approaches to obtain spatially heterogeneous estimates of direct and indirect effects. In particular, geographically weighted regression (GWR) is existing methodology for regression on spatial data that can be applied to implement spatial mediation analyses. The ability to leverage spatial effects in mediation could have many potential applications in a wide range of epidemiologic studies.

Methods/Statistics

Spatial case-crossover design: a new method for disentangling the spatial distribution of heat-related hospitalizations in California Kristen Hansen* Kristen Hansen Tarik Benmarhnia Armin Schwartzman

Many studies have examined the effect of heat waves on various health outcomes including hospital admissions. But few have explored the fine-scale spatial variability over a wide spatial domain in order to identify vulnerable areas while taking into consideration the spatial structure of the data. In this study, we compared a few approaches for addressing this problem proposing a novel spatiotemporal method. We use California, USA as a case because California has widely varying climate, elevation, and uneven distribution of population. We propose a spatial extension of the case-crossover design where we match heat wave to similar non-heat wave days (based on time varying covariates) for comparison of hospitalization rates in small spatial regions (zip codes) on both absolute and relative scales. We extend to use Bayesian Hierarchical models to leverage spatial correlation in the data set. For comparison, we apply the Kulldorff method of cluster detection across the state. We find that the Kulldorff method fails to recognize areas where zip code centroids are far apart from each other and population is relatively low. Our approach detects regions both in urban and rural areas of California, however more precision is found in urban areas both on relative and absolute scales. The Bayesian Hierarchical model extension has more precision and still detects those rural as well as urban areas. Future steps include the consideration of the isotropy assumption in Bayesian hierarchical models. This approach is able to leverage spatial data to get local estimates all across California that can help guide local level policy making on both relative and absolute scales and can help statewide efforts to reduce heat wave health impacts. This methodology can be used in other regions and other environmental exposures as well to help guide policy in a changing climate.

A structured approach to evaluating life course hypotheses: Moving beyond analyses of exposed versus unexposed in the omics context Yiwen Zhu* Yiwen Zhu Andrew J. Simpkin Matthew J. Suderman Alexandre A. Lussier Esther Walton Andrew D.A.C. Smith Erin C. Dunn

Life course epidemiology provides a framework for studying the hypothesized effects of exposures that vary over the life course, on health outcomes. As a theory-driven analytic method, the structured life course modeling approach (SLCMA) simultaneously assesses possibly-competing life course hypotheses and determines which hypothesized effect is most supported by observed data.

In this study, we performed simulations and empirical analyses to evaluate the performance of the SLCMA when applied to genome-wide DNA methylation (DNAm). Using simulations, we compared five statistical inference tests used with SLCMA (n=700), assessing the family-wise error rate (FWER), statistical power, and confidence interval coverage to determine whether inference based on these tests was valid in the presence of substantial multiple testing and small effects, two hallmark challenges of inference from omics data. In the empirical analyses, we evaluated the time-dependent relationship of childhood abuse with genome-wide DNAm (n=703). In the simulations, selective inference and max-|t|-test performed best: both controlled FWER and yielded moderate statistical power when the effect size is sufficiently large. Empirical analyses using SLCMA revealed time-dependent effects of childhood abuse on DNAm. Our findings show that SLCMA, applied and interpreted appropriately, can be used in high-throughput settings to examine time-dependent effects underlying exposure-outcome relationships over the life course. We provide recommendations for applying the SLCMA in omics settings, discuss the assumptions required to interpret the effects causally, and encourage researchers to move beyond analyses of exposed versus unexposed in omics studies.

Grandparenthood and mortality: a Swedish national multi-generation cohort study Can Liu*
Can Liu Alessandra Grotta Josephine Jackisch Ylva Almquist Olof Stephansson

Grandparenthood may affect health both positively and negatively. Previous findings were biased by comparing those lived long enough to have grandchildren to those not.

To answer "Does grandparenthood affect mortality of the grandmother or the grandfather?", we emulated a series of hypothetical randomized yearly trials in 2004-2016, using a national multi-generation cohort of all people born in 1953 and lived in Sweden in 1963 and their descendant family members with health, socioeconomic and demographic information from Swedish national registers. They were followed until death, emigration, or the end of 2017, whichever came first. Members of the control group were censored when becoming grandparents (per-protocol effect). We use pooled logistic regression models to estimate gender- and lineage-specific hazard ratios (HRs) of mortality, comparing grandparents to those not being grandparents, adjusting for time-varying confounders. We also stratified the analysis by whether a grandparent was living in the same county as the first grandchild.

Maternal grandmothers [HR 0.76, 95%CI 0.56-1.05] and paternal grandfathers [HR 0.81, 95%CI 0.65-1.01] had lower mortality than women and men not being grandparents. The protective effect of paternal grandfatherhood was more pronounced among grandfathers living in the same county as their grandchildren [HR 0.75, 95%CI 0.58-0.96] than those living in a different county [HR 0.96, 95%CI 0.71-1.30]. In contrast, the association between maternal grandmotherhood and mortality did not differ substantially by distance. Maternal grandfatherhood and paternal grandmotherhood were not associated with mortality [HR 0.86 95CI% 0.67-1.10 and 0.93, 95%CI 0.72-1.20].

Becoming a maternal grandmother or a paternal grandfather was associated with a positive effect on health. Living close to the grandchild was especially protective for paternal grandfathers. Becoming a maternal grandfather or a paternal grandmother did not affect mortality.

DAG: continuous treatment of grandparenthood and survival

Child mortality (cease to be grandparent) is assumed to be negligible

Time varying confounder
- Days of inpatient care
- Comorbidity index
- Income
- cohabitation status

Time-constant confounder
- age at having the first child
- sex of first child
- number of children
- percentage of daughter among all children
- education at 49
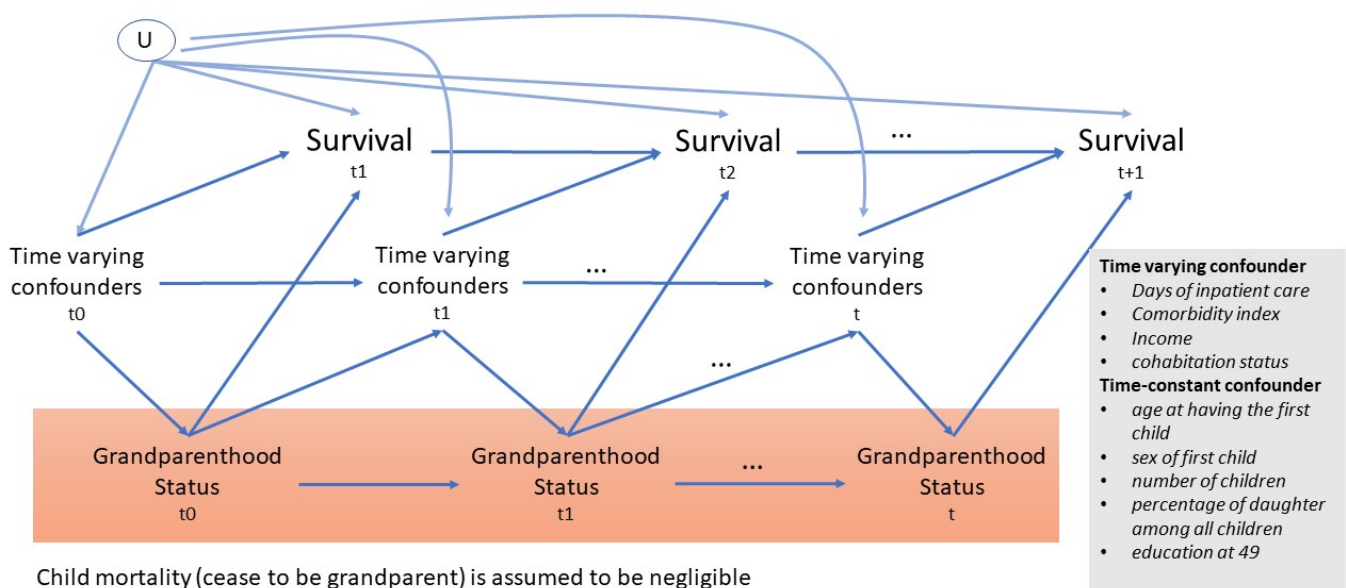
DAG With Omitted Objects Displayed (DAGWOOD): An overlay for DAGs for revealing assumptions and generating graphical causal models

Noah Haber* Noah Haber Mollie Wood Sarah Wieten Alexander Breskin

Directed acyclic graphs (DAGs) are frequently used in epidemiology as a guide to causal inference assumptions. However, in a typical DAG, the assumptions of sharp causal nulls and correct model specification are denoted in the DAG by the absence and the assumed direction of the arcs, respectively. These assumptions lie hidden in the negative space between nodes.

We propose an algorithmically generated overlay on the existing DAG structure which addresses this gap: the DAG with omitted objects displayed (DAGWOOD). DAGWOODs add two classes of objects on top of a DAG: exclusion restriction pathways (ERPs) and misdirection or reverse pathways (MRPs). ERPs are a superset of both known unmeasured and unknown unmeasured confounding pathways. Known unmeasured ERPs include any items which are known by the analysts to be potentially biasing but not modelled empirically, often due to lack of data. Unknown unmeasured ERPs represent any and all potential unknown biasing pathways which are assumed to be negligible. MRPs represent alternative pathways that could be drawn between two objects, e.g., if a variable controlled for as a confounder was in fact a collider. The ERPs and MRPs correspond to both a graphical overlay and a list of key assumptions for any given causal model. All these assumptions must be justifiable as being negligible or non-existent for an estimate from a causal model to be justifiable as being unbiased.

The DAGWOOD framework 1) makes explicit and organizes the most important causal model assumptions, 2) reinforces best DAG practices, 3) provides a framework for critical evaluation of causal models, and 4) can be used in iterative processes for generating causal models. While it is inherently impossible to fill in the space beyond our best theoretical understanding, DAGWOODs provide a vehicle to directly confront and address the most important assumptions to improve causal inference.
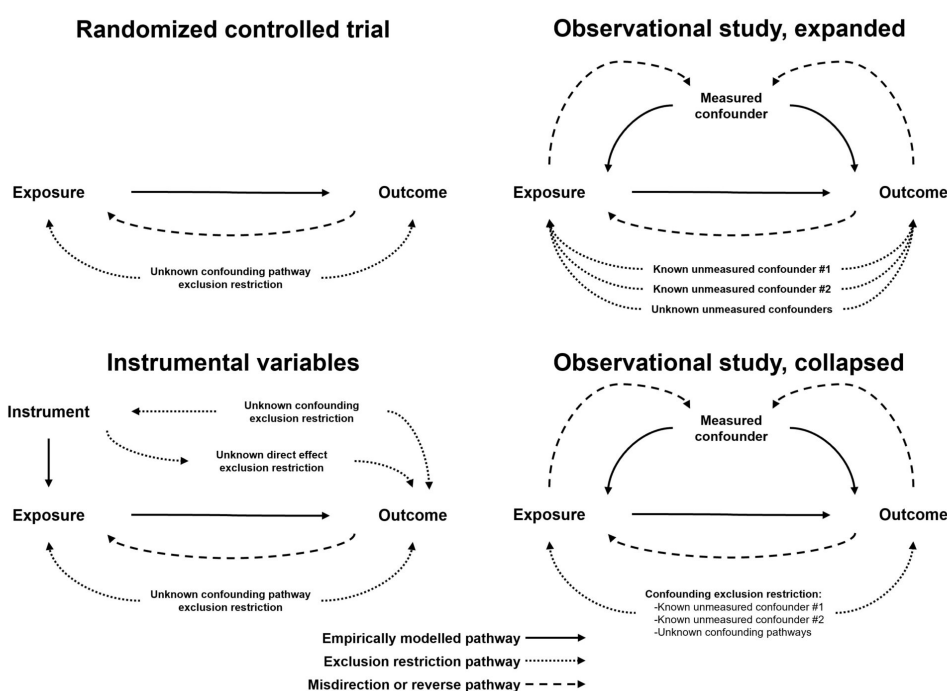
The Functional Synthetic Control Method: Redefining Synthetic Control Using Functional Data Analysis Aaron Shev* Aaron Shev Andrew Farris Rose Kagawa Hannah Laqueur

We propose a modification to the Synthetic Control Method (SCM) using the tools of functional data analysis. The SCM is 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. SCM creates a counterfactual time trend for the treated unit in the absence of the treatment by taking the weighted average of pre-intervention outcomes from selected donor regions. The selection of donors relies on often arbitrarily chosen pre-intervention observations of the outcome, and the observations chosen can impact the values of the weights applied to the donor pool. Our objectives are to incorporate functional representations of the data into SCM and to compare the performance of this approach with traditional SCM. We reframe the panel data as functional data by assuming the outcome for each unit is continuous over the observation period but observed only at discrete time points. Operationally, this is done by representing each unit's outcome as a linear combination of a basis of continuous functions, such as cubic B-splines. The proposed method uses the coefficients corresponding to each basis function as together they provide a concise numerical summary of the shape and trend of each unit. We conduct a Monte Carlo simulation to compare the SCM to functional SCM. In a preliminary simulation, on average the RMSE was 22% smaller in the pre-treatment period and 1% greater in the post-treatment period for functional SCM when no treatment effect was present. The functional synthetic control method provides better donor selection and replaces an arbitrary step of the analysis with a data driven process. Additionally, it requires little extra computation time, and can be used in conjunction with other augmentations of the SCM making it an attractive choice and a valuable contribution to the synthetic toolbox.

Co-exposure (Z) amplification bias: A threat to the validity of mixtures epidemiology Marc
G. Weisskopf* Marc G. Weisskopf Thomas F. Webster

Background/Aim
Environmental epidemiologists are increasingly concerned with analysing simultaneous exposure to
multiple toxicant exposures and increasing effort is being devoted to establishing methods to
analyze exposure mixtures in epidemiological studies. Co-exposures in this setting can cause a form
of Z-amplification bias, which we refer to as co-exposure amplification bias. Understanding, the
properties of this bias amplification is critical for mixtures epidemiology.

Methods
Through the use of Directed Acyclic Graphs (DAGs) we describe data structures underlying different
reasons for correlated mixtures of exposures. From these we deduce the potential for bias
amplification when including multiple exposures together in analytic models.

Results
When correlation between co-exposures is caused by a variable that is unrelated to the outcome of
interest, then the possibility of co-exposure amplification bias is high when the exposures are
considered together in analytic models. When correlation between co-exposures is caused by a
variable that is also related to the outcome of interest, then adjustment for both exposures helps
reduce confounding. When both reasons for co-exposure correlation are present, the effects on co-
exposure bias become more complicated and can go in both directions. In this case, the distribution
of sources of exposure to the contaminants will influence which direction the bias is likely to go.

Conclusions
Co-exposure amplification bias poses an important potential problem to the analysis of health effects
of exposure mixtures. Careful consideration of the structure giving rise to correlated exposures is
critical and may have implications for statistical approaches to analyzing the data.

A simulator to inform Alzheimer's disease and dementia trial design Scott Zimmerman* Scott Zimmerman Melinda Power Teresa Filshtein Sarah Ackley Megha Mehrotra Kan Gianattasio Jingkai Wei Audra Gold Maria Glymour

Optimal trial design should incorporate the best available evidence from observational studies regarding how trial participant characteristics, intervention intensity and duration, and outcome assessments would shape trial results. Qualitative judgments are often used to incorporate prior evidence on these elements into trial design because there are few systematic quantitative tools. We develop a simulation tool using an R Shiny app to aid in evaluating proposed trial designs. We show initial validation results using an example of interventions on type 2 diabetes management to prevent Alzheimer's disease and related dementias. The simulation software allows for evaluation of anticipated effect sizes and power of hypothetical RCTs of blood glucose management interventions on memory outcomes. Users can vary trial design elements including sample size, sample composition, effect size of the intervention on blood glucose, and follow-up time. The simulation model is parameterized from a previously developed statistical model, based on a presumed causal structure of the effect of blood glucose on a memory score, which was fit to data from the Health and Retirement Study (HRS) and the Atherosclerosis Risk in Communities (ARIC) study. Comparing our simulation to the ACCORD-MIND trial (approximately matching intervention intensity, duration, and sample size, and scaling memory measures for comparison), we show an anticipated effect size of -0.041 (-0.428, 0.324) SD, compared to -0.037 (-0.417, 0.335) SD in the original trial (both at 3.3 years of follow-up). Significant outcome differences by study arm were not detectable in simulation until 10 years after enrollment, long after the 3.3 years of follow-up in ACCORD-MIND.
To design better RCTs, it is important to systematically use observational evidence to anticipate how effects may vary depending on sample composition, intervention and outcome assessment. Simulation studies provide a mechanism to evaluate proposed trials.

Bounds on the average causal effect of prenatal alcohol exposure on ADHD – a Mendelian randomization study
Elizabeth Diemer* Elizabeth Diemer Marcus Munafo Luisa Zuccolo Henning Tiemeier Sonja Swanson

Background: Point estimation in Mendelian randomization (MR), an application of the instrumental variable model proposing single nucleotide polymorphisms (SNPs) as instruments, requires additional assumptions beyond the three instrumental conditions. Bounding approaches, which do not require additional point estimating assumptions, are infrequently applied in instrumental variable models, possibly because bounds from a single proposed instrument are often wide. However, MR approaches proposing multiple SNPs as instruments may lead to narrower bounds.

Aim: This project aimed to estimate bounds on the average causal effect of prenatal alcohol exposure on offspring ADHD in a British birth cohort study (N=4457), proposing 10 maternal SNPs as instruments.

Methods: We first applied the instrumental inequalities to all possible combinations of the 10 SNPs to identify violations of the MR conditions. We then computed bounds on the average causal effect assuming: 1) that all SNPs in a combination were marginally and jointly valid instruments, 2) that all SNPs in a combination were marginally but not jointly valid instruments, and 3) that at least a certain number of SNPs were marginally valid instruments.

Results: The instrumental inequalities failed to hold for all sets with >4 SNPs, indicating at least 6 were not valid instruments. Bounds assuming at least one SNP was a marginally valid instrument (-0.522, 0.469) barely improved on assumption-free bounds (-0.531,0.469). Bounds became tighter as larger numbers of SNPs were assumed to be jointly valid instruments, and occasionally identified the direction of effect, though bounds from different sets of proposed instruments varied substantially (see Figure).

Conclusions: Our results suggest that, when proposing multiple SNPs as instruments, it is possible to narrow bounds on the average causal effect. Variation in the bounds under different assumptions indicates that this analysis is highly dependent on said assumptions.

Average causal effect of any vs. no alcohol consumption in pregnancy on offspring ADHD
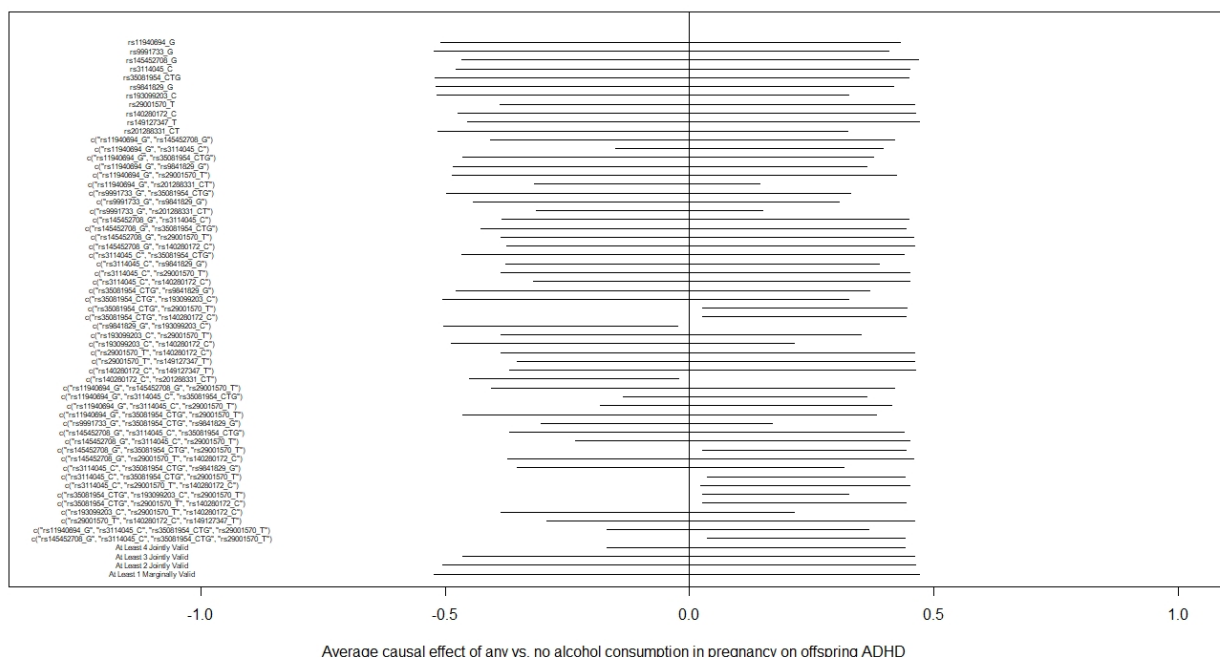
Use of directed acyclic graphs (DAGs) in applied health research: review and recommendations
Peter Tennant* Peter Tennant Wendy Harrison Eleanor J Murray Kellyn F Arnold Laurie Berrie Matthew P Fox Sarah C Gadd Claire Keeble Lynsie R Ranker Johannes Textor Georgia D Tomova Mark S Gilthorpe George TH Ellison

BACKGROUND:
Directed acyclic graphs (DAGs) are an increasingly popular approach for identifying confounding variables that require adjustment when estimating causal effects in observational data. This review examined the use of DAGs in applied health research to inform recommendations for improving their transparency and utility in future research.

METHODS:
Original health research articles published during 1999-2017 mentioning "directed acyclic graphs" or similar or citing the DAGitty software package were identified from Scopus, Web of Science, Medline, and Embase. Data were extracted on the reporting of: estimands, DAGs, and adjustment sets, alongside the characteristics of each article's largest DAG.

RESULTS:
A total of 234 articles were identified that reported using DAGs. The distribution of publication year, first author country, and journal citation category are shown in Figure 1. A fifth (n=48, 21%) reported their target estimand(s) and half (n=115, 48%) reported the adjustment set(s) implied by their DAG(s). Two-thirds of the articles (n=144, 62%) made at least one DAG available. Diagrams varied in size but averaged 12 nodes (IQR: 9-16, range: 3-28) and 29 arcs (IQR: 19-42, range: 3-99). The median saturation (i.e. percentage of total possible arcs) was 46% (IQR: 31-67, range: 12-100). 37% (n=53) of the DAGs included unobserved variables, 17% (n=25) included super-nodes (i.e. nodes containing more than one variable), and 34% (n=49) were arranged so the constituent arcs flowed in a consistent direction. None evaluated the assumptions of their DAG against their data.

CONCLUSIONS:
There is substantial variation in the use and reporting of DAGs in applied health research. Although this partly reflects their flexibility, it also highlights some potential areas for improvement. The review therefore offers several recommendations to improve the reporting and use of DAGs in future research.
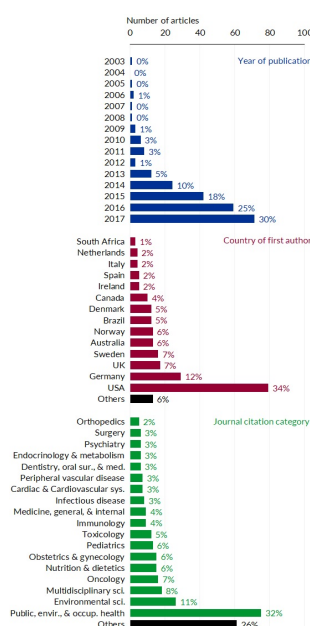
Is lack of reproducibility a crisis, or data behaving as expected? Rebecca Nash* Rebecca Nash W. Dana Flanders Rich F. MacLehose Thomas P. Ahern Lindsay J. Collin Timothy L. Lash

Concerns about lack of reproducibility in scientific research have been prominent recently. Funding agencies and journal editors have developed and promoted guidelines for reproducible research and investigators are often asked to describe how their work can be replicated. The term "reproducibility crisis" has been coined by some in the scientific community to describe the influx of findings that have not been replicated by others. However, little consideration has been given, in this context, to the influence of selection pressures resulting from reliance on significance testing to identify findings that merit attention.

If the alternative hypothesis is true, overlaps the positive side of the null distribution, and the distribution of a parameter under the alternative hypothesis overlaps the rejection region for a given test, then on average, a statistically significant result overestimates the true effect. If power is 50% or lower, a statistically significant result is guaranteed to overestimate the truth. In many research settings, low power is not unusual.

A replication study, however, is not subject to the selection pressure of statistical significance, and more likely to yield an unbiased estimate, if there is no other source of bias. Replication results therefore regress towards the mean of the alternative distribution. Original results could be adjusted for this inflation, but this rarely occurs.

The Center for Open Science published an account of the reproducibility of psychological studies. We used their publicly available dataset with original and replication results and power information. We show that the original results, adjusted for the inflation using methods derived from Copas 1999, correspond well to the replication results. So long as results are selected for attention based on statistical significance, they ought to be adjusted for the expected inflation before publication. This strategy will reduce the appearance of poor reproducibility.

LATEBREAKER

Methods/Statistics

Inter- and intra-researcher reliability of anthropometric measurements in the SAYCARE Study Gabriela Vatavuk-Serrati* 3647] Vatavuk-Serrati Heráclito B. de Carvalho Francisco Leonardo Torres-Leal Ariclécio Cunha de Oliveira Augusto César F. De Moraes

Background: Anthropometric measures are frequently used in epidemiologic studies to assess body composition. Therefore, it is important to obtain reliable measurements among different examiners. **Objective:** To test the inter- and intra-researcher reliability of anthropometric measurements across the three centers of the SAYCARE (South American Youth/Child cARdiovascular and Environmental) Cohort Study in Brazil. **Methods:** A training workshop was conducted in July 2019 in Fortaleza to standardize anthropometric measurements across researchers from Sao Paulo, Fortaleza, and Teresina who participate in the SAYCARE Cohort Study. The training consisted of theoretical and practical sessions. An experienced researcher measured weight, height, circumferences (arm, neck, waist, and hip) and skinfolds (biceps, triceps, subscapular, and suprailiac) of children between 5 and 11 years of age, and these measurements were considered the reference for the inter-researcher reliability. Researchers took the same anthropometric measurements of the participants before they received the training and after, and those were compared to assess the intra-researcher reliability. Every measurement was performed three times, and the average of them was used for the analyses. **Results:** The sample was composed of 9 children (55.6% male) with a mean body mass index (BMI) of 16.06 kg/m2 (95% CI: 14.97, 17.16). Inter-researcher reliability varied between 0.9 and 0.944 for weight and height, between 0.875 and 0.944 for arm, neck, waist and hip circumferences, and was 0.944 for all skinfold measurements. Intra-researcher reliability varied between 0.9 and 0.944 for weight and height, between 0.875 and 0.944 for the circumferences, and between 0.929 and 0.944 for biceps, triceps, subscapular and suprailiac skinfolds. **Conclusion:** Inter- and intra-researcher reliability were ranked from good to excellent for all the measurements according to WHO parameters across the SAYCARE Cohort Study centers in Brazil.

Geographic variation in the oral microbiome of Agricultural Health Study applicators Ian D. Buller* 3647] Buller Emily Vogtmann Mary H. Ward Christian Abnet Rashmi Sinha Yunhu Wan Mitchell H. Gail Catherine C. Lerro Dale P. Sandler Laura Beane Freeman Rena R. Jones

Background Geographic location of individuals may partially explain heterogeneity in the composition of their microbiota, but studies are limited, including within the United States.

Methods We evaluated the spatial variation of oral microbial communities in a subset of participants in the Agricultural Health Study (AHS), a cohort of pesticide applicators (mostly male farmers) and their spouses in Iowa (IA) and North Carolina (NC). Excluding spouses residing at the same geocoded address, buccal cell specimens were analyzed for 1,432 applicators aged 19-84 years (IA, N=962; NC, N=470) using 16S rRNA gene sequencing. We compared richness of observed species (rarefaction: 20,000 reads) within and between the two states using the intraclass correlation coefficient (ICC), a measure of spatial clustering (Moran's I), and non-spatial linear models including age, sex, and smoking status as covariates. Within state, we also evaluated the relationship of Euclidean distance between applicators and beta diversity using an index of overall community composition (a Bray-Curtis dissimilarity matrix; BCD; rarefaction: 20,000 reads) with the Mantel statistic (999 simulations) based on Pearson's correlation (r).

Results Species richness varied more within each state than between states (ICC=0.067; 95% CI:-0.11-0.243) but there was no evidence of spatial clustering within either state (IA: global Moran's I=0.001; p=0.531, NC: global Moran's I=-0.002; p=0.930). Residuals were not spatially autocorrelated for either state (IA: p=0.537, NC: p=0.78), indicating that variation in species richness could be explained with a non-spatial model. BCD was not significantly correlated with distance within either state (IA: r=0.001; p=0.445, NC: r=-0.017; p=0.826).

Conclusions In this novel evaluation, we did not demonstrate significant spatial variation in the oral microbiota of AHS applicators within or between study states. Future studies will incorporate occupational and environmental predictors.

Methods/Statistics

Measure-at-risk sampling in case-control studies Michael D. Garber* 3647] Garber Lauren E. McCullough Stephen J. Mooney Michael R. Kramer Kari E. Watkins R.L. Felipe Lobelo W. Dana Flanders

Transient exposures are difficult to measure in epidemiologic studies, especially when both the status of being at risk for an outcome and the exposure change over time, as when measuring built-environment risk on transportation injury. Contemporary 'big data' generated by mobile sensors can improve measurement of transient exposures. Unfortunately, exposure information generated by these devices typically only samples the experience of the target cohort of interest and thus must be used in a case-control framework.

We present a method, which we call measure-at-risk sampling. Its goal is to estimate the denominator of an incidence rate ratio (exposed to unexposed measure of the at-risk experience) for a cohort. From the cohort, the method samples the measure of the at-risk experience, e.g., person-time, rather than sampling individuals or moments. We describe sufficient conditions for the ratio of the exposed to unexposed at-risk measure to consistently estimate that of the cohort (examples in Figure). We describe the method for individual-level person time and individual- and place-level person-distance. We illustrate the method with data from a smartphone app used to record bicycling.

The method extends an established case-control sampling principle: sample the at-risk experience of a cohort study such that the sampled exposure distribution approximates that of the cohort. It is distinct from density sampling in that the sample remains in the form of the at-risk measure, which may be continuous, such as person-time or person-distance. This aspect may be both logistically and statistically efficient if such a sample is already available, for example from 'big data' sources like aggregated mobile-sensor data.
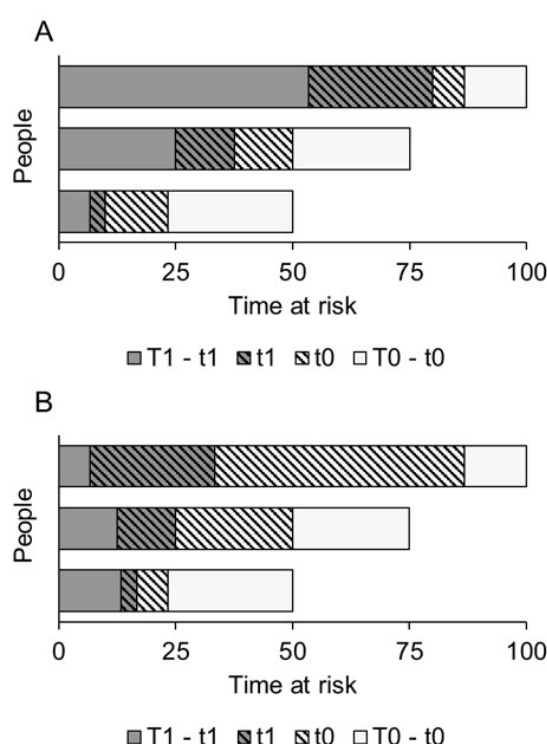
Optimizing misclassification errors in rare outcome studies Hayden Smith* Hayden Smith
Rossanna Rosa

Background: Imbalanced data can be defined as having an outcome prevalence less than or equal to
10%. The application of classification algorithms to imbalanced data can result in disproportionate
rates of false positives and false negatives. Objective: To present post hoc sampling and analytic
options for addressing misclassification errors in rare outcome studies.

Methods: An antimicrobial stewardship project was conducted to create preliminary classification
rules for identifying extended spectrum beta-lactamase (ESBL) bacteremia in an Emergency
Department (ED) in the United States. Retrospective data for a 44-month period were collected for
point of care information. Patient variables included: age; history of ESBL in prior 2-years; care
facility residence; central line; and documented antibiotic use in the prior 6-months. An initial
classification tree was fit to 80% of data. Next, comparator approaches were applied (e.g., cost
matrix, priors, adaptive synthetic sampling, etc.) to address the outcome imbalance. Trees were
trimmed via cross-validation. The initial and cost matrix-based trees were then applied to a 20%
holdout set.

Results: The study included 442 ED patients with a blood culture. Ten percent of patients had
confirmed ESBL; median age 68 (IQR: 57-81) years, 14% resided in a care facility, 44% had prior
antibiotics, and 4% had a history of ESBL. Clinical gestalt and initial tree had 48% and 66% accuracy
in the holdout set, respectively; with the tree including one split (i.e., history of ESBL). The cost
matrix-based tree had 80% accuracy with two splits (i.e., care facility residency and history of ESBL
in non-residents), see Figure. This tree had an 85% probability of classifying more cases than the
initial tree as revealed in a supplemental Bayesian model.

Conclusions: Rates of false positives and false negatives can be optimized in rare outcome studies. In
the presented study, directed methods were able to identify additional outcome cases in a holdout
set.
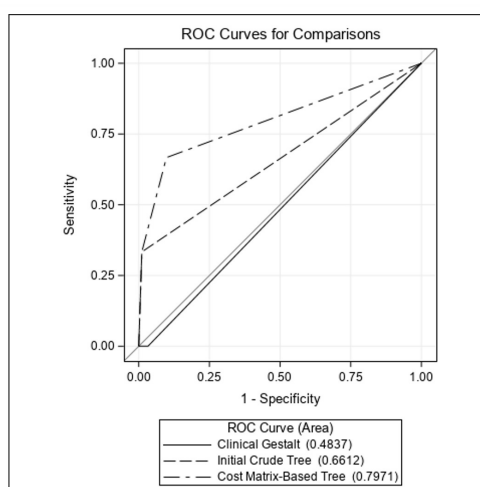
Figure. Emergency Department providers' "Clinical Gestalt", "Initial Crude Classification
Tree" and post hoc adjustment for imbalanced outcome tree (i.e., "Cost Matrix"
penalizing false negatives 10 times more than false positives) for preliminary
identification of extended spectrum beta-lactamase bacteremia status in holdout
patients with blood culture in a United States Emergency Department located in the
Midwest. Initial tree had a 14% (95%: 6%, 33%) and cost-matrix-based tree had a 31%
(95% CI: 10%, 53%) greater area under the curve compared to provider's Clinical Gestalt.

Methods/Statistics

Efficient and robust methods for causally interpretable meta-analysis: transporting inferences from multiple randomized trials to a target population Issa J Dahabreh* Sarah Robertson Issa J Dahabreh Jon A Steingrimsson Lucia C Petito Miguel A Hernán

For many causal questions, evidence is available from several randomized trials that recruit individuals from different underlying populations. Decision-makers need to synthesize the trial evidence and transport inferences to some target population that is chosen on substantive grounds. Meta-analysis is an umbrella term for methods that attempt to synthesize findings across multiple trials. A commonly overlooked problem, however, is that standard meta-analysis methods may produce results that do not have a clear causal interpretation when each trial includes individuals from a different population, and treatment effects vary across those populations. We present methods for causally interpretable meta-analyses that combine information from multiple randomized trials to estimate potential (counterfactual) outcome means and average treatment effects in a target population. We obtain identification results for transporting causal inferences from a collection of independent randomized trials to a new target population in which experimental data are not available. We propose augmented inverse probability weighting estimators for potential outcome means and average treatment effects in the target population that use covariate, treatment, and outcome data from the collection of trials, but only covariate data from the target population sample. We show that the estimators are doubly robust, in the sense that they remain consistent and asymptotically normal under misspecification of some of the models on which they rely. We report simulation studies to evaluate the finite sample performance of both augmented inverse probability weighting estimators (doubly robust) and non-augmented alternatives (outcome model-based or weighting). We demonstrate the methods using data from the HALT-C multi-center randomized trial that compared peginterferon alfa-2a vs. no treatment for patients with chronic hepatitis C.

Methods/Statistics

Visualizing study results with p-value functions versus Bayesian posteriors Hayden L. Smith*
Hayden Smith

Background: The reproducibility crisis involves many issues. Options for addressing null hypothesis significance testing (NHST), magnitude, and estimate directionality related to p-values include the use of p-value functions and Bayesian posteriors. Objective: to present study results using p-value functions and Bayesian posteriors to compare their respective definitions and graphical displays.

Methods: A hospital-based study was conducted at a Midwestern tertiary center to decrease the number of vancomycin days in the adult ICU. At the center, patients typically received a methicillin-resistant Staphylococcus aureus (MRSA) screening via culture, which takes 2-days until results are received. A project was conducted to switch clinician practices to polymerase chain reaction (PCR) testing, which takes 2-hours until results are received. This change in practice should decrease vancomycin days in patients with a negative screening due to earlier drug discontinuation. Changes in PCR versus culture screening rates were examined using a frequentist approach via plotted p-value functions and Bayesian posteriors with non-informative priors.

Results: Patients screened for MRSA using PCR in the pre-intervention period was 14% (49/356) compared to 98% (313/321) in the post-intervention period; this change represented an 84% improvement in practice. Alpha level selections for the estimate can be seen with in the p-value function and posterior plots (Figure). Both visualizations allow readers to visualize directionality, magnitude, and precision of result. Key distinctions between approaches is in their interpretations, which will be described at the conference along with additional study details.

Conclusions: Analytic recommendations regarding NHST and reproducibility are being presented in literature. P-value functions and posteriors provide a transparent option for visualizing information about results. However, intended audiences need to understand the unique interpretations of each method.
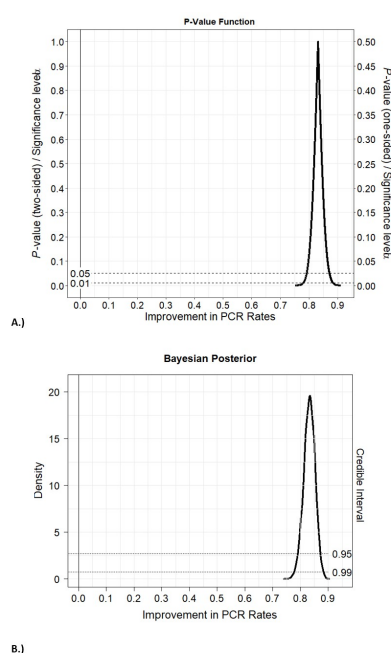
Figure. Rate difference for adult Intensive Care Unit patients screened for MRSA with PCR versus culture after implementing an antimicrobial stewardship project. A.) p-value function with alpha (i.e., 0.05, 0.01) applied as dashed lines. B.) Bayesian posteriors with flat prior and credible interval (i.e., 0.95%, 0.99) applied as dashed lines.

Molecular

Association of hygiene hypothesis indicators with prevalence of antinuclear antibodies in US adolescents Jesse Wilkerson* Jesse Wilkerson Helen Meier Dale Sandler Frederick Miller Gregg Dinse Christine Parks

Background: Recent evidence suggests increasing prevalence of autoimmunity as measured by antinuclear antibodies (ANA) in U.S. adolescents. According to the hygiene hypothesis, improved hygiene and cleaner environments in early childhood lead to declining exposure to infections and other immune challenges, resulting in improper immune responses to later-life exposures. We examined associations of common hygiene hypothesis indicators with ANA prevalence in adolescents in the National Health and Nutrition Examination Survey (NHANES) over a 25-year timespan.
Methods: The study sample included 2,709 NHANES participants aged 12-19 years across several survey cycles from 1988-2012, for whom ANA levels (measured by Hep-2 immunofluorescence assay) were available. We used logistic regression to estimate associations of asthma, allergies, and infection antibodies with ANA positivity, adjusting for age, sex, race/ethnicity, body mass index, education, smoking status, and time period (NHANES survey cycle). Associations were also examined within individual time periods.
Results: The prevalence of ANA positivity in adolescents increased from 5.0% in 1988-1991 to 12.8% in 2011-2012. ANA prevalence was associated with diagnosis of asthma before the age of 6 (OR: 2.05, CI: 1.07–3.95) and with current hay fever (OR: 1.63, CI: 0.88–3.00). Fewer than 2% of those with ANA positivity in 1988-1991 had been diagnosed with asthma, compared with 18% in 1999-2000, and 27% in 2003-2004 and 2011-2012. ANA prevalence trended negatively with antibodies to Helicobacter pylori (OR: 0.50, CI: 0.24–1.02), Hepatitis A (OR: 0.80, CI: 0.47–1.36), and Herpes Simplex Virus-1 (OR: 0.76, CI: 0.49–1.18).
Conclusions: Results suggest the observed increase in ANA prevalence among U.S. adolescents is associated with an increase in asthma prevalence and a lower prevalence of common infections seen over 25 years, consistent with the hygiene hypothesis.

Molecular

The relationship between bulky DNA adducts and long interspersed nuclear element-1 DNA methylation in healthy colon tissue Priyanka Gogna* Priyanka Gogna Kaitlin Boyd Vikki Ho Thomas E. Massey Roger Godschalk Frederik-Jan van Schooten Will D. King

Background
Evidence suggests that environmental chemicals may increase cancer risk through genotoxic and epigenetic pathways. Bulky DNA adducts are a non-specific measure of structurally-related DNA adducts that may reflect exposures to chemicals like heterocyclic aromatic amines (HAAs) and polycyclic aromatic hydrocarbons (PAHs), common carcinogens found in meats cooked at high temperatures and combustion-related processes. A decrease in DNA methylation of long interspersed nuclear element-1 (LINE-1) has been linked to an increase in colorectal cancer risk. This study examined the relationship between bulky DNA adducts and LINE-1 DNA methylation levels measured in healthy colon tissue.

Methods
The present study was conducted within a cross-sectional investigation of first-time colonoscopy patients (N=198). Pinch-biopsies were taken from normal appearing mucosa. Bulky DNA adduct levels were measured using a 32P-postlabelling assay; LINE-1 DNA methylation was measured using high resolution melt curves. The relationship was quantified via multivariable linear regression. Age and sex were considered a priori confounders, while other lifestyle variables were assessed using backwards elimination.

Results
A one standard deviation increase in bulky DNA adducts was associated with a 0.16 standard deviation decrease in LINE-1 DNA methylation (p=0.02), after adjustment for age, sex, and BMI. This suggests a negative linear relationship between DNA adduct formation and LINE-1 DNA methylation.

Conclusions
Increasingly, epigenetic mechanisms have been identified as important in colon carcinogenesis. Our results suggest that chemical exposures leading to adduct formation may impact cancer risk partially through an influence on epigenetic mechanisms occurring in healthy tissue. Further understanding how different biomarker measures may relate informs on their use as established biomarkers of exposure and early disease for patients in the future.

Molecular

Relationships between air pollution indicators and markers of inflammation during pregnancy Priyanka Gogna* Priyanka Gogna Will D. King Markey Johnson Premkumari Kumarathasan Paul J Villeneuve Bruce Lanphear Tye E Arbuckle Michael M Borghese

Background
Outdoor air pollution, which can lead to changes in important biological processes, including inflammation, is associated with adverse pregnancy and birth outcomes including hypertension, preeclampsia, diabetes, preterm birth, and low birth weight. Pregnancy-specific biological processes, such as increased estrogen production and altered metabolism, can impair the body's ability to detoxify air pollution exposures, highlighting the need to study exposures during pregnancy. Relatively few studies have directly evaluated associations between outdoor air pollution and markers of inflammation, especially during pregnancy. We are currently examining the relationship between PM2.5 and NO2 as indicators of air pollution, with markers of inflammation during pregnancy in a cohort of Canadian women. Results from this analysis are forthcoming and will be presented in June.

Methods
This study is nested within the Maternal-Infant Research on Environmental Chemicals (MIREC) study, a Canadian pregnancy cohort. Residential PM2.5 and NO2 exposures were estimated using a combination of satellite-based and land-use regression models to generate overall pregnancy and trimester specific averages. We measured C-reactive protein, Interleukin-6, and Interleukin-8 in a sub-cohort of women within MIREC who had a singleton live birth and provided a plasma sample during the third trimester (n=1,588). Regression analyses will be used to quantify the relationships of interest, controlling for a comprehensive set of confounders, and assessing both pregnancy average and trimester specific exposure windows. Non-linearity of the dose-response curve will be assessed using splines.

Relevance
Current evidence suggests that the effects of air pollution on human health outcomes can occur at low doses. The proposed study of low-dose air pollution exposures in relation to markers of inflammation will help identify underlying mechanisms of the relationship between air pollution and pregnancy and birth outcomes.

Characteristics of Human Oral Microbial Community: Findings from Three Large US Cohorts

Dantong Shao* 3647] Shao Emily Vogtmann Rashmi Sinha Jianxin Shi Anil Chaturvedi Xing Hua Yunhu Wan Mitchell Gail J. Gregory Caporaso Linda Liao Laura Beane Freeman Neal Freedman Christian Abnet

Background The human oral microbiome plays important roles in human health and disease. Oral microbial communities may be related to a variety of demographic and lifestyle factors, which must be understood to allow modelling this exposure with health outcomes.

Methods The participants were from National Institutes of Health-AARP Diet and Health Study (NIH-AARP), Agricultural Health Study (AHS) and Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial (PLCO). A case-cohort sampling design was used and a sampling weight for each participant was calculated according to cancer status, age, sex, and tobacco use. DNA was extracted from oral wash specimens which were collected before cancer diagnosis and the 16S rRNA V4 gene region was sequenced using Illumina MiSeq and processed using QIIME2. Weighted linear regression was used to evaluate the associations of demographics with microbiome richness (alpha diversity measured as observed species) within each cohort then meta-analyzed in R.

Results 2407, 2180, and 2611 healthy participants and patients with cancer were selected from NIH-AARP, AHS and PLCO cohorts, representing populations of 22197, 33061, and 38793 people with oral wash specimens. Microbiome richness was inversely associated with age (P<0.001), while men and more educated individuals had higher richness than women (P<0.001) and the less educated (P=0.03), respectively. Tobacco smokers had lower richness than non-smokers and the richness decreased as the smoking intensity increased. In contrast, alcohol drinking was associated with higher richness. However, we had limited power to detect an association with race/ethnic group. In a full multivariable model, age, sex, tobacco, and alcohol explained 7% of the overall variance in oral microbial richness.

Conclusion Our work provides a comprehensive description of oral microbial richness in three large-scale US epidemiologic studies and suggests a modest but discernable contribution of lifestyle factors.
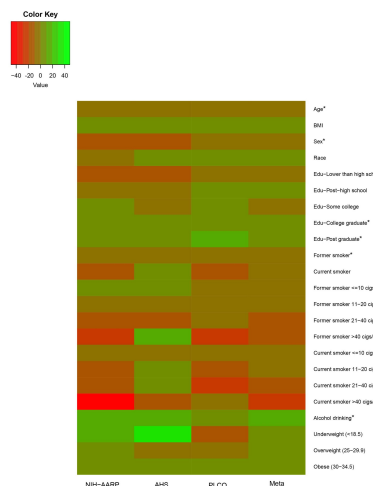
Figure 1. The heatmap of weighted standardized coefficients (Beta) for the correlation between demographics and oral microbial alpha diversity for each cohort and the meta-estimates.
*p<0.05

Joinpoint regression analysis of trends in incidence rates of multiple sclerosis in Kuwait: 1980-2019

Saeed Akhtar* Saeed Akhtar Raed Alroughani Jarrah Al-Abkal

Background: Multiple sclerosis (MS) is an inflammatory disorder of central nervous system causing demyelination and axonal injury. Temporally, a tendency for increasing MS incidence has been recorded worldwide. This retrospective cohort study sought to quantify trends in the age-standardized incidence rates (ASIRs) (per million person-years) of MS in Kuwait from 1980 through 2019, overall and by subcohorts defined by age at MS onset, sex and nationality.

Methods: MS incidence data from 1980 through 2018 were obtained from the Kuwait National MS Registry. For 2019, MS incident cases' data were estimated using multiple imputation. Using mid-year relevant Kuwait population as denominator and the World Standard Population as a reference, MS ASIRs overall and by subcohorts defined by age at onset (0-19, 20-39, 40+ years), sex (male, female) and nationality (Kuwaiti, non-Kuwaiti) were computed. Joinpoint regression analysis was conducted to estimate annual percent change (APC) and its 95% CI overall and by subcohorts.

Results: During 1980-2019, an overall, MS ASIR was 32.3 (95% CI: 19.8, 44.8) with a significant (p < 0.001) joinpoint (1980-2013, APC = 11.2; 95% CI: 9.5, 12.9; 2013-2019, APC = -23.4; 95% CI: - 37.1, - 6.6) (Fig 1). Eight of twelve subcohorts had significantly (p < 0.05) increasing trends in MS ASIRs. In four of these eight subcohorts, one significant (p < 0.05) joinpoint was observed including Kuwaiti females aged 0-19 years (1980-2009, APC = 81.6; 95% CI: 58.7, 107.7), Kuwaiti females, aged 20-39 years (1980-2004, APC = 104.9; 95% CI: 34.7, 211.9), non-Kuwaiti females aged 0-19 years (1990-2019, APC = 78.0; 95% CI: 25.1,153.3) and Kuwaiti males, aged 0-19 years (1980-2009, APC = 34.9; 95% CI: 4.3, 74.4).

Conclusions: From 1980 through 2013, Kuwait had an overall significantly increasing trend in MS ASIRs followed by a significant declining drift during the subsequent period from 2013 through 2019. The underlying factors modulating MS risk in Kuwait need further studies.
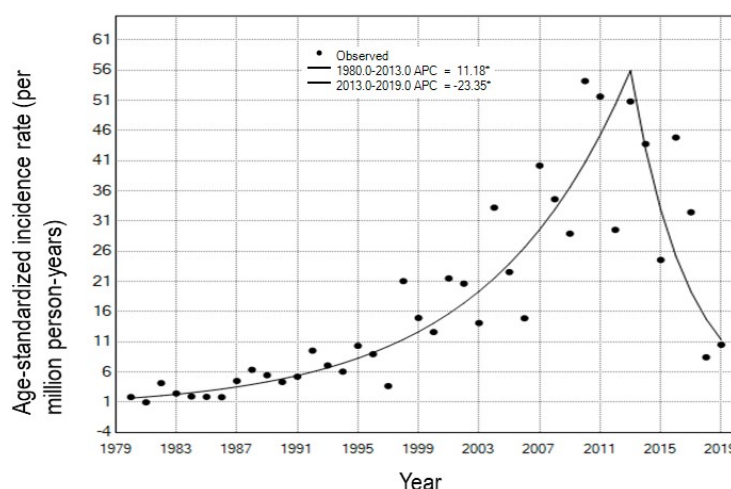
Fig 1. Trend in multiple sclerosis age-standardized incidence rates (per million of person-years) in Kuwait: 1980-2019 (* indicates the APC (annual percent change) is significantly different from zero at alpha = 0.05)

Nationwide study of therapeutic plasma exchange versus intravenous immunoglobulins in Guillain-Barré Syndrome Hind Beydoun* Hind Beydoun May A. Beydoun Sharmin Hossain Alan B. Zonderman Shaker M. Eid

Background: Guillain-Barré Syndrome (GBS) is an autoimmune disease with worldwide incidence of 0.4 to 4 per 100,000. We compared outcomes of therapeutic plasma exchange (TPE) versus intravenous immunoglobulin (IVIG) among hospitalized patients diagnosed with GBS, using the 2002-2014 Nationwide Inpatient Sample.

Methods: In a retrospective cohort study involving 6,642 records (2,637 TPE and 4,005 IVIG), treatment type was examined as predictor of length of stay, total charges and in-hospital death with regression modeling using risk adjustment and propensity scoring to control for confounders.

Results: Compared to those receiving IVIG, patients who underwent TPE experienced prolonged hospitalization by ≈7.5 days, greater hospitalization costs by ≈$46,000, and worse outcome in terms of in-hospital death with an odds ratio of 2.78 and a 95% confidence interval of (1.99, 3.88). Results did not change after controlling for confounders through risk adjustment, propensity score adjustment or matching. For hospitalization charges and in-hospital death, but not for length of hospital stay, propensity-score adjusted models yielded more conservative estimates as compared to risk-adjusted models. There were no statistically significant interaction effects between treatment and sex or between treatment and time period (2002-2007, 2008-2014) in relation to the three outcomes of interest.

Conclusions: TPE may be associated with poorer healthcare utilization outcomes compared to IVIG, regardless of the method applied to control for confounders, although confounding by indication could not be ascertained.

Neurology

Association of antecedent cardiovascular disease and medication use with the risk of developing ALS: a population-based nested case-control study
Hoda S. Abdel Magid* Hoda Abdel Magid Barbara B. Topol Valerie McGuire Jessica Hinman Edward Karasakis Lorene M. Nelson

Background: Antecedent cardiovascular diseases (CVD) and medication use, may play a role in the risk of developing amyotrophic lateral sclerosis (ALS). We investigated the association between hypertension, ischemic heart disease, heart failure, acute myocardial infarction, and atrial fibrillation with the risk of developing ALS. We also examined associations with use of angiotensin-converting enzyme inhibitors (ACEIs), angiotensin II receptors blockers (ARBs), calcium channel blockers, beta blockers, and antiarrhythmics. Methods: We conducted a population-based nested case-control study in the national Medicare fee for service population, which included 3,714 enrollees ages 65 and above with newly diagnosed ALS between 2006-2014. Cases were compared with 18,750 sex-, age, county, and enrollment-matched controls. Odds ratios (OR) and 95% Confidence Intervals (CIs) for the association between antecedent CVD or medication use and ALS were estimated using conditional logistic regression models adjusting for diabetes, obesity, tobacco use, socioeconomic status, and controlling for confounding by indication. Medication use was identified through claims pharmacy data, similarly analyzed, and further analyzed using a dose response approach.

Results: The fully adjusted OR for any CVD diagnosis was 0.93 (95% CI 0.86–1.02) when using an a priori-defined clean period of 24-months prior to ALS diagnosis. Our results varied across cause-specific CVD diagnoses. We observed inverse associations for heart failure (OR 0.79; 95% CI 0.70–0.89) and atrial fibrillation (OR 0.81; 95% CI 0.76–0.92), and no associations with hypertension, IHD, or acute MI. ALS risk was reduced with use of ACEIs (OR 0.84; 95% CI 0.77–0.91), calcium channel blockers (OR 0.64; 95% CI 0.59–0.70), and beta blockers (OR 0.76; 95% CI 0.71–0.83). ALS risk decreased with increased duration of calcium channel blocker and beta blocker use. Conclusion: Our findings suggest CVD conditions and medication use may be protective for ALS.

Figure 1: Association of Antecedent Cardiovascular Disease and Medication Use with the Risk of developing ALS among Medicare Enrollees 2006-2014* (Cases N: 3,714; Controls N: 18,750)

CVD Condition
HTN: Hypertension
AMI: Acute Myocardial Infarction
IHD: Ischemic Heart Disease
HFA: Heart Failure
AFI: Atrial Fibrillation
ANY: Any Cardiovascular Disease

CVD Medication
ARB: Angiotensin II Receptor Blocker
ACE: Angiotensin-Converting-Enzyme Inhibitors
BBL: Beta Blocker
CAC: Calcium Channel Blocker
AAR: Antiarrhythmic

Odds ratios adjust for sex, birthyear, county, race/ethnicity, tobacco, obesity, SES

Nutrition/Obesity

Intake of antioxidant supplements and risk of keratinocytes cancers in women: A prospective cohort study Yahya Mahamat-saleh* Yahya Mahamat-Saleh Isabelle Savoye Iris Cervenka Marie Al Rahmoun Francesca Romana Mancini Marie-Christine Boutron-Ruault Marina Kvaskoff

Background: Experimental studies suggested that antioxidants could protect against skin carcinomas. However, epidemiological studies on antioxidant supplement use in relation to basal-cell carcinoma (BCC) and squamous-cell carcinoma (SCC) risks yielded inconsistent findings, and few prospective studies have been conducted to date. We aimed to investigate intake of antioxidants supplements and risk of keratinocytes cancers (KCs).
Methods: E3N (Etude Epidémiologique auprès de femmes de l'Education Nationale) is a prospective cohort of 98,995 French women aged 40–65 years in 1990. Intakes of antioxidants from diet were estimated via a validated food questionnaire in 1993, and antioxidant supplements use through questionnaires in 1995. We used Cox proportional hazards regression models to compute hazard ratios (HRs) and 95% confidence intervals (CIs) adjusted for age and main known skin cancer risk factors.
Results: Over 1995-2014, 2425 BCC and 451 SCC cases were diagnosed among 63,063 women. We found positive relationships between vitamin A supplement use and KCs risk (HR=1.37, 95% CI= 1.15-1.62), particularly with BCC (HR=1.40, 95% CI=1.17–1.69); and between vitamin E supplement use and risk of both BCC (HR=1.21, 95% CI=1.03–1.52) and SCC (HR=1.43, 95% CI=1.03–1.99). However, while intake of beta-carotene supplement was associated with increased SCC risk (HR=1.59, 95% CI=1.00–2.54), there was not associated with BCC risk, although with no heterogeneity across KC types (Pheterogeneity=0.21). Vitamin C supplement was also not associated with KCs.
Conclusion: These findings suggest that intake of vitamin A or E supplement was associated with an increased KCs risk in women. Further studies with information on doses and duration of supplements and the ability to examine their underlying mechanisms are needed.

Nutrition/Obesity

Association between Child's Obesity and of Maternal Perception of Child's Overall Health: A Multi-Racial Cohort of Children JacKetta R Cobbs* JacKetta Cobbs Pamela Ferguson John Vena Kelly Hunt

Objective: Over the years, several studies have reported maternal misperceptions of child's obesity status, but few studies have examined the relationship between child's measured obesity status and maternal perception of child's health, life satisfaction, and stress; therefore, our objective was to examine this association.

Methods: A cross-sectional study of the Environmental Influences on Child Health Outcomes NICHD Fetal Growth Studies cohort of 4-8 year old children was conducted. Linear regression models were used to examine the association between child overweight (85th to 95th BMI percentile) and obesity (≥ 95th BMI percentile) and the NIH 7-item PROMIS General Health v1.0, 4-item Life Satisfaction, and 4-item Psychological Stress surveys. These surveys assessed mother's perception of child's overall health.

Results: Of the 805 children, 48.2% were female, 27.3% were non-Hispanic white, 31.2% were non-Hispanic black, 28.8% were Hispanic and 12.7% were Asian. Obesity, but was not associated with being overweight, was associated with lower positive health scores [-0.96 (95%CI: -1.50, -0.43)]. Nor being overweight was associated with life satisfaction, or psychological stress scores. Interestingly, the association between child obesity and mother perception of child general health was modified by child race-ethnic group. Obesity was associated with lower general health scores among non-Hispanic white [-1.52 (95%CI: -2.97, -0.06)], non-Hispanic black [-1.30 (95%CI: -2.17, -0.44)], and Hispanic [-0.90 (95%CI: -1.70, -0.11)] children. However, obesity was associated with higher maternal perceived general health among Asian children [4.09 (95%CI: 1.34, 6.85)].

Conclusion: Maternal perception of child's overall health varied depending on adiposity status as well as racial-ethnic group. Future studies should identify cultural differences that may influence mother's perception of child's overall health as well as the relationship between obesity and overall health.

Nutrition/Obesity

Group-based trajectory modelling of body mass index and body size over the life course: a scoping review Vanessa De Rubeis* Vanessa De Rubeis Alessandra Andreacchi Isobel Sharpe Charles D.G. Keown-Stoneman Laura N. Anderson

Group-based trajectory modelling has been applied to identify distinct trajectories of growth across the life course; however, the methodology and outcomes of these studies during the adult life period have not been reviewed. Objectives of this study were to describe the methodological approaches for group-based modelling of growth across the life course and to summarize outcomes across studies. A scoping review with a systematic search was conducted in four databases (Medline, EMBASE, CINAL, and Web of Science) in January 2019. All studies were screened by two independent abstractors at title and abstract-level, and at full-text. Studies that used a group-based procedure to identify trajectories on any statistical software were included. There were no restrictions on year of publication, language, or study design. Studies were excluded if they only evaluated growth ≤18 years. Data were extracted on study characteristics (journal, country, year, study design), trajectory methodology (model fit, shape, software and approach, number and name of trajectories), and measures of growth. A total of 52 studies were included and most were published from 2013-2019. PROC TRAJ in SAS was used by 29 studies, other procedures used include TRAJ in STATA, FIML in Mplus, and lcmm in R. The Bayesian Information Criterion was used by almost all studies (n=48) to determine the number of trajectories that optimally fit the data. Body mass index was the most common measure of growth reported (n=37). The mean number of identified trajectories was 4 (range 3 to 16) and the mean number of growth measures was 6.5. Group-based trajectory modelling is emerging as an increasingly used method in epidemiologic research. A range of statistical methods have been used, and all studies have identified at least 3 discrete trajectories. Understanding the unique life course growth trajectories in populations is important and may provide further insight for population health interventions.

Nutrition/Obesity

Body Mass Index, Waist Circumference, Waist-to-Hip Ratio, and Percent Body Fat in Relation to Health Care Use in the Canadian Longitudinal Study on Aging Alessandra Andreacchi* Alessandra Andreacchi Laura Andeson Lauren Griffith Emmanuel Guindon

Obesity has been associated with increased health care use, but it is unclear whether this is consistent across all measures of obesity. The objectives of this study were to compare obesity defined by four anthropometric measures, including body mass index (BMI), waist circumference (WC), waist-to-hip ratio (WHR), and percent body fat (%BF), and to estimate the associations with health care use among Canadian adults.

A prospective cohort study was conducted with individuals aged 45-85 years from the Canadian Longitudinal Study on Aging (n=30,097). All anthropometric measures were collected by trained research assistants and body fat was measured using dual-energy x-ray absorptiometry. Obesity was defined as BMI ≥30.0 kg/m2, WC ≥88cm for females and ≥102cm for males, WHR ≥0.85 for females and ≥0.90 for males, and %BF >35% for females and >25% for males. Approximately 18 months later, self-reported health care use, including contact with a general practitioner, medical specialist, emergency department, and being a patient in a hospital overnight, in the past 12 months was collected. Logistic regressions adjusted for age, education, income, urban/rural, marital status, smoking status, and alcohol use, and stratified by sex were used.

Among females, the prevalence of obesity defined by BMI was 28%, by WC was 45%, by WHR was 37%, and by %BF was 75%. Among males, the prevalence of obesity defined by BMI was 30%, by WC was 40%, by WHR was 88%, and by %BF was 71%. All measures of obesity were associated with increased odds of all health care use. For example, among women, BMI-defined obesity was associated with having reported seeing a general practitioner (OR=1.19, 95% CI: 1.01, 1.40) and being a patient in a hospital overnight (OR=1.65, 95% CI: 1.41, 1.93) in the past 12 months.

The prevalence of obesity varied substantially depending on the anthropometric measure used to define obesity, however all measures were strongly associated with increased health care use.

Nutrition/Obesity

Effect of Citrus and Green Vegetable Intake on Lung Diseases among Adults in the United States: An Application of Propensity Score Using 2007-2016 NHANES Data Tianjiao Shen*

Tianjiao Shen Mohammed S. Orloff Mohammed Elfaramawi

Background: Epidemiological evidence supports that citrus and green vegetable intake improves lung function. The risks of common chronic lung diseases, including chronic obstructive pulmonary disease (COPD) and asthma, are associated with less consumption of fruits or vegetables. However, the effects of dietary intake on COPD/asthma are commonly biased by insufficient adjustment of other food components.

Methods: 17818 adults in the United States from the 2007-2016 National Health and Nutrition Examination Survey were used to assess the association between citrus fruits/dark-green vegetables intake and COPD/asthma. Dietary intake was assessed by 24-hour dietary recall; fruits/dark-green vegetables consumption was binarized into no intake (reference) versus any intake. Selected covariates for the propensity score (PS) model included gender, age, race, education, marital status, Body Mass Index, binge drinking, blood cadmium, physical activity, smoking status, energy intake, and the 9 types of other foods. The effect of fruits/dark-green vegetables intake on COPD/asthma was estimated by inverse probability of treatment weighting using the PS.

Results: Compared to no intake, any intake of citrus were associated with a protective effect on asthma [OR(95% CI) = 0.84 (0.71, 0.98)], but not associated with chronic bronchitis that is a subtype of COPD [OR(95% CI) = 1.00 (0.78, 1.27)]. Compared to no intake, any intake of dark-green vegetables were associated with a protective effect on chronic bronchitis [OR(95% CI) = 0.71 (0.55, 0.91)], but not associated with asthma [OR(95% CI) = 1.07 (0.88, 1.30)]. Emphysema, another subtype of COPD, was not associated with the intake of citrus [OR(95% CI) = 0.86(0.59, 1.26)] or dark-green vegetables [OR(95% CI) = 0.64 (0.36, 1.12)].

Conclusion: In this representative sample of US adults, citrus consumption is associated with lower asthma risk; dark-green vegetables intake is associated with lower chronic bronchitis risk.

Markers of Vitamin D Metabolism and Reproductive Outcomes Among Women with Proven Fecundity Sunni Mumford* Sunni Mumford Alexandra Purdue-Smithe Keewan Kim Elizabeth DeVilbiss Samrawit Yisahak Josh Freeman Jessica Zolton Lindsey Sjaarda Neil Perkins Robert Silver Enrique Schisterman

Background: Sufficient levels of total 25-hydroxyvitamin D (25(OH)D), the primary circulating form of vitamin D, have been linked with lower risk of pregnancy loss and higher risk of live birth, though it is unknown whether modifiers of vitamin D metabolism and bioavailability may underlie the associations. Thus, our purpose was to assess the relationship between markers of vitamin D metabolism and live birth and pregnancy loss.

Methods: Women aged 18-40 years and trying to conceive were followed for ≤6 cycles while attempting pregnancy and throughout gestation if they conceived. We assessed total 25(OH)D, vitamin D binding protein (VDBP), calcium, parathyroid hormone (PTH), and fibroblast growth factor (FGF23) in serum at baseline (n=1185), from which free and bioavailable (sum of free and albumin-bound) 25(OH)D were calculated. We estimated RRs using log-binomial models adjusted for confounders.

Results: 47% had sufficient total 25(OH)D, ≥30 ng/mL. Total, free, and bioavailable 25(OH)D concentrations were associated with increased risk of live birth (total RR per 10 ng/mL 1.05, 95% CI: 1.00, 1.10; free RR per pg/mL 1.01, 95% CI 1.00, 1.03; bioavailable RR per ng/mL 1.03, 95% CI: 0.99, 1.07), and reduced risk of pregnancy loss (total RR per 10 ng/mL 0.88, 95% CI: 0.78, 1.00; free RR per pg/mL 0.96, 95% CI 0.92, 1.00; bioavailable RR per ng/mL 0.90, 95% CI: 0.81, 1.00). PTH was associated with decreased risk of live birth (RR per pg/mL 0.97, 95% CI: 0.93, 1.02) and increased risk of pregnancy loss (RR 1.09, 95% CI: 0.98, 1.21). No associations were observed with VDBP, calcium, and FGF23.

Conclusions: Higher preconception total, free, and bioavailable 25(OH)D, and lower PTH concentrations, were associated with higher live birth and lower pregnancy loss risk. Associations between total 25(OH)D and pregnancy outcomes appear to be driven by free and bioavailable 25(OH)D, suggesting that these may be relevant markers of vitamin D metabolism for reproductive outcomes.

Nutrition/Obesity

Association of Circulating Bile Acids with Abdominal Obesity and Non-Alcoholic Fatty Liver Disease in Guatemala Jessica L. Petrick* Jessica Petrick Andrea A. Florio Christian S. Alvarez Alvaro Rivera-Andrade Maria F. Kroker-Lobos Neal D. Freedman Mariana Lazo Eliseo Guallar John D. Groopman Katherine A. McGlynn

Non-alcoholic fatty liver disease (NAFLD) is characterized by fat deposition in the liver which is not attributable to excessive alcohol consumption and is closely associated with abdominal obesity. NAFLD affects 10-30% of the world population, with an especially high prevalence in Latin America (>30%). Persons with NAFLD are at an increased risk of death due to type 2 diabetes, cardiovascular disease, and liver cancer. Bile acids have roles in numerous metabolic processes, and disruption of bile acid homeostasis can lead to dysregulated energy balance, inflammation, and ultimately, liver disease. Secondary bile acid dysregulation has also been shown to promote hepatocarcinogenesis in animal models. While bile acids are potentially involved in NAFLD, studies to-date are small, and no studies have investigated this in a Hispanic population. Thus, we investigated whether circulating bile acids were associated with abdominal obesity and NAFLD in a cross-sectional study of adults aged 40 or older from 5 departments in Guatemala. Using liquid chromatography, we quantitated 15 primary and secondary bile acids in serum from 444 study participants. Prevalence odds ratios (PORs) and 95% confidence intervals (CIs) were calculated for associations between bile acid levels and abdominal obesity (waist circumference: ≥90 cm for men and ≥80 cm for women, prevalence=73%) and a non-invasive estimate of NAFLD (approximated by fatty liver index [FLI] >60, prevalence=59%) using log-binomial regression. Higher levels of glycine- and taurine-conjugated primary bile acids were associated with a 21-42% higher prevalence of both central obesity (e.g., POR per unit increase in log2 glycocholic acid=1.30, 95% CI: 1.06–1.59) and NAFLD (POR=1.42, 95% CI: 1.14–1.78). This study provides evidence from a population with a high prevalence of NAFLD that higher conjugated primary bile acid levels, but not secondary, are associated with increased prevalence of abdominal obesity and NAFLD.

Nutrition/Obesity

Are infant birth weight and gestational age related to parent feeding practices when children are toddlers?

KATHRYN KRUPSKY* KATHRYN KRUPSKY Sarah A. Keim Rebecca Andridge Bharathi Zvara Sarah E. Anderson

Parent feeding practices are strategies parents use to shape child eating. These practices may influence children's diet and risk for obesity. The reciprocal nature of parent-child interactions makes it challenging to discern temporality in associations between feeding practices and child weight status. Feeding practices like restrictive feeding may elevate a child's risk for obesity, but children's weight might shape parents' feeding practices. Few studies assessed the influence of child weight status on later parent feeding practices. We examined associations between children's birth weight (BW), gestational age (GA) and parent feeding practices when children were 2-years. Data are from an on-going prospective cohort study of 299 parent-child dyads from central Ohio. BW and GA were extracted from children's medical records. BW-for-GA z-scores were calculated using 2017 US natality data. We surveyed parents when children were 24-months on 6 feeding strategies: mealtime structure, consistency of mealtimes, child control of intake, parent control of intake, between mealtime grazing and encouraging clean plate. We accounted for potentially non-linear relationships between BW-for-GA and feeding strategies using restricted cubic splines, adjusted for child sex, parent race/ethnicity, marital status, education, and income. We found a marginally significant non-linear relationship between BW-for-GA and child control of intake (partial $F = 2.60$; $p = 0.05$), where child control of intake was greatest among the smallest children, and a marginally significant linear relationship between BW-for-GA and between mealtime grazing ($F = 3.89$; $p = 0.05$), where predicted between mealtime grazing scores decreased as BW-for-GA increased. Both effects did not persist after adjusting for covariates. Children's BW may not impact feeding practices in toddlerhood, but continued exploration of parent-child interactions may contribute to more effective recommendations for child feeding.

Citrus intake and risk of skin cancer in the European prospective investigation into cancer and nutrition cohort (EPIC) Yahya Mahamat-Saleh* Yahya Mahamat-Saleh Iris Cervenka Marie Al-Rahmoun Francesca Mancini Gianluca Severi Reza Ghiasvand Marit Veierod Saverio Caini Domenico Palli Edoardo Botteri Marie-Christine Boutron-Ruault Marina Kvaskoff

Recently, two large prospective cohort studies in the US reported positive and linear associations between citrus intake and the risks of melanoma and keratinocyte cancers. These associations are highly plausible biologically, since citrus products are rich in furocoumarins, which exhibit carcinogenic and phototoxic effects. However, as pointed out by several authors, epidemiologic studies are lacking. We aimed to examine the potential association between citrus intake and skin cancer risk.

EPIC is an ongoing multi-center prospective cohort initiated in 1992 and involving ~520,000 participants who have been followed-up in 23 centers from 10 European countries. Dietary data were collected at baseline using validated country-specific dietary questionnaires. We used Cox proportional hazards regression models to compute hazard ratios (HR) and 95% confidence intervals (CI).

During a mean follow-up of 13.7 years, 8,448 skin cancer cases were identified among 270,112 participants. We observed a positive linear dose-response relationship between total citrus intake and skin cancer risk (HR=1.10, 95%CI=1.03–1.18 in the highest vs. lowest quartile; Ptrend=0.001), particularly with basal cell carcinoma (BCC) (HR=1.11, 95%CI=1.02–1.20, Ptrend=0.007) and squamous cell carcinoma (SCC) (HR=1.23, 95%CI=1.04–1.47, Ptrend=0.01). Citrus fruit intake was positively associated with skin cancer risk (HR=1.08, 95%CI=1.01–1.16, Ptrend=0.01), particularly with melanoma (HR=1.23, 95% CI=1.02–1.48; Ptrend=0.01), although with no heterogeneity across skin cancer types (Phomogeneity=0.21). Citrus juice was positively associated with skin cancer risk (Ptrend=0.004), particularly with BCC (Ptrend=0.008) and SCC (Ptrend=0.01), but not with melanoma (Phomogeneity=0.02).

Our study suggests moderate positive linear dose-response relationships between citrus intake and skin cancer risk. However, studies with available biomarker data and the ability to examine sun exposure behaviors are warranted to clarify these associations.

Nutrition/Obesity

Circulating 25-hydroxyvitamin D level, vitamin D intake, and risk of skin cancers: A systematic review and dose-response meta-analysis of prospective studies Yahya Mahamat-Saleh* Yahya Mahamat-Saleh Dagfinn Aune Sabrina Schlesinger

Background: Sun exposure is a major environmental risk factor for skin cancers and is also an important source of vitamin D. However, while experimental evidence suggests that vitamin D may have a protective effect on skin cancer risk, epidemiologic studies investigating the influence of 25-hydroxyvitamin D (25(OH)D) level and/or vitamin D intake on skin cancer risk are conflicting. A systematic review and dose-response meta-analyses of prospective studies was conducted to clarify these associations.

Methods: Relevant studies were identified by searching in the PubMed database up to 30th August 2019. Random effects dose-response meta-analyses were used to estimate summary relative risks (SRRs) and 95% confidence intervals (CIs).

Results: Overall, thirteen prospective studies were included. Circulating 25(OH)D level was associated with higher risks of melanoma (SRR (95% CI) per 30 nmol=1.42; (1.17; 1.72) , n=6 studies) and keratinocyte cancer (KC) (SRR (95% CI) per 30 nmol/L = 1.30; (1.13; 1.49), n=8 studies). The SRR (95% CI) per 30 nmol/L increase in 25(OH)D level was 1.41 (1.19; 1.67), n=4 and 1.57 (0.64; 3.86), n=3 for basal cell carcinomas (BCCs) and squamous cell carcinomas (SCCs), respectively; and no difference for type of skin cancer was observed. However, while we found that vitamin D intake (from diet, supplemental and total) was not associated with risks of melanoma and SCC, vitamin D intake was associated with slightly increased BCC risk, albeit with no heterogeneity across skin cancer type.

Conclusion: This meta-analysis suggests positive associations between circulating 25(OH)D level and risk of melanoma and KC; however, this finding is most likely confounded by sun exposure. However, we found no associations between vitamin D intake skin cancers, except positive associations with BCC risk.

Nutrition/Obesity

Effect of sugar-sweetened beverage intake on adolescent breast density Lara Yoon* Lara Yoon Camila Corvalán Ana Pereiras John Shepherd Karin B. Michels

Background: Frequent sugar-sweetened beverage (SSB) intake has been associated with weight gain and early menarche in adolescents. How SSB intake relates to breast development in young girls remains unclear.

Methods: We evaluated the association between intake of SSB (beverages with added sugar including soda, flavored milk, milk-substitutes, fruit juice, coffee, tea, sport drinks, and powdered drinks) and breast composition in 374 adolescent girls enrolled in the Growth and Obesity Cohort Study in Santiago, Chile from April 2013 to February 2016. Dietary SSB intake was assessed bi-annually using the multiple-pass 24-hour recall method. Cumulative updating was used to obtain mean SSB intake (mL/day). SSB intake categories were created based on the distribution of intake in our cohort with consideration of Reference Amounts Customarily Consumed for beverages (0-30 mL, 30-360 mL, >360 mL). Breast composition (fibroglandular volume [FGV], percent fibroglandular volume [%FGV], total breast volume) was measured at Tanner stage 4 (B4) using dual-energy X-ray absorptiometry. Linear regression models were used to analyze the association between SSB intake and breast outcomes.

Results: A total of 881 dietary recalls were available for 374 girls prior to the breast density assessment. The mean ± SD breast FGV, %FGV, and total breast volume at B4 were 86.5 ± 35.2 cm3, 41.7% ± 16.5%, and 232.2 ± 114.4 cm2, respectively. The mean SSB intake was 343.2 ± 212.0 mL/day. Compared to girls who consumed 30-360 mL/day of SSB, girls who consumed < 30 mL/day had a modest increase in FGV and total breast volume (FGV: β, 13.0 [95% CI, -2.0-27.9]; total breast volume: β, 36.5 [95%CI, 4.9-68.2]). There was no association between SSB intake and breast composition when comparing girls who consumed 30-360 mL to those who consumed more than 360 mL/day of SSB.

Conclusion: We observed little evidence that SSB intake was associated with overall breast composition in adolescent Chilean girls.

Nutrition/Obesity

Prenatal variation in blood arsenic and mercury concentrations by substituting white rice with other grains Pi-I D. Lin* Pi-i Lin Andres Cardenas Mohammad L. Rahman Marie-France Hivert Sheryl L. Rifas-Shiman Tamarra James-Todd Emily Oken

Background: Rice accumulates arsenic (As) and mercury (Hg) more readily compared to other grains, but data are lacking on the relative exposure from different food sources. We performed a causal analysis to evaluate the effect of substituting white rice with other grain items on erythrocyte As and Hg concentrations in pregnancy.

Methods: In the first trimester [median (IQR) 9.6 (2.1) weeks gestation], 1206 pregnant women in the Project Viva cohort (recruited 1999-2002 in eastern MA) used food frequency questionnaires to report intake of commonly consumed grain items and provided blood for erythrocyte As and Hg measurements. To estimate variations in As and Hg by hypothetical food substitution, we used a macronutrient substitution model. Specifically, we assumed the consumption of total grain remained constant and calories from white rice would be replaced only by calories from other grain items; and fitted a multivariable linear regression model with log-transformed As or Hg as the dependent variable and included all grain item, except white rice, as the independent variables. The model controlled for total grain intake, and adjusted for potential confounders, including age, parity, education, household income, marital status, race/ethnicity, pre-pregnancy BMI, smoking, hemoglobin level, sex of the child, and seafood intake.

Results: Consumption of white rice and seafood were weakly correlated [shrimp (Spearman r=0.17); dark fish (r=0.16); and other fish (r=0.11), breaded fish (r=0.09), canned tuna (r=0.01), all p<0.001]. After accounting for covariates, substituting each serving of white rice with other grains was associated with lower As and Hg (Figure 1). Replacements with brown rice and other grains did not have a significant effect.

Conclusion: Using statistical modeling, we found that substituting white rice with other grains during pregnancy was associated with lower erythrocyte concentrations of As and Hg.

Figure 1. Relative percent difference in median erythrocyte arsenic (As) and mercury (Hg) concentrations among pregnant women in Project Viva by substituting white rice with other grains (per serving/day)

Nutrition/Obesity
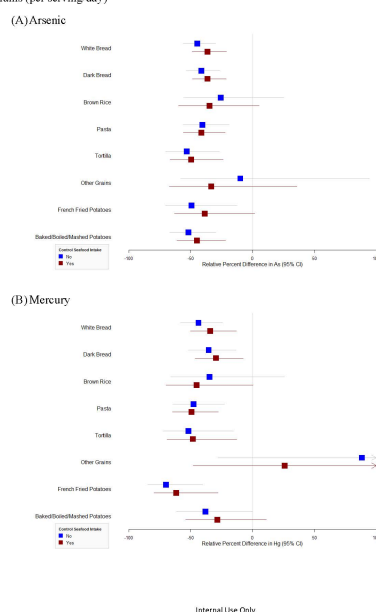
Early Exposure to Animals in Relation to Childhood Body Mass Index Pamela L Ferguson*
Pamela Ferguson John Vena Brian Neelon JacKetta Cobbs Sarah Commodore Kelly Hunt

Background: Some studies have found children exposed early in life to animals appear to have lower risks of obesity, asthma, and allergies. A possible mechanism is that animal exposure positively alters child's gut microbiome. Study results disagree on timing and type of animal exposure that may affect childhood obesity.

Methods: We analyzed early exposure of children to animals in relation to body mass index (BMI) at ages 4-8 years in the Environmental Contributors to Child Health Outcomes [ECHO] NICHD Fetal Growth Studies cohort. Of the 831 children with BMI measured, 744 (89.5%) had complete data and were included in analysis. Outcome was child's BMI percentile (adjusted for gender and age) categorized as normal/underweight (<85), overweight (85 to <95), and obese (≥95). The main exposure was having a dog in the home and/or regular contact with farm animals during the first year of life (most exposures were to dogs). Covariates were race/ethnicity (Asian, Black, Hispanic, White), maternal education (up through high school degree, at least some college or more), food assistance (received Federal food aid and/or free school meals, none) and mother's report of child activity level (high, low). We used a partial proportional odds logistic regression model, allowing food assistance to have unequal slopes.

Results: Children not exposed during their first year to dogs and/or farm animals have 1.49 (95% CI: 1.02, 2.19) times higher odds of being in a higher weight category compared to a lower weight category than those exposed to animals. Other factors that were significantly associated with heavier weight were increased maternal BMI, being Hispanic (vs White), and low activity. Having food assistance was associated with obesity but not overweight.

Conclusion: These results provide additional evidence that exposure to dogs and/or farm animals in early life is associated with lower BMI in childhood, after adjusting for race, activity, and maternal socioeconomic factors.

Association between animal exposure and childhood overweight and obesity.

Effect	Odds Ratio Estimates (95% CI)
No 1st year exposure to dog/farm animals (reference=exposure)	1.49 (1.02, 2.19)
Maternal BMI (kg/m²)	1.08 (1.05, 1.11)
Race/ethnicity (reference=White)	
Asian	0.53 (0.26, 1.08)
Black	1.32 (0.76, 2.27)
Hispanic	2.11 (1.25, 3.58)
Child physical activity (reference=high activity)	1.55 (1.10, 2.19)
Mother has HS degree or less (reference=at least some college)	1.25 (0.84, 1.87)
Received food assistance (reference=no assistance)	
Overweight outcome	0.95 (0.60, 1.50)
Obese outcome	1.96 (1.03, 3.73)

Nutrition/Obesity

Sugary Drink Consumption across Social Groups among Canadian Adults Christine Warren*
Christine Warren Douglas Manuel Laura Anderson David Hammond Erin Hobin Mahsa Jessri JoAnne
Arcand Lindsay McLaren Mary L'Abbé Heather Manson Laura Rosella Ye (Lennon) Li Brendan Smith

Background: Sugary drink (SD) consumption is associated with increased risk of chronic disease. In
Canada, little is known about whether SD consumption is socially patterned. Our objective was to
estimate the prevalence of SD consumption and mean energy intake from SD among consumers
across socioeconomic position (SEP) in Canadian adults. Methods: A cross-sectional analysis was
conducted using 24-hour dietary recalls from respondents of the nationally representative 2015
Canadian Community Health Survey-Nutrition (n=13,519, >19 years, 53% female). SDs were
defined as beverages containing free sugars. Sex-specific weighted multivariable linear regression
estimated the prevalence of SD consumption and, among consumers, mean energy intake from SD
(kcal/day) across SEP (household income adequacy quintile, food security, and education) adjusted
for age, energy reporting status, and recall day. Results: In females, prevalence of SD consumption
was inversely related to income (Q1:57% [95%CI:51-63] vs Q5:43% [95%CI:35-51]) and food security
(insecure:63% [95%CI:54-71] vs secure:51% [95%CI:48-51]), but not education. No social patterns in
the prevalence of SD consumption were found in males. In females, mean energy from SD was
inversely related to food security (insecure:189 kcal/day [95%CI:150-233] vs secure:164 kcal/day
[95%CI:149-180]) and education (less than high school:202 kcal/day [95%CI:154-258] vs bachelor
degree or above:158 kcal/day [95%CI:134-183]). In males, more pronounced patterns were found
across food security (insecure:263 kcal/day [95%CI:221-308] vs secure:217 kcal/day
[95%CI:199-235]) and education (less than high school:251 kcal/day [95%CI:208-297] vs bachelor
degree or above:192 kcal/day [95%CI:173-213]). In both sexes, no differences in mean energy from
SD were observed across income. Conclusion: SD consumption is socially patterned in Canadian
adults. Population-level interventions that reduce SD consumption overall and across SEP are
warranted.

The Association Between Childhood Adversity and Dietary Quality Francisco Marquez*
Francisco Marquez Patricia Markham-Risica Karen Jennings-Mathis Audrey Tyrka

Self-medicating behaviors, such as unhealthy food intake, may explain the association between childhood adversity and obesity. The Healthy Eating Index (HEI) can reveal differences in dietary quality among survivors of childhood adversity. To assess the association between childhood adversity and dietary quality, we used the HEI in a sample from the Lifestyle Influences of Family Environment study (LIFE). Demographic and dietary data were obtained for 145 participants using formal interviews and interviewer-administered 24-h recalls. Dietary quality was measured using the 2015 HEI scoring algorithm. Demographic differences were assessed using Fisher's exact tests and analysis of variance. The association between childhood adversity and dietary quality was assessed through linear regression. To determine the robustness of this association, a step process of multiple linear regression was employed. Confounders were determined a-priori and included in the final model if they had a p-value < 0.2. Variables included in the final model were sex and age. Bootstrap CIs were used to validate model results. Differences in HEI component scores were assessed using Kruskal-Wallis tests. The mean ± SD HEI score for all participants was 54.6 ± 12.8. Individuals with childhood adversity had a 5.0 lower overall HEI score when compared to those without a history of childhood adversity 95% CI (0.87, 9.2). After adjusting for age and sex, childhood adversity was associated with a 5.2 lower HEI score 95% CI (1.1, 9.4). HEI component scores indicated that individuals with childhood adversity were significantly more likely to have lower whole grain (0.9 versus 2.7) and total dairy (4.3 versus 6.2) scores. Childhood adversity was associated with lower measures of dietary quality. These results warrant further exploration of dietary and behavioral pathways mediating the association between childhood adversity and obesity.

Overall HEI Score by Group
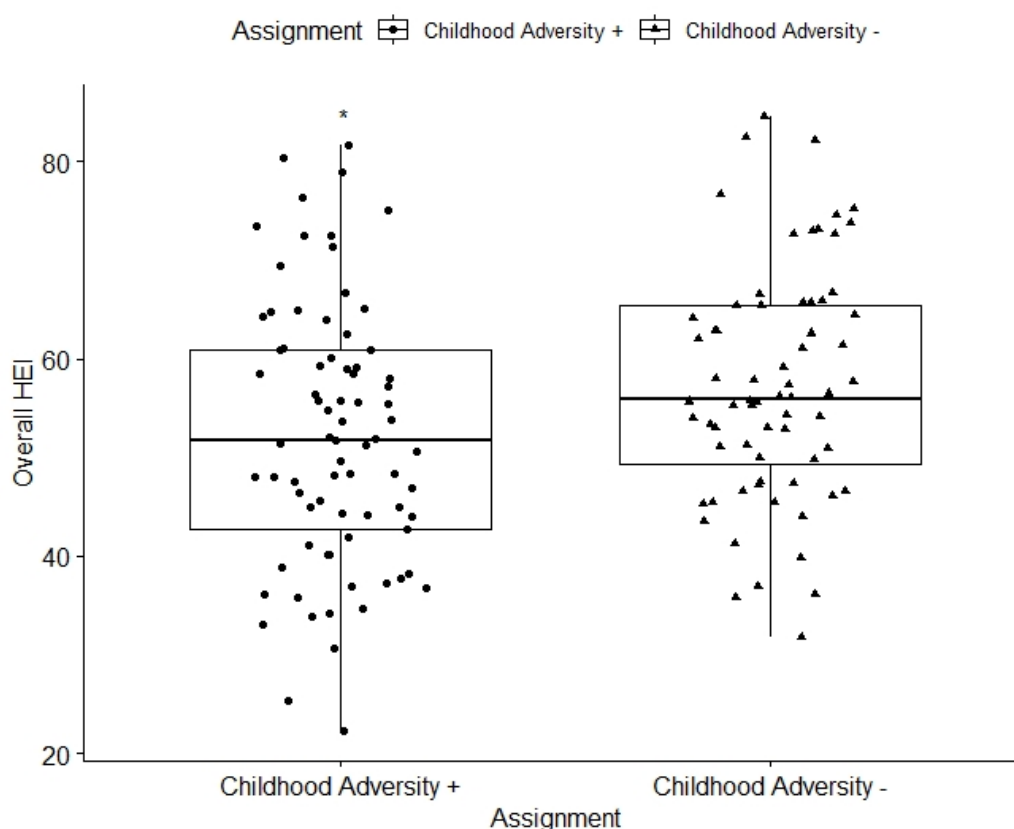
Exposure to polyunsaturated fatty acids and mercury from seafood and its relation with metabolic syndrome in Mexican children and adolescents Yanelli Rodriguez Carmona* Yanelli Rodríguez-Carmona Larissa Betanzos-Robledo Alejandra Cantoral-Preciado Wei Perng Martha María Tellez-Rojo Karen E. Peterson Erica C. Jansen

Background: Seafood intake has been associated with lower cardiovascular risk due, in part, to the anti-inflammatory effects of Omega-3 polyunsaturated fatty acids (PUFAs), such as Eicosapentaenoic acid (EPA) and Docosahexaenoic acid (DHA). However, its methylmercury (MeHg) content has been associated with increased risk of diverse cardiovascular events. We evaluated the independent relationships of PUFAs and MeHg, after mutual adjustment, on metabolic syndrome.
Methods: The study included 321 youth (9-17 yrs) from the ELEMENT birth cohort in Mexico City. Plasma DHA and EPA (% of total fatty acids), height, weight, blood pressure, Tanner staging (pre- vs post-pubertal), food frequency (FFQ) and physical activity (hrs/week) questionnaires were collected. We calculated the Metabolic syndrome Risk Z-score (MetRisk Z-score) as the sum of waist circumference, fasting glucose and insulin, triglycerides/HDL ratio and mean blood pressure Z-scores. Non-seafood PUFAs and seafood MeHg intakes (mg/d) were estimated (FFQ). Multiple sex-stratified linear models included plasma PUFAs and seafood MeHg as predictors (in quartiles, Q) with MetRisk Z-score as the outcome, adjusting by energy intake, socioeconomic status, physical activity, non-seafood PUFAs intake, plasma PUFAs and Tanner staging.
Results: Plasma EPA was not associated with the MetRisk Z-score in the whole sample, however, an inverse association was observed in girls (Q4 vs Q1: β= -1.60; 95% CI= -2.98,-0.21) and a positive association in boys (Q3 vs Q1: β= 1.82; 95% CI=0.22,3.42). Plasma DHA was inversely associated with MetRisk Z-score across the sample and by sex. No association was found between the seafood MeHg intake and MetRisk Z-score.
Conclusions: After adjusting for seafood MeHg intake, plasma DHA was associated with lower MetRisk Z-score in both sexes, whereas EPA levels were associated with the MetRisk Z-score negatively in girls and positively in boys. No association was found for MeHg and MetRisk Z-score.

Table 1. β and 95% confidence intervals for the multiple linear regressions between plasma DHA and EPA percentages, seafood MeHg intake and the MetRisk Z-score

	All (n=310)		Girls (n=157)		Boys (n=153)	
	β	95% CI	β	95% CI	β	95% CI
DHA %[a]						
Q2	-1.25	-2.29 , -0.20	-1.16	-2.6 , 0.27	-1.10	-2.63 , 0.42
Q3	-0.70	-1.72 , 0.32	-0.92	-2.36 , 0.51	-0.29	-1.75 , 1.17
Q4	-2.18	-3.21 , -1.14	-1.40	-2.75 , -0.05	-2.78	-4.46 , -1.09
EPA %[a]						
Q2	-0.08	-1.1 , 0.95	-0.46	-1.78 , 0.86	0.37	-1.21 , 1.95
Q3	0.41	-0.66 , 1.47	-1.37	-2.76 , 0.02	1.82	0.22 , 3.41
Q4	-0.50	-1.58 , 0.58	-1.60	-2.98 , -0.21	0.68	-0.96 , 2.32
MeHg (mg/day)[b]						
Q2	0.65	-0.43 , 1.74	-1.00	-2.36 , 0.35	0.33	-1.33 , 2.00
Q3	-0.01	-1.06 , 1.03	0.24	-1.19 , 1.66	0.96	-0.58 , 2.51
Q4	-0.24	-1.31 , 0.84	0.16	-1.28 , 1.6	0.37	-1.14 , 1.89

Abbreviations: MetRisk Z-score, Metabolic syndrome Risk Z-score; DHA, Docosahexaenoic acid; EPA, Eicosapentaenoic acid; MeHg, methylmercury; CI, confidence intervals.
[a] DHA and EPA models were adjusted for total energy intake (kcal/day), socioeconomic status (low, middle and high), physical activity (hours/week), non-seafood PUFAs intake (mg/day), seafood MeHg intake (mg/day) and pubertal status (pre- vs post-pubertal).
[b] MeHg models were adjusted for total energy intake (kcal/day), socioeconomic status (low, middle and high), physical activity (hours/week), plasma PUFAs % and pubertal status (pre- vs post-pubertal).

Validity of Billing Codes for Obesity in the Pediatric Population Apryl Susi* Apryl Susi
Elizabeth Hisle-Gorman Cade Nylund

Background: Obesity is a common chronic disease which negatively impacts child and adult health.
Epidemiologic studies often identify obesity by International Classification of Diseases (ICD) codes in
insurance claims. Validation studies of ICD-9/10 codes for adult obesity indicates under-coding,
however, ICD code obesity validation studies have not been reported in children.
Objective: To evaluate the validity of child ICD-9/10 obesity billing codes as compared to vitals data
over time and by sex.
Methods: Children aged 2-17 with height and weight data in 2009-17 in the Military Health System
were included. BMI-for-age percentiles were calculated using Center for Disease Control and
Prevention's 2000 growth chart standards; BMI over the 95th percentile was classified as obese. In-
and outpatient records for the same year were assessed for ICD coding for obesity. Yearly sensitivity
and specificity were calculated overall and by gender.
Results: 1,704,790 unique children were included, contributing 5,707,949 years of observation.
51.2% were male. Annually, 580,000-660,000 children had a measured height and weight,
11.6-13.2% were obese by BMI percentiles, and 2.0-3.5% from ICD codes. Sensitivity of coded
obesity increased from 14.8% in 2009 to 29.3% in 2017 overall, from 13.3-28.0% in males, and from
16.6-31.0% in females, which was consistently 3-4 percentage points above males. Specificity ranged
from 99.8-99.9% in all populations and remained stable across all years.
Discussion: ICD codes should not be used to determine obesity when BMI is available. In the
absence of BMI, researchers and practitioners should know ICD codes only identify 30% of children
with obesity. An obesity ICD code indicates almost certain obesity, lack of a code does not exclude
obesity. Despite improved sensitivity, 70% of obese children did not receive an ICD code. Males are
less likely to receive an ICD code for obesity than females when presenting with a BMI above the
95th percentile.

Sensitivity of Coded Obesity
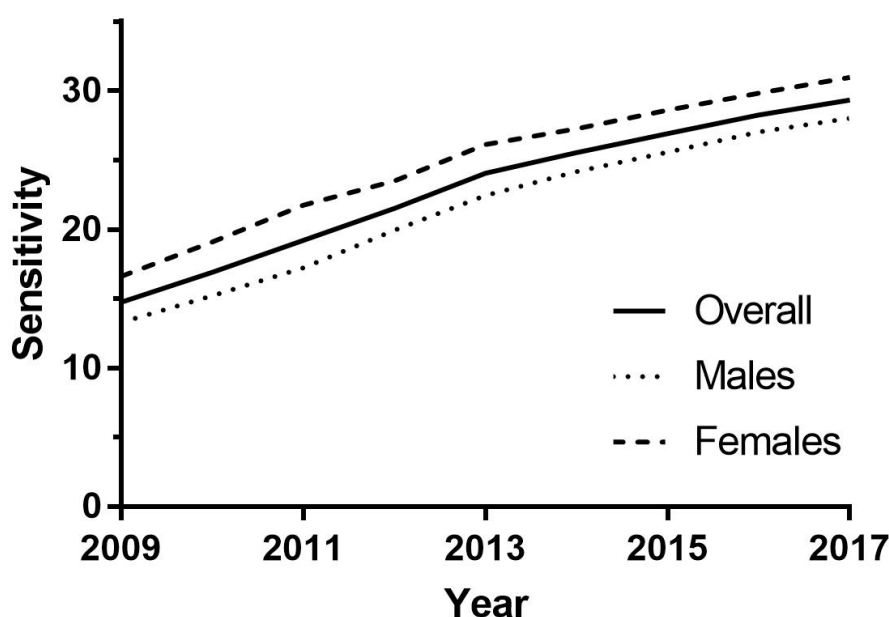
Dietary Factors and PFAS Plasma Concentrations in Childhood Shravanthi M Seshasayee*
Shravanthi M Seshasayee Sheryl L. Rifas-Shiman Jorge E. Chavarro Pi-I D. Lin Sharon Sagiv Emily
Oken Abby F. Fleisch

Background: Perfluoroalkyl substances (PFASs) are stain-repellant chemicals with long half-lives
(3-7 years) that may contaminate foods through bioaccumulation, food packaging, and processing.
Investigation of dietary sources of PFASs in children is limited.
Methods: We studied 559 Boston-area children with food frequency questionnaire data (89 food
items) in early childhood (median age 3.3 years) and plasma concentrations of six PFASs measured
in mid-childhood (median age 7.7 years) in 2006-2010. We used reduced rank regression (RRR), a
dimension reduction approach that accounts for both a priori (dietary intake) and a posteriori
(PFAS) variations to identify distinct dietary patterns most strongly associated with the six PFASs.
We adjusted analyses for annual household income, maternal education, and child race/ethnicity.
Results: Perfluorooctane sulfonate (PFOS) and perfluorooctanoate (PFOA) were the most prevalent
PFASs [e.g., PFOS median (IQR) was 4.5 (3.0) ng/dL]. RRR identified six dietary patterns that
together explained 18% of variance in PFAS plasma concentrations. The dietary pattern most
strongly associated with the six PFASs included greater intake of ice cream, salad dressing, non-
chocolate candy, lettuce, butter, white rice, fish, and soda and lower intake of margarine (Figure 1).
This pattern explained 9% of PFAS variance and closely correlated with PFOS ($\rho=0.85$), PFOA
($\rho=0.84$), and perfluorodecanoate ($\rho=0.71$).
Conclusion: Consistent with PFAS exposure from multiple sources, including textiles, we found diet
to explain only a modest amount of PFAS variability. The dietary pattern most strongly associated
with PFAS plasma concentrations confirmed possible bioaccumulation of PFAS in fish and identified
several packaged items for which further investigation of PFAS-contamination may be warranted.

Figure 1. Top twenty-five food item loadings corresponding to the RRR-derived early childhood
dietary pattern most explanatory of variance in PFAS plasma concentrations in mid-childhood.[a]
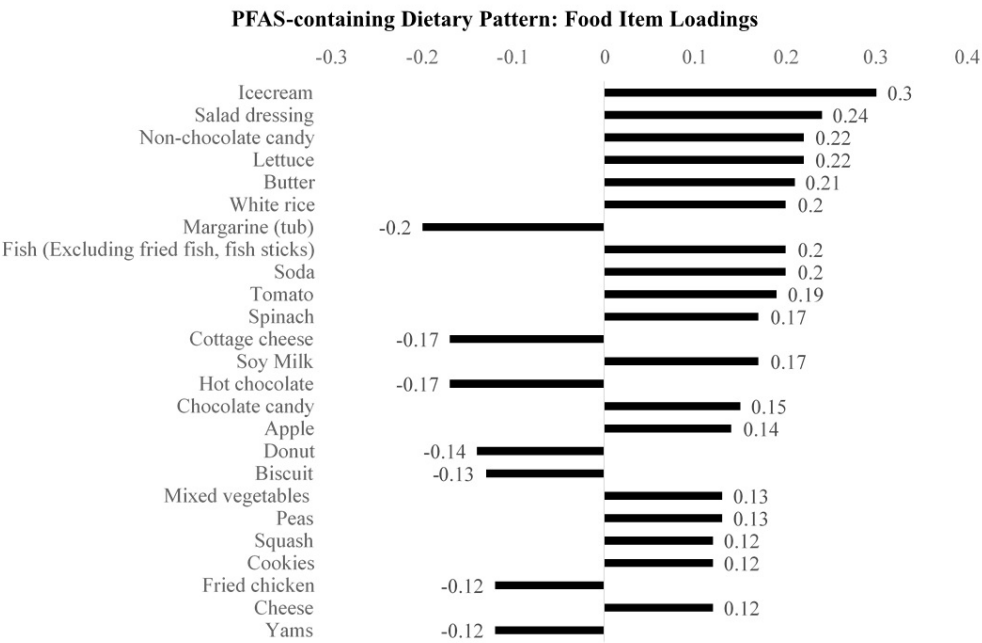
Abbreviation: PFAS – Perfluoroalkyl substances
[a] Adjusted for annual household income, maternal education, and child race/ethnicity

Milk consumption and risk of mortality from all-cause, cardiovascular disease and cancer in older people Xiang Jun Wang* Xiang Jun Wang

Background: Milk as a common diet is recommended by many guidelines, but the results on the association of milk consumption with the risk of cardiovascular disease (CVD) or cancer were contradictory. Moreover, evidence regarding milk consumption and mortality risk in Chinese is scarce.

Objective: We examined the associations of milk consumption with the risk of all-cause, CVD and cancer mortality in a low milk consumption population using data from the Guangzhou Biobank Cohort Study.

Design: 18,214 participants aged 50+ years without CVD history at baseline (2003-6) were included. Causes of death were identified through record linkage. Cox proportional hazards regression was used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs).

Results: Of the 18,214 participants, 12,670 (69.6%) did not consume milk, 2,669 (14.7%) had moderate (1-3 portions/week; 1 portion=250 ml) and 2,875 (15.8%) had high (3+ portions/week) consumption. During an average follow-up of 11.5 (standard deviation=2.3) years, 2,697 deaths occurred, including 917 CVD and 1,029 cancer deaths. Compared with no consumption, the adjusted HR (95% CIs) of all-cause, CVD, ischemic heart disease (IHD) and stroke mortality for moderate milk consumption was 0.92 (0.81-1.04), 0.72 (0.57-0.92), 0.57 (0.38-0.85) and 0.77 (0.63-0.94), respectively. High consumption was associated with a higher risk of total cancer and esophagus cancer mortality, with the adjusted HR (95% CIs) being 1.33 (1.12-1.57) and 3.20 (1.21-8.43) respectively. No significant association of high consumption with lung cancer, liver cancer, gastrointestinal cancer, or colorectal and anal cancer was found.

Conclusions: In our sample of Chinese with much lower milk consumption than those in the West, compared with no consumption, moderate milk consumption showed a lower risk of CVD mortality, but high milk consumption showed a higher risk of total cancer mortality. Further studies are warranted to verify the differential effects of milk on CVD and cancer.

The association Between Mediterranean Diet and Depressive Symptoms in Boston Area Puerto Rican Adults Over Time Natalia Palacios* Neha Sahasrabudhe Lee, Jong Soo Punnett, Laura Tucker, Katherine L. Palacios, Natalia

Background: Studies evaluating the protective effect of Mediterranean diet on depression are limited, particularly among the minority populations.
Objective: The aim of this study was to examine the potential longitudinal association between Mediterranean diet (MeD diet) and self-reported depressive symptoms in the Boston Puerto Rican Health Study (BPRHS) cohort.
Methods: We examined the association between MeD diet and CES-D score (Center for Epidemiologic Studies Depression scale) using a repeated measures mixed-effect model in 1498 BPRHS participants with 3 follow-up visits over 5 years. We adjusted all our models for age, sex, Body Mass Index (BMI), education, alcohol use, smoking, physical activity, chronic medical conditions score, plasma vitamin B6, marital status, food security status, income to poverty ratio, antidepressant use, tangible support and study visit. We also conducted sensitivity analyses restricted to participants without diabetes and to participants with complete CES-D and MeD diet score at all 3 visits.
Results: Depressive symptoms decreased significantly over time in all participants (β= -0.88, 95% CI =-1.03, -0.73). Stronger adherence to MeD diet produced a larger decrease in depressive symptoms score longitudinally over the course of 5 years (β= -1.7, 95% CI= (-3.3, -0.2) comparing highest vs. lowest MeD diet tertile; P-trend=0.02). This association was stronger in sensitivity analyses restricted to 825 participants without diabetes and among 866 participants with complete measures of CES-D and MeD diet score at all 3 visits (β =-1.9, 95% CI= (-3.5, -0.3); p-trend: 0.02) and (β=-2.0, 95% CI= (-3.9, -0.2); p-trend= 0.02) respectively, comparing highest versus lowest MeD diet tertile. We did not observe a significant interaction between MeD diet score and time in our longitudinal analyses.
Conclusion: Higher adherence to the MeD diet was associated with lower depressive symptoms score over 5 years in this cohort of Puerto Ricans.

Nutrition/Obesity

The association Between Serum 25(OH)D and Depressive Symptoms in Boston Area Puerto Rican Adults Over Time

Natalia Palacios* Neha Sahasrabudhe Lee, Jong Soo Punnett, Laura Tucker, Katherine L. Palacios, Natalia

Background: Several studies have reported a protective effect of vitamin D on depression, but research examining this association in minority populations is limited.

Objective: The aim of this study was to evaluate the potential cross-sectional and longitudinal association between serum 25-hydroxyvitamin D (25(OH)D) concentration and self-reported depressive symptoms in the Boston Puerto Rican Health Study (BPRHS) cohort.

Methods: We examined the association between serum 25(OH)D and CES-D (Center for Epidemiologic Studies Depression scale) using a repeated measures mixed effect model in 1498 BPRHS participants with 3 follow-up visits over 5 years. All models were adjusted for age, sex, Body Mass Index (BMI), season of blood collection, education, smoking, alcohol use, physical activity, chronic medical conditions score, plasma vitamin B6, fruits and vegetable servings/day and study visit. We also conducted sensitivity analyses restricted to study participants not taking vitamin D supplements and those with complete data on serum 25(OH)D and CES-D at all 3 visits.

Results: Depressive symptoms decreased significantly over the course of follow-up in all participants ($P<0.01$). Serum 25(OH)D concentration was not associated with depressive symptoms score either cross-sectionally at baseline (β = -0.85, 95% CI = -2.80,1.10, comparing participants deficient in 25(OH)D to those with sufficient levels; P-trend=0.59) or longitudinally over three waves of follow-up (β = -0.41 ; 95% CI = -1.95,1.13; P-trend=0.93) in this cohort. We observed similar associations in the sensitivity analyses restricted to 1312 participants not taking vitamin D supplements and among 887 participants with complete measures of serum 25(OH)D and CES-D score at all 3 visits. We did not observe a significant interaction between serum 25(OH)D and time in our longitudinal analysis.

Conclusion: Serum 25(OH)D concentration was not associated with depressive symptoms in this cohort of Puerto Ricans.

Nutrition/Obesity

Categorizing community type for epidemiologic evaluation of food and physical activity resources in the United States Tara Patricia McAlexander* Tara McAlexander Yasemin Algur Brian S. Schwartz David Lee Karen R. Siegel Jamese Johnson Nora Lee Victoria Ryan Leslie McClure

Background: United States (US) communities include rural, exurban, small towns and cities, micropolitan and metropolitan core, and suburban settings. Food and physical activity resources vary across these settings, posing measurement, interpretation, distributional, and analytic challenges for their use in epidemiologic research. Appropriate classification of and stratification by community type can minimize these challenges.
Objectives: To review existing community classification methods and propose a novel approach for classifying communities across the US for evaluation of community and environmental domains relevant to obesity and type 2 diabetes (T2D).
Methods: Studies of community conditions and health commonly use US Census tract boundaries to define communities, but most studies have been confined to urban areas or have ignored how community type influences measurement and analysis. We obtained the US Department of Agriculture's 2010 10-level Rural-Urban Commuting Area (RUCA) codes for all Census tracts in the contiguous US and evaluated how classification changed after modifying: 1) RUCA codes based on percentage of Census tract land area within Census-defined urban clusters and urbanized areas; and 2) division of urban Census tracts based on land area.
Results: Original RUCA classifications grouped 59% of all Census tracts, including suburban and sprawling regions, as highly urban. Modified classification designated 24% of Census tracts as urban, 36% as surrounding areas, 16% suburban or small town, and 25% rural. Distributions of tract-level measures of food and physical activity resources showed improved differentiation by community type.
Conclusions: Modified community type categorization improved differentiation of community types for evaluating community and environmental domains relevant to obesity and T2D.

LATEBREAKER

Nutrition/Obesity

Body composition parameters for healthy individuals Rita Mattiello* 3647] Mattiello Marina A. Amaral Lisiane Marçal Perez Eduardo Mundstock Wilson Canon Montanez

Background: Body composition (BC) measures are important health parameters. Reference values from bioelectrical impedance analysis parameters are lacking for healthy community-dwelling individuals. The aim of the study was to estimate the percentile distribution of BC parameters for healthy individuals and to investigate the association with age.

Methods: A cross-sectional study of healthy Brazilian individuals aged 5 years and older, both sexes. The following BC parameters were assessed: percent body fat, percent lean mass, fat mass index, and fat-free mass index. The relationships between BC parameters and age were analyzed using a quantile regression model (25th, 50th and 75th percentiles).

Results: Of 1241 participants, with median age of 27.0 (range 5 to 99) years, 651 (53%) were female and 777 (74%) were Caucasian. Using quantile regression analysis, BC variables were associated with age in males and females, respectively: Percent body fat (P50 estimate: 0.16 95CI: 0.12 to 0.21; P <.0001; 0.26 95CI: 0.22 to 0.30; P <.0001); Percent lean mass (P50 estimate: -0.14 95CI: -0.18 to -0.10; P <.0001; -0.24 95CI: -0.28 to -0.20; P <.0001); Fat mass index (kg/m^2) (P50 estimate: 0.08 95CI: 0.06 to 0.09; P <.0001;0.10 95CI: 0.08 to 0.12; P <.0001) and, fat-free mass index (kg/m^2) (P50 estimate: 0.12 95CI: 0.09 to 0.15; P <.0001; 0.05 95CI: 0.04 to 0.07; P <.0001).

Conclusions: This study describes the reference values for most clinical BC parameters in percentiles stratifying by different life cycles and sex.

Reliability of the Saycare Dietary Inflammatory Index in Children and Adolescents Livia Garcia* 3647] Azevedo-Garcia Augusto César F. De Moraes Francisco Leonardo Torres-Leal Juan Carlos Aristizabal Gabriela Berg Heráclito B. de Carvalho

Background: Chronic inflammation may be associated with the development of chronic diseases and it's directly associated with diet. The validation of tools that assess inflammatory dietary patterns in young populations that allow valid and reliable results to be obtained is important in order to guide disease prevention strategies for adult life. **Objective:** To test the reliability of a Food Frequency Questionnaire (Ffq) to assess the consumption of pro-inflammatory food in South American children and adolescents**. Methods:** The Saycare (South American Youth/Child cARdiovascular and Environmental) is a multicenter, observational feasibility study performed in a sample of 3- to 18-year-old children (n= 166) and adolescents (n= 110) attending private and public schools from seven South American cities (Buenos Aires, Lima, Medellin, Montevideo, Santiago, Sao Paulo, and Teresina). Participants answered the Ffq twice with a two-week interval. We selected pro-inflammatory food and summarized these groups (sugar-sweetened beverages, high-sugar, red meat, processed-meat and high-fat) in a Saycare Dietary Inflammatory Index**.** The reliability of the Ffq was analyzed by correlation coefficients for each food, food group and index. **Results:** The sample was characterized by total of 166 children (54.2% female; 45.8% male) and 110 adolescents (56.2% female; 43.8% male). For the index we had an average consumption of pro-inflammatory food: 166 grams/day;121 grams/day and a Spearman's coefficients of 0.60;0.59 in children and adolescents, respectively. Depending on the food group, reliability analyzes resulted in Spearman's coefficients from 0.67 to 0.41. The group that obtained the highest correlation coefficient was sugar-sweetened beverages. **Conclusion:** The Saycare Ffq shows moderate reliability for all pro-inflammatory food and the Index and can be used to measure the intake of pro-inflammatory food groups in pediatric population from low- to middle-income countries.

Nutrition/Obesity

Early life household environments in relation to trajectories of food responsiveness Erica Jansen* Erica Jansen Niko Kaciroti Julie Lumeng Katherine Rosenblum Alison Miller

Introduction: Early life socioeconomic status and unstable household environments can predict long-term chronic disease risk. Eating behaviors established during childhood are one potential mechanism. We evaluated whether household-level factors were associated with trajectories of food responsiveness.

Methods: The sample included 397 children (4 years old at baseline) from a low-income cohort followed up to 5 times over 7 years. At each visit, parents completed the Childhood Eating Behavior Questionnaire, which includes a food responsiveness (FR) subscale (i.e., eating in response to external cues vs. hunger). Group-based trajectory models were used to identify distinct trajectories of FR. Multinomial logistic models were used to evaluate predictors of trajectory membership. Baseline household predictors included household food insecurity, income-to-needs ratio, the Chaos, Hubbub, And Order Scale (CHAOS; measure of household disorganization), and sleep hygiene (routines followed prior to bedtime). All models were adjusted for child age, sex, and maternal depression.

Results: Three distinct FR trajectories were identified: low, slightly increasing FR (Group 1; 42.8% of the sample), medium, fluctuating FR (Group 2; 43.1%), and high, steady FR (Group 3; 14.0%). In bivariate analysis, household food insecurity, lower income-to-needs, more chaos, and worse sleep hygiene predicted higher membership in Groups 2 and 3 compared to Group 1. In multivariable analysis, lower sleep hygiene remained associated with higher odds of Group 3 membership (OR=2.59, 95% CI 1.19 to 5.75). Greater household chaos was associated with higher odds of Group 2 vs Group 1 membership (OR=1.11, 95% CI 1.01 to 1.21).

Conclusion: Children from households with less structure during early childhood had higher trajectories of food responsiveness. Findings suggest that dysregulated eating could be a possible mechanism through which unstable early home environments may shape long-term disease risk.

Food Responsiveness Trajectories
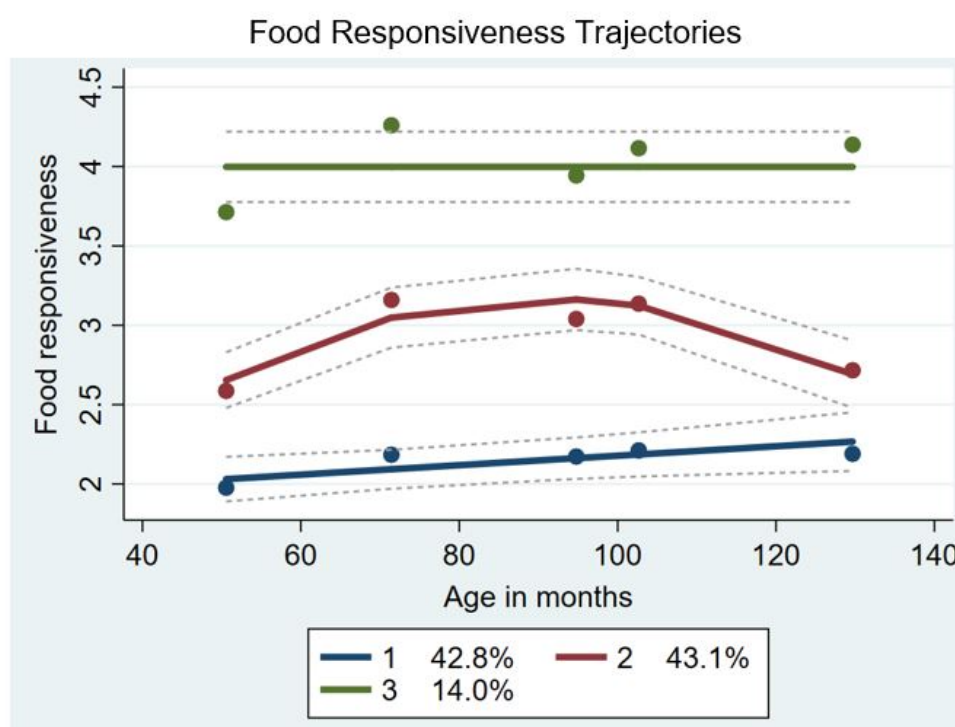
Epidemiological pattern and the ability of body adiposity indicators in identifying adolescent metabolic syndrome – a nationwide study in Taiwan

Wei-Ting Lin* Wei-Ting Lin Chun-Ying Lee Yu-Ting Chin Pei-Wen Wu David W. Seal Chien-Hung Lee

Adolescent metabolic syndrome (MetS) has been demonstrated to have a predictive ability for several metabolic-related diseases in adulthood. Body adiposity index (BAI) and abdominal volume index (AVI) are two recently proposed noninvasive adiposity indicators that simultaneously consider the influence of height, hip and waist circumference on body weight. The aims of this study are to investigate epidemic patterns and correlates for the gathering of MetS risk components and evaluate the discriminative ability of the BAI and AVI in identifying adolescent MetS. We evaluated 1920 representative adolescents aged 12-18 years with a comprehensive questionnaire survey, body measurements and clinical examinations collected in the 2010-2011 National Nutrition and Health Survey in Taiwan. The MetS diagnostic criteria defined by the Taiwan Pediatric Association (TPA) was used to evaluate adolescent MetS. Survey modules were used to adjust for sampling weights in all analyses. Multinominal regression models were used to assess the effect of BAI and AVI on the adolescent MetS. The area under receiver operating characteristic (AU-ROC) curves was used to evaluate the discriminative ability of the BAI and AVI in determining TPA-defined adolescent MetS. The prevalence of TPA-defined MetS was 5.0% and 3.1% in boys and girls, respectively. Increased BAI and AVI were associated with an increased risk of MetS in girls and boys (all p<0.001). Compared to adolescents with <85th levels of BAI and AVI, 11.8-fold or above risks were found in adolescents with ≥95th levels of BAI and AVI. The discriminative capability of AVI in identifying adolescent MetS was higher than that for BAI in both genders (p≤0.005 in boys (figure A) and in girls (figure B)). In conclusion, using BAI and AVI to assist the screening of adolescent MetS may be a feasible strategy in Taiwan. AVI presents a better discriminative capability in determining adolescent MetS than BAI in both genders.

Occupational
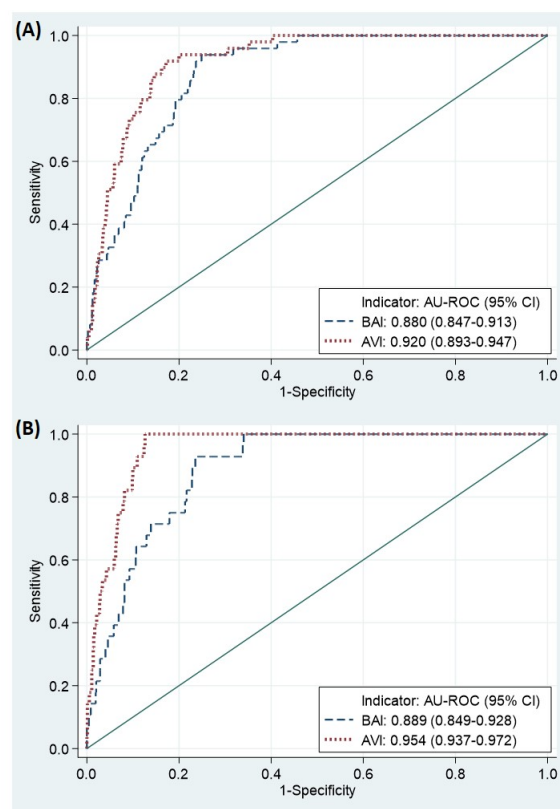
The Epidemiology of Behavioral Health among Soldiers with a Medical Discharge FY2017-FY2018 Theresa N. Faller* Theresa Faller Jamie Carreno Davidson Tanja C. Roy

Background: Overall, the rate of behavioral health (BH) problems is up to 15 times higher among US Army Soldiers compared to civilians, and women are at higher risk compared to men. Prevention and management of these diagnoses may prevent service attrition and increase quality of life for Soldiers. This study describes the prevalence of BH problems among medically discharged Soldiers as there is little available research to date.

Methods: A cohort study was conducted among active duty Soldiers who were medically discharged from October 2016 – September 2018 using data from the Soldier Performance, Health, and Readiness (SPHERE) Database, a repository of Army medical, administrative, and performance data. Medical discharges were identified from Certificates of Release or Discharge. BH diagnoses were identified using ICD-10 codes from medical records. Risk of BH diagnoses were assessed using logistic regression.

Results: From October 2016 – September 2018, 4.6% of the 34,000 medical discharges were related to BH. There was no difference by sex in the odds of a BH related discharge. Among all discharged Soldiers, 56.3% had at least one BH diagnosis in the 6 months prior to discharge. The most common disorders were adjustment disorder (15.1%), PTSD & acute stress disorder (12.8%) and depression (12.1%). Men had lower odds of adjustment disorder (OR: 0.833 [0.777-0.894]) and depression (OR: 0.643 [0.596-0.693]) compared to women. There was no difference in the odds of PTSD.

Conclusion: Our findings using recent data were consistent with rates of BH diagnoses in other Soldier populations and were higher than in civilian cohorts. There was no difference in risk of a BH related discharge in men compared to women, while risk of specific BH diagnoses varied. This suggests women may be at a higher risk for only certain diagnoses and not overall. Further studies should clarify the effect of BH on medical discharge and whether mitigating risk will lower risk of discharge.

Occupational

Prevalence of lung cancer among ever-employed adults — National Health Interview Survey, 2004–2018 Jacek Mazurek* Jacek Mazurek Girija Syamlal

In 2016, 218,229 persons were newly diagnosed with lung cancer, and 148,869 people died of lung cancer. An estimated 85% of lung cancer cases have been attributed to smoking. Workplace exposures can cause lung cancer in a previously healthy worker. To assess the industry- and occupation-specific prevalence of lung cancer among ever-employed adults, 2004–2018 National Health Interview Survey data for participants aged 18 years and over who were employed at any time prior to the interview were analyzed. Participants who had ever been told by a doctor or other health professional that they had cancer or a malignancy of any kind and indicated that it was a lung cancer were considered to have lung cancer. Information on respondents' longest held job industry and occupation was analyzed. Data were weighted to produce nationally representative estimates. During 2004–2018, an estimated annualized 534.8 thousand (prevalence 244.8 per 100,000) adults employed at any time prior to the survey had ever been diagnosed with lung cancer. The majority of persons with lung cancer were aged >65 years (64.9%, 907.2 per 100,000), White, non-Hispanic (82.7%, 292.9), former cigarette smokers (62.5%; 680.3), living in the South (42.6% 287.4), and had high school education or less (55.3%, 346.8). Lung cancer diagnosis was nearly equally distributed among ever-employed men (49.9%, 246.5 per 100,000) and women (50.1%; 242.3). An estimated 49.4% of ever-employed adults had information on longest held job. Lung cancer prevalence was highest among adults in the transportation and warehousing (469.4 per 100,000) industry and in production occupations (437.6). These findings might assist health professionals in identifying workers in industries and occupations with a high lung cancer prevalence who should be evaluated for possible lung cancer. Continued surveillance is important to assess lung cancer prevalence and trends by respondents' industry and occupation.

Occupational

Older Workers: An Investigation of Work-related Fatal Injuries due to Falls Thomas Schenk*
Thomas Schenk

The proportion of older workers (age ≥ 65 years) continues to rise in the U.S. as the aging baby-boom generation continues working later in life. The U.S. Bureau of Labor Statistics projects labor force participation to increase the fastest for older workers through 2024. Although older workers represent a small fraction of the U.S. work force, they suffer a disproportionate number of work-related fatalities. From 2015 through 2018, older workers accounted for 5% of the hours worked in the U.S., while they sustained 14% of all fatal work-related injuries. Using injury frequency and hours-worked data from the U.S. Bureau of Labor Statistics, Census of Fatal Occupational Injuries for 2015 through 2018, fatal injury rates (IR= # fatal injuries / hours worked) were calculated for older workers and for those under 65 years of age. Injury rate ratios (IRR) were used to compare cause-specific injury rates of older workers to the corresponding rates of workers under 65 years of age (IRR= IR≥65yrs/IR<65yrs). Falls, slips, and trips had the largest injury rate ratio of any cause category (IRR= 5.37, 95% CI 4.95-5.83). Focusing on falls, slips, and trips revealed that older workers suffer higher rates of fatal injuries compared to younger workers for falls due to tripping (IRR= 26.72, 95% CI 18.61-39.32), falls due to slipping (IRR= 16.59, 95% CI 10.97-25.11), falls on the same level (IRR= 14.9, 95% CI 12.61-17.61), and falls to a lower level (IRR= 3.95, 95% CI 3.58-4.37). Older workers' rates of fatal injury were two to eight times greater than the rates of workers under 65 for all other fall categories of 25 feet or less. As the U.S. labor force grows older, the findings of this investigation point to a need for injury prevention and the importance of maintaining walking surfaces in a safe, well-lit condition and continued training on safe work practices for all work at elevations.

Identifying Fitness Test Plateaus with Nonlinear Trends Among Soldiers Taking the Army Physical Fitness Test (Disclaimer: The Views Expressed in this Presentation are Those of the Authors and Do Not Reflect the Official Policy of the Department of Army, Department of Defense, or the U.S. Government) Soothesuk Kusumpa* 3647] Kusumpa Kathryn Taylor Melissa Richardson Tanja Roy

Army Physical Fitness Test (APFT) scores from the U.S. Army may provide insight into implementation of future performance tests. The literature suggests there exists a plateau effect in physical performance as number of assessments increase. To date, there has been no investigation into the non-linearity of APFT performance as number of attempts increase. This study evaluates the relationship between test attempts and test scores among all Soldiers graduating Basic Combat Training (BCT) in 2017**.**

The study population was followed through Nov 2019 with their first 6 recorded APFT scores being considered for analyses. Soldiers who completed a combined BCT and Advanced Individual Training were excluded from the study. Number of tests attempts were evaluated for both linear and non-linear relationships with APFT score. Non-linearity was evaluated using generalized additive mixed models with penalized cubic splines. Linearity was assessed with linear mixed models. Each model was adjusted for age, race, and time between tests**.** To select the model with the best fit, we used Akaike's Information Criteria.

For both Female and Male Soldiers, the non-linear models with 5 degrees of freedom produced the best fit. Female Soldiers (n=7,287) gained 10 to 12 points from 1st to 2nd test. A plateau was observed after the 2nd test with successive tests having minimal changes. Male Soldiers (n=30,951) gained 6 points from 1st to 3rd test. The plateau began between the 2nd and 3rd test, with a subsequent deficit in test scores.

Repetitive physical fitness test attempts may contribute to a plateau effect and in some cases result in a performance deficit. Recognizing multiple test attempts and any plateau may inform learning curve analysis (e.g. Soldier performance over time) and future test development. When using longitudinal data with large populations, relying solely on linear regression methodology may produce incorrect interpretations of trends.
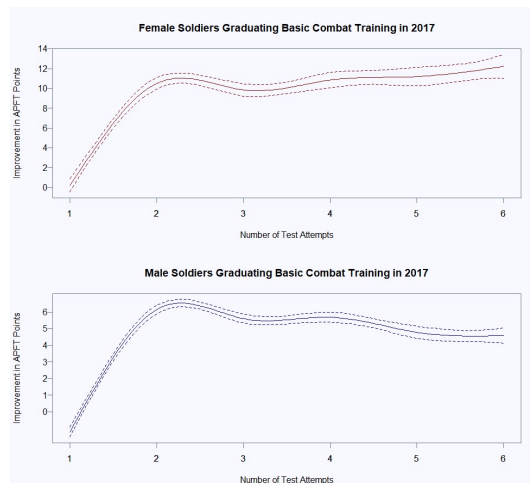
Social Support moderates the effects of Asthma-COPD Overlap Syndrome on Health-related Quality of Life in World Trade Center Health Registry Enrollees, 2015-2016 James E. Cone*
James Cone Asieh Kazem Haghighi Jiehui Li Rafael de la Hoz Cristina Pollari Jennifer Brite

Background: Asthma-chronic obstructive pulmonary disease (COPD) Overlap Syndrome (ACOS) is a newly defined form of chronic airway disease, and has not been well studied among 9/11-exposed populations with increased prevalence of asthma. ACOS is associated with poorer Health Related Quality of Life (HRQOL) than asthma or COPD alone. We examined whether social support moderated the effect of ACOS on HRQOL in an exposure cohort of World Trade Center Health Registry (WTCHR) enrollees.

Methods: This is a longitudinal study, including enrollees with complete data on 9/11/01 exposure at their 2003-2004 enrollment, and data on asthma and/or COPD diagnoses and age of at least 25 years at the time of the 2015-2016 (Wave 4) WTCHR survey. Probable ACOS was defined at Wave 4 as self-reported post-9/11 physician-diagnosed asthma and either emphysema, chronic bronchitis, or COPD. Social support was measured at Wave 4 using a 5-question scale, summed and categorized as quartiles from 1=low to 4= high social support. HRQOL, also assessed at Wave 4, was defined as number of days of poor physical or mental health out of the past 30 days. We evaluated whether the effect of ACOS on HRQOL was moderated by social support using multivariable logistic regression and linear regression.

Results: Of 36,864 participants, 29,911 were eligible for this analysis, and 1,495 (5.0%) had probable ACOS. Enrollees with ACOS had significantly poorer HRQOL than those with either asthma or COPD alone. After adjusting for age, education, gender, physical and mental health comorbidities and smoking status, we found that higher levels of social support moderate the effects of probable ACOS on HRQOL (Figure 1).

Conclusion: Probable ACOS in those with WTC exposures is associated with significantly poorer HRQOL, which is moderated by higher social support. Further study of ACOS is needed to understand and prevent the development of this and other occupationally- and environmentally-related airway diseases.

Other
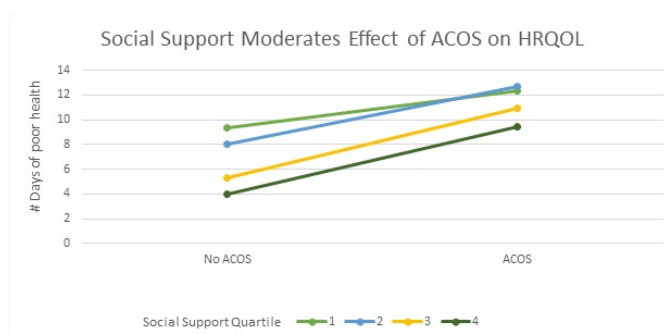
Body Mass Index and Readmission after Surgery: A Complicated Relationship Hsin-Hui Huang* Hsin-Hui Huang Madhu Mazumdar David Forsh Jashvant Poeran

Background: Body mass index (BMI) is consistently linked to complications including readmission. Previous studies have ignored potential age-BMI modification and BMI categorizations by the Centers for Disease Control and Prevention (CDC) may not adequately capture optimal thresholds. We aimed to study this potential modification and optimal threshold definitions in a cohort with two distinct age extremes: hip fracture repair surgery.

Methods: Among 236,006 hip fracture repair surgeries (National Surgical Quality Improvement Program, 2012-2017) multivariable regression models measured the association between 30-day readmission and BMI. We applied an interaction term between age (dichotomized based on the median, 70 years) and BMI. BMI was modeled as 1) continuous, 2) CDC categories (underweight: ≤18, normal: 19-24, overweight: 25-29, obese: ≥30 kg/m2); and 3) categorical applying a supervised machine learning discretization method, the Class-Attribute Contingency Coefficient (CACC) method resulting in three (≤22, 23-36, and ≥37 kg/m2) and two categories (≤22 and ≥23 kg/m2) in those aged <70 ('young') and ≥70 ('old') years, respectively. Odds ratios (OR) and 95% confidence intervals (CI) are reported.

Results: In the young group (n=119,870), increasing BMI (per 10 units) is associated with increased readmission odds (OR 1.12 CI 1.06-1.17); this association is reversed (OR 0.90 CI 0.86-0.93) in the old group (n=116,136). Among CDC BMI categories 'overweight' (compared to 'normal') was associated with decreased readmission odds in both groups (OR 0.82 CI 0.73-0.92 and OR 0.88 CI 0.82-0.94) while lower odds were also observed for 'obese' in the old group (OR 0.90 CI 0.83-0.97). Similar patterns were observed when applying the CACC categorization, however with fewer categories.

Conclusion: Associations (and directions of effect) between BMI and readmission differ based on patient age in this cohort; the CACC method provides a parsimonious alternative to CDC BMI categories.

Other

Epidemiology Beyond Its Limits Maret L. Maliniak* Maret Maliniak Lauren E. McCullough Avnika B. Amin Julia M. Baker Davit Baliashvili Julie Barberio Chloe M. Barrera Carolyn A. Brown Lindsay J. Collin Alexa A. Freedman David C. Gibbs Maryam B. Haddad Eric W. Hall Sarah Hamid Kristin R. Harrington Aaron Holleman John A. Kaufman Mohammed A. Khan Katie Labgold Veronica C. Lee Amyn A. Malik Laura M. Mann Kristin J. Marks Izraelle McKinnon Kristin N. Nelson Zerleen S. Quader Katherine H. Ross Supriya Sarkar Monica P. Shah Iris Yuefan Shao Jonathan P. Smith Kaitlyn K. Stanhope Marisol Valenzuela-Lara Miriam E. Van Dyke Kurt Vyas Timothy L. Lash

Background: Twenty-five years ago, journalist Gary Taubes published a Special News Report in Science titled "Epidemiology Faces Its Limits," which questioned the utility of nonrandomized epidemiologic research. To bolster his case, he selected numerous examples of research topics he viewed as unlikely to have public health implications. Studies have since accumulated for these associations. We evaluated the current evidence of the public health importance of these selected topics.

Methods: We identified all exposure-outcome associations mentioned by Taubes in his 1995 paper and collated meta-analyses and policy statements/scientific evaluations published by authoritative bodies pertaining to them. At least two independent reviewers assessed whether the public health consensus for each association was causal, non-causal, or indeterminate. Further independent review resolved discrepancies. Causal associations were those with meta-analysis results and a statement of causality by an authoritative body.

Results: Of the 70 exposure-outcome associations identified, we excluded 14 duplicates and 3 associations too vaguely worded for evaluation; 53 associations remained for assessment of causality. Among these, 11 were considered causal by Taubes, and our group concurs. An additional 10 associations, previously doubted by Taubes, were viewed as causal by our group and have explicit policy recommendations pertaining to them. They include associations between alcohol consumption and breast cancer, residential radon exposure and lung cancer, and use of tanning devices and melanoma. Of the remaining, our group viewed 6 as non-causal and 26 as indeterminate.

Conclusion: Twenty-five years later, epidemiology has reached beyond its limits. Many associations selected by Taubes as examples to denigrate epidemiologic research have proven to have important public health implications. This history should inform current debates about the reproducibility of epidemiologic research results.

Age dependent associations between patient characteristics and NAFLD, using NHANES data Syed Naqvi* Syed Naqvi Anthony Nunes, PhD

The prevalence of non-alcoholic fatty liver disease (NAFLD) in the US is projected to increase to over 100 million patients within 10 years and costs nearly $300 billion annually. The spectrum of NAFLD ranges from steatosis only to non-alcoholic steatohepatitis (NASH), NASH may progress to cirrhosis, hepatocellular carcinoma, or death. Research goal is to describe characteristics of NAFLD patients within stratum of age and to report age specific NAFLD prevalence and prevalence ratios by demographic and clinical characteristics. We hypothesize that age dependent associations between demographic/clinical characteristics and NAFLD can provide epidemiological insight to inform the development of diagnostic and treatment guidelines. Distributions of patient characteristics are reported by NAFLD, and within the following age groups: 18 and younger, 19-49, 50-64, 65-74, and 75+. Prevalence estimates and prevalence ratios of NAFLD are provided separately for each age group within strata of demographic and clinical characteristics of the NHANES participants.
The study population included 16,655 participants with data available from Mobile Examination Center (MEC) component of NHANES. Of this, 14,623 participants had sufficient data to determine NAFLD status. Prevalence of NAFLD generally increased with age; however, we observed a slight decline in prevalence among those over the age of 74. Prevalence ratios were calculated for various demographic and clinical factors and notable heterogeneity was observed across age groups. For example, the prevalence ratio of NAFLD for obese (>=30BMI) vs. non obese (<30 BMI) was 19.44 for patients below age of 18, and prevalence ratio steadily declined with increasing age to 2.75 for age group 75+. Similarly, prevalence ratio for diabetic vs. nondiabetic patients decreased from 3.99 for age group younger than 18 to 1.68 for 75+ age group. This descriptive hypothesis generating study should be followed-up with confirmatory analyses.

Other

Exposure to the World Trade Center disaster and exam performance among New York City public school students: a difference-in-differences analysis Erin Takemoto* Erin Takemoto Sean Locke Joan Casey Dana Goin Ingrid Giesinger Charon Gwynn Howard Alper Mark Farfel Robert Brackbill

The World Trade Center (WTC) disaster exposed children to environmental toxins, caused emotional and physical traumas, and disrupted the academic school year. WTC exposure health effects are well-documented; impacts on education outcomes, which have been associated with health over the life course, are not. We examined the WTC disaster's impact on math and English language arts (ELA) exam performance among 3rd and 6th grade New York City public school students.

Schools with 3rd or 6th grade classes and available address data in 2001 were geocoded to two exposure groups: exposed (0-1.5 miles from the WTC site) and unexposed (>6 miles from the WTC site). Propensity score matching was used to identify unexposed schools with similar exam performance to the exposed schools in the three years prior to the WTC disaster (1998-2001). Up to 3 unexposed schools were matched with replacement within a radius of 0.2*SD of the propensity score to each exposed school. Among matched sets, we conducted difference-in-differences analyses using linear mixed models to examine WTC impact on student-level continuous exam scores, taken in the spring of 2001 and 2002, among children in exposed versus unexposed schools. Random intercepts accounted for school-level clustering. Weighted models accounted for the variable matching ratio and were controlled for student-, school-, and area-level variables.

After matching, our study population included 8,175 3rd grade students in 10 exposed and 27 unexposed schools and 8,391 6th grade students in 5 exposed and 15 unexposed schools. WTC disaster exposure was associated with a decrease in 3rd grade math exam performance by 4 points (95% CI: -7.4, -1.1); we observed no differences in 3rd grade ELA or 6th grade math or ELA exam performance.

WTC disaster exposure had a small impact on math exam performance among 3rd graders, suggesting exposure to the WTC disaster, or other disasters, may have important implications beyond physical health effects.

Figure. Difference-in-differences estimates of the effect of the World Trade Center disaster exposure on subject-specific exam scores for New York City 3rd and 6th grade public school students (2001-2002).
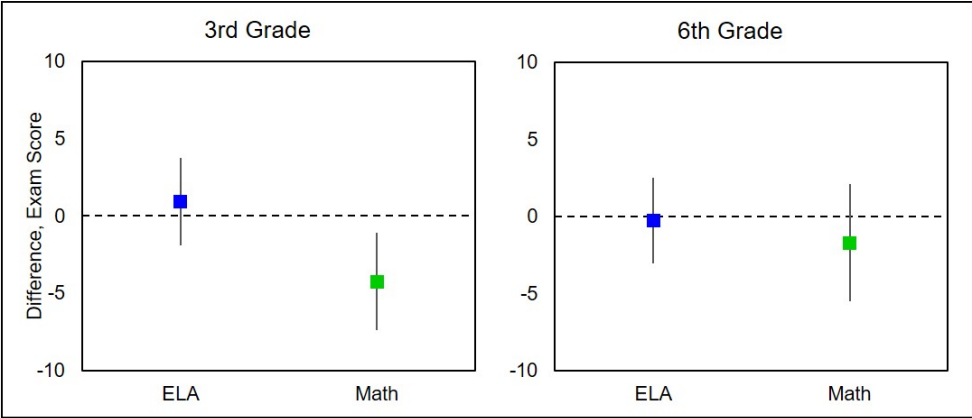
Abbreviations: ELA, English language arts
Models adjusted for: student level (race/ethnicity, English language learner, special education status, free/reduced price lunch eligibility), school level (total enrollment, teacher to pupil ratio), and area level (proportion of children living in poverty) variables.

Epidemiology is a Disruptive Field that Introduces Innovative Ideas Adan Becerra* 3647]
Becerra Olugbemiga Ekundayo Maynor Gonzalez Ashley Holub Meliha Salahuddin Tosin Onasanya Shanshan Li

Introduction: Characterizing the value and contributions of research papers by using bibliometric indices is an important goal for all scientists, including epidemiologists. One such paper-level metric recently developed is the disruption index, which varies between −1 and 1, and corresponds to science that *develops* ideas already proposed or *disrupts* a field by proposing new ideas, respectively. Here, we benchmark the disruptive index portfolio of epidemiology and compare it to all other scientific fields in PubMed. Methods: Using a publicly available dataset of calculated disruption indices for all PubMed papers published between 1954-2014, we defined the "Epidemiology Universe" as all papers published by the journals *Epidemiology, American Journal of Epidemiology, and International Journal of Epidemiology* (N=19,751) and all other papers in PubMed were defined as the "PubMed Universe" (N= 12,722,631). We compared mean disruption indices (absolute scale and percentile scale) between the "Epidemiology Universe" and the "PubMed Universe" using a Welch two-sample t-test. We generated kernel density curves of both groups and arbitrarily plotted 3 of the top 100 most disruptive papers in the "Epidemiology Universe" (one from each journal). Results: The Epidemiology Universe had a higher mean disruptive index score compared to the PubMed Universe (0.0023 versus -0.00055, difference = 0.0028, 95% CI= 0.0024, 0.0033). On the percentile scale, this corresponds to the average Epidemiology paper being in the 51st percentile versus the 49th percentile for the average PubMed paper. Conclusions: Using a bibliometric index that measures the degree to which a paper disrupts a field with new innovation, we find that epidemiology, as a field, is more disruptive than the PubMed Universe. Future analyses will use natural language processing to extract common themes in disruptive epidemiology papers.
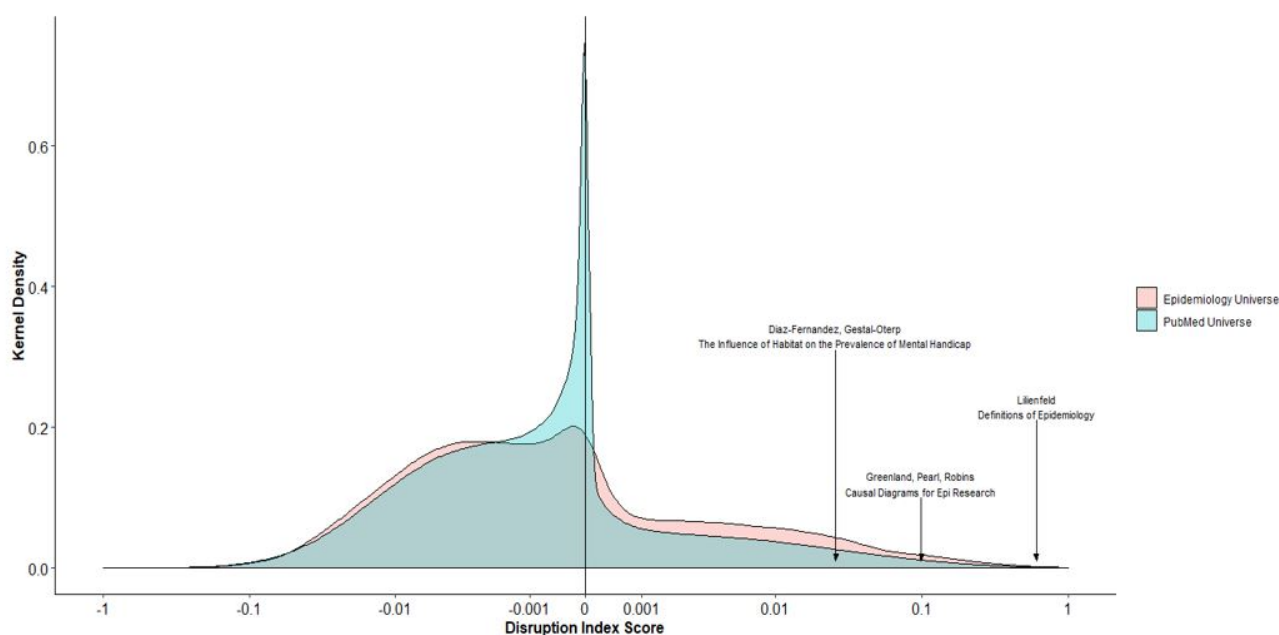
A comparison of childhood asthma case definitions based on parent-reported data Ruth J. Geller* Ruth Geller Janice A. Espinola Kohei Hasegawa Jonathan M. Mansbach Ashley F. Sullivan Carlos A. Camargo

Purpose: To identify the optimal research definition of asthma using only parent-reported data from children up to 5 years of age.

Methods: We analyzed data from a multicenter, prospective cohort study of 921 infants hospitalized for bronchiolitis. Follow-up was conducted via biannual parent telephone interviews. Three asthma definitions were developed using parent-reported data: (1) clinician diagnosis by age 5 years ("broad definition"), (2) clinician diagnosis by age 5 years with either asthma medication use (inhaled bronchodilator, inhaled or systemic corticosteroids, or montelukast) or asthma symptoms during age 4-4.9 years ("epidemiologic definition"), and (3) clinician diagnosis by age 5 years with either long-term inhaled corticosteroid use or asthma symptoms during age 4-4.9 years ("strict definition"). Definitions were evaluated using bivariate and multivariable associations with known asthma risk factors: family history of asthma and eczema and infant demographic factors (male sex, Black or Hispanic race/ethnicity [referent: non-Hispanic White]).

Results: The prevalence of asthma at age 5 years was approximately 30% for all three asthma definitions: 294/875 (34%) by the broad definition, 235/875 (27%) by the epidemiologic definition, and 229/875 (26%) by the strict definition. Asthma risk factors had similar associations with all three asthma definitions (Fig. 1).

Conclusions: Parent report of clinician-diagnosed asthma correlates well with known risk factors for asthma. We recommend using the epidemiologic definition in observational research limited to parent-reported data since this definition likely balances sensitivity vs. specificity. Future work will compare parent-reported asthma diagnosis against medical record data and measurement of airway inflammation and bronchial reactivity.

Figure 1. Associations of asthma risk factors with 3 definitions of childhood asthma using parent-reported data, from multivariable logistic regression models
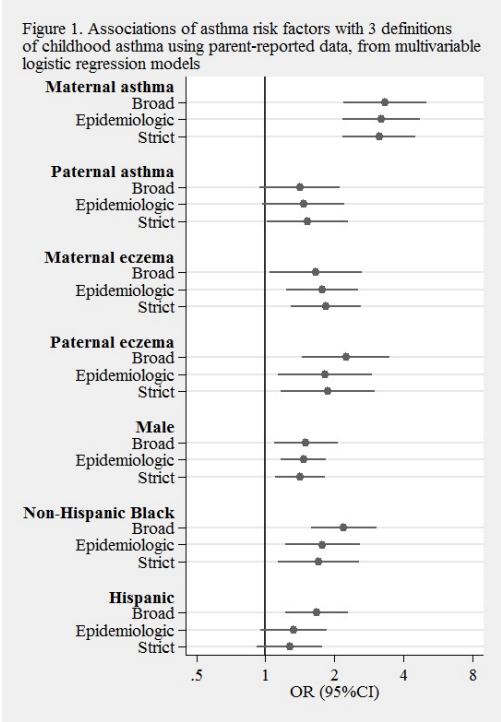
Maternal Occupational Exposure to Polycyclic Aromatic Hydrocarbons and the Risk of Isolated Congenital Heart Defects among Offspring Jenil Patel* Jenil Patel Wendy N Nembhard Maria D Politis Carissa M Rocheleau Peter H Langlois Gary M Shaw Paul A Romitti Suzanne M. Gilboa Tania A. Desrosiers Tabassum Insaf Philip J Lupo The National Birth Defects Prevention Study

Very few population-based studies have explored the association between women's gestational occupational exposures to polycyclic aromatic hydrocarbons (PAHs) and risks of congenital heart defects (CHDs) in their offspring despite suggestive evidence from animal model studies. We conducted a case-control study to assess the overall association and potential for exposure-response relation between maternal occupational PAH exposure during early pregnancy and CHDs using 4,775 CHD cases and 7,734 non-malformed control infants from the NBDPS (1997-2011).
Job information collected in the NBDPS maternal interview was used to assess occupational exposures to PAHs. Expert industrial hygienists estimated cumulative exposure to PAHs from exposure intensity and frequency scores, work duration, and work hours blinded to case/control status. After generating quartiles for cumulative exposure to PAHs during early pregnancy, we estimated crude and adjusted odds ratios (ORs) with 95% confidence intervals (CIs) using unconditional logistic regression for quartiles of PAHs exposure and CHD subphenotypes. Final models were adjusted for maternal age at delivery, education, race/ethnicity, smoking, anticonvulsant use, folic acid supplementation, and study center.
The prevalence of estimated PAH exposure was the same among mothers of cases and controls (10.2%). After multivariate adjustment, women in the highest quartile of PAH exposure were more likely to have offspring with two subphenotyoes of CHDs: conotruncal heart defects as group (OR 1.41; 95%CI 1.00-2.00) and tetralogy of Fallot (ToF) (OR 1.83; 95% CI 1.21-2.78), compared to mothers with no exposure. No other associations were observed.
We observed a moderate association of PAHs with conotruncal heart defects, which is consistent with evidence from animal models. While our study adds to the growing evidence on the role of PAHs on the risk of structural birth defects, a need for future studies with larger populations is indicated.

Maternal diabetes and risk for birth defects, by race and ethnicity, National Birth Defects Prevention Study, 1997-2011 Sarah C. Tinker* Sarah Tinker Suzanne M. Gilboa Cynthia A. Moore D. Kim Waller Regina M. Simeone Shin Y Kim Denise J. Jamieson Lorenzo D. Botto Sarah Fisher Jennita Reefhuis

Maternal pregestational diabetes (PGD) is a strong risk factor for birth defects. It is unclear whether the increased risk for birth defects associated with PGD differs by maternal race and ethnicity. We analyzed data from the National Birth Defects Prevention Study, a multi-site population-based case-control study of birth defects. Cases were from surveillance systems at up to 10 sites during 1997-2011; controls were randomly selected from the same population. Mothers of cases and controls participated in a computer-assisted telephone interview. We defined PGD as self-reported type 1 or 2 diabetes diagnosed before pregnancy. We used logistic regression to assess the association between PGD and birth defects, adjusting for pregestational obesity, and stratified by maternal race and ethnicity. We analyzed data from 37,655 mothers, 800 (2.1%) with PGD. Most of the adjusted odds ratios (aORs) for Hispanic and non-Hispanic black (NHB) mothers were stronger than those for non-Hispanic white (NHW) mothers. For hydrocephaly, the aORs for NHW, NHB, and Hispanic mothers were 3.4 (95% confidence interval [CI]: 1.3, 8.7), 14.8 (95% CI: 6.1, 35.8), and 20.6 (95% CI: 7.9, 53.8), respectively. For cleft lip with or without cleft palate the aORs were 1.9 (95% CI: 1.1, 3.3), 5.2 (95% CI: 2.7, 10.2), and 8.0 (95% CI: 3.3, 19.2) for NHW, Hispanic, and NHB mothers, respectively. Stronger associations with PGD were observed for Hispanic mothers than for NHW or NHB mothers for tetralogy of Fallot (aORs: 13.2, 3.9, and 2.5, respectively), hypospadias (aORs: 16.5, 1.9, and 1.6, respectively), and sacral agenesis (aORs: 278.6, 51.4, and 87.0, respectively). The differences we observed by race and ethnicity may reflect factors, potentially related to access to care, that influence glycemic control before pregnancy, which can substantially reduce the risk for birth defects.
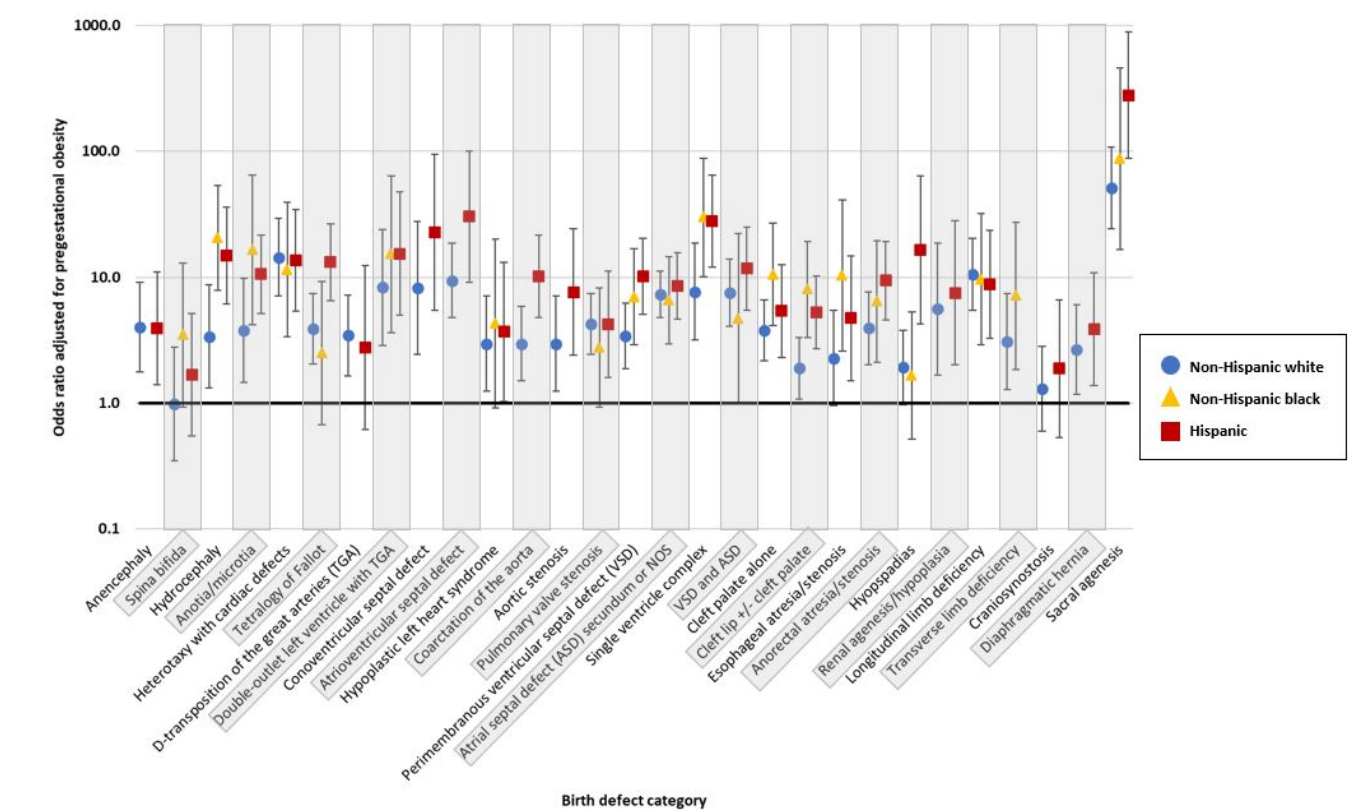
Patient Education and Knowledge Regarding Labor Induction Valery A. Danilack* Valery Danilack Leah Siegel-Reamer Liana Lum Cailey Kesselring E. Christine Brousseau Kate M. Guthrie

Introduction: Over 25% of deliveries in the U.S. involve labor induction, but there is concern about how little women understand about this process. We conducted postpartum qualitative interviews to elucidate women's knowledge and expectations of labor induction.

Methods: We recruited women who underwent labor induction during their most recent delivery from our hospital's postpartum unit. We conducted semi-structured qualitative interviews within two months of delivery. Research questions included expectations for the labor induction, sources of information, and explanations by medical staff before and during the process. Clinical details about the induction were obtained from the electronic medical record.

Results: From April-September 2018, we interviewed 36 women; 18 with a vaginal delivery and 18 with a cesarean delivery. The most common sources of information included prenatal care and friends or family; other sources included the internet, online forums, and videos/television. Knowledge of labor induction was influenced by how long before the induction a woman knew she would be induced and by the extent to which she sought information about induction. Seven women admitted knowing nothing about induction at the time of hospital admission. Women knew more about the use of oxytocin to stimulate contractions and less about cervical ripening methods. All women provided a reason for labor induction in the interview that was in agreement with their medical record. Women's accounts of the methods received throughout the labor induction process were also accurate. Women would like to be better informed of the overall process of labor induction and the expected sequence of events. However, women reported that hospital staff explained individual parts of the induction well.

Conclusions: Women would benefit from increased prenatal education from trusted sources in order to be more knowledgeable about the possible trajectory, duration, and components of labor induction.

Source of information about labor induction, frequency cited, and descriptions	Sample quotes Women are identified by parity and indication for induction
Prior Delivery 15 women with knowledge or expectations based on prior deliveries	"…When I had my first child a resident tried to do this Foley catheter balloon thing … she tried three or four times … and I bled more trying to get that thing in than my actual delivery. So, it was a horrible experience … which made me fear it on my third one." - Parity 2, Hypertensive Disorder
Prenatal Care 25 women received information from conversations with nurses, providers, or prenatal care classes or pamphlets	"My doctor explained it to me beforehand. When I came here, it actually happened the way she said it's gonna go, so I already knew what they were going to do, and that's what they did, so no surprises there." - Parity 0, Premature Rupture of Membranes
Friends or Family 18 women received information from friends, family, or support groups	"Everyone was either telling me their horror story of getting induced or, once in a while, there was someone who says how it's nice and quick and everything goes smoothly, so just people's opinions in general coming at you at totally different angles makes you a nervous wreck." - Parity 0, Late term
Social Media 7 women received information from social media groups or reading/participating in forums	"It was a lot to take in with all the different answers that girls and women were throwing out there. 'Cause I was on those social media groups a lot asking questions, too … I would rather talk to somebody who knows from experience than look up information." - Parity 0, Late term
Reputable Websites 6 women received information from hospital websites, national organizations, or peer reviewed academic research	"I also went through my graduate program website with databases and looked at journal articles … just to see what were the different types of induction that I might be looking at, and what was more commonly used…" - Parity 0, Other
Other Internet 15 received information from "Googling" or other internet sources besides social media or reputable websites	"Yeah, I Google everything, and I really shouldn't be doing that … No one should be doing that…" - Parity 0, Fetal Growth Restriction "I looked a lot of things up on YouTube. I watched labor and birth deliveries and how it went." - Parity 0, Late term
Television 2 women received information from TV shows	"Yeah. They gave me the pill, but I wasn't expecting the pill … I watch those baby shows where they give you the Pitocin and it goes through your system and active labor and everything. That's what I thought was gonna happen. I thought they were just gonna give me that." -Parity 1, Late term

Using Prenatal Tests to Estimate Pregnancy Start in Health Insurance Claims Data Jennifer Lyons* Jennifer Lyons Steven Bird Danijela Stojanovic Judith Maro Darren Toh Elnara Eynullayeva Andrew Petrone Rajani Rajbhandari Lockwood Taylor

Background: Identifying pregnancy start in administrative claims can be difficult in the absence of gestational age codes and for non-live birth deliveries. Our study aimed to develop a claims-based algorithm using codes for routine prenatal tests and fertility procedures to classify the timing of pregnancy start.

Methods: Using data from 16 health plans from 1/1/06-1/31/18, we identified live birth pregnancies and assigned a reference pregnancy start date using a previously validated algorithm. We defined 16 tests and procedures using ICD-9-CM and ICD-10-CM codes and used clinically recommended timing to estimate pregnancy start. We quantified the days difference between the reference start date and each estimated start date and defined performance as the proportion of estimated start dates that occurred within two weeks of the reference start date. We developed three algorithms by adding the prenatal tests in order of performance. We calculated the proportion of pregnancies captured by each algorithm and the median difference in days between the reference and algorithm identified start dates.

Results: Among 4,727,266 pregnancies, 97.9% had at least one prenatal test of interest. Performance ranged from 90.6% (nuchal translucency) to 20.1% (first trimester ultrasound). Algorithm 1 included the six highest performing tests (≥80%), captured 81.6% of pregnancies, and had a median difference of 5 days (IQR=7) compared to the reference start date. Algorithms 2 and 3 had lower cut offs for test performance (≥70% and ≥60%) and included 87.6% and 97.9% of pregnancies with median differences of 6 days (IQR=7) and 6 days (IQR=8), respectively, compared to the reference start date.

Conclusion: Our algorithms used routine prenatal tests and fertility procedures to define pregnancy start in a population of commercially- and Medicaid-insured pregnant women with live birth deliveries. Future research will assess the accuracy of these algorithms in non-live birth deliveries.

Association between body mass index and folate insufficiency indicative of neural tube defects risk among non-pregnant women of childbearing age in the United States, NHANES, 2007-2010

Vijaya Kancherla* Vijaya Kancherla Meryna Manandhar Hind Beydoun

Background: Maternal folate status during periconceptional period is associated with neural tube defects (NTD) in the offspring. We examined the association between body mass index (BMI) categories and blood folate concentrations, and specifically, red blood cell (RBC) folate concentrations indicative of NTD risk among non-pregnant women of child-bearing age (20-44 years) in the U.S.

Methods: We used data from 2007-2010 US National Health and Nutrition Examination Survey (NHANES). Overweight, obesity, and strata within obesity, were examined. Serum and RBC folate concentrations were examined as continuous and categorical variables. RBC folate concentrations were grouped indicating high ($\leq$585 nmol/l) and elevated risk (586-747 nmol/l) for NTDs. Unadjusted and adjusted prevalence odds ratios (aPOR) and their 95% confidence intervals (CI) were estimated using logistic regression.

Results: Of the 30,878 participants, 25.6% were overweight, 32.7% obese, and 32.3% had RBC folate concentration indicting NTD risk (<748 nmol/L). Overweight was not associated with RBC folate level for NTD risk; however, a marginally significant negative association was noted for overall obesity and RBC folate concentrations indicative of elevated NTD risk (aPOR=0.76; 95% CI=0.45, 1.00). A significant protective association was noted between Class 3 obesity (BMI $\geq$40 kg/m2) and folate concentration indicative of high NTD risk ($\leq$585 nmol/L) (aPOR=0.46; 95% CI=0.24, 0.89).

Conclusions: The prevalence of RBC folate concentrations indicating elevated or high NTD risk varied by level of obesity among non-pregnant women of child-bearing age. Further studies are needed to understand the folate pathway in overweight and obese women and subsequent NTD risk in their offspring.

Associations between prenatal maternal exposure to per- and polyfluoroalkyl substances (PFAS) and polybrominated diphenyl ethers (PBDEs) with birth outcomes among pregnant women in San Francisco

Stephanie Eick* Stephanie Eick Elizabeth K. Hom Thepaksorn Monika Izano Lara Cusing June-Soo Park Amy Padula Erin DeMicco Tracey Woodruff Rachel Morello-Frosch

Per- and polyfluoroalkyl substances (PFAS) and polybrominated diphenyl ethers (PBDEs) are used in consumer products for their oil and water repellent and flame retardant properties, respectively. However, there is growing concern about their potential harm to the developing fetus. Therefore, we examined the association between prenatal measures of PFAS and PBDEs in maternal serum during the 2nd trimester of pregnancy, with low birth weight (LBW; <2500 grams) and preterm birth (PTB; gestational age <37 weeks). Participants enrolled in this study were part of the Chemicals in Our Bodies cohort (N=510), which includes a diverse group of pregnant women from the San Francisco Bay Area. Women enrolled in this cohort were recruited between 2014 and 2018. Adjusted logistic regression models showed a slightly elevated odds of LBW associated with increasing concentrations of PFAS congeners, specifically PFNA (odds ratio [OR]= 1.56, 95% confidence interval [CI]= 0.85, 2.77), PFOS (OR=1.03, 95% CI= 0.59, 1.74), PFOA (OR=1.62, 95% CI= 0.87, 2.96), Me-PFOSA-AcOH (OR=1.05, 95% CI= 0.59, 1.77), PFHxS (OR=1.24, 95% CI= 0.70, 2.11). We also observed a slightly increased odds of PTB associated with higher concentrations of PFNA (OR=1.32, 95% CI= 0.78, 2.17), PFOA (OR=1.54, 95% CI= 0.89, 2.63), and Me-PFOSA-AcOH (OR=1.10, 95% CI= 0.71, 1.67). There was no evidence of an association between PBDEs exposures and LBW or PTB. Our findings suggest that prenatal exposure to PFAS may be associated with LBW and PTB, although future studies with more statistical power are needed to confirm these findings.
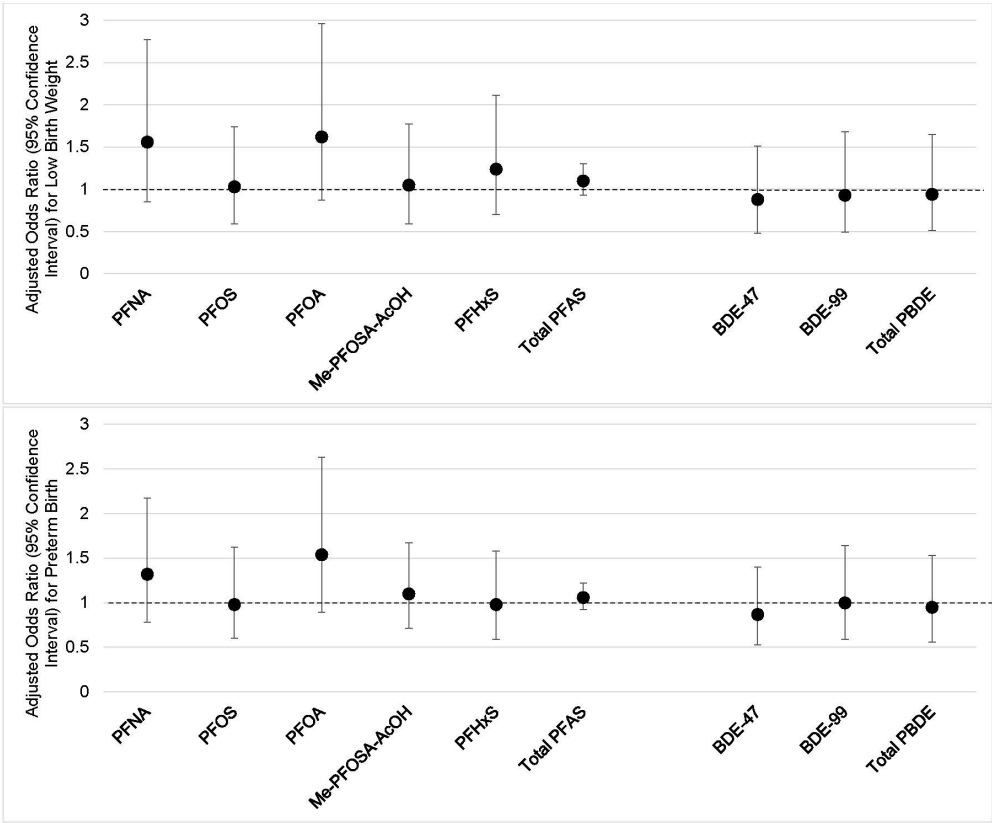
Using Data Science Methods to Identify School and Home Risk Factors Related to Asthma and Allergy Symptoms among School-aged Children in NY Xinlei Deng* Xinlei Deng Connie Jiang Ian Ryan Wangjian Zhang Bo Ye Tia Marks Yanji Qu George Thurston Xiaobo, Romeiko Shao Lin

Background
Few prior studies comprehensively assessed all major indoor environmental exposures from school and home settings on these outcomes, due to constraints of traditional methods. This study aimed to address these gaps by examining important school and home indoor factors for the allergy and asthma symptoms from various indoor exposures through machine-learning methods and provide a well-rounded understanding of asthma and allergy symptoms.

Methods
The Student Health and Physical Environment study was conducted in 2017-2019 using a cross-sectional design of randomly selecting 10 public schools in New York State. Home-related environment questionnaires and air quality measurements in school were collected. Indoor factors in school and home settings were examined for asthma and allergy symptoms. Random forest and decision tree models were applied to select important variables and interpret their relationships respectively.

Results
For asthma, the top five positively contributed factors were family allergy rhinitis (10.40%), pollen trigger (5.48%), bedroom carpet (3.58%), tobacco trigger symptom (2.98%) and secondhand smoking (2.56%), For allergy, the top 5 positively contributed factors were pollen trigger (10.88%), higher paternal education (7.33%), bedroom carpet (5.28%), family allergy rhinitis (4.78%) and higher mother education (4.25%). Decision tree model performed very well for each outcome (Asthma: AUCInternal_validation = 0.797, AUCCross_validation = 0.753, AUCExternal_validation = 0.812; Allergy: AUCInternal_validation = 0.819, AUCCross_validation = 0.790, AUCExternal_validation = 0.829) and suggested that tobacco trigger symptom was the leading factor in asthma symptoms, while pollen trigger and family allergy rhinitis were the leading factors in allergy symptoms.

Conclusion
Among many discovered risk factors, family history, tobacco trigger symptom and pollen trigger were the lead risk factors for asthma and allergy. Further studies are needed to confirm our findings.
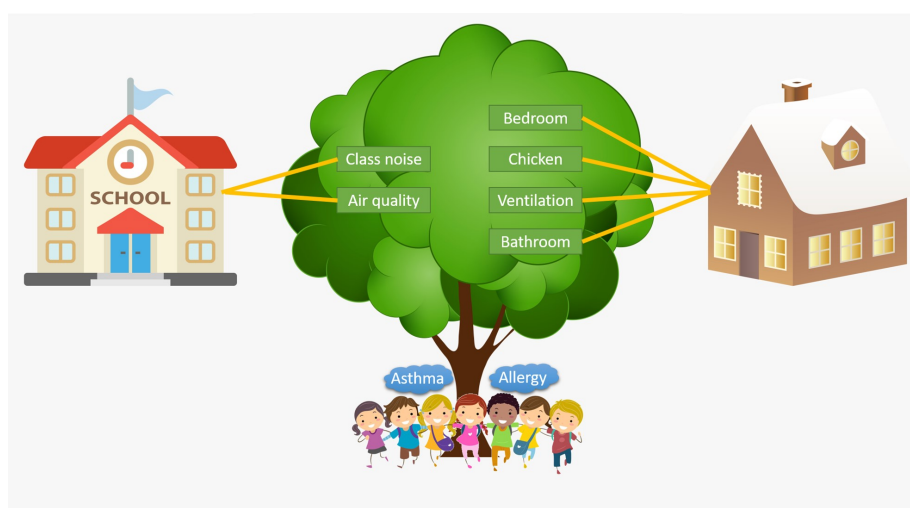
Over-the-counter analgesic use and reproductive outcomes Kerry S. Flannagan* Kerry Flannagan Lindsey A. Sjaarda Sunni L. Mumford Jeannie G. Radoc Victoria C. Andriessen Neil J. Perkins Jessica R. Zolton Robert M. Silver Enrique F. Schisterman

Over-the-counter analgesic use is common among women and may be perceived as safe, though it has been associated with risks to fecundability and pregnancy viability. However, the overall literature remains inconclusive, and many existing studies rely on retrospective or non-specific measurement of medication use. We examined urinary detection of acetaminophen and ibuprofen exposure in relation to fecundability, live birth, and pregnancy loss.

We followed 1218 women for up to 6 menstrual cycles while attempting conception and throughout resulting pregnancies. We classified women as positive or negative for acetaminophen and ibuprofen use while attempting conception and in early pregnancy with urine immunoassays. We estimated fecundability OR (FOR) and CI using discrete Cox proportional hazards models and RR of live birth and pregnancy loss with log binomial models. Covariates included age, race, BMI, education, use of other drugs and medications, time since last pregnancy, number of prior pregnancy losses, and usual menstrual pain severity. Acetaminophen and ibuprofen were adjusted for each other.

While trying to conceive, 147 (12%) and 396 (33%) participants tested positive for acetaminophen and ibuprofen, respectively; during pregnancy, 39 (5%) and 52 (7%) pregnant women tested positive, respectively. Preconception acetaminophen use was related to lower fecundability (FOR 0.74; 95% CI 0.57, 0.96) whereas ibuprofen was not (FOR 0.97; 95% CI 0.82, 1.16). Neither drug was associated with live birth (acetaminophen RR 0.90; 95% CI 0.70, 1.17; ibuprofen RR 0.93; 95% CI 0.78, 1.11) or pregnancy loss (acetaminophen RR 0.91; 95% CI 0.58, 1.43; ibuprofen RR 1.20; 95% CI 0.89, 1.61).

While we did not find an association between acetaminophen or ibuprofen and miscarriage, our results suggest that acetaminophen may be detrimental to fecundability. Future research should address dosage and duration of use of these drugs in relation to these outcomes.

Assessing joint effects of blood lead and air pollution on children's 3rd grade standardized test scores in New York City birth cohort from 1994 to 1998 Meeraj Kothari* Meeraj Kothari Jeanette A. Stingone Katharine H. McVeigh

Background: Ambient air pollution and elevated blood lead levels have been associated with poor academic outcomes among children. As these exposures co-occur, we aimed to estimate the joint effects of early-life exposure to lead and air pollution on children's academic outcomes.

Methods: Data for 167,394 children born between 1994 and 1998 in New York City were obtained through administrative data linkages of the birth registry, educational records and lead poisoning prevention program. Census tract at birth was used to assign annual average ambient concentrations of 40 air pollutants using the 1996 National Air Toxics Assessment. NY State 3rd grade standardized test scores for math were normalized by birth year of the child. Maximum venous blood lead level was assessed by the children's healthcare provider and the median age of measurement was 12 months. Multiple imputation was performed using predictive mean matching to impute missing blood lead data. Elastic net, a type of penalized regression, was used for selection of air pollutants. Multiple linear regression models were fit including potential confounders identified through directed acyclic graph analysis and results were pooled using Rubin's rules.

Results: The elastic net analysis identified 9 out of 40 air pollutants to be linearly correlated with standardized math scores. For each 5 mcg/dL increase in blood lead, the standardized math score was 4.1% (95% CI: 3.3%, 4.9%) lower, adjusting for potential confounders. The estimated effect of the identified air pollutants was similar across strata of blood lead levels, although slightly smaller in magnitude among children with higher blood lead levels.

Conclusions: Maximum venous blood lead levels and air pollution were individually associated with the standardized math scores, upon adjusting for potential confounders. We did not observe a larger effect of air pollutant exposure among children with elevated blood lead levels in stratified analyses.

Gestational and Postpartum Weight Trajectories among Women With and Without Asthma in the Breathe, Wellbeing, Environment, and Lung Function Study (B-WELL-Mom) Danielle Stevens* Danielle Stevens William Grobman Leah Lipsky Matthew Rohn Andrew Williams Jenna Kanner Seth Sherman Zhen Chen Pauline Mendola

Aberrant weight gain during pregnancy and post-partum weight retention have been associated with adverse outcomes for women and their offspring. We examined whether weight trajectories across pregnancy and postpartum differed between women with (n=291) and without (n=98) asthma enrolled in a prospective cohort study at two U.S. hospitals. Piecewise linear mixed models examined whether there were significant differences in weight gain between asthmatic and non-asthmatic women throughout gestation and in the postpartum period. Secondary analyses assessed whether early pregnancy BMI (kg/m2) modified the associations of interest, and whether baseline asthma atopy, control, onset, or corticosteroid use impacted the observed associations. All models adjusted for age, race/ethnicity, income, marital status, maternal education, cigarette smoking, parity, breastfeeding exclusivity and duration, postpartum depression, study site, and early pregnancy BMI. In a typical 40-week gestation, women with asthma gained 3 lbs excess weight than women without asthma (27.7 lbs (25.6, 30.0) and 24.8 lbs (21.1, 28.6), respectively). This excess weight gain was retained up to 3 months postpartum (asthma: 15.1 lbs (13.1, 17.2) and no asthma: 11.9 lbs (8.5, 15.4)). With respect to early pregnancy BMI, this pattern was similar among overweight (BMI 25-30) and obese (BMI ≥ 30) women, but no differences in weight gain by asthma status were observed among women with BMI < 25. Corticosteroid use – specifically inhaled corticosteroid use – contributed to excess gestational weight gain but not postpartum weight retention. Future research should assess whether this weight gain contributes to adverse maternal and offspring health outcomes in pregnancies impacted by asthma.

Predicting Prolonged Length of Stay in Hospitalized Children with RSV Krista Wollny* Krista Wollny Amy Metcalfe

Background: Respiratory Syncytial Virus (RSV) is the most common cause of respiratory tract infections in children. The hospital course is challenging to predict due to the absence of specific treatments for RSV. The overarching aim of this study is to predict prolonged length of stay in children admitted to the hospital with RSV.

Methods: We examined the National Inpatient Sample (NIS), which contains 20% of all hospitalizations in the United States. Children <5 years diagnosed with RSV were included. The primary outcome was prolonged length of stay (≥7 days). Logistic regression models were developed using bootstrapped samples of the NIS data from 2016. Internal validation was completed using the 2016 data. Data from 2015 were used to test for the external validity of the models.

Results: The first model included age, transport, intubation, comorbidities (congenital cardiac disease, chronic lung disease, neuromuscular disease, trisomy 21 and immunosuppression), location, and teaching status. Model 1 had an AUROC curve of 0.7228 (95% CI: 0.7056-0.7388). A second model was developed to examine if the number of comorbidities a child had could replace the specific comorbidities. Model 2 had an AU ROC curve of 0.7222 (95% CI: 0.7062-0.7395). Both models performed similarly in the external validation analysis.

Conclusion: The analysis suggests that the variables that predict a prolonged length of stay for RSV include younger age, transport from an acute care hospital, intubation, increased number of comorbidities, urban hospitals and teaching hospitals. Future studies could explore the clinical presentation of children with RSV that predicts prolonged length of stay.

Perinatal & Pediatric

Application of propensity score matching and inverse probability of treatment weighting to assess a community-based nutrition intervention in Armenia Arin A. Balalian* Arin A. Balalian Vahe Khachadourian Hambardzum Simonyan Sharon Daniel

Child malnutrition is a major issue in conflict zones. Numerous interventions have sought to reduce malnutrition. Nonetheless, elimination of malnutrition—one of the sustainable development goals—could be achieved by evidence-based interventions.

The aim of the current study was to use propensity score matching and inverse probability weighting to assess the causal effect of a community-based multidisciplinary intervention on children's two main outcomes: anemia and stunting.

In 2016, a quasi-experimental study was conducted to compare the communities exposed and not exposed to a community-based multidisciplinary program, including food supplementation and healthcare capacity-building components in a chronic conflict zone in the northeastern border of Armenia. We included 6month to 6-year-old children and their caregivers in the study.

In 2016, 983 children were included in the study. We matched 308 exposed children with unexposed children based on propensity scores. The entire sample was used to calculate relative risks using inverse probability weighting. The relative risk of average treatment effect among treated for stunting among children from the exposed communities estimated by propensity score matching was 1.58 (95% CI 0.97–2.57). Nevertheless, children who took part in the program had a lower relative risk of anemia (0.31; 0.21–0.45). The relative risk for average treatment effect in entire population and average treatment effect among treated, estimated by inverse probability weighting, were substantially lower for stunting (1.10, 0.71–1.72 and 1.21, 0.79–1.64, respectively), though similar for anemia (0.35, 0.24–0.50 and 0.32, 0.23–0.46, respectively).

The program was successful in reducing the risk of anemia among children in exposed communities; nonetheless the impact on stunting is uncertain. Marginal models could be used for similar quasi-experimental settings when the causal effect of intervention in population is of interest.

Paternal arsenic exposure increases risk of myelomeningocele among offspring in a highly-exposed population Gwen Tindula* Gwen Tindula Sudipta Kumer Mukherjee Sheikh Muhammad Ekramullah DM Arman John Obrycki David Christiani Maitreyi Mazumdar

Neural tube defects, severe birth defects that occur when the neural plate fails to close in early gestation, continue to be a pressing public health concern, despite advances in prevention from folic acid supplementation. Arsenic, a chemical naturally occurring in soils, has been shown to induce neural tube defects in animal models and could serve as a risk factor for neural tube defects in humans. Given the limited research on arsenic neurotoxicity in humans, we investigated the relationship between arsenic and risk of myelomeningocele, a common and severe form of neural tube defect, in a case control study in Bangladesh. We also explored the interaction between arsenic levels and maternal serum folate. We analyzed arsenic in maternal and paternal toenail samples collected at the child hospital visit using inductively coupled plasma mass spectrometry. A total of 276 participants (156 cases and 120 controls) were included in the analysis. On average, parents of cases had higher levels of arsenic in toenails than parents of controls. Maternal toenail arsenic levels were not significantly related to case status in the main effect model. In the paternal model, a 1-unit increase in the natural logarithm of toenail arsenic was significantly associated with 75% greater odds of being a case (adjusted odds ratios: 1.75) compared to being a control after adjusting for maternal serum folate level, parental age, child age, birth facility, and child sex. Results did not suggest an interaction between paternal arsenic and maternal serum folate. The findings from this study provide novel insight into the role of arsenic in neural tube defect risk in humans and add to the growing body of literature of the influence of paternal environmental factors on child health outcomes.

Perinatal & Pediatric

Current prevalence of periconceptional folic acid supplement use and its determinants in Germany: Findings from a cross-sectional study Vijaya Kancherla* Vijaya Kancherla Clara Wegner Anke Lux Andrea Köhn Dirk Bretschneider Kristina Freese Mathias Heiduk Anke Redlich Daniela Schleef Gerhard Jorch Anke Rissmann

Background: Many countries in Europe, including Germany, do not have mandatory fortification of staple foods with folic acid to prevent neural tube defects (NTDs). Alternately, these countries rely on voluntary intake of folic acid supplements by women of reproductive age as a primary prevention strategy for NTDs. Studies in the past in the European region show sub-optimal prevalence of folic acid supplement use in spite of programs educating women about folic acid. We examined periconceptional folic acid supplement use among women of childbearing age and factors associated with it in a large population-based sample in Germany.
Methods: We conducted a cross-sectional survey targeting all maternity units in Magdeburg, Saxony-Anhalt, Germany between January and July, 2019. Data were collected using interviews. Prevalence of periconceptional folic acid supplement use was assessed among pregnant women and women in their early post-partum period. Logistic regression was used to estimate prevalence odds ratios (POR) and 95% confidence intervals (CI) for predictors. Interaction was assessed for pregnancy intention and folic acid awareness.
Results: A total of 1004 women (228 pregnant and 776 in post-partum) participated in the study with a response rate of 94.3%. Prevalence of folic acid supplement use was 41.5% (95% CI=37.7, 45.7). Multivariable analysis showed age, educational qualification, marital status, pregnancy intention, parity, and awareness of folic acid's importance as significant predictors of periconceptional folic acid supplement use. There was no significant interaction with pregnancy intention or folic acid awareness. Information about folic acid obtained from books, doctors, friends, media, pharmacy, and relatives, but not partners, increased the likelihood of periconceptional folic acid use.
Conclusions: Less than 50% of women in the study took periconceptional folic acid. Targeted promotion of timely folic acid supplement use should be done by gynaecologists and primary care

Evaluation of appropriateness of hospital admission for preterm labor concerns Marni Jacobs* Marni Jacobs Carolina Martinez Louise Laurent

Pregnant women with signs or symptoms of preterm labor are often admitted to the hospital as it is difficult to predict who is at risk for preterm delivery. This study examines 97 women with singleton pregnancies < 34 weeks gestational age (GA) admitted to the hospital from January – December 2016 for possible preterm labor. Time from initial hospitalization to delivery and associations with characteristics at initial presentation were examined using Fisher's exact test. Mean GA at admission was 28.9±3.4 weeks and GA at delivery was 35.0±5.0 weeks (44.3% preterm). Overall, 29 women (30%) delivered within one week of admission; of those, nearly half (n=14, 48%) delivered within the first 24 hours. Two-thirds (n=64) delivered ≥ 30 days after initial hospitalization. Among those with presentation details (n=87), 21 (25%) were admitted for short cervix only, while 39 (45%) presented with uterine contractions. Women who delivered within the first week were more likely to have contractions at initial presentation (21/28, 75%) than those who delivered after the first week (18/59, 31%, p = 0.0006), and were more likely to have been transferred from an outside hospital (37% vs. 13%, p = 0.02). However, 46% presenting with contractions delivered more than one week after admission. Only 3 women admitted for a short cervix (14%) and 4 with other preterm labor symptoms (abdominal pain, vaginal bleeding, discharge) (15%) delivered within one week, with 2 of the patients with short cervix or other symptoms being noted to have advanced cervical dilation. Our findings suggest that many admissions for preterm labor may be unnecessary, potentially incurring increased costs and stress. Providers could consider outpatient management of women presenting with signs or symptoms other than contractions or advanced cervical dilation. Future work will consider additional markers for preterm labor and compare outcomes in women discharged home from triage rather than admitted to the hospital.

Perinatal & Pediatric

Preterm birth and violence during pregnancy: A 7-year population-based birth cohort study in Ontario, Canada Erica Erwin* Erica Erwin Kat Denize Yanfang Guo Daniel J Corsi Kari Sampsel Katherine A Muldoon

Background: Globally, an estimated 15 million babies are born preterm per year. Violence and abuse during pregnancy can cause serious psychological and physiological stress that can impact the health of newborns including prematurity. We evaluate this association between abuse during pregnancy and preterm birth within a provincial birth registry in Ontario, Canada.

Methods: This study is a 7-year retrospective population-based birth cohort study (1apr12 to 31mar19) using data from the Ontario Birth Registry (Better Outcomes Registry & Network, BORN) and the Canadian Census. Abuse during preconception and/or pregnancy is a mandatory question in Ontario and is defined in the registry as a self- disclosed threat of or actual physical, sexual, psychological, emotional or financial abuse. Preterm birth was defined as a birth between 20 and 37 weeks gestation. We used a log binomial regression model with a log-link function to estimate the adjusted relative risk (aRR) of preterm birth between pregnancies where abuse was disclosed compared to unexposed pregnancies. The model was adjusted for maternal age, median neighborhood income quintiles and population size.

Results: Between 2012-2019, there were 715,725 pregnancies in Ontario and 18,236 (2.55%) cases of abuse disclosed during pregnancy. The prevalence of preterm birth was 9.65% among pregnancies where abuse was disclosed, compared to 7.16% in unexposed pregnancies. The risk of preterm birth was 33% higher among pregnancies where abuse was disclosed, even after adjusting for the potential confounding effects of age, income and community size (aRR 1.33 95% CI: 1.27-1.39).

Conclusion: Preventing preterm births begins with healthy pregnancies. This study has documented a 33% increase in the risk of prematurity among women who disclose abuse during pregnancy. Screening for violence within routine prenatal care should be included into assessments for risk of preterm birth and other adverse perinatal outcomes.

The effect of gestational age at delivery on the association between pre-pregnancy BMI and perinatal death. Jeffrey N Bone* Jeffrey Bone KS Joseph Robert Platt Sarka Lisonkova

Introduction
The pathophysiology of obesity-associated perinatal death is not fully understood. Increased rates of perinatal death in women with higher pre-pregnancy body-mass-index (BMI) may be partly due to lower gestational age (GA) at delivery. Our aim was to quantify the indirect effect of pre-pregnancy BMI on perinatal death mediated through differences in GA at delivery.

Methods
The study included all singleton births at ≥20 weeks' gestation in British Columbia, 2004-2017; pregnancy terminations and births missing with BMI were excluded (28%). Pre-pregnancy BMI categories were: underweight (BMI 30m/kg2). Data were obtained from the British Columbia Perinatal Database Registry. The proportion of the association between BMI and perinatal death mediated by GA at delivery (in weeks) was estimated using natural effect models, adjusted for potential confounders. Sensitivity analyses examined potential effect of unmeasured confounding between BMI and perinatal death, and GA and perinatal death.

Results
In a total of 392,820 women, the proportions of underweight, overweight, and obese women were 6.0%, 20.6%, and 12.8%, respectively. Women with higher BMI had lower GA at delivery. Perinatal mortality was elevated in overweight (AOR=1.22, 95% CI 1.08-1.37) and in obese women (AOR = 1.55, 95% CI 1.36-1.77). Mediation analysis estimated 63.1% of the association between obesity and perinatal death was mediated by GA at delivery (natural indirect effect AOR =1.32, 95% CI 1.23-1.42, natural direct effect AOR=1.18, 95% CI 1.05-1.32). Similar, but smaller effects were seen when comparing overweight vs normal BMI.
Estimated effects were moderately robust to unmeasured confounding.

Conclusion
Under specific assumptions, the results suggest that about 60% of the association between pre-pregnancy obesity and perinatal death is mediated by the lower GA among obese women.

Perinatal & Pediatric

Impact of postnatal growth on neurodevelopmental impairment by sex at 2 years of corrected age in a European cohort of very preterm children Rym El Rafei* Rym El Rafei Pierre-Henri Jarreau Mikael Norman Rolf Felix Maier Henrique Barros Patrick Van Reempts Pernille Pedersen Marina Cuttini Jennifer Zeitlin

Background: Extra-uterine growth restriction (EUGR) is prevalent among very preterm (VPT) infants and has been associated with impaired neurodevelopment; some research suggests that boys may be more vulnerable to the effects of poor growth. We investigated postnatal growth during the neonatal hospitalization and neurodevelopment at 2 years of corrected age (CA) by infant sex in a VPT cohort. Methods: Data come from the EPICE (Effective Perinatal Intensive Care in Europe) population-based cohort of births <32 weeks of gestation from 11 European countries (N=4196 infants discharged home <50 weeks' postmenstrual age and followed up at 2 years CA). Postnatal growth was measured by (1) the difference in Z-scores of discharge weight and birthweight (using Fenton's postnatal charts and a fetal growth chart) and (2) weight-gain velocity based on Patel's exponential model. Moderate to severe neurodevelopmental impairment was assessed using a parent-report questionnaire (standardized questions for motor, visual and hearing function and PARCA-R for non-verbal cognition). Published cut-offs were used to define EUGR as none, moderate and severe for each indicator. We estimated risk ratios (RR) adjusting for maternal and neonatal characteristics overall and by sex.
Results: The prevalence of impairment at 2 years of CA was 16.8%; it was higher for boys (19.7%) than girls (13.7%). Severe EUGR, defined by delta Z-scores and velocity indicators was moderately associated with impairment after adjustment: RR: 1.2, 95% Confidence Intervals (IC): 0.9-1.6 and RR: 1.3, 95%CI 1.0-1.5, respectively, but this reflected a stronger association for boys (RR: 1.7, 95%CI: 1.3-2.3 and RR: 1.5, 95% CI: 1.2-2.0, respectively) and no association for girls.
Conclusion: We found an association between EUGR and neurodevelopment at 2 years among VPT boys but not girls. Understanding why boys have increased susceptibility to the effects of poor growth is needed to develop appropriate management strategies.

What measures should be used to compare postnatal growth among preterm infants in international research? Rym El Rafei* Rym El Rafei Pierre-Henri Jarreau Mikael Norman Rolf Felix Maier Henrique Barros Patrick Van Reempts Pernille Pedersen Marina Cuttini Jennifer Weitlin

Background: Extrauterine growth restriction (EUGR) is prevalent among very preterm (VPT) infants and is related to poor neurodevelopment. International research on this topic is limited by the absence of consensual measures of postnatal growth. This study compared EUGR prevalence in a European VPT cohort using different indicators.

Methods: Data come from the EPICE (Effective Perinatal Intensive Care in Europe) cohort of births <32 weeks of gestational age (GA) from 11 European countries (N=6,260 infants discharged home <50 weeks of postmenstrual age). Five EUGR indicators were defined based on: discharge-weight percentiles using (1) Fenton charts and (2) Intergrowth-21st (IG) charts; delta-Z-score measures (discharge weight-birthweight Z-scores) using (3) Fenton for both discharge and birthweights (4) Fenton for discharge weight and a fetal growth reference for birthweight; weight gain velocity using (5) Patel's exponential model. Maternal and neonatal characteristics were used to adjust for case-mix. Mean birthweight at 40 weeks' GA per country was used to investigate whether differences in population size correlate with VPT EUGR prevalence.

Results: Greater than two-fold differences in EUGR prevalence were observed between countries for all indicators. The country-level prevalence of discharge weight <10th percentile using Fenton and IG charts were strongly correlated with population size (Spearman's rho: -0.84 (P<.001) and -0.87 (P<.001), respectively). Delta Z-scores using the fetal growth reference and weight-gain velocity were independent of the country's term birthweight, but high variation persisted in EUGR prevalence even after case-mix adjustment.

Conclusion: High variability in EUGR prevalence among VPT infants exists between European countries, regardless of the indicator. The correlation of discharge weight percentiles with population size suggests that common norms should not be used to assess VPT growth in international research.

Figure 1: correlation of unadjusted and adjusted EUGR prevalence defined as discharge weight under the 10th percentile of Fenton postnatal charts, with term birthweight by country
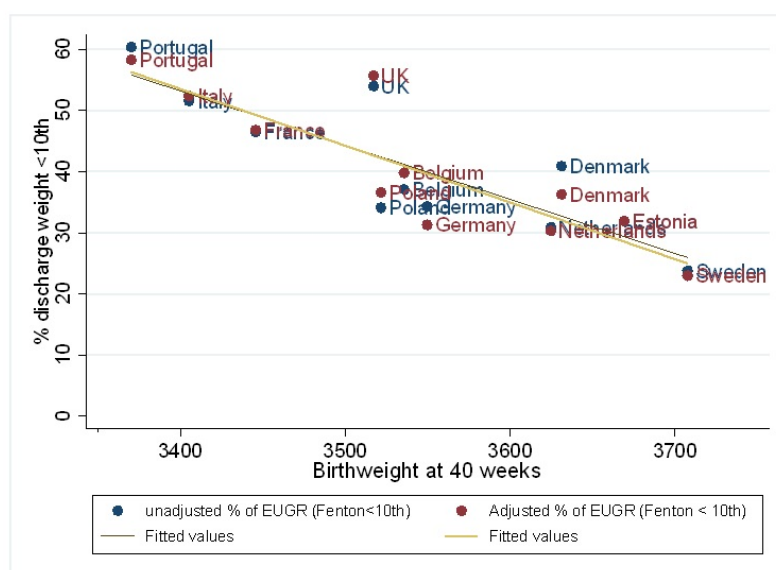
Note: Spearman's rho = -0.84, P<.001 and -0.89, P<.001 for unadjusted and adjusted RR, respectively. Adjustments for maternal (age, parity, foreign born) and neonatal (gestational age, small for gestational age, sex, feeding at discharge, any severe neonatal morbidity, bronchopulmonary dysplasia) characteristics

Adequacy of Nutritional Intake in Dichorionic Twin Pregnancies: Results from the NICHD Fetal Growth Studies
Samrawit F. Yisahak* Samrawit Yisahak Sunni L. Mumford Stefanie N. Hinkle Katherine L. Grantz Roger B. Newman William A. Grobman Jagteshwar Grewal

OBJECTIVE: Twin pregnancies generate greater nutritional demands than do singleton pregnancies. Due to the paucity of longitudinal dietary data in non-singleton pregnancy cohorts, the adequacy of dietary intake in women carrying twins is largely unknown. Using data from a prospective multi-site U.S. study, we longitudinally compared the nutritional intake of women with twin pregnancies to the Dietary Reference Intake recommendations.

METHODS: The dietary intake of 148 women carrying twins was assessed in each trimester using a self-administered food frequency questionnaire. We examined changes in total energy and macronutrient composition using repeated measures ANOVA and false discovery-rate adjustment. In the absence of generally recognized twin-specific recommendations, we quantified the proportion of women whose total energy intake was below the trimester-specific Estimated Energy Requirements (EER) for women with singleton pregnancies and whose percent energy from macronutrients was outside the Acceptable Macronutrient Distribution Range (AMDR). We accounted for differential loss to follow-up using inverse probability weighting.

RESULTS. Total energy intake by women carrying twins (1987 ± 867 kcal/day; 21667 ± 1029 kcal/day; 2282 ± 1116 kcal/day, p=0.10) increased only modestly in each trimester. Macronutrient composition did not change significantly (Figure). At each trimester, 62.3%, 69.6%, and 71.7% of women had total energy intake below the EER recommended for singleton gestations. Most women also had total fat intake above the AMDR (Figure).

CONCLUSION: Women with twin pregnancies did not make substantial changes in energy and macronutrient intake as gestation progressed. A majority of these women also failed to meet trimester-specific EERs set for singleton pregnancies. The consequences of this failure should be investigated further, but it may be a contributor to the third trimester slowing of fetal growth typical of twin gestations.

Figure: Trimester-Specific Total Energy Intake and Macronutrient Composition among Women with Dichorionic Twin Pregnancies in the NICHD Fetal Growth Studies
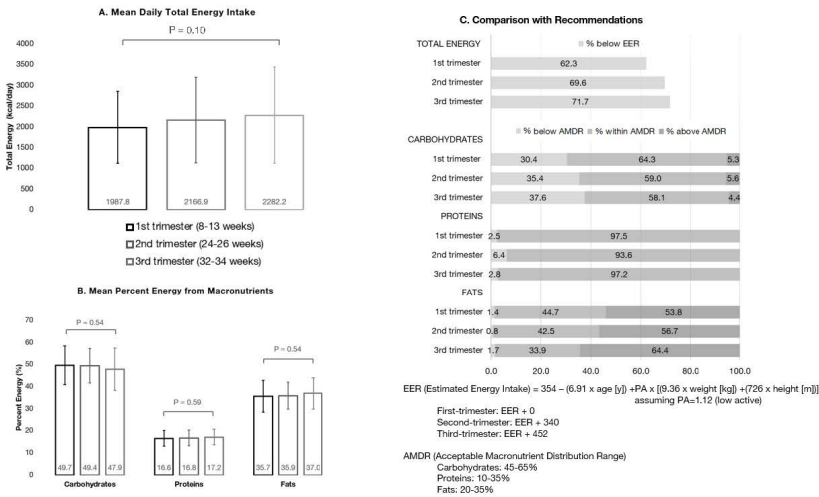
Significance of presenting the absolute and relative measures of association between neonatal abstinence syndrome and health insurance status Amna Umer* Amna Umer Christa Lilly Candice Hamilton Janine Breyel Collin John

The incidence of neonatal abstinence syndrome (NAS) is higher in Medicaid-financed births vs. privately insured births. A few state level studies have demonstrated this association on the relative scale only. The main objective of this study was to examine the association of NAS and health insurance status for the state of West Virginia (WV). We compare our findings to another state-level study in Wisconsin (WI) (Atwell et al., 2016) and demonstrate the importance of presenting both the absolute and relative measures of association. We used Project WATCH surveillance system data for all WV residents' births, N= 30,902. The effect size was calculated on the relative scale (risk ratio (RR) and odds ratio (OR)) and on the absolute scale (risk difference (RD)) along with its 95% CI. We also calculated the number needed to harm (NNH), by computing the reciprocal of the RD. The odds of NAS for Medicaid-insured newborns in WV was 6.72 times that of privately insured group (OR = 6.72; 95% CI: 5.74, 7.87). For the absolute measure of association, the excess risk (RD) associated with NAS in the Medicaid vs. privately insured newborns was 68.60 cases per 1000 live births. The NNH was 14.58 (95%CI: 13.60 – 15.70). Our results are similar to WI on the relative scale (OR = 8.4; 95% CI: 7.4 – 9.5). However, on the absolute scale in WI the RD was 10.5 cases per 1000 live births in the Medicaid vs. private insurance group. The NNH showed that for every 15 newborns enrolled in Medicaid in WV and every 95 enrolled in WI, one additional newborn will be diagnosed with NAS. Although on the relative scale our findings are similar, on the absolute scale we observed more than 6 folds increase in the risk of NAS in the Medicaid vs. privately insured newborns in the state of WV. Thus, by reporting both the relative (RR and/or OR) and the absolute (RD) measures of this association, our study was able to better illustrate the magnitude of this association for the state of WV.

A 7-year investigation of violence and abuse during pregnancy: Prevalence, patterns and prevention strategies Erica Erwin* Katherine Muldoon Erica Erwin Kathryn Denize Yanfang Guo Daniel Corsi Kari Sampsel

Background: Pregnancy can increase economic and psychological stress and escalate the risk of violence, posing serious risks to maternal and fetal health. This study was designed to estimate the annual and age-specific rates of abuse among pregnant women in the province of Ontario, Canada.

Methods: We conducted a 7-year retrospective population-based cohort study (April 1st, 2012 to 31 March, 2019) using data from the Ontario Birth Registry (Better Outcomes Registry & Network, BORN). The sample includes a comprehensive capture of all pregnancies that resulted in a live or still birth in a hospital, home or birth centre among Ontario residents. Screening for abuse during pregnancy is a mandatory question and is defined as 'a self-disclosed threat of or actual physical, sexual, psychological, emotional or financial abuse'. The annual standardized rate was calculated per 1,000 births, age stratified rates were calculated by age group (18 and under, 19-24, 25-29, 30-34, 35-39, 40+). Poisson regression models were used to estimate the rate ratio (RR) and 95% Confidence Interval (CI) across the 7-year period. Stratified models were run for each age group.

Results: Out of 715,725 births registered between 2012-2019, there were 18,236 (2.55%) cases of abuse disclosed during pregnancy, ranging from 2,463 to 2,766 per year. The annual rate of abuse was 25.5 per 1,000 pregnancies. Abuse was documented across all age groups, with the highest rates among adolescents 18 years and under (81.63 per 1,000) and 19-24 years (46.72 per 1,000). The overall rate of abuse remained stable over time (RR:1.00, 95% CI:0.94-1.06), as did the rates in each age group.

Conclusion: While under-ascertainment is an ongoing challenge, over 18,000 pregnancies in Ontario were identified through a universal screening program. Abuse was seen across all age groups, with highest rates among adolescent pregnancies. The rates remained consistently high and stable over time.

The Impact of a Lifestyle Intervention on Physical Activity among Latinas with a History of Abnormal Glucose Tolerance in Pregnancy: Estudio PARTO Kathryn A. Wagner* Kathryn Wagner Sarah Burkart Bess H. Marcus Penelope Pekow Milagros C. Rosal JoAnn E. Manson Barry Braun Lisa Chasan-Taber

Low physical activity (PA) in the postpartum period is associated with an increased risk of developing type 2 diabetes, particularly for women with a history of gestational diabetes mellitus. However, postpartum PA trials are sparse and often failed to include Latinas, who experience disproportionately high rates of diabetes and low rates of PA. We therefore assessed the impact of a culturally modified, motivationally targeted, individually-tailored intervention on postpartum PA and PA self-efficacy among participants in Estudio PARTO, a randomized trial conducted in Western Massachusetts from 2013-17. Latinas who screened positive for GDM were randomized to a Lifestyle Intervention (LI, n=100) or to a comparison Health and Wellness control group (HW, n=104) during late pregnancy. Exercise goals in LI were to meet American Congress of Obstetrician & Gynecologists (ACOG) guidelines for postpartum PA, while there was no mention of exercise behavior change in the HW group. The Pregnancy Physical Activity Questionnaire (PPAQ) was used to measure total PA at baseline (24-28 weeks gestation), and at 6 weeks, 6 months and 12 months postpartum. Based on an intent-to-treat analysis using mixed effects models, we observed no significant group by time interaction with regard to PA nor self-efficacy measures. However as compared to baseline levels, women in the LI group had significant increases in MVPA at 6 months (mean change=24.5 MET-hrs/wk, p=0.03) and 12 months postpartum (30.9 MET-hrs/wk, p=0.05). Similarly, women in the HW group had significant increases in MVPA at 6 months (mean change=49.1 MET-hrs/wk, p=0.002) and 12 months postpartum (27.6 MET-hrs/wk, p=0.01). In contrast, only the LI group experienced significant increases in vigorous PA at 6 months (1.7 MET-hrs/wk, p=0.03) and 12 months postpartum (1.3 MET-hrs/wk, p=0.03). In this randomized trial among high-risk Latina women, both groups benefitted from participation in a culturally targeted intervention.

Support for Nutritional Depletion in the Relation between Short Interpregnancy Intervals and Increased Birth Defect Risk Julie M. Petersen* Julie Petersen Mahsa M. Yazdy Kelly D. Getz Marlene T. Anderka Martha M. Werler

Short interpregnancy intervals have been associated with increased risks for adverse perinatal outcomes, including birth defects. One proposed explanation for such associations is nutritional—in particular folate—depletion; however, there is little empirical support. We aimed to evaluate birth defect risks in relation to short interpregnancy intervals—alone and in combination with multivitamin and folic acid intake—using data from the National Birth Defects Prevention Study, a U.S. population-based case-control design (1997-2011). Eligible participants were multiparous, with the prior interpregnancy interval of <24 months, and prior pregnancy resulting in singleton livebirth. Cases included 8 non-cardiac and 6 cardiac defect groups (n=3,274); controls were non-malformed liveborn infants (n=2,575). Interpregnancy interval was categorized as <6 (primary index), 6-11, 12-17, and 18-23 (reference) months. Multivitamin supplementation was classified as any use 28 days before to 56 days into the study pregnancy. Low folic acid intake was defined as no supplementation and estimated dietary folate <400 µg/day. Short intervals were associated with increased risks for several defects (ORs ranged 1.2-2.3). Although estimates were imprecise, the increased risks associated with short intervals occurred only or were stronger among those with no multivitamin use (ORs ranged 1.4-2.3) or low folic acid intake (ORs ranged 1.7-3.3) compared to those with longer intervals without these dietary risk factors; conversely, the associations were weaker or absent among women with only short intervals but neither dietary risk factor (ORs ranged 1.1-1.7). Our study provides empirical evidence that nutritional depletion may underlie the associations between short interpregnancy intervals and birth defect risks. Regular supplementation is recommended for all women of childbearing potential; if sustained during postpartum, it may help to avoid depletion before the start of the next pregnancy.
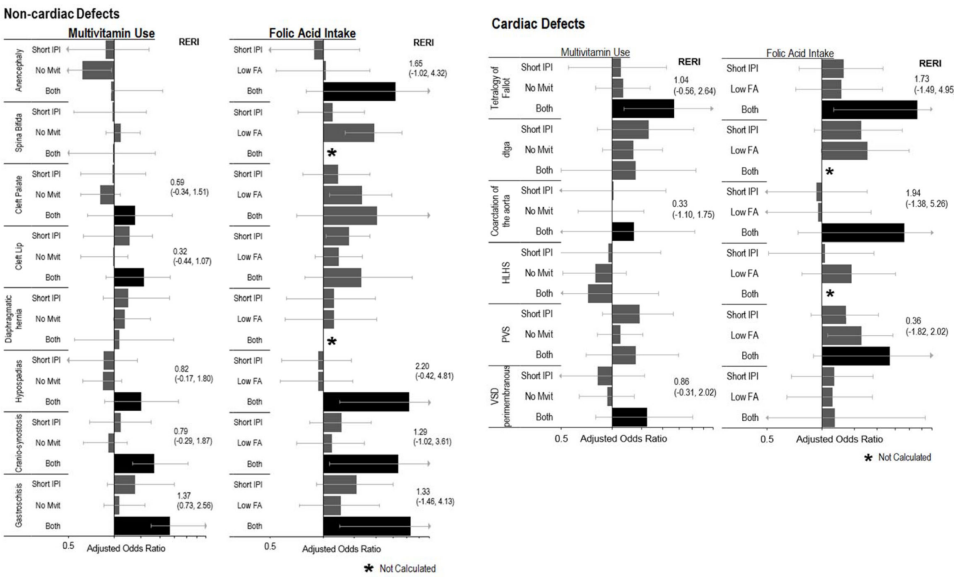
Blood pressure change during pregnancy and preterm delivery Fanfan Chan* Fanfan Chan
Songying Shen Peiyuan Huang Xueling Wei Jinhua Lu Lifang Zhang Xiaoyan Xia Kar Keung Cheng
Huimin Xia Xiu Qiu

Background
Pregnant women experience substantial changes in blood pressure (BP). The effect of these changes
on preterm birth is elusive. We aimed to explore the association between changes in maternal BP
and preterm delivery.

Methods
This study included pregnant women recruited between February 2012 and June 2016 in the Born in
Guangzhou Cohort Study, China. The participants' BP between 13 and 41 gestational weeks was
measured at their rountine antenatal visits and information at delivery was collected. Linear mixed
models were applied to capture BP trajectories for term, spontaneous and iatrogenic preterm
delivery. BP trajectories for women with various gestational length (34~40 weeks) were also
presented.

Results
Of 19,299 women included in the analysis, the number of iatrogenic preterm, spontaneous preterm
and term delivery was 170 (0.88%), 668 (3.47%) and 18,391 (95.64%), respectively. The BP
trajectories of the three groups were all J-shaped (Figure 1). Women with iatrogenic preterm
delivery had the highest BP throughout pregnancy, followed by those with spontaneous preterm and
term delivery. Systolic BP for women with iatrogenic preterm, spontaneous preterm and term
delivery reached the nadir at around 18 weeks of gestation, with values being 111.93 (95%CI
110.59, 113.27), 108.41 (95%CI 107.87, 108.95) and 107.01 (95%CI 106.91, 107.12) mmHg,
respectively, and all increased consecutively till delivery. With regard to diastolic BP, nadirs were
reached at around 22 weeks of gestation with values being 67.02 (95%CI 65.91~68.12), 64.10
(95%CI 63.65~64.55) and 62.70 (95%CI 62.62~62.78) mmHg, respectively. Further, women with
shorter gestational length had higher BP throughout pregnancy.

Conclusion
Women with spontaneous preterm delivery had higher BP throughout pregnancy than women with
term delivery, as did those with iatrogenic preterm delivery. Maternal BP was inversely associated
with gestational length.
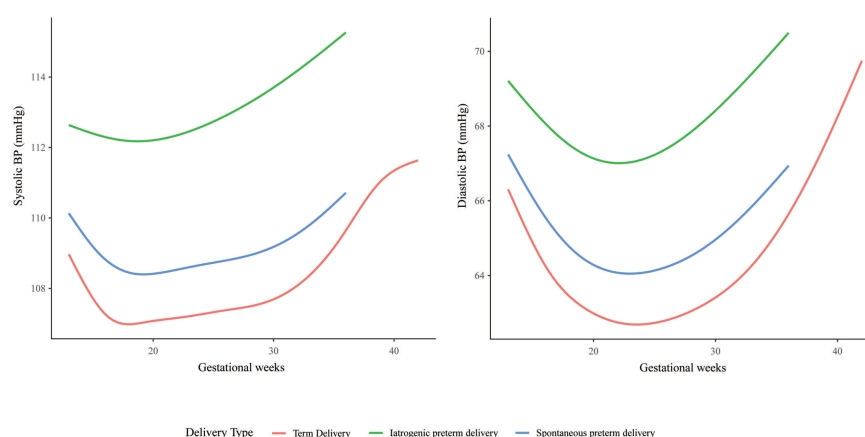
Figure 1. Blood pressure trajectories among women with iatrogenic and spontaneous preterm and term delivery

Prenatal Folate Revisited: Maternal Folate Status During Pregnancy and Brain Developmental Trajectories in Offspring

Runyu Zou* Runyu Zou Hanan El Marroun Henning Tiemeier Tonya White

Emerging evidence shows that low maternal folate levels during pregnancy are associated with offspring neurodevelopmental abnormalities even in the absence of neural tube defects. However, the relationship between prenatal maternal folate status and offspring brain development in later childhood has rarely been investigated. Embedded in the population-based Generation R Study, we examined the temporal association of maternal folate status during pregnancy with downstream brain development in 1237 children of Dutch origin using linear regression and linear mixed models. Maternal folate concentrations were measured from venous blood in early gestation and folate concentrations below 7 nmol/L were defined as 'deficient' in the main analyses. Child structural neuroimaging data, including volumetric measures and surface-based metrics were assessed using magnetic resonance imaging (MRI) at age 9-11 years. In addition, measures of child head circumference using fetal ultrasound in the third trimester and total brain volume using MRI at age 6-8 years were used for longitudinal analysis with repeated assessments. After adjusting for covariates, maternal folate deficiency during pregnancy was associated with a smaller total brain volume (B=-34.6 cm3, 95%CI -67.6 to -1.7) as well as less surface area in the postcentral region of the right hemisphere and less gyrification in the precuneus region of the left hemisphere. Analysis of the repeated measurements showed that children exposed to deficient folate concentrations in utero had persistently lower brain volume compared to controls from the third trimester onwards (β=-0.3, 95%CI -0.6 to -0.1). Consistent results were obtained from sensitivity analysis using a less rigorous folate deficiency cut-off value (8 nmol/L) or targeted maximum likelihood estimation (TMLE). These findings suggest the importance of adequate folate intake during pregnancy on offspring brain development in childhood.

Figure. Maternal folate status during pregnancy and child brain developmental trajectories
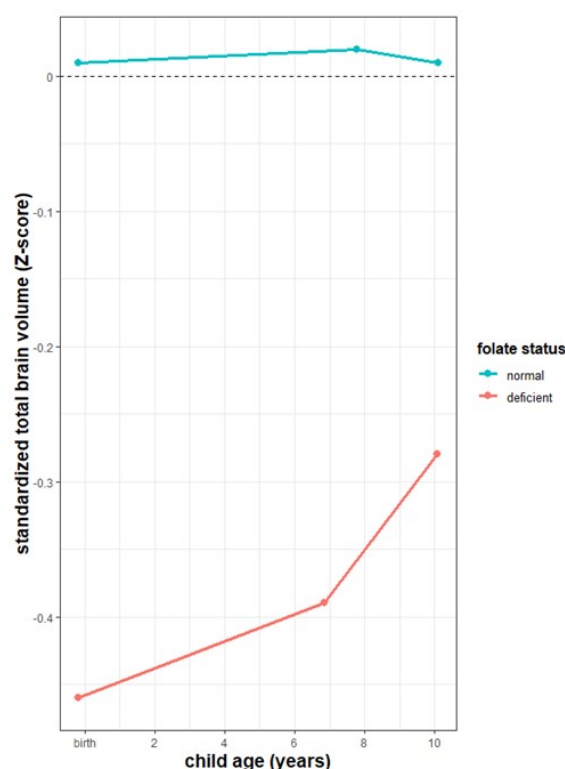
The Role of Type 1 Diabetes in the Contribution to Fetal Overgrowth: Asian-Caucasian Disparities Yanfang Guo* Yanfang Guo Mark Walker Shi Wu Wen

Background: It has been known that the clinical and immunologic characteristics of type 1 diabetes mellitus (T1DM) in Asian populations are quite different from those of Caucasians. Little is known for the Asian-Caucasian differences in the contribution of T1DM to large-for-gestational-age (LGA) neonates. Our study is to compare the impact of T1DM on LGA neonates between Asian and Caucasian women.

Method: A population-based retrospective cohort study was conducted among Asian and Caucasian women who had perinatal screening and resulted in a singleton birth in an Ontario hospital between April 2015 and March 2018. Multivariate log-binomial regression models were used to estimate the adjusted relative risks (aRRs) and 95% confidence intervals (CIs) of T1DM on LGA (birth weight>90th percentile for gestational age and sex) among Asian and Caucasian women. Top six contributors to LGA between Asian and Caucasian women were compared by using multivariate logistic regression models.

Results: Among total 235,258 eligible women, 69.4% are Caucasian women and 30.6% are Asian women. The prevalence of T1DM and LGA neonates were 0.5% and 11.0% for Caucasian women, 0.2% and 5.0% for Asian women, respectively. The association between T1DM and LGA neonates in Caucasian women (aRR: 4.18, 95% CI [3.84, 4.55]) was stronger than that in Asian women (aRR: 2.11, 95% CI [1.24, 3.59]). T1DM is the third strongest contributor to LGA neonates in Caucasian women, following excessive gestational weight gain and high body mass index. However, T1DM is the sixth contributor of LGA in Asian women, following excessive gestational weight gain, high body mass index, gestational diabetes, advanced maternal age and type 2 diabetes.

Conclusion: T1DM in Caucasian women plays stronger roles in LGA neonates than that in Asian women. Clinicians should be aware of racial disparities of effects of T1DM on fetal overgrowth when developing management strategies of pregnant women with T1DM.

Perinatal & Pediatric

Prenatal Exposure to Antidepressants and the Risk of Attention Deficit Hyperactivity Disorder in Childhood: Findings from a nationwide cohort study Buket Öztürk* Buket Öztürk Vera Ehrenstein Henrik Toft Sørensen Lars Pedersen

Background: Results from observational studies that examined the association between prenatal exposure to antidepressants and the risk of Attention Deficit Hyperactivity Disorder (ADHD) in childhood remain inconsistent.

Objectives: To estimate the causal effect of prenatal exposure to antidepressants on the risk of ADHD in childhood, by triangulating results using approaches with different key sources of potential bias.

Methods: We created a pool of all singleton live-born children in Denmark in 1997-2016 and performed following analyses: Restricted analyses, by comparing prenatally antidepressants-exposed vs. unexposed children restricted to, i) Children of formerly antidepressants-exposed mothers, ii) Children of mothers with a diagnosis of depression. Active-comparator analysis, by comparing prenatally antidepressants-exposed children with children of mothers exposed to talk therapy. Sibling design analysis, by comparing prenatally antidepressants-exposed children with their unexposed siblings. We also performed several sensitivity analyses. We used Cox regression to calculate hazard ratios (HR) and 95% confidence intervals (CI) as a measure of relative risk of ADHD.

Results: The study included 1,223,201 children from which 27,522 were prenatally exposed to antidepressants. The number of children with ADHD was 947 in the exposed and 30,772 in the unexposed. Restricted analyses provided HRs of i) 1.19 (1.09-1.29) and ii) 1.21 (1.00-1.45). Active-comparator analysis showed an HR of 1.22 (1.10-1.36) and sibling design analysis an HR of 1.09 (0.89-1.33). The sensitivity analyses indicated some residual confounding.

Conclusion: There was a slightly elevated risk of ADHD in children prenatally exposed to antidepressants compared with unexposed children. Triangulation and sensitivity analyses suggested that this might be due to residual confounding. Our study thus did not provide strong evidence for a causal effect of prenatal antidepressant exposure on the risk of ADHD.

Household alcohol use and child behavior problems in South Africa: Results from the Asenze Study Marine Azevedo Da Silva* Marine Azevedo Da Silva Rachel Gruver Chris Desmond Silvia Martins Leslie Davidson

Childhood exposure to alcohol use by household adults has been associated with a range of problem behaviors in children. Most of the research in this area has focused on higher income countries. However, patterns of alcohol use, family dynamics, and childhood behavior problems may be considerably different in low- and middle-income countries (LMIC). We explored the association between household alcohol use and behavior difficulties among South-African children.

We used data from the Asenze study, a population-based cohort of South African children and their caregivers. Household alcohol use, Alcohol Use Disorders Identification Test (AUDIT), and child behavior (using the Strengths Difficulties Questionnaire) were assessed when children were 6-8 years old, in 2010-2012 (wave 2). We performed logistic regression analysis to examine the association between household alcohol use and child behavior problems. The sample, those with complete data, included 1383 children under the care of 1248 adults.

Hazardous household drinking (20%) was associated with overall child behavior problems (OR=1.49, 95% CI 1.00-2.21) after controlling for sociodemographic characteristics, child and caregiver HIV status, and caregiver post-traumatic stress. Hazardous alcohol use by the caregiver (4%) was associated with overall (OR=2.01, 95% CI 1.02-3.95), externalizing (OR=2.00, 95% CI 1.03-3.92), and internalizing (OR=2.60, 95% CI 1.36-4.96) child behavior problems. There was no association between hazardous use by other people in the household (15%) and child behavior problems.

Household alcohol use, primarily by the caregivers, is associated with childhood behavioral difficulties in this population. It supports the need for interventions to reduce the prevalence of household alcohol use. Long-term follow-up to understand the full impact of household alcohol exposure on child and adolescent mental health in LMIC settings is needed.

Effects of prenatal smoking and drinking on birth outcomes: results from the Safe Passage Study Ayesha Sania* Ayesha Sania Lauren C. Shuffrey Nicolò Pini Hein J. Odendaal Amy J. Elliott Michael M. Myers William P. Fifer

Objective: To examine the role of prenatal drinking and smoking on birth outcomes in two perinatal cohorts, one from the USA and one from South Africa.

Method: Pregnant women were enrolled from perinatal clinics in Northern Plains, USA (n=4468) and Cape Town, South Africa (n=6374). Data on daily drinking and weekly smoking was collected at up to four prenatal visits. Exposure categories of drinking and smoking were identified using cluster analyses. Linear regressions were used to estimate the effects of exposure on birthweight and gestational age, and binomial regressions to estimate effects on preterm birth and small for gestational age (SGA). Models were adjusted for maternal age, education, income, employment status, marital status, height, parity, antenatal care, and prenatal depression.

Result: Prenatal smoking was associated with a reduction in birthweight in a dose-response manner. Compared to non-smokers, and controlling for drinking, birthweight was 171 g (standard error, SE 20 g), 162g (SE 14 g) and 104 g (SE 11 g) lower among high, moderate, and low continuous smokers, respectively. SGA incidence was 70% (95% CI: 1.1, 2.5) higher among high continuous smokers and 35% (95% CI: 0.98, 1.89) higher among moderate continuous smokers. Controlling for smoking, there was a small increase in gestational length (0.16 to 0.48 weeks) and a reduction in the incidence of preterm birth (RR, 0.60 95% CI: 0.49, 0.72) among women who drank throughout the pregnancy. Mean birthweight was 105 g (SE 20g) lower among high continuous drinkers and 85 g (SE 22g) lower among low continuous drinkers. Further analyses showed there was a synergistic interaction between drinking and smoking evident by a large reduction in birthweight in dual exposure group.

Conclusion: Parental smoking and drinking caused significant fetal growth restriction in two ethnically and racially diverse perinatal cohorts. All women should be warned of the risk posed by smoking and drinking during pregnancy.
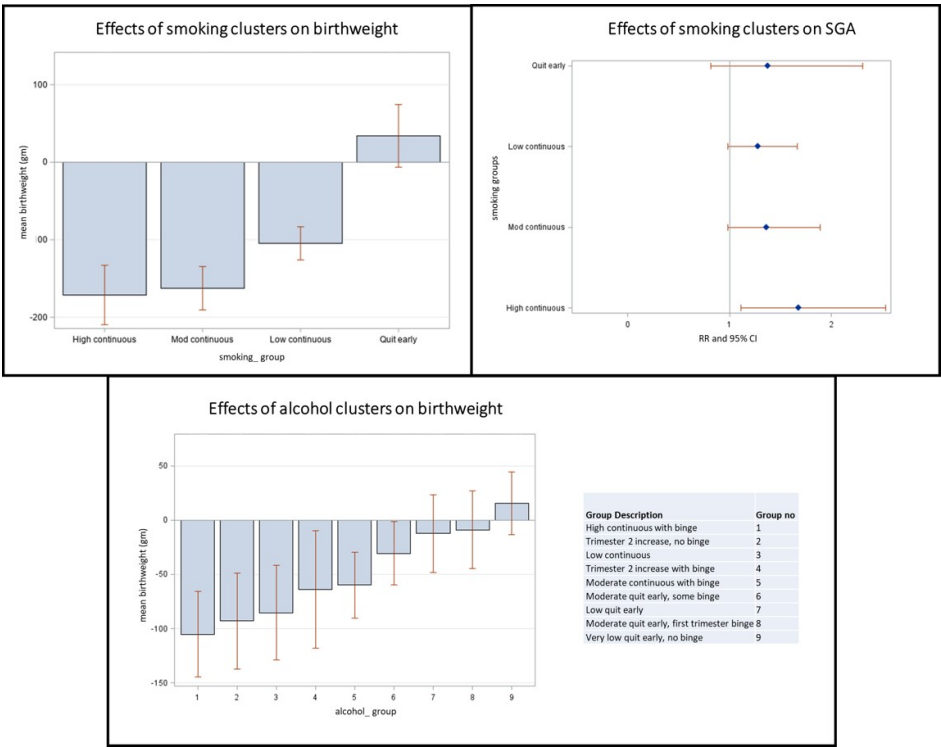
Environmental quality and associations with birthweight-for-gestational age deciles for infants born term and preterm in Portland, OR Lynne C. Messer* Lynne Messer Monica Jimenez Alison Krajewski Christine L Gray Jyotsna Jagai Kristen Rappazzo Danelle Lobdell

Residents of urban neighborhoods experience adverse exposures simultaneously (e.g., traffic exhaust, manufacturing emissions, water contamination), often close to home. We created a census tract-level environmental quality index (trEQI) with data representing five domains (air, built, land, sociodemographic, water) and merged the continuous trEQI (2010) with 2010-2014 birth record data to construct a geographically defined cohort in Portland, OR. The effects of environmental quality were expected to vary by infant's birthweight for gestational age (BWforGA) so we evaluated the OR trEQI and deciles of the size-for-gestational-age distribution separately for term and preterm infants, with unconditional quantile regression, in models adjusted for continuous and quadratic maternal age, categorical education, partnership status, and payment type. Approximately 5% of the 91,520 cohort infants were preterm. Lower environmental quality was associated with lower continuous birthweights among infants born term (beta coefficient (b) = -7.3; 95%CI: -13.2, -1.4) and preterm (b = -41.6; 95%CI: -76.0, -7.3), but estimates varied across the BWforGA continuum (Figure 1). The largest decrements in birthweights were seen for term infants born in the 70th, 80th, and 90th percentiles of BWforGA (b= -12.7; 95%CI: -20.6, -4.7, b= -12.3; 95%CI: -21.5, -3.2; and b= -12.5; 95%CI: -23.9, -1.2, respectively). Among preterm infants, those in the 10th and 20th percentiles of BWforGA had the largest decrements associated with lower environmental quality (b= -122.6; 95%CI: -211.9, -33.2 and b= -105.3; 95%CI: -178.7, -31.9, respectively). The strongest associations between poor environmental quality and BWforGA were seen for the most vulnerable infants (smallest preterm infants), and associations with environmental quality were not uniform across the BWforGA continuum. Addressing environmental quality is a critical public health intervention with maternal and child health equity implications.

Term- and preterm-stratified change in continuous birthweight *, within deciles of birthweight for gestational age categories, for a one-unit change in continuous census tract-level EQI score (2010) in one Oregon metropolitan area (2010-2014)
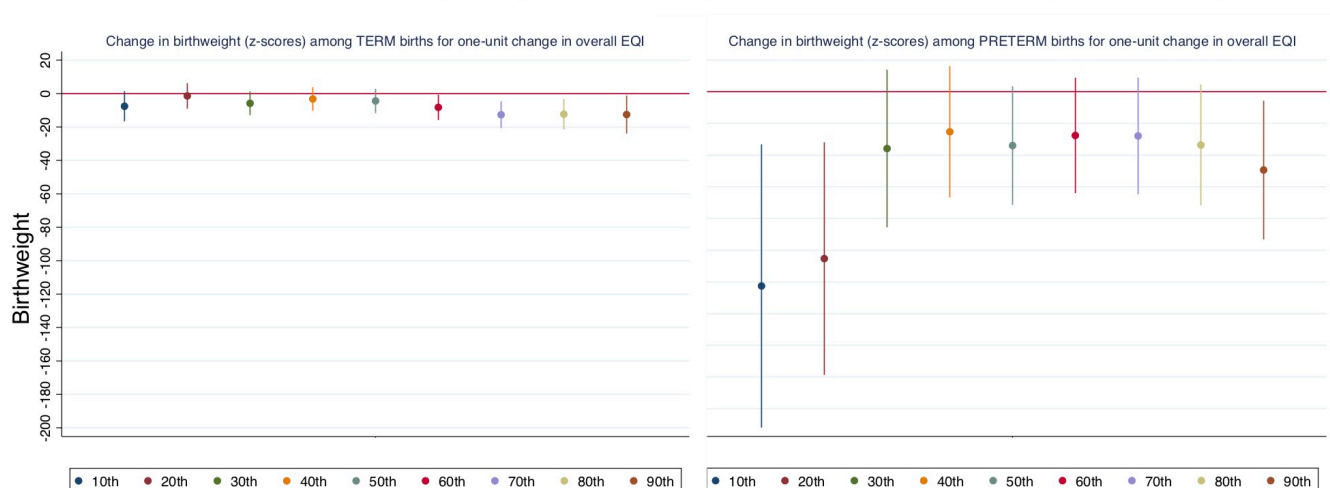
* models adjusted for continuous and quadratic maternal age, categorical maternal education, dichotomous partnership status and payment type

Association between pregnancy experiences and offspring biological age estimates Alonzo T. Folger* Alonzo Folger Lili Ding Kimberly Yolton Robert T. Ammerman Judith B. Van Ginkel Katherine A. Bowers

Background. Epigenetic age has emerged as a tool to predict chronological age with high accuracy across multiple tissue types. Epigenetic clocks have been developed from statistical models that include DNA methylation (DNAm) across multiple CpG sites and ages. Predicted epigenetic age can be used to estimate accelerated biological age, a potential biomarker for health and developmental risk. Prenatal experiences can impact an offspring's developmental trajectory, and these effects may be detected using predicted epigenetic age. We hypothesized a significant association between pregnancy experiences (uplifts and hassles) and offspring age acceleration estimated using 2 epigenetic clocks. Methods. 53 women and their offspring were followed from pregnancy (visit 1) to 3-5 weeks of age (visit 2); 40 dyads were followed to 2-years (visit 3). We collected the Pregnancy Experiences Scale (PES) among other measures during pregnancy and offspring buccal epithelial DNA at visits 2 and 3. DNAm data were generated using the Illumina Infinium MethylationEPIC BeadChip. We used the Horvath pan-tissue and PedBE (pediatric-specific) clocks to derive predicted age. General linear models were used to examine associations between PES scores and age acceleration, defined as the residual between predicted age and chronological age. Results. Correlations were observed between chronological and predicted age for the Horvath clock (Pearson: 0.84, p<0.01) and the PedBE clock (Pearson: 0.97, p<0.01). Increased positive feelings about pregnancy experiences was significantly associated with lower age acceleration measured neonatally with the PedBE clock (beta: -0.009, 95% CI: -0.015, -0.003). Although non-significant, similar effects were observed with the Horvath clock. We did not observe significant relationships at visit 3. The estimates were adjusted for maternal age, race and smoking status. Conclusion. Positive pregnancy experiences may buffer offspring from accelerated biological aging.
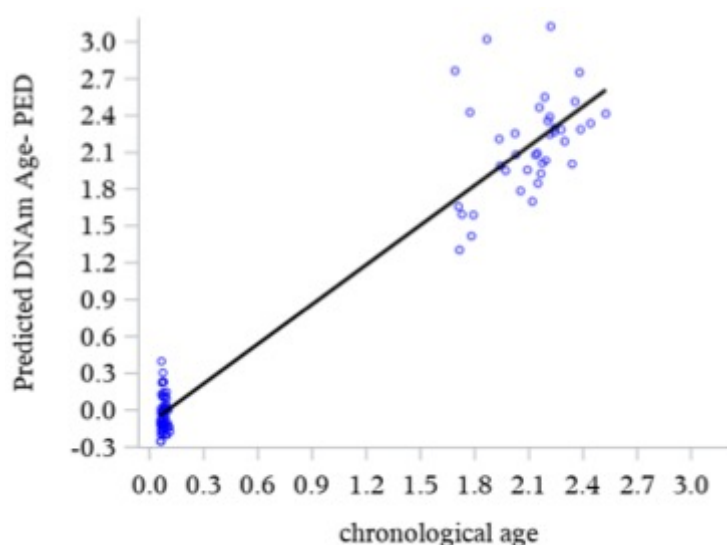
Maternal characteristics associated with gestational weight gain in France Melissa Amyx*
Melissa Amyx Jennifer Zeitlin Béatrice Blondel Camille Le Ray

Adequate gestational weight gain (GWG) is essential for optimal pregnancy outcomes. Currently no national guidelines on GWG exist and few studies have investigated GWG in France. Our objectives were to provide nationally-representative estimates of GWG and GWG adequacy and identify risk factors for inadequate or excessive GWG in France. Singleton livebirths from the French National Perinatal Survey 2010 (N=13455) and 2016 (N=11395) were included. GWG was calculated as women's end of pregnancy minus prepregnancy weight (kg) and categorized as inadequate, adequate, or excessive by prepregnancy BMI (under-[<18.5], normal [18.5-24.9], over-[25-29.9] weight; obese≥30 kg/m2) using 2009 Institute of Medicine (IOM) thresholds. We estimated average GWG and the proportion of women in each GWG category. Adjusted polytomic logistic regression identified characteristics associated with inadequate or excessive GWG. Average GWG was 13.0 (+/-5.6) kg, with 28.6% of women gaining inadequately, 39.5% adequately, and 31.9% excessively. Risk factors for inadequate GWG included underweight prepregnancy BMI (adjusted OR [aOR] 1.4, 95%CI 1.2, 1.5), being foreign-born and arriving in France in the year of pregnancy (aOR 1.5, 95%CI 1.1, 2.0), and insufficient prenatal care (aOR 1.2, 95%CI 1.1, 1.4). Conversely, the strongest risk factors for excessive GWG were overweight (aOR 3.0, 95%CI 2.8, 3.3) or obese prepregnancy BMI (aOR 3.1, 95%CI 2.8, 3.4) and decreased/stopped smoking in pregnancy (aOR 2.5, 95%CI 2.2, 2.8: ≥10 cigarettes/day prepregnancy and stopped; aORs 1.4-1.5 for lesser decreases); additional risk factors included primiparity (aOR 1.3, 95%CI 1.2, 1.4), lower education (aORs 1.1-1.5), and not working/stopping working earlier in pregnancy (aORs 1.1-1.5). In France, inadequate and excessive GWG, per 2009 IOM guidelines, are common. For optimal outcomes, additional support for at risk groups is needed, including nutritional support for women quitting smoking or with high or low BMI.

Prenatal influences on childhood health: what role for mums and dads? Kayleigh Easey*
Kayleigh Easey Gemma Sharp

Background: It is widely recognised that pregnant mothers can influence the health and characteristics of their children via non-genomic "maternal effects", but there are still gaps in our understanding regarding causality and the range and mechanism of effects. Consequently, current public health advice in pregnancy can be inconsistent, misleading and not based on robust, empirical evidence of causation. Additionally, there is increasing evidence that fathers can also exert "paternal effects" on the child health, but very little advice is currently offered to fathers-to-be.

Aim: To better understand whether and how both maternal and paternal health behaviours in the prenatal period causally influence offspring health outcomes in childhood.

Methods: By combining existing questionnaire and 'omics data from six European birth cohorts, and "triangulating" evidence from multiple causal inference methods (Mendelian randomization, sibling comparisons, negative control designs), this project explores causal relationships and interactions between maternal and paternal prenatal health behaviours (smoking, alcohol, fat/sugar in diet, body mass index, caffeine and physical activity) and childhood outcomes including birth weight, cleft lip/palate, IQ and educational attainment. It also explores the role of DNA methylation as a potential molecular mediator of parental influences on offspring health.

Results: Through well-powered meta-analysis of epigenome-wide association studies, the project has already shown that maternal and paternal pre-pregnancy BMI are associated with offspring methylation to a similar degree, suggesting associations are better explained by genetic or shared environmental factors than a causal mechanism. The project is now exploring the other aforementioned exposures and outcomes.

Impact: Findings will identify the most appropriate prenatal targets (mothers, fathers, or both parents) for more effective public health to improve child health.

Perinatal & Pediatric

A scoping review of maternal, newborn, and child health research in Ethiopia Jenna Daniel* Grace Chan Delayehu Bekele Jenna Daniel Bezawit Hunegnaw Matthew Kennedy Ronke Olowojesiku Misrak Getnet Sarah Unninayar Lisanu Taddesse Grace Chan

A scoping review of maternal, newborn, and child health research in Ethiopia

Background: Despite significant reductions in maternal and child mortality over the last decade, much work remains to improve maternal, newborn, and child health (MNCH) in settings, such as Ethiopia, where a disproportionate majority of global deaths occur. To prioritize research questions, more information is needed to understand the current knowledge of MNCH and identify remaining gaps. The aim of this scoping review is to describe the body of published MNCH research conducted in Ethiopia.

Methods: A search strategy conducted in PubMed/MEDLINE, EMBASE, and the WHO African Index Medicus identified 7,827 unique articles for screening. Two researchers independently reviewed titles, abstracts, and full-texts; abstracted data; and reconciled differences. Descriptive analyses were conducted.

Results: We included 2,289 studies in the scoping review. Preliminary results indicate an exponential increase in MNCH research in Ethiopia over the last decade, with 74% of articles published between 2010-2019 compared to 1946-2009. The majority of the studies (80%) were conducted in Addis Ababa and the four agrarian regions compared to the pastoralist and semi-pastoralist regions (7%). The most common target populations were children less than 10 years of age (30%), pregnant women (27%) and women of reproductive age (26%), compared to newborns (8%) and postpartum women (3%). Sixty-three percent of studies were cross-sectional design; 6% were prospective cohort studies, and 2% were randomized control trials.

Conclusion: To our knowledge, this is the first scoping review to describe the landscape of MNCH research in Ethiopia. Understanding the depth of existing knowledge of MNCH in Ethiopia will support the prioritization and development of future research questions. Additional studies are needed to focus on the neonatal and postpartum period.

Comparing methods to assess the association between gestational weight gain and adverse perinatal outcomes

Megan Richards* Megan Richards Matthew Strickland Natalie Rosenquist Lyndsey Darrow

Background: Gestational weight gain (GWG) is associated with many adverse outcomes; however, there is debate over the best way to analyze GWG as an exposure while accounting for gestational age. Methods: We estimated and compared associations between GWG and three perinatal outcomes [cesarean delivery (CS), small for gestational age (SGA) and large for gestational age (LGA)] using four previously proposed methods to operationalize GWG, all applied to the same data stratified by pre-pregnancy body mass index (BMI): (1) Institute of Medicine (IOM) categories of GWG; (2) 10lb categories of GWG adjusting for gestational age using indicator variables; (3) weight gain for gestational age z-scores, and; (4) a survival analysis using week-specific interpolated GWG. Data were obtained from birth records in California (2007-2017; n=5,031,913), Oregon (2008-2017; n=421,920), and Nevada (2010-2017; n=262,001); years were selected based on availability of pre-pregnancy BMI. Methods 1-3 used log-binomial models; method 4 used a Cox proportional hazards model. Results: In general, the approaches yielded similar patterns of associations with the outcomes. For example, among women with a normal BMI (n=2,675,078): (1) Using IOM categories, women who had excess GWG were 1.17(CI: 1.17, 1.18) times as likely to have a CS compared to those who had adequate GWG. (2) After adjusting for gestational age, women who gained ≥40lbs compared to 20-29lbs were 1.11(CI: 1.10, 1.11) times more likely to have a CS. (3) Women who had a z-score of 0.5-1.5 were 1.15(CI: 1.14, 1.15) times more likely to have a CS compared to women who had a z-score between -0.5-0.5. (4) The HR for CS associated with a 10lb increase in GWG was 1.13(CI: 1.13, 1.13). For women who had higher GWG, estimated RRs for LGA were less comparable. Conclusion: Although the conclusions from the four methods to operationalize GWG accounting for gestational age were similar, each effect measure has a different interpretation.

Misclassification of Neonatal Abstinence Syndrome (NAS) surveillance estimates: is considering the positive predictive value (PPV) enough? Katie Labgold* Katie Labgold Penelope Howards

Infant withdrawal from opioids, known as Neonatal Abstinence Syndrome (NAS), is a major public health concern. NAS surveillance commonly uses hospital discharge data. State-specific validation studies have noted that discharge data consistently over-estimates the NAS prevalence in medical records because of imperfect positive predictive values (PPVs). Yet, variation in the negative predictive value (NPV) has not been explored and can yield substantial bias for rare outcomes. The purpose of this study was to inform our understanding of NAS burden by investigating the variability of NAS prevalence under several NAS misclassification scenarios. We used publically available 2010 New Jersey inpatient hospital data from the Healthcare Cost and Utilization Project. We identified infant live-birth records and non-iatrogenic NAS cases using discharge international classification of disease (ICD)-9 codes. Surveillance data was adjusted using outcome misclassification bias models to reflect an expected NAS prevalence under a range of PPV and NPV scenarios. We varied PPV from 50-100% and NPV from 99.9-100%. The 2010 surveillance NAS prevalence was 0.44%. Under the range of PPV and NPV scenarios, we calculated an adjusted prevalence ranging from 0.22-0.54% (fig.1). Most scenarios had an adjusted NAS prevalence below the surveillance prevalence. However when the PPV was high (≥80%) and the NPV was imperfect (<100%), there were a few scenarios where the surveillance data underestimates the adjusted NAS prevalence. Our results for New Jersey suggest that in states with a lower PPV, surveillance data will consistently over-estimate the medical record NAS prevalence. Yet, in states with a higher PPV, surveillance data can either slightly over- or under-estimate the medical record NAS prevalence depending on the NPV. Future research should incorporate additional misclassification concerns and improve upon limitations of current misclassification bias models for NAS surveillance.

Figure 1. Prevalence of NAS under Varying PPV & NPV Scenarios, NJ 2010
Hospital Discharge Prevalence Indicated by Dotted Line (0.44%)
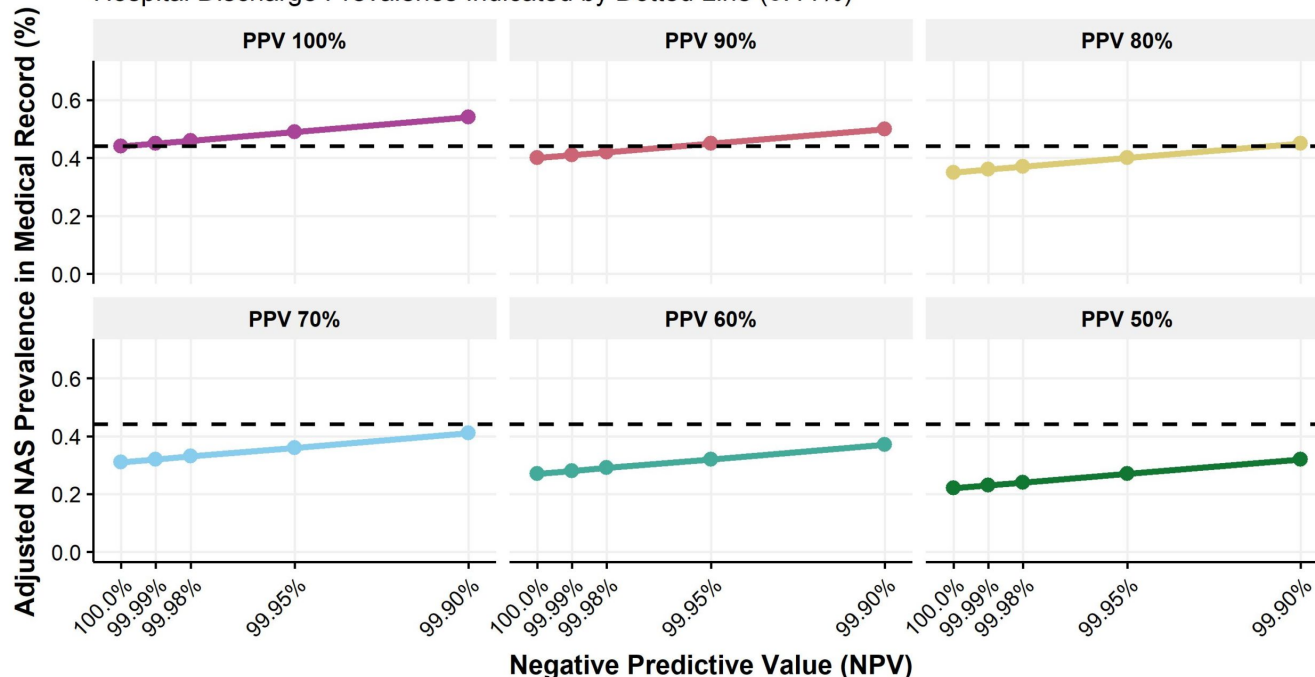
In utero exposure to metal mixtures (cadmium, lead, mercury, manganese, and selenium) and child blood pressure: the Boston Birth Cohort Mingyu Zhang* 3647] Zhang Tiange Liu Eliseo Guallar Xiaobin Wang Noel T Mueller

Introduction:

Exposure to heavy metals (e.g., cadmium [Cd], lead [Pb], and mercury [Hg]) in pregnancy may lead to higher offspring blood pressure (BP), while trace minerals (e.g., manganese [Mn] and selenium [Se]) may have protective, antioxidant effects that modify heavy metal-BP associations. To our knowledge, no study has examined the co-exposure of heavy metals and trace minerals.

Objective:

To examine the individual and joint effect of *in utero* exposure to Cd, Pb, Hg, Mn, and Se on child BP.

Methods:

We used data from the Boston Birth Cohort (enrolled 1998-2015). Metals were measured in maternal red blood cells 24-72 hours after delivery and were ln-transformed. We calculated child systolic BP (SBP) percentile based on the 2017 American Academy of Pediatrics hypertension guidelines. We examined associations of metals with SBP using linear regression models. We also used Bayesian Kernel Machine Regression (BKMR) to model metal co-exposures, allowing for interactions and non-linear effects. We adjusted for confounders including maternal age at delivery, race/ethnicity, education, and smoking status in pregnancy.

Results:

Our analytic sample comprised 1,273 mother-child pairs. Of the mothers, 61% were Black/African American and 9% smoked in pregnancy. Of the children (age range 3-15 years), 50% were girls. In the multivariable-adjusted linear models, Se and Mn were inversely associated with SBP: an IQR increment in ln(Se) and ln(Mn) were associated with a 2.02 (95% CI: 0.18, 3.85) and 1.84 (95% CI: 0.02, 3.67) percentile lower child SBP, respectively. These results were confirmed in the BKMR models (Figure). We observed evidence of interactions between Mn and Cd (P-interaction = 0.013), with a stronger inverse Mn-SBP association when Cd was higher. Mn was also more protective among current smokers, compared to former or never smokers. There were no associations between Cd, Pb, or Hg with child SBP in linear regression or BKMR models.

Conclusion:

Higher Se and Mn in pregnancy are associated with lower child BP. Mn appeared to be more protective among children born to mothers who had high Cd or smoked in pregnancy.

Figure. Associations between ln-transformed metal 1 and child SBP percentile by different quantiles (0.1, 0.5, 0.9) of metal 2 estimated using the BKMR models. Se and Mn were inversely associated with SBP. There is also evidence of interactions between Mn and Cd, with a stronger inverse Mn-SBP association when Cd was higher.
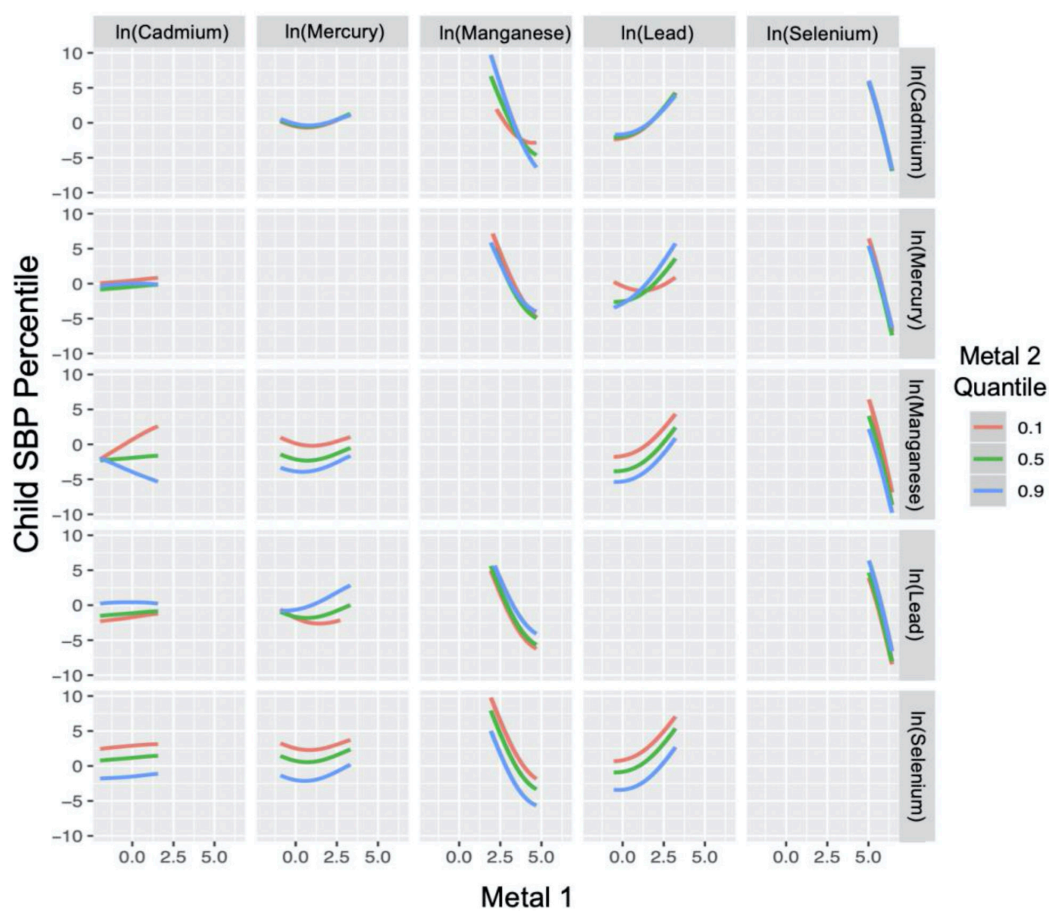
LATEBREAKER

Perinatal & Pediatric

Increasing Prepregnancy Obesity Class in Twin Pregnancy is Associated with Decreased Gestational Weight Gain Amy R. Nichols, MS, RD* 3647] Nichols Radek Bukowski Paul J. Rathouz Tomislav Urban Saralyn F. Foster Rachel Rickman Elizabeth M. Widen

Twin pregnancies have increased in recent decades but the Institute of Medicine (IOM) twin gestational weight gain (GWG) recommendations remain provisional and do not differentiate by obesity severity. Among nationally representative mother-twin triads, we describe GWG across prepregnancy BMI categories.

US Vital Statistics records for 160,602 twins born 2014–2016 were examined. Analysis of variance or chi^2 assessed associations between BMI (<18.5kg/m^2 underweight, 18.5–24.9 normal, 25–29.9 overweight, ≥30 obesity) and BMI obesity class (class I: 30–34.9kg/m^2, II: 35–39.9, III: ≥40), total GWG and meeting provisional IOM GWG recommendations (below, met, above). Multivariable linear regression models identified associations between BMI category and GWG, adjusting for covariates at delivery, and how maternal height, age, ethnicity and education predicted total GWG.

Prepregnancy, 2.7% of women were underweight, 25.6% overweight and 28.3% had obesity (class I: 43.4%; II: 35.4%; III: 21.2%). GWG was 18.4±6.1kg (mean±SD) for underweight, 18.6±6.1 for normal weight, 17.2± 7.7 for overweight and 14.1±8.4 for obesity (class I: 15.2±8.2kg; II: 13.5±8.3; III: 12.2±8.6). A majority of normal weight (43.9%) and overweight (43.9%) women met provisional IOM GWG recommendations; those with obesity tended to gain below IOM or lose weight (38.1%), especially class III (48.5%). Compared to normal weight, estimated GWG was lower in overweight (b=-1.2 95%CI -1.3, -1.1) and across obesity classes (class I: b=-3.2 95%CI -3.3, -3.1; II: b=-4.9 95%CI -5.0, -4.7; III: b=-6.1 95%CI -6.3, -6.0). Height (b=0.11 %95CI 0.11, 0.12) and higher education (b=1.0 95%CI 0.91, 1.08) were positively associated with GWG, while Black (b=-0.63 95%CI -0.73, -0.53) or Asian (b=-1.80 95%CI -1.96, -1.65) ethnicity was inversely associated with total GWG.

While many women met provisional twin recommendations, optimal maternal weight change that balances risk for mothers and infants requires further investigation.

Using propensity scores to understand the counterfactual in youth e-cigarette initiation

Natasha Sokol* 3647] Sokol Justin Feldman

Background: E-cigarettes have shown promise as smoking cessation aids, but their potential to initiate youth nicotine dependence has generated debate over their role in harm reduction. Since 2014 youth use has increased rapidly, with some evidence suggesting a "gateway" effect for cigarette smoking, although smoking rates have continued to decline. To understand the overall public health impact of e-cigarettes, we investigate the counterfactual scenario: what would have happened to youth cigarette smoking if e-cigarettes had not been available?

Methods: We used Monitoring the Future data (12th grade). For five years prior to widespread e-cigarette availability (2009-2013), we generated survey-weighted gender-stratified predictive logistic models for the odds of current cigarette use, incorporating sociodemographic, family, alcohol and school variables, and a linear time trend. Models predicted smoking propensity scores for participants in 2014-2018. We compared actual smoking prevalence each year (2014-2018) to predicted prevalence, and estimated e-cigarette use in never smokers (2016-2018) among tertiles of cigarette smoking propensity.

Results: Current smoking declined faster than predicted. By 2018, prevalence was 7.6% (95% CI: 7.1, 8.1) vs. a predicted 9.7% (95% CI: 9.4, 10.0). Among non-smokers in 2016-2018, vaping prevalence was highest (23.5%; 95% CI: 22.2, 24.9) among those with the highest predicted probability of smoking, and lowest (3.8%; 95% CI: 3.3, 4.4) among those with the lowest.

Conclusions: The decline in current smoking among 12th graders has hastened since e-cigarettes became available. Among never smokers, vaping is most common among youth who would have had a high likelihood of becoming cigarette smokers prior to e-cigarettes' popularization, and extremely uncommon among those with low likelihood. The actual public health impact of e-cigarettes is highly contingent on all aspects of their relationship with smoking behaviors among youth and adults.

The association between maternal pre-pregnancy BMI, gestational weight gain and child adiposity among a diverse cohort of children aged 4-8 years Kelly J Hunt* 3647] Hunt for the ECHO-FGS study group.

Objective: To examine the association between maternal pre-pregnancy BMI, gestational weight gain (GWG), and child adiposity as measured by BMI, waist circumference and percent body fat in a racial/ethnically diverse cohort.

Study Design: In this cohort study of women without major chronic diseases before pregnancy, we examined the association between pre-pregnancy BMI, GWG, and child adiposity. Children ages 4-8 years (n=816) participating in the Environmental Influences on Child Health Outcomes (ECHO)-NICHD Fetal Growth Studies (FGS) were assessed. Maternal pre-pregnancy BMI, GWG, and child adiposity was ascertained by trained study staff. Multinomial logistic and linear regression models were used. All models included demographic factors (child's age, sex, and race-ethnic group; mother's age and education), childhood factors (household poverty, marital status and child activity level), gestational age at delivery, pre-pregnancy BMI and GWG.

Results: The odds of child obesity (≥95th BMI percentile) increased for each unit increase in maternal pre-pregnancy BMI [OR=1.12 (95% CI: 1.08, 1.17)], but also increased independently with kg GWG [OR=1.05 (95% CI: 1.01, 1.08)] as did the odds of high child waist circumference (≥85th percentile) [pre-pregnancy BMI OR=1.09 (95% CI: 1.06, 1.13); GWG OR=1.04 (95% CI: 1.01, 1.06)]. As pre-pregnancy BMI increased, child mean fat mass (β [95% CI]: 0.14 [0.09, 0.19]), fat free mass (β [95% CI]: 0.11 [0.07, 0.16]), waist circumference (β [95% CI]: 0.30 [0.21, 0.39]), and BMI z-score (β [95% CI]: 0.05 [0.04, 0.07]) increased. GWG was also associated with child fat mass (β [95% CI]: 0.05 [0.01, 0.09]), fat free mass (β [95% CI]: 0.08 [0.05, 0.12]), waist circumference (β [95% CI]: 0.13 [0.06, 0.20]) and BMI z-score (β [95% CI]: 0.02 [0.01, 0.03]).

Conclusions: Maternal pre-pregnancy BMI and GWG were independently and positively associated with child fat mass, percent body fat, fat free mass, waist circumference and BMI.

Vaping and cigarette smoking during pregnancy and risk of small for gestational age Mir M Ali* 3647] Ali Victor M Cardenas Lori A Fischbach Wendy N Nembhard

This study estimates the effect of maternal exposure to tobacco (including electronic nicotine delivery systems (ENDS)) during pregnancy on giving birth to a neonate that is small for gestational age (SGA). PRAMS (Pregnancy Risk Assessment Monitoring System) collects state-specific, population-based data on maternal exposures (including exposure to cigarettes, ENDS and other tobacco products) before, during, and shortly after pregnancy. The Arkansas PRAMS data was used to calculate risk ratios (RRs) to estimate the effect of using ENDS only, cigarettes only, ENDS and cigarettes (dual use), and other tobacco products on SGA. The study also assesses the effect of cigarette smoking cessation during pregnancy on the risk of SGA among cigarette smokers and dual users. A sensitivity analysis corrected for misclassification due to under-reporting of tobacco use, using values for sensitivity and specificity obtained from comparing self-reported tobacco use to serum cotinine and hair nicotine levels. Adjusting for maternal age, race/ethnicity, education, and alcohol consumption, the RRs for SGA among cigarette smokers and dual users were 1.6 (95% CI: 1.0, 2.6) and 1.8 (95% CI: 1.0, 3.4) respectively. The RR estimates increased after correcting for tobacco use misclassification, going from a RR of 1.6 among cigarette smokers to 1.9 and 3.3, based on sensitivity and specificity estimates from serum cotinine and hair nicotine levels, respectively. Similarly, the RR estimates among dual users increased from 1.8 to 2.0 and 5.3, respectively. The RRs among cigarette smokers and dual users who stopped smoking cigarettes during pregnancy compared to non-tobacco users were 1.2 (95% CI: 0.6, 2.4) and 2.9 (95% CI: 1.4, 6.3) respectively. Our results are consistent with the hypothesis that maternal exposure to cigarette smoking and ENDS use increases risk for SGA. Dual use, but not cigarette-only use, elevated the risk for SGA after cigarette smoking cessation.

Vitamin D Mitigates the Intergenerational Association between Maternal Preeclampsia and Childhood Blood Pressure Mingyu Zhang* 3647] Zhang Guoying Wang Xiaobin Wang Noel T Mueller

Introduction:

Preeclampsia, a pregnancy-specific complication, is the leading contributor to maternal morbidity and mortality. It is also associated with adverse child health outcomes including elevated blood pressure (BP). We recently found that Vitamin D is protective against elevated BP in childhood, yet no studies to our knowledge have examined whether Vitamin D could be a *modifiable* target to mitigating the association of preeclampsia and child BP.

Methods:

We used data from the Boston Birth Cohort. We ascertained preeclampsia diagnosis from medical records. We calculated child systolic BP (SBP) percentile based on the 2017 American Academy of Pediatrics hypertension guidelines. We examined the modifying role of cord blood 25(OH)D as both a continuous variable and a categorical variable by quartiles. We used linear mixed models with random intercepts and adjusted for confounders including maternal age at delivery, race/ethnicity, education, smoking status, and pre-pregnancy BMI.

Results:

Our analytic sample included 754 mother-child pairs with 6,669 BP observations from 3 to 18 years of age. 62% of the mothers were Black/African American and 50% of the children were girls. Median cord blood 25(OH)D was 12.2 (IQR: 7.9-17.2) ng/mL. Compared to children born to mothers with no preeclampsia, those born to mothers with preeclampsia had 5.34 (95% CI: 1.37, 9.30) percentile higher SBP. Children born to preeclamptic mothers had 3.47 (95% CI: 0.77, 6.18) percentile decrease in SBP per 5 ng/mL increment in cord blood 25(OH)D. The **Figure** shows the difference in SBP percentile comparing children born to mothers with vs. without preeclampsia by quartiles of Vitamin D levels. The differences changed in a dose-dependent manner depending on different levels of cord blood Vitamin D (P-interaction = 0.007).

Conclusion:

We found that higher Vitamin D attenuated or even eliminated the associations between maternal preeclampsia and high child BP. Optimizing maternal Vitamin D levels during pregnancy may help prevent high BP and cardiovascular disease among children born to preeclamptic mothers.

Estimating misclassification bias resulted from pregnancy loss on the association between interpregnancy interval and preterm birth Gizachew Tessema* 3647] Tessema Siri Håberg Gavin Pereira Maria Magnus

A paucity of studies explored how intervening pregnancy loss (miscarriages and induced abortions) contributes to interpregnancy interval (IPI) misclassification and whether this misclassification translates into bias in estimated the effect of IPI on adverse birth outcomes. We identified all registered pregnancies (n=167,012), with at least two consecutive pregnancies per mother, occurring between 2008 and 2016 in Norway. The information on all pregnancies and subsequent outcomes (livebirth, stillbirth, miscarriage, and induced abortions) came from three national registries (Birth Register, the General Practitioner, and Patient Register) in Norway. We first defined IPI using the conception date of the index pregnancy (pregnancy following the interval) and the event date of the previous pregnancy, irrespective of pregnancy outcomes. We then calculated IPI among pregnancies that restricted to livebirth or stillbirth. We independently assessed the association between the two IPIs and preterm births (PTB). Logistic regression analysis was conducted. Adjusted odds ratios (aOR) and 95% confidence interval (CI) were estimated after adjustment for maternal age, parity, and year of birth. In the study, 4.7% of pregnancies resulted in PTB. There were about 12% of pregnancies occurred in <6 months after delivery or termination of pregnancies irrespective of their outcomes. However, when pregnancy losses were not accounted, there were only 4.4% births occurred in <6 months following livebirth or stillbirth, indicating over 60% of IPIs were misclassified. After adjustment for confounders, there was a modest overestimation of odds of short IPI (<6 months) (aOR=1.96, 95% CI: 1.77-2.17) for IPI that restricted to livebirth/stillbirth on PTB as compared to the odds of short IPI that accounted pregnancy loss (aOR=1.63, 95% CI: 1.50-1.76). There was a significant misclassification bias associated with pregnancy loss which should not be ignored when assessing the effect of IPI on PTB.

A Population-Based Study to Quantify the Risks of Opioid Analgesics in Pregnancy Susan B. Brogly* 3647] Brogly Maria P. Velez Martha M. Werler Wenbin Li Andi Camden Astrid Guttmann

Background: An estimated 2-4% of US pregnancies are exposed to opioid analgesics for pain. We sought to determine the risks of prenatal opioid analgesics independent of biases that may have affected other studies.

Methods: Using universal coverage administrative health data for Ontario, Canada we assembled a cohort of mother-infant pairs without opioid use disorder and with an estimated date of confinement from Apr 2013-Mar 2018 (N=627,283). Since July 2012 all opioid analgesic prescriptions were recorded in the linked Narcotic Monitoring System database. Risk ratios between opioid analgesic exposure (any vs. none & 1st, 2nd, 3rd trimester vs. none) and preterm birth, small for gestational age (SGA) birth and stillbirth were estimated. Inverse probability treatment weighting with *a priori* confounders (age, SES, parity, obesity, diabetes, pain, comorbidity score) and high dimensional propensity scores (HDPS) was used for confounding adjustment.

Results: 4.1% of pairs were exposed to opioid analgesics, mainly codeine (2.2%), morphine (1.1%) or oxycodone (0.8%). HDPS performed better for confounding control than *a priori* confounders alone. The adjusted preterm birth risk was higher in opioid exposed vs. unexposed pairs (1st trimester: 1.37, 95% CI: 1.29-1.46; 2nd: 1.39, 95% CI 1.30-1.49; 3rd:1.09, 95% CI: 1.01-1.18), and was 26% higher with codeine in the 1st or 2nd trimester and 35-44% higher with morphine in the 1st, 2nd or 3rd trimester. An ~10% higher SGA risk was observed only for 1st trimester opioid analgesic, codeine or morphine exposure. Stillbirth was higher in pairs with 1st or 2nd trimester exposure to any opioid analgesic, codeine (1st: 2.19, 95 % CI 2.03-2.36; 2nd 2.02, 95% CI: 1.85-2.20) or morphine (1st: 1.27, 95% CI: 1.07-1.51; 2nd 1.16, 95% CI: 0.97-1.38).

Conclusion: Prenatal opioid analgesics, particularly 1st or 2nd trimester exposure, is associated with a higher risk of preterm birth, SGA and stillbirth after accounting for confounding by indication.

Immunity and Infection and the Developing Infant Gut Microbiome in the New Hampshire Birth Cohort Study Yuka Moroishi* 3647] Moroishi Jiang Gui Juliette Madan Emily Baker Anne G. Hoen Lucas Salas Todd Everson Carmen Marsit Zhigang Li Margaret R. Karagas

The interplay between the developing immune system and microbiome is a critical process during infancy. We examined whether blood immune cell composition at birth in umbilical cord (inferred by DNA methylation profiling) related to the early infant gut microbiome (assessed by 16S and metagenomic sequencing) and in turn examined whether the infant gut microbiome influences occurrence of infections among infants the New Hampshire Birth Cohort Study. We used penalized regression to select possible microbial taxa associated with immune cells. Relative abundance of *Bifidobacterium* bifidum was related to proportion of B cells, CD4+ T-lymphocytes, CD8+ T-lymphocytes, Natural killer cells, and nucleated red blood cells. Several microbial taxa associated with upper and lower respiratory tract infections, acute respiratory symptoms, fever, and eczema over the first year of life. Our findings give clues to the development of gut microbiome and immunity in early life.

Perinatal & Pediatric

Descriptive epidemiology of neonatal visits to emergency departments in Ontario, Canada: a population-based record linkage study Michaela Smith* Michaela Smith Deborah Weiss Mélissa Langevin Nick Barrowman Ann E. Sprague Deshayne B. Fell Katherine A. Moreau Thierry Lacaze-Masmonteil Roger L. Zemek JoAnn Harrold

Background: Infants and neonates present frequently to the Emergency Department (ED) for care, but there is relatively little research examining when and why ED visits occur in the neonatal period (first 28 days of life). Our objective was to determine the prevalence, incidence, timing, and reasons for neonatal ED visits using a large population-based cohort and record linkage across multiple databases.

Methods: We extracted a one-year birth cohort (March 1, 2016 to February 28, 2017) from a population-based birth registry in Ontario, Canada. This cohort, representing all births in the province, was linked to national health administrative databases which capture all hospital admissions and ED visits. Prevalence and incidence rates of neonatal ED visits were calculated using standard statistical techniques. ED visits were also characterized by age of neonate, access to primary care, maternal age, infant sex, and diagnosis code (assessed using the International Classification of Diseases 10th Revision).

Results: 9.6% (13,190/136,967) of infants visited the ED in the neonatal period; 8.2% (n=11,158) were single visits and 1.5% (n=2032) visited 2+ times. In this period, the incidence rate of ED visits was twice as high in days 1-14 versus days 15-28, at 6.65 per 1000 days of follow-up (95% CI 6.52, 6.78) and 2.99 (2.92, 3.07), respectively. The median age at first ED visit was 10 days old, but most occurred on the fourth day of life. Across all visits, the most frequent diagnosis was neonatal jaundice (19.0%), followed by parental fears in a healthy infant (5.0%). In most cases (88.2% of visits), parents reported having access to a family physician. Visit rates were higher among male infants and younger mothers (under 25 years) regardless of parity.

Conclusions: Approximately 10% of infants visit the ED in the neonatal period, most frequently in the first 14 days after birth. A large proportion of ED visits can be attributed to neonatal jaundice and parental concerns.

Incidence of neonatal ED visits

	Total ED visits	Total person-time (days)	Rate (per 1000 days)	95% CI Lower bound	95% CI Upper bound
First 28 days	15 696	3 405 229	4.61	4.54	4.68
Days 1-14	10 010	1 506 031	6.65	6.52	6.78
Days 15-28	5 686	1 899 198	2.99	2.92	3.07

Incidence rate twice as high in first 14 days v. second 14 days
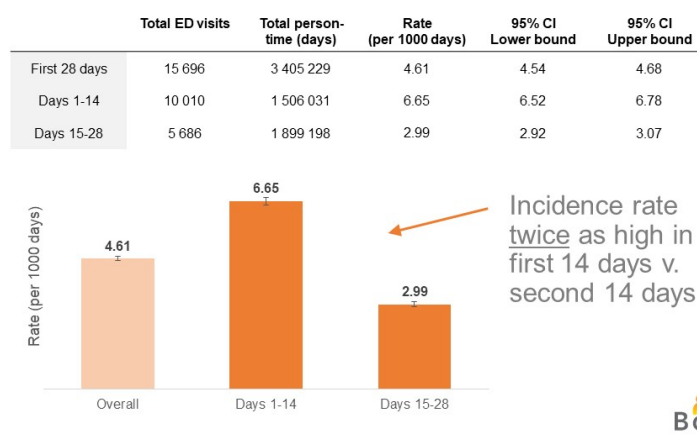
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Ontario

Prevalence of Developmental Delay among Children born Late-preterm and Early-term in Early Childhood: The All Our Families Study Nikki Stephenson* Nikki Stephenson Jessica Walsh Muci Wu Sheila McDonald Suzanne Tough

Background: Births between 34 and 38 gestational age (GA) account for 30% of all live births, and unlike infants born before 34 weeks GA they do not receive routine developmental follow-up. However, these infants born late-preterm (34-37 weeks GA) and early-term (37-39 weeks GA) are at increased risk of poorer social and health outcomes when compared to infants born full-term (39-40 weeks GA). It is not feasible to routinely follow up one-third of all live births with extensive assessment, thus it must be determined who among these late-preterm and early-term births would benefit most from additional support.

Objectives: 1) Determine the distribution of GAs at birth; 2) Compare the prevalence of delays by developmental domain for children born late-preterm and early-term at 2, 3 and 5 years.

Methods: The All Our Families Study is a prospective pregnancy cohort of 3200 women from Calgary, Canada, which collected information on birth, child health and development outcomes (Ages & Stages Questionnaire domains: communication, gross motor, fine motor, problem-solving, and personal social skills). Medical records were linked with self-report questionnaires completed twice in pregnancy, at 4 months post-partum, and 1, 2, 3 and 5 years postpartum. Chi-square analysis and 95% CIs were used to compare prevalences of developmental delays.

Results: GA specific prevalences were: late-preterm 4.54%, early-term 24.47%, and full-term 54.69%. Children born late-preterm experience more problem-solving delays at 2 years, problem-solving and fine motor delays at 3 years, and problem-solving, fine motor, and gross motor, and personal social delays at 5 years when compared to their full-term counterparts (table 1).

Conclusion: The results of this study indicate developmental delay occurring before five is correlated with gestational age at birth. Developmental delay may become more pronounced through the preschool years, and research on the trajectories of longer-term outcomes is necessary.

Table 1: Prevalence estimates of developmental delay (according to ASQ-3) by gestational age at birth at 2, 3 and 5 years of age

ASQ Domain	2 Year			p-value	3 Year			p-value	5 Year			p-value
	Late-Preterm	Early-Term	Full-Term		Late-Preterm	Early-Term	Full-Term		Late-Preterm	Early-Term	Full-Term	
	n = 60	n = 302	n = 644		n = 88	n = 428	n = 964		n = 71	n = 356	n = 825	
	% (95% CI)				% (95% CI)				% (95% CI)			
Communication	23.21	11.60	13.99	0.0642	8.75	5.99	4.48	0.1573	8.22	7.44	7.59	0.9737
	(13.97-36.01)	(8.52-15.61)	(11.59-16.80)		(4.23-17.25)	(4.14-8.59)	(3.36-5.95)		(3.74-17.13)	(5.25-10.45)	(6.03-9.52)	
Gross motor	19.64	13.17	12.23	0.2782	20.00	12.64	11.67	0.0919	17.57	8.62	6.04	0.0008
	(11.21-32.12)	(9.87-17.35)	(9.98-14.90)		(12.62-30.20)	(9.87-16.04)	(9.82-13.81)		(10.48-27.96)	(6.25-11.78)	(4.65-7.81)	
Fine motor	17.86	8.20	11.22	0.0717	25.32	16.89	13.89	0.0143	12.33	7.20	5.46	0.0483
	(9.88-30.13)	(5.64-11.78)	(9.07-13.82)		(16.95-36.03)	(13.70-20.64)	(11.88-16.17)		(6.54-22.05)	(5.04-10.17)	(4.15-7.16)	
Problem-solving	25.45	15.14	11.71	0.0095	21.25	13.14	9.51	0.0018	5.41	3.94	1.44	0.0050
	(15.68-38.54)	(11.6-19.53)	(9.5-14.35)		(13.63-31.57)	(10.32-16.60)	(7.84-11.49)		(2.04-13.55)	(2.43-6.34)	(0.84-2.46)	
Personal social	23.21	14.42	12.54	0.0739	7.50	6.90	4.69	0.1650	16.90	10.81	7.09	0.0121
	(13.97-36.01)	(10.97-18.73)	(10.26-15.24)		(3.41-15.72)	(4.90-9.65)	(3.54-6.18)		(9.05-27.66)	(8.14-14.22)	(5.58-8.96)	

Parents' perspectives on using children's shed deciduous teeth for environmental health research Tania Desrosiers* Tania Desrosiers Neasha Graves Kathleen Gray

Background: Deciduous teeth develop in utero and are a stable biomatrix in which prenatal exposures can be measured. Shed teeth are thus a valuable resource for epidemiologic studies of environmental risk factors for perinatal and pediatric outcomes. In this qualitative study, our aim was to explore parents' perspectives on using children's teeth for environmental health research.

Methods: Parents of children 5-15 years were recruited to attend focus groups in demographically diverse areas of North Carolina in 2019. A semi-structured interview tool was used to guide moderated discussion about cultural practices related to losing teeth and perspectives on participating in research that utilize children's teeth. Discussions were recorded and transcribed; transcripts were coded and analyzed using qualitative content analysis.

Results: Participants (n=19) were predominantly female (84%), had a college degree (69%), and self-identified as black (47%) or white (47%). Whereas all parents exchanged money for shed teeth, only 63% saved teeth. Four recurring themes emerged: 1) Parents demonstrated lack of knowledge about how teeth develop and relate to exposures in pregnancy; 2) Parents expressed concerns related to privacy of information and DNA from teeth; 3) Parents held conflicting opinions about the benefits of learning that children were prenatally exposed to an environmental contaminant, particularly without any recommended follow-up or treatment; 4) Parents were generally in favor of using shed teeth for research, and wondered whether they should be saving children's teeth for unanticipated needs in the future.

Conclusions: We identified several potential barriers to participation to consider when designing responsive informed consent and study protocols for collecting deciduous teeth as biomarkers of the fetal exposome. Our study also reveals an opportunity to encourage parents to save shed teeth for clinical or research applications.

Gestational organophosphate esters exposure and thyroid hormone disruption in newborns: The HOME Study Zana Percy* Zana Percy Ann Vuong Joseph Braun Yingying Xu Maria Ospina Antonia Calafat Andy Hoofnagle Kim N. Dietrich Changchun Xie Bruce P. Lanphear Kim Cecil Kimberly Yolton Aimin Chen

Production of organophosphate esters (OPEs) has risen and OPEs have replaced polybrominated diphenyl ethers as flame retardants in consumer goods. Animal and human studies suggest that OPEs may be associated with thyroid hormone (TH) disruption, but few cohort studies have examined this association. We quantified OPEs in the urine of 298 healthy pregnant women in the HOME Study from Cincinnati, Ohio (enrolled in 2003-2006) at three times (16 and 26 weeks' gestation, delivery), and THs in newborn cord serum. We used generalized estimating equations (GEE) to assess associations between OPE concentrations at each time and cord serum THs. We also examined dose-response using quartiles from each time. We adjusted for mother's age at delivery, education, race, infant year of birth, and infant sex. Each natural log-unit increase in urinary bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) at 16 and 26 weeks was associated with a 0.02 (95% CI: -0.004, -0.04) ng/dL reduction in free T4 and a 0.22 (95% CI: -0.03, -0.41) ug/dL reduction in total T4, respectively. For each natural log-unit increase, urinary di-n-butyl phosphate (DNBP) at 16 weeks was associated with a 0.14 (95% CI: 0.02, 0.27) uIU/mL increase in cord blood thyroid stimulating hormone (TSH), and DNBP at delivery was associated with a 0.29 (95% CI: -0.01, -0.58) ug/dL decrease in cord serum total T4. In dose-response analyses, increased urinary DNBP and diphenyl phosphate (DPHP) at delivery were associated with increased cord serum TSH; bis-2-chloroethyl phosphate (BCEP), BDCIPP, DPHP, and DNBP at delivery were inversely associated with some thyroid hormones (Figure 1). These results suggest that gestational exposure to OPEs may affect newborn thyroid function.

Association between life-course maternal adversity and longitudinal measures of infant behavior

Katherine Bowers* Katherine Bowers Lili Ding Qin Kiki Sun Kimberly Yolton Robert T Ammerman Judith Van Ginkel Alonzo Folger

Background. Despite reductions in health care disparities, children from socioeconomically disadvantaged families have a higher risk of impaired neurobehavioral outcomes. Home visiting (HV) programs aim to improve developmental and behavioral outcomes for families living in poverty by focusing on the first 1,000 days of life, a critical window of brain development. But, even within impoverished families, variability exists in response to HV services and the prevalence of adverse behavioral outcomes. The PRegnancy and Infant DEvelopment (PRIDE) Study was initiated to understand the timing and types of adversity that may contribute to poorer behavioral outcomes and to understand the role of DNA methylation in these associations within families in poverty. Methods. In the pilot wave, 56 pregnant mothers participating in Every Child Succeeds, a HV program in Cincinnati, OH, were enrolled in the PRIDE Study and followed postnatally to measure infant neurobehavior at 1 month (n=53), 24 months (n=40) and 36 months (n=27). A battery of assessments measured maternal early-life and prenatal adversity. Infant behavior was assessed using the NICU Network Neurobehavioral Scale (1 month) and Child Behavior Checklist (CBCL) (24 and 36 months). Descriptive statistics summarized demographics at each study visit. Adjusted coefficients (maternal age and race) describing the association between maternal adversity and infant behavioral outcomes were generated using linear regression. Results. Early-life adversity, multiple prenatal measures of perceived general and pregnancy-associated stress, and maternal depression were associated with worse behavioral outcomes (both externalizing and internalizing) at 24 months (Table 1). For most measures the association persisted through 36 months, though some were not statistically significant. Conclusion. Adversity both in early life and during pregnancy is associated with poorer offspring behavioral outcomes at 24 and 36 months.

Table 1. Association between maternal stress and adversity in pregnancy and offspring behavioral impairment at 24 and 36 months.

Dependent Variable	Independent Variables*	24 months		36 months	
		Coefficient	P value	Coefficient	P value
CBCL** Internalizing symptoms	Early Life Adversity	0.72	0.25	0.50	0.45
	Psychological Distress	0.31	0.03	0.39	0.01
	Depression	0.51	0.03	0.86	0.002
	Perceived Stress	0.38	0.04	0.57	0.01
	Ratio Frequency hassles:uplifts	-1.46	0.21	-0.2	0.87
	Ratio Intensity hassles:uplifts	-6.98	0.02	-1.40	0.75
CBCL Externalizing symptoms	Early Life Adversity	1.696	0.01	0.81	0.24
	Psychological Distress	0.494	<0.001	0.41	0.017
	Depression	0.731	0.002	0.40	0.22
	Perceived Stress	0.598	0.002	0.29	0.25
	Ratio Frequency hassles:uplifts	-1.463	0.21	-0.20	0.87
	Ratio Intensity hassles:uplifts	-6.979	0.02	-1.40	0.75
CBCL Total score	Early Life Adversity	1.282	0.04	0.80	0.25
	Psychological Distress	0.424	0.002	0.43	0.01
	Depression	0.683	0.003	0.69	0.03
	Perceived Stress	0.519	0.01	0.46	0.07
	Ratio Frequency hassles:uplifts	-1.913	0.09	-0.61	0.63
	Ratio Intensity hassles:uplifts	-8.467	0.004	-5.45	0.20

*Early Life Adversity measured by Adverse Childhood Experiences scale; Psychologic Distress as measured by Brief Symptom Inventory-18 total score; Depression measured by Edinburgh Postnatal Depression Scale; Perceived Stress measured by Perceived Stress Scale-10; Ratio of frequency and intensity of uplifts measured by Pregnancy Experience Scale-Brief.
**CBCL- Child Behavior Checklist

What does the target trial emulation framework add to pharmacoepidemiology? A systematic review focusing on active-comparator, new-user studies. Kazuki Yoshida* Kazuki Yoshida Sizheng Steven Zhao Houchen Lyu Daniel H. Solomon Kazuki Yoshida

OBJECTIVE To clarify the additional benefits of the target trial emulation framework beyond the typically recommended active-comparator with new-user design in pharmacoepidemiology, we conducted a focused methodological systematic review of observational comparative effectiveness studies to identify design issues that might have been avoided by explicitly specifying target trials.

METHODS We chose comparative effectiveness studies of biological disease modifying antirheumatic drugs for rheumatoid arthritis as an example because many active-comparator, new-user design studies have been published. We searched papers through August 2019. We multiply reviewed each paper for the components of the target trial emulation: eligibility criteria, treatment strategies, assignment procedures, follow-up period, outcome, causal contrasts of interest, and analysis plan (Table). Each study's actual description was taken as the "emulation protocol," and we considered the corresponding "implied target trial protocol." We assessed for emulation failures that would have been avoided with an explicit target trial protocol (see Table).

RESULTS We found 31 studies comparative effectiveness studies that used an active-comparator, new-user design. 16 included post-baseline information for baseline eligibility. No studies explicitly specified the treatment strategies beyond the names of the initiated drugs, without mention of allowed treatment changes during follow-up. 13 studies described a priori confounders; none cited literature supporting the confounders. 5 studies failed to specify the follow up duration. 3 used "unnatural" composite outcomes to avoid missingness. 26 did not specify causal contrasts of interest. 2 claimed per-protocol analyses, but failed to address post-baseline selection bias.

CONCLUSION Explicit target trial protocols are likely valuable even in active-comparator, new-user design comparative effectiveness studies.

Table 1. Issues identified in the 31 studies reviewed for their design descriptions ("emulation protocol") and reasons why these do not correspond to well-defined "target trials" (emulation failure).		
Design Component	Issues in "emulation protocol"	Reasons for emulation failure (i.e., whether the implied hypothetical trial is well-defined and natural)
1. Eligibility criteria	Post-baseline data requirement (16 studies).	Impossible to use future data at enrollment.
	Differential eligibility for each arm (3 studies).	Breaks the notion of one group of people randomized to 2+ arms.
2. Treatment strategies	Mixing prevalent users and new users (1 study)	Impossible to assign/randomize to "*having* used drug A for X months"
	Not defining treatment strategies beyond "initiate drug A at baseline" (31 studies)	Implied protocol leaves everything up to the treating physician and patient (See also item 6)
3. Assignment procedures	Weak substantive justification for confounder selection (31 studies)	Broken randomization (due to insufficient emulation of randomization)
4. Follow-up period	Unspecified follow-up duration in longitudinal analyses (5 studies)	Infeasible to conceive an RCT with unspecified duration. Analysis results may lack interpretability.
5. Outcome	Joint outcome of remaining on treatment *and* having a good disease activity response to avoid missingness (3 studies)	Rather unnatural outcome for a real RCT although technically possible.
6. Causal contrasts of interest	Failure to clarify the estimand of interest (26 studies)	Problem also common in clinical trials
7. Analysis plan	Intention-to-treat type analysis among those with follow up	Deviates from the intention-to-treat principle (all randomized should be analyzed)
	Per-protocol analyses did not account for post-baseline selection bias	Problem also common in clinical trials

Pharmacoepidemiology

Causal estimands for comparing outcomes of brand and generic drugs using observational data: a narrative review Marissa Seamans* Marissa Seamans

Generic drugs have saved over $1 trillion in the healthcare system as low-cost alternatives to brand-name drugs. Generics are approved based on demonstration of their bioequivalence to their corresponding brand products under the assumption that products with the same active ingredients and equivalent rates of absorption will be therapeutically exchangeable in clinical practice. However, questions arise about the real-world exchangeability of brand and generic drugs due to differences in the products' ingredients or patterns of drug adherence. Given that randomized clinical trials comparing generics to their brand counterparts are not required and therefore seldom sought, questions about the comparative effectiveness and safety of brand and generics must be answered using observational data with clearly defined estimands. We reviewed the breadth of estimands that may be considered by regulators, clinicians, and patients to examine the therapeutic equivalence of generic and brand drug use. We identified situations that might require each estimand and illustrate with examples from the literature. Finally, we provide guidance on the design and analysis of future observational studies to target estimands comparing outcomes of brand and generic drugs.

Impact of hospitalization and medication switching on future adherence to oral anticoagulant in high-risk atrial fibrillation patients Thanh Phuong Pham Nguyen* Thanh Phuong Pham Nguyen Yong Chen Dylan Thibault Charles E. Leonard Sean Hennessy Allison Willis

Objectives: Oral anticoagulants (OACs) are recommended in high-risk atrial fibrillation (AF) patients to prevent stroke and systemic thromboembolism. Hospitalization represents an opportunity to enhance patients' adherence to chronic therapies. We aimed to examine the impact of hospitalization and medication switching after discharge on patients' future adherence to OACs. Methods: A quasi-experimental pre-post study design was implemented using commercial insurance healthcare claims from the 2009-2016 Optum Insight Data Mart. We identified adult AF patients on OAC with a random hospitalization after OAC initiation and evaluated OAC adherence 6 months before and after hospitalization. Adherence was estimated by the proportion of days covered (PDC). Difference-in-difference analysis via a generalized linear model was employed to compare pre- and post-hospitalization PDCs by reasons for hospitalization (i.e., bleeding versus nonbleeding-related reasons), adjusting for imbalanced baseline characteristics between groups. Change to adherence when switching OAC at discharge was also examined.
Results: We identified 22,429 individuals who met inclusion criteria (median age 74 years, 52.4% male, 77.2% white, and 4.5% admitted for bleeding). After covariate adjustment, there was a reduction in PDC after discharge in both groups (7.8% and 4.7%, respectively; p<0.0001). We noted a larger reduction by 3.2% (p=0.0003) in PDC in the bleeding group vs. those hospitalized for other reasons. We unexpectedly found a smaller decline in PDC by 3.4% (p=0.0342) in patients who switched from warfarin to a direct-acting OAC compared to other switchers after discharge, regardless of the reason for hospitalization.
CONCLUSIONS: These results suggested that hospitalization could temporally be associated with a reduction in OAC adherence. Better strategies are needed to improve OAC adherence, particularly after hospitalization and during transition of care across different settings.

Pharmacoepidemiology

Transition from ICD-9-CM to ICD-10-CM and measurement of pregnancy episodes in the U.S. health insurance claims data

Amir Sarayani* Amir Sarayani Xi Wang Thuy Thai Yasser Albogami Nakyung Jeon Almut G Winterstein

Prior to October 2015, pregnancy cohorts assembled from U.S. health insurance claims databases rely on International Classification of Diseases-Ninth revision (ICD-9) codes. Our objective was to extend existing pregnancy identification algorithms into the ICD-10 era and evaluate performance. We used a national private insurance database (2006-2017) to develop and test the algorithm. We considered validated ICD-9 diagnosis and procedure codes to identify claims for live birth, stillbirth, ectopic pregnancy, abortions, and prenatal screening visits to identify pregnancies with unknown outcomes. We then mapped these codes to the ICD-10 coding system using General Equivalent Mapping tools and reconciled the outputs with literature and expert opinion. Both versions were applied to the respective coding period to identify pregnancies, assign gestational age, estimate conception, and define individual pregnancy episodes. We required 45 weeks of health plan enrollment from the episode start date to ensure the capture of all pregnancy endpoints. We identified 7,060,675 pregnancy episodes, of which 50.1% had insurance enrollment during pregnancy. The pregnancy episodes with live-born deliveries comprised the majority (76.5%) of the cohort, followed by the abortions (20.3%). The annual prevalence for all types of pregnancies was stable across the ICD transition period except for post-term pregnancies, which increased from 0.5% to 3.4% after the ICD transition. We observed that ICD codes with gestational age information were available for 86.8% of live-born deliveries in the ICD-10 era compared to 23.5% in the ICD-9 era. The patterns of prenatal tests remained stable across the transition period. In conclusion, the translation of existing ICD-9 pregnancy algorithms into the new ICD-10 codes appeared valid. New codes for gestational age can potentially improve the precision of conception estimates and minimize measurement biases in the ICD-10 era.

A pharmacoepidemiologic approach to evaluate real-world hormonal contraceptive failure using administrative claims data Amir Sarayani* Amir Sarayani Joshua D. Brown Amie J. Goodin Brian Cicali Carl Henriksen Stephan Schmidt Almut G. Winterstein

Accurate estimation of pregnancy conception is a challenge of pharmacoepidemiologic studies. In a novel application, we aimed to study the effectiveness of oral contraceptives (OC), where misclassification of conception relative to OC use may obscure effect estimates. We used a large claims database to determine OC failure (i.e., conception) among patients receiving anticonvulsants (AC) for epilepsy or bipolar disorder, where the expected OC failure risk varies depending on drug-drug interaction (DDI) between the type of AC and OC. In cohort A, we identified females aged 12-48 who had AC drugs with no DDI (full effect of OC). In cohort B, patients had AC drugs with known DDI (diminished effect of OC). In both cohorts, we excluded patients with infertility or hormonal imbalances during a 6-month look-back period and followed patients from their first day of concomitant use. We allowed for cohort re-entry if we observed a gap in treatment for more than 15 days. The outcome was conception during concomitant AC/OC use, measured with a validated algorithm that estimates gestational age based on identified pregnancy endpoints. We estimated adjusted incidence rates, the relative and absolute risk using a generalized estimating equation model after standardized mortality ratio weighting via exposure propensity score. In cohort A, we identified 89,777 OC episodes with an adjusted contraception failure rate of 16.1 (95% CI 14.5-17.8) per 1000 person-years. In cohort B, we observed a higher incidence rate of 22.9 (18.7-28.0) among 18,964 OC episodes. The relative risk of contraception failure in cohort B was 1.43 (1.13-1.78), and the rate difference was 6.8 (1.9-11.7). The findings were robust in several sensitivity analyses. Our study showed that it is feasible to estimate the contraception failure rates for oral contraceptives using real-world data and pharmacoepidemiologic methods with adequate sensitivity to detect the expected impact of a drug-drug interaction.

Patient Characteristics Associated with Concurrent VA and non-VA Prescriptions among Post-9/11 Veterans Receiving Long-term Opioid Therapy in Oregon: 2014-2019 Jonah Geddes* Jonah Geddes Sarah Andrea, PhD MPH Tess A. Gilbert, MHS Lawrence Cook, PhD Kathleen Carlson, PhD

Research Objective:
Veterans receiving Department of Veterans Affairs (VA)-prescribed long-term opioid therapy (LTOT) and concurrent non-VA psychotropic medications may have greater risk for opioid-related adverse events. For Post-9/11 Veterans in Oregon receiving VA LTOT, we examined associations between sociodemographic and clinical characteristics and concurrent non-VA opioid or sedative/hypnotic prescriptions.

Study Design:
We linked VA administrative data to Oregon prescription drug monitoring program data for Post-9/11 Veterans that used Oregon VA outpatient services between 2014 and 2019. We restricted to Veterans receiving LTOT (≥5 milligram morphine equivalents of opioids in any 90 out of 104-days). We defined concurrent non-VA prescriptions as those with ≥1 day of overlap with VA opioid prescriptions from the fill date. Associations between patient characteristics and likelihood of overlap were estimated using logistic regression; multivariable models were specified using directed acyclic graphs.

Principal Findings:
Among 3,846 Veterans who received VA LTOT during the study period, there were 831 (21.6%) who received concurrent non-VA opioids and/or sedative/hypnotics. We found that women (aOR=1.4; 95% CI: 1.0-1.8), those living rurally (aOR=1.6; 95% CI: 1.3-1.8), those with low versus high annual VA utilization (aOR=2.4; 95% CI: 1.2-4.8), Veterans Choice Program participants (aOR=1.2; 95% CI: 1.0-1.4), and those with pain (aOR=2.8; 95% CI: 1.1-7.1), posttraumatic stress disorder (aOR=1.3; 95% CI: 1.1-1.6) or traumatic brain injury (aOR=1.2; 95% CI: 1.0-1.5) diagnoses were more likely to have concurrent non-VA prescriptions. Veterans with cancer diagnoses were less likely to have concurrent prescriptions (aOR=0.5; 95% CI: 0.4-0.7).

Conclusions:
Understanding patient characteristics associated with concurrent psychotropic medications may allow for greater identification of high-risk individuals and the provision of interventions during key touchpoints of care.

Geographic Variation in Anticoagulant Use and Resident, Facility, and County- Level Characteristics Associated with Treatment Among United States Nursing Home Residents with Atrial Fibrillation Matthew Alcusky* Matthew Alcusky Jonggyu Baek Jennifer Tjia David McManus Kate Lapane

Objective:
To quantify geographic variation in anticoagulant use and explore what resident, facility, and county characteristics were associated with anticoagulant use in an older clinically complex population with atrial fibrillation.

Methods:
Long-stay nursing home residents (>65 years) with diagnosed atrial fibrillation and >6 months of Medicare fee-for-service enrollment were studied. The point prevalence of oral anticoagulant use was estimated on December 31st, 2014, 2015, and 2016 using a repeated cross-sectional design. Multilevel logistic models evaluated the extent to which variation in anticoagulant use between counties could be explained by resident, facility, and county characteristics, and state of residence. Proportional changes in cluster variation (PCV), intraclass correlation coefficients (ICC), and adjusted odds ratios were estimated.

Results:
Among 86,736 nursing home residents from 11,860 facilities and 1,694 counties, 71% were ≥ 80 years, 50% had a CHA2DS2-Vasc ischemic stroke risk score of >5 (>2 is high risk), and 45% used oral anticogulants. Older age, recent bleeding, cognitive impairment, and antiplatelet use had strong negative associations with treatment. Most states had counties in the highest (48%-58%) and lowest (31%-41%) quintiles of anticoagulant use. Compared with the null model, adjustment for resident characteristics increased variation between counties (PCV: -18.4%). The full model explained 56.6% of between-county variation. Within-county correlation was a small proportion (ICC<2.2%) of total variation.

Conclusion:
In this older adult population at very high-risk for ischemic stroke, less than half received anticoagulants. Nursing home residents with similar characteristics were treated differently across counties, and variation in treatment was partially attributable to the characteristics of facilities and counties. Comparative evidence and refinement of predictive algorithms specific to the nursing home setting may be warranted.

Dealing with treatment-confounder feedback and sparse follow-up in longitudinal studies - an application of the marginal structural model with a multiple sclerosis cohort Mohammad Ehsanul Karim* Mohammad Ehsanul Karim Helen Tremlett Feng Zhu John Petkau Elaine Kingwell

The interferon-betas are widely prescribed platform therapies for patients with multiple sclerosis (MS). We accessed a cohort of patients with relapsing onset MS from British Columbia, Canada (1995-2013) to examine the potential survival advantage associated with interferon-beta exposure using a marginal structural model. Accounting for potential treatment-confounder feedback between comorbidity, MS disease progression and interferon-beta exposure, we found an association between cumulative interferon-beta use of at least 6 months and improved survival (hazard ratio = 0.63, 95% confidence interval 0.47-0.86). We also assessed potential effect modifications by sex, baseline age or baseline disease duration, and found these factors to be important effect modifiers. Sparse follow-up due to variability in patient contact with the health system is one of the biggest challenges in longitudinal analyses. We considered several single-level and multi-level multiple imputation approaches to deal with sparse follow-up of the disease progression information, and both types of approaches produced similar estimates. Compared to ad hoc imputation approaches, such as linear interpolation and last observation carried forward, all multiple imputation approaches produced smaller treatment effect estimates, although the direction of effect and conclusion drawn concerning the survival advantage remained the same.

Reproductive

Peri-pubertal serum dioxins, furans and PCBs are longitudinally associated with reproductive hormones throughout adolescence among Russian Boys Bora Plaku-Alakbarova*

Bora Plaku-Alakbarova Paige Williams Jane Burns Susan Korrick Oleg Sergeyev Mary Lee Sergey Rudnev Boris Revich Russ Hauser

Background. Dioxins, furans and polychlorinated biphenyls (PCBs) are ubiquitous environmental pollutants linked with altered timing of pubertal onset and maturation in boys. We examined whether peri-pubertal exposures to dioxins, furans and PCBs were associated with reproductive hormones during adolescence in the Russian Children's Study.

Methods: From 2003-2005, 516 Russian boys were enrolled at ages 8-9 years; 45 serum dioxins, furans, and PCBs were quantified at study entry and empirically grouped into 8 exposure clusters using variable cluster analysis. Serum reproductive hormones were measured biennially through age 19. Longitudinal mean response models were used to model the association between chemical clusters and serum levels of total testosterone (adjusted for sex hormone binding globulin), follicle stimulating hormone (FSH), and luteinizing hormone (LH).

Results. A 1-SD increase of the cluster 2 score (representing tetra/penta PCBs 44, 49, 52, 87, 101, 110, 149, with chlorines at 2,2',5') was associated with decreased serum testosterone in early and late puberty, with the greatest decline (52%, 95% CI 40-64%) occurring at age 8. The same 1-SD increase in cluster 2 was associated with an 8-37% decline in serum LH from ages 8-13, with the highest decline of 37% (95% CI 19-56%) occurring at age 8. Also, a 1-SD increase in cluster 4 score (tri/tetra PCBs 28, 66, 77, 81, with chlorines at 4,4') was associated with a 15-19% decline in testosterone at ages 10-15, with the highest decline of 19% (95% CIs 14%, 25%) occurring near age 12. However, a 1-SD increase in cluster 4 was associated with increased FSH, with the highest gains (12-14%) observed after age 16. No significant associations were observed with other exposure clusters.

Conclusion. Peri-pubertal exposures to tri- and penta-chlorinated PCBs with chlorines at the 2,2',5' or 4,4' positions may alter serum levels of testosterone, FSH and LH during puberty.

Reproductive

Pelvic inflammatory disease in North Carolina emergency departments Dayna Neo* Dayna
Neo Erika Samoff Mara Larson Anna Cope

Background: Pelvic inflammatory disease (PID) is an infection of the upper female reproductive
organs that can lead to infertility, chronic pelvic pain, and ectopic pregnancies. In 2017, 308 cases
were reported to the North Carolina (NC) health department. We aimed to quantify PID diagnoses in
NC emergency department (ED) visits.

Methods: The NC Disease Event Tracking and Epidemiology Collection Tool (NC DETECT) tracks all
ED visits in NC. We identified PID diagnoses among female patients of reproductive age (15-44
years) between 2008 and 2017 using ICD9/10-CM codes, and calculated the yearly prevalence of PID
at the patient level. We assessed the number of PID visits per patient each year, and examined
yearly PID prevalence by age, median neighborhood income based on zip code, insurance status, and
provider region.

Results: A total of 54,502 ED visits among 51,847 women had a diagnosis code for PID between
2008 and 2017. Most (95.5%) women with PID only had one ED visit, while 4.5% had >1 PID visit in
the same calendar year. PID prevalence among women who visited the ED decreased from 1.0%
(n=6,189) to 0.6% (n=4,371) between 2008 and 2017 (Figure 1). For each year, PID prevalence was
highest among women aged 20-24 years, covered under Medicaid, and whose provider was in the
coastal region of NC. Between 2008 and 2016, PID prevalence was highest among women whose
median neighborhood income was less than $37,999, and in 2017, it was highest among women
whose median neighborhood income was between $38,000 - $47,999. While the overall prevalence
of PID decreased between 2008 - 2016, we observed a slight increase in PID between 2016 – 2017.

Conclusion: More cases of PID were identified among ED patients than was reported to the health
department. Although PID prevalence has declined since 2008 among women visiting the ED,
disparities associated with PID persist in NC.

Figure 1. Pelvic inflammatory disease trend, 2008 – 2017

Reproductive
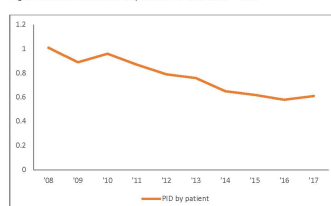
Is it too little or too late? Associations between sleep duration and midpoint, and fecundability Joshua Freeman* Joshua Freeman Brian Whitcomb Elizabeth Bertone-Johnson Laura Balzer Lindsey Sjaarda Neil Perkins Keewan Kim Jeannie Radoc Robert Silver Victoria Andriessen Alexandra Purdue-Smithe Enrique Schisterman Sunni Mumford

Research in animal models and studies of night shift work has shown that extremes of sleep deprivation and disrupted sleep timing are related to perturbations in reproductive hormones and menstrual cycle characteristics, and thus potentially disrupting reproduction. To date, few studies have characterized relationships between habitual sleep characteristics and reproductive outcomes and it is unclear how these may be related to fecundability. Thus, our aim was to prospectively examine how habitual sleep duration and midpoint (a proxy of chronotype) are related to fecundability among women attempting natural pregnancy. Women, aged 18-40, with a history of 1-2 pregnancy losses were followed for up to 6 cycles while attempting to conceive (n=1220). Preconception sleep characteristics assessed in baseline questionnaires were used to calculate average sleep duration and midpoint (midpoint between bedtime and wake time). Sleep variables were categorized based on sleep guidelines and prior research. Fecundability odds ratios (FOR) were estimated adjusting for sociodemographic characteristics, drug use, sleep aid use, and mutually adjusted for sleep duration or midpoint. Overall, 64.9% (n=797) conceived. Short sleep duration and long sleep duration were reported by 14.8% (<7 hours; n=180), and 11.4% (≥9 hours; n=139), and late sleep midpoints were reported by 13.5% (≥5:00 AM; n=165). Neither short or long sleep duration (short FOR: 1.16, 95% CI: 0.92, 1.46, <7 vs. 7-9 hours; long FOR: 0.87, 95% CI: 0.66, 1.14, ≥9 vs 7-9 hours) or late sleep midpoint (FOR: 0.88; 95% CI: 0.68, 1.13; ≥5:00 vs. <5:00 AM) were associated with fecundability. Among couples attempting natural conception, habitual preconception sleep duration and midpoint were not associated with fecundability and our results are potentially reassuring for women attempting to conceive. However, further investigation regarding sleep quality is needed.

Reproductive

The influence of fine particulate matter on the association between residential greenness and ovarian reserve Audrey Gaskins* Audrey Gaskins Kelvin Fong Lidia Mínguez-Alarcón Brent Coull Joel Schwartz Itai Kloog Russ Hauser Peter James

Background: Natural vegetation, or greenness, is thought to improve health through its ability to buffer and reduce environmental exposures as well as relieve stress and mental fatigue. In concert, these effects could help mitigate the detrimental effects of air pollution on reproductive aging in women.

Methods: Our analysis included 565 women attending the Massachusetts General Hospital Fertility Center (2004-2014) who had a measured antral follicle count (AFC), a marker of ovarian reserve. We calculated peak residential greenness in the year prior to AFC using 250m2 normalized difference vegetation index (NDVI) from satellites. Validated spatiotemporal models estimated daily residential exposure to particulate matter <2.5µm (PM2.5) for the 3 months prior to AFC. Poisson regression models were used to estimate the association between peak greenness, average PM2.5 exposure, and AFC adjusted for age, BMI, smoking status, education, year, and season.

Results: The women in our analysis, had peak greenness exposures ranging from 0.07 to 0.92 with a standard deviation (SD) of 0.18. There was no main effect of peak residential greenness on AFC; however, higher exposure to PM2.5 was associated with lower AFC (-7.7% per 2 µg/m3 95% CI -11.1, -4.2). There was a significant interaction between exposure to PM2.5 and peak greenness on AFC (P-interaction<0.001). Among women with an average exposure of 7 µg/m3 to PM2.5 (the 10th percentile), a SD increase in residential peak greenness was associated with a 6.2% (95% CI 2.2, 10.3) higher AFC. Conversely, among women with a PM2.5 exposure of 12 µg/m3 to PM2.5 (the 90th percentile), a SD increase in residential peak greenness was associated with a 5.9% (95% CI 1.0, 10.6) lower AFC.

Conclusions: Residing in an area with high levels of greenness may slow reproductive aging in women only when exposure to PM2.5 is low.

Reproductive
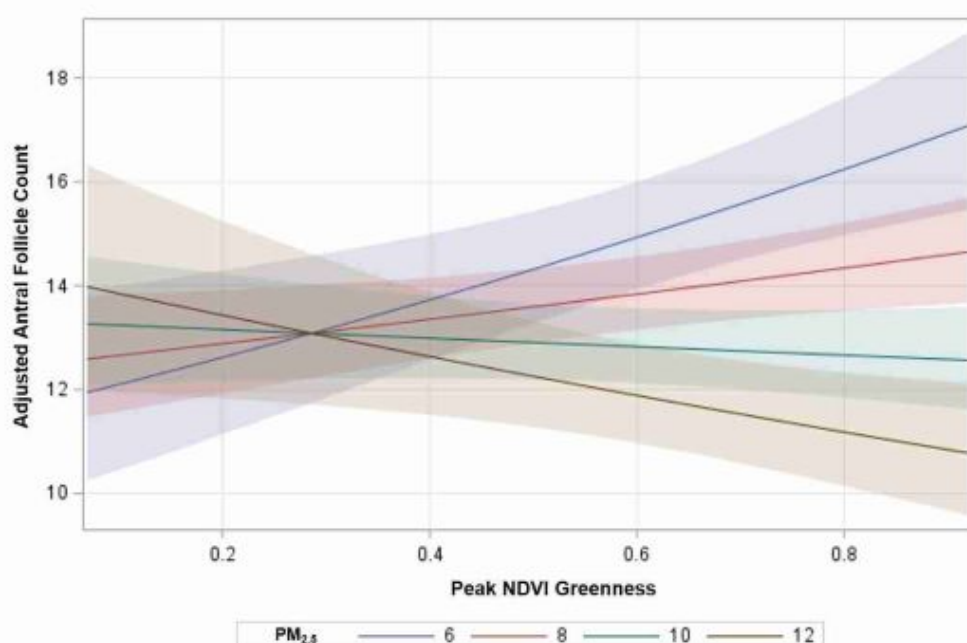
Leukocyte telomere length and fecundability, live birth, and pregnancy loss Alexandra*

Alexandra Purdue-Smithe Keewan Kim Lindsey Sjaarda Neil J. Perkins Enrique Schisterman Robert M. Silver Sunni L. Mumford

Telomere length is influenced by a variety of endogenous and exogenous factors, such as body mass index, smoking, and oxidative stress, and is therefore considered a marker of cumulative cellular aging or biologic age. Longer telomere length has been associated with higher levels of circulating reproductive hormones, greater parity, and reduced risk of polycystic ovary syndrome, suggesting a role of telomere length in human reproduction. However, the relationship between telomere length, as a marker of biologic age, and fecundability and fertility is unknown. We therefore evaluated associations of preconception leukocyte telomere length with fecundability, live birth, and pregnancy loss among 1,228 participants of the EAGeR trial, which included women aged 18-40 years who were attempting to conceive. Preconception leukocyte telomere length was measured at baseline using polymerase chain reaction and reported as a ratio (T/S) in relation to population-specific standard reference DNA. The T/S ratio for each participant was then converted to base-pairs using the following formula: Base-pairs = 3274 + 2413(T/S ratio). We estimated associations of telomere length with fecundability, live birth, and pregnancy loss using Cox proportional hazards models and log-binomial models adjusted for age, body mass index, smoking, and other factors. In both unadjusted and adjusted models, preconception telomere length was not associated with fecundability (adjusted fecundability odds ratio (FOR) per 1,000 base-pairs = 1.03; 95% CI = 0.85, 1.26), live birth (adjusted relative risk (RR) per 1,000 base-pairs = 1.13; 95% CI = 0.80, 1.60), or pregnancy loss (adjusted RR per 1,000 base-pairs = 1.14; 95% CI = 0.81, 1.60). These findings suggest that leukocyte telomere length, as a marker of biologic age, is not importantly related to fecundability or fertility among healthy reproductive-age women.

Preconception and very early pregnancy biomarkers of oxidative stress and reproductive outcomes Carrie Nobles* Carrie Nobles Pauline Mendola Sunni Mumford Robert Silver Keewan Kim Lindsey Sjaarda Neil Perkins Enrique Schisterman

Background: Oxidative stress is a key biologic pathway for a range of physiologic, lifestyle and environmental factors to impact reproduction. Despite the unique susceptibility of reproductive processes to oxidative stress, the relationship of isoprostanes, stable markers of oxidative stress, with pregnancy and pregnancy loss is little explored.

Methods: The EAGeR trial enrolled 1,228 women attempting pregnancy with 1-2 prior pregnancy losses. Pregnancy was determined by measurement of hCG and pregnancy loss by absence of clinical confirmation or an observed loss following a positive hCG. Isoprostanes 8-iso-PGF2α, its metabolite 2,3-dinor-iPF2α-III, and stereoisomers 5-iso-PGF2α-VI and 8,12-iso-iPF2α-VI were measured in urine prior to conception and at 4 weeks' gestation. Covariate-adjusted standardization for creatinine accounted for dilution. Discrete Cox proportional-hazards and log-binomial models estimated fecundability and pregnancy loss adjusting for participant characteristics.

Results: Preconception isoprostane levels were higher among women who were younger, nulliparous, had higher BMI and who smoked. Higher preconception 8-iso-PGF2α and 2,3-dinor-iPF2α-III were associated with lower fecundability (OR 0.88, 95% CI 0.80, 0.97 and OR 0.87, 95% CI 0.79, 0.97, respectively, per interquartile range [IQR]), and higher preconception 8,12-iso-iPF2α-VI with increased risk of pregnancy loss (RR 1.14, 95% CI 1.00, 1.29 per IQR). Among pregnancies (n=797), isoprostane levels increased from preconception to 4 weeks' gestation (e.g. median 61% [IQR -18, 180%] increase for 8-iso-PGF2α). Higher 8-iso-PGF2α and 2,3-dinor-iPF2α-III at 4 weeks' gestation were associated with lower risk of pregnancy loss (RR 0.75, 95% CI 0.60, 0.94 and RR 0.80, 95% CI 0.68, 0.94, respectively, per IQR).

Conclusions: Isoprostanes may serve as a marker for both the reproductive harm of oxidative stress and the success of pro-oxidant processes including implantation and early placentation.

Relationships Between Psychosocial Stressors Among Pregnant Women in San Francisco: a Path Analysis Stephanie Eick* Stephanie Eick Dana Goin Monika Izano Lara Cushing Erin DeMicco Amy Padula Tracey Woodruff Rachel Morello-Frosch

Pregnant women who experience psychosocial stress, such as depression and anxiety, are at an increased risk for adverse pregnancy outcomes. Few studies have examined the associations between multiple stressors from different sources, such as poor neighborhood quality, food insecurity, stressful life events, and financial hardship, which may be important to better understand the etiology of adverse outcomes. We developed a conceptual model indicating the relationship between psychosocial stressors among pregnant women. Women in this analysis were enrolled in Chemical in Our Bodies, a diverse pregnancy cohort in San Francisco (N=510). Path analysis, a subset of structural equation modeling, was used to examine associations between eleven perceived and objective measures of stress. Psychosocial stress was assessed via questionnaire at the 2nd trimester and included: perceived stress, depression, neighborhood quality, community status, stressful life events, caregiving, discrimination, financial hardship, job strain, food insecurity, and unplanned pregnancy. We identified perceived stress and discrimination as strong predictors of depression (β=0.76, 95% confidence interval [CI]=0.59, 0.96; β=3.76, 95% CI=1.60, 5.85, respectively). Our model additionally indicated that food insecurity, job strain, and stressful life events influenced depression both directly (β=2.67, 95% CI=1.13, 4.04; β=1.63, 95% CI=0.29, 3.07; β=0.43, 95% CI=0.15, 0.70, respectively) and indirectly through the mediating pathway of increased perceived stress. Our study included diverse measures of psychosocial stress not previously explored in this context and identified food insecurity, discrimination, job strain, neighborhood quality, and perceived stress as important factors associated with depressive symptoms. These findings highlight the complex relationships between stressors and improve our understanding of the pathways leading to depression, an important clinical outcome.
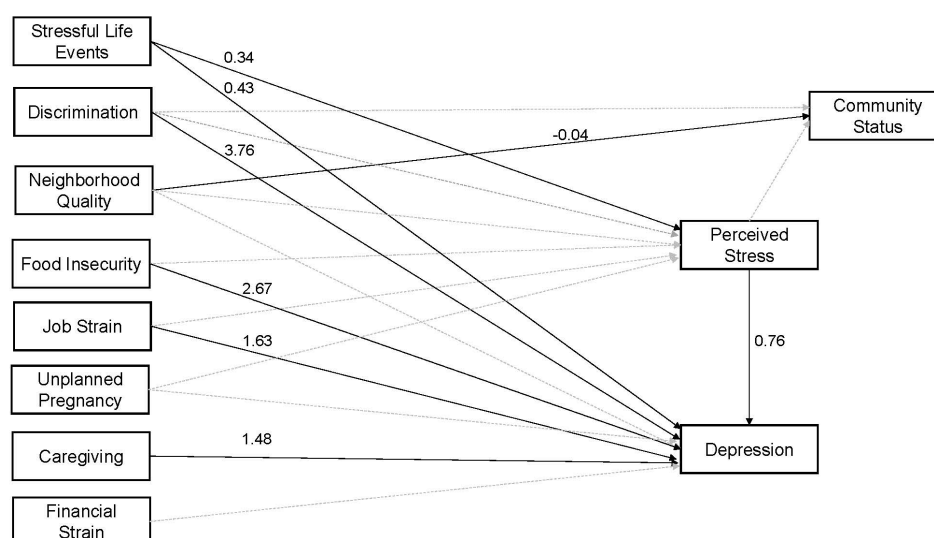
Test re-test reliability of a self-reported reproductive history questionnaire among women of childbearing age Kimberly L. Parra* Kimberly Parra Rachelle L. Begay Leslie V. Farland Leslie K. Dennis

Women's reproductive health histories are used increasingly to assess risk of gynecological disorders in clinical practice and epidemiological research. However, reliability studies of reproductive health histories have been limited or produced mixed agreement. We employed a test-retest reliability study using a women's health survey that was self-administered online (n=66). Participants were re-tested with the same survey 3-4 weeks later for the consistency of their responses (n=36). Women of reproductive age (24-49 years) enrolled in a graduate nursing program in Tucson, Arizona were asked to participate in the study. A 36-item, structured survey adapted from the World Endometriosis Research Foundation (EPHect Questionnaire) was self-administered to participants online and re-tested for the consistency of their responses using reliability coefficients, Cohen's kappa (k) and intraclass correlation coefficient (ICC). The survey included items on menstruation, hormone-use, fertility, pelvic pain, and early perinatal factors. Excellent reliability was attained for age at menarche, first coil/IUD, and first pregnancy (Intraclass Correlation Coefficient >0.93). Questions that elicited excellent reliability were having a period in the last 3 months and ever being pregnant (kappa (k)=1.00). Menstrual cycle and hormonal factors had good reliability (k >0.61), Age estimations related to first hormone-use and first pain with periods were less consistent. Severity of pelvic pain during last period had fair reliability (k=0.54). Kappas for factors related to pelvic pain during the last 12 months ranged from 0.44 to 0.78. The survey was administered graduate nursing students which may limit generalizability of our findings. Our findings will improve the quality of data collection in clinical practice and in the research of women's health histories by helping to identify the most reliable questions for ascertaining self-reported reproductive factors.

Reproductive

Is preconception adiposity related to human offspring sex ratio? Elizabeth A. DeVilbiss* Elizabeth DeVilbiss Alexandra C. Purdue-Smithe Lindsey A. Sjaarda Sunni L. Mumford Neil J. Perkins Joshua R. Freeman Robert M. Silver Enrique F. Schisterman

Background: Unfavorable reproductive conditions leads to bias towards fewer male offspring. An example is obesity, but mechanisms are unknown. Thus, we explored the relationship between leptin, which is secreted by adipose tissue, and offspring sex ratio.
Methods: Among 1228 women attempting pregnancy in the EAGeR trial, we used log-binomial regression to estimate RRs and 95% CIs for male live birth in women with higher preconception leptin (tertile 2: 11.22-26.24 ng/mL, tertile 3: >26.24 ng/mL) relative to the lowest tertile (<11.22 ng/mL). To determine when mechanisms relating to male survival occur, we estimated RRs among all women completing the trial, women becoming pregnant, and women having a live birth, employing inverse probability weights to account for probabilities of withdrawal, pregnancy, and live birth. Models were stratified by preconception high sensitivity C-reactive protein (CRP), a marker of systemic inflammation, and adjusted for age, physical activity, and either CRP, BMI, or waist to hip ratio.
Results: Among all women completing follow-up, women in the highest tertile of preconception leptin had a lower probability of male live birth (RR=0.67; 95% CI: 0.51, 0.87). Adjustment for and stratification by CRP produced similar findings, as did adjustment for waist to hip ratio. Adjustment for BMI attenuated findings (RR=0.85; 95% CI: 0.57, 1.26). Among pregnancies and live births, relationships persisted among women with low CRP (pregnancies: RR=0.72; 95% CI: 0.51, 1.02; live births: RR=0.78, 95% CI: 0.57, 1.07).
Conclusions: Among women with high preconception leptin, production of male offspring is reduced, independent of low-grade inflammation. Between confirmation of pregnancy and live birth, this relationship persists only among women with low CRP.

Reproductive

Pregnancy history and adenomyosis risk: Results from a population-based case-control study employing two control groups Kristen Upson* Kristen Upson Sawsan (Suzie) As-Sanie Victoria L. Holt

Adenomyosis, characterized by the invasion of endometrial glands and stroma into the myometrium, is associated with substantial morbidity. Since trophoblast invasion in early pregnancy and pregnancy-related surgical procedures may disrupt the endometrial-myometrial border, we investigated pregnancy history in relation to adenomyosis risk. We used data from a case-control study of adenomyosis conducted among female enrollees ages 18-59 of a large, integrated healthcare system in Washington State. We identified incident, pathology-confirmed cases of adenomyosis diagnosed 2001-2006 (n=386). We employed two control groups: 1) randomly selected enrollees with intact uteri matched to cases on age ("population controls", n=323) and 2) hysterectomy controls (n=233). Data on pregnancy history, including gravidity, parity, history of cesarean delivery and dilation and curettage, were collected from in-person interviews. We used logistic regression to estimate the OR and 95% CI, adjusting for age, reference year, and menarche age. In analyses using population controls, we observed an increased odds of adenomyosis with ever being pregnant (OR 3.5, 95% CI: 2.0-5.9). As for number of pregnancies, the odds of adenomyosis increased 30% with each additional pregnancy (OR 1.3, 95% CI: 1.2-1.4). We then evaluated pregnancy-related surgical procedures, additionally adjusting for gravidity. We did not observe an association with dilatation and curettage history among gravid women (OR 1.0, 95% CI: 0.7-1.5), nor an association with number of cesarean deliveries among parous women (1 vs. 0: OR 0.9, 95% CI: 0.5-1.4; ≥2 vs. 0: OR 1.2, 95% CI: 0.7-2.1). In our analyses using hysterectomy controls, we observed similar patterns of associations that were attenuated in magnitude, except for an association between dilatation and curettage history and adenomyosis (OR 2.2, 95% CI: 1.3-3.5). Our results indicate that pregnancy, but not cesarean delivery, is associated with increased adenomyosis risk.

Reproductive

Combined oral contraceptive use and blood lead concentrations Kristen Upson* Kristen Upson Quaker E. Harmon Janet E. Hall Lauren E. Wise Ganesa Wegienka Erik J. Tokar Donna D. Baird

Oral contraceptive use is common, with 151 million users worldwide. Since toxic metal lead is stored in bone and estrogen can influence bone formation and turnover, we investigated the association between current use of estrogen-containing combined oral contraceptives (COCs) and blood lead concentrations. We used enrollment data from the Study of Environment, Lifestyle & Fibroids (SELF), a cohort of 1693 African American women ages 23-35 years. Blood lead concentrations were measured in whole blood samples from 1548 participants (91% of cohort) and data on current COC use were collected by telephone interview and questionnaire. After excluding current users of depot medroxyprogesterone acetate (DMPA), contraceptive vaginal ring, or patch, and those with a history of blood clot, angina, heart attack, or stroke, the investigation included 1379 participants. We used linear regression to estimate the percent difference in blood lead concentrations and 95% CI between current COC users and non-users, adjusting for age, education, smoking, alcohol intake, past DMPA use, and birth in last year. At enrollment, 13% of participants (n=177) reported current COC use. The geometric mean blood lead concentration among COC users and non-users was 0.57 µg/dl (95% CI: 0.54-0.61) and 0.70 µg/dl (95% CI: 0.68-0.72), respectively. After adjustment, current COC users had blood lead concentrations that were 8% lower than non-users (95% CI: -14%, -2%). We then conducted analyses to address potential residual confounding from smoking, a substantial source of lead, and unmeasured factors associated with lead exposure and choosing COCs. We observed a similar association when we restricted the study population to never smokers (-6% lower, 95% CI: -12%, 1%) and compared current and past COC users (-9% lower, 95% CI: -16%, -2%). Our results indicate current COC use is associated with lower blood lead concentrations. Estrogen in COCs may limit bone turnover and mobilization of lead from bone.

Associations between soluble receptor for advanced glycation end product (sRAGE) and fecundability and fertility in women attempting pregnancy Keewan Kim* Keewan Kim Edwina H. Yeung Lindsey A. Sjaarda Carrie J. Nobles Neil J. Perkins Elizabeth A. DeVilbiss Joshua R. Freeman Samrawit Yisahak Alexandra C. Purdue-Smithe Sonia L. Robinson Robert M. Silver Enrique F. Schisterman Sunni L. Mumford

The soluble receptor for advanced glycation end products (sRAGE) binds to advanced glycation end products (AGEs), that are produced endogenously or obtained mainly through intakes of heat-processed foods, to mitigate reactive oxygen species production and inflammatory damage. Elevated levels of sRAGE have been observed in women with recurrent pregnancy loss and pregnancy complications. Though sRAGE is a more reliable biomarker than AGEs, few studies have examined its relation with pregnancy outcomes in a large population study. We thus investigated associations between preconception levels of serum sRAGE and time-to-pregnancy, pregnancy loss, and live birth among women attempting pregnancy. 1,228 women aged 18-40 years and with 1-2 prior pregnancy losses were followed up for 6 menstrual cycles while attempting pregnancy and throughout pregnancy if they conceived. Levels of sRAGE were determined in serum samples collected at baseline. Discrete Cox models and log-binomial regressions were used to calculate fecundability odds ratio (FOR), RRs, and 95% CI. For models evaluating pregnancy loss, inverse probability weights were used to account for potential selection bias by restricting to pregnant women. Models were adjusted for age, BMI, race, smoking, physical activity, serum cholesterol, fat-soluble micronutrients, C-reactive protein (CRP), and free fatty acids. In our data, mean (standard deviation) levels of sRAGE were 1,183 (460) pg/mL and levels were higher in women of BMI <25 kg/m2 and CRP <1.95 mg/L. Serum sRAGE (per 200 pg/mL increase) was not strongly associated with fecundability (FOR 1.03, 95% CI 0.99, 1.07), pregnancy loss (RR 0.96, 95% CI 0.91, 1.02), and live birth (RR 1.02, 95% CI 1.00, 1.04). Though sRAGE, a reliably measured component of the AGE-RAGE axis, may have a role on fecundability and fertility, its impact during preconception may be small among healthy women attempting pregnancy.

Reproductive

Male dietary fat intake and fecundability: a preconception cohort study Lauren A. Wise*
Lauren Wise Amelia K. Wesselink Sydney K. Willis Ellen M. Mikkelsen Katherine L. Tucker Kenneth J. Rothman Elizabeth E. Hatch

Background: Higher intakes of saturated fat and trans fatty acids have been associated with poor semen quality and low testosterone levels, whereas higher intakes of omega-3 fatty acids have been associated with improved semen quality in some studies. There have been few preconception cohort studies of male diet and fecundability. Methods: We examined the association between male dietary fat intake and fecundability in Pregnancy Online Study (PRESTO), a North American preconception cohort study (2013-2020). Men aged ≥21 years completed an online baseline questionnaire about their medical history, socio-demographics, anthropometrics, and lifestyle factors. Ten days after enrollment, men completed a validated food frequency questionnaire (DHQ II). Female partners completed bimonthly follow-up questionnaires for up to 12 months or until pregnancy. Analyses were restricted to 446 couples attempting conception for ≤6 cycles at entry. We used proportional probabilities regression to estimate fecundability ratios (FR) and 95% CIs for the associations of % energy from total fat and fat subtypes (saturated, monounsaturated, polyunsaturated, trans, omega-3, omega-6) with fecundability, adjusting for energy intake and other potential confounders. Results: We observed little association between total fat, saturated fat, mono-or poly-unsaturated fat, or trans fat intake and fecundability. FRs (95% CIs) comparing the top vs. bottom quartiles of dietary fat intake were 1.00 (0.73-1.36) for trans fatty acids, 1.15 (0.84-1.57) for omega-3 fatty acids, 0.78 (0.56-1.08) for omega-6 fatty acids, and 1.23 (0.93-1.64) for the ratio of omega-3 to omega-6 fatty acids. Conclusion: We observed little overall association between male intake of total fat, and most fat subtypes, and fecundability. Weak associations were seen for intakes of omega-6 fatty acids and the ratio of omega-3 to omega-6 fatty acids, though associations were imprecise.

Reproductive

Male red and processed meat intake and fecundability in a North American preconception cohort Sydney K. Willis* Sydney Willis Lauren A. Wise Amelia K. Wesselink Ellen M. Mikkelsen Katherine L. Tucker Anne Sofie D. Laursen Kenneth J. Rothman Elizabeth E. Hatch

In the United States, steroid hormones are often administered to cattle for growth promotion. There are concerns that intake of animal tissue containing residual hormone levels, as well as environmental chemicals, may adversely affect human reproduction. Red meat is also a major source of iron, selenium, zinc, and vitamin B12, which may be important determinants of male reproductive function. Prior research on meat intake and male fertility has been limited to studies of semen parameters, and results have been inconsistent. We evaluated the association between male meat intake and fecundability, the per-cycle probability of conception, in Pregnancy Study Online, a prospective preconception cohort study of North American couples. At enrollment, men completed a baseline questionnaire and a validated food frequency questionnaire, on which we ascertained information on intake of red and processed meat. Female partners completed bi-monthly follow-up questionnaires to ascertain pregnancy status. The analysis included 446 men attempting to conceive for ≤6 cycles at study entry. We used proportional probabilities regression models to estimate fecundability ratios (FR) and 95% CIs, adjusting for male and female age, diet quality, BMI, income, and education; and male energy intake, race/ethnicity, sleep, depression, sugar-sweetened beverage and alcohol intake, and physical activity. We observed a dose-response association between increased red meat and processed meat intake and improved fecundability. The FR comparing intake of ≥7 vs.<2 servings/week of red meat was 1.65 (95% CI: 1.11-2.47). The FR comparing intake of ≥4 vs. <1 serving/week of processed meat was 1.29 (95% CI: 0.83-2.01). Results were similar when restricting to men without a history of infertility. While results are imprecise, we found some evidence that higher consumption of red meat and processed meat by males during preconception may be associated with improved fecundability.

Risk of miscarriage in women with chronic diseases: a Norwegian registry study Maria C.
Magnus* Maria Christine Magnus Nils-Halvdan Morken Knut-Arne Wensaas Allen J.

Background: There are data suggesting that thyroid disorders and cardiovascular disease may be
associated with a woman's risk of miscarriage. However, the role of maternal chronic diseases more
broadly has not been explored. A wider exploration may provide clues about underlying mechanisms
of miscarriage.
Objective: To prospectively study the risk of miscarriage in relation to a range of pre-existing
chronic diseases.
Methods: We identified all registered pregnancies (n= 593,009) in Norway for the period 2010-2016
using information from national health registries (birth, patient and general practitioner databases).
Chronic diseases (20 different conditions) were defined by diagnostic codes used in primary and
specialist care. We estimated the association between maternal chronic conditions and risk of
miscarriage using logistic regression while adjusting for the woman's age at the start of pregnancy.
Results: An increased risk of miscarriage was seen in women with a pre-existing diagnosis of chronic
kidney disease (adjusted OR 1.68; 95% CI: 1.14, 2.48), hypertension (adjusted OR 1.15; 95% CI:
1.06, 1.24), type 2 diabetes (adjusted OR 1.36; 95% CI: 1.20, 1.55) and endometriosis (adjusted OR
1.26; 95% CI: 1.17, 1.36). After accounting for the potential competing risk of induced abortions, we
also observed an increased risk of miscarriage among women with polycystic ovarian syndrome
(adjusted OR 1.84; 95% CI: 1.27, 2.65), celiac disease (adjusted OR 1.21; 95% CI: 1.05, 1.40) and
type 1 diabetes (adjusted OR 1.13; 95% CI: 1.03, 1.24)
Conclusion: A range of maternal chronic diseases were associated with increased risk of
miscarriage.

Prenatal exposure to maternal stress and telomere length in newborns Susannah H Leisher*
Susannah Leisher Abraham Aviv Ian McKeague Pam Factor-Litvak Ezra Susser Katrina Kezios
Ronald Wapner Matthew Hoffman

Background There is a growing literature on associations between telomere length and health outcomes, and adverse prenatal exposures, including stressors, have been associated with decreased length. We aimed to assess evidence for an association between maternal prenatal stress and newborn leukocyte telomere length (LTL) at birth.

Methods This was a retrospective cohort study of 564 mother-father-infant trios from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-to-be. We used data on stress-related exposures (perceived stress, depression, anxiety, racism) and possible mediators (perceived social support, resilience) via validated questionnaires. We used generalized linear models to assess associations between stress and newborn LTL (measured by Southern blot), adjusting for all stress-related exposures, maternal and paternal LTL, and other covariates, and testing for mediation and for interaction by sex and race/ethnicity.

Results Mean newborn LTL was 9.51 (SD 0.69) kilobases. We found a decrease of 23 base pairs (95% confidence interval 8, 38) in telomere length at birth for every one-unit increase in maternal perceived stress in the first trimester; this effect appeared dose-dependent, with a decrease of 291 bp in infants of mothers with highest compared to lowest first-trimester perceived stress scores. The effect was stronger in boys. Sensitivity analyses were compatible with these results.

Conclusions In the largest study to date of maternal stress and telomere length, using a gold-standard measure for telomere length and multiple measures of prospectively-collected stress data, we found evidence for shorter telomere length at birth in infants whose mothers had higher perceived stress in the first trimester. Limitations included small numbers of non-Hispanic African-Americans. Further research should attempt to replicate our findings in placental tissue. Biological plausibility should also be investigated.

Qualitative acceptability comparison of 28-day orally administered dimethandrolone undecanoate vs 11β-methyl-19-nortestosterone dodecylcarbonate vs placebo for male contraception Frances Fernando* Frances Fernando Diana Blithe

Introduction: Current male contraceptive options are limited to vasectomy and condoms. Dimethandrolone undecanoate (DMAU) and 11β-methyl-19-nortestosterone dodecylcarbonate (11β-MNTDC) are novel progestogenic androgens under development for male hormonal contraception. These compounds cause gonadotropin suppression, which blocks endogenous testosterone production (causing suppression of spermatogenesis), while providing adequate androgen replacement to prevent symptoms of hypoandrogenism. We evaluated user-experiences of DMAU, 11β-MNTDC and placebo via acceptability questionnaires.

Methods: DMAU and 11β-MNTDC were evaluated in two separate placebo-controlled studies. Healthy male volunteers were randomized to receive oral doses of active drug or placebo daily (with food) for 28 days. Protocol outcomes included safety, gonadotropin suppression, tolerability and acceptability. Acceptability questionnaires obtained after treatment were analyzed via a chi-square test.

Results: Participants (38 DMAU, 30 11β-MNTDC, 28 Combined Placebo) who completed questionnaires had similar demographic characteristics. Men randomized to active drug (either DMAU or 11β-MNTDC) showed more willingness to use the agent (66% DMAU, 87% 11β-MNTDC) compared to placebo recipients (46%, p=0.007). Most participants (87% of DMAU users, 73% of 11β-MNTDC users and 68% of placebo users) expressed satisfaction with the regimen and most of the men, (82% of DMAU users, 90% of 11β-MNTDC users and 78% of placebo users) would recommend the study regimen to others.

Conclusions: Men overall had a satisfactory experience with oral DMAU and 11β-MNTDC. Most stated that they would use the method, if available, and would recommend it to others. Oral DMAU and 11β-MNTDC appear to be highly acceptable male contraceptive prototypes and warrant longer-term studies to assess spermatogenic suppression.

Unintended pregnancy among racial/ethnic and sexual minority college women: An application of a quantitative intersectional analysis Colleen Reynolds* Colleen Reynolds Ariel Beccia Brittany Charlton

Purpose
This study quantified the separate and intersectional associations of race/ethnicity and sexual minority status on the risk of unintended pregnancy.
Methods
We analyzed cross-sectional survey data from the National College Health Assessment between Fall 2015 and Spring 2018. We used multivariable log-binomial regression to estimate the relative risk (RR) of unintended pregnancy among college-attending women aged 18-25 (N =177,592). We estimated multiplicative and additive (relative risk due to interaction, RERI) interaction between race/ethnicity and sexual orientation on the risk of unintended pregnancy; 95% confidence intervals (CIs) were estimated using 500 bootstrap replicates.
Results
Compared to heterosexual non-Hispanic white women, the following groups had increased risks of unintended pregnancy: sexual minority non-Hispanic white, heterosexual racial minority, and sexual minority racial minority women. Notably, sexual orientation was not associated with unintended pregnancy among racial minority women. We did not find evidence for an additive interaction between race/ethnicity and sexual orientation (RERI=-0.19; 95%CI=-0.68, 0.34), but we found a multiplicative interaction (RR=0.76; 95%CI=0.59, 1.00).
Discussion
Our findings illustrate that statistical interactions are scale dependent. Intersectional research should not assume the nature of the interactions between identities, but rather explore associations on both the additive and multiplicative scales. More broadly, our findings suggest the need to move beyond "double jeopardy" approaches to quantitative intersectional research and consider the broader factors that may uniquely shape the health status of groups at the nexus of particular social identities. For example, non-Hispanic white sexual minority women may have particular difficulty accessing contraception. By contrast, health care providers may emphasize contraceptive use for racial minority women, regardless of sexual orientation.

Relative Risk of Unintended Pregnancy

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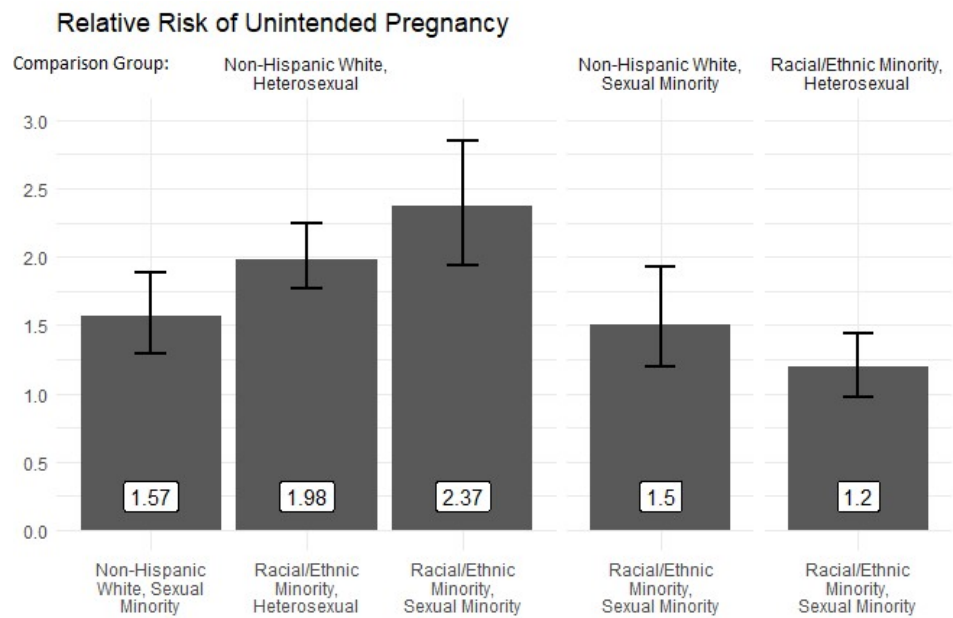
Preconception antibiotic use and spontaneous abortion: a prospective study Holly Crowe*
Holly Crowe Lauren Wise Amelia Wesselink Charles Horsburgh Ellen Mikkelsen Elizabeth Hatch

Antibiotic use may increase the risk of spontaneous abortion (SAB) through increased oxidative stress or disruption of the reproductive tract microbiome. In a North American preconception cohort study, we examined the association between antibiotic use and SAB risk. From 2013 through 2019, we enrolled 10,921 female pregnancy planners; 5,793 conceived during 12 months of follow-up and 1,084 (19%) experienced SAB. At baseline, we collected data on antibiotic use in the past 4 weeks, including type and indication for use. Pregnancy losses at <20 gestational weeks were reported on follow-up questionnaires completed preconceptionally and in early and late pregnancy. We used Cox regression models, with gestational weeks as the time scale, to estimate hazard ratios (HR) and 95% CIs, adjusting for demographics, lifestyle, and reproductive history. Overall, 458 women (8%) reported using antibiotics in the four weeks before baseline, most commonly penicillins (24%) and macrolides (9%). Respiratory infections (31%) and urinary tract infections (UTI) (27%) were the most common indications for antibiotic use. Overall, preconception antibiotic use showed little association with SAB (HR=1.05, CI: 0.85-1.30). Use of penicillins (HR=1.01, CI: 0.65-1.55), macrolides (HR=0.87, CI: 0.41-1.82), or nitrofurantoin (HR=1.11, CI: 0.53-2.34) was not appreciably associated with SAB, while use of cephalosporins was associated with increased risk (HR=1.63, CI: 0.87-3.06), although estimates were imprecise. Antibiotic use was associated with a slightly increased risk of SAB when used for UTI (HR=1.27, CI: 0.87-1.84) or pelvic/vaginal infections (HR=1.58, CI: 0.96-2.61), but not for respiratory infections (HR=0.94, CI: 0.64-1.37), indicating potential confounding by indication. Overall, our findings provide little support for the hypothesis that preconception antibiotic use is associated with SAB.

Reproductive

Development of a maternal health specific neighborhood stress index Jessica Meeker* Jessica Meeker Mary Regina Boland

Introduction. Pregnancy related deaths in the US have doubled from 7.2 to 18.0 deaths per 100,000 live births between 1987 and 2014; however the cause remains disputed. We seek to design a socio-demographic neighborhood stress index to understand the effect of social and built environment factors upon poor maternal birth outcomes. Existing indices are often outcome dependent, not comprehensive, and focus on where the mother lives at the end of pregnancy only. Methods. This study utilizes EHR data for a cohort of pregnant patients in the University of Pennsylvania Health System. The primary exposure is the stress index (a continuous predictor bounded from 0-10). The index is comprised of a myriad of singular exposures including violent crime, poverty, vacant housing, and access to healthy food, walkability, segregation, & education. Logistic regression with a lasso penalty on the predictors will be utilized to create the index, which will be designed to specifically predict the maternal health outcomes of study. We will then validate our index on 80% of our data to determine the prediction performance. Results. The first iteration of the index was designed to predict having a cesarean delivery. Utilizing logistic regression with a lasso penalty, neighborhood poverty and racial distribution seemed to be the most significantly predictive for a cesarean delivery. However, in this model we did not include crime, food access, or walkability, so we anticipate the index to change when these additional variables are assessed. Discussion. Socio-demographic variables at the census tract level are often used in health disparities research; however, these measures are often highly correlated and introduce statistical issues due to collinearity. Therefore, our study creates an index that is maternal health specific, methodologically overcomes the issue of collinearity, and can also be used as a model for other health researchers in creating their own outcome specific index.

Rural-urban differences in maternal mortality trends in the US, 1999-2017: Accounting for the impact of the pregnancy checkbox Lauren Rossen* Lauren Rossen Lindsay Womack Sayeedha Uddin Amy Branum

States incrementally adopted a pregnancy checkbox on death certificates between 2003-2017 to improve ascertainment of maternal mortality. Inconsistent measurement by states over time has made it difficult to estimate national maternal mortality rates, trends, and related disparities (e.g., rural-urban).

Data on maternal deaths (while pregnant or within 42 days) and corresponding denominators (numbers of live births) were drawn from mortality and birth data from 1999-2017. Log-binomial regression models were used to examine the impact of the pregnancy checkbox and predict number of maternal deaths per 100,000 live births from 1999-2017 under two scenarios: 1) assuming all states had the checkbox from 1999-2017; and 2) assuming no states had the checkbox. The impact of the checkbox and related trends over time were estimated by urban/rural residence, adjusting for age, race/ethnicity, and state. County of residence was categorized as large urban (counties in large central or large fringe metropolitan areas), medium/small urban (counties in medium or small metropolitan areas), or rural (non-metropolitan counties). Sensitivity analyses examined the potential impact of outcome misclassification. Results will be updated when 2018 data become available.

The implementation of the checkbox increased identification of maternal deaths (averaged over 2003-2017) by an estimated 7.53 deaths per 100,000 live births (95% CI: 6.25–8.81) in large urban areas, 11.57 (95% CI: 9.56–13.57) in medium/small urban areas, and 16.55 (95% CI: 12.85–20.25) in rural areas. Predicted trends assuming that all states had adopted the checkbox throughout the entire period suggested that maternal mortality rates declined in large urban areas from 1999-2017 (average annual change = -0.23, 95% CI: -0.39–-0.07, p=0.006) from 22.51 in 1999 to 20.87 in 2017. In contrast, predicted maternal mortality rates increased in rural areas (0.60, 95% CI: 0.18–1.02, p=0.005) from 20.88 in 1999 to 34.38 in 2017.

Reproductive
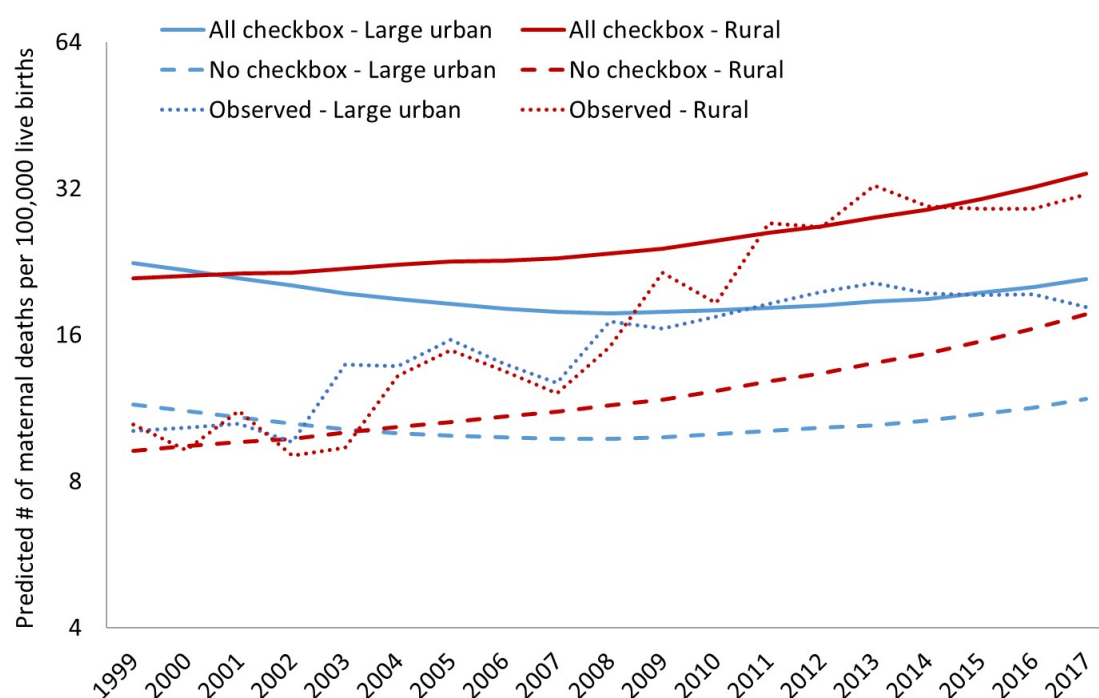
The Association of Substance Use Disorders with Unintended and/or Mistimed Pregnancy in a Clinical Sample of Women from Three Prenatal Care Sites, 2016-17 Kelsey C. Coy*

Kelsey Coy Jean Y. Ko Kathryn Gilstad-Hayden Steven J. Ondersma Grace Chang Tiffany Blake-Lamb Kimberly Yonkers

Background: Little research examines the prevalence of mistimed/unintended pregnancy among women with any substance use disorder (SUD); this analysis addresses this gap.

Methods: Secondary analysis of survey data from three prenatal care sites in Connecticut, Massachusetts, and Michigan, 2016-17 (n=1115). Chi-square tests (p<0.05) were used to assess differences in sociodemographic characteristics among women with any SUD (DSM-V criteria from self-report; includes heroin, stimulants, prescription drug, alcohol, or marijuana) versus those without. Modified Poisson regression with robust error variance was used to calculate adjusted prevalence ratios (aPR), controlling for sociodemographic and substance use variables, to estimate the association of having a pregnancy that was self-reported to be mistimed (pregnancy happened at the wrong or not quite right time) and/or unintended (pregnancy was not intended or intentions kept changing) with having any SUD.

Results: In this ambulatory healthcare sample, 15.5% of women had any SUD. Women with any SUD were more likely to be ≤ 24 years old, unmarried, on public assistance, living in unsafe neighborhoods, or living with someone using drugs. They were also more likely to have less than a high school education, a previous pregnancy, a child and family services case ever opened, self-reported depression/anxiety, self-reported pain/discomfort, a partner, friend, or parent with substance use problems, and tobacco use in the month before pregnancy compared to women without SUD. Almost three in four women with any SUD reported a mistimed/unintended pregnancy. The prevalence of mistimed/unintended pregnancy was 17% higher among women with any SUD compared to women without SUD (aPR: 1.17; 95% CI: 1.05-1.31) after adjustment.

Conclusions: Mistimed/unintended pregnancy was higher among women with any SUD. Delivery of recommended health services, including patient-centered contraceptive counseling, can address needs in women with SUD.

Association of pregnancy conditions with risk of early natural menopause Christine Langton*
Christine Langton Brian Whitcomb Alexandra Purdue-Smithe Lynnette Sievert Susan Hankinson
JoAnn Manson Bernard Rosner Elizabeth Bertone-Johnson

Early menopause, defined as the cessation of ovarian function before the age of 45 years, affects approximately 10% of women and is associated with increased risk of cardiovascular disease and other chronic conditions. It has been hypothesized that conditions during pregnancy may impact the formation of the initial cohort of follicles and the rate of oocyte atresia in the fetal ovary, thereby influencing menopause timing. As research on the developmental origins of menopause timing is limited, we evaluated associations of birth weight and gestational age with early menopause among 108,887 nurses in the prospective Nurses' Health Study II.

Nurses were 25-42 years old and premenopausal at baseline, and provided information on their birth weight, gestational age at birth and their mother's pregnancy smoking history. In 2001, nurses' mothers (n~35,900 women) also provided this information, which was used to classify exposure status; otherwise, nurses' reports were used. Menopause status and age at menopause were assessed every 2 years (1989-2017). We used Cox proportional hazards models to estimate hazard ratios (HRs) and 95% confidence intervals (CIs), adjusting for lifestyle, dietary, and reproductive factors, and maternal smoking.

During 1.7 million person-years of follow-up, 2,579 women experienced early natural menopause. In multivariable models, lower birth weight and preterm birth were each associated with higher risk. Compared with birth weight of 7 to 8.4 pounds, women weighing =2 weeks prematurely, compared to those with term births, the HR for early menopause was 1.18 (95% CI, 1.03-1.35).

In this large, prospective study lower birth weight and preterm birth, were associated with higher risk of early menopause. Our results support future research to identify in utero exposures that affect offspring health.

Reproductive

Folate-Sensitive Birth Defects and Family History of Down Syndrome in the National Birth Defects Prevention Study Maria D. Politis* Maria D. Politis Jenil Patel Philip J. Lupo Suman Maity Paul A. Romitti Marilyn L. Browne Gary M. Shaw Mary M. Jenkins Wendy N. Nembhard

Women with a history of Down syndrome-affected pregnancies have increased risk of neural tube defects (NTDs) in subsequent pregnancies. The association between family history of Down syndrome and NTDs and increased risk of other potential folate-sensitive defects is unknown. We aimed to examine whether family history of Down syndrome was associated with folate-sensitive birth defects, specifically NTDs, orofacial clefts, hydrocephaly and conotruncal heart defects, in offspring. We used data from the National Birth Defects Prevention Study to compare maternal self-reported family history of Down syndrome in 9,947 birth defect cases to 11,750 unaffected controls. Crude and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were estimated using logistic regression. To assess for potential selection bias, sensitivity analysis among a subset of primiparous women was conducted. Family history of Down syndrome was 1.38% (95% CI: 1.17-1.59) among controls and 1.59% (95% CI: 1.34-1.83) among cases. Infants with NTDs were 1.67 times more likely to have a family history of Down syndrome than controls after adjusting for potential confounders (95% CI: 1.20-2.32). Among primiparous women, infants with NTDs were 1.99 times more likely to have a family history of Down syndrome compared to controls (95% CI: 1.13-3.52). Infants with other folate-sensitive birth defects were more likely to have family history of Down syndrome than controls. This provides initial evidence that the interplay between Down syndrome and risk of folate-sensitive birth defects goes beyond maternal pregnancy history. If confirmed, parental family history of Down syndrome could be considered in counseling women about potential increased risks of folate-sensitive birth defects among their offspring.

Neighborhood Socioeconomic Status and Breastfeeding Initiation and Duration Among Primiparous Black Women Yvette Cozier* 3647] Cozier Michele K Griswold Sybil L Crawford Donna J Perry Sharina D Person Lynn Rosenberg Julie R Palmer

Black women in the U.S. have significantly lower rates of breastfeeding compared with white women and other racial/ethnic groups. Residential neighborhood influences individual behavior by establishing community norms and values. Due to racial segregation, black women tend to live in more disadvantaged neighborhoods than do white women irrespective of individual education. We assessed the association between neighborhood socioeconomic status (NSES) and breastfeeding initiation (BI) and duration among participants in the Black Women's Health Study a prospective follow up of US black women begun in 1995 when women were aged 21-69. Biennial follow-up questionnaires collected information on incident births. Residential addresses were geocoded to year 2000 US census data measuring area deprivation, combined into a summary score, and divided into quartiles. We used logistic regression, adjusting for body mass index, years of education, occupation, marital status, and geographic region, to estimate ORs and 95% CIs. Overall, 30% of BWHS participants live in high poverty neighborhoods, defined as one in which 20% or more of residents subsist on incomes below the federal poverty level. From 1997 to 2005, there were 2,813 primiparous women with a mean age of 32 years; 71% had ≥16 years of education. Overall, 81% initiated breastfeeding, of which 51% continued for ≥ 6 months. The ORs for BI and duration of ≥ 6 months for women residing in the lowest compared to the highest quartile of NSES were 0.59 (95% CI: 0.43-0.81) (P_{trend}=0.0002) and 0.63 (95% CI: 0.45-0.87) (P_{trend}=0.0005), respectively. In a cohort of Black women, living in a low- relative to high-resource community was associated with non-initiation of breastfeeding and with shorter breastfeeding duration among those who did initiated breastfeeding, independent of their own educational status. Further research addressing neighborhood-level barriers to breastfeeding is warranted.

Maternal adverse childhood experiences are associated with binge drinking and street drug use in pregnancy in a dose-dependent fashion Cheryl L Currie* Cheryl L Currie

Background: The objective of this study was to examine the role that maternal adverse childhood experiences (ACEs) may play in binge drinking and street drug use in pregnancy within a large community-based sample of middle and upper-middle income women who were well-educated, predominantly Caucasian and married, had planned their pregnancy, and were receiving prenatal care. The role that ACEs may play in substance misuse in pregnancy is not well understood in this sociodemographic. Methods: Data were derived from the All Our Families prospective cohort study collected in Alberta, Canada between 2008-2011 (N = 1663). Three mailed surveys were completed by women during and after pregnancy. An established scale examined maternal ACEs before 18 years. Binge drinking and street drug use in pregnancy were assessed using yes/no questions at 34-36 weeks gestation. Separate adjusted logistic regression models tested associations between ACE score, binge drinking, and street drug use in pregnancy adjusted for a range of confounders. Results: Most women (63%) reported at least 1 ACE, with 14% reporting 4 or more. Binge drinking and street drug use in pregnancy were reported by 10% and 3% of women; respectively. In adjusted models, a woman's ACE score was significantly associated with binge drinking and street drug use in pregnancy in a moderate, dose-response fashion. Overall, ACEs resulted in 2 to 4-fold increase in the odds of substance misuse in pregnancy. Conclusions: Maternal ACEs were common in this sample of women with moderate to high socioeconomic status, and impacted the next generation through substance misuse in pregnancy. These findings combine with others to speak to the public health significance of maternal ACEs on substance misuse in pregnancy across the socioeconomic spectrum. Findings raise questions about whether physicians should screen and recommend interventions for women of child-bearing age with elevated ACE scores as part of routine preventative care.

Inflammation and conception, what is the role of vitamin D status? Anne Marie Jukic* Anne Marie Jukic Clarice Weinberg Sunni Mumford Anne Steiner

Data from women with polycystic ovary syndrome or endometriosis suggest that inflammation may contribute to ovulatory disorders or subfertility. At the same time, higher levels of vitamin D have been associated with improved fecundability, perhaps by modulating inflammation. Our objective was to examine the association between pre-conception high sensitivity C-reactive protein (hs-CRP) levels and fecundability independently, and within levels of vitamin D. We excluded values of hs-CRP above 10mg/L and categorized the remaining values according to clinical criteria (3). We used data from a prospective study of women trying to conceive a pregnancy, Time to Conceive, a cohort of women over age 30 who were therefore at higher risk of both subfecundity and chronic inflammation. Blood samples drawn early in the participants' pregnancy attempts, and in the early follicular phase, were analyzed for serum hs-CRP and 25OHD. Pregnancy attempt time was the number of menstrual cycles of attempt prior to enrollment (treated as left truncation) plus the number of menstrual cycles from enrollment to either a positive pregnancy test or censoring. We used discrete-time-to-event models to examine hs-CRP and time to pregnancy alone and stratified by 25OHD level. The overall mean of hsCRP was 1.6mg/L (median=0.86). Mean hs-CRP level was higher among women with vitamin D deficiency (<20ng/ml, N=19) and lowest among women with a 25OHD level of 30ng/ml or more. There was no overall association between hs-CRP and fecundability. However, when the 25OHD level was 30ng/ml (N=361), higher hsCRP was associated with increased fecundability: FR(CI): 1.4 (0.40, 5.3) and 2.9 (1.4, 6.1). Our results suggest that vitamin D level may modify the effects of chronic inflammation on fecundability.
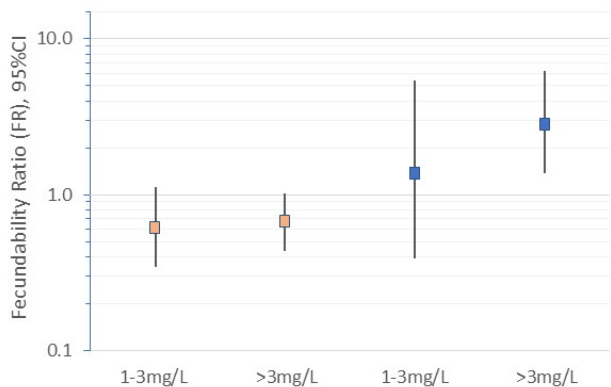
Associations between hsCRP and fecundability, among women with vitamin D deficiency (25OHD <20 ng/ml), orange squares, and among women with vitamin D sufficiency (≥30ng/ml), blue squares.

Respiratory

Longitudinal predictors of emphysema severity in a cohort of HIV-infected smokers Andreas Teferra* Andreas Teferra Amy K. Ferketich Jamaal Saleh Mahmood Alalwan Janice Drake Meghan Connors Philip Diaz

Introduction: HIV infection is an independent risk factor for the development of emphysema, but the progression of the disease in HIV-infected individuals is poorly understood. We examined predictors of change in emphysema severity in a cohort of HIV-infected smokers.
Methods: Participants were 94 HIV-infected current smokers with at least 10 smoking pack-years at baseline. Emphysema severity was assessed at baseline and follow-up using high-resolution computed tomography (HRCT) scans, with each lung lobe assigned a 0-5 score according to the percentage of the lobe that was affected. The aggregated scores indicated total emphysema severity. Data on smoking history, biological markers of HIV and pulmonary function tests including spirometry and single breath diffusing capacity for carbon monoxide (DLCO) were also collected. Predictors of emphysema severity were assessed by fitting a marginal Poisson model accounting for with-in participant correlated measurements.
Results: The average follow-up was 7.8 ± 1.1 years. Participants were 43.6 ± 8.7 years old at baseline, 84% male and 53.2% non-Hispanic white. Emphysema severity increased from baseline (2.9 ± 3.8) to follow-up (3.4 ± 4.4). Improvements in DLCO % predicted and ratio of forced expiration in 1 second to forced vital capacity (FEV1/FVC %) were related to a reduction in severity over the follow-up period; with a 10% increase in each measure relating to a RR of 0.80 [95% CI: 0.72-0.89] and 0.83 [95% CI: 0.74-0.94], respectively. Decline in HIV viral load was an independent predictor of a decrease in emphysema severity [RR: 0.79 95% CI: 0.64-0.99], whereas an additional 10 pack-years of smoking from baseline suggested worsening severity [RR: 1.06 95% CI: 0.99-1.13]. Conclusion: Controlled HIV infection and improvements in pulmonary function were predictors of reduction in emphysema severity among HIV-infected smokers. Continued smoking even among established smokers may relate to worsening severity.

Respiratory

Value of Quality Control Over-Reading (QC) in the Epidemiologic Studies W. Braxton
Jackson* W. Braxton Jackson Matthew D. Curry Mark R. Bodkin Kaitlyn G. Lawrence Dale P. Sandler

Background: Centralized expert review of spirometry is a common, but costly, quality control (QC)
practice in large-scale epidemiologic studies of lung disease. Modern spirometers provide
computerized QC feedback to examiners. Expert review may exclude tests, but studies have shown
that it can also recover a substantial proportion of tests judged as technically unacceptable by
spirometer software. However, the scientific benefit of centralized QC remains unclear in terms of
differential misclassification of outcome by exposure status or related bias in effect estimates.
Methods: We explored the relationship between smoking and lung function in a prospective study of
the health effects of a major oil spill disaster to examine the value of centralized spirometry QC. The
analysis included adult participants who met 2005 American Thoracic Society acceptability and
reproducibility criteria (three acceptable tests with ≤150mL difference between the largest and
second largest FVC curve and FEV1 curve) either before (N=6,466) or after (N=7,488) centralized
review. Lifetime smoking was categorized as current, former, or never. Lung function limitation was
defined as forced expiratory volume in 1 second (FEV1) ≤70% predicted. Effects were assessed by
adjusted multivariable linear and modified Poisson regression. RESULTS : Current smokers had an
elevated prevalence of function limitation compared to non-smokers after adjustment in both the
QC'd (PR:1.54, 95%CI:1.33,1.78) and non-QC'd (PR:1.54, 95%CI:1.33,1.79) data sets, as did former
smokers former smokers QC (PR:1.14, 95%CI:0.95,1.37) vs. non-QC (PR:1.16, 95% CI:0.96,1.40).
CONCLUSIONS: We found elevated prevalence of lung function impairment in current smokers. The
effect size and precision of the findings were similar regardless of whether the data was reviewed by
an expert or not. Epidemiologists should consider the costs and benefits of QC when designing
studies, especially when lung function is not the primary outcome.

Respiratory

Respiratory Hospitalizations and Wildfire Smoke: A spatio-temporal analysis of the October 2007 firestorm in San Diego County Rosana Aguilera* Rosana Aguilera Kristen Hansen Alexander Gershunov Sindana D. Ilango Paige Sheridan Tarik Benmarhnia

Wildfire smoke adversely impacts respiratory health as fine particles can penetrate deeply into the lungs. Epidemiological studies of differential impacts typically focus on population subgroups in terms of vulnerability to wildfire smoke. Such information is useful to target and customize smoke warnings and mitigation actions for specific individuals. In addition to individual vulnerability, it is also important to assess spatial patterns of health impacts to identify vulnerable communities and tailor public health actions during wildfire smoke events. We assess the spatio-temporal variation in respiratory hospitalizations in San Diego County during a set of major wildfires in 2007, which lead to a substantial public health burden. Analyzing the spatio-temporal evolution of exposure is necessary due to variations in smoke plume extent, particularly in this region where the most damaging wildfires are associated with strong wind conditions that spread flames and smoke particles. We propose an extension of the case-crossover analysis that explicitly considers the spatial variation of respiratory health associated with smoke exposure, compared to reference periods before and after wildfires. We find the highest excess hospitalizations in areas covered by and immediately downwind of wildfires, and that excess hospitalizations tend to follow the distribution of smoke plumes across space and time.

LATEBREAKER

Respiratory

Identifying Associations between Ambient Environmental Exposures and Pediatric Asthma Emergency Department Visits by Asthma Season Using a Bayesian Time-Stratified Case Crossover Design Matthew Bozigar* 3647] Bozigar Andrew Lawson John Pearce Erik Svendsen John Vena

Background: Numerous ambient air pollutants have been linked with asthma emergency department (ED) visits. However, seasonal variation in estimated associations is less understood.

Objective(s): We 1) used innovative methods in a Bayesian framework to 2) identify single pollutant associations with asthma ED visits.

Methods: We assessed ED visits with a primary diagnosis of asthma among the age 5-19 population of South Carolina (SC) from 2005 to 2014. Highly resolved spatio-temporal exposure estimates were obtained for 12 pollutants and two weather factors. We innovatively defined seasons by periods of relative burden specific to the study location's "asthma seasons", and included variable selection in a time stratified Bayesian case crossover design to estimate associations.

Results: Disproportionate burdens were observed for males (58.5% of ED visits), children ages 5-9 (46.9%), African Americans (68.0%), children on public insurance (e.g., Medicaid, 58.3%), and children living in the central Midlands region of SC (52.4%). An overall positive association was observed with NO_x (OR_{IQR}: 1.086, 95% CI: 1.052, 1.117) and PM_{10} (OR_{IQR}: 1.043, 95% CI: 1.025, 1.062). In Fall, the peak asthma burden season (47.5%), the association with PM_{10} was stronger (OR_{IQR}: 1.210, 95% CI: 1.156, 1.262) and EC was also positively associated (OR_{IQR}: 1.073, 95% CI: 1.044, 1.103).

Discussion: Fall allergens, such as ragweed antigens, attached to particles of respirable size are a potential major allergenic driver of ED visits in SC, though confirmation is needed. Finding overall associations with NO_x and EC underscored the potential adverse health impacts of fuel combustion, the assumed source. Additional research is needed into the SC Spring asthma season with the second highest burden, as no air pollutants were significantly associated. In a changing climate, combined air pollution and allergen health effects research and projecting future trends are needed. Our methodology is transferrable and reproducible for any location and time-varying exposures.

Screening

External validation of chronic kidney disease prediction scores and development of a short non-invasive easy-to-use screening tool for routine use in general practice Susanne Stolpe* Susanne Stolpe Cornelia Blume Börge Schmidt Raimund Erbel Karl-Heinz Jöckel Andreas Stang

Chronic kidney disease (CKD) is a relevant problem for public health regarding individual and societal implications. Patients often remain unaware of a CKD until more serious stages. Screening populations at higher risk for CKD can be cost-effective. However, CKD prediction scores are rarely externally validated and implemented.

We wanted firstly to externally validate CKD prediction scores, and secondly, select a score suitable for self-completion by patients to screen for unknown CKD in general practice.

From literature, we identified 6 CKD prediction scores using non-invasive variables only. For external validation, we used baseline data from the German Heinz-Nixdorf-Recall -Study (HNRS) comprising 4,841 participants aged 45-79 years from the general population. We defined CKD as eGFR <60ml/min/1.73m². We evaluated the scores' discrimination and calibration.
We modified the best performing score for use as patient self-completion questionnaire. We tested its diagnostic criteria in 6,556 patients (18-99 years) unaware of their CKD status (CKD prevalence 20%) from a joint database ("Kern-DB") of four large German CKD related cohort studies. In Kern-DB patients, prevalence of hypertension, diabetes and old age were high, and comparable to the risk factor profile of patients in medical practice where a CKD prevalence of 30% can be expected.

External validation resulted in c-statistics of 0.68-0.73. The ‚Modified SCORED' performed best. Its items (N=7) reflect main CKD risk factors. As patients rarely know about proteinuria we skipped this item. Applying the remaining score parameters on age, sex, hypertension, diabetes, myocardial infarction, and heart failure to the patients selected from Kern-DB yielded c=0.70, 70% sensitivity, 61% specificity. Predicted values were 31% (positive) and 61% (negative).

Our short screening tool supports physicians to get an indication for in-depth CKD diagnosing in high-risk patients according to the guidelines.

Screening

Association of dental care and colorectal cancer screening in older adults: a national level study in the United States Sanda Cristina Oancea* S. Cristina Oancea Narysse Nicolet

Background: Both frequent dental care and colorectal cancer screening are important in prevention of oral diseases and colorectal cancer respectively. The present study addresses the gap in literature by exploring the association between visiting a dentist/dental clinic and getting screened for colorectal cancer.

Methods: Survey data from the 2018 Behavioral Risk Factor Surveillance System was analyzed using weighted and adjusted logistic regression models. The final study sample consisted in 161,109 United States adults aged 50-75 years who have never been diagnosed with cancer. The outcome variable was the receipt of colorectal cancer screening. Dental visits were categorized as: within the past year (less than 12 months), within the past 2 years (1 year but less than 2 years), within the past 5 years (more than 2 years but less than 5 years), more than 5 years, or never.

Results: Compared to individuals who went for dental care 5 or more years ago or never, the weighted and adjusted odds of receiving colorectal cancer screening were significantly greater among individuals who went for dental care within the past year (OR=2.02; 95% CI: 1.85-2.20), within the past two years (OR=1.28; 95% CI: 1.15-1.43), or within the past 5 years (OR=1.26; 95% CI: 1.13-1.40).

Conclusion: The findings indicate that there is a significant association between the receipt of dental care and colorectal cancer screening among US's older residents. Additionally, receiving dental care within the last year is significantly greater associated with the receipt of colorectal cancer than receiving dental care more than 1 year ago. Due to the growing US population of elderly individuals and increased risk of colorectal cancer during those years, programs should be implemented to address the disparities in preventative care.

Screening for Undiagnosed Atrial Fibrillation in Primary Care: Primary Care Physician Perceptions about Current and Future Practice Jeffrey M. Ashburner* Jeffrey Ashburner Priscilla R. Lee Colin M. Rivet Aimee K. Lin Courtney E. Leonard Ana T. Trisini Lipsanopoulos Leila H. Borowsky Wyliena Guan Xinye Li Yuchiao Chang Shaan Khurshid Patrick T. Ellinor Daniel E. Singer David M. McManus Steven A. Lubitz Steven J. Atlas

Background:
Atrial fibrillation (AF) is the most common cardiac arrhythmia and associated with a 5-fold increased risk of stroke. AF may be asymptomatic, so screening for undiagnosed AF is appealing. European and Australian/New Zealand guidelines recommend electrocardiogram (ECG) screening, while U.S. guidelines currently do not.

Methods:
We conducted a large (n=35,309) pragmatic cluster-randomized trial (ClinicalTrials.gov NCT03515057) in a U.S. primary care network to assess the efficacy of population-based AF screening in older patients using a handheld ECG at clinic visits. Following the trial, we surveyed primary care providers (PCPs) about how they assessed heart rhythm and opinions about AF screening.

Results:
The survey response rate was 76% (81% intervention; 71% control) among 170 physicians and 28 nurse practitioners. Intervention and control responses were similar, so were combined except as noted. 93% of PCPs reported routinely assessing pulse pattern at visits. Most PCPs (85%) believe AF screening should be done during primary care visits. Intervention PCPs exposed to use of a handheld ECG during the trial favored this as a screening method (86%), while control PCPs favored pulse palpation (65%). PCPs were less certain whether screening should be done outside of office visits with patch monitors (17% yes, 36% no, 47% unsure) or consumer devices (22% yes, 24% no, 54% unsure). Of PCPs who support screening with personal devices, 71% believed patients should be able to share results via a patient portal. PCPs were uncertain about the burden of AF required to treat intermittent AF, though many had a low threshold (Figure).

Conclusion:
Clinic-based AF screening, which will largely detect undiagnosed persistent AF, is widely supported by PCPs. PCPs appear less certain about screening done outside of clinic visits. This may be due to recognition that more paroxysmal AF may be detected and the burden of AF at which to recommend oral anticoagulation is unclear.

Figure: What is the minimum duration of a single AF episode that would lead you to recommend oral anticoagulation (OAC) for a patient with a CHA2DS2-VASc of 3 and paroxysmal AF?
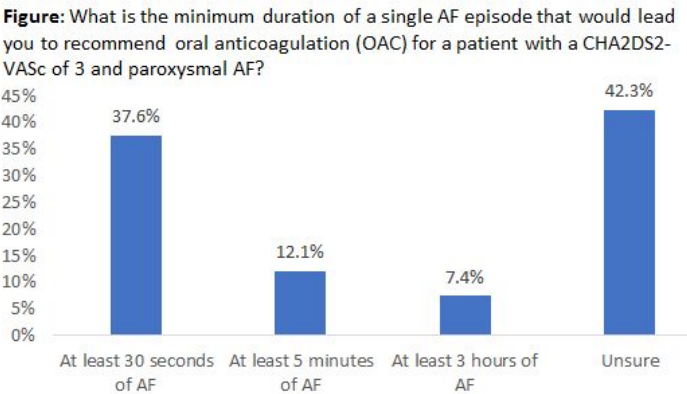
Social

The association between social network structure and composition with physical activity: The Cardiovascular and Metabolic Diseases Etiology Research Center (CMERC) cohort So Mi Jemma Cho* So Mi Jemma Cho Hokyou Lee Jee-Seon Shim Yousik Youm Hyeon Chang Kim

Evidence suggests that physical activity (PA) engagement is often shaped through myriad of structural aspects of social relationships. We compared social network structure, components, and tie strengths variables across participants with varying levels of PA and identified the relationship between social network structure and PA.

From middle-aged, community-dwellers, we collected network structure (density and components), composition, and tie strengths among network members using the "name generator" module. We calculated metabolic equivalent of task (MET)-min/week performed during everyday and leisure activities from the 7-Day Physical Activity recall. We employed multivariable linear regression to assess the association between network structure and PA. As supplementary analyses, we have also examined the association with the moderate vigorous physical activity (MVPA) and wrist-worn accelerometer measurements.

Participants engaged in higher PA had lower network density compared to the less active counterpart. The network members of the highest PA quartile were older, acquainted with for longer duration, and more likely to be composed of same sex and cohabiting members (in male only). After adjusting for socioeconomic status and comorbidities, network density was inversely associated self-reported PA in both male (β=-564.01, p=0.0506) and female (β=-627.00, p<0.0001). Yet, the association was not maintained in both self-reported and accelerometer-assessed MVPA. However, the objective MET showed inverse association with network density, only in female. In contrast, network component was positively associated with self-reported MET (male, β=104.16, p<0.0001; female, β=55.96, p<0.0001), which remained statistically significant with self-reported MVPA but not with accelerometer-based measurements.

Understanding of the role of social network structures in a population that can largely benefit from appropriately-designed intervention can help attain optimal level of PA.

Do health and developmental problems modify the effects of residential mobility on youth socioeconomic position among low-income families? Results from a housing voucher experiment Nicole Schmidt* Nicole Schmidt Naomi Thyden Huiyun Kim Lan Liu Pam Joshi Toben Nelson Theresa Osypuk

Moving to lower poverty neighborhoods may be a mechanism to improve socioeconomic position (SEP), particularly for low-income families, but myriad health problems may also hinder upward residential and SEP mobility. This study leveraged an experimental design, to examine potential heterogeneous effects of voucher-induced residential mobility using the Moving to Opportunity (MTO) study. Volunteer families living in public housing were randomized (in 1994-1998) to 1 of 3 groups: to receive (1) a Section 8 rental subsidy voucher with housing counseling and requirement to move to a low-poverty neighborhood ("low poverty treatment"), (2) a "Section 8" voucher only, or (3) no voucher (control group). We tested whether MTO treatment effects on adolescent (ages 15-20, N=3600) and grown child (ages 21-30, N=3100) education and employment (SEP, measured in 2008-2010) were modified by baseline child health and developmental problems, using intent-to-treat regression. We hypothesized that children without baseline health/developmental barriers would experience improved SEP, but results were opposite—treatment was beneficial for youth with baseline health problems. Adolescents in the low poverty treatment (vs. controls) who required special medicine at baseline were more likely to be enrolled in school 10-15 years later (B(SE) = 0.88(0.34), 95%CI = 0.21, 1.55; trt-modifier interaction p=.031). Grown children in the low poverty treatment (compared to controls) who had baseline learning problems were more likely to have a HS diploma or GED 10-15 years later (B(SE) = 0.49(0.26), 95%CI = -0.01, 1.00; trt-modifier interaction p=.047). Subgroup effects for low poverty treatment without health barriers and for both Section 8 groups were nonsignificant. There were no treatment interactions with health/development on college enrollment, current employment, or youth idleness. Housing vouchers with locational constraints may help low-income families with health problems improve SEP.

The association between indicators of socioeconomic position and DNA methylation: A systematic review Janine Cerutti* Janine Cerutti Yiwen Zhu Alexandre Lussier Jiaxuan (Jessie) Liu Erin C. Dunn

Socioeconomic position (SEP), one of the most commonly measured concepts in epidemiology, is a major determinant of health across the life course. However, the biological mechanisms explaining this relationship are not yet well-understood. One widely pursued hypothesis is that the socioeconomic environment causes DNA methylation (DNAm) marks to bind to DNA, which may influence gene activity and subsequent long-term health without altering the sequence of the genome. The goal of this systematic review was to summarize the current state of the field on the association between SEP and DNAm, in order to guide future epigenetic studies in this space. We focused on multiple types of SEP indicators and DNAm data in human samples spanning the entire life course.

We performed a systematic search of empirical articles that examined the association between any SEP exposure and DNAm, published from inception through September 17, 2019. The 37 studies found varied considerably by research design and life course stages examined (Figure 1). We also found that different SEP indicators – spanning income, education, occupation, and other domains – associated with DNAm in most studies. Studies that individually analyzed multiple SEP exposures found little to no overlap in DNAm profiles between measures, suggesting that different indicators represent different underlying constructs of SEP that may affect biological processes independently. We also found evidence that the timing and duration of SEP may differentially impact DNAm patterns.

SEP is a complex, yet important social factor that should continue to be investigated and taken into account in epigenetic studies. Future studies should carefully and thoughtfully consider how to conceptualize and measure different indicators of SEP given their domain- and timing- dependent impacts. These efforts will inform intervention and prevention efforts aimed at reducing the ill effects of socioeconomic disadvantage across the life course.
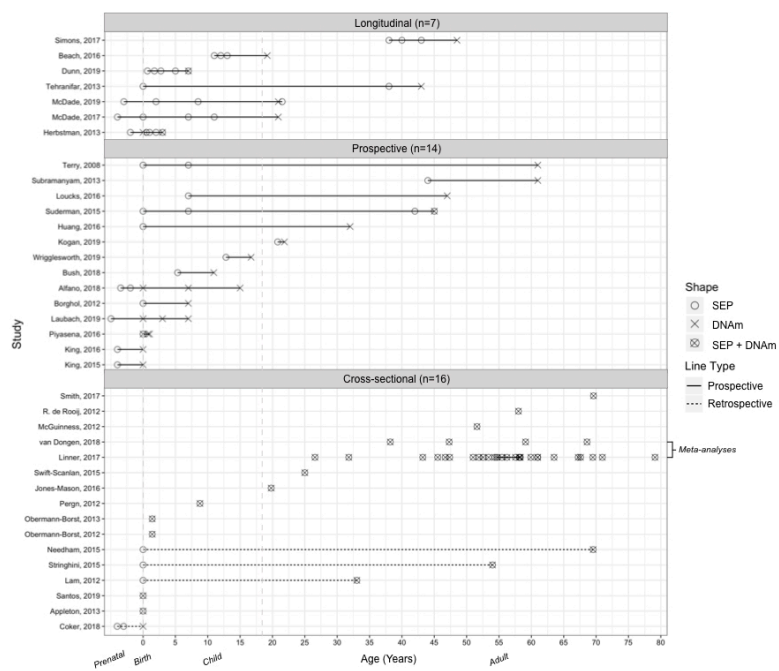
Viewing the Graduate Record Examination (GRE) score does not harm nor help applicants regardless of their racial/ethnic minority status: a randomized study Kristina Dang* Kristina Van Dang Francois Rerolle Kala Mehta Kirsten Bibbins-Domingo Maria Glymour Meghan Morris

Background. Whether requiring GRE scores for PhD applicants affects the diversity of the admitted cohort is uncertain. We designed a randomized study of applications to 2 PhD programs in population health to assess whether including applicant GRE scores differentially affects reviewers' scores for underrepresented minorities (URM) applicants.

Methods. Completed applications were quadruplicated and randomly assigned to 2 reviewers blinded to GRE score and 2 reviewers unblinded (N=14 reviewers). Reviewers read and assigned scores (1-10, 1 being best) for: research experience, academic training, level of institutional support, research potential, and overall impression. UCSF defines URM as African American/Black, Filipino, Hmong, Vietnamese, Hispanic/Latinx, Native American/Alaska Native, Native Hawaiian/Other Pacific Islander, or two or more. We used linear mixed models to evaluate the effect of the reviewer seeing the GRE scores and whether it was modified by URM status; with fixed effects for reviewers and random effects for each applicant.

Results. Among 198 applicants, 39 (19.6%) were URM. The average reviewer score for URM applicants was 3.62 (SD=1.58) and for non-URM applicants 3.72 (SD=1.96). In mixed models, scores were not significantly different for applications including the GRE compared to applications with the GRE removed, both among non-URM applicants (b=0.15; 95% CI: -0.03, 0.33) and URM applicants (b=0.02, 95% CI:-0.36, 0.40). We failed to find evidence that blinding to GREs differentially affected URM compared to non-URM students (b for interaction= -0.13, 95% CI:-0.55, 0.29).

Conclusions. In this randomized study, we found little statistical evidence that using GRE scores in admissions decisions affects either URM applicants or non-URM applicants when applying to our graduate programs. Although this study has a small sample, the confidence interval suggests large harms are unlikely and many other factors had much larger effects on outcomes.

Figure. Randomized study of GRE on admissions
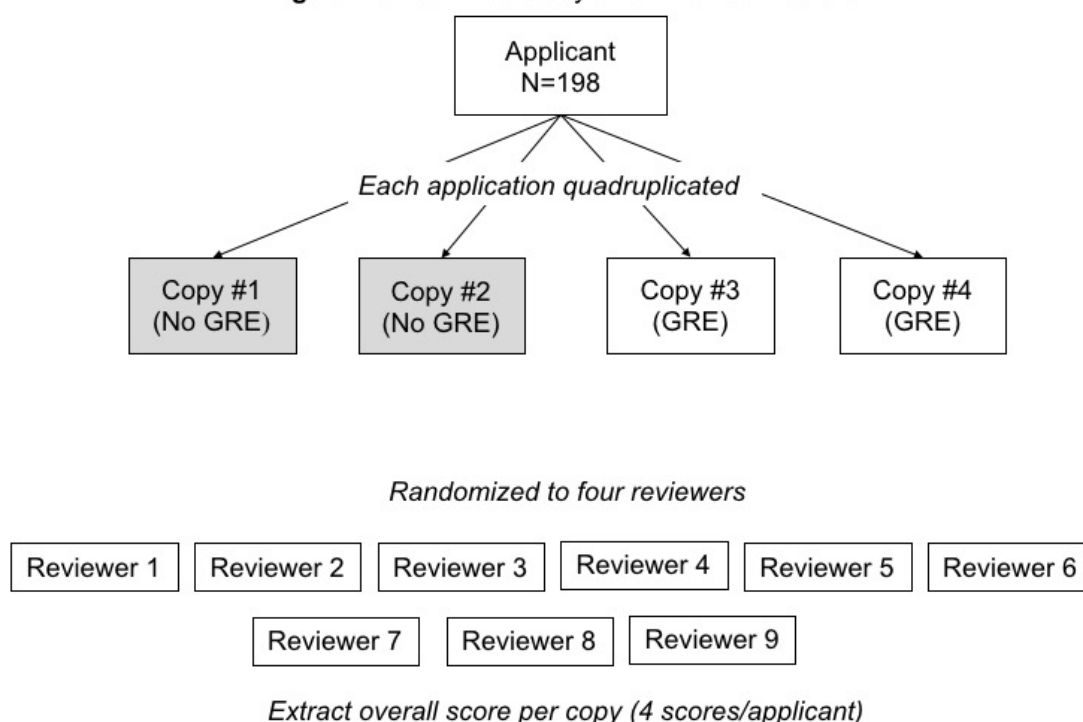
Creating a census tract measure of exposure to structural vulnerability Shanice Battle, MPH*
Shanice Battle

Although many theories have been developed to study the association between structural disadvantage and health, the constructs that underlie this disadvantage are understudied in empirical analyses. In particular, it is unclear whether it is possible to measure exposure to structural factors and how to best account for the multidimensional nature of structural disadvantage in empirical measures. A review of previous research suggests this disadvantage can be described as structural vulnerability that consists of three correlated dimensions - affluence, disadvantage and social vulnerability (AF, DA and SV, respectively). The aim of this paper is to create a measure of structural vulnerability based on census tract data linked to participants in the American's Changing Lives study (n=3617). A confirmatory factor analysis was conducted using census tract indicators of AF, DA and SV to compare uni-dimensional, bi-factor and three factor models using model fit criteria and factor interpretability. While the three factor model was deemed best in terms of strong factor loadings and fit indices, results are consistent with previous challenges in sufficiently measuring exposure to structural risk factors. Furthermore, the fit of the models varied across census tracts of subgroups of adult men and women ages 25 and older when divided by race and gender.

Longitudinal Associations between Discrimination and Telomere Length: The Multi-Ethnic Study of Atherosclerosis (MESA) Elleni Hailu* Elleni Hailu Belinda Needham Tene Lewis Jue Lin Teresa Seeman Ana Diez Roux Mahasin Mujahid

Prior studies have documented links between experiences of discrimination and short Leukocyte Telomere Length (LTL), a marker of cellular aging. However, no study to-date has investigated the longitudinal relationship between discrimination and LTL change. Additionally, whether the association varies across sociodemographic characteristics remains poorly understood. Using data from the Multi-Ethnic Study of Atherosclerosis Stress Ancillary Studies I&II (n=1080, age range=45-84), our study aimed to assess the association between baseline reports of discrimination and 10-year changes in LTL, and possible effect modification by race/ethnicity, gender, and age. Discrimination was assessed using both the Major Experiences of Discrimination Scale (MDS; none,1 domain, >/=2 domains) and the Experiences of Discrimination Scale (EDS; none, low, moderate, high). Change in LTL was defined as Regression to the Mean corrected 10-year difference in the ratio of Telomeric DNA to Single Copy gene (T/S). Linear Regression models found no associations between discrimination and LTL change or effect modification by race/ethnicity. However, there was evidence to suggest effect measure modification by gender ($P(X^2) = 0.03$) and age ($P(X^2) = 0.14$) only for MDS, after adjusting for socio-demographic characteristics, health behaviors, and health conditions. Among men, reporting major discrimination in >/=2 domains was found to be protective against telomere length attrition (Beta=0.024, 95% CI: -0.004,0.052) compared to reporting no discrimination. For those between ages 55 and 64, reporting major discrimination in >/=2 domains was associated with faster 10-year LTL attrition (Beta=-0.029, 95% CI: -0.064,0.006). There was no association between MDS and LTL for women or other age groups (45-54 years; 65+ years). Results indicate that domain specific discrimination may have differential impacts on accelerated cell aging across gender and age and warrant the need for continued investigation.

Probing the association between county jail incarceration and county mortality: A hypothesis-generating analysis Sandhya Kajeepeta* Sandhya Kajeepeta Seth Prins

Introduction: Mass incarceration has collateral consequences for community health, which are reflected in county-level health indicators including county mortality rates.

Objective: To explore the previously documented relationship between changes in county jail incarceration rates and subsequent county mortality rates across the United States, we conducted a longitudinal analysis of national administrative data from 1987-2016, stratified by cause of death.

Methods: Jail data were obtained from the Bureau of Justice Statistics. Mortality data were obtained from the Centers for Disease Control and Prevention. We fit one-year-lagged quasi-Poisson two-way fixed effects models controlling for all unmeasured stable county characteristics and measured time-varying confounders, including county poverty and crime rates.

Results: We considered eight common causes of death and found that chronic lower respiratory disease, substance use disorder, and suicide were the most strongly associated with change in county jail incarceration rate. A within-county increase in jail incarceration rate from the first to second quartile was associated with a 7.6% (95% CI: 6.0, 9.3) increase in chronic lower respiratory disease mortality, a 5.2% (95% CI: 0.2, 10.5) increase in substance use disorder mortality, and a 4.2% (2.4, 6.0) increase in suicide, after adjusting for confounders.

Discussion: We present three theorized mechanisms that may underlie the observed cause-specific associations: Racialized Political Economy – Material Pathways, Racialized Political Economy – Psychosocial Pathways, and Direct Pathogenic Effects of Jail Incarceration. Findings generate novel hypotheses concerning the pathways through which jail incarceration impacts community health, to be tested in future research.

Social

The Association Between Use of Family Planning Clinics or Planned Parenthood for Healthcare, Marital Status, and Risk of Preterm Birth among African American Women

Shawnita Sealy-Jefferson* Shawnita Sealy-Jefferson Kenya Moyers Shibani Chettri Natalie C. Brooks Brittney Butler Rhonda Dailey Dawn P. Misra

Family planning clinics and Planned Parenthood fill a critical healthcare need for women who are minoritized, unmarried, and economically disadvantaged. However, no prior studies have examined the joint impact of using this type of healthcare and marital status on risk of preterm birth (PTB) among African American women. We used in-depth interview and medical record data from the Life-course Influences on Fetal Environments Study (2009-2011, n=1,385) of postpartum African American women to answer this research question. PTB was defined as birth before 37 completed weeks of gestation. We used log binomial regression models (unadjusted and adjusted for age, educational attainment, and income) to estimate prevalence ratios (PR) and 95% CIs. We included an interaction term (p<0.10 cutoff) between self-reported use of family planning clinics or Planned Parenthood for healthcare in the past year (yes/no) and marital status (married/not married). In our study, 16.3% of participants had a PTB (n=226) and 13.6% reported using family planning clinics or Planned Parenthood for healthcare in the past year (n=188). In the overall sample, use of family planning clinics or Planned Parenthood for healthcare in the past year was not associated with risk of PTB (aPR: 0.75, 95% CI: 0.50, 1.11). However, marital status modified the association (p for interaction: 0.007). Among unmarried women (n=991), those who reported using family planning clinics or Planned Parenthood for healthcare during the past year (compared to those who did not) had lower PTB risk in unadjusted (PR: 0.55, 95% CI: 0.33, 0.91) and adjusted models (PR: 0.57, 95% CI: 0.33, 0.96). Conversely, results among married women (n=393) were in the opposite direction and were not strong (unadjusted PR: 1.74, 95% CI: 0.93, 3.29; adjusted PR: 1.67, 95% CI: 0.87, 3.24). Future studies should examine potential mediators of the reported association, to identify novel intervention targets for PTB among African American women.

Neighborhood Context as a Contributor to Sleep Differences in a Bi-national Cohort of Puerto Rican Young Adults Ryan Saelee* Ryan Saelee Ayana April-Sanders Hector R. Bird Glorisa Canino Cristiane Duarte Shakira Suglia

Background: Few studies have examined differences in dimensions of sleep among bi-national cohorts of Puerto Rican young adults and neighborhood contextual factors that may contribute to those differences. This study examined 1) sleep quality differences between living in San Juan, PR compared to South Bronx, NY, 2) the association between neighborhood factors and sleep quality, and 3) whether these neighborhood factors explained geographic differences in sleep quality among Puerto Rican young adults.

Methods: Participants (n=655; mean age=22.4 years) were from the Boricua Youth Study Health Assessment, a study of cardiovascular health among Puerto Rican young adults. Sleep quality was a summary score (lower score representing better sleep) from the Pittsburgh Sleep Quality Index. Neighborhood factors included summary scores from self-reported scales on collective efficacy, safety, and hazards. Study site (San Juan vs. South Bronx) was used to determine participant residence. Sociodemographic factors included gender, age, parental socioeconomic status and participant education. Multivariable linear regression was used for analyses.

Results: Adjusting for sociodemographic factors only, participants in San Juan had better sleep quality than those in South Bronx (β=-.77, 95% CI: -1.32, -.21). In separate adjusted models, greater collective efficacy (β=-.07; 95% CI: -.12,-.01), safety (β=-.44; 95% CI: .04, .84), but less hazards (β=-.03; 95% CI: -.08, .01) were related to better sleep quality. Controlling for neighborhood factors together, those in San Juan still had better sleep quality but the association was attenuated by 27% (β=-.56, 95% CI: -1.14, .02).

Discussion: Results suggest that neighborhood context may partially explain sleep differences for young adult Puerto Ricans living in two social contexts. Future studies should explore whether other neighborhood and contextual factors contribute to these sleep differences.

Social

Unpacking Neighbourhood Inequities: Investigating the Longitudinal Relationship between Income Inequality and Mental Health among Mothers Living in Calgary, Alberta

Samuel "Sammy" Lowe* Samuel Lowe Darcy Reynard Sheila McDonald Roman Pabayo

Objectives: To explore the relationship between neighbourhood income inequality (NII) and absolute income inequality and maternal depression and anxiety over time.

Methods: Data were analyzed from 2,412 mothers who participated in the All Our Families pregnancy cohort study and followed from <25 weeks pregnancy to 3 years postpartum. Depression was measured using the Edinburgh Postnatal Depression Scale (depressed score ≥10) and the Centre for Epidemiologic Studies Depression Scale (depressed score ≥16). Anxiety was measured using the Spielberger State Anxiety Inventory (anxiety score ≥40). Growth curve modeling was used to quantify the relationship between NII (z-transformed Gini index) and absolute income, adjusting for mother's baseline age, education, marital status, history of mental illness, ethnicity, and neighbourhood median household income and level of poverty.

Results: At baseline, NII was not a significant predictor of depression. However, mothers with high household income had a 21.8% (OR=0.78, 95%CI 0.63-0.96) reduction in the odds of being depressed for every one standard deviation increase in NII after follow-up. NII was not associated with depression among mothers from moderate/low household incomes. High household income mothers also had a 17.3% (OR=0.83, 95%CI 0.71-0.96) reduction in the odds of having anxiety for every one standard deviation increase in NII at baseline, and an 18.5% (OR=0.81, 95%CI 0.67-0.99) reduction after follow-up. NII was not associated with anxiety among mothers from moderate/low household incomes.

Conclusion: At baseline, mothers with high household income living in high inequality areas experienced a decreased risk of anxiety. Over time, higher income inequality was associated with decreased odds for adverse mental health outcomes among high income mothers.

Understanding the Impact of Obtaining Affordable Housing and Case-Management on Residents' Health Care Utilization and Cost Hannah Cohen-Cline* Hannah Cohen-Cline Jannate Ahmed Megan Holtorf

Access to stable housing is a powerful strategy for impacting health care utilization and quality and improving population health, and has been linked to lower health care expenditures, decreased use of acute health care such as emergency department visits and inpatient stays, and increased connection to primary care. However, housing alone is not always enough to improve wellbeing, and residents often still need assistance to address other social needs. This study assessed the impact of obtaining housing through an affordable housing and case-management program in Southern Oregon on residents' social needs and health care utilization and cost. We used administrative housing data to identify our population, and combined this with Medicaid claims and enrollment data to determine study eligibility, define cases and controls, and construct our health care outcomes. Our study sample included adults 18 years of age or older who had at least 6 months of Medicaid coverage during our study window, 2015 to 2018. Cases were defined as adults who obtained housing through the affordable housing program during our study window, while controls were defined as those who remained on the waitlist. Our health care outcomes were per member per year (PMPY) use of primary care, emergency department visits, inpatient stays, outpatient mental health visits, and dental care, as well as total costs of care. We then developed linear regression models to compare the health care outcomes between cases and controls. Cases used significantly less emergency department (difference: -0.61, p=0.034) and inpatient utilization (PMPY difference: -0.13, p=0.023), compared to controls. Cases also had significantly lower total costs of health care, compared to controls (PMPY difference: $-1794.25, p=0.022). Obtaining stable and affordable housing with case-management may lead to more optimal use of health care, which can ultimately improve population health and lower health care costs.

Social

Social determinants of microcephaly and delayed childhood neurodevelopment following in utero exposure to Zika virus Grace Power* Grace Power

A dramatic increase in microcephaly cases detected in newborns in Brazil during the 2015-16 Zika virus (ZIKV) epidemic lead to the declaration of a public health emergency of international concern by WHO. The implications associated with adverse outcomes from in utero exposure to ZIKV, such as microcephaly and neurodevelopmental delays, are substantial at a household as well as health systems and a broader societal level. Understanding risk factors following congenital ZIKV infection is therefore of high importance.

As a result of the socioeconomic disparities evident in Brazil, several studies demonstrated increased levels of microcephaly in economically deprived urban areas during the recent ZIKV outbreak. While these studies play an important role in generating hypotheses, they use a geographically defined group as the unit of observation. Not only is aggregate data bias a risk, but socioeconomic risk factors at the individual and household level remain insufficiently evaluated.

This study set out to explore associations between socioeconomic position and immediate as well as longer-term adverse health outcomes following in utero exposure to ZIKV. This was achieved by using data collected during the ZIKV epidemic from February 2016 to September 2017 in the State of Rio de Janeiro, Brazil. The results obtained indicate evidence of a consistent relationship between unfavourable socioeconomic indicators and microcephaly. In addition, the direction of association for adverse socioeconomic factors revealed that the most deprived children with prenatal exposure to ZIKV are at greater risk of neurodevelopmental delays. Conclusions drawn from this analysis have the capacity to i) identify target populations indicative of the most at risk group in the event of a future epidemic and ii) alleviate the risk of longer-term neurodevelopmental disability in children with in utero exposure to ZIKV, thus supporting health attainment and poverty reduction in Brazil.

Social

Individual-level residential mobility, neighbourhood socioeconomic change and premature death: a population-based cohort study Emmalin Buajitti* Emmalin Buajitti Laura Rosella

Background
Area-level residential mobility can be used to measure neighbourhood socioeconomic status (nSES). However, ecological measures mask individual-level characteristics of movement, including whether movers migrated to areas of higher or lower nSES. We leveraged residential histories from Ontario's health insurance program to explore health characteristics and premature mortality outcomes associated with residential mobility in individuals.
Methods
We followed 20,164 respondents from the 2000-01 cycle of the Canadian Community Health Survey for 15 years. Using postal codes from 5 years post-interview, respondents were categorized as: moved to same or better nSES, moved to worse nSES, did not move and nSES stayed the same or better, or did not move and nSES worsened.
We compared baseline characteristics according to residential mobility group. Using sequential Cox models, we estimated the unadjusted, age-sex adjusted, age-sex-SES adjusted, risk factor-adjusted (+smoking, alcohol, physical activity and BMI) and health status-adjusted (+multimorbidity) premature mortality risk associated with residential mobility.
Results
Respondents who moved were more likely to be young, male, and low-income than those who did not move. After age-sex-SES adjustment, risk of premature mortality was 1.39 times higher in those who moved to same or higher nSES, compared to those who did not move and nSES stayed the same or improved (95%CI 1.12, 1.72). For those moving to worse nSES, the hazard ratio for premature mortality was 1.21 (95%CI 0.92, 1.58). After adjustment for baseline risk factors and multimorbidity, the association was attenuated and no longer significant.
Conclusions
Residential mobility is an individual-level indicator of socioeconomic status that has not been well-studied in the literature. An association between residential mobility and premature mortality was observed, but was reduced after adjustment for confounding by baseline risk factors and health characteristics.

Social

Strong upward residential mobility and preterm birth: A sibling control design in California, 2005-2015 Samantha Gailey* Samantha Gailey Tim A. Bruckner

Background: Recent research finds that strong upward neighborhood mobility may contribute to improved birth outcomes. It remains unclear, however, whether upward mobility confers benefits to births delivered by non-Hispanic (NH) black and Hispanic, as well as NH white, women. In this study, we use a sibling-linked dataset to test whether strong upward mobility (i.e. moving from a very high to a very low disadvantage neighborhood) corresponds with a reduced odds of preterm birth (PTB). We examine NH white, NH black, and Hispanic mothers separately given distinct mobility patterns and risks of PTB.

Methods: We use a matched-sibling design for 892,084 sibling-pairs delivered by mothers with consecutive singleton live births in urban California neighborhoods from 2005 to 2015. We linked mother's residential address at each birth to a census-derived index of urban neighborhood disadvantage and defined strong upward mobility as moving from a very high to a very low disadvantage neighborhood. We estimated conditional logistic regression models predicting the odds of PTB (<37 weeks' gestation) in the sibling delivered after the move, controlling for the risk of PTB in the sibling delivered before the move, as a function of strong upward mobility, separately for NH white (N=240,188), NH black (N=52,609), and Hispanic (N=446,833) mothers.

Results: Strong upward mobility (relative to no change in neighborhood disadvantage) varies inversely with the odds of PTB in NH black mothers (OR=0.75, 95% CI: 0.56, 0.99). However, this association does not reach statistical detection in NH white or Hispanic mothers.

Conclusions: NH black mothers, but not NH white or Hispanic mothers, who experience strong upward neighborhood mobility exhibit a lower than expected risk of PTB in siblings delivered after moving. If replicated, our findings suggest that policies, programs, and structures that enable opportunities for upward neighborhood mobility among NH black women may reduce racial disparities in PTB.

Table 1. Odds ratios and 95% confidence intervals predicting the probability of PTB at time 2 (after move) as a function of strong upward mobility (vs. no change) in NH white, NH black, and Hispanic mothers who lived in very high disadvantage neighborhoods at time 1 (before move), controlling for preterm birth at time 1 and maternal covariates (not shown).

Parameter	NH white		NH black		Hispanic	
	OR	95% CI	OR	95% CI	OR	95% CI
Strong upward mobility	0.97	(0.81, 1.16)	0.75	(0.56, 0.99)	0.92	(0.80, 1.05)
Preterm birth (time 1)	4.00	(3.57, 4.48)	3.19	(2.91, 3.50)	3.06	(2.93, 3.19)

Social

Neighborhood Socioeconomic Status and Mortality in the Nurses' Health Study Nicole V. DeVille* Nicole DeVille Shilpa N. Bhupathiraju Boyang Chai Isabel Holland Hari S. Iyer Ichiro Kawachi Francine Laden Jaime Hart

Background: An extensive body of literature shows associations between individual-level socioeconomic status (SES) and risk of mortality, and a growing body of literature supports associations between area-level (i.e. neighborhood) SES variables and mortality, even after accounting for individual-level SES and other known risk factors. Our objective was to examine associations between neighborhood SES (nSES) and incident all-cause, non-accidental mortality in a nationwide cohort of U.S. women. Methods: We used time-varying Cox proportional hazards models, conditioned on age (in months, updated every time period) and follow-up cycle (questionnaire period), to assess the relationship between nSES and mortality among women in the Nurses' Health Study (NHS) between 1986-2014. Incident mortality was ascertained from the National Death Index, and nSES was determined for the Census tract of each residential address based on the closest decennial Census or American Community Survey. We examined the association with quintiles of nSES variables and created a nSES score by summing the z-scores of selected variables, such that increasing scores were associated with affluence. Demographic, lifestyle (e.g. diet, physical activity, smoking), and individual-level SES factors were ascertained through biennial questionnaires. Results: After adjustment for potential confounders, increasing nSES score was statistically significantly associated with decreased risk of all-cause mortality (HR=0.97, 95%CI: 0.96, 0.97 for a 1 SD increase (4.33)). For individual measures, the associations comparing the fifth to first quintiles ranged from 0.88 (95%CI: 0.83, 0.93) for percent of households receiving interest or dividends, to 1.09 (95%CI: 1.04, 1.14) for percent of households in poverty. Most nSES measures were associated with mortality. Conclusions: In the NHS cohort with extensive follow-up and information on potential confounders, nSES measures were associated with all-cause mortality.

Social

Does the union make us strong? Labor union membership, self-rated health, and mental illness: a parametric g-formula approach Jerzy Eisenberg-Guyot* Jerzy Eisenberg-Guyot Stephen J. Mooney Wendy E. Barrington Anjum Hajat

Introduction: Union members enjoy better wages and benefits than non-members, which can improve health. However, the longitudinal relationship between unionism and health remains uncertain, partially because of healthy-worker bias, a bias that cannot be addressed without high-quality data and methods that account for treatment-confounder feedback and structural non-positivity. Applying one such method, the parametric g-formula, to Panel Study of Income Dynamics data, we analyzed the longitudinal relationships between union membership, poor/fair self-rated health (SRH), and moderate mental illness (Kessler K6 > 4).

Methods: Our union membership and SRH analyses included 16,719 respondents followed between 1985 and 2017, while our union membership and mental-illness analyses included 5,838 respondents followed between 2001 and 2017; all respondents were employed at baseline. Using the parametric g-formula, we contrasted cumulative incidence of the outcomes under two hypothetical interventions, one in which all employed-person-years were set to union-member employed-person-years (union intervention), and one in which no employed-person-years were set to union-member employed-person-years (non-union intervention). We also examined whether the intervention effects varied by gender, gender-race, or gender-education in stratified models. CIs were calculated via non-parametric bootstrapping.

Results: The cumulative incidence of the outcomes during follow-up under no intervention was 47% for poor/fair SRH and 45% for moderate mental illness. Overall, the union intervention did not reduce incidence of poor/fair SRH (RR: 1.01, 95% CI: 0.94, 1.09; RD: 0.01, 95% CI: -0.03, 0.04) or moderate mental illness (RR: 1.02, 95% CI: 0.91, 1.12; RD: 0.01, 95% CI: -0.04, 0.06) relative to the non-union intervention (Figure 1). These effects largely did not vary by subgroup.

Conclusion: We found little evidence that union membership reduces incidence of poor/fair SRH or mental illness.
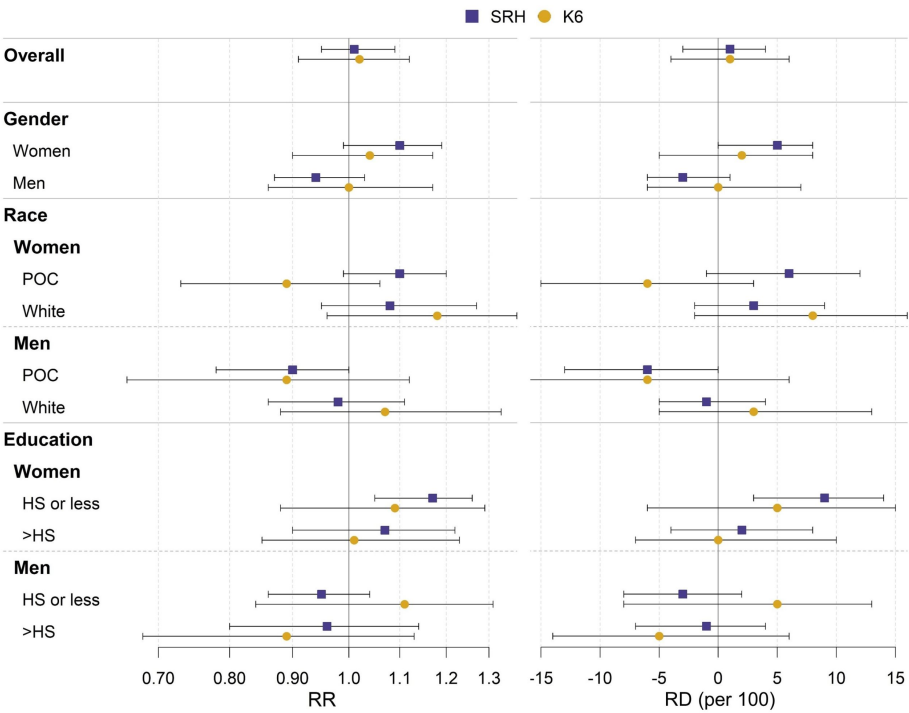
Sleep disparities among White, Black, and Hispanic sexual minority compared to heterosexual women: Findings from the Sister Study Erline E. Martinez-Miller* Erline Martinez-Miller Symielle A. Gaston Dale P. Sandler Chandra L. Jackson

Sexual minorities may experience greater stress than heterosexuals, which could negatively affect sleep with implications for physical and mental health. Racial/ethnic minorities who are also sexual minorities appear to face additional burden, yet little is known about sleep among sexual minorities or variation by race/ethnicity. Among 50,792 eligible adult female Sister Study participants, we assessed cross-sectional associations between sexual orientation (heterosexual, sexual minority: bisexuals and homosexuals) and sleep at enrollment (2003-2009). We also examined race/ethnicity (non-Hispanic White [NHW], non-Hispanic Black [NHB], and Hispanic) as a modifier. Self-reported sleep measures were average duration/night (<6, 6, 7-8, and 9 hours), debt ≥2 hours between maximum and minimum sleep, latency ≥30 minutes, and medication use (prescription drug and melatonin). Adjusting first for sociodemographic factors and self-rated health and then for perceived sexual discrimination, we estimated prevalence ratios (PRs) and 95% CIs using Poisson regression with robust variance estimators. Among participants (mean age: 55 years), 2% identified as sexual minorities, 86% were NHW, 9% NHB, and 5% Hispanic. Although most sleep measures did not differ by sexual orientation, among NHBs, sexual minorities had a higher prevalence of short sleep (PR [95%CI]: 1.36 [1.02, 1.82]) than heterosexuals, even after adjusting for perceived sexual discrimination. Sexual minorities overall had a higher prevalence of sleep medication use than heterosexuals (1.13 [1.01, 1.28]) with some racial/ethnic variation (NHW: 1.06 [0.94, 1.20], NHB: 1.77 [1.11, 2.81], Hispanic: 1.21 [0.62, 2.36]). Future sleep research among sexual minorities is warranted, and the roles of social stressors related to sexual orientation, especially those that might differ by race/ethnicity, should be explored further for potential intervention targets.

Figure 1. Adjusted* cross-sectional associations of sexual orientation with sleep duration and sleep medication use**, overall and by race/ethnicity: the Sister Study (2003-2009; N=50,792).

Sexual minority: homosexual and bisexual vs. heterosexual
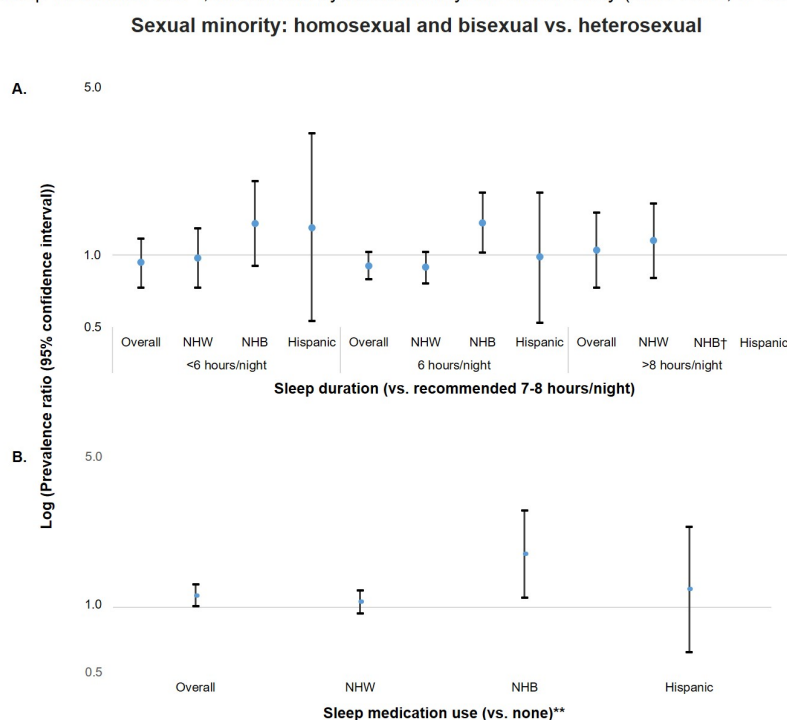
Abbreviations: NHW, non-Hispanic White; NHB, non-Hispanic Black.
*Models adjusted for age, nativity, region of residence, marital status, educational attainment, annual household income, occupation, and self-rated health.
**Sleep medication use include drug prescription medication and melatonin.
†Unable to present estimates for NHB and Hispanic models for >8 hour sleep durations vs. 7-8 hours due to positivity limitations.

Neighborhood deprivation and epigenetic age acceleration Kaitlyn Lawrence* Kaitlyn Lawrence Jacob Kresovich Katie O'Brien Thanh Hoang Zongli Xu Jack Taylor Dale Sandler

Neighborhood deprivation is associated with reduced life expectancy and higher all-cause mortality. Biologic age, which accounts for physiologic variation among individuals of the same chronologic age, may be influenced by living in a low socioeconomic status (SES) area. Epigenetic clocks utilize blood-based DNA methylation patterns to estimate biologic age and may be sensitive markers of biologic aging. However, few prior studies have evaluated whether living in a low SES area can influence biologic age measured by epigenetic clocks. We assessed the relationship between neighborhood deprivation and epigenetic age metrics. The Sister Study is a large prospective cohort study of women aged 35-74 years. We used data from a case-cohort study of breast cancer in non-Hispanic white participants with measured blood DNA methylation data (n=2,632). We measured genome-wide methylation at 450,000 CpG sites and used values to estimate epigenetic age following methods published for 4 epigenetic clocks - Hannum, Horvath, PhenoAge, and GrimAge. Metrics were regressed on chronologic age to estimate differences, or 'age acceleration' and transformed into z-scores. Participants were assigned neighborhood deprivation scores at the census-block group level based on their primary address at cohort entry using the 'Area Deprivation Index'. We estimated associations between deprivation and age acceleration using linear regression. Comparing the highest quartile of neighborhood deprivation to the lowest, there was a positive association with age acceleration estimated by Hannum (Beta: 0.20, 95% Confidence Interval (CI): 0.04, 0.37), PhenoAge (Beta: 0.28, 95% CI: 0.13, 0.43), and GrimAge (Beta: 0.41, 95% CI: 0.25, 0.57), but not Horvath clocks. Increasing quartiles of deprivation were associated with GrimAge in a dose-dependent manner (p<0.001). The biological consequences of residing in low SES neighborhoods appear to be quantified by methylation-based markers of aging.

Social

Dynamic residential movement and depression among people who were affected by the 9/11 disaster Sungwoo Lim* Sungwoo Lim Sze Yan Liu Jennifer Brite Cristina Pollari Aldo Crossa Sean Locke

Residential instability, marked by frequent moves, is associated with mental health, but causal inference on this relationship is challenging due to time-varying exposure, time-varying confounding, and the role of changing social environments. We tested the hypothesis that a frequent residential moving experience over 8 years is associated with higher risk of depression and lower likelihood of social integration among adults exposed to the 9/11 disaster. To address violations of causal assumptions, we used longitudinal Targeted Maximum Likelihood method. Data for this study came from a 4-wave longitudinal survey from the World Trade Center Health Registry. The study sample included 38,495 adults who participated in both Wave 1 and Wave 2. We then measured residential movement using geocoded annual address records, and depression using the Personal Health Questionnaire Depression Scale. We accounted for any differences in baseline and time-varying covariates by residential movement at 2007-14 when estimating risk of depression, unmet health needs, and high social integration at Wave 4 (2015-16). From 2007-14, most enrollees (68%) did not move, and 6% moved at least once every 4 years. The remaining 26% moved less frequently (e.g., only moving in 2007-10). Frequent moving versus no moving was associated with risk of depression (RR = 1.2, 95% CI: 1.06, 1.37). Residential movement was neither associated with unmet health needs nor high social integration, except for those with frequent moving who were less likely to report high social integration (RR = 0.91, 95% CI: 0.85, 0.97). These findings show the importance of social networks in understanding increased risk of depression associated with housing instability. For individuals experiencing frequent residential moving, especially those who have been affected by traumatic events, support for social connection to new communities should be considered as an effective preventive measure against depression.

Social

Impact of individual-level income on health-related quality of life after a colorectal cancer diagnosis varies with neighborhood socioeconomic status context Jamaica R Robinson*

Jamaica Robinson Amanda I Phipps Wendy E Barrington Lianne Sheppard Philip Hurvitz Polly A Newcomb

Background. Evidence indicates individual-level income inequalities are primary drivers of persistent disparities in health-related quality of life (HRQoL) after a colorectal cancer (CRC) diagnosis. Contextual findings also suggest that living in a low socioeconomic status neighborhood (nSES) is related to lower HRQoL in cancer patients. However, research of HRQoL in CRC cases has yet to explore income effects within the context of nSES. Methods. We included data from 1339 population-based CRC cases diagnosed 2016-2018 in the Seattle-Puget Sound region. We focused on the effects of annual household income, reported by cases for a time period two years before CRC diagnosis, and an nSES index constructed from cases' geocoded residential addresses and American Community Survey block group-level data. We measured overall HRQoL after a recent CRC diagnosis using the Functional Assessment of Cancer Therapy - Colorectal (FACT-C) survey, in which differences of 5-8 points are considered clinically meaningful. We evaluated income effects, independently and jointly with nSES, on overall HRQoL after CRC using generalized linear models with robust standard errors to account for within-neighborhood dependence and to control for mild violation of linear regression assumptions. Results. After adjusting for case demographics, having a lower income before diagnosis (p-trend: <0.01) was independently related to reporting lower overall HRQoL after CRC. Effects in the lowest income category (<\$30K/year) were largest given living in a low nSES neighborhood (B:-13.74, 95% CI:-19.00, -8.47). Conclusion. Lower income levels are associated with poorer HRQoL in recently diagnosed CRC cases, especially among cases living in low nSES neighborhoods. Future research should evaluate these associations in other CRC populations, and assess whether effects are mediated by supportive care access, so as to improve knowledge of potential intervention targets.

Association between Neighborhood Poverty and Blood Lead Level Severity in Milwaukee County, Wisconsin Children, 2014-2016 Sarah Laurent* Helen Meier

Introduction: Childhood lead poisoning is a serious public health concern due to the negative health outcomes resulting from exposure during early developmental years. Milwaukee County has the highest rate of childhood lead poisoning in Wisconsin and contains areas of concentrated socioeconomic disadvantage. We examined the effect of neighborhood socioeconomic disadvantage on lead exposure severity in children in Milwaukee County between 2014 – 2016.

Methods: Data come from the Wisconsin Department of Health Services childhood lead surveillance program (N=61,029) and the U.S. Census Bureau. Ordinal logistic regression was used to evaluate the association between blood lead level severity (< 5 µg/dL = low, 5 – 14 µg/dL = elevated, 15 – 44 µg/dL = high, ≥ 45 µg/dL = severe) and percent of families that fall below the poverty line in each census tract (< 15% = low, 15-29% = moderate, ≥ 30% = high). All models were adjusted for sex, age and race/ethnicity and interaction terms were included to evaluate the effect of race/ethnicity in modifying the association between neighborhood poverty level and blood lead level.

Results: Stark differences in blood lead level severity by neighborhood poverty and race/ethnicity were observed. Greater than 60% of children with elevated, high or severe blood lead levels lived in census tracts with high poverty and African American children were disproportionately represented in more severe blood lead level categories. Children living in high poverty neighborhoods had greater odds of higher blood lead levels than those living in low poverty neighborhoods (OR = 3.60, 95%CI: 2.80, 4.64). The association of neighborhood poverty and childhood blood lead level severity varied by race/ethnicity.

Conclusion: Children are not equally exposed to lead in Milwaukee County. Minority and high poverty communities bear a higher burden of lead exposure. Lead exposure prevention efforts should be targeted to protect these vulnerable populations.

Social

The Role of Alcohol in Neighborhood Disadvantage and Cardiometabolic Factors in People Living with HIV Tekeda Ferguson* Tekeda Ferguson Aubrey S. Madkour David A. Welsh Patricia E. Molina Katherine P. Theall

Neighborhood factors may play a key role in the development of comorbidities, as they are important contexts that shape health and behavior. Unhealthy alcohol use is common among people living with HIV (PLWH) and is associated with worse outcomes and risk of morbidity. We hypothesize that unhealthy alcohol use mediates the association between concentrated neighborhood disadvantage (CDI) and cardiometabolic factors. We examined this in the New Orleans Alcohol use in HIV (NOAH) Study (n=365). Hypertension (HTN) was defined as a mean systolic ≥130-139 or diastolic blood pressure ≥80-89 mmHg. Metabolic syndrome (MS) was defined as having 3 of 5 conditions: HTN, high-density lipoproteins (≤40 (men)/50 (women)), triglycerides (≥ 150mg/dl), glucose (≥100 mg/dl), or waist circumference >88(women)/102(men). Alcohol use was assessed with the Alcohol Use Disorders Identification Test, Timeline Follow Back Calendar, and biomarker, phosphatidylethanol. Multilevel regression and mediation analyses by alcohol were performed adjusting for age, race, smoking, and viral load. Participants were 83.6% African American and 69% male with a mean age 48.2 ±10.4. MS was prevalent in 36%, HTN 66%, diabetes 14%, and 27% were obese. There was substantial clustering of cardiometabolic outcomes by neighborhood, with intra-class correlations (ICC) near or greater than 20% for BMI, diabetes, HTN, and MS. CDI explained a significant proportion of the variance in diabetes (ICC dropped, 18% to 8%) and the likelihood of having diabetes increased by 33% (OR = 1.33 (1.02, 1.74)). There was an indication of medication by alcohol use but not alcohol use disorder for HTN, metabolic syndrome, or diabetes. Our results suggest a significant role of social environmental factors on cardiometabolic comorbidities among PLWH, with marginal mediation by alcohol. There is a critical need for a deeper understanding of the roles that social determinants at the community level play in alcohol use and comorbidities.

Social

Ignoring the Cost of Color on Black Maternal Health: The Influence of Skin Color, Gendered Skin Tone Bias and Prepregnancy Body Mass Index. Jaime Slaughter-Acey* Jaime Slaughter-Acey Dawn P Misra

Research highlighting racial disparities in obesity in the US is ample. Yet, this work fails to recognize the complexity of race classification and thus, its intersection with other aspects of social identity (eg, gender, skin color). Using data from 1410 Black women, age 18-45 yrs, enrolled in the Lifecourse Influences on Fetal Environment Study, this study examined the association between women's skin tone, gendered colorism (skin tone bias) and prepregnancy BMI, kg/m2. Self-reported skin tone was categorized as Dark, Medium, Light, and Very Light brown. Gendered colorism was assessed by asking women to report how often the opposite sex finds them attractive due to their skin color (Very Often, Fairly Often, and Not Often). Results: For gendered colorism, the proportion of women who reported that men found them attractive due to their skin tone "Very Often" varied by skin tone, Dark-25.7%, Medium-22.9%, Light-30.9% and Very Light-46.1%. In ordinal logistic regression models adjusted for age, birth place, and parity, skin tone predicted gendered colorism; women with darker skin, relative to Very Light, were less likely to report men found them attractive due to their skin tone. Mean (SD) BMI also varied by women's skin tone (Dark: 30.4[7.8], Medium: 29.1[7.9], Light: 28.3[7.0], and Very Light: 27.7[6.9]); and gendered colorism category (Very Often: 27.7[6.9], Fairly: 29.3[7.8], Not Often: 30.2[7.7]). Linear regression controlling for age, parity, and birth place showed skin tone was associated with BMI. Compared to dark brown women, Medium (β=-1.29; 95%CI: -2.43, -0.15), Light (β=-1.90; 95%CI: -3.17, -0.64), and Very Light (β=-2.34; 95%CI: -3.81, -0.88) women had a lower BMI. Upon further control for gendered colorism, skin tone remained associated with BMI, though, the association was attenuated. Findings suggest that racialized experiences related to skin tone, our most visible physical attribute, intersect with gender to shape Black women's prepregnancy BMI.

Is eviction poisonous?: A survival analysis of eviction and lead poisoning in a national urban birth cohort Gabriel L. Schwartz* Gabriel Schwartz Kathryn M. Leifheit Lisa Berkman Mariana Arcaya Jarvis Chen

Background
Eviction is common among low-income families in the US and may impact children's health, particularly outcomes linked to housing. Yet research investigating connections between eviction and young people's health using causal inference methods is scant. We test whether eviction is prospectively associated with incident lead poisoning, a condition causing long-term impairment whose primary determinant is poor housing quality.

Methods & Findings
We analyze data from 2,708 children (contributing 6,636 observations) in the Fragile Families study, a national urban birth cohort that oversampled unmarried mothers. We apply weights to account for time-varying confounding and potential selection bias, fitting a cross-lagged, proportional hazards marginal structural model and treating eviction as cumulative over time. We estimate that an eviction multiplies children's prospective hazard of lead poisoning by 2.45 times (p=0.064; 95% CI=0.95, 6.32), such that evicting our whole sample in their first year of life would yield a 1 in 10 chance of being poisoned by age 3 compared to a 1 in 21 chance were no one evicted. This gap compounds as evictions accumulate. Because Fragile Families measures only a subset of evictions, misclassification likely makes these results conservative. We discuss potential effect modification by renting status and to whom these results generalize.

Conclusions
Eviction is a powerful longitudinal predictor of lead poisoning, potentially causally so. Confidence intervals are wide, though this may be driven by low statistical power and conservative statistical procedures. Our results provide strong motivation for further research on what mediates this relationship and for re-examining this question using more complete eviction measures and larger datasets. In the meantime, our large estimated effect, combined with the life-long consequences of lead poisoning for children, warrant urgent attention from medical providers and policymakers.

Estimated hazard of lead poisoning over time, by eviction history
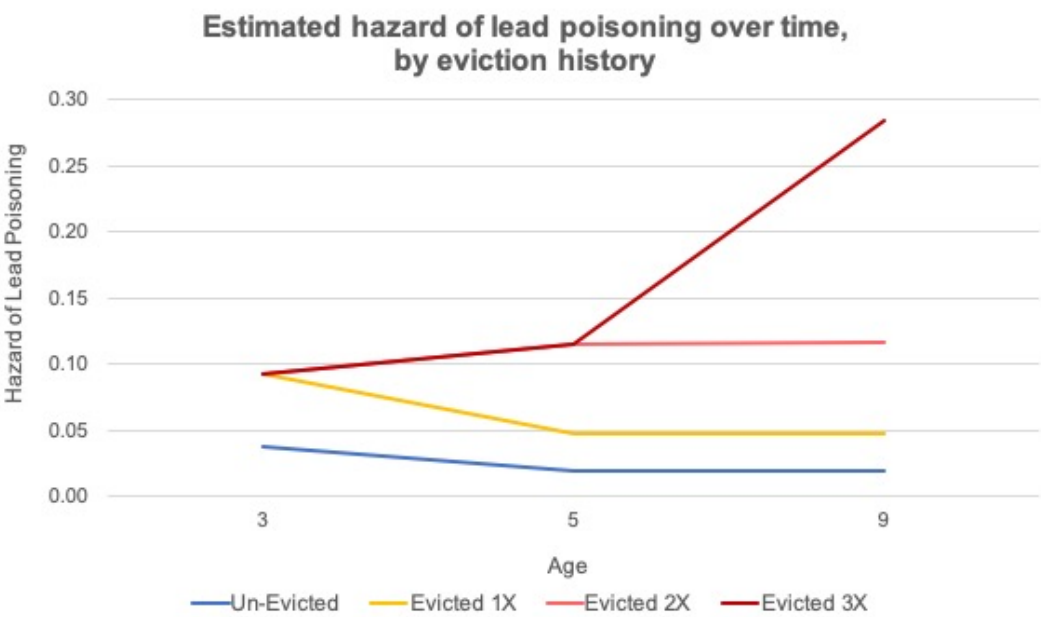
LATEBREAKER

Social

Disparities in HIV-related risk among trans women sex workers and effects of a targeted, anti-sex-trafficking policy Caitlin M. Turner* 3647] Turner Sean Arayasirikul Erin C. Wilson

Background: Sex work is a means of survival for many trans women (TW) and disproportionately exposes them to violence, institutionalization, and HIV risk. We assessed social and HIV-related disparities for trans women who do sex work (TWSW) compared to those who do not, and evaluated whether the US 2018 "Allow States and Victims to Fight Online Sex Trafficking Act" and "Stop Enabling Sex Traffickers Act" (FOSTA-SESTA) affected these disparities.

Methods: Generalized estimating equations (GEE) characterized longitudinal differences in social and HIV-related outcomes for TWSW compared to TW not engaged in sex work enrolled in the Trans*National cohort study (n=428) after adjusting for social transition and race/ethnicity. We compared the adjusted, pre-to-post law changes in outcomes for TWSW versus TW not engaged in sex work using difference-in-differences analyses.

Results: Over 18 months, TWSW compared to those not engaged in sex work had higher adjusted odds of experiencing transphobic hate crimes (aOR=2.88; 95%CI=1.65–5.01), engaging in condomless anal intercourse (aOR=3.32; 95%CI=1.87–5.44), or being recently incarcerated (aOR=3.17; 95%CI=1.53–6.56); TWSW also had a higher mean number of income sources (adjusted mean=1.20; 95%CI=1.02–1.42). One difference-in-differences analysis showed additive interaction: the adjusted mean number of income sources reported by TWSW compared to those not engaged in sex work decreased from pre- to post-FOSTA-SESTA (from 1.81 to 1.54 for TWSW and 1.48 to 1.45 for TW not engaged in sex work; p=0.050).

Conclusions: Numerous disparities exist for TWSW in San Francisco and FOSTA-SESTA may have reduced income sources for TWSW compared to those not engaged in sex work. Preliminary findings show that FOSTA-SESTA may not exacerbate other disparities; however, these analyses are likely underpowered and require more post-law data with a larger number of TWSW. This highlights the urgent need for long-term follow-up data of TW to precisely analyze policy effects, especially given the recent enactment of a number of other policies targeting TW.

Religious service attendance and mortality: do epidemiologic cohorts have the right covariates to avoid selection bias? Diane Lauderdale* Diane Lauderdale L. Phil Schumm Chuanhong Liao

Cohorts have repeatedly found that more frequent religious service attendance is strongly protective of mortality. The potential for selection bias is always acknowledged. The dominant methodological strategy has been to control for baseline sociodemographics and health conditions; more recent work has used marginal structural models for time-varying covariates. However, these approaches are fundamentally limited by covariates traditionally collected in cohorts. We use a nationally representative longitudinal study of older adults, the National Social Life, Health and Aging Project (NSHAP), which was largely designed by social scientists and includes some domains rarely measured in epidemiology. NSHAP collected three waves of data (2006, 2011, 2016), each with frequency of religious attendance (6 levels). Here we focus on a rich set of social network, psychological, and functional status variables to identify novel potential confounders. About 50% change religious frequency between waves. We model religious attendance with mixed-effects ordinal logit models including both the respondent-level mean of the potential confounder (capturing between-person association) and the difference from his or her overall mean at each timepoint (capturing within-person association), adjusting for demographics and including a respondent-level random intercept. Models account for the complex sample design. The largest and most highly significant between-person associations include network variables (relatives nearby, number of friends), functional variables (hearing; difficulty walking, dressing, bathing, toileting, eating), and psychological variables (4 of the big 5 personality traits: openness, conscientiousness, extraversion, neuroticism; feeling isolated). The strongest within-person associations were functional measures. As we complete National Death Index linkage, we can fully assess religious attendance and mortality in marginal structural models.

Traumatic childhood experiences are associated with a higher prevalence of multiple metabolic abnormalities in adulthood among a racially/ethnically diverse cohort of US women Symielle Gaston* Symielle Gaston Christine Parks Dale Sandler Chandra Jackson

Traumatic childhood experiences (TCEs) may negatively affect stress-response pathways and behaviors contributing to metabolic syndrome (MetS) in adulthood. MetS affects about one-third of U.S. women, but few studies have investigated TCEs and MetS in diverse samples of women. To investigate the association between TCEs and MetS, we used cross-sectional data collected from 2003 to 2012 among 35,389 U.S. White, Black, and Hispanic women in the Sister Study. Self-reported TCEs prior to age 18 years were categorized as major accident, natural disaster, household dysfunction, major illness, and sexual, physical, or psychological/emotional trauma. MetS was defined as having ≥3 metabolic abnormalities (measured abdominal obesity; diagnosis of/medications for pre-hypertension/hypertension, dyslipidemia, borderline or type 2 diabetes). Adjusting for age, race/ethnicity, and childhood socioeconomic position and region of residence, Poisson regression with robust variance was used to estimate prevalence ratios (PRs) and 95% CIs for MetS in those with versus without TCEs. We also tested for modification by race/ethnicity. Mean age was 54.6 years and 89% were White, 7% Black, and 4% Hispanic. MetS prevalence was highest among Black women (23% vs. 11% White and 15% Hispanic). History of TCEs was highest among Black women (55% vs. 50% White and 51% Hispanic) and was associated with 16% higher prevalence of MetS overall (PR=1.16 [95% CI: 1.10-1.23]). All traumas were positively associated with MetS (PRrange: 1.16 [household dysfunction] - 1.36 [major accident]). Associations were generally similar by race/ethnicity. However, physical trauma in childhood was not associated with MetS among Black and Hispanic women but was associated with METs among White women (PR=1.43 [95% CI:1.25-1.64]). TCEs were associated with a higher prevalence of MetS, suggesting that most early life traumas may contribute to MetS in adulthood among a racially/ethnically diverse population of women.

Substance Use

E-cigarette use among current and former adult cigarette smokers in the US: National Health Interview Survey (NHIS), 2018 Rime Jebai* Rime Jebai Mohammad Ebrahimi Kalan Semiu Olatunde Gbadamosi Boubakari Ibrahimou

Introduction:
Recently, electronic cigarettes (e-cigarettes) have seen a dramatic surge in use among young adults leading to increased susceptibility to nicotine dependence. Few studies have explored the association between e-cigarette use and cigarette smoking in the US. The aim of this study was to examine e-cigarette use among current and former cigarette smokers using nationally representative data of US adults.
Methods:
Data of adults aged 18 years and older participating in the 2018 NHIS were analyzed. E-cigarette status was measured as current and daily use. Cigarette smoking was categorized into current, former (quit ≤1, 2-3, 4-5, and >6 years before data collection), and never smokers. Logistic regression models were performed to identify the association between cigarette smoking status and e-cigarette use.
Results:
Of the 25,417 adult respondents, current and daily e-cigarette users were 1.86% and 1.38%, respectively. Compared to current cigarette smokers, adults who quit cigarette smoking ≤1 year (aOR=4.15, 95% CI: 2.65-6.50), 2-3 years (3.78, 2.37-6.04), and 4-5 years (4.05, 2.49-6.59) were more likely to be daily e-cigarette users after adjusting for age, sex, race and other tobacco use. Former smokers who quit cigarette ≥6 years (0.29, 0.16-0.52 vs. current smokers) and never cigarette smokers (0.08, 0.05-0.13 vs. current smokers) had lower odds of daily e-cigarette use. Similarly, former smokers who quit cigarettes ≥6 years (0.14, 0.08-0.26 vs. current smokers) and never cigarette smokers (0.13, 0.09-0.18 vs. current smokers) had lower odds of current e-cigarette use.
Conclusion:
Findings suggest that young adults who were current and former cigarette smokers who quit ≤5 years were more likely to be daily e-cigarette users. However, never and long-term former cigarette smokers were less likely to be current and daily e-cigarette users. Future longitudinal studies are needed to better understand the reasons for e-cigarette use among this population.

Prevalence of heavy episodic drinking and substance use treatment among US college students: results from the national Healthy Minds Study Lynsie R. Ranker* Lynsie Ranker Sarah K. Lipson

Alcohol misuse is a widely recognized problem on college campuses. Prior research shows over 40% of undergraduates engage in heavy episodic drinking (HED, 4+/5+ drinks in a single setting for females/males) at least once in the past 2 weeks. While research shows lower prevalence of alcohol consumption among students of color and those from low socioeconomic backgrounds, little is known about HED and treatment access in these growing groups. Using the 3 most recent waves of panel survey data from the Healthy Minds Study (2015-2018), we explored prevalence of alcohol consumption in the past 2 weeks, frequent HED (3+ times) in the past 2 weeks, and substance use disorder (SUD) diagnosis among students aged 18-29 from 60 US campuses (N=119,068). Stratified analyses and multivariable regression with response propensity weights were used to examine variations by race/ethnicity and first-generation status (neither parent completed college). In the overall sample (mean age 21.2), 61% reported alcohol use and 23% reported 3+ HED episodes in the past 2 weeks. Roughly 1% of the sample reported SUD diagnosis compared to 1.6% of those reporting recent alcohol consumption. While alcohol use was most common among white, non-Hispanic compared to other racial/ethnic groups, prevalence of frequent HED was similar across racial/ethnic groups (19.8-24.2%) with the exception of Asian students (15.9%). There were reduced odds of SUD diagnosis among Asian, Black, Latinx, and Middle Eastern students compared to white, non-Hispanics. While alcohol consumption was less common among first-generation (54.9%) than non-first-generation students (64.5%), frequent HED was similar, and odds of SUD diagnosis was lower. Results suggest similar prevalence of frequent HED across race/ethnicity and first-generation status. Yet, SUD diagnosis lags behind for minority groups. Results underscore a need for further research into associations between HED and SUD diagnosis during the pivotal college years.

Table: Racial/ethnic identity and first-generation status and alcohol use, binge drinking, and substance use disorder diagnosis among US college students (2015-2018) ages 18-29

	n (% of sample)	Any Alcohol Use in the past 2 weeks n = 119,068			Harmful Binge drinking in the past 2 weeks[a] n = 76,205			Substance use disorder diagnosis (ever)[d] n = 76,205		
		%	OR (95% CI)	aOR[c] (95% CI)	%	OR (95% CI)	aOR[c] (95% CI)	%	OR (95% CI)	aOR*** (95% CI)
Racial and ethnic identity										
American, Alaskan Native, or Pacific Islander[b]	444 (0.4)	53.6	0.59 (0.45, 0.77)	0.65 (0.49, 0.86)	22.2	0.89 (0.56, 1.42)	0.99 (0.63, 1.57)	1.5	1.32 (0.46, 3.77)	1.46 (0.51, 4.16)
Asian/Asian American[b]	15471 (11.6)	45.8	0.42 (0.40, 0.45)	0.36 (0.34, 0.38)	15.9	0.59 (0.52, 0.67)	0.62 (0.54, 0.70)	0.4	0.40 (0.26, 0.61)	0.38 (0.25, 0.59)
Black/African American[b]	4963 (5.7)	46.9	0.45 (0.41, 0.49)	0.58 (0.54, 0.64)	21.6	0.86 (0.74, 1.01)	0.99 (0.84, 1.16)	0.9	0.79 (0.44, 1.40)	0.94 (0.52, 1.71)
Hispanic/Latinx	11749 (10.3)	57.8	0.69 (0.65, 0.73)	0.83 (0.78, 0.88)	23.1	0.94 (0.86, 1.03)	1.02 (0.93, 1.11)	0.8	0.69 (0.49, 0.97)	0.67 (0.47, 0.96)
Middle Eastern, Arab, or Arab American[b]	1360 (1.1)	38.5	0.31 (0.27, 0.36)	0.32 (0.27, 0.37)	20.2	0.79 (0.60, 1.05)	0.86 (0.65, 1.15)	0.7	0.57 (0.19, 1.67)	0.57 (0.19, 1.69)
Multi-Racial[b]	6836 (5.8)	59.7	0.74 (0.69, 0.80)	0.77 (0.72, 0.84)	19.8	0.77 (0.69, 0.86)	0.79 (0.71, 0.89)	1.4	1.19 (0.84, 1.70)	1.16 (0.81, 1.66)
Other[b]	1381 (1.3)	56.2	0.66 (0.57, 0.76)	0.67 (0.57, 0.79)	22.6	0.92 (0.70, 1.20)	1.00 (0.77, 1.32)	2.0	1.72 (0.95, 3.12)	1.44 (0.78, 2.66)
White[b]	76864 (63.8)	66.7	Ref	Ref	24.2	Ref	Ref	1.1	Ref	Ref
First generation college student										
Yes	33091 (31.5)	54.9	0.67 (0.65, 0.70)	0.72 (0.69, 0.75)	21.0	0.85 (0.80, 0.91)	0.93 (0.87, 1.00)	1.0	0.92 (0.71, 1.19)	0.84 (0.64, 1.11)
No	85977 (68.5)	64.5	Ref	Ref	23.7	Ref	Ref	1.1	Ref	Ref

Note: all sample sizes are unweighted, all percents and ORs are weighted results

[a] consuming 4/5 drinks in one sitting 3 or more times in a row in the past 2 weeks (among those who have consumed alcohol in the past 2 weeks)

[b] Non-hispanic

[c] aOR: adjusted for age, sex at birth, gender identity, sexual orientation, importance of religion, residence location, and race/ethnicity or first generation status (dependent on exposure)

[d] among those who consumed alcohol in the past 2 weeks

Substance Use

Using Latent Class Analysis to Understand Comorbidity of Substance Use and Internalizing and Externalizing Symptoms in Adults
Courtney Blondino* Courtney Blondino Robert Perera Elizabeth Prom-Wormley

The economic burden and mortality rates of substance use disorders are increasing and may be due to unaddressed comorbidity between substance use and internalizing and externalizing mental disorder symptoms. Details regarding how use of substances and mental disorder symptoms group together will improve the understanding of the underlying etiology associated with comorbidity.

Data from adult participants (18 years and older) in the first wave (2013-2014) of the Population Assessment of Tobacco and Health Study (N= 32,320) were used to study the comorbidity of current substance use behaviors (i.e., cigarettes, e-cigarettes, alcohol, marijuana, and prescription drugs not prescribed) and internalizing and externalizing symptoms using latent class analysis. Model parsimony and fit criteria were used to determine the most optimal class solution. Three-step method was used to determine significant associations between demographic factors and latent class membership. Analyses were performed in Mplus Version 8.4.

A four-class solution was most optimal: low symptom (N= 20974, 64.9%), internalizing (N= 5229, 16.2%), externalizing (N= 3304, 10.2%), and highly comorbid (N= 2810, 8.7%). The highly comorbid class had higher conditional probabilities for all items compared to the other classes, except for alcohol use, which was highest for the externalizing class. The internalizing class had higher conditional probabilities for cigarette, e-cigarette, marijuana and prescription drugs not prescribed compared to the externalizing class. Participants who were white, female, younger, and had lower levels of socioeconomic status had greater odds for membership in the internalizing and the highly comorbid classes relative to low symptom class.

Findings detail the degree to which specific substance use and mental disorder symptoms function together. Results support population-level prevention and intervention of substance users who experience varying levels of mental disorder symptoms.
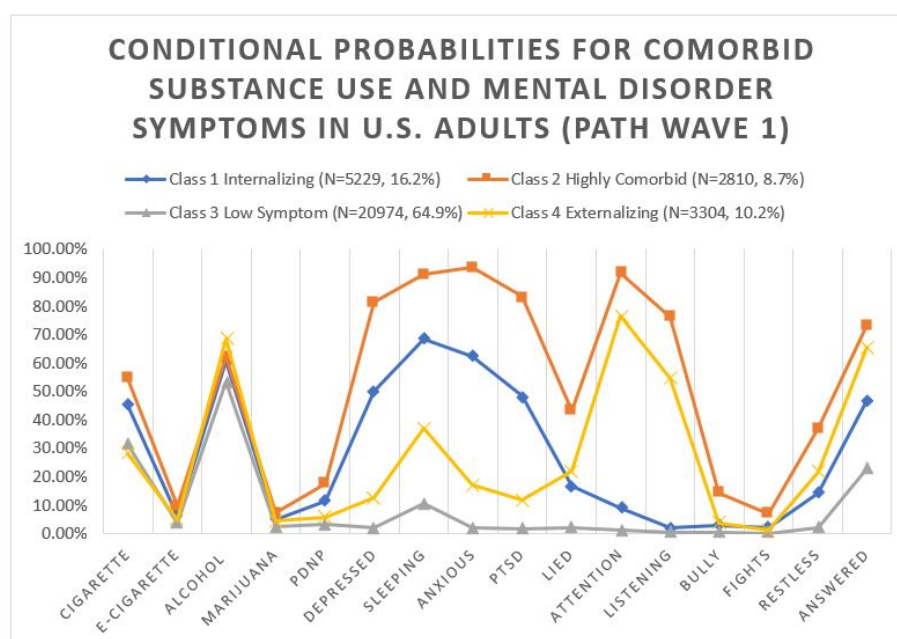
Substance Use

Self-Report of Polysubstance Use and Cessation Among Pregnant Women Marina Jenkins*

Marina Jenkins Erin Nacev Deborah Ehrenthal

Substance use during pregnancy may be a key risk factor for adverse perinatal outcomes. Polysubstance use can be a source of confounding in substance literature that does not include all common substances. The objectives of this analysis were to describe prenatal polysubstance use and to analyze cessation patterns.

Data from the Wisconsin Pregnancy Risk Assessment Monitoring System (PRAMS) for 2016-2017 were analyzed and weighted to reflect the population. PRAMS includes women's self-reported substance use for: tobacco, opioids, cannabis, cocaine, heroin, amphetamines, tranquilizers, and hallucinogens. Most substance use was reported as occurring during pregnancy and in the month before pregnancy; smoking in the last three months of pregnancy and in the three months before pregnancy. Women who report substance use before but not during pregnancy were considered as having successfully quit (cessation). Descriptive statistics were used to describe the number of substances used and percent who quit each substance entering pregnancy. T-tests were used to assess whether mean number of substances reported in pregnancy was higher among those who did not quit each substance.

Overall, 2,384 individuals had complete substance use data; 26.7% reported use of any substance before pregnancy and 19.0% during pregnancy. Of those who reported any substance during pregnancy, the mean number of substances reported was 1.3 (SE=.04), the range was 1-7, and 20.7% reported more than one. The percent who reported cessation ranged from 24.8% for tranquilizers to 91.5% for hallucinogens. The mean number of substances used during pregnancy was higher among women who did not quit for all substances (p.05).

Maternal polysubstance use is rare, but may hinder cessation efforts. Interventions to prevent prenatal substance use should address polysubstance use. Maternal substance use research should assess multiple substances to avoid confounding.

Adverse outcomes of hepatitis C virus infection among people who inject drugs in the direct-acting antiviral era Mirsada Serdarevic* Mirsada Serdarevic Brooke R. MacDonald1 Matthew Cvitanovich Tzu-Chun Chu Rachel Stewart Esther Fasanmi Rohit P. Ojha

Background: Several states have Medicaid policies that preclude people who inject drugs (PWID) from treatment with direct-acting antivirals for hepatitis C virus (HCV) despite no contraindications for ongoing injection drug use (IDU). Lack of treatment may increase the risk of adverse outcomes related to HCV infection among PWID, but these risks have not been systematically assessed. Therefore, we aimed to estimate the risk of adverse hepatic and extrahepatic outcomes of HCV infection among PWID in the direct-acting antiviral era.

Methods: We used data from the Hepatitis C Virus Outcomes Registry (HEPCOR), which is a longitudinal registry that includes people diagnosed with HCV infection in a safety-net health system in Texas. Eligible patients were aged >18 years, had a positive HCV-RNA test between January 1, 2014 and December 31, 2016 with follow-up through June 30, 2019, IDU, no history of HCV treatment, and no history of the outcomes of interest (cirrhosis, hepatocellular carcinoma [HCC], and cardiovascular disease [CVD]) at the time of HCV diagnosis. We used a competing-risk framework with death as the competing risk to compute 2-year cumulative incidence for each of the three outcomes.

Results: Our study population comprised 1,537 PWID with HCV infection, of whom 63% were aged >50 years, 65% were male, and 57% were non-Hispanic White. Cumulative incidence of the outcomes of interest over two years is illustrated in the Figure. Specifically, the 2-year cumulative incidence of cirrhosis, HCC, and CVD were 13.1% (95% confidence limits [CL]: 11.1%, 15.5%), 6.1% (95% CL: 4.8%, 7.7%) and 21.4% (95% CL: 18.3%, 24.9%).

Conclusions: We observed a high risk of adverse hepatic and extrahepatic outcomes for PWID with HCV infection within a short follow-up period, which could be attributable to delayed HCV diagnosis. Our findings emphasize the need for improving HCV screening and removing restrictions to direct-acting antivirals for this population.

Figure. Cumulative incidence of cardiovascular disease (CVD), cirrhosis, and hepatocellular carcinoma (HCC) following hepatitis C virus infection among people who inject drugs.

Substance Use
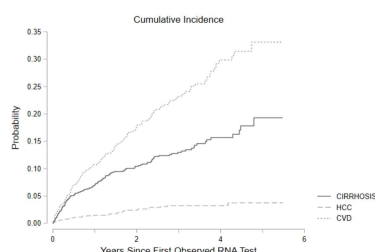
Epidemiology of Prenatal Opioid Use and Associated Maternal Characteristics in Ontario, Canada Andi Camden* Andi Camden Teresa To Joel G. Ray Tara Gomes Li Bai Kinwah Fung Astrid Guttmann

Confounding by indication is a critical threat to validity in research designed to understand health effects of prenatal opioid exposure; however, there is a lack of knowledge of the epidemiology of maternal opioid use & influence of maternal characteristics associated with type of opioid therapy. 1) To estimate the rate of any opioid use & type of opioid use during pregnancy; 2) To describe concurrent maternal factors by type of opioid therapy used in pregnancy. Population-based cohort study of all hospital live & stillbirths from 2014-2017 in Ontario, Canada.

Multiple linked administrative databases were used to identify maternal opioid use (prescription & health care) & demographic, social, pharmacologic & medical characteristics. Estimated rate of maternal opioid use & examined maternal characteristics by opioid therapy in pregnancy.

The rate of opioid use in pregnancy was 56/1000 births. Decreasing analgesic use influenced trend in overall prescription opioid rate; however, other indicators of opioid use (neonatal abstinence syndrome, opioid-related health care) remained stable. Maternal characteristics varied by opioid type & duration. Dose-response trends in vulnerability among women with 90+ days of analgesic use in pregnancy contrasted with 30-89 days & intermittent use, with respective rates of 48%, 39%, 23% for social assistance, 21%, 15%, 10% for 3+ previous live births & 74%, 71%, 53% for high medical comorbidities. Similar social vulnerabilities between women with chronic analgesic use & buprenorphine - respective rates of 48% vs. 47% for social assistance, 21% vs. 28% for 3+ previous live births & 4% vs. 6% for victim of violence.

We provide the first population-based estimates of opioid use in pregnancy in Canada across multiple opioid therapies in one study. Findings suggest heterogeneity within & between opioid therapy, and identify high-risk groups & confounders, which can inform studies on the impact of multiple maternal risk factors & opioid use on child health.

Figure. Rate of Prescription Opioid Use per 1000 Hospital Births Overall and by Type, Ontario, Canada, 2014 to 2017
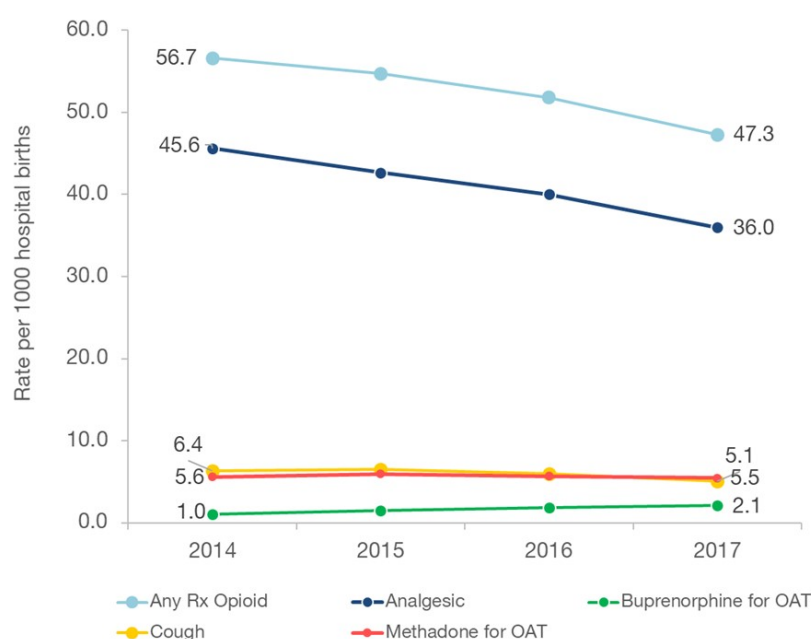
Data Source: Maternal prescription opioid records from the Narcotic Monitoring System.

Identifying Prenatal Opioid Exposure in Health Administrative Data for Public Health Surveillance and Epidemiologic Research Andi Camden* Andi Camden Teresa To Joel G. Ray Tara Gomes Li Bai Kinwah Fung Astrid Guttmann

Accurate estimation of prenatal opioid exposure is needed for surveillance & epidemiologic research but can be challenging with health administrative data. Reasons include varying definitions & methods to identify prenatal opioid exposure (POE) & neonatal abstinence syndrome (NAS).
1) To evaluate the impact of using different definitions of maternal opioid use & NAS in the estimation of POE; 2) To investigate whether maternal phenotypes vary by the type of definition used for POE.
Population-based cross-sectional study of all hospital births from 2014-2017 in Ontario, Canada. Multiple linked population-based health administrative databases were used to identify opioid-related pre- & perinatal ED visits & hospitalizations, as well as community-based opioid prescriptions. We examined how pre-conception & in-pregnancy maternal phenotypes varied by using different approaches to ascertain POE.
There were 9591 live/stillbirths with POE. Ascertainment of POE was highest using maternal prescription drug data (78%) & infant hospital records with NAS diagnoses (46%). Maternal phenotypes varied by data source used for POE ascertainment. Opioid-related health care during pregnancy identified a high-risk phenotype, in contrast to those ascertained through prescription data, with respective rates of 63% vs. 54% for using social assistance, 30% vs. 8% for polydrug use, 22% vs. 6% for alcohol use, 26% vs. 19% for 3+ live births, 13% vs. 5% for victim of violence, 12% vs. 6% for involvement in criminal justice system & 64% vs. 17% for a history of mental health & addictions hospital care.
Conclusion: Ascertainment of POE differs by health administrative data source & ability to link records. Prescription drug data identified the highest number of opioid-exposed births and, with linked health care records, is useful to identify illicit opioid use and additional risk factors. Clinically meaningful differences in maternal phenotypes of opioid users by method used to ascertain POE.

Figure. Prenatal Opioid Exposure by Data Source. Included are all Hospital Births in Ontario, Canada, 2014 to 2017.

Substance Use
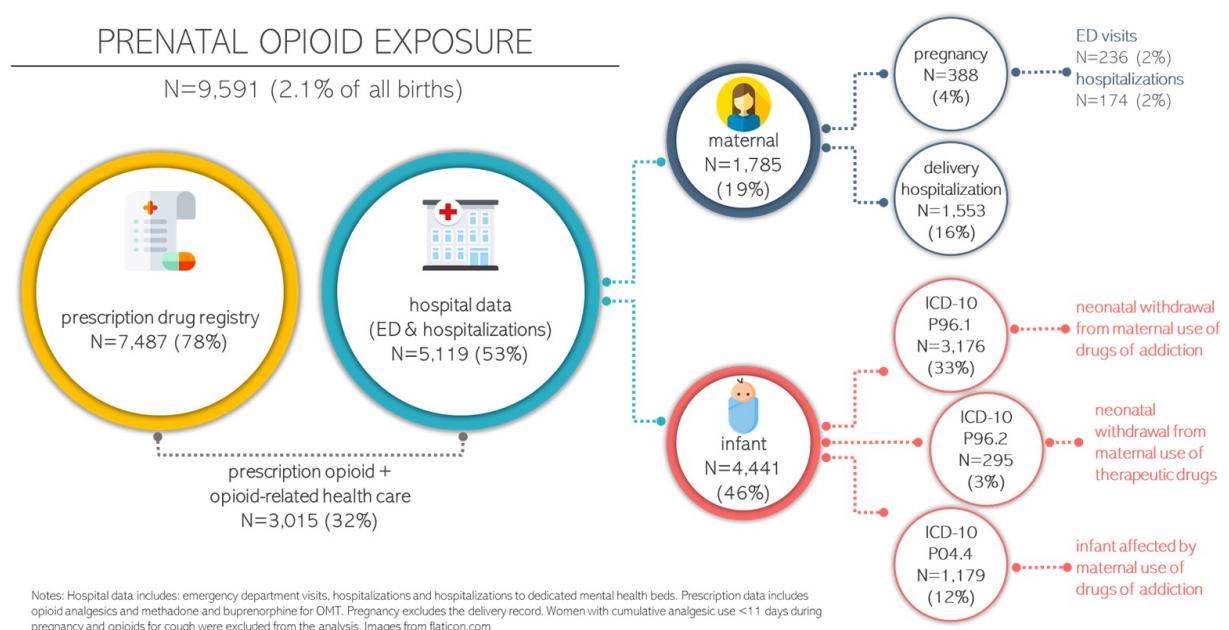
An Examination of Relationships Between Recreational Cannabis Legalization and Alcohol Purchasing Collin Calvert* Collin Calvert Darin Erickson

Whether recreational cannabis legalization impacts alcohol consumption is a key question as cannabis policy evolves, given the adverse health effects alcohol. Relatively little research has examined this question. This study examined the association between recreational cannabis legalization and the alcohol purchasing. We used data from the Nielsen Consumer Panel to calculate monthly alcohol by volume (ABV) purchased for different types of beverages (beer, wine, spirits, and all alcohol products) at the state level. To account for differences in state population sizes, we divided each dependent variable by the respective state's population to calculate per capita measures of ABV purchased in liters per 1,000 people. Changes in ABV purchase rate for each type of alcoholic beverage in states that have legalized recreational cannabis (Colorado, Washington, and Oregon) were compared to states that had not legalized recreational cannabis. We included data on purchases five years prior to legalization and all years following legalization. Change in per capita ABV was estimated using difference-in-differences (DiD) models. To test the robustness of our results, we also fit DiD models comparing each state that has legalized recreational cannabis to all of the states that have not legalized recreational cannabis. We found largely significant decreases in ABV purchased. Washington showed significant increases in ABV purchased of beer and liquor. When comparing to all states that have not legalized recreational cannabis, significance for most beverages was lost but directionality remained largely consistent. Overall findings suggest a minor decrease in per capita ABV purchased associated with recreational cannabis legalization. Privatization of alcohol outlets in Washington may have contributed to increases in ABV purchased. Future studies should examine additional states as more time passes and more post-legalization data becomes available.

Substance Use

Prescription Opioid Laws and Opioid-Related Harm: Identifying salient opioid policy features with machine learning Silvia S. Martins* Silvia Martins Emilie Bruzelius Jeanette A. Stingone Christine M. Mauro Stephen Crystal Corey Davis Kara E. Rudolph Katherine M. Keyes Magdalena Cerda

Aims: To identify prescription opioid-related laws that distinguish US counties with high vs. low opioid prescribing rates using machine learning approaches from 2006 to 2017.
Methods: The primary outcome was high versus low opioid prescribing counties (outpatient prescribing records maintained by IQVIA Xponent obtained from the CDC), using a threshold of ☐100 prescriptions per 100 persons annually as the cutoff. In the entire period, about 30% of counties were identified as high opioid prescribing counties. Prescription opioid law exposure variables included: Prescription Drug Monitoring Programs (PDMPs), pain management clinic laws (PMCs), and initial prescribing limitations for prescription opioids. To identify combinations of prescription opioid policies that were most predictive of high opioid prescribing counties, we applied a multi-stage machine learning approach stratified by time periods 2006-2009 (the "prescription opioids period"), 2010-2012 (the "heroin period"), 2013-2017 (the fentanyl period"). Analyses were conducted in R.
Results: From 2006 to 2009, the PDMP feature that allows non-physician delegates to access prescribing data was the policy that most consistently distinguished high vs. low opioid prescribing counties. From 2010 to 2012, the following PMC laws: mandatory registration fee, cash payment and record keeping requirements, were the policies that most consistently distinguished high vs. opioid prescribing counties. From 2013 to 2017, the policies that most consistently distinguished high vs. low opioid prescribing counties included PMC laws (mandatory registration fees, providers allowed to prescribe, cash payments).
Conclusion: PMC laws seem to be the most important prescription opioid policy laws related to the identification of high-opioid prescribing when using a machine learning approach. Further understanding on how opioid laws can best interact with efforts to expand treatment and reduce harms is needed.
Funding: R01DA048572 (Cerda & Martins).

Opioid use disorder trends from 2002 to 2017 by cigarette smoking status in the United States Maria Parker* Maria Parker Andrea Weinberger

Background: There have been significant increases in opioid use and opioid-related overdose deaths in the United States (US). While cigarette smoking remains disproportionately high among individuals with opioid use disorder (OUD), it is unknown whether trends in OUD differ by cigarette smoking status. This study examined: (1) differences in OUD by smoking status, and (2) trends in the prevalence of OUD by cigarette smoking status over time.

Methods: Data were harnessed from US National Surveys on Drug Use and Health, annual cross-sectional, nationally representative samples of individuals aged 12 and older. Past-year OUD prevalences were estimated each year from 2002 to 2017 among current daily, current non-daily, former, and never cigarette smokers (combined analytic sample n = 891,548). Linear time trends of OUD were assessed using logistic regression models.

Results: In 2017, OUD was significantly more common among current daily smokers (2.6%) and current non-daily smokers (1.5%) compared to former (0.5%) or never smokers (0.2%). Overall, the prevalence of OUD increased among US individuals between 2002 and 2017, although trends differed by smoking status. Adjusting for background characteristics, the prevalence of OUD increased significantly among daily smokers (AOR = 1.05, 95% CI: 1.04, 1.07), non-daily smokers (AOR = 1.03, 95% CI: 1.01, 1.05), and former smokers (AOR = 1.05; 95% CI: 1.02, 1.09), but decreased among never smokers (AOR = 0.98; 95% CI: 0.97, 0.99).

Conclusions: In the US, the prevalence of OUD was higher among current cigarette smokers relative to former and never smokers. OUD increased among current and former smokers, in contrast to a decrease in OUD among non-smokers from 2002 to 2017. Although OUD increased among those with both current and former smoking, OUD remains significantly lower among former versus current smokers. Cigarette smoking may be important to address alongside efforts to reduce OUD and harmful consequences of OUD.

Substance Use

Association of state cannabis liberalization with self-directed and interpersonal violence injuries Ellicott Matthay* Ellicott Matthay Holly Elser Mathew V. Kiang

Background: Cannabis liberalization policies are rapidly being adopted across the US, yet evidence on population health impacts of these policies remains sparse. Cannabis policies may promote or deter violence by changing patterns of substance use. For example, cannabis can substitute or complement alcohol, which strongly promotes violent behavior.
Methods: We applied a differences-in-differences approach to study the association of adoption of state medical and recreational cannabis policies with changes in county-quarter-level rates of medical visits for self-directed or interpersonal violence-related injuries. We measure outcomes using Optum, a demographically representative database of medical claims from a large, private healthcare network of over 60 million beneficiaries in all 50 states and Washington DC, 2003-2017. Because there is important heterogeneity in the content of cannabis policies, we employed a latent class analysis to categorize exposure using NIH policy data on up to 364 possible cannabis provisions in each state-month.
Results: In preliminary analyses, we identified 288,000 self-directed and 251,000 interpersonal violent injuries during the study period. We identified four classes of cannabis policies varying in stringency and maturity across states and time. The association of each policy class with violent injury rates will be tested using negative binomial models that account for spatiotemporal autocorrelation, accommodate lagged effects of policies on health, and control for state fixed effects, year fixed effects, and a range of state-specific time-varying potential confounders.
Discussion: Characterizing cannabis policies beyond "medical" and "recreational" is feasible, and may be important for accurate measurement of health impacts. Measuring impacts on self-directed and interpersonal violence may additionally provide a key indicator of the population health consequences and inform future implementation and adoption of cannabis policies.

Substance Use

Medication-assisted treatment and postpartum health care utilization among pregnant women with opioid use disorder in Maine, 2010-2017 Katherine A. Ahrens* Katherine Ahrens Marjorie C. Meyer Carole A. McBride

The objective of this research was to estimate the prevalence of medication-assisted treatment, and its association with 12-month postpartum hospitalization and emergency department (ED) visits among pregnant women with opioid use disorder (OUD) in Maine. We used data from the Maine All Payer Claims Database, a repository of healthcare claims data for the majority of residents with health insurance in Maine. We restricted the analysis to women covered by Medicaid because substance use disorder-related claims are currently not available from commercial payers. OUD was identified among pregnant women if they had at least one OUD diagnosis code (ICD-9/10) or medication-assisted treatment code during the 5 months leading up to delivery month. Consistent treatment (evidence of buprenorphine or methadone treatment for each of the 5 months prior to delivery) was compared with inconsistent and no treatment for risk of hospitalizations and ED visits in the first 12 months postpartum using log binomial regression. Risk ratios (RR) were adjusted for age at delivery, rurality, delivery type (vaginal vs. C-section), hospital level of care, and any prescription claim during pregnancy for benzodiazepines and antidepressants, separately. During 2010-2017, 35,916 deliveries in Maine were paid for, in part, by Medicaid. OUD among pregnant women increased from 7.1% (SE=0.4%) in 2010 to 12.1% (SE=0.5%) in 2017; consistent treatment among women with OUD increased from 45.3% (SE=2.8%) in 2010 to 58.3% (SE=2.3%) in 2017. Among women with OUD and continuous Medicaid coverage in the first year postpartum (n=3058), consistent treatment was associated with lower risk of hospitalization compared with inconsistent treatment (RR=0.72, 0.54-0.97) and lower risk of ED visits compared with no treatment (RR=0.87, 0.80-0.94). Consistent medication-assisted treatment during pregnancy results in decreased 12-month postpartum emergency health care utilization among women with OUD covered by Medicaid.

Table: Medication-assisted treatment for pregnant women with opioid use disorder in Maine and 12-month postpartum hospitalization and emergency department visits, 2010-2017

Medication-assisted treatment during pregnancy*	N (%)	At least one hospitalization (%)**	Adjusted risk ratio (95% CI)***	Adjusted risk ratio (95% CI)***	At least one ED visit (%)**	Adjusted risk ratio (95% CI)***	Adjusted risk ratio (95% CI)***
Total	3694 (100)	8.1			50.6		
Consistent treatment	2082 (56)	6.9	0.72 (0.54, 0.97)	0.75 (0.56, 1.01)	48.2	0.96 (0.88, 1.05)	0.87(0.80, 0.94)
Inconsistent treatment	867 (23)	10.0	Ref	1.04 (0.74, 1.46)	50.5	Ref	0.90 (0.81, 0.99)
No treatment	745 (20)	9.6	0.96 (0.69, 1.35)	Ref	57.1	1.11(1.00, 1.23)	Ref

*Buprenorphine and/or methadone treatment for each of the 5 months leading up to delivery month

**Hospitalizations and emergency department visit follow-up restricted to 3058 women with continuous insurance coverage

***Adjusted for: age at delivery, rurality, delivery type (vaginal vs. C-section), hospital level of care, and any prescription claim during pregnancy for benzodiazepines and antidepressants, separately

Trends in cannabis use and attitudes towards legalization and use among Australians from 2001-2016: An age-period-cohort analysis Navdep Kaur* Navdep Kaur Katherine M. Keyes Ava Hamilton Wendy Swift Cath Chapman Michael Livingston Tim Slade

Objective
The changing landscape of cannabis legalization and availability in Australia necessitate the monitoring of changes in use and attitudes. This study aims to estimate period and cohort effects of past-year cannabis use, attitudes towards cannabis criminalization, and attitudes towards cannabis legalization.

Methods
Data were drawn from the 2001-2016 Australian National Drug Strategy Household Survey (N=145,168 respondents 18-79 years old, size varied for each model based on availability of outcome and covariate data (~107,000-127,000 per model). Hierarchical age-period-cohort models estimated period and cohort effects of past-year cannabis use (stratified by sex and education), attitudes towards cannabis criminalization, and attitudes towards cannabis legalization.

Results
Approximately ten percent of participants reported past-year cannabis use in 2016. Past-year cannabis use decreased in young adults ages 18-35 (24.3 % to 17.7%) and slightly increased in middle adults ages 36-55 (8.36% to 10.5%) and older adults ages 56-79 (0.6% to 3.01%). We found positive period effects for past-year cannabis use and negative cohort effects for younger cohorts. Older cohorts had 1.1 to 1.5 times log odds of past-year cannabis use compared to the overall mean, whereas younger cohorts had -2.0 to -2.9 times log odds compared to the overall mean. Results were consistent by sex and education. We also found negative period effects over time for attitudes towards criminalizing use and a positive cohort effect for younger cohorts. Lastly, we observed positive period effects for supporting legalization beginning in 2007 and negative cohort effects for younger cohorts.

Conclusion
Overall cannabis use prevalence is increasing in Australia, yet prevalence is decreasing among younger cohorts. Variance in legalization support prevalence is also increasing, signaling discordance between use and attitudes among young adults with potentially predicting increases in use over time.

Figure 1. Hierarchical age-period-cohort estimates of period and cohort effects of past-year cannabis use among 18-79 year olds in six waves of the Australian National Drug Strategy Household Survey from 2001-2016
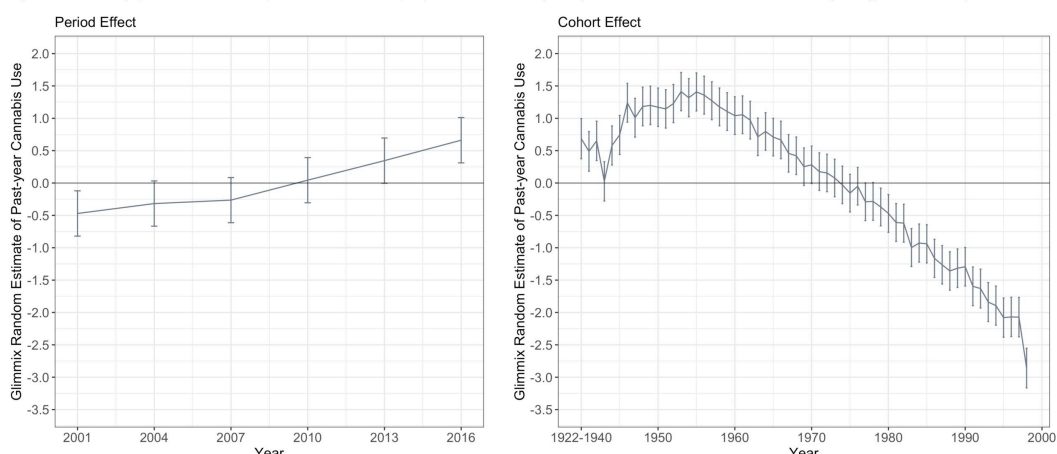
Elimination of hepatocellular carcinoma among people who inject drugs by intervening on hepatitis C virus infection Mirsada Serdarevic* Mirsada Serdarevic Tzu-Chun Chu Brooke R. MacDonald Jeff Claassen Rachel A. Stewart Rohit P. Ojha

Background: Injection drug use (IDU) is associated with hepatocellular carcinoma (HCC) incidence, for which the primary hypothesis is mediation by hepatitis C virus (HCV) infection. Nevertheless, the potential magnitude of HCC elimination by intervening on HCV is unknown. We aimed to assess the magnitude of HCC elimination through hypothetical intervention on HCV in relation to IDU.

Methods: We used electronic medical records at an urban safety-net health system in Texas to identify individuals who were aged 18 – 64 years, received care between 2013 and 2017 with follow-up through 2018, and had no history of HCC. IDU prior to HCV diagnosis was defined by self-report and an algorithm based on International Classification of Diseases version 9 Clinical Modification (ICD-9-CM) codes. HCV infection defined as a positive HCV-RNA test and HCC diagnoses were validated using data from the institutional oncology registry. We used a counterfactual framework to assess the magnitude of 5-year HCC risk after a hypothetical intervention on HCV in this population. We estimated the total and controlled direct effects as risk differences (RD) using stabilized inverse probability weighted marginal structural models and covariate adjustment for the exposure-outcome and mediator-outcome relations. We also estimated the proportion of HCC cases eliminated.

Results: Our study population comprised 61,077 individuals, of whom 12% reported a history of IDU and 0.14% developed HCC. History of IDU had higher 5-year risk of HCC compared with no IDU (RD=0.87%, 95% confidence limits [CL]: 0.37%, 1.4%). The controlled direct effect translated to elimination of 23% of 5-year HCC cases (RD=0.67%, 95% CL: 0.04%, 1.3%).

Conclusions: If assumptions for estimating controlled direct effect hold, our results suggest that intervening on HCV only partially reduces HCC incidence in relation to IDU. Longer follow-up could reveal a larger effect, but short-term expectations may need to be tempered.

Substance Use

Disparities in substance use disorder treatment use and perceived need by sexual identity among adults in the United States Anna Krasnova* Anna Krasnova José E. Diaz Morgan M. Philbin Pia M. Mauro

Aim:
Lesbian, gay and bisexual (LGB) individuals who meet criteria for substance use disorders (SUD) may have different perceptions and more difficulty accessing substance use treatment than their heterosexual peers. We estimated SUD treatment use and perceived SUD treatment need by gender, comparing LGB adults who report SUD to their heterosexual peers.

Methods:
The 2015-2017 National Survey on Drug Use and Health included n=13,261 adults 18 years or older with past year DSM-IV SUD who reported sexual identity (i.e., heterosexual, gay/lesbian or bisexual). Outcomes included past-year: 1) any SUD treatment; 2) specialty SUD treatment; 3) perceived need for SUD treatment. Weighted multivariable logistic regression models estimated odds of each outcome by LGB identity, stratified by gender and adjusted for socio-demographics.

Results:
Among adults meeting SUD criteria, SUD treatment use was similar among men (10.9%) and women (10.0%), as was specialty SUD treatment (men: 7.1%; women 7.3%), and perceived treatment need (men: 4.8%; women 5.4%). In adjusted models, the odds of reporting any SUD treatment or specialty SUD treatment use did not differ by sexual identity for men or women. However, bisexual women had higher odds than heterosexual women of reporting perceived SUD treatment need (aOR=1.63; 95% CI=1.10-2.44), as did bisexual men (aOR=2.36; 95% CI 1.19-4.71) and gay men (aOR=2.33; 95% CI 1.33-4.09) compared to heterosexual men.

Conclusions:
While SUD treatment use was low among adults who met SUD criteria overall, LGB individuals, particularly bisexual women and men, and gay men reported higher perceived need for SUD treatment. As perceived SUD treatment need is associated with subsequent treatment seeking behavior, SUD treatment services need to not only be tailored for LGB individuals, but also motivate people to engage in care services and reduce other barriers to facilitate timely treatment among this marginalized population who perceives a need for treatment.

Substance Use

Childhood and Adult Adversities: Clusters by Race/ Ethnicity and Substance Use Behaviors

Jessica Friedman* Jessica Friedman Jeanie Santaularia Darin Erickson Susan M. Mason

Background

The primary aim of this study is to better understand how childhood and adult adversities cluster together by race/ethnicity and how these clusters are associated with substance use including alcohol, binge drinking, tobacco, e-cigarettes and marijuana use. Previous research indicates that while ACEs are common across all racial/ ethnic groups, they occur at higher rates among women and persons of color. One explanation is that women of different backgrounds are deferentially exposed to adversities. This may influence disparities in substance use behaviors.

Methods

We used latent class analysis in the combined 2015 and 2018 years of the College Student Health Survey, a large state surveillance system of 2- and 4-year Minnesota college students, to identify clusters of childhood adversities plus highly correlated adult adversities among women aged 18-25. Analyses were stratified across racial/ethnic groups. The distal outcome procedure was used to regress each substance use outcome on each adversity class separately in White, Black, Asian, and Latina women.

Results

In the combined 2015/2018 sample, the seven-class model was selected for Whites and the four-class models were selected for Black, Asian and Latinas using numerous recommended criteria. Differences across racial/ethnic groups clusters included the presence of a lifetime sexual assault only cluster in the White, Black and Asian that did not exist among the Latinas. All racial/ ethnic groups had a low adversity cluster. Across all racial/ ethnic groups, unique clusters of adversity emerged with higher- adversity clusters indicating disparities in predicted probabilities of specific substance use behaviors.

Conclusions

The assessment of adversity clusters revealed distinct patterns of lifetime adversity by race/ethnicity. Understanding the unique pattern of adversity in women with different racial/ethnic backgrounds can inform targeted prevention of adversity and its impacts.

Substance Use

Association between e-cigarette use and sleep deprivation in American 18-24 year-old adults: Results from the 2018 BRFSS Sina Kianersi* Sina Kianersi Yijia Zhang Molly Rosenberg Jon Macy

Sleep deprivation is linked to various adverse health outcomes in young adults, such as depression, obesity, and weakened learning ability. Previous studies have found an association between cigarette smoking and sleep deprivation. However, very few studies have assessed the association between e-cigarette use and sleep deprivation. This is an important question given the rapid increase in e-cigarette use among young adults in recent years. We used cross-sectional data from the 2018 Behavioral Risk Factor Surveillance System Survey (BRFSS) to estimate this association, selecting participants aged 18 to 24 (N = 26,005). In 2018, 15.7% [95% CI: 15.1%, 16.2%] of BRFSS participants aged 18 to 24 reported current use of e-cigarette. Current (every day or some days) e-cigarette users were 34% more likely to report sleep deprivation, compared to those who had never used e-cigarettes [Prevalence ratio (PR) (95% CI): 1.34 (1.25, 1.43)]. This association remained significant when we adjusted for different confounders that included sociodemographic characteristics and other health behaviors. Importantly, the association decreased after adjusting for cigarette smoking [PR (95% CI): 1.17 (1.08, 1.27)] but maintained statistical significance. These findings suggest that e-cigarette use might be related to sleep deprivation in young adults. Interventions that target lowering e-cigarette exposure in the young adult non-smokers might be useful to improve sleep in this population.

KDE plots: number of sleep hours by e-cigarette exposure status, 2018 BRFSS

Substance Use
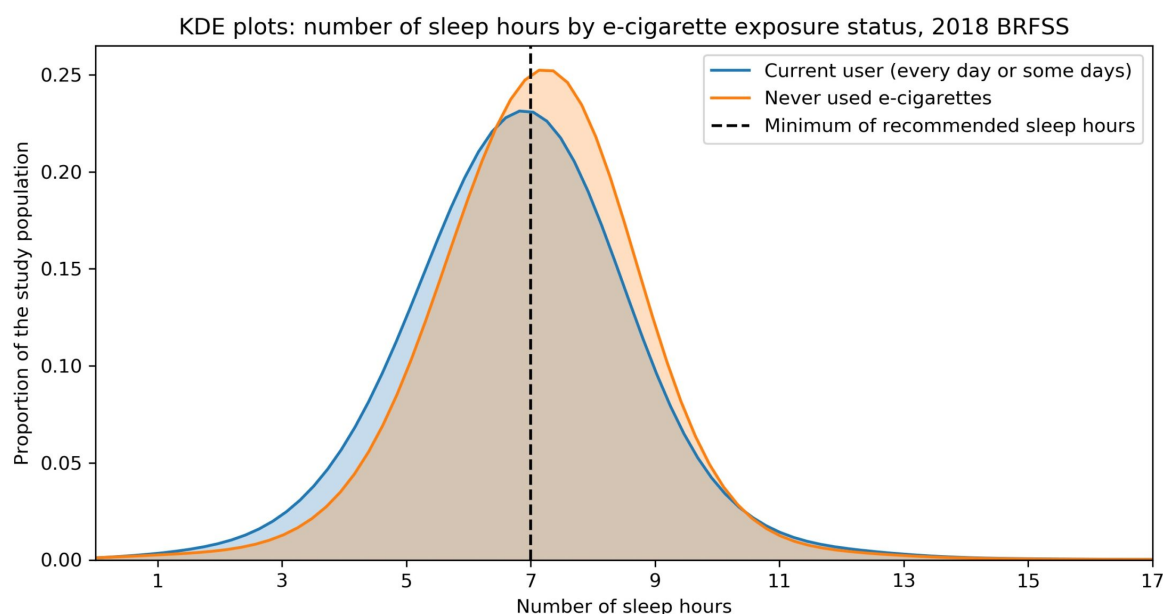
Trajectory Patterns of Alcohol Use in Patients with HIV in northern Vietnam Kumi Smith*
Kumi Smith Latkin, Carl A Sripaipan, Teerada Ha, Tran Viet Quynh, Bui Xuan Go, Vivian F

Background: Results of the REDART trial in northern Vietnam found that a targeted intervention to reduce alcohol consumption in patients living with HIV was highly effective. A better understanding of participants' longitudinal alcohol consumption following the intervention can provide insights into its mechanisms and potential applications.

Methods: Consumption patterns were documented by asking participants to recall daily use over in the prior 30 days at each follow-up visit (3, 6, 12 months). Group-based trajectory models identified common consumption trajectories and multinomial logistic regression models assessed the relationship between trajectory group membership and trial arm. Models were adjusted for demographic variables, baseline consumption, and a scale indicating readiness to reduce consumption.

Results: We identified five trajectory groups. A predicted 44% of participants were labeled as exhibiting "consistently low" alcohol consumption; 19.7% as "consistently high," 14.9% as "declining," 12.2% as "late increasing," and 9.3% as "rise and fall." Those randomized to the intervention group were more likely to be in the "consistently low" consumption group than in any other group, though findings lacked statistical significance for the "declining" and "consistently high" groups. Older age, being an ethnic minority (non-Kinh), and heavy drinking at baseline were predictive of membership in a suboptimal trajectory groups, while higher baseline readiness scores were protective against it.

Conclusion: Most REDART participants followed a consistently low consumption trajectory, to which intervention arm participants were more likely to belong. Yet a wide variety of other consumption trajectories were also observed, including several suboptimal patterns. Insights from such analyses can inform screening strategies to identify and engage with individuals who face higher risk of suboptimal trajectory patterns, and for tailored interventions to address their concerns.
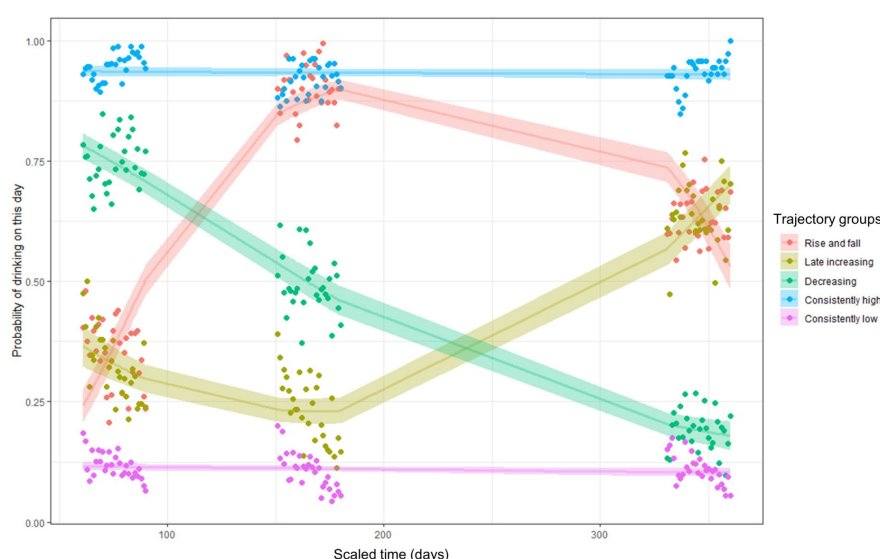
Figure 1. Longitudinal trajectory groups of alcohol consumption patterns among participants of an alcohol reduction intervention for people living with HIV in northern Vietnam. Data is shown for the three follow-up visits after the intervention taking places on days 90, 180, and 360. Using the Timeline Followback method, participants were asked to recall and describe their daily alcohol use over the prior 30 days. Points represent the observed proportion of each latent group who reported drinking on a Timeline Followback day. Lines and 95% confidence intervals represent the posterior probability of membership in each group.

Substance Use

Association between prescription opioid supply and fatal drug poisonings in the United States David S. Fink* David Fink Katherin M. Keyes Charles Branas Paul Gruenewald Magdalena Cerda Deborah H. Hasin

Background: Greater area-level prescription opioid supply is associated with more fatal drug poisonings in many, but not all studies. Heterogeneity across studies may arise from methodological variation in modeling this association. This analysis aimed to investigate three potential sources of this heterogeneity: geographic unit used to aggregate data, measures of prescription opioid supply and type of fatal drug poisoning, holding constant two common sources of bias, inadequate adjustment for potential confounders variables and spatial autocorrelation of nearby counties.
Methods: We measured associations between county-level prescription opioid supply and fatal drug poisonings in 2006-2016 across 3,109 U.S. counties. Comparisons were made across geographic aggregation, type of fatal drug poisonings, and measure of prescription opioid supply. We used Bayesian Poisson conditional autoregressive models, adjusting for compositional and contextual differences across counties.
Results: County-level analyses showed that in descending order, prescription opioid supply was most associated with deaths due to opioids only, prescription opioids only, any drug, and heroin. Regarding geographic aggregation, county-level analyses produced estimates smaller in magnitude than state-level estimates. All results were robust to the two different measures of prescription opioid supply.
Discussion: We found a positive association between prescription opioid supply and fatal drug poisonings robust to type of drug poisoning, level of aggregation, and measure of prescription opioid supply. Given consistent results across the methodological sources of variation, previous heterogeneity of effect estimates may arise from inadequate adjustment for potential confounding and/or spatial autocorrelation, two sources of bias we held constant throughout.

Substance Use

Is the effect of moving with a housing voucher subsidy on alcohol use modified by health vulnerability? Naomi Thyden* Naomi Thyden Nicole Schmidt Spruha Joshi Theresa Osypuk Huiyun Kim Toben Nelson

Neighborhood context may be a cause of alcohol use among adolescents, but effects may be contingent on baseline health. However, prior evidence has focused on observational data which is threatened by confounding. We leveraged a housing voucher experiment, the Moving to Opportunity (MTO) study, to test whether youth with more baseline health/developmental vulnerability showed weaker effects of the MTO voucher treatment on alcohol use. Volunteer low-income families in public housing were randomized in 1994-1998 to 1 of 3 conditions: to 1) receive a Section 8 housing subsidy voucher, 2) receive a housing voucher in a low poverty neighborhood combined with housing counseling ("low poverty treatment"), or 3) no voucher (control group). Alcohol use was assessed 10-15 years later in youth ages 10-20, in 2008-2010, N=4600. Using intention to treat regression models, we tested treatment interactions with baseline health vulnerabilities as modifiers. We hypothesized that the protective effects of MTO voucher treatment on alcohol use would be present among youth without health/developmental problems at baseline. However, we found the opposite pattern; compared to controls, MTO pooled voucher treatment was protective on ever-drinking alcohol, only if youth had baseline health vulnerability, e.g., behavior problems (OR= 0.26, 95% CI (0.09, 0.72); treatment-modifier interaction p=.02) or problems at school (OR= 0.46, (0.26, 0.82); interaction p=.02). MTO low-poverty treatment (vs. controls) was also protective for amount of drinks, on times they drank, if youth had baseline health problems requiring special medicine/equipment (OR= 0.50 (0.32, 0.80); interaction p=.01). Treatment effects were nonsignificant among youth without health/developmental vulnerabilities. We saw similar patterns but weaker effects for past month drinking and binge drinking. For low-income adolescents, housing vouchers may protect against alcohol use for those with health/developmental problems.

Substance Use

Is simple random sample for a state level study valid for regional estimates? Amna Umer*

Amna Umer Christa Lilly Candice Hamilton Aileen Baldwin Janine Breyel Collin John Stefan Maxwell

The objective of this study was to examine key characteristics of a sample drawn using simple random sampling technique and compare it to the population parameters. The West Virginia (WV) Office of Laboratory Services (OLS) receives dried blood spot (DBS) specimens of all infants born in the state as part of the WV Newborn Screening. In order to estimate the prevalence of prenatal alcohol exposure for the state and six Substance Abuse and Mental Health Services Administration (SAMHSA) regions a sample of DBS were selected and tested for Phosphatidylethanol. The sample size was calculated as 1,825 using the sample size formula for prevalence studies [n = Z2 P (1-P) / d2, Z = 1.96, P = prevalence, and d =precision]. There were 4,580 births in the 3 months from which the DBS sample was randomly selected from each month (n =610) after manually shuffling the DBS using hat-and-draw method. Project WATCH collects data on all infants born in the state as part of the mandatory surveillance system since 1998. The results of the DBS were matched with the Project WATCH file and 1,729 cases were matched (94.17%). Since the recommended sampling technique would have been stratified random sample for regional estimates, we wanted to assess the representativeness of this sample for the six SAMHSA regions. Using the population level data from Project WATCH we compared the key sample characteristics for the six regions to the population parameters. The results showed that the sample was a representative sample of the target population for the state as well as for the regional estimates (Table 1). Enumerating an exhaustive list of 4,580 DBS and splitting into sub-population groups by regions for performing stratified random sampling technique would have been labor and resource intensive. For a large-scale epidemiological study, a simple random sample is a reasonable method for sample selection to make inferences about the population and sub-population when resources are limited.

Table 1: Comparing key sample (n = 1,729) characteristics to the population (N= 4,580) parameters

	Population	Sample	Substance Use during pregnancy		Neonatal Abstinence Syndrome		Smoking during Pregnancy		Teen Pregnancy	
	N	n	N	n	N	n	N	n	N	n
SAMHSA Regions	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)
1	260 (6.73)	92 (6.25)	53 (20.38)	20 (21.74)	23 (8.85)	7 (7.61)	68 (26.15)	26 (28.26)	15 (5.77)	5 (5.43)
2	372 (9.63)	132 (8.97)	59 (15.86)	26 (19.7)	14 (3.76)	4 (3.03)	78 (20.97)	23 (17.42)	31 (8.33)	9 (6.82)
3	358 (9.27)	152 (10.33)	50 (13.97)	20 (13.16)	11 (3.07)	3 (1.97)	74 (20.67)	32 (21.05)	32 (8.94)	12 (7.89)
4	960 (24.85)	364 (24.75)	132 (13.75)	49 (13.46)	55 (5.73)	20 (5.49)	183 (19.06)	67 (18.41)	47 (4.9)	18 (4.95)
5	1160 (30.03)	424 (28.82)	177 (15.26)	55 (12.97)	60 (5.17)	18 (4.25)	265 (22.84)	80 (18.87)	73 (6.29)	29 (6.84)
6	753 (19.49)	307 (20.87)	116 (15.41)	55 (17.92)	45 (5.98)	20 (6.51)	226 (30.01)	90 (29.32)	69 (9.16)	26 (8.47)
WV Residents	3863 (84.34)	1471 (85.08)	587 (15.2)	225 (15.3)	208 (5.38)	72 (4.89)	894 (23.14)	318 (21.62)	267 (6.91)	99 (6.73)
			Medicaid Health Insurance		White Race		No of Previous Pregnancies ≥1		Maternal Education ≤10 grade	
			N	n	N	n	N	n	N	n
SAMHSA Regions			Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)	Freq (%)
1			78 (31.58)	23 (26.74)	231 (92.4)	83 (92.22)	198 (76.15)	69 (75)	14 (5.38)	3 (3.26)
2			242 (66.3)	82 (63.08)	300 (82.19)	107 (82.95)	262 (70.43)	97 (73.48)	37 (9.95)	13 (9.85)
3			207 (58.97)	84 (56.76)	338 (97.41)	144 (97.3)	255 (71.23)	104 (68.42)	33 (9.22)	15 (9.87)
4			450 (47.82)	169 (47.34)	880 (93.12)	330 (92.18)	649 (67.6)	242 (66.48)	81 (8.44)	32 (8.79)
5			603 (56.41)	222 (56.06)	1036 (90.24)	370 (88.73)	830 (71.55)	318 (75)	73 (6.29)	28 (6.6)
6			446 (61.77)	186 (63.05)	699 (94.33)	286 (94.08)	540 (71.71)	232 (75.57)	68 (9.03)	33 (10.75)
WV Residents			2026 (54.83)	766 (54.25)	3484 (91.78)	1320 (91.29)	2734 (70.77)	1062 (72.2)	306 (7.92)	124 (8.43)

Supervised consumption service use and non-fatal overdose among people who inject drugs in Toronto, Canada Zachary Bouck* Ayden Scheim Zachary Bouck Paula Tookey Shaun Hopkins Ruby Sniderman Gary Garber Stefan Baral Thomas Kerr Sean Rourke Dan Werb

Background: Over 40 sanctioned supervised drug consumption services (SCS) operate in Canada, with the primary goal of reducing overdose mortality. Arguments against SCS have included the potential for elevated risk of non-fatal overdose mediated by risk compensation among SCS clients. We therefore estimated the association between frequency of SCS use and recent accidental, non-fatal overdose among people who inject drugs (PWID).
Methods: PWID aged 18+ in Toronto were recruited to a longitudinal cohort beginning 11/2018. This analysis includes baseline data from participants recruited by 10/2019. Our primary exposure was self-reporting performing 'all or most' (75-100%), 'some' (25-74%), or 'few' (<25%) versus none of one's injections within an SCS in the past six months. Multivariable modified Poisson regression was used to estimate associations between frequency of SCS use and non-fatal overdose in the past six months. To address the potential for unmeasured confounding influencing any SCS use, we repeated analyses after restricting to SCS users.
Results: Of 603 participants [mean age=44.2, 31.5% female], most reported SCS use (25.9%, all/most; 28.9%, some; 30.0%, few) versus no use (15.3%), with 37.9% reporting an overdose. In adjusted regression analyses, compared to no use, any frequency of SCS use was not significantly associated with recent overdose: all/most (adjusted prevalence ratio [aPR] = 1.44, 95% CI 0.93-2.24); some (aPR= 1.20, 95% CI 0.77-1.86); few (aPR= 1.49, 95% CI 0.97-2.30). Among SCS users (n=511), more frequent SCS use was not associated with recent overdose.
Discussion: SCS use was not associated with increased prevalence of non-fatal overdose after accounting for potential confounders reflecting the vulnerable client population engaged by SCS. These results build on existing findings from the pre-fentanyl era, collectively challenging the risk compensation hypothesis related to SCS use.

Substance Use

Evaluating Intended and Unintended Effects of Opioid Prescribing Policies in a Safety-Net Health Clinic

Christopher Rowe* Christopher Rowe Kellene Eagen Jennifer Ahern Phillip O. Coffin

Safely reducing opioid prescribing is a key strategy in combatting the opioid epidemic. There is limited evidence on specific prescribing policies that maximize benefits, such as reductions in inappropriate prescribing, and minimize harms, such as patient pain or transitions to illicit opioids. We examined the effects of two policies intended to reduce inappropriate opioid prescribing in a public safety-net clinic in San Francisco, CA, including new guidelines for managing prescription opioid refills and using patient urine toxicology testing. We used a difference-in-differences approach to compare the changes in three outcomes (mean prescribed opioid dose in morphine milligram equivalents [MME], proportion of patients reporting heroin use, proportion reporting non-prescribed opioid analgesic use) between samples of patients of the clinic with new policies (n=157) and a control clinic (n=125). Associations for each outcome and post-policy period were estimated using separate linear regression models with indicator variables for the treated clinic and post-policy period, an interaction between the two, and cluster-robust standard errors. The policies were associated with a clinically meaningful reduction in mean prescribed opioid dose in the first two to three post-policy years, but this association attenuated in the final year (Year 1 = -51.6 MME, 95%CI = [-93.5, -9.7]; Year 2 = -90.0 [-160.0, -20.1]; Year 3 = -73.1 [-149.0, 2.8]; Year 4 = -44.4 [-130.9, 42.1]). The policies were not related to changes in heroin or non-prescribed opioid analgesic use. The two policies facilitated rapid reductions in mean opioid dose but no apparent change in illicit opioid use, suggesting that these policies may be an effective and safe means of reducing opioid prescribing in similar patient populations. However, the control clinic achieved reductions of nearly the same magnitude over a longer timeframe, suggesting that dose reductions are obtainable via more gradual means.

Figure 1A: Raw Outcome Plot of Mean Prescribed Opioid Dose by Year and Clinic
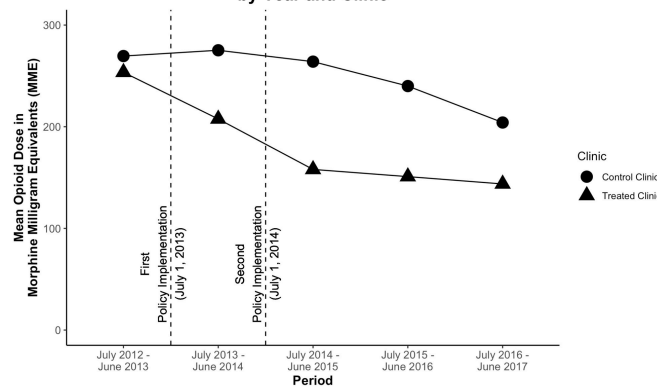
Figure 1B: Difference-in-Difference Association Estimates of Prescribing Policies on Mean Prescribed Opioid Dose

Substance Use
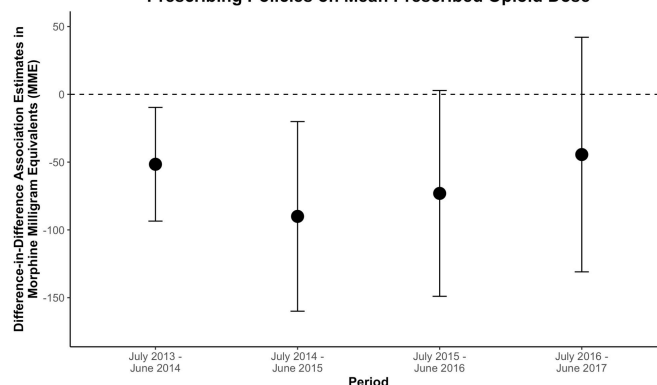
Estimates of opioid use disorder prevalence from a regression-based multi-sample stratified capture-recapture analysis Jeong Eun Min* Jeong Eun Min Lindsay Pearce Fahmida Homayra Joshua Barocas Mike Irvine Amanda Slaunwhite Gina McGowan Bohdan Nosyk

Background: An epidemic of opioid overdose has spread across North America, with illicit drug-related overdose emerging as a leading cause of death in recent years. Regional estimates of opioid use disorder (OUD) prevalence are urgently needed to adequately address the opioid overdose epidemic and to identify priority areas for targeted public health intervention. Our objective is to estimate the annual prevalence of OUD in British Columbia (BC), Canada, from 2000 to 2017.
Methods: We performed a multisample stratified capture-recapture analysis to estimate OUD prevalence in BC. The analysis included individuals identified from 3 administrative databases (hospital discharge abstracts, physician billing claims, and prescription drug records) for 2000-2011 and 4 databases (those 3 databases and emergency department visits) for 2012-2017, linked at the individual level. Cases were stratified by age group, sex and health authority of residence. Negative binomial regression models on the counts of individuals within these strata were used to estimate prevalence, adjusting for dependency between databases. We considered alternative capture period definitions, covariate selection criteria, the use of additional datasets and an alternative estimation procedure (conditional logit regression) to assess the robustness of our results.
Results: OUD prevalence in BC among people aged 12 years or older was 1.0% (N=33,349 individuals) in 2000 and increased to 1.4% (N=57,415) in 2011. Between 2013 and 2017 prevalence increased from 1.5% to 1.9% (N=84,721). The greatest increases in prevalence were observed among females ≤ 30 years old and males ≤ 44 years old, with 35.8% and 44.0% increases from 2013 to 2017 (Figure).
Conclusions: In BC, the OUD prevalence was 1.9% among people 12 years or older in 2017. We estimated that prevalence has increased twofold since 2000, particularly among younger males.

Substance Use
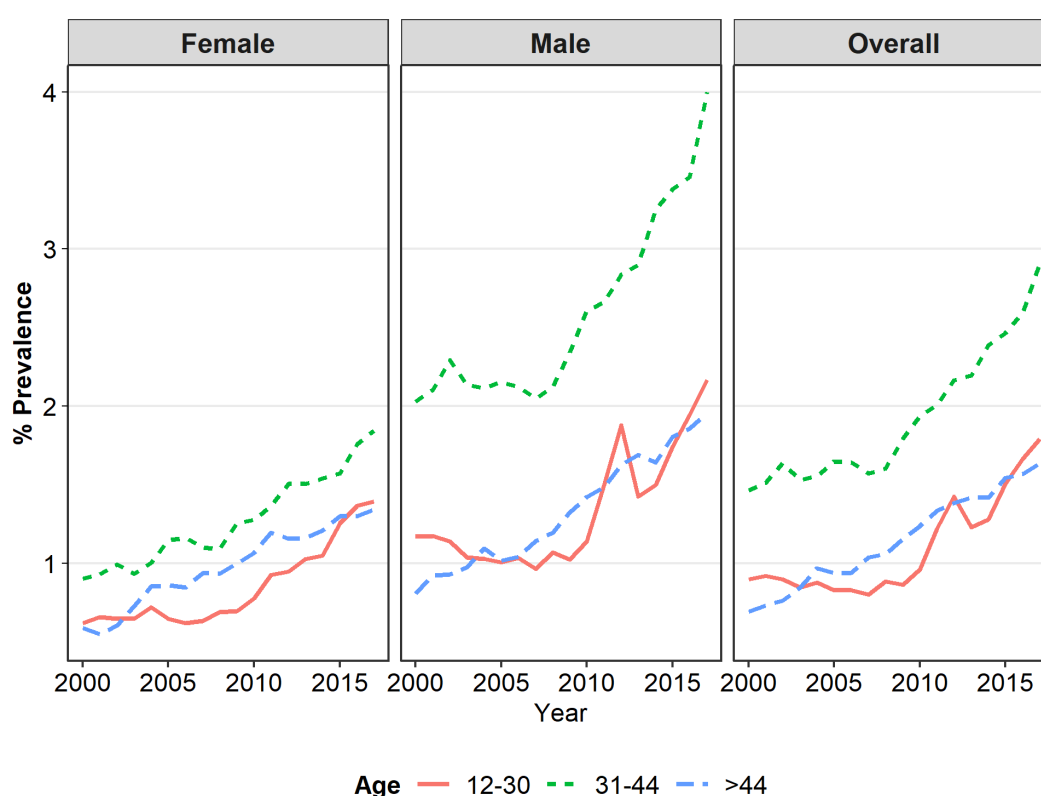
Wearable alcohol monitors for alcohol use data collection among college students: feasibility and acceptability Sina Kianersi* Molly Rosenberg Christina Ludema Sina Kianersi Kristen Jozkowski Lucia Guerra-Reyes Patrick C. Shih Peter Finn

Introduction: Our understanding of the epidemiology of alcohol use and alcohol-related harms on college campuses is limited by the traditional use of self-reports to measure alcohol use. Wearable alcohol monitors are a newly developed technology that passively collect objectively measured information on alcohol use. These alcohol monitors measure sweat-based transdermal alcohol concentration (TAC), and are integrated into devices worn on the wrist. The aim of this pilot study was to assess the feasibility and acceptability of using wearable alcohol monitors in a college student population.

Methods: In September 2019, we enrolled n=5 Indiana University undergraduate students in a pilot study to wear alcohol monitor wristbands continuously over a 5-day period. Concurrently, participants completed daily surveys querying details about their alcohol use in the previous 24 hours. We measured acceptability at endline with the Acceptability of Intervention Measure (AIM) scale (min=1, max=5). We measured feasibility with process measures: 1) amount of alcohol monitor data produced, and 2) correlation between drinking events identified by the alcohol monitors and drinking events reported by participants.

Results: Overall, participants reported high acceptability of the wearable alcohol monitors with a mean AIM score of 4.3 (range: 3.3 to 5.0). Feasibility of monitor use was also high: all participants were able to successfully use the alcohol monitors, producing a total of 24 out of 25 possible days of alcohol monitoring data. The number of drinking events detected by the alcohol monitors largely corresponded with self-reported drinking events (see Figure), and the self-reported number of drinks during a drinking event was correlated with the area under the curve of each drinking event peak (Pearson's r=0.6, p=0.02).

Conclusions: Wearable alcohol monitors are a promising data collection tool for more objective real-time measures of alcohol use in college student populations.
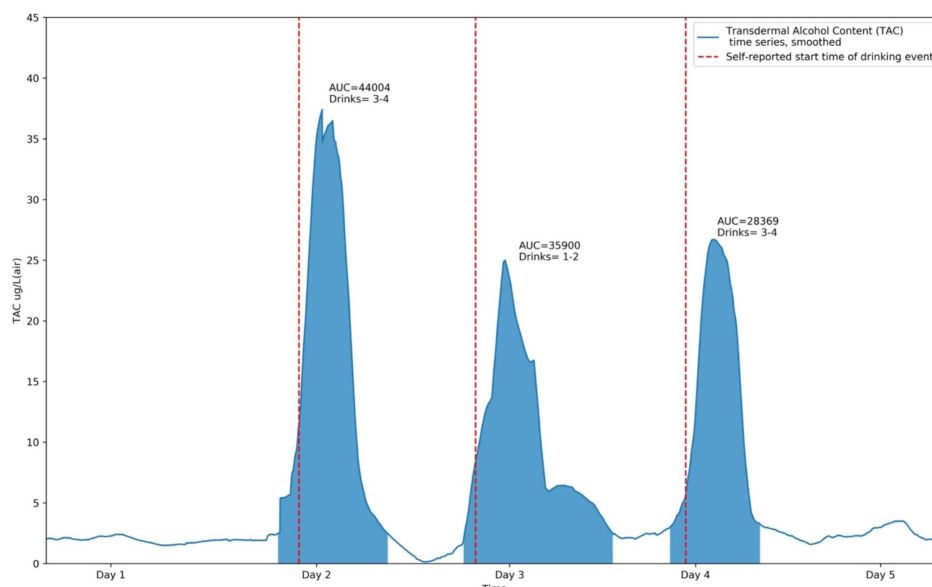
Figure. Example alcohol monitor data produced by pilot participant over 5 days, annotated with self-reported drinking events and drinking amounts, September 2019.

Substance Use

Drug and alcohol use disorder following early life exposure to tetrachloroethylene (PCE)-contaminated drinking water Ann Aschengrau* Ann Aschengrau Alexandra Grippo Michael Winter Margaret Shea Richard Saitz

Background: Exposure to neurotoxic solvents such as tetrachloroethylene (PCE) has been associated with adverse behavioral consequences in studies of highly exposed adults in workplace settings. However, little is known about possible adverse effects of lower exposure levels commonly seen in community settings. We recently observed that drug and alcohol use was more frequent among adults from Cape Cod Massachusetts who were exposed to high levels of PCE-contaminated drinking water during gestation and early childhood. Using newly collected data from a population-based retrospective cohort study, the current analysis examines whether early life exposure to PCE-contaminated drinking water is associated with the diagnostic criteria for alcohol and drug use disorder later in life.
Methods: Three-hundred and sixty-three subjects with prenatal and early childhood PCE exposure, and 255 unexposed subjects were studied. Individuals (median age: 40 years) completed questionnaires on the eleven established diagnostic criteria (e.g., hazardous use, interpersonal problems related to use) for lifetime drug and alcohol use disorder and confounding variables. A validated leaching and transport model was used to estimate exposure to PCE-contaminated water.
Results: Exposure to high PCE levels (>=67th percentile) during early life was associated with the lifetime presence of one or more diagnostic criteria for drug use disorder (adjusted RR: 1.7, 95% CI: 1.2-2.5) but not alcohol use disorder (adjusted RR: 1.0, 95% CI: 0.9-1.2). Individuals with one or more diagnostic criteria for drug use disorder were more likely to use multiple illicit drugs and misuse prescription medications than unaffected individuals (79.7% versus 23.3%).
Conclusions: These results suggest that exposure to PCE-contaminated drinking water during early life may increase the risk of drug use disorder later in life. Future analyses will examine the contribution of social stressors to this association.

Substance Use

Influence of Family and Community Socioeconomic Status on the Risk of Adolescent Drug Use Ann Aschengrau* Ann Aschengrau Alexandra Grippo Michael Winter

Purpose: This study determined the influence of family and community socioeconomic status (SES) on adolescent drug use. Because drug use during this developmental stage increases the risk of subsequent mental, physical and social problems, it is important to consider both family and community characteristics in its etiology.
Methods: The present analysis examined the influence of family and community SES on the use of marijuana, inhalants, heroin, cocaine/crack, psychedelics/hallucinogens, Ritalin without a prescription, and club drugs in a population-based retrospective cohort study. Self-administered questionnaires were used to obtain information on adolescent drug use. Family SES was gathered from birth certificate data on maternal educational level and paternal occupation. Community SES characteristics at birth, age 10 and age 18 were obtained from the US Census Bureau. Generalized estimating equation analyses were used to account for non-independent outcomes arising from several children from the same family and to control for confounding variables.
Results: An increased risk of adolescent drug use was associated with lower maternal education, non-white collar occupations among fathers, and lower community median income, and poverty and unemployment levels at age 18. The strongest associations were seen for the use of multiple drugs (adjusted RR: 1.7, 95% CI: 1.4-2.2), inhalants (adjusted RR: 2.5, 95% CI: 1.5-2.2), crack/cocaine (adjusted RR: 2.8, 95% CI: 1.7-4.5), psychedelics/hallucinogens (adjusted RR: 1.8, 95% CI: 1.4-2.4), and club/designer drugs (adjusted RR: 1.8, 95% CI: 1.2-2.7) among adolescents whose mothers had only a high school education. Null or weak associations were observed for marijuana use.
Conclusions: These results suggest that the use of certain drugs during adolescence is associated with both family and community SES measures. However, maternal education appears to have the greatest influence on use.

Substance Use

Exposure calls to the US poison control centers involving cannabidiol: 2000–2019 Silvia Perez-Vilar* Silvia Perez-Vilar Sara Karami Cindy M. Kortepeter Michelle C. Hines Kira Leishear

In June 2018, the US Food and Drug Administration (FDA) approved the first prescription cannabidiol (CBD) product. The 2018 Farm Bill removed cannabis and derivatives that contain ≤0.3% tetrahydrocannabinol from the cannabis definition in the Controlled Substances Act, but preserved FDA's authority to regulate products containing cannabis or cannabis-derived compounds under the Federal Food, Drug, and Cosmetic Act (FD&C Act) and the Public Health Service Act. We aimed to describe patterns and trends of calls to the US poison control centers (PCCs) involving CBD exposure as part of FDA's review of available safety data on CBD. The American Association of Poison Control Centers' (AAPCC) National Poison Data System (NPDS) captures near real-time data on calls to PCCs. We used CBD generic and product codes (excluding cannabis and nabiximols) to extract data on human exposure calls involving CBD during January 2000–April 2019. We described call counts overall and by calendar year, age group, gender, call reason, and number of exposures. We identified 1,041 calls. Of these, 92% described use of unapproved plant-based CBD. Gender distribution was similar with 0.4% of females being pregnant at the time of exposure; 40% of the calls referred to CBD exposure in children aged <18 years. There were no calls related to CBD in 2000–2013; subsequently, calls ranged between 3 in 2014 and 519 in 2018. NPDS categorized most calls as unintentional exposures (45%), intentional exposures (30%), or adverse reactions (21%). The most frequent co-exposures were benzodiazepines (16%) and cannabis (mostly dried plant) [15%]. There was a sharp increase in calls regarding CBD since 2016. Most CBD exposure calls described unapproved CBD. As per the label of the currently FDA-approved CBD product, some benzodiazepines may result in potential drug interactions with CBD.
Disclaimer: This abstract reflects the views of the authors and should not be construed to represent FDA's views or policies.

Substance Use

Phosphatidylethanol (PETH) in newborn residual dried blood spots for late prenatal alcohol exposure detection Amna Umer* Amna Umer Christa Lilly Candice Hamilton Aileen Baldwin Janine Breyel Collin John Stefan Maxwell

Phosphatidylethanol (PETH) is a direct metabolite of ethanol and is a phospholipid formed in the red blood cell membranes only in the presence of alcohol. A positive PETH in newborn dried blood spots (DBS) defined as a cut-off of □8 ng/ml (Jones et al., 2011 and Baldwin et al., 2015) or □21 ng/ml (Bakhireva et al., 2017) and is indicative of prenatal alcohol exposure (PAE) 2 – 4 weeks before delivery. Due to the complex alcohol metabolism and individual variations in PETH formation, degradation, and elimination, PETH concentrations cannot differentiate between the various levels of alcohol consumption. However, as no amount of drinking is safe during pregnancy the main objective of this study was to demonstrate the varying prevalence rates of late PAE based on varying PETH cut-offs. Method: 1,830 newborn DBS in the West Virginia Newborn Screening Repository were randomly selected and analyzed for PETH. The prevalence rates were calculated using three cut-offs that include □2 ng/ml (limit of detection (LOD)), □8 ng/ml, and □ 21ng/ml. Results: The results show the prevalence of late PAE at PETH cut-offs of □2 ng/ml, □8 ng/ml, and □21 ng/ml were 28.57% (95%CI: 26.11– 30.03), 8.03% (95%CI: 6.84 – 9.22), and 1.85% (95%CI: 1.26 – 2.44) respectively. Conclusion: No amount of alcohol consumption is safe during pregnancy and PETH formation cannot occur in the absence of alcohol thus decreasing the PETH cut-off level to LOD in newborn DBS may increase the sensitivity for detecting any alcohol use in late pregnancy. This may help in identifying true prevalence rates of PAE in large-scale population-based epidemiological studies as well as provide basis for resource allocation geared towards this mother infant dyad.

Individual EMS Disposition in the Prehospital Setting to Predict Future Opioid Overdose and Mortality Michaela F. George* Michaela George Lillie Valliere Haylea Hannah Karina Arambula Rochelle Ereman Michaela F. George

There have been over 400,000 deaths related to prescription opioids in the US since 1999, with the highest prevalence among individuals age 45-54 years old. However, adults between the ages of 18 and 34 have the highest prevalence of misuse of prescription opioids. With accidental overdoses as a leading cause of death, Marin County is just one community that is heavily impacted by this ongoing epidemic. Statistics related to non-fatal and fatal opioid overdoses are difficult to accurately count due to the differing ways counties may categorize cause of death, diagnoses, and other contributing factors. However, looking at 911 calls gives us a baseline for community-based non-fatal opioid overdoses encountered by Emergency Medical Services (EMS) to further characterize the burden of opioid overdoses. A cross-sectional study was conducted by Marin County's Health and Human Services using EMS data and death records. This study determined if an individual's disposition from EMS can be used to predict future outcomes for individuals with opioid use disorder. Whether the patient refuses treatment/transport or accepts treatment/transport may allow us to find patterns that will predict outcomes such as experiencing another overdose or being at a higher risk for all-cause or overdose mortality. If our findings show that one disposition yields more favorable outcomes for those experiencing a suspect opioid overdose, this could implicate a solution to intervene at the EMS level. Interventions such as providing patients with resources and facilitating treatment for addiction in the prehospital setting could mean that EMS personnel reach more individuals and thus make a larger impact.

Fatal & Non-Fatal Opioid Overdoses in Marin County: Using EMS and county data to locate the presence of fentanyl, naloxone distribution, and repeat overdoses events Michaela F. George* Michaela George Josette Rojo Haylea Hannah Karina Arambula Rochelle Ereman Michaela F. George

In recent years, the United States has been greatly affected by prescription drug overdose deaths, 68% of which are caused by opioids. Like many communities nationwide, Marin County in California is deeply affected by the opioid epidemic with accidental overdose being one of the leading causes of injury-related death. This study examines how fatal and non-fatal opioid overdoses in Marin County are associated with factors such as suspected fentanyl involvement, naloxone administration (EMS and in the community), and repeat overdose events. A cross-sectional study was conducted by Marin County's Health and Human Services using data collected from EMS dispatch calls and vital statistical records. Logistic regression was used to study the relationship between fatal and non-fatal overdoses and factors associated with the EMS event such as suspected fentanyl involvement, use of naloxone, and repeat suspect overdose. A spatial analysis was conducted using a Geographical Information System software examining the distribution of fatal and non-fatal overdoses in Marin County in relation to three variables: suspected fentanyl involvement, presence of naloxone, and whether the incident was a repeat overdose. With the findings of the study, the authors hope to suggest effective interventions to address fentanyl hot spots and increase the distribution of naloxone especially in areas with high risk of fatal and non-fatal overdoses. Additionally, these results will inform on-going efforts locally to offer naloxone trainings to communities affected by the hot spots to teach of its harm reduction properties and how to properly use a kit when encountering an overdose. Trusted messengers and case managers can be utilized in hard-to-reach communities such as the homeless community to easily access trainings. Lastly, understanding factors associated with repeat non-fatal overdoses in Marin County will allow health professionals to understand and predict patterns in overdoses.

Substance Use

The relationship between self-reported non-injection cocaine use and hepatitis C in the United States Alison E. Simmons* Alison Simmons David Fisman Susan Bondy

Hepatitis C is a bloodborne pathogen that causes chronic hepatitis, which may lead to cirrhosis and/or hepatocellular carcinoma. It is commonly transmitted among people who inject drugs through sharing of contaminated needles. There is also evidence that transmission may occur through the sharing of contaminated nasal and oral non-injection implements. Studies to date have not conclusively established a relationship between intra-nasal and oral cocaine use and hepatitis C. In this study, the association between cocaine use and hepatitis C among people who do not inject drugs was examined.

Data from 2011–2012, 2013–2014, and 2015–2016 cycles of the National Health and Nutrition Examination Survey were analyzed. Multivariable logistic regression was used to test for an association between cocaine use and hepatitis C among individuals who never injected an illicit substance. Covariates included age, income, race, education, and number of lifetime sex partners.

In the unadjusted model, those who reported non-injection use of cocaine had 3.84 (95% CI: 2.07, 7.12) times the odds of having hepatitis C compared to those who did not use cocaine. In the adjusted model, those who reported non-injection use of cocaine had 2.92 (95% CI: 1.45, 5.91) times the odds of having hepatitis C compared to those who did not use cocaine.

This study elucidates an understudied at-risk group of individuals who report intra-nasal or oral cocaine use and have a higher risk of HCV compared to individuals who do not report cocaine use. These individuals should be the target of harm reduction interventions to reduce the transmission of hepatitis C.

Substance Use

The Relationship between Buprenorphine Waiver Certifications and Acute Hepatitis C Virus Incidence in the United States, 2013-2017 Daniel Brook* Daniel Brook Christian Adams Christine Hannah Kathryn Vivian David William

Background: The United States (US) is currently experiencing an epidemic of hepatitis C virus (HCV) infection spread primarily through shared injection drug equipment by people with opioid use disorder. The Drug Addiction and Treatment Act of 2000 allows buprenorphine, an evidence-based medication for opioid use disorder, to be prescribed by physicians through waivers. The relationship between buprenorphine and HCV is unknown. Syringe service programs (SSPs) prevent the spread of HCV, but many communities do not have access to them. We aim to assess the relationship between buprenorphine availability and HCV incidence.

Methods: We obtained buprenorphine waiver certification data from the Substance Abuse and Mental Health Services Administration and calculated the patients per 100 people in each state that can be served via a waiver. We obtained acute HCV incidence data by state from the Centers for Disease Control and Prevention and SSP data from amFAR. We created three multivariable negative binomial models using a generalized estimating equation, selecting covariates through a directed acyclic graph. We also assessed for effect measure modification (EMM) by state SSP status.

Results: A higher than median buprenorphine availability in 2012 was associated with a higher acute HCV incidence in 2013-2017 (IRR: 1.66 95% CI: 0.91, 3.02). Higher buprenorphine availability per 100 persons in 2012 was associated with a higher acute HCV incidence in 2013-2017 (IRR: 2.90 95% CI: 1.05, 7.99). Higher buprenorphine availability per 100 persons in 2012-2016 was associated with a higher acute HCV incidence in 2013-2017 (IRR: 1.98 95% CI: 0.86, 4.52). We found no evidence of EMM on these relationships by SSP status.

Conclusion: Our ecological association model demonstrates that increasing buprenorphine availability was associated with a higher incidence rate of acute HCV in the US in 2013-2017. These results should be followed with a causal analysis of this relationship.
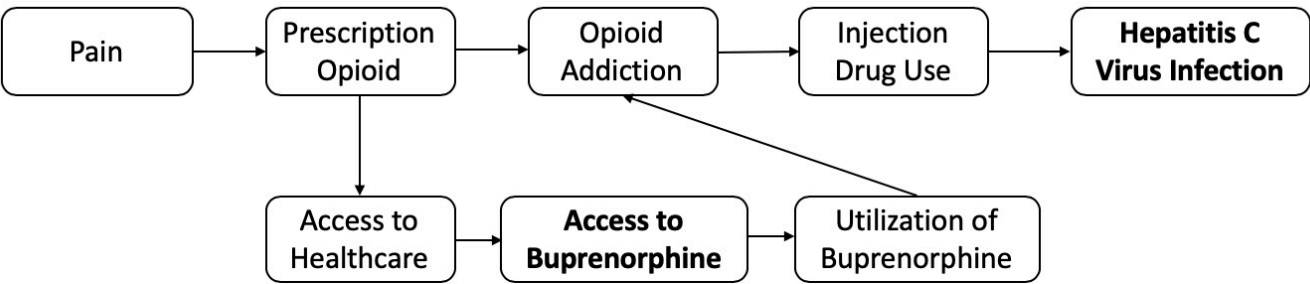
Figure 1: The relationship between access to buprenorphine and Hepatitis C Virus Infection.

Substance Use

US Drug Overdose Mortality: 2008-2017 Increases Affect Younger People Who Use Drugs

Dhruv S. Gaur* Dhruv Gaur Brendan P. Jacka Traci P. Green Elizabeth A. Samuels Scott E. Hadland Maxwell S. Krieger Jesse L. Yedinak Brandon D.L. Marshall

Introduction. Drug overdose mortality remains a public health crisis in the United States (US). Overdoses involving synthetic opioids other than methadone (hereafter "synthetic opioids"), including fentanyl and its analogs, are the primary contributor to overdose mortality.
Methods. Using the US National Vital Statistics System multiple cause of death data for 2008-2017, we analyzed age-specific overdose death rates by region (East or West of the Mississippi River) and by differences in racial, ethnic, and urbanicity distribution for young people (aged 15-34 years). Overdose deaths were defined using ICD-10 Codes X40–X44, X60–X64, X85, and Y10–Y14, including all overdose deaths and separately, deaths involving synthetic opioids. Age-adjusted mortality rates were compared using z-tests (number of deaths was >100) or non-overlapping confidence intervals for gamma distribution (<100 deaths).
Results. In 2008, the age distribution of overdose mortality was similar in eastern and western states, with adults aged 45-54 experiencing the highest overdose burden (Figure, Panel A). Thereafter, the age burden of mortality shifted in eastern states, with people aged 25-30 experiencing the highest overdose mortality rates by 2017 (Figure, Panel B). In 2008-2017, overdose mortality among young people in eastern states increased by 147% compared to 39% in western states. This was driven by overdoses involving synthetic opioids, which increased by 2413% in the east and 725% in the west. Groups experiencing the highest increases in rates of opioid overdose death were Black and Hispanic people and people living in large metropolitan areas.
Conclusion. Driven by the emergence of synthetic opioids, the burden of drug overdose mortality increasingly affects young people, particularly in eastern states. These changes, along with significant increases among people of color and in urban areas, highlight the need for targeted interventions to reduce opioid overdose risk in diverse populations.

Substance Use

Investigating the impact of socio-environmental characteristics on substance-use acute outcome disparities by sexual orientations using linked longitudinal population-based data
Celine Teo* Celine Teo Sukhdeep Kaur Antony Chum

Background
There is global evidence that lesbian, gay and bisexual (LGB) individuals report higher rates of substance use compared to the general population. However there is a lack of population-based estimate of this disparity in Canada. Our study intends to use population-based health administrative data to examine substance-use acute outcomes (SUAO) across sexual orientations, i.e. ambulatory care, hospitalizations, and mortality data. There is strong evidence that socio-environmental characteristics influence the risk of SUAO in the general population, but these relationships are poorly understood in the LGB population.
Methods
Participants from our study is drawn from the Canadian community health surveys and are linked to their longitudinal health administrative data from 1999-2019 (n=938,600). We used a mixed-effect zero-inflated Poisson regression to model the number of SUAOs in each person-year predicted by: sexual orientation, age, year dummies, and sociodemographic factors. Random-intercepts are used to account for within-person serial dependence. We used interactions to understand whether socio-environmental characteristics such as LGB population density and LGB hate-crimes uniquely impacts the risk of LGB SUAOs.
Results
Preliminary descriptive results indicate that the general population experience SUAO at the rate of 442 per 100,000 person-year (95% CI 368-571) and LGB individuals experience SUAO at the rate of 1635 per 100,000 person-year (95% CI 1385-1824). Further analysis will be conducted. These will include models to understand if model results differ by substance types (e.g. alcohol, cannabis, and other drugs) and gender-stratified analysis since the outcome may differ by gender.
Conclusions
Our project will provide evidence to inform Canadian health service providers and community organizations to provide additional interventions targeted at LGB individuals.

Substance Use

Early buprenorphine initiation and healthcare utilization among insured patients with opioid use disorder in the US, 2010 – 2018 Tianyu Sun* Tianyu Sun Stephen Kogut Natallia Katenka Ashley Buchanan

Buprenorphine (bup) was approved by the FDA for opioid use disorder (OUD). This study was aimed to evaluate the association between early buprenorphine (bup) initiation versus late/no-treatment and health outcomes including the number of opioid overdoses, overdose-related cost, number of any emergency department (ED) visits, and total healthcare cost (medical and prescription). This retrospective cohort study used Optum's deidentified Clinformatics® Data Mart Database. Adults with OUD diagnosis during 2010 - 2018 were included. They were required to be continuously enrolled for baseline (1 year before OUD diagnosis) and follow-up period (1 year after OUD diagnosis). The early bup initiation was defined as receiving bup for OUD within 30 days after the first OUD diagnosis. A generalized linear model was used to compare 4 outcomes among the early initiators to deferred/untreated patients. We adjusted for age, gender, depression, chronic pain, anti-depressant usage, alcohol abuse, polypharmacy, year of OUD diagnosis, previous opioid usage, previous overdose, Charlson comorbidity index, baseline total healthcare cost, and social economic status (SES) such as race, education level, etc. Accounting for the missingness in SES variables, multiple imputation was applied to generate 20 datasets with complete baseline information, assuming variables in the model have an existing joint distribution. Results were combined using Rubin's estimator of variance. A total of 55,608 patients were included, 10.2% were early bup initiators. Comparing to untreated/late initiators, the early initiators had 12% fewer opioid overdose related visits (95% CI 0.02, 0.21), 32% less opioid overdose related cost (95% CI 0.29, 0.36), 13% fewer ED visits (95% CI 0.12, 0.15), 23% less total healthcare cost (95% CI 0.20, 0.25) during follow-up. Early bup initiation was associated with fewer opioid overdoses, fewer ED visits, less opioid related cost, and less total healthcare cost.

New and Persistent Marijuana Users: Characteristics, Patterns of Use, and Differences by State Medical Marijuana Law Status Natalie Levy* Natalie Levy Luis Segura Emilie Bruzelius Silvia Martins

Background-Marijuana use is common and increasing in the United States. Increases are attributed in part to social and policy changes, including medical marijuana legalization. Characterizing individuals who initiate marijuana use overall and by state medical marijuana law (MML) status may illuminate patterns of use and generate hypotheses about the impact of MMLs on initiation.

Methods-Using 2013-17 National Surveys on Drug Use and Health data, new users were defined as past-year users who first used marijuana in the survey year or prior two years; all others were considered persistent past-year users. Annual counts and proportions by initiation were estimated. Characteristics of new and persistent users were compared overall and new users were compared by state MML status. Analyses were conducted in R software v3.6.1 accounting for the complex survey design and using survey weights.

Results-The number of new marijuana users increased from 2013-17; however, new users as a proportion of past-year marijuana users (15.2% [14.8%-15.6%]) did not change nor differed by state MML status. Most new users were <25 years old (12-17 years: 41.3% [39.9-42.7%]; 18-25 years: 48.3% [46.9-49.8%]) versus 31% of persistent users (12-17 years: 2.8% [2.7-2.9%]; 18-25 years: 28.1% [27.4-28.7%]). A larger percentage of persistent (60.5% [59.6-61.3%]) than new users (48.5% [47.5-52.5%]) were male. The median number of days using marijuana in the past year was 10 [IQR: 2, 52] for new users versus 60 [IQR: 10-260] for persistent users. No differences in marijuana use disorder were observed. Among new users, no differences in demographics or patterns of use were observed by state MML status.

Conclusion-New users are younger and use marijuana less than persistent users but new users in MML and non-MML states share similar characteristics and patterns of use. Additional work might explore changes in characteristics of new users over time and directly evaluate the impact of MMLs on initiation.

Neighborhood disorder and harmful alcohol use: Comparison of approaches for assigning neighborhood exposure Lynsie R. Ranker* Lynsie Ranker Jennifer Weuve Craig S. Ross Ziming Xuan Karin Tobin Adam J. Milam Abby Rudolph

Indices of neighborhood disorder are associated with risk behaviors such as heavy alcohol use and other drug use. Studies often use residential address as the primary exposure site, yet exposure in other activity spaces may correlate better with risk behaviors. We evaluated the association between neighborhood disorder and harmful alcohol use, but with two different neighborhood exposure assignments based on (1) residential address and (2) different activity spaces and the amount of time spent in each. Our data included baseline responses from participants in an HIV prevention study, who lived in Baltimore City. Respondents reported locations and the amount of time during a typical week in the past 6 months where (if applicable) they lived/slept, worked, socialized, and injected drugs. Using data from the Neighborhood Inventory for Environmental Typology Instrument we calculated objective neighborhood disorder scores for participants (residential score and activity-weighted score). Participants also completed the Alcohol Use Disorder Identification Test (AUDIT-10) scale. 394 participants had complete location information, AUDIT score, and key covariates (mean age=49.2, 56.6% male). Neighborhood disorder scores ranged from 5-32; the mean residential disorder score was 20 (standard deviation [SD], 5.6) and the mean activity-weighted disorder score was 19.6 (SD 5.3). 24% of the sample reported harmful alcohol use (AUDIT of 8+; mean score=5.5, SD 7.6). The adjusted prevalence ratio (PR) of harmful alcohol use per SD higher residential neighborhood disorder was 1.15 (95%CI 0.96–1.38). Results were driven by physical disorder, rather than social disorder or violence, alcohol and other drugs domains. Activity-based exposure results were similar (PR=1.10, 95%CI 0.91–1.32), possibly due to limited mobility across neighborhoods in this sample. Understanding exposure to disorder at a neighborhood level may help explain risk behaviors and highlight priorities for intervention.

Table: Unadjusted and Adjusted* Model Results for Residential and Activity-Weighed Exposure+ and harmful alcohol use (AUDIT score of 8 or higher) with a standard deviation increase in disorder score (n=394)

Binomial Models	Total Disorder		Physical Disorder		Social Disorder		Violence, Alcohol, and Other Drugs Disorder	
	PR	95% CI	PR	95% CI	PR	95% CI	PR	95% CI
Residential, Unadjusted	1.15	0.96, 1.38	1.15	0.96, 1.39	1.08	0.92, 1.27	1.11	0.92, 1.32
Residential, Adjusted	1.14	0.94, 1.37	1.14	0.95, 1.38	1.06	0.90, 1.26	1.11	0.92, 1.33
Activity-space, Unadjusted	1.11	0.93, 1.33	1.12	0.93, 1.34	1.06	0.90, 1.26	1.11	0.93, 1.32
Activity-space, Adjusted	1.10	0.91, 1.32	1.11	0.93, 1.33	1.05	0.88, 1.25	1.08	0.90, 1.30

*Adjusted for age, sex at birth, sexual orientation, race and education status
+Activity weighted includes where they slept/lived, earned money, injected drugs (if applicable), and socialized

Substance Use

Incident Smoking and Alcohol Consumption in Japanese Atomic Bomb Survivors: The Lifespan Study of Japanese Atomic Bomb Survivors (LSS) Matthew Dekker* Matthew Dekker Mai Utada Benjamin French Amanda Phipps Eric Grant

o Background
Stressful early life experiences may be associated with risky health behavior later in life. Previous work on Japanese atomic bomb survivors has focused primarily on radiation driven health effects, though it is plausible that individuals exposed to the atomic bombs as children may have also experience higher levels of later life smoking and alcohol consumption than those with lower levels of exposure.
o Purpose
Using data from the Lifespan Study of Japanese Atomic Bomb Survivors, this study sought to identify differences in smoking/alcohol consumption by exposure to the atomic bombs in individuals who were 16 year old or younger at the time of the blasts.
o Methods
Simple stratified analyses were run comparing estimates of smoking and alcohol consumption (ever/never and amount consumed) across groups defined by distance from the blast hypocenter (three categories : <2 km, 2-<2.5km, 2.5-10km) as well as by radiation dose category (0–0.005 Gy, 0.005–.5Gy, 0.5–1Gy, ≥1Gy) and in-city status (not-in-city versus in-city) with estimates being compared by city and sex due to potential confounding.
o Result
No meaningful differences were observed between groups as defined by distance from the blast hypocenter or radiation dose. These results held when both distance and dose were defined using different categories as well as when included as continuous variables. Not-in-city individuals, however, differed in several areas from their in-city counterparts, particularly in the proportion having reported ever consuming alcohol (females: Hiroshima - 41% vs. 9%, Nagasaki – 33% vs. 7%).
o Conclusions
The strongest associations were observed comparing in city to not-in-city individuals, however there may be unmeasured differences in these groups. The lack of observed association when measuring exposure by dose and distance may be due to extreme baseline rates of smoking and alcohol consumption.
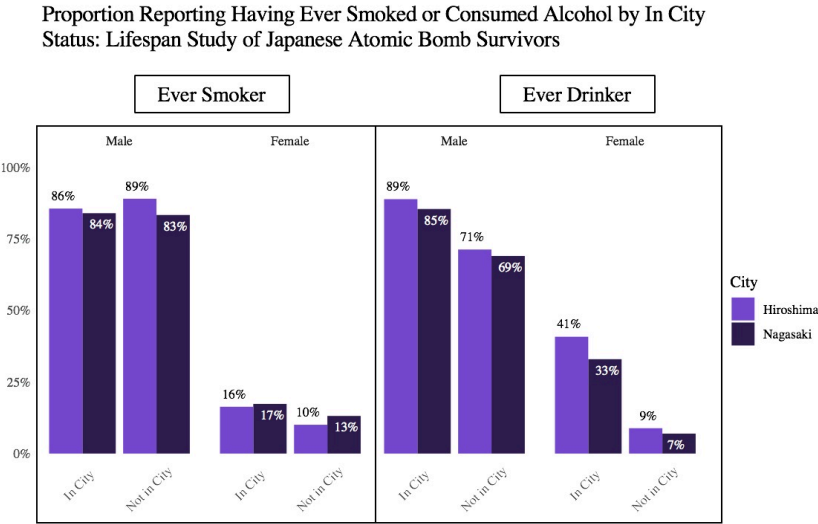
Proportion Reporting Having Ever Smoked or Consumed Alcohol by In City Status: Lifespan Study of Japanese Atomic Bomb Survivors

Self-reported opioid use and mortality risk among patients with HIV engaged in care
Seashore (Yu) Li* 3647] Li Joella Adams Brandon Marshall Jennifer Edelman Christopher Rentsch Declan Barry Kirsha Gordon Robert Kerns

Aim: To examine the association between long-term patterns of opioid use and mortality risk among patients with HIV (PWH).

Methods: Survey data between 2002 and 2018 on 3,658 participants in the Veterans Aging Cohort Study (VACS) study was analyzed for a total of 22,684 person-years of observation. We used joint trajectory modeling (accounting for dropout) to group patients into trajectories of two contemporaneous longitudinal measures: self-reported opioid use (regardless of reason or source) and VACS Index 2.0 scores. Cox proportional hazards model was used to estimate the unadjusted and adjusted hazard ratios [HR] comparing stable, infrequent opioid use, and other opioid trajectory memberships and mortality. Covariates included sociodemographic characteristics, HIV, clinical factors, and prescribed medications.

Results: Dual trajectory modeling accounting for dropout resulted in the following classifications of opioid use: 25% with no lifetime use, 62% with stable, infrequent use, 8% with escalating use and 6% with de-escalating use. Compared to those with stable, infrequent use, escalating use and de-escalating use had higher risk of death (unadjusted HR [95% CI]: 1.27 [1.13, 1.43] and 1.76 [1.54, 2.02], respectively). In adjusted analyses, overall differences in mortality by opioid trajectory group did not remain significant (p-value=0.25), although the direction of effects were similar. In sensitivity analyses targeting drop out, the distribution of opioid use trajectory membership changed, but did not affect the overall pattern of results.

Conclusion: PWH with escalating compared with other patterns of opioid use have increased mortality risk, although this relationship may be confounded by other factors. In trajectory modeling with non-random missing data, methods to account for differential drop out should be used.

Kaplan-Meier survival estimates

Self-reported opioid use and mortality risk among patients with HIV engaged in care

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Kaplan-Meier survival estimates

Risk of emergency department visits immediately after release from New York City jails for individuals with opioid use disorder Teena Cherian* 3647] Cherian Monica Katyal Kelsey Burke Andrew Biundo Ryan McDonald Joshua Lee Ross MacDonald Sean Murphy Sungwoo Lim

Release from jail incarceration may spur emergency department (ED) utilization among individuals with opioid use disorder (OUD). We examined if incarceration is associated with elevated risk of ED visits within 1 year of jail release among adults with OUD. Data from New York City (NYC) Health + Hospitals/Correctional Health Services' electronic health records and New York State Statewide Planning and Research Cooperative System ED visit records from 2011-2017 were matched. The study cohort included incarcerated adults (≥18 years old) in NYC jails who had OUD ascertained by clinical diagnostic criteria and were released to the community. A comparison group included adults who were not in the study cohort and had ≥1 opioid-related ED visit. Number of ED visits during 1 year after jail release (cohort) or average jail release date (comparison group) was counted, censoring for time reincarcerated. Accounting for baseline characteristics, rates of ED visits were compared between groups via multivariable Poisson log-linear regression modeling. Of 13,904 individuals released from jail and matched to ED visit records, 88% were male and 38% were black. The mean (± standard deviation) age was 42±11 years. Of 116,385 individuals in the comparison group, most were male (64%) and white (67%) with mean age of 38±14 years. The average number of ED visits during 1 year post-release for study and comparison groups was 4 and 1 visits, respectively. Accounting for age, sex, race, and year of latest discharge from jail, formerly incarcerated individuals were more likely to have had an ED visit (RR: 3.98; 95% CI:3.93-4.04). Individuals with OUD and recent incarcerations were more likely to seek care at EDs than comparison individuals with ≥1 opioid-related visit. Disruptions or lack of access to regular health care and life challenges associated with community reentry might contribute to poor health utilization outcomes among this vulnerable population.

Factors Associated with Ever And Current Blunt Use Among Florida Youth Mohammad Ebrahimi Kalan* 3647] Ebrahimi Kalan Ziyad Ben Taleb Rime Jebai Tera Anderson Zoran Bursac Wasim Maziak

Introduction: Cigar blunting has become a popular mode of consuming marijuana among youths in the US. Little is known about the prevalence and factors associated with ever and current blunt use among youths. This study assessed the prevalence and correlates of ever and current blunt use among youths in Florida. **Methods:** Data came from the 2018 Florida Youth Tobacco Survey (FYTS), a school-based representative sample of middle school (n= 30,021), and high school students (n= 28,051) in 67 counties. This study sample is comprised of 55, 807 students who responded to the blunt use question as never, ever, or current (past 30-day) use. Assessed covariates were demographic characteristics, ever and current tobacco products use, and status of asthma. Weighted multinomial regression analysis was performed to examine the association between covariates and blunt use. Adjusted odds ratios (aORs) and 95% confidence intervals (95% CIs) were reported. **Results:** Overall, the weighted prevalence of ever and current blunt use among adolescents were 9.3% and 13.7%, respectively. Females were more likely to be ever (aOR=1.27, 95% CI=1.15-1.41) and current (1.19, 1.07-1.33) blunt users compared to males. Non-Hispanic (NH) Blacks had greater odds of being ever (1.95, 1.69-2.24) and current (2.38, 2.07-2.74) blunt users compared to NH Whites. Hispanics were more likely to be ever (1.15, 1.02-1.30) blunt users compared to NH Whites. High-schoolers had greater odds of being ever(2.97, 2.66-3.31) and current (2.30, 2.06-2.56) blunt users compared to middle-schoolers. Living with someone who smokes cigars was associated with greater odds of current blunt use (1.39, 1.18-1.64). Ever vaping marijuana THC oil in an e-cigarette device was associated with ever (4.54, 3.55-5.81) and current (12.64, 10.06-15.88) blunt use. Ever and current use of e-cigarettes, cigarettes, hookah, cigars, and smokeless tobacco was significantly associated with ever and current blunt use (p<0.05 for all). Adolescents who currently had asthma were more likely to be current (1.18, 1.00-1.40) blunt users than those without asthma. **Conclusions:** Blunt use prevalence is high among Florida youth. To prevent and reduce the rate of blunt use among youth, statewide tobacco prevention strategies must take into account the popularity of blunt use among youth.

LATEBREAKER

Substance Use

Bully victimization and increased risk of vaping among Texas high school students: analysis of the 2017 Texas Youth Risk Behavior Survey Timothy Ihongbe* 3647] Ihongbe

Introduction

Bullying and vaping among adolescents in the United States is a major public health concern. Bully victimization has been associated with substance use in adolescents. However, the association of bully victimization with vaping in adolescents is unclear. This study aims to examine the independent association between bully victimization and vaping among Texas high school students.

Methods

This study utilized the 2017 Texas Youth Risk Behavior Survey (N = 2,113). Bully victimization was measured as experiencing either traditional bullying or electronic bullying, or both simultaneously, and vaping was measured as a binary variable (Yes/No). Multivariate logistic regression, accounting for the complex survey design and confounding variables, was used to examine the association.

Results

The prevalence of past-year bully victimization was 24.7%. Over one in ten students (10.3%) reported vaping during the past 30 days. The odds of vaping in students who experienced bullying was 1.81 (95% CI=1.03-3.19), compared to students who did not experience bullying.

Conclusions

Findings show that bullying in high school students is independently associated with greater likelihood of vaping. Healthcare providers, school counselors, and educators should be aware of this association while developing intervention programs to address bullying and vaping in high school students.

Substance Use

Applying a flexible, efficient, nonparametric indirect effect estimator to explain differences in opioid treatment responsivity Kara Rudolph* Kara Rudolph Ivan Diaz Sean X Lou Matisyahu Shulman John Rotrosen Edward V Nunes

Drug overdose deaths have increased exponentially with opioids being a primary contributor. A recent comparative effectiveness trial, X:BOT, of extended-release naltrexone (XR-NTX) versus buprenorphine-naloxone (BUP-NX) to prevent opioid relapse was conducted in N=570 patients. Although the treatments, once initiated resulted in similar relapse risk in aggregate, responsiveness differed between homeless vs non-homeless patients. Reasons for these differences have not yet been explored.

Participants were randomized, treated, and followed weekly for up to 24 weeks. We use a novel nonparametric, efficient and robust estimator of interventional indirect effects to estimate mediation path-specific treatment differences on opioid relapse. Our estimator incorporates machine learning into model fitting and accounts for: 1) the presence of a post-treatment, intermediate variable (induction into treatment) and 2) multiple, high-dimensional mediators. We assess the extent to which differences in mediation pathways may explain differences in overall treatment effects on abstinence outcomes between homeless and non-homeless participants.

Homeless patients were nearly 20% less likely to relapse on XR-NTX vs. BUP-NX whereas non-homeless patients were 18% more likely to relapse on XR-NTX. Much of this discrepancy can be explained by differing path-specific effects through the intermediate variable of induction and mediators of adherence and depressive symptoms. Homeless patients on XR-NTX adhered to treatment more of the time and had lower depressive scores over the 24-week follow-up. The opposite was true of nonhomeless patients on XR-NTX. The indirect effect through these mediators explains most of the beneficial effect of XR-NTX in homeless patients (12.7% reduced risk of relapse, 95% CI: 2.7-22.6) and nearly all of the worse effect in nonhomeless patients (19.6% increased risk of relapse, 95% CL: 12.6, 26.5).

LATEBREAKER

Substance Use

Shifting Trends in Opioid Overdose Deaths, Harris County, Texas, 2013-2019 Bethanie Van
Horne* 3647] Van Horne Dorothy Mandell Molly Amelia Eisenhart

While the opioid epidemic is prevalent nationwide, the impact varies greatly within and across
regions.
In Harris County, Texas, home to Houston, cocaine had been a leading cause of overdose death for
decades. However, over the last decade opioid overdoses have increased. As agencies have
increased
their capacity to respond to this new trend, a question arises as to how these deaths track and
compare
to deaths attributed to cocaine. This study was designed to assess whether the geospatial pattern for
deaths attributed to cocaine differed significantly from those attributed to opioids. Recently released
overdose data from 2013-2019 from the Harris County Institute of Forensic Sciences were used.
Place of
injury was geocoded using automated geocoding. The substances attributed to the overdose death
were
coded with a text-based algorithm. Deaths were exclude if a hospital address was given as the place
of
injury, the injury occurred outside Harris County, the person was not between 15 and 64 years old,
or
the manner was suicide or homicide. For the purpose of these analyses, only deaths that were
attributed to cocaine or opioids alone were included (n=1910). All analyses were conducted using
ArcMap and were population corrected at census tract. Preliminary results of point pattern analysis
showed significant differences between cocaine and opioid attributed deaths. Opioid deaths were
more
geospatially distributed and were shifted to the northwest of Harris County, whereas cocaine was
concentrated in central Houston. Hotspot analyses (Getis-Ord Gi*) were also calculated (Figure 1).
Over
time, opioid deaths have shifted from being a suburban phenomenon to, more recently, occurring in
the
center of the county in areas similar to that of historic and current cocaine overdose deaths. These
data
have implications for where outreach efforts and overdose reversal drugs are needed and provide a
look
at how the distribution of these deaths have changed.

2013-2017

Translational & Implementation Science
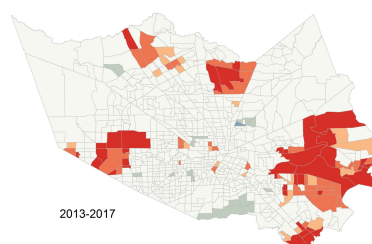
Secondhand smoke exposure in multiunit housing serving low-income residents in New York City: Evaluation of a federal smoking ban in public housing findings using a natural experiment design, 2018-2019 Elle Anastasiou* Elle Anastasiou Katarzyna Wyka Albert Tovar Terry Gordon Brial Elbel Donna Shelley Lorna E. Thorpe

Background: In July 2018, the U.S. Department of Housing and Urban Development passed a rule requiring public housing authorities to implement smoke-free housing (SFH) policies.
Objective: We measured objective secondhand smoke (SHS) incursions immediately before and 12 months after implementation of a federal SFH policy in a purposeful sample of 21 high-rise buildings (>15 floors) in New York City (NYC): 10 NYC Housing Authority (NYCHA) buildings subject to the policy and 11 low-income private sector buildings with no SFH policy where most residents received 'Section 8' federal housing subsidies.
Methods: Prior to SFH policy, we invited participants from non-smoking households (NYCHA n=157, Section 8 n=118) to enroll into a longitudinal air monitoring study to track SHS exposure in homes for 7-day stretches, using: 1) nicotine concentration from passive, bisulfate-coated filters and 2) particulate matter <2.5 µm (PM2.5) from low-cost particle monitors. In common areas (n=91 stairwells and hallways), we measured nicotine concentration and performed visual inspections for cigarette butts. We then conducted two post-policy air monitoring sessions at 6 months (December 2018-March 2019) and 12 months (May 2019-September 2019) post-SFH policy.
Results: We observed slightly larger declines in nicotine concentration in NYCHA hallways compared to Section 8 hallways from pre-policy to 12 months post-policy (difference-in-difference [DID], -0.43 µg/m3, 95% CI -1.26, 0.40). Findings were similar for cigarette butt visual inspections. There was no differential change over time in nicotine concentrations measured in non-smoking households (DID, -0.04 µg/m3, 95% CI -0.24, 0.15) or stairwells (DID, 0.03 µg/m3, 95% CI -0.99, 1.06). Findings suggest greater declines in PM2.5 for Section 8 buildings compared to NYCHA buildings.
Conclusions: Evidence suggests nicotine concentrations in hallways of NYC public housing buildings may be decreasing as a result of SFH policy implementation.

Designing trials for transport: : optimizing trials for translation to diverse Megha L.
Mehrotra* Megha L. Mehrotra Maya Petersen Scott C. Zimmerman David V. Glidden Elvin Geng

Background
Transportability is a causal framework that formalizes how an effect estimated in one population can
be used to identify the effect in another population. Insights from transportability can expedite a
trial's public health impact. However, researchers rarely design trials to ensure that the study's
results can be translated to external settings, and as a result, trials often can't meet the necessary
assumptions for transport. We introduce the concept of a transportable trial: a trial designed to
maximize the potential for its results to be transportable to external settings.

Methods
Guided by transportability theory, we describe key elements of a hypothetical transportable trial
including characteristics of the study population, study measurements, and data availability. We
compare these characteristics to those of pragmatic trials, a popular trial design that aims to
facilitate translation of evidence from trials to practice.

Results
To increase the chances of meeting the transport assumptions, a transportable trial collects
individual-level measurements of important proximal causes of the outcome (including mediators,
causes of mediators, and causes of the outcome). Additionally, it includes study populations that are
heterogeneous with respect to these proximal causes of the outcome. Finally, to ensure that the
trial's data can be used in transport estimators, researchers should plan to make individual-level
data available to other researchers, policy-makers, and public health departments who intend to
transport the results to a new setting. Some of these design choices may be in direct tension to the
goals (or usual practice) of pragmatic trials, which often minimize measurements to mimic usual
clinic settings.

Conclusions
Trial design choices motivated by the principles of transportability can improve translation of trial
results to a wider range of possible target settings.
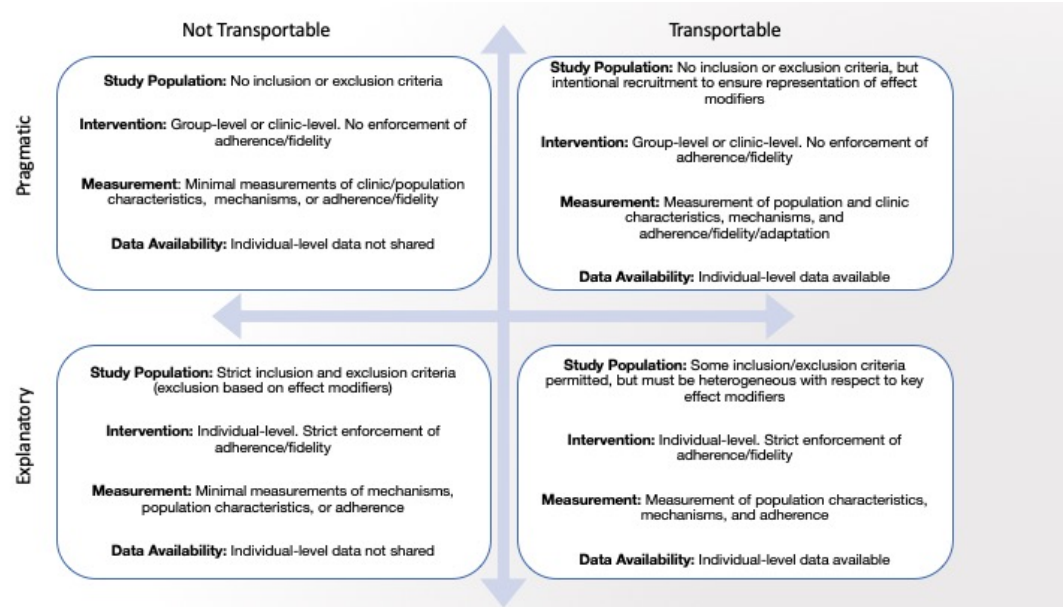
Association of Physical Activity with Mammographic Density Kezhen Fei* Kezhen Fei Russell B. McBride Joseph H. Rothstein Stacey E. Alexeeff Xiaoyu Song Lori C. Sakoda Valerie McGuire Ninah Achacoso Luana Acton Rhea Y. Liang Jafi A. Lipson Daniel L. Rubin Martin J. Yaffe Alice S. Whittemore Laurel A. Habel Weiva Sieh

Background: High mammographic density is a common and strong risk factor for breast cancer that may account for up to one third of the population attributable risk in the US. A better understanding of the relationship of modifiable lifestyle factors, such as physical activity, with mammographic density could inform strategies to reduce breast cancer risk.

Methods: We examined associations of physical activity with percent density (PD), absolute dense area (DA), and nondense area (NDA) in a population-based study of 19,899 women screened using full-field digital mammography (FFDM) Hologic or General Electric machines. Overall physical activity was estimated by the metabolic equivalent of task (MET) using standard methods, and MD measurements were measured centrally using the Cumulus semi-automated method. Machine-specific effects were estimated using multivariable linear regression, and combined using random effects meta-analysis.

Results: Physical activity was positively associated with PD (Ptrend=0.0023), unassociated with DA (Ptrend=0.7050), and inversely associated with NDA (Ptrend<0.0001) adjusting for age, BMI, reproductive factors, alcohol use, and family history of breast cancer. The inverse association of physical activity with NDA was stronger in normal and overweight women than in obese women. In mediation analyses, the positive association of physical activity with PD remained significant after adjusting for DA (Ptrend<0.0001), but was no longer significant after adjusting for NDA (Ptrend=0.4020).

Conclusion: These findings indicate that higher intensity or duration of physical activity may be associated with modestly higher PD through lower NDA, which reflects the amount of breast fat, rather than higher DA, which reflects the amount of fibroglandular tissue. Reductions in breast cancer risk from increased physical activity do not appear to be mediated through lower mammographic density, and are likely to involve independent biological pathways.

Severe maternal morbidity and subsequent risk of postpartum cardiovascular events Abigail Cartus* Abigail Cartus Marian P. Jarlenski, MPH, PhD Katherine P. Himes, MS, MD Ashley I. Naimi, PhD Lisa M. Bodnar, RD, MPH, PhD

Severe maternal morbidity (SMM) refers to a collection of potentially life-threatening peripartum complications (e.g. sepsis, eclampsia) that may impact maternal health. To investigate the association between SMM and risk of cardiovascular events postpartum, we used administrative healthcare data from Pennsylvania Medicaid, 2016-2018, including deliveries with gestational age at delivery from 20-42 weeks and no observed history of non-SMM cardiovascular events (N=137,488). We defined SMM as any ICU admission or any ICD-10 diagnosis or procedure code for SMM occurring antepartum, intrapartum, or ≤ 42 days postpartum. We defined cardiovascular outcomes as any ICD-10 diagnosis code for atrial fibrillation, heart failure, ischemic heart disease, or stroke occurring from 43 days to a mean (SD) follow-up of 352 (270) days postpartum. We used multivariable logistic regression adjusted for maternal race, age, obesity, hypertension, and parity to generate adjusted risk differences. The cumulative incidence of SMM was 45 per 1,000 deliveries (n=4507), while 6.0 per 1000 deliveries had any cardiovascular event > 42 days postpartum (n=785). Deliveries with SMM had a higher incidence of any cardiovascular event than deliveries without SMM (28/1000 compared to 4.9/1000). Cumulative incidences of individual cardiovascular events per 1,000 deliveries were 2.4 (ischemic heart disease), 2.0 (stroke), 1.4 (heart failure), and 0.60 (atrial fibrillation). Compared to deliveries without SMM, deliveries with SMM had 18 excess cases of any cardiovascular event (adjusted risk difference 18 (95% CI 14, 22), 8.8 (6.2, 11) excess cases of heart failure, 6.6 (4.1, 9.1) excess cases of stroke, 5.2 (2.9, 7.5) excess cases of ischemic heart disease, and 1.4 (0.2, 2.6) excess cases of atrial fibrillation. These findings suggest that women who experience SMM may be particularly vulnerable to gaps in care around the 42-day postpartum cutoff and constitute a high-risk population requiring specialized care after delivery.

Women's Health

Exposure to parabens in relation to prospectively-assessed metabolic syndrome among Mexican women undergoing a menopausal transition: Findings from the Study of Early Life Exposures in Mexico to Environmental Toxicants (ELEMENT)

Astrid N. Zamora* Astrid Zamora Erica Jansen Karen E. Peterson Deborah Watkins Juan Alfredo Tamayo-Orozco Martha M. Téllez-Rojo Ana Baylin Brisa N. Sánchez John D. Meeker Marcela Tamayo-Ortiz

Introduction: Evidence suggests that exposure to endocrine-disrupting chemicals (EDCs) can influence risk of Metabolic Syndrome (MetS) in general adult populations, but is unclear whether EDCs impact women during the menopausal transition, a life course period characterized by an increased risk of MetS due to hormonal changes. Parabens are a class of EDCs found in personal care and beauty products; thus, women may be at increased risk of exposure. We examined whether paraben exposure in mid-adulthood is prospectively associated with MetS among women of peri-/menopausal age.

Methods: Urinary parabens (butyl-paraben (BP), ethyl-paraben (EP), methyl-paraben (MP), propyl-paraben (PP)) were measured in 2008 in 72 women from the Early Life Exposures in Mexico to ENvironmental Toxicants (ELEMENT) cohort. MetS components (i.e. fasting blood glucose, triglycerides, HDL cholesterol, fasting blood pressure (bp), waist circumference) were assessed in a follow-up visit approximately 10 years later. Using logistic regression models, we regressed diastolic and systolic bp, components of MetS and overall MetS, respectively on log-transformed paraben metabolite concentrations, adjusting for age.

Results: At follow-up, the mean age in years among women was 45.6 (± 5.8) and the prevalence of MetS was 33%. For every one interquartile range (IQR) unit increase in the concentration of BP, PP, MP, and EP, the odds ratios for high diastolic blood pressure were 2.6 (95% CI: -0.5 5.7), 4.7 (95% CI: 0.9, 8.5), 3.1 (95% CI: -0.7, 7.0), 1.6 (95%CI: -2.7, 5.9) higher, respectively. The association for PP was statistically significant at a p-value of 0.02.

Conclusion: Pilot analyses suggest paraben metabolites are among EDCs that may predict higher blood pressure in peri-/menopausal women 10 years later. Longitudinal studies with larger sample size that account for hormonal changes are necessary to confirm these findings.

The Relationship Between Adverse Childhood Experiences and Maternal Depression in Rural Pakistan

Katherine LeMasters* Katherine LeMasters Brooke S. Staley Lisa Bates Esther O. Chung Ashley Hagaman Elissa Scherer Siham Sikander Elizabeth Turner Joanna Maselko

Background: Adverse childhood experiences (ACEs) increase risk for depression in adulthood. While the prevalence of perinatal depression is nearly 20% in low- and middle-income countries, little work examines the relationship between ACEs and maternal depression in these settings. This study estimates the overall relationship between ACEs and depression and assesses which specific ACEs are associated with increased risk among women in rural Pakistan.

Methods: Data come from the 36-month postpartum wave of the Bachpan birth-cohort in rural Pakistan (n=889). Major depressive episodes (MDE) were assessed with the Structured Clinical Interview for DSM-IV (SCID) and depressive symptom severity with the Patient Health Questionnaire-9. ACEs were measured with an adapted ACE International Questionnaire, and both total ACEs and separate grouped domains (i.e., home violence) were analyzed. Multivariable Poisson and linear mixed models were used for analyses.

Results: About 23% of women had MDE and 17% had moderate depressive symptoms. The majority (58%) experienced at least one ACE domain, most commonly home violence (38%). Total ACE score was associated with poor mental health. Women experiencing four or more ACEs had the most pronounced increase in symptom severity (Mean Difference (MD)=3.37; 95% CI=1.67,5.06). Exposure to specific ACE domains, such as family distress, was also positively related to MDE (Prevalence Ratio=1.45; 95% CI=1.11,1.89) and symptom severity (MD=1.87; 95% CI=0.65,3.10).

Conclusions: These findings highlight women's lifelong experiences as important factors to understanding current mental health in rural Pakistan. They also signal the need for a life course perspective for addressing women's mental health. Global health practitioners should address women's ACEs within mental health interventions to ensure that they receive appropriate psychosocial and mental health support.

Figure 1: Maternal ACEs and Depression, Bachpan Cohort, Pakistan, N=889
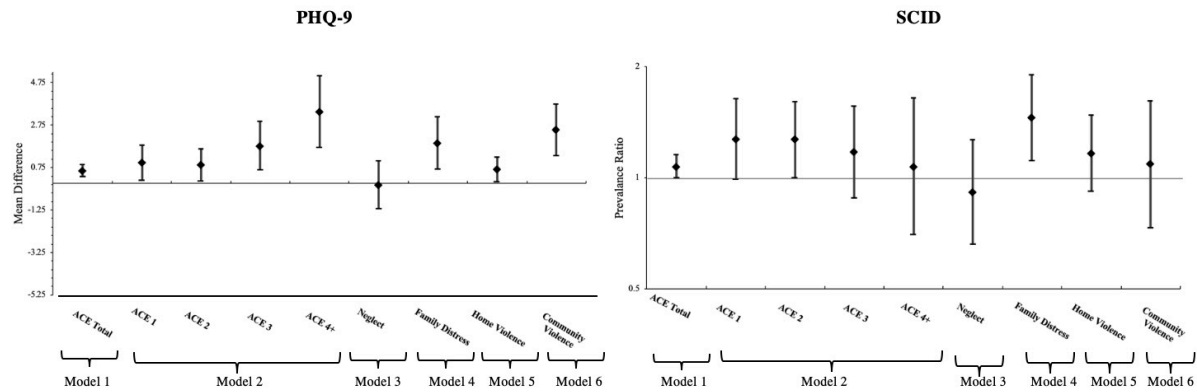
All models adjusted for clustering and used probability weights. Adjusted for maternal age, women's education, and mental health problems in natal family as confounders. Adjusted for people per room, number of living children, and living with child's grandmother for missingness associations and for trial arm and assessor. SCID models were conducted using log-Poisson regressions accounting for inflated variance
PHQ-9 models were conducted using mixed effects models with an identity link
Neglect Domain contains emotional neglect and physical neglect. Family Distress Domain includes alcohol or drug abuser in the household; incarcerated household member; someone depressed, mentally ill, institutionalized, or suicidal; or no or one parent, parental separation, or divorce. Home Violence Domain includes physical abuse, emotional abuse, or household member treated violently. Community Violence Domain includes bullying, community violence, or collective violence.

Women's Health

Estimating the prevalence of hirsutism in a cohort of young African-American women Helen Chin* Helen Chin Donna Baird

Hirsutism, a common symptom of hyperandrogenism, is characterized by excess, male pattern terminal hair growth in women, and can be a clinical characteristic of polycystic ovary syndrome (PCOS). The modified Ferriman-Gallwey (mFG) score (0-36) is a common scale used to diagnose hirsutism. The mFG assesses hair growth patterns on 9 areas of the body using illustrations depicting varying degrees of dark hair growth on a scale of 0 (no terminal hair) to 4 (typical male pattern hair growth). It was developed in a predominantly white population (n=161), and an arbitrary cutoff of 8 was used as evidence of hirsutism, a cutoff that has continued to be used. The prevalence of hirsutism in the general population and in racially and ethnically diverse groups is not established but estimates range from 5-10%. Using data from the Study of Environment, Lifestyle and Fibroids, a cohort of young African-American women, we estimated the prevalence of hirsutism using the mFG. The instrument was a supplemental questionnaire introduced at the 3rd study visit. It was presented to 1568 of the 1693 participants, and data are available for 98%. Most women (70%) reported some dark hair growth on at least one area of the body, and 10% of women had hirsutism (a score of 8 or more). Dark hair was reported most commonly on the upper lip, lower face and neck, stomach, and below the belly button. Reporting long menstrual cycles vs. normal cycles was associated with hirsutism (PR=2.3, 95% CI: 1.4, 3.7), as was reporting doctor diagnosed PCOS vs. no PCOS (PR= 2.4, 95% CI: 1.5, 3.7). These results contribute to the establishment of population-specific normative ranges for excess hair growth on both the total body and individual body areas. Minimal missing data suggests women are comfortable answering questions about their hair growth patterns. Incorporating these types of questions in large cohort studies provides an opportunity to study the epidemiology of hirsutism in diverse populations.

Urinary Tract Infections Among Older Adult Women in the United States: Findings from the Urologic Diseases in America Project Lydia Feinstein* Lydia Feinstein Julia B Ward Kevin C Abbott Tamara Bavendam Ziya Kirkali John Lim Erline Martinez-Miller Casey Pierce Brian R Matlaga

Introduction: Urinary tract infections (UTIs) are the most common outpatient infections and occur more often in women than men, with older adult women at highest risk. As part of the Urologic Diseases in America project, we assessed trends in the burden of UTI and its clinical management among women aged ≥65 years using 10-years of administrative claims data.

Methods: We analyzed data from female beneficiaries in the 2007-2016 Centers for Medicare & Medicaid Services Medicare 5% Sample (N≈365,000 annually). UTI was defined as an outpatient claim with a UTI-related diagnosis code followed by a pharmacy claim for an anti-infectious agent within 72 hours. UTI prevalence was calculated annually and averaged across the study period. Among UTI cases (N=730,224), we assessed trends in UTI-related medication use, 12-month UTI recurrence following initial infection, and comorbid conditions.

Results: From 2007-2016, the average annual prevalence of UTI was 13%, with little change over time (range: 12-13%). Women experienced a mean of 2 UTI episodes annually, with 21% experiencing at least 3 episodes annually. The 12-month cumulative probability of UTI recurrence was 44%, with most recurrent infections occurring within the first 6 months (Figure 1). The most commonly used medications to treat UTI were quinolones (41%), urinary anti-infectives (20%), and sulfonamides (15%). Approximately 35% of UTI cases were prescribed medications for longer than 7 days. Comorbid conditions were common among women with UTI, particularly diabetes mellitus (33%), ischemic heart disease (32%), and chronic kidney disease (21%).

Conclusions: There is a high UTI burden among older adult women in the United States. UTI recurrence is common, which may warrant closer monitoring for drug resistance in this population. Treatment duration for many women appeared to be longer than what guidelines typically suggest (3-7 days), representing an opportunity for practice improvement.

Figure 1. 12-month cumulative probability of UTI recurrence among female Medicare beneficiaries aged ≥65 years, 2007-2016
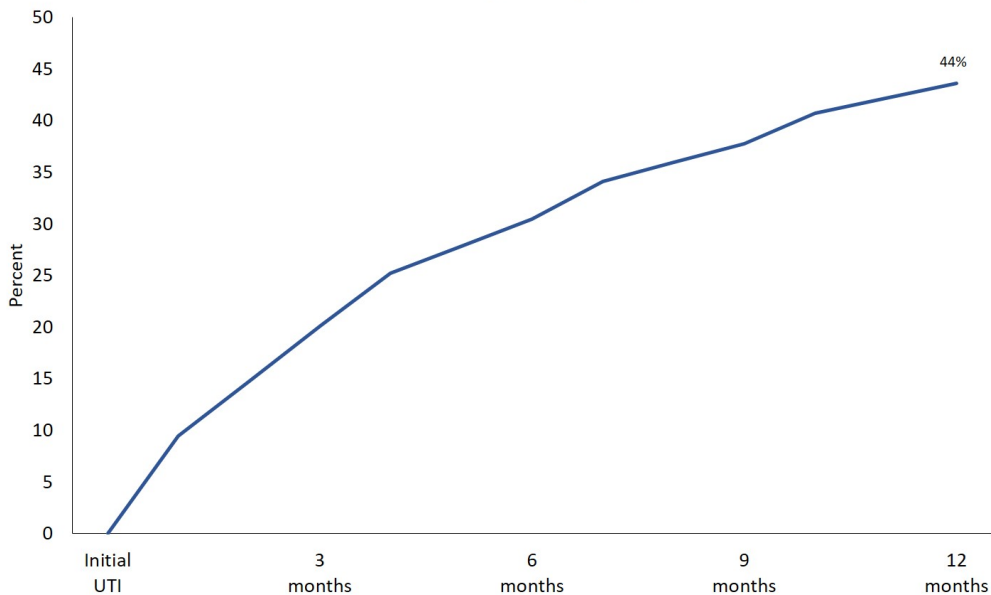
Frequency of opioid dispensing after surgical abortion in the US Liza R Gibbs* Liza Gibbs

Julia A Pisc Kari P Braaten Brian T Bateman Elizabeth M Garry

Background: Over 800,000 induced abortions occur annually in the US, of which 2/3 are surgical. NSAIDs, not opioids, are recommended for pain management after surgical abortion. Objective: Characterization of opioid fills among US commercially insured women after surgical abortion. Methods: Women aged 15-50y with an outpatient claim for dilation and curettage or evacuation surgical abortion (D&C/D&E) were identified in IBM MarketScan 2015-2018, excluding those with >1 opioid fill in the prior 90d, evidence of opioid dependence or abuse in the prior 180d (baseline), or spontaneous abortion or mifespristone use in 7d prior. The frequency of oral opioid dispensing within 7d after abortion, refill in 6w after initial fill, chronic use (≥6 fills) in 1y after abortion or initial fill, and median morphine milligram equivalent (MME) total dose of initial fill were described. Multivariable logistic regression was used to evaluate predictors of opioid fill. Results: Among 28,304 women who underwent induced surgical abortion, 8.3% had an opioid fill within 7d. The strongest predictors of opioid fill were non-Northeast region [aOR(95%CI) West: 8.25(7.23-9.42); South: 7.74(6.75-8.87); Midwest: 5.12(4.37-5.98)], moderate sedation for the procedure [1.57(1.36-1.80)], and baseline depression [1.41(1.24-1.61)]. The median(IQR) MME dose was 75(50-113), which was increased for women with abortion complications [90(75-150)]. Of those with an opioid fill and 6w follow-up (N=2,257), 10.0% had a refill. Complication was the strongest predictor of refill [2.98(1.59-5.59)]. Among women with 1y follow-up, chronic use was identified among 2.2% of women with an initial fill (N=1,396), versus 0.3% among those without (N=13,942). Conclusion: The frequency of an opioid fill after surgical abortion among commercially insured women was high given recommendations that NSAIDs be used for clinical analgesia. Opioid prescribing contrary to recommendations may increase the potential for misuse or abuse.

Predictors of opioid dispensing following surgical abortion

* Provider type not mutually exclusive

Women's Health
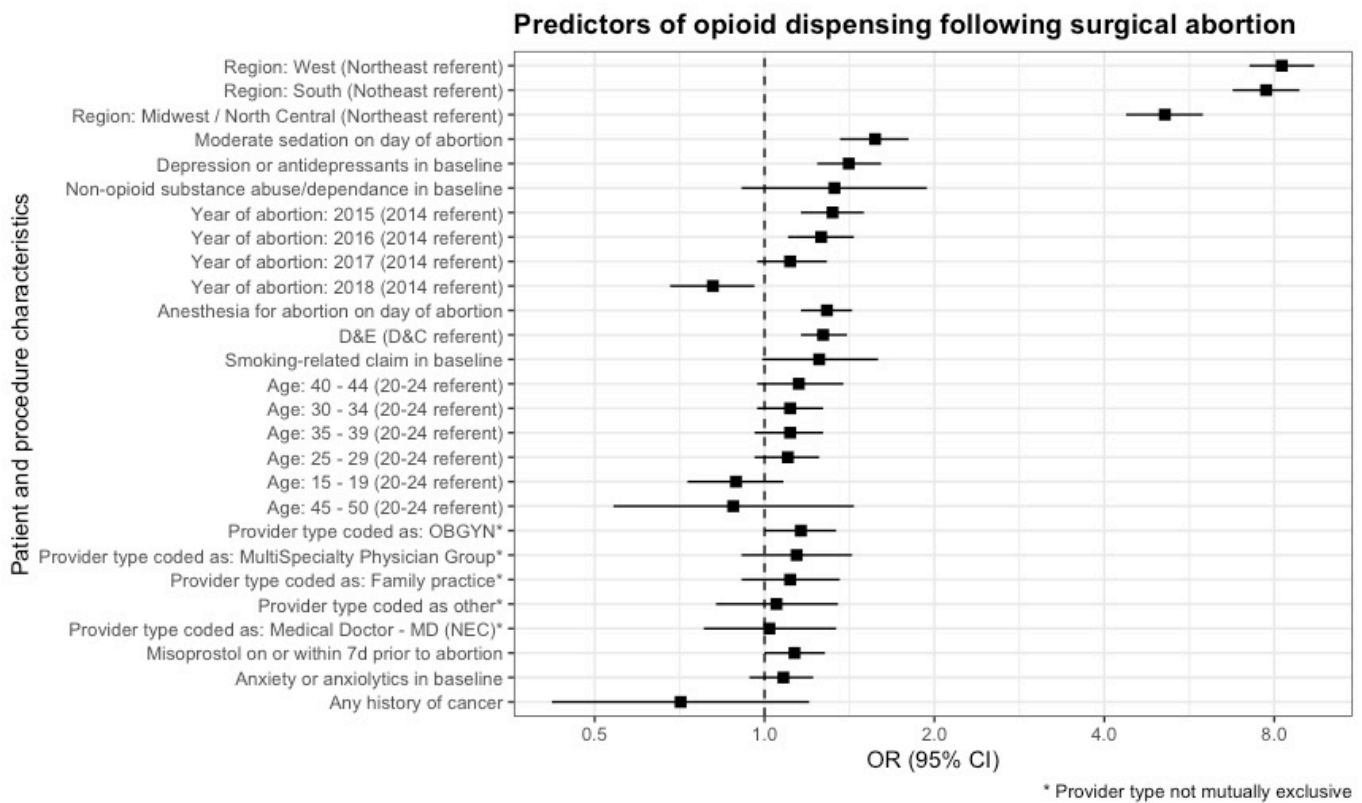
Neighborhood deprivation and preterm birth: The mediating influence of neighborhood violence Timothy Ihongbe* Timothy Ihongbe Juan Lu

Background: Neighborhood deprivation has been reported to be associated with preterm birth. Neighborhood violence may mediate the association; however, the mediating influence of neighborhood violence has been unexplored in epidemiologic studies. This study, using a geographically defined cohort of women in Richmond city, Virginia, aimed to examine the mediating influence of neighborhood violence on the association between neighborhood deprivation and preterm birth.

Methods: Merged data from the vital statistics live birth records, police crime reports, and census data for Richmond city, Virginia, between 2006 and 2015 was analyzed. Data had a 2-level hierarchical structure with live births nested in 66 census tracts. Neighborhood deprivation was measured using the Neighborhood Deprivation Index (NDI) based on a previously validated algorithm. Multilevel structural equation modeling was used to examine the mediating influence of neighborhood violence on the association between neighborhood deprivation and preterm birth.

Results: Prevalence of preterm birth in the study population was 10.1% and the violence rate was 114.1 per 1000 youth population in Richmond city during the study period. The median NDI score across all census tracts was 0.09, with an interquartile range of –0.69 to 0.76. There was a significant direct effect between neighborhood deprivation and preterm birth (β=0.304, 95% CI=0.231, 0.377). However, the indirect effect of neighborhood deprivation on preterm birth through neighborhood violence was not significant (β=0.063, 95% CI= –0.025, 0.151).

Conclusions: Although, neighborhood deprivation was significantly associated with increased risk of preterm birth in women in Richmond city, Virginia, neighborhood violence does not mediate the association between neighborhood deprivation and preterm birth.

Figure 1. Unstandardized effects (β and SE) of neighborhood deprivation on preterm birth, Richmond city, Virginia, 2006-2015

Table 1. Direct and indirect effects of neighborhood deprivation on preterm birth, Richmond city, Virginia, 2006-2015

Neighborhood deprivation	Preterm birth	
	β	95% CI
Total effect	0.367	0.239, 0.495*
Direct Effect	0.304	0.231, 0.377*
Indirect Effect	0.063	–0.025, 0.151

* 95% CI does not contain 0

Women's Health

Lead exposure during pregnancy and its longitudinal association with BMI among Mexican women Laura C. Arboleda-Merino* Laura Arboleda-Merino Nicole Kasper Erica C. Jansen Brisa Sanchez Deborah J. Watkins Marcela Tamayo-Ortiz Adriana Mercado-Garcia Martha Maria Tellez-Rojo Karen E. Peterson

Introduction: Pregnancy is a vulnerable period for higher lead (Pb) exposure in mothers, as Pb stored in bone is released into the blood during increased, pregnancy-related bone turnover. Pregnancy Pb exposure is associated with hypertension and gestational diabetes, but its association with adiposity is unclear. Thus, we examined the long term association between blood Pb levels during pregnancy (pregnancy Pb) and BMI during postpartum and into the peri-/menopausal period.
Methods: The geometric means of pregnancy Pb were calculated in 588 Mexican women. BMI was measured at up to 7 follow up visits from 1 month to 21 years postpartum. In linear regression models, we evaluated the association between pregnancy Pb and BMI at each visit adjusting for weeks postpartum, and baseline (first prenatal visit) characteristics including BMI, age, years of education, and parity. We evaluated the longitudinal association between exposure and outcome using mixed models.
Results: Participants were 26.5 (SD=5.5) years old at baseline, with a BMI of 25.7 (SD = 4.0). Average pregnancy Pb was 5.2 (SD= 3.4) ug/dL, with an interquartile range of 3.7 ug/dL. In adjusted models, one IQR-increase in pregnancy Pb was associated with 0.20 (95% CI= -0.34, -0.06, p=0.006) and 0.15 (95% CI= -0.30, -0.008, p=0.04) kg/m2 lower BMI at 1 and 4 months post-partum, respectively, and 0.66 (95% CI= 0.07, 1.24, p= 0.03) kg/m2 higher BMI at 21 years post-partum. In adjusted mixed models including a pregnancy Pb and time interaction, one IQR-increase in pregnancy Pb was related to 0.16 (95% CI= -0.30, -0.03, p= 0.02) kg/m2 lower BMI throughout follow-up, with evidence that the direction of this association reversed over time (p for interaction=0.07).
Conclusion: Findings suggest an inverse association between blood Pb levels during pregnancy and BMI in the early postpartum period, but the relationship changed over time such that women with higher pregnancy Pb levels had higher BMI during peri-/menopause.

Mental health among women with young children in South Africa; a nationally representative study Elysia Larson* Elysia Larson Ellen Moscoe

Background: Mental health disorders are an important source of morbidity in sub-Saharan Africa, but there is strikingly little nationally representative evidence on their incidence across the lifecourse. In particular, depression among women with young children contributes to women's poor mental health around the world and is especially relevant in high-fertility settings with low access to mental health services.

Methods: We used 5 waves of longitudinal data from South Africa's National Income Dynamics Study (2008-2017) to assess the prevalence of depressive symptoms among women with children under 1 and 5 years old, as measured by the 10-item Center for Epidemiologic Studies Depression scale (CES-D-10). The primary outcome was the continuous CES-D-10 score while the secondary outcome was an indicator of CES-D-10>10 which indicates depression. Regression models included linear time trends, controlled for age, race, and household income, and standard errors were clustered to reflect the sampling design.

Results: Between 2008-2017, the proportion of women with CES-D-10 scores exceeding the cut-off for depression fell from 32% to 20% among women who have children, and from 24% to 15% among women with no children. We found that having a child under 1 year of age was associated with CES-D-10 scores that were 0.15 points higher (95% CI 0.01-0.28, p=0.028) than for all other women, and having a child under 5 years of age was associated with CES-D-10 scores that were 0.20 points higher (95%CI 0.1-0.30, p<0.001) than for women without children under five.

Conclusions: In a context of high health system use for childbirth, but low access to mental health care, the risk of depressive symptoms for women with young children is very high. Ongoing research using longitudinal, multilevel models to estimate the effect of childbirth on depression incidence will shed light on important periods during the life course for mental health evaluation and intervention.

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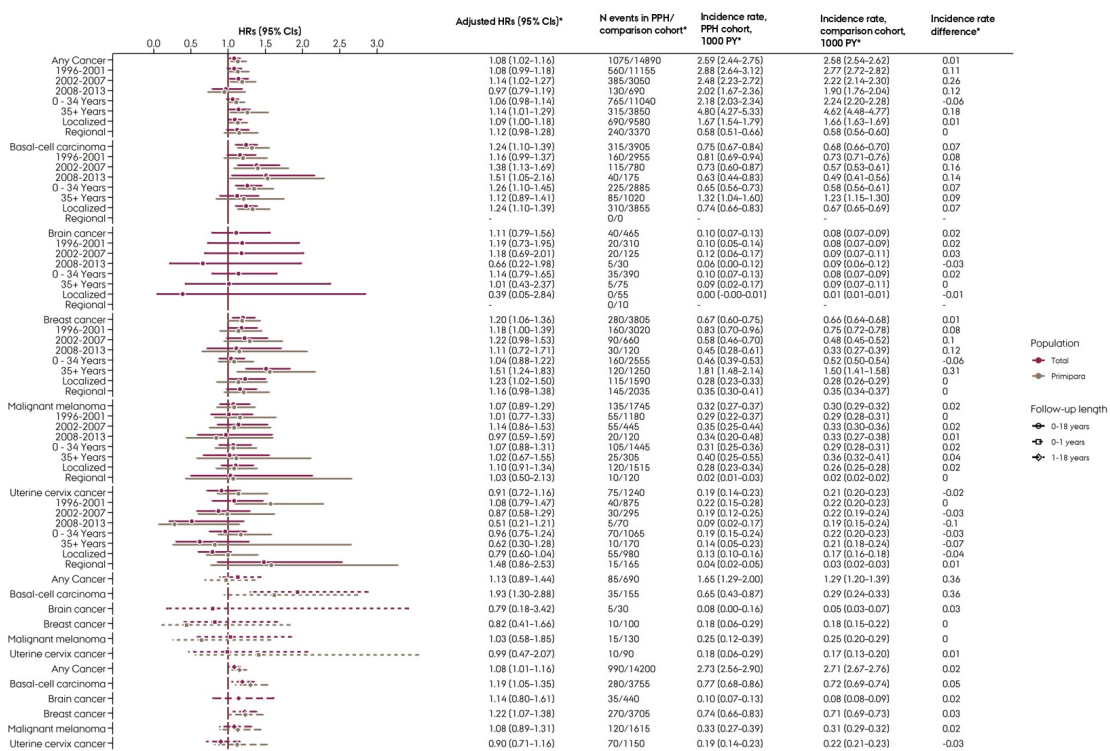## Postpartum hemorrhage as a marker of cancer: a population-based nationwide cohort study in Denmark

Elena Dudukina* Elena Dudukina Katalin Veres Erzsébet Horváth-Puhó Henrik Toft Sørensen Vera Ehrenstein

Background: Risk factors leading to postpartum hemorrhage (PPH) that are unrelated to pregnancy are not a common target for investigation. We hypothesized that PPH may be a marker of clinically silent cancer.

Methods: We used the Danish registries to assemble a population of women cancer-free before the delivery date and having a singleton, 1996-2013 (n=587240). The PPH cohort included women with an incident hospital diagnosis of PPH between the delivery date and the end of 12th postpartum week. Eligible women without PPH comprised a comparison cohort. For both cohorts, we computed incidence rates of any cancer, common site-specific cancers, and cancers with local vs regional spread. We used Cox proportional hazards model to compute hazard ratios (HRs) of cancer (with the 95% CIs), adjusted for calendar period, age, chronic pulmonary disease, obesity, diabetes, subfertility, smoking, and parity. We followed the cohorts until the diagnosis of cancer, death (competing event), emigration, or study end, whichever was the earliest. We computed cancer HRs by the calendar year, age group, and follow-up length. We repeated the analyses for primiparous women.

Results: The PPH cohort comprised 51224 and 27885 women in the total and primiparous populations, respectively. PPH cohort was at 1.1-fold (0.9-1.4) increased hazard of any cancer within the first year of follow-up and at 1.1-fold (1.0-1.2) increased hazard of any cancer at 18 years of follow-up. The HR for the primiparous population was 1.0 (0.7-1.4) in the first year and 1.1 (1.1–1.2) at 18 years of follow-up. The differences in cancer rates (per 1000 PY) were small (Figure).

Conclusion: The magnitude of the association between PPH and cancer was small and possibly driven by unmeasured moderately different lifestyles in women from PPH and comparison cohort. We found no evidence for the hypothesis of PPH being a marker of clinically silent cancer.

	Adjusted HRs (95% CIs)*	N events in PPH/comparison cohort*	Incidence rate, PPH cohort, 1000 PY*	Incidence rate, comparison cohort, 1000 PY*	Incidence rate difference*
Any Cancer	1.08 (1.02–1.16)	1075/14890	2.59 (2.44–2.75)	2.58 (2.54–2.62)	0.01
1996-2001	1.08 (0.99–1.18)	560/11155	2.88 (2.64–3.12)	2.77 (2.72–2.82)	0.11
2002-2007	1.14 (1.02–1.27)	385/3050	2.48 (2.23–2.72)	2.22 (2.14–2.30)	0.26
2008-2013	0.97 (0.79–1.19)	130/690	2.02 (1.67–2.36)	1.90 (1.76–2.04)	0.12
0 - 34 Years	1.06 (0.98–1.14)	765/11040	2.18 (2.03–2.34)	2.24 (2.20–2.28)	-0.06
35+ Years	1.14 (1.01–1.29)	315/3850	4.80 (4.27–5.33)	4.62 (4.48–4.77)	0.18
Localized	1.09 (1.00–1.18)	690/9580	1.67 (1.54–1.79)	1.66 (1.63–1.69)	0.01
Regional	1.12 (0.98–1.28)	240/3370	0.58 (0.51–0.66)	0.58 (0.56–0.60)	0
Basal-cell carcinoma	1.24 (1.10–1.39)	315/3905	0.75 (0.67–0.84)	0.68 (0.66–0.70)	0.07
1996-2001	1.16 (0.99–1.37)	160/2955	0.81 (0.69–0.94)	0.73 (0.71–0.76)	0.08
2002-2007	1.38 (1.13–1.69)	115/780	0.73 (0.60–0.87)	0.57 (0.53–0.61)	0.16
2008-2013	1.51 (1.05–2.16)	40/175	0.63 (0.44–0.83)	0.49 (0.41–0.56)	0.14
0 - 34 Years	1.26 (1.10–1.45)	225/2885	0.65 (0.56–0.73)	0.58 (0.56–0.61)	0.07
35+ Years	1.12 (0.89–1.41)	85/1020	1.32 (1.04–1.60)	1.23 (1.15–1.30)	0.09
Localized	1.24 (1.10–1.39)	310/3855	0.74 (0.66–0.83)	0.67 (0.65–0.69)	0.07
Regional	-	0/0	-	-	-
Brain cancer	1.11 (0.79–1.56)	40/465	0.10 (0.07–0.13)	0.08 (0.07–0.09)	0.02
1996-2001	1.19 (0.73–1.95)	20/310	0.10 (0.05–0.14)	0.08 (0.07–0.09)	0.02
2002-2007	1.18 (0.69–2.01)	20/125	0.12 (0.06–0.17)	0.09 (0.07–0.11)	0.03
2008-2013	0.66 (0.22–1.98)	5/30	0.06 (0.00–0.12)	0.09 (0.06–0.12)	-0.03
0 - 34 Years	1.14 (0.79–1.65)	35/390	0.10 (0.07–0.13)	0.08 (0.07–0.09)	0.02
35+ Years	1.01 (0.43–2.37)	5/75	0.09 (0.02–0.17)	0.09 (0.07–0.11)	0
Localized	0.39 (0.05–2.84)	0/55	0.00 (-0.00–0.01)	0.01 (0.01–0.01)	-0.01
Regional	-	0/10	-	-	-
Breast cancer	1.20 (1.06–1.36)	280/3805	0.67 (0.60–0.75)	0.66 (0.64–0.68)	0.01
1996-2001	1.18 (1.00–1.39)	160/3020	0.83 (0.70–0.96)	0.75 (0.72–0.78)	0.08
2002-2007	1.22 (0.98–1.53)	90/660	0.58 (0.46–0.70)	0.48 (0.45–0.52)	0.1
2008-2013	1.11 (0.72–1.71)	30/120	0.45 (0.28–0.61)	0.33 (0.27–0.39)	0.12
0 - 34 Years	0.96 (0.88–1.22)	160/2555	0.46 (0.39–0.53)	0.52 (0.50–0.54)	-0.06
35+ Years	1.51 (1.24–1.83)	120/1250	1.81 (1.48–2.14)	1.50 (1.41–1.58)	0.31
Localized	1.23 (1.02–1.50)	115/1590	0.28 (0.23–0.33)	0.28 (0.26–0.29)	0
Regional	1.16 (0.98–1.38)	145/2035	0.35 (0.30–0.41)	0.35 (0.34–0.37)	0
Malignant melanoma	1.07 (0.89–1.29)	135/1745	0.32 (0.27–0.37)	0.30 (0.29–0.32)	0.02
1996-2001	1.01 (0.77–1.33)	55/1180	0.29 (0.22–0.37)	0.29 (0.28–0.31)	0
2002-2007	1.14 (0.86–1.53)	55/445	0.35 (0.25–0.44)	0.33 (0.30–0.36)	0.02
2008-2013	0.97 (0.59–1.59)	20/120	0.34 (0.20–0.48)	0.33 (0.27–0.38)	0.01
0 - 34 Years	1.07 (0.88–1.31)	105/1445	0.31 (0.25–0.36)	0.29 (0.28–0.31)	0.02
35+ Years	1.02 (0.67–1.55)	25/305	0.40 (0.25–0.55)	0.36 (0.32–0.41)	0.04
Localized	1.10 (0.91–1.34)	120/1515	0.28 (0.23–0.34)	0.26 (0.25–0.28)	0.02
Regional	1.03 (0.50–2.13)	10/120	0.02 (0.01–0.03)	0.02 (0.02–0.02)	0
Uterine cervix cancer	0.91 (0.72–1.16)	75/1240	0.19 (0.14–0.23)	0.21 (0.20–0.23)	-0.02
1996-2001	1.08 (0.79–1.47)	40/875	0.22 (0.15–0.28)	0.22 (0.20–0.23)	0
2002-2007	0.87 (0.58–1.29)	30/295	0.19 (0.11–0.26)	0.22 (0.19–0.24)	-0.03
2008-2013	0.51 (0.21–1.21)	5/70	0.09 (0.02–0.17)	0.19 (0.15–0.24)	-0.1
0 - 34 Years	0.96 (0.75–1.24)	70/1065	0.19 (0.15–0.24)	0.22 (0.20–0.23)	-0.03
35+ Years	0.62 (0.30–1.28)	10/170	0.14 (0.05–0.23)	0.21 (0.18–0.24)	-0.07
Localized	0.79 (0.60–1.04)	55/980	0.13 (0.10–0.16)	0.17 (0.16–0.18)	-0.04
Regional	1.48 (0.86–2.53)	15/165	0.04 (0.00–0.06)	0.03 (0.02–0.03)	0.01
Any Cancer	1.13 (0.89–1.44)	85/690	1.65 (1.29–2.00)	1.29 (1.20–1.39)	0.36
Basal-cell carcinoma	1.93 (1.30–2.88)	35/155	0.65 (0.43–0.87)	0.29 (0.24–0.33)	0.36
Brain cancer	0.79 (0.18–3.42)	5/30	0.08 (0.00–0.16)	0.05 (0.03–0.07)	0.03
Breast cancer	0.82 (0.41–1.66)	10/100	0.18 (0.06–0.29)	0.18 (0.15–0.22)	0
Malignant melanoma	1.03 (0.58–1.85)	15/130	0.25 (0.12–0.39)	0.25 (0.20–0.29)	0
Uterine cervix cancer	0.99 (0.47–2.07)	10/90	0.18 (0.06–0.29)	0.17 (0.13–0.20)	0.01
Any Cancer	1.08 (1.01–1.16)	990/14200	2.73 (2.56–2.90)	2.71 (2.67–2.76)	0.02
Basal-cell carcinoma	1.19 (1.05–1.35)	280/3755	0.77 (0.68–0.86)	0.72 (0.69–0.74)	0.05
Brain cancer	1.14 (0.80–1.61)	35/440	0.10 (0.07–0.13)	0.08 (0.08–0.09)	0.02
Breast cancer	1.22 (1.07–1.38)	270/3705	0.74 (0.66–0.83)	0.71 (0.69–0.73)	0.03
Malignant melanoma	1.08 (0.89–1.31)	120/1615	0.33 (0.27–0.38)	0.31 (0.29–0.32)	0.02
Uterine cervix cancer	0.90 (0.71–1.16)	70/1150	0.19 (0.14–0.23)	0.22 (0.21–0.23)	-0.03

Population: Total, Primipara

Follow-up length: 0-18 years, 0-1 years, 1-18 years

* Presented for the total population. The HRs were adjusted for chronic pulmonary disease, obesity, diabetes, subfertility, smoking, and parity (in the total population)

Women's Health

Association of lifetime interpersonal violence with urinary tract infections and painful bladder symptoms in a multiethnic cohort of community-dwelling middle-aged to older women in California Eva Raphael* Eva Raphael Stephen K. Van Den Eeden Cesar Hernandez Michael Schembri David Thom Alison Huang

Background

Prior research suggests that women are more likely to present with genitourinary complaints and infections in the immediate aftermath of exposure to interpersonal violence, but little is known about longer-term effects on urinary function and risk over their lifetime. We examined relationships between interpersonal violence exposures and bladder pain and UTI in community dwelling older women.

Methods

We examined cross-sectional data from a multiethnic cohort of 2,016 women aged 40 to 80 years enrolled in Kaiser Permanente Northern California, an integrated health care delivery system. During interviews in 2008-2012, women completed questionnaires about interpersonal violence exposures, as well as ever having an antibiotic-treated UTI and any painful bladder symptoms in the prior 3 months. We examined the association of each type of interpersonal violence with: a) ever having a UTI and b) current painful bladder using logistic regression models.

Results

Among the 2,016 women, 36% were Caucasian, 22% Black, 23% Latina and 20% Asian. Twenty-seven percent reported at least one lifetime interpersonal violence exposure, 60% ever had a UTI, and 22% reported pain with urination. Lifetime experience of physical intimate partner violence (IPV) was strongly associated with ever having a UTI (OR 1.52, 95% CI 1.18, 1.97), emotional or verbal IPV (OR 2.00, 95% CI 1.58, 2.53), and sexual assault (OR 1.68, 95% CI 1.32, 2.13). Lifetime experience of physical IPV was associated with any current bladder pain symptoms (OR 1.36, 95% CI 1.04, 1.79), as was emotional or verbal IPV (OR 1.32, 95% CI 1.03, 1.69), and sexual assault (OR 1.44, 95% CI 1.12, 1.86).

Conclusions

Lifetime experience of interpersonal violence was associated with ever having a UTI and current painful bladder symptoms in middle-aged to older women. Findings from this large community-based cohort suggest that interpersonal violence may be an under-recognized marker of risk for painful bladder and UTI.

	Number of participants/Total (%)	OR (95% CI)	P-value*
Women with ever having an antibiotic-treated UTI	1197/2002 (59.8)		
Physical IPV			
Yes	212 (67.9)	1.52 (1.18, 1.97)	<0.01
No	957 (58.2)		
Emotional/verbal IPV			
Yes	303 (72.1)	2.00 (1.58, 2.53)	<0.01
No	866 (56.5)		
Sexual assault			
Yes	263 (69.2)	1.68 (1.32, 2.13)	<0.01
No	893 (57.2)		
Women with at least mild bladder pain in the last 3 months	447/2016 (22.2)		
Physical IPV			
Yes	86 (27.2)	1.36 (1.04, 1.79)	0.03
No	356 (21.5)		
Emotional/verbal IPV			
Yes	112 (26.5)	1.32 (1.03, 1.69)	0.03
No	331 (21.4)		
Sexual assault			
Yes	106 (27.7)	1.44 (1.12, 1.86)	<0.01
No	331 (21.1)		

*P-values derived from Chi-Square test of association.

Women's Health

A retrospective cohort study of race and ethnicity, pre-pregnancy weight, and pregnancy complications Ruchi Tiwari* Ruchi Tiwari Daniel A. Enquobahrie Pandora L. Wander Ian Painter Vivienne Souter

Objective: To examine relationships between race/ethnicity, pre-pregnancy overweight/obesity status, and pregnancy complications.
Methods: We conducted a retrospective cohort study among mothers with singleton live births in hospitals contributing to the Obstetrical Clinical Outcomes Assessment Program database (N=72,697). Race was categorized as Non-Hispanic White (NH-W), NH African-American (NH-AA), Hispanic, NH Asian (NH-A), NH American Indian/Alaskan Native (NH-AI/AN), and NH Native-Hawaiian/Other Pacific Islander (NH-NHP). Overweight/obesity status was defined as body mass index (BMI)≥25kg/m2. Pregnancy complications evaluated were gestational diabetes (GDM), pre-eclampsia, and cesarean delivery(CS). We fitted adjusted and unadjusted stratified Poisson regression models with robust standard errors. Interaction terms were used to assess the statistical significance of interactions between race/ethnicity and pre-pregnancy overweight/obesity status.
Results: Among women with overweight/obesity, Hispanics had a lower risk of CS as compared to NH-W (aRR:0.89;95%CI:0.84-0.93). Similarly, among women with overweight/obesity, Hispanic and NH-NHP had a lower risk of preeclampsia (aRR:0.74;95%CI:0.66-0.82 and aRR:0.64;95%CI:0.44-0.92, respectively) and NH-AA had a greater risk of GDM (aRR:1.23;95%CI:1.07-1.42) when compared with NH-W women. These associations were not present among normal-weight. Women with overweight/obesity, when compared with women with normal-weight, had an increased risk of GDM and CS among all race/ethnicities except AI/AN and NH-NHP, respectively (p-values<0.05). The multiplicative interaction terms between race/ethnicity and overweight/obesity status were significant for all three complications (interaction p-values<0.05).
Conclusion: Pre-pregnancy overweight/obesity status modifies associations of race/ethnicity with pregnancy complications. Conversely, race/ethnicity modifies associations of pre-pregnancy overweight/obesity status with pregnancy complications.

Women's Health

Sister Study: Predictors of Incomplete Enrollment in a Prospective Cohort of Breast Cancer

W. Braxton Jackson* W. Braxton Jackson M. Elizabeth Dale P. Sandler

Background: The Sister Study is examining environmental and familial risk factors for breast cancer and other diseases in a cohort of sisters of women who have had breast cancer. The study design required completing two telephone interviews and a home visit. Of the women who started the enrollment process, 50,844 completed all required activities (2003-2009). However, 3,066 completed only some of the required activities and thus were not fully enrolled. Those partially enrolled did not receive follow-up questionnaires but are followed for mortality. An understanding of predictors of incomplete enrollment could enhance future cohort enrollment and retention efforts as well as address questions of generalizability. Methods: We examined demographic, lifestyle, and health characteristics of fully and partially enrolled women to identify predictors of incomplete enrollment using adjusted modified Poisson regression to estimate adjusted prevalence ratios (PR) and 95% confidence intervals. Results: Multiple characteristics independently predicted partial enrollment, including timing of enrollment (late vs early recruitment period: PR 1.41; 95% CI, 1.28-1.56), age (35 to 39 vs 70 to 79 years: PR 2.21; 95%CI, 1.71-2.86), race (non-Hispanic black vs white: PR 2.34; 95% CI, 2.12-2.58), marital status (single/divorced/widowed vs married: PR 1.46; 95% CI, 1.35-1.59), history of other cancer (yes vs no: PR 1.33; 95% CI, 1.14-1.54), current smoking (yes vs no: PR 1.68; 95% CI, 1.52-1.87), and perceived stress (high vs low: PR 1.70; 95% CI, 1.43-2.02). Having more than one sister with breast cancer or one with breast cancer before the age of 45 did not affect enrollment status. Conclusion: Enrollment status (complete vs incomplete) varied by characteristics assessed early in the enrollment process. Future studies may consider flagging women with characteristics that increase the risk of incomplete enrollment and implement tailored strategies to ensure full participation.

Use of depot medroxyprogesterone acetate reduces fibroid growth and incidence: a prospective study Quaker Harmon* Quaker Harmon Stacy Patchel Donna Baird

Use of depot medroxyprogesterone acetate (DMPA), a long-acting progesterone contraceptive, has been associated with reduced fibroid prevalence. Prospective data to evaluate the association between DMPA and fibroid growth and incidence has been lacking. The Study of Environment Lifestyle & Fibroids (SELF) followed 1693 black women age 23-35 at enrollment from the Detroit area with ultrasound every 20 months for 4 visits (5 years). A subset of fibroids could be matched across consecutive visits and change in their volumes was used to calculate 18-month growth rates. Women without fibroids at baseline with at least 1 follow-up visit were included in an analysis of incidence. Questionnaire data was used to quantify DMPA exposure at each visit. Cumulative duration of DMPA use (months) and time since last use of DMPA (years) were explored singly and jointly (using relevant categorical cut points to create joint exposure variables). All models were adjusted for time-varying age, and time since last birth. In addition, growth models included fibroid volume and number; while incidence models included body mass index and months between visits. At enrollment women had a mean age of 29 years and 20% had used DMPA within 4 years of baseline. SELF has strong follow-up, 93% have at least 2 ultrasounds and 77% have all 4 ultrasounds, with a median 19 months between visits. Among 421 women with growth data on 1-6 fibroids, the crude fibroid growth rate was 78% increase in volume per 18 months. DMPA use within the last 4 years reduced fibroid growth 33% (95% CI -42%, -22%). Among the 1123 women who were fibroid free at baseline, 26% had incident fibroids over 5 years. Use of DMPA for at least 10 months within the last 4 years was associated with a decreased incidence of fibroids (RR 0.7, 95% CI 0.7, 1.0). Consistent with known associations with fibroid prevalence, use of DMPA within 4 years also slows the growth of prevalent fibroids and decreases the risk of incident fibroids.

Physiologic effects of chronic stress among African American sexual minority women

Tubanji Walubita* Tubanji Walubita William M. Jesdale, PhD Sarah N. Forrester, PhD

African American individuals and sexual minority women have worse health when compared to White individuals and heterosexual women, respectively. African American, sexual minority women face a unique combination of chronic stressors due to their multiple marginalized identities. Allostatic load is a measure of the physiologic effects of chronic exposure to stress. An increase in allostatic load indicates dysregulation of body systems, which often leads to poor health outcomes. The association between sexual orientation and allostatic load among African American women has not previously been explored. We hypothesized that African American women who self-identify as lesbian and bisexual will have higher allostatic load scores than African American women who self-identify as heterosexual. We used data from the National Health and Nutrition Examination Survey, a cross-sectional, population-based survey. The participants in the study are African American women who self-identify as lesbian, bisexual, or heterosexual. The sexual orientation of the participants was collected from the Sexual Behavior Questionnaires. Allostatic load was measured using nine biomarkers from the examination and laboratory data. Any biomarker value that falls outside the clinical range will equate to a positive count for that biomarker; therefore, the potential range for allostatic load will be 0-9. In the first (2015-2016) of eight waves of data to be analyzed (2001-2016), 9 African American women identified as lesbian, 17 as bisexual, and 376 as heterosexual. In preliminary findings, African American lesbian women and African American bisexual women had an average of 9 total allostatic load markers, as compared to an average of 8.46 among African American heterosexual women. The findings from this study will reveal the association between sexual orientation and allostatic load among African American women and will provide insight into the relationships between chronic stress and poor health.

Women's Health

The association between menstrual cycle characteristics and vulvodynia Bernard Harlow*
Julia Bond Vanessa Estibeiro Allison Juntunen Alexis Mccullough Bernard Harlow

Introduction: Despite its high estimated lifetime prevalence of 8-13% of women, the etiology of unexplained vulvar pain (vulvodynia) remains largely uncharacterized. Menstrual cycle characteristics may play a role in the development or presentation of vulvodynia, due to hormonal influences and/or the use of menstrual hygiene products. No studies to our knowledge have evaluated an association between menstrual cycle characteristics and vulvodynia.
Methods: We used data from a case-control study recruited from the administrative database of a large healthcare network. Approximately 30,000 women aged 18-40 years were screened for vulvar pain via a mailed survey, and a sample of 223 clinically-confirmed cases of vulvodynia and 226 age-matched controls were ultimately included. The study asked detailed questions about menstrual cycle characteristics during three periods: early life (years after menarche), the year before the onset of vulvar pain, and present day. We also assessed menstrual hygiene characteristics, including use of tampons or sanitary pads, and symptoms of pre-menstrual syndrome (PMS).
Results: Cases had higher odds of shorter cycle lengths (<25 weeks) (OR 2.5, 95% CI 1.1-5.8) and self-perceived heaviness of flow (OR 1.9, 95% CI 1.1-3.5) prior to onset of vulvar pain compared to comparable time periods among controls. These associations tended to be consistent across the three time-periods assessed. Additionally, cases had higher odds of experiencing PMS symptoms (muscle stiffness, insomnia, mood swings, etc.), and reporting that PMS symptoms interfered with daily functioning most or all of the time (OR 2.7, 95%CI 1.1-6.6).
Discussion: Our study is the first to evaluate the association between menstrual characteristics and vulvodynia. Our findings could suggest that hormonal characteristics that influence menstruation may also play a role in the etiology of vulvodynia.

Impact of the Affordable Care Act on breast pumps and breastfeeding by health insurance type Summer Hawkins* Summer Hawkins Krisztina Horvath Christopher F. Baum

The Affordable Care Act (ACA) required private insurance plans to provide breast pumps (BP) with no cost sharing effective Aug 2012. Medicaid expansion and Marketplace insurance occurred in Jan 2014 for most states. Despite the known benefits of breastfeeding, disparities persist. Whether access to pumps increases breastfeeding remains unknown.

Our study aims were twofold. We first examined associations between the ACA insurance reforms in 2012 and 2014 with rates of BP claims per 100,000 live births between Medicaid enrollees and the privately-insured using All Payer Claims Databases (APCD) from Massachusetts, Maine, and New Hampshire in 2011-2015. We next examined associations between monthly rates of BP claims per state-insurance-maternal age group from APCDs with breastfeeding initiation and for ≥4 weeks using Pregnancy Risk Assessment Monitoring System (PRAMS) data. We report average marginal effects by insurance type from adjusted regression models.

In the first model, among privately-insured women the ACA-related 2012 (0.313[0.282-0.345]) and 2014 reforms (0.139[0.111-0.166]) were associated with increases in rates of BP claims. Only the 2014 reforms were associated with increases in rates of BP claims among Medicaid enrollees (0.333[0.303-0.362]). In the second set of models, rates of BP claims in the month women gave birth were associated with increases in breastfeeding initiation among the privately-insured (0.098[0.016-0.180]), but not Medicaid enrollees (0.016[-0.100-0.132]). In contrast, rates of BP claims were associated with increases in breastfeeding for ≥4 weeks for both the privately-insured (0.201[0.096-0.306]) and Medicaid enrollees (0.197[0.072-0.323]).

We found evidence that increases in BP claims as a result of the ACA-related insurance reforms translated into higher breastfeeding initiation and duration among privately-insured women. While Medicaid expansion increased BP claims for enrollees, it resulted in gains in breastfeeding duration only.

Women's Health

Planned mode of birth after previous cesarean section and women's use of psychotropic medication in the first year postpartum: a population-based record linkage cohort study

Kathryn Fitzpatrick* Kathryn Fitzpatrick Maria Quigley Daniel Smith Jennifer Kurinczuk

Background: Policy in many high-income settings supports giving pregnant women with previous cesarean section a choice between planning an elective repeat cesarean section (ERCS) or planning a vaginal birth after previous cesarean (VBAC), provided they do not have contraindications to VBAC. Despite the potential for this choice to influence women's mental health, evidence about the associated effect to counsel women and identify potential targets for intervention is limited. This study investigated the association between planned mode of birth after previous cesarean and women's subsequent mental health, inferred from their use of psychotropic medication in the first year postpartum. Methods: A population-based cohort study of 31,131 women with one or more previous cesarean sections who gave birth to a term singleton in Scotland between 2010-2015 without a history of being dispensed psychotropic medications in the year before birth was conducted using linked Scottish national datasets. Cox regression was used to investigate the association between planned mode of birth and being dispensed psychotropic medications in the first year postpartum adjusted for socio-demographic, medical, pregnancy-related factors and breastfeeding. Results: Planned VBAC (n=10,220) compared to ERCS (n=20,911) was associated with a reduced risk of the mother being dispensed any psychotropic medication (respective rates 10.6 versus 13.2 per 100 person-years, adjusted hazard ratio[aHR] 0.85, 95% CI 0.79-0.92), an antidepressant (8.8 versus 11.4 per 100 person-years, aHR 0.83, 95% CI 0.76-0.90), and at least two consecutive antidepressants (6.4 versus 8.6 per 100 person-years, aHR 0.83, 95% CI 0.75-0.91) in the first year postpartum. Conclusions: Women giving birth by ERCS may be more likely than those having a planned VBAC to experience mental health problems in the first year postpartum. Further studies are needed to replicate and explore the reasons behind this new finding.

Women's Health

Association of anthropometric factors with anti-Mullerian hormone levels Nydjie P. Grimes*

Nydjie Grimes Brian W. Whitcomb Alexandra Purdue-Smithe Katherine W. Reeves Susan E. Hankinson Bernard A. Rosner JoAnn E. Manson Elizabeth R. Bertone-Johnson

Previous studies have suggested that menopause may occur later in overweight women than lean women. However, results from studies of adiposity and anti-Müllerian hormone (AMH), an established marker of ovarian aging and time to menopause, have been less consistent, with some studies observing lower AMH levels among women with higher body mass index (BMI) and others finding no association. We assessed the association of anthropometric factors with AMH levels among participants in the Nurses' Health Study 2. Participants (n=1619) were aged 32-49 years when providing premenopausal blood sample in 1996-99; AMH was measured using an ultra-sensitive ELISA assay (picoAMH). Weight at age 18 and height were self-reported in 1989, and weight was reported at time of blood collection. BMI was calculated as weight (kg)/ height (m2). Waist and hip circumferences were self-reported in 1993 and used to derive waist-to-hip ratio. AMH values were natural log transformed for analysis, then exponentiated for interpretability. In multivariable linear regression models adjusting for age, smoking, infertility, assay characteristics, and other factors, we observed the suggestion of a non-linear, J-shaped relation of BMI and AMH levels. For BMI at blood collection, mean AMH levels were lowest in women with BMI 18.5-22.5 kg/m2 (mean = 1.1 ng/mL). In comparison, levels were 10-30% higher in underweight women (BMI <18.5 kg/m2), and in those with BMI 22.5-24.9, and 25.0-27.4 kg/m2. The highest levels were observed in overweight and obese women; for example, compared to those with BMI 18.5-22.5 kg/m2, AMH levels were 67% higher in women with BMI 27.5-29.9 (P = 0.06) and 69% higher for ≥30 (P = 0.03). Non-linear patterns in mean AMH levels were observed for BMI at age 18 and waist-to-hip ratio. These results are consistent with studies of BMI and menopause timing and provide some additional support for a non-linear relation of adiposity and age at menopause.

Do Organophosphate Esters Disrupt Maternal Thyroid Function? Giehae Choi* Giehae Choi Alexander Keil David B. Richardson Julie Daniels Kate Hoffman Gro Dehli Villanger Amrit k. Sakhi Cathrine Thomsen Amy H. Herring Samantha S.M. Drover Rachel Nethery Stephanie M. Engel

Background. Organophosphate esters (OPEs) may influence thyroid function, which during pregnancy can adversely affect women and the developing fetus. There have been no studies of OPEs exposure and thyroid dysfunction during pregnancy.

Aim. To characterize relationships between OPE exposures and thyroid function among pregnant women.

Methods. 498 euthyroid women who provided bio-samples at 17 weeks' gestation were selected from the Norwegian Mother, Father and Child cohort. Diphenyl phosphate (DPHP), di-n-butyl phosphate (DnBP), bis(2-butoxyethyl) hydrogen phosphate (BBOEP), and bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) were measured in urine. Total triiodothyronine (TT3), total thyroxine (TT4), and thyroid stimulating hormone (TSH) were measured in blood. We estimated % changes in TT3, TT4, TSH, and TT3:TT4 ratio per interquartile range (IQR) increase in specific gravity (SG) standardized OPEs using linear models. We adjusted for parity, season of sample collection, maternal smoking, age, education, depression, phthalate metabolite concentrations, and dietary iodine, selenium, and alcohol intake. OPE concentrations below the limit of detection (LOD) were multiply imputed from truncated log-normal distributions, as well as missing covariates. Estimates were pooled using Rubin's rules.

Results. DPHP and DnBP were detected in nearly all samples (96% and 94% respectively), while BBOEP (51%) and BDCIPP (21%) were detected less frequently. Increased DPHP was associated with slightly lower TT4 [beta: -0.24% (95% CI: -1.00, 0.52)] and slightly higher TSH [3.01% (0.27, 5.81)]. However, DPHP was also associated with higher TT3 [0.92% (0.04, 1.81)]. The TT3:TT4 ratio and DPHP appeared nonlinearly associated (Fig.1). No other OPE was associated with thyroid function.

Conclusions. DPHP exposure during pregnancy was associated with altered maternal thyroid function, although there was a lack of consistency in the direction across thyroid biomarkers.
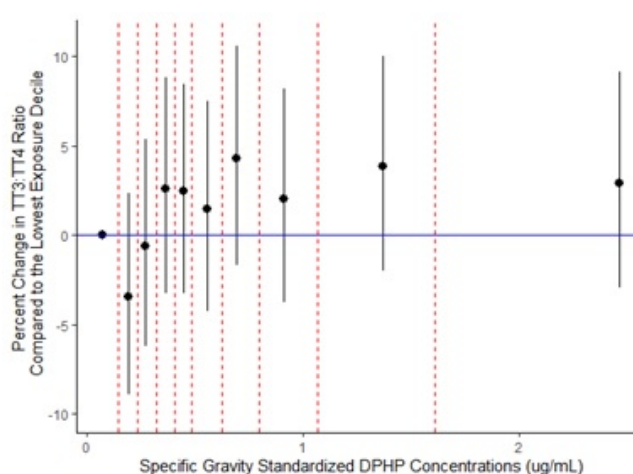
Fig.1. Percent change in total triiodothyronine to total thyroxine ratio (TT3:TT4 ratio) compared to the lowest decile of specific gravity standardized diphenyl phosphate (DPHP). Dotted vertical lines represent lowest 10th, 20th, 30th, 40th, 50th, 60th, 70th, 80th, and 90th deciles of exposure.

Association between pre-pregnancy body mass index and risk of preterm birth in more than 1 million Asian American mothers Rui Gao* 3647] Gao Buyun liu

Background: Asian Americans are among the fastest growing subpopulations in the United States. Previous studies have reported race/ethnic disparities in the association between maternal pre-pregnancy obesity and risk of preterm birth in the general population. However, evidence from the Asian American population, among whom obesity is usually defined with different cutoff points of body mass index (BMI) from other racial/ethnic groups, is lacking. **Methods:** We conducted a population-based cohort study using nationwide birth certificate data from the US National Vital Statistics System 2014-2018. All Asian mothers who had a singleton live birth were included. According to Asian American-specific cutoffs, pre-pregnancy BMI was classified into underweight (BMI<18.5 kg/m^2), normal weight (BMI 18.5-22.9 kg/m^2), overweight (BMI 23.0-27.4 kg/m^2), Class I Obesity (BMI 27.5-32.4 kg/m^2), Class II Obesity (BMI 32.5-37.4 kg/m^2), and Class III Obesity (BMI ≥ 37.5 kg/m^2). Preterm birth was defined as gestational age less than 37 weeks. Multivariable logistic regression models were used to estimate the odds ratio (OR) of preterm birth. **Findings:** We included 1081341 Asian American mother-infant pairs in our analysis. The rate of preterm delivery was 6.51% (n=70434), ranging from 4.95% in East Asian mothers to 8.30% in Southeast Asian mothers. Compared with mothers with normal weight, the adjusted OR was 1.04 (95% CI 1.01-1.07) for underweight mothers, 1.18 (95% CI 1.16-1.20) for overweight mothers, 1.41 (95% CI 1.37-1.44) for mothers with Class I Obesity, 1.69 (95% CI 1.63-1.76) for mothers with Class II Obesity and 1.78 (95% CI 1.66-1.90) for mothers with Class III. Similar pattern of associations was observed in Asian American mothers across different country origins. **Conclusions:** Among Asian Americans, being overweight or obese in the pre-pregnancy period significantly associated with an increased risk of preterm birth. The risk of preterm birth increased with increasing obesity severity.

Prospective association between dysmenorrhea and chronic pain development and effect modification by the Big Five personality traits Rui Li* 3647] Li Benjamin Chapman Todd A. Jusko Donna A. Kreher Adrienne Bonham Christopher Seplaki

Dysmenorrhea, or menstrual pain, is a leading cause of lost work hours among women of reproductive age. Despite some evidence linking dysmenorrhea to pain chronicity, it is unknown whether dysmenorrhea increases the risk for developing chronic pain among women generally and whether personality traits modify that risk.

Our data are from the nationally representative and longitudinal Midlife in the United States (MIDUS) cohort. Dysmenorrhea was classified as some or a lot menstrual discomfort at MIDUS 1 (M1, 1995), and chronic pain defined as persistent pain of a few months to many years reported at M2 (2004) and M3 (2013). The Big Five personality traits were assessed at all waves. Among 525 women aged 25-62 at baseline, the relative risk of chronic pain from M2 to M3 associated with dysmenorrhea was estimated by Poisson regression models accounting for correlated observations and adjusting for demographic, lifestyle, and psychosocial factors. Effect modification was explored by interacting dysmenorrhea with the normalized scores of traits calculated as the mean of M1 and M2 measures.

The 10-year cumulative incidence of chronic pain was 35% and 23% in women with and without dysmenorrhea. Dysmenorrhea was associated with a 40% greater risk (95% CI, 5%-87%) of chronic pain, which did not change with missing data imputation, exclusion of women with gynecological surgeries, and additional adjustments of age of menarche, duration of hormone/birth controls use and parity. Extraversion, openness to experience, and agreeableness attenuated the association (β interaction ranged -0.14 to -0.08) despite non-significance.

In this study of community-dwelling women of reproductive age, dysmenorrhea is associated with a greater risk of chronic pain. Whether early management of dysmenorrhea reduces chronic pain-related burden in women deserves future research. Our preliminary findings of risk modification by personality traits need replication with larger samples.

Women's Health

Endometriosis, psoriasis and psoriatic arthritis: A prospective cohort study Holly R. Harris*
Holly Harris Karen Moreno Nascimento Korkes Eunyoung Cho Marina Kvaskoff Tricia Li Stacey
Missmer

Objective: Endometriosis has been associated with both immunologic and pain disorders. Our
objective was to examine the bi-directional associations between endometriosis, psoriasis and
psoriatic arthritis (PsA).

Design: A prospective cohort study using data collected from 92,613 premenopausal women from
1991-2009 as part of the Nurses' Health Study II cohort.

Methods: Cases of laparoscopically-confirmed endometriosis were identified on biennial
questionnaires. History of physician diagnosed psoriasis and psoriatic arthritis (PsA) were confirmed
by supplementary questionnaires. Multivariable Cox proportional hazards models were used to
calculate hazard ratios (HR) and 95% confidence intervals (CI) with each condition as the exposure
and the outcome.

Results: During 18 years of follow-up, 3908 incident cases of laparoscopically-confirmed
endometriosis, 655 cases of psoriasis, and 111 cases of PsA were reported. When psoriasis was
considered the exposure, psoriasis with concomitant PsA was associated with a higher risk of
endometriosis diagnosis (HR=1.96; 95% CI=1.13-3.39). In contrast, no association was observed
between psoriasis alone and endometriosis diagnosis (HR=0.81; 95% CI=0.55-1.18). When
laparoscopically-confirmed endometriosis was considered the exposure there was a suggestive, but
not statistically significant, association with risk of PsA (HR=1.78; 95% CI=0.90-3.55) and to a lesser
extent psoriasis (HR=1.28; 95% CI=0.94-1.73).

Conclusions: In this large cohort study, psoriasis with concomitant PsA (but not psoriasis alone) was
associated with a higher risk of endometriosis. The mechanisms underlying these associations that
suggest synergy of immune, inflammatory and pain pathways, remain to be elucidated. Analyses
with additional years of follow-up in this cohort are ongoing.

Women's Health

Glycemic index, glycemic load, fiber, and gluten intake and risk of laparoscopically-confirmed endometriosis Holly Harris* Holly Harris Myriam Afeiche Kathryn Terry Leslie Farland Jorge Chavarro Stacey Missmer

Objective: Prospective data on modifiable dietary factors and incident endometriosis are scarce. Therefore, our objective was to investigate the association between carbohydrate quality (dietary glycemic index [GI] and glycemic load [GL]), fiber intake (total fiber, legume, vegetable, cruciferous vegetable, fruit, and cereal fibers), and gluten intake and diagnosis of laparoscopically-confirmed endometriosis.

Design: The prospective Nurses' Health Study II cohort using data collected from 81,789 premenopausal women from 1991-2013.

Materials and Methods: Diet was assessed with a validated food frequency questionnaire every four years. Multivariable Cox proportional hazards models adjusted for race/ethnicity, menstrual cycle length, parity, age at menarche, body mass index, recent gynecologic/breast exam, and total calories, were used to calculate HRs and 95% CIs.

Results: During 22 years of follow-up, 3793 incident cases of laparoscopically-confirmed endometriosis were reported. Women in the highest quintile of GI had a 12% (95% CI=1.02-1.24) higher risk of endometriosis diagnosis than those in the lowest quintile. No association was observed for GL. Higher intake of fruit and cereal fiber was associated with a lower risk of endometriosis (highest vs lowest quintile HR=0.89; 95% CI=0.80-0.98 and 0.90; 95% CI=0.81- 1.00, respectively). In contrast, cruciferous vegetable fiber intake was associated with higher risk (highest vs lowest quintile=1.17; 95% CI=1.06-1.30). Gluten intake was associated with a lower risk (highest vs lowest quintile=0.82; 95% CI=0.72-0.93). When evaluated by history of infertility, the associations with GI and gluten were only apparent among women who had never reported infertility.

Conclusions: Our findings suggest that modifiable dietary factors, such as carbohydrate quality measured with GI, specific types of fiber intake, and gluten are associated with endometriosis diagnosis and some of these associations may vary by fertility status.