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Abstracts

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Methods

Considering pregnancies as repeated versus isolated events: An empirical comparison of common approaches across selected perinatal outcomes Shalmali Bane*, Suzan Carmichael, Julia Simard, Maya Mathur,

Despite published guidance on how to address repeated pregnancies to the same individual, a variety of approaches are observed. While some of these approaches are supported by the chosen research question, others are consequences of constraints inherent to a given dataset (e.g., missing parity). We compared common cohort selection and analytic approaches used for epidemiological research.

Using vital records linked to hospital discharge records for singletons, we created four cohorts: (1) all births (2) randomly selected one birth per individual (3) first observed birth per individual (4) primiparous births. Sampling of births was not conditional on cluster. Study outcomes were severe maternal morbidity (SMM) and preeclampsia/eclampsia, and the independent variables were self-reported race/ethnicity (as a social factor) and systemic lupus erythematosus. We assessed the distribution of maternal characteristics, the prevalence of outcomes, overall and stratified by parity, and risk ratios (RRs). Among all births, we compared RRs from three analytic strategies: with standard inference, cluster-robust inference, and adjusting for parity.

Outcome prevalence was consistently lowest among all births and highest among primiparous births. RRs differed for study outcomes across all four cohorts, with the most pronounced differences between the primiparous-birth cohort and other cohorts. Robust inference minimally impacted the confidence bounds of estimates, compared to the standard inference, (e.g., lupus-SMM association: 4.01, 95% CI 3.54-4.55 vs. 4.01, 95% CI 3.53-4.56), while adjusting for parity slightly shifted estimates.

Researchers should consider the alignment between methods used, sampling strategy, and research question. This could include refining the research question to better match possible inference, considering alternative data sources, and acknowledging data limitations. If parity is an established effect modifier, stratified results should be presented.

Assessment of DistillerSR's Machine Learning Capabilities for Maternal Risk Outcome Research Maxwell Dodge*, Ke Pan, Austin Heuer, Nicholas Kassebaum, Maegan Dirac,

Background: Systematic reviews (SR) for meta-analyses are time and resource intensive. Oftentimes, they require researchers to review thousands of papers in order to extract only a few dozen sources. Using data from a fully completed SR we evaluated the ability of the DistillerSR machine learning algorithm to accurately rank and bulk exclude sources at the title and abstract stage.

Methods: A SR used to identify data regarding the risk of obstructed labor with nonoptimal maternal anthropometry was used to evaluate an SR protocol developed for use with DistillerSR. The initial search string returned 1,866 hits; as fully executed by human reviewers, 895 were included in full text review and 59 were extracted. We then used title and abstract screening results as training data to feed into a DistillerSR project to test a protocol that used AI. The protocol consisted of dual screening with interrater reliability checks to train the reviewers, activating AI reprioritization to present references in descending likelihood of inclusion, and single screening remaining references while iteratively bulk excluding sources with the lowest likelihood of inclusion. Using the scores assigned from DistillerSR we then tested to see if our 59 sources were included using our protocol and, if so, if this resulted in fewer total title abstract screenings and/or full-text reviews carried out by human reviewers.

Results: Using our SR protocol, AI reprioritization in DistillerSR successfully included all relevant sources and enabled the earlier identification of pertinent sources. However, it did not allow for any bulk exclusion of sources based on the predicted scores in this SR.

Conclusion: Although employing DistillerSR's machine learning algorithm doesn't guarantee a shorter screening time, it can facilitate the earlier generation of preliminary model results. Additionally, it can also reduce screening errors when double screening is not feasible, freeing up resources for other projects.

Understanding the impact of selection biases inherent in pregnancy research across different causal inference approaches: a simulation study Basma Dib*, Ellen Caniglia, Sean Brummel, Roger Shapiro, Sonja Swanson,

Randomized trials and observational studies that study the effect of pre-/during-pregnancy treatments on maternal and neonatal outcomes often have inherent forms of selection or collider-stratification bias. For example, these studies often restrict analyses to those who had a livebirth, those with a specified gestation duration, and/or those with complete follow-up. These selection factors and the outcome of interest frequently have unmeasured or even unknown shared causes which may induce bias in estimating the effect of treatment. Though such selection biases can affect all causal inference approaches, what is unknown is the extent to which the biases meaningfully impact different analytic approaches in pregnancy studies. We conducted a simulation study to assess and compare the magnitude and direction of selection biases in a hypothetical study of treatment effect on pregnancy outcomes across three different causal inference methods: inverse probability weighting (IPW), instrumental variable (IV), and sibling comparison design (SCD) analysis. We generated simulated data for various scenarios under two main conditions: (1) presence of loss to follow-up and (2) presence of a competing event. For each scenario, we generated 500 samples of data, each with a sample size of 10,000, and estimated an average causal effect. In presence of loss to follow-up, the mean bias in the risk difference estimates increased with a stronger association of loss to follow-up with treatment and outcome, with estimates obtained from IPW analysis and SCD analysis biased to nearly the same extent and in the same direction. The estimates obtained from IV analysis were consistently more biased by about one percentage point in the same direction. The mean bias varied across which causal estimand was targeted in light of the competing event. Our simulation study provides insight on the extent to which different analytic methods are impacted by selection bias in pregnancy research.

Pre-Pregnancy and First-Trimester Hair Cortisol Predicts Preterm Birth in Pregnant Women in Perú: A Causal Inference Model Richard G. Künzel*, Yinxian Chen, Sixto E. Sanchez, Marta B. Rondon, Nelida I. Pinto, Elena Sanchez, Clemens Kirschbaum, Linda Valeri, Karestan C. Koenen, Bizu Gelaye,

Approximately 87% of pregnant women in Perú have experienced at least one traumatic life event. Traumatic life events and other forms of psychological stress have frequently been associated with preterm birth (PTB), but the underlying biological mechanisms remain unclear. A promising biological mechanism is the hypothalamic-pituitary-adrenal (HPA) axis, a system involved in both, stress, and pregnancy regulation.

Investigating N = 1,808 pregnant Peruvian women, we examined the effect of pre-pregnancy and first-trimester hair cortisol (HCC) and hair cortisone concentrations (HCNC), which are novel chronic biomarkers of the HPA axis, on the risk of PTB. Using propensity scores to create stabilized inverse probability weights, we construct marginal structural models for causal association estimation.

While both independent one-log-unit increases from the population-mean pre-pregnancy HCC (Risk Ratio (RR) = 0.87; 95%CI: 0.64, 1.19) and HCNC (RR = 0.82; 95%CI: 0.59, 1.14) were associated with decreased risk of PTB, first-trimester HCC (RR = 1.50; 95%CI: 1.13, 2.01) and HCNC (RR = 1.41; 95%CI: 1.06, 1.87) were linked to increased PTB risk. Interestingly, if HCNC had been elevated in both, pre-pregnancy and first trimester, the increased PTB risk due to the elevated first-trimester HCNC would have been attenuated (RR = 1.07; 95%CI: 0.75, 1.52) compared to a HCNC increase only in the first trimester (RRpre-pregnancy*first trimester = 0.76, 95%CI: 0.63, 0.91). Furthermore, the HCNC/HCC ratio, which is thought to represent 11β-HSD-2 activity, was negatively associated to PTB in all occurrences.

Our findings show that corticosteroid levels before and in early pregnancy are linked to PTB risk. Moreover, our results implicate that the temporal trajectory of chronic corticosteroid concentrations, which may be influenced by previous experiences of traumatic life events or psychological distress, is crucial for PTB prediction.

Maternal prenatal cannabis use disorder and risk of autism spectrum disorder in offspring: A data linkage cohort study Abay Tadesse*, Berihun Dachew, Getinet Ayano, Kim Betts, Rosa Alati,

Abstract

Background: Few studies have investigated the link between in-utero cannabis exposure and an increased risk of autism spectrum disorder (ASD) in offspring, with these previous studies relying on maternal self-reports of cannabis use. In this study, we used large-population-based linked data and a robust diagnostic tool to investigate the association between cannabis use disorder (CUD) and the risk of ASD in offspring.

Methods: This population-based cohort study was conducted by participating 222,534 mother-offspring pairs using linked data derived from health data registries in New South Wales (NSW), Australia. Data were drawn from the Perinatal Data Collection (PDC), encompassing all live birth cohorts from January 2003 to December 2005. This dataset was linked with the NSW Admitted Patient Data Collection (APDC) and Ambulatory Mental Health Data collections (AMB-MH) using mothers and offspring unique identification. The exposure variable, prenatal CUD, and the occurrence of ASD in offspring, the primary outcomes of interest, were identified using the International Classification of Diseases-Australian Modification (ICD-10-AM). The associations were explored using Generalized Linear Models (GLMs) with a binomial family regression model. Additionally, gender-specific sensitivity analyses were carried out.

Results: After accounting for relevant confounders, we found a three-fold increased risk of ASD in the offspring of mothers with maternal prenatal CUD [RR = 3.1 (95% CI 2.13 – 4.41)] compared to non-exposed offspring. In our stratified analyses, a significant gender difference was observed; female offspring have a higher risk of ASD than their male counterparts [RR = 4.7 (95% CI 2.56, 9.12) versus RR = 3.0 (95% CI 1.70, 4.16)]. Furthermore, we noted a slightly increased risk of childhood ASD among those exposed to both CUD and tobacco smoking [RR = 3.28 (95% CI 2.11, 4.90, p < 0.01)].

Conclusion: This study shows that maternal prenatal CUD is linked to a higher risk of ASD in offspring, with a stronger risk in female offspring. Further research is needed to understand these gender-specific effects and the relationship between maternal CUD and ASD risk in children.

Adverse Childhood Experiences and Utilization of Preventive Healthcare among Children in Rural Communities in the United States (NHIS 2022) Mary Labuhn*, Andrew Williams,

Background. Children residing in rural communities have increased risk for Adverse Childhood Experiences (ACEs), and children in rural communities are less likely to receive preventive healthcare. Additionally, the associations between ACEs and health behaviors may be sex specific. Given rural-urban disparities in chronic health conditions, examination of drivers of these disparities is needed.

Methods. Data for children between the ages of 9 and 17 (weighted n=3,949,102) were collected from the 2022 National Health Interview Survey. Sample included those identified as residing in "nonmetropolitan" areas according to the 2013 NCHS Urban-Rural Classification. Physician visit in the past 12 months (yes/no) and dental visit in the past 12 months (yes/no) were self-reported. Participants self-reported (yes/no) to 8 ACEs (high ACEs ≥1). Logistic regression estimated odds ratios and 95% confidence intervals for associations between ACEs and doctor visit and dental visit, adjusted for demographic and healthcare factors.

Results. Children with ≥1 ACE were 28% less likely (OR=0.71,95%CI:0.78,0.79) to visit a doctor and 48% less likely (OR=0.52,95%CI0.51,0.52) to visit a dentist, compared to children with 0 ACEs. Further, boys had decreased odds (OR=0.23,95%CI0.23,0.23) while girls had increased odds (OR=1.23,95%CI:1.22,1.25) of visiting a doctor within 1 year. Both boys (OR=0.22,95%CI:0.22,0.23) and girls (OR=0.87,95%CI 0.86,0.88) had decreased odds of visiting a dentist.

Discussion. For children living in rural communities, those with ≥1 ACE were less likely to have a recent doctor or dentist visit. We observed sex differences, such that boys with ≥1 ACE were significantly less likely to have had a recent doctor or dentist visit than girls with ≥1 ACE. A higher prevalence of particular ACES, such as "lacking basic needs" among boys may explain the observed differences by sex. Further research is warranted to best inform prevention efforts in rural communities.

Child health and development

Food Insecurity in Early Life and Obesity Risk Across Childhood and Adolescence in the Environmental influences on Child Health Outcomes (ECHO) Program Izzuddin Aris*, Allison Wu, Pi-I Lin, Mingyu Zhang, Huma Farid, Monique Henderson, Yeyi Zhu, Assiamira Ferrara, Rana Chehab, Emily Barret, Susan Carnell, Carlos Camargo Jr, Su Chu, Hooman Mirzakhani, Rachel Kelly, Sarah Comstock, Rita Strakovsky, Thomas O'Connor, Jody Ganiban, Anne Dunlop, Dana Dabelea, Carrie Breton, Theresa Bastain, Shohreh Farzan, Christine Call, Tina Hartert, Brittney Snyder, Sara Santarossa, Andrea Cassidy, Michael O'Shea, Lacey McCormack, Margaret Karagas, Cindy McEvoy, Akram Alshawabkeh, Emily Zimmerman, Brent Coull, Ndidiamaka Amuthah-Onukagha, Michele Hacker, Tamarra James-Todd, Emily Oken,

Background: Limited access to healthy foods, resulting from residence in neighborhoods with low food access or from household food insecurity, is a public health concern. The contribution of these exposures in early life to child obesity remain understudied.

Methods: We used data from cohorts participating in the nationwide ECHO program. Participant inclusion required a geocoded residential address or response to a food insecurity question in pregnancy (mean 32.4 gestational weeks) or early childhood (mean 4.3 years) and information on child body mass index (BMI). We identified low-income-low-food-access (LILA) neighborhoods using the US Food Access Research Atlas as low-income neighborhoods where the nearest supermarket is >0.5 miles for urban or >10 miles for rural areas. Mixed-effects models estimated associations of LILA neighborhoods and household food insecurity in pregnancy or early childhood with risk of obesity (age and sex-specific BMI ≥95th percentile), adjusting for sociodemographic and prenatal characteristics.

Results: Of 24,919 pregnant participants from 55 cohorts with neighborhood food access data, 23.2% resided in LILA neighborhoods. Residence in LILA (vs. non-LILA) neighborhoods in pregnancy was associated with higher risk of obesity at 5 (risk ratio 1.30; 95% CI 1.15-1.46), 10 (1.60; 1.30-1.96), and 15 years (1.92; 1.44-2.57). Similar findings were noted for residence in LILA neighborhoods in early childhood. Of 1,452 pregnant participants from 11 cohorts with household food security data, 6.4% experienced food insecurity. Household food insecurity in early childhood, but not pregnancy, was associated with child obesity at 10 years although estimates were highly imprecise (2.82; 1.09-7.30).

Conclusion: Residence in LILA neighborhoods in early life is associated with higher subsequent risk of child obesity. Future studies should examine whether investing in neighborhood resources to improve food access in early life would prevent obesity in children.

Associations between Exposure to Extreme Ambient Heat and Neural Tube Defects in Georgia Sarah LaPointe*, Lauren Beagle, Xiaping Zheng, Vijaya Kancherla, Abby Mutic, Howard Chang, Audrey Gaskins,

Hyperthermia is a well-known animal teratogen, yet evidence on how maternal exposure to extreme ambient heat during periconception affects risk of neural tube defects (NTDs) in offspring is limited. Thus, the objective of this study was to estimate the association between exposure to extreme heat in the periconceptional period and NTDs, including spina bifida and anencephaly, in offspring. This case-control study in Georgia (1994-2017) included 825 isolated NTD cases and 3,300 controls identified using fetal death and birth records and matched 1:4 on county of residence and year of delivery. To define exposure to extreme ambient heat, we calculated the number of consecutive days that daily apparent temperature exceeded the county-specific 95th percentile during periconception. We calculated adjusted odds ratios and 95% confidence intervals to measure the association between ambient heat exposures during an eight-week periconception period (2 weeks prior to and 6 weeks following last menstrual period) and any NTDs using conditional logistic regression models adjusted for maternal age and month and year of last menstrual period. The adjusted odds ratios for NTDs were 1.09 (95% CI 1.01, 1.16), 1.18 (95% CI 1.03, 1.36), and 1.28 (95% CI 1.04, 1.58) for exposure to 1-2, 3-5, and 6 or more consecutive days of extreme heat during periconception, respectively, compared to no days of extreme heat exposure. Weekly analysis of extreme heat exposure indicated a consistently elevated odds of offspring NTDs from 2 weeks prior to 6 weeks after last menstrual period, largely driven by increased odds of spina bifida across the periconception period. In conclusion, we found positive, dose-response associations between extreme ambient heat exposures during periconception and NTDs. Our results highlight another potential health threat posed by climate change for pregnant women and offspring.

Oral contraceptives and uterine fibroid development in a prospective ultrasound study of Black and African American women Christine Langton*, Donna Baird, Quaker Harmon,

Uterine fibroids are highly prevalent benign tumors of the uterine muscle. Fibroids are the leading indication for hysterectomy, and Black and African American women are disproportionally burdened. Fibroids are dependent on estrogen and progesterone and oral contraceptives (OCs) alter these hormone levels. Studies examining the relationship between OCs and fibroids have had mixed results, and none utilized ultrasounds to prospectively assess fibroid incidence and growth.

We evaluated the association between OCs and fibroid development among 1,610 self-identified Black/African American women aged 23-35 years in the Study of Environment, Lifestyle & Fibroids. A standardized ultrasound examination was conducted at 4 clinic visits over 5 years to detect fibroids ≥0.5 cm in diameter. OC use was assessed at each visit and age at first use was reported at enrollment and derived thereafter. We used Cox regression to estimate hazard ratios (HRs) and 95% CIs for the association between OCs (time-varying current use and age at first use) and incident fibroids. Fibroid growth was defined as change in log-volume per 18 months for fibroids matched at successive visits. Incidence and growth models were adjusted for time-varying demographic and reproductive factors.

Of 1,232 fibroid-free participants at enrollment, 122 (10%) were current OC users, 79 (6%) first used OCs before age 15 years, and 295 (24%) developed incident fibroids over the study. Current OC use was not associated with risk of incident fibroids compared to no current use (aHR=1.15; 95% CI: 0.79, 1.69), yet was associated with a 13.7% reduction in fibroid growth (95% CI: -24.2%, -1.7%). Risk of incident fibroids was decreased for those who began using OCs before age 15 (aHR=0.53; 95% CI: 0.30, 0.94), but average fibroid growth differed little by age at first use.

Results from this ultrasound-based, prospective fibroid study add important data to understanding the complex relationship between OC use and fibroids.

Subjective sleep health and menstrual cycle characteristics in a North American prospective cohort study Chad M. Coleman*, Traci N. Bethea, Tanran R. Wang, Andrea S. Kuriyama, Julia C. Bond, Wendy Kuohung, Yael I. Nillni, Lauren A. Wise, Amelia K. Wesselink,

Introduction: Menstrual cycle disturbances affect up to 30% of reproductive-aged individuals. Few studies have examined the effect of sleep on menstrual cycle characteristics.

Methods: We estimated the associations of subjective sleep duration and quality with menstrual cycle characteristics in Pregnancy Study Online, a web-based North American preconception cohort study (2013-2023). Eligible participants were aged 21-45 years, assigned female sex at birth, and not using contraception or fertility treatment. On the baseline questionnaire, participants reported sleep duration (hours/day) in the past month. Beginning in October 2020, we assessed sleep quality in the past month via the Pittsburgh Sleep Quality Index (PSQI). On a follow-up questionnaire completed 8 weeks after baseline, participants reported menstrual cycle characteristics, including regularity, cycle length, bleed length, flow volume, intermenstrual bleeding, and menstrual pain. We used log-binomial regression models to estimate prevalence ratios (PRs) and 95% CIs adjusting for socio-demographic, behavioral, and reproductive factors.

Results: Short (<6 hours/day) and long (≥9 hours/day) sleep durations were associated with increased prevalence of prolonged bleed length (≥7 days; PRs vs. 7-<9 hours/day=2.10 [CI: 0.99-4.45] and 1.64 [CI: 0.89-2.99], respectively) and intermenstrual bleeding (PRs=1.59 [CI: 1.01-2.51] and 1.50 [CI: 1.05-2.14], respectively). Relative to good sleep quality (PSQI ≤5), poor sleep quality (PSQI >5) was associated with prolonged bleed length (PR=1.44 [CI: 0.93-2.23]), intermenstrual bleeding (PR=1.13 [CI: 0.88-1.45]), and severe menstrual pain (PR=1.29 [CI: 1.09-1.53]). Sleep duration and quality were not appreciably associated with other menstrual characteristics.

Conclusions: Sleep duration and quality were associated with menstrual cycle disturbances in this cohort. As sleep is a modifiable health behavior, this work may inform interventions to improve gynecologic health.

Associations between early-life menstrual characteristics and gestational diabetes in a large US cohort Zifan Wang*, Donna Baird, Michelle Williams, Anne Marie Jukic, Allen Wilcox, Jukka-Pekka Onnela, Russ Hauser, Brent Coull, Shruthi Mahalingaiah,

BACKGROUND: Associations between early-life menstrual characteristics and gestational diabetes (GDM) or recurrent GDM remain unclear.

METHODS: Participants from the Apple Women's Health Study, a US digital cohort, who consented, enrolled in 11/2019-9/2023, provided reproductive history, and were without diabetes prior to index pregnancy and aged ≥18 at first pregnancy were included (N=30,473). Age at menarche was recalled in years. Time from menarche to cycle regularity was categorized as follows: referent (<1, 1-2, 3-4 years) and prolonged time to regularity (PTR) (>5 years, not yet regular, or regular after hormones). GDM was recalled for each pregnancy. We restricted to pregnancies of ≥24 weeks with a live birth. Recurrent GDM was defined as having GDM in 2 or more pregnancies. We evaluated the associations [odds ratios (ORs) (95% CIs)] of age at menarche and PTR with GDM at first pregnancy (logistic regression), across all eligible pregnancies (cluster-weighted generalized estimating equation), and GDM recurrence among those with ≥2 pregnancies (multinomial logistic regression), adjusted for potential confounders and age at pregnancy.

RESULTS: Of the eligible first pregnancies (N=20,591), 6% reported GDM. In those with ≥2 pregnancies (N=17,512), 8% had GDM once, and 4% had recurrent GDM. A 1-year younger menarche was associated with higher odds of GDM in first pregnancy [1.04 (1.00, 1.08)], across all pregnancies [1.04 (1.01, 1.08)], and recurrent GDM [1.08 (1.02, 1.14)]. Similar associations were observed for early (<11 years) but not for late (≥16 years) menarche. PTR was associated with higher odds of GDM in first pregnancy [1.34 (1.15, 1.56)], across multiple pregnancies [1.23 (1.10, 1.38)], and recurrent GDM [1.31 (1.07, 1.61)].

CONCLUSIONS: Earlier menarche and PTR are associated with higher odds of GDM and GDM recurrence. These findings extend the literature and suggest early-life windows to be explored for better understanding risk factors for GDM.

Endometriosis and hypertriglyceridemia, why we care about severity and typology? Karen Schliep*, Leslie Farland, Anna Pollack, C. Matthew Peterson, Kathryn Rexrode, Emmanuel Adediran, Bin Yan, Rachael Hemmert, Rachel Myer, Madeline Paulsen, Michael Varner,

While plausible mechanisms exist for an association between endometriosis and hypertriglyceridemia, prior studies have shown inconsistent findings, possibly due to the inability to assess endometriosis severity or subtypes. Among 473 premenopausal individuals undergoing gynecologic laparoscopy, regardless of clinical indication, the present study assessed the association between non-fasting serum triglycerides and incident endometriosis. Participants were recruited in Salt Lake City and San Francisco (2007–2009). Surgeons completed an operative report immediately after surgery to capture revised American Society for Reproductive Medicine staging (I−IV) and typology of endometriosis (superficial endometriosis [SE], ovarian endometrioma [OE], and deep infiltrating endometriosis [DE]). We collected biospecimens, anthropometrics, and self-reported sociodemographics at baseline. We evaluated the association between endometriosis diagnosis, stage, typology, and triglyceride concentrations using non-fasting female cutpoints (normal <175mg/dL vs hypertriglyceridemia ≥175mg/dL) via generalized linear models. Among the cohort, 108 women (23%) had high triglycerides. Endometriosis was associated with a slightly higher prevalence of high triglycerides (adjusted prevalence ratio (aPR): 1.41, 95% CI: 0.93, 2.12). We found stronger associations by stage and type. Compared to no endometriosis, women with moderate to severe stage endometriosis had 2.03 (95% CI: 1.13, 3.63) higher adjusted aPR for hypertriglyceridemia. Women who were diagnosed with DE combined with OE had a 4.01 higher aPR (95% CI: 2.56, 6.29) for hypertriglyceridemia. In sum, we found that endometriosis staging and typology correlated more strongly with hypertriglyceridemia compared to diagnosis alone. A limitation of this study is not having fasting blood draws; however, prior research has shown that non-fasting triglyceride levels are a better predictor of cardiovascular risk than fasting triglycerides.

Long-term cardiometabolic trajectories of women with diagnosed and probable PCOS in a diverse cohort of parous women Wei Perng*, Kyle Salmon, Sheryl Rifas-Shiman, Lianne Chen, Victoria Fitz, Maryam Kazemi, Jan Shifren, Emily Oken, Jorge Chavarro, Kyle Salmon

Polycystic ovary syndrome (PCOS) is an underdiagnosed female endocrinopathy that contributes to metabolic risk across the lifespan. Here, we investigated metabolic trajectories across 3 (average age 37±5 years), 7, 12, and 17-year post-enrollment visits with respect to PCOS status in 557 parous women in Project Viva.

The exposure was PCOS status comprising 3 levels: 1) PCOS diagnosis (dx), per medical records or self-reported clinical dx; 2) probable PCOS, among women with no dx but ≥2 of the following: cycle length<21 or ≥35 days, free testosterone >75th %ile, or elevated anti-Müllerian hormone (AMH) >75th %ile; and no PCOS (referent). Outcomes were body composition (% fat mass; body mass index [BMI]), glycemia (HbA1c, fasting glucose, insulin), and adipokines (leptin, adiponectin). We ran linear mixed models with PCOS status as a fixed effect predictor and random effects for individual ID. Confounders included longitudinal age and baseline weight status, marital status, and income.

70.6% of participants identified as White, 12.8% as Black, 6.5% as Hispanic, 5.8% as Asian, and 4.3% as >1 race or other racial group. Nearly 10% (9.7%) of women had a PCOS dx, 9.2% had probable PCOS, and 81.1% had no PCOS. At baseline, obesity prevalence was 43.9%, 19.6%, and 16.9% for dx, probable, and no PCOS, respectively. Over follow-up, the PCOS dx group had the highest adiposity and leptin, and least favorable glycemia. Women with dx PCOS had 2.0% (95% CI: 0.2, 3.8) higher fat mass and 0.3% (0.1, 0.6) higher HbA1c than those with no PCOS, whereas these outcomes were comparable for probable vs. no PCOS (p=0.23 for % fat mass; p=0.36 for HbA1c). On the other hand, adiponectin – which reflects insulin sensitivity – was lower in both PCOS dx and probable PCOS vs. no PCOS.

While the PCOS dx group generally had the least favorable metabolic profile across 12 years of follow-up, serum adiponectin was lowest among women with probable PCOS, despite this group being leaner, on average, than the PCOS dx group. The prevalence of probable PCOS in this general-risk setting suggests substantial underdiagnosis of PCOS, particularly among lean women. Further, the lower insulin sensitivity in this group highlights the importance of assessing biochemical profiles (e.g., androgens, AMH) among women with irregular cycles, even in the absence of obesity.

Impact of ambient temperature on preterm birth: A multi-city analysis in Japan Shuhei Terada*, Hisaaki Nishimura, Naoyuki Miyasaka, Takeo Fujiwara,

Background: Preterm birth (PTB) is a major public health concern, with its prevalence on the rise in recent decades. Although low and high ambient temperatures have been suggested as potential contributors to PTB in the US and China, regional heterogeneity in access to maternal and child healthcare has also been reported, making it challenging to discern the specific impact of temperature on PTB apart from healthcare access. Using the strengths of the Japanese integrated universal maternal and child healthcare system, this study aimed to assess the association between exposure to ambient temperature and PTB.

Methods: This is a time-stratified case-crossover study. We identified 214,050 PTB cases among 1,908,168 registered singleton live births in 46 prefectures (excluding Okinawa) in the Japan Perinatal Registry Network database between 2011 and 2020. Prefectural meteorological data were obtained from the regional weather stations closest to the respective prefectural offices. Conditional Poisson regression incorporating a distributed lag non-linear model was employed to estimate the associations between daily mean temperature and PTBs for a lag of 28 days in each prefecture, adjusting for relative humidity, air pollution (PM2.5 and ozone), and holidays. We combined the effect estimates from 46 prefectures using a random-effects meta-analysis, yielding pooled relative risks (RRs).

Results: We observed a U-shaped relationship between the mean temperature and pooled RRs of PTB with a significantly higher risk at both low and high temperatures, without evidence of regional heterogeneity ($I2 = 13.9\%$, $P = 0.14$). Compared to 16.0°C, the adjusted RRs were 1.11 (95% confidence interval [CI]: 1.03, 1.19) at 2.9°C (the mean of the 5th percentile) and 1.07 (95% CI: 1.00, 1.15) at 28.6°C (the mean of the 95th percentile).

Conclusions: Both low and possibly high temperatures were associated with an increased risk of PTBs.

Prenatal Ambient Air Pollutant and Climatic Factors Mixture Exposure and Fetal Growth

Stefania Papatheodorou*, Katie Senechal, Michael Leung, Anna Modest, Michele Hacker, Antonella Zanobetti,

Introduction: Research linking prenatal ambient air pollution and climatic factors with fetal growth has largely considered one factor at a time. Real-life exposure involves exposure to mixtures of pollutants and climatic factors; not considering joint effects/effect modification by co-exposures contributes to misleading results.

Methods: We used ultrasound measures of biparietal diameter (BPD), head circumference, femur length, and abdominal circumference (AC), in addition to birth weight, from 9,446 pregnancies that were delivered at the Beth Israel Deaconess Medical Center from 2011-2016. Weekly prenatal pollutant exposures were estimated using satellite-based hybrid chemical-transport models, including nitrogen dioxide (NO_2), ozone(O_3), particulate matter ($PM_{2.5}$), and high-resolution data for temperature and relative humidity. We examined associations between weekly-averaged prenatal pollution mixture levels and outcomes using Bayesian Kernel Machine Regression-Distributed Lag Models (BKMR-DLMs) to identify susceptibility windows for each component and estimate a potentially complex mixture exposure-response relationship including nonlinear effects and interactions. We adjusted for sociodemographic and clinical characteristics, seasonal and long-term trends, and area-level factors.

Results: BKMR-DLMs identified the stronger effect for temperature at early gestation predicting lower BPD in mid-pregnancy (up to -0.10 z-score (95% CI -0.16 to -0.04) at 16 to 23 weeks). There was a negative association between birthweight z-scores and exposure to mixtures of air pollutants, where up to -0.18 (95% CI -0.23 to -0.13) or approximately 88 g decrease in birthweight, comparing the 75th percentile to the median level of exposure to the air pollutant mixture could occur. There was evidence for interactions between O_3, PM2 5, and temperature.

Conclusion: In this multi-pollutant model, we identified a strong association between exposure to higher temperature in early pregnancy and mid-pregnancy fetal brain measurements and a strong association between air pollutants and birthweight.

Neighborhood Socioeconomic Conditions and Disparities in Birth Weight: Investigating Mediation by Prenatal Exposure to Multiple Air Pollutants Nan Ji*, Erika Garcia, Rima Habre, Shohreh F. Farzan, Theresa M. Bastain, Carrie V. Breton,

Background: Despite the strong evidence that prenatal air pollutant exposure is impacted by neighborhood socioeconomic (NSES) and associated with downstream birthweight (BW), the mediating role of prenatal exposure to multiple air pollutants in the NSES and BW relation has not been examined. Our study examined the mediation effect of multiple air pollutants during pregnancy in the association between NSES and BW. **Methods**: BW were abstracted from medical records for women participating in the Maternal and Developmental Risks from Environmental and Social Stressors (MADRES) study—a pregnancy cohort of predominantly low-income Hispanic/Latina women in Los Angeles. One-year averaged Child Opportunity Index overall and from the social and economic domain (COI and COI-SE) before pregnancy were obtained based on participant's residential address. Primary mediators were pregnancy-averaged concentrations of 10 air pollutants. Mediation effects of these pollutants were examined using a regression-based approach (cmest R package) and adjusting for potential confounders (N = 702). **Results**: Compared to those exposed to the lowest quartile, women exposed to the 4th quartile of COI and COI-SE had heavier babies at birth, with increased BW of 41.9 grams (g ; 95%CI: -5.8 g, 89.6 g) and 34.4 g (-11.4 g, 80.2 g), respectively. Nitrogen dioxides (NO2) exposure during pregnancy was found to mediate 10.0 g (0.1 g, 19.9 g) and 8.5 g (0.1 g, 16.9 g) of the observed NSES-BW association. **Conclusions**: Women living in high-opportunity neighborhoods (high COI and COI-SE) before pregnancy delivered infants with higher BW. These positive associations were partially mediated by NO2 exposure during pregnancy. Our next steps include (1) using structural equations modeling to assess the mediation effect of trimester-specific air pollutants; (2) using dimension-reduction approaches to assess the mediation effect of air pollutant mixtures.

Air pollutants and plasma total folate among pregnant women in Canada, 2008-2011 Tyler Smith*, Amanda MacFarlane, Joseph Braun, Eric Lavigne, Markey Johnson, Bruce Lanphear, Ana Maria Siega-Riz, Raji Balasubramanian, Gina Muckle, Mandy Fisher, Jillian Ashley Martin, Tye E. Arbuckle, Youssef Oulhote,

Introduction: Gestational folate metabolism is essential for fetal development but may be disrupted by environmental exposures. We estimated associations between first-trimester air pollutants and first- and third- trimester plasma total folate concentrations among pregnant women in Canada.

Methods: The Maternal-Infant Research on Environmental Chemicals (MIREC) Study enrolled pregnant women (n=1,983) at 11 sites in 10 cities in Canada from 2008 to 2011. We estimated average daily NO2, O3, PM2.5, and SO2 at maternal residences in the first trimester using measurements from National Air Pollution Surveillance (NAPS) stations. We measured plasma total folate in the first and third trimesters (ranges: 6-14 and 32-34 gestational weeks, respectively) using LC-MS/MS. Linear regression models with multiple imputation using chained equations were used to estimate percent change in plasma total folate associated with a 2-fold increase in each pollutant, adjusting for maternal age, education, race, country of birth, income, folic acid supplementation, healthy eating index, and study site.

Results: Median (IQR) average daily NO2, O3, PM2.5, and SO2 were 16.6 (7.1, 27.3) ppb, 22.8 (18.3, 28.5) ppb, 8.6 (5.3, 11.3) µg/m3, and 1.1 (0.6, 1.8) ppb, respectively, in the first trimester. Median (IQR) plasma total folate was 96 (78, 118) and 98 (74, 133) nmol/L in the first and third trimesters, respectively. In the first trimester (n=1,846), NO2 and SO2 were inversely associated with plasma total folate (ß: -3.1% [95% CI: -5.6, -0.5] and -2.3% [95% CI: -4.2, -0.3], respectively). In the third trimester (n=1,604), O3 was inversely associated with plasma total folate (ß = -10.0%; 95% CI: -17.3, -2.1).

Discussion: In cross-sectional and prospective analyses of pregnant women in Canada, ambient air pollutant exposures were inversely associated with plasma total folate. By reducing the availability of folate in pregnancy, air pollutants may impair fetal development, including neurodevelopment.

Exposure to racial discrimination is associated with a 'dose-dependent' increased risk of placentally mediated adverse pregnancy outcomes Sarah Heerboth*, Ebony Carter, Nadia Charguia, Rebecca Fry, Tracy Manuck,

Intro: Racial discrimination is consistently implicated in obstetric disparities. We sought to quantify the extent to which discrimination is associated with placentally-mediated pregnancy complications (plac-comps).

Methods: Primary analysis of a prospective cohort. Participants identifying as Black, White, and/or Hispanic, with singleton, non-anomalous gestations were recruited <22 weeks, 2017-2022, and completed the Krieger Scale, which includes evaluation of discrimination across 9 domains (e.g., school, work). The primary outcome was a diagnosis of plac-comps (any of the following: preeclampsia, gestational hypertension, birthweight <10% for gestational age and sex, placental abruption).

Results: 435 individuals (43% Black, 38% White, 19% Hispanic) were included; 71 (16%) had plac-comps. Surveys were completed at a mean of 17.1 (IQR 16.0-19.7) weeks. Compared to those without plac-comps, individuals with plac-comps were more likely to report discrimination in ≥1 domain (57% vs. 35%, p<0.001), in a greater number of domains (mean 1.8 vs. 0.9, p<0.001), and specifically regarding getting credit/a loan (14% vs. 5%, p=0.007), in public (25% vs. 16%, p=0.048), at stores/restaurants (41% vs. 15%, p<0.001), and at work (31% vs. 15%, p=0.001). Compared to those without plac-comps, those with plac-comps reported worrying more during childhood about racial discrimination against others (49% vs. 30%, p<0.001) and themselves (46% vs. 27%, p<0.001) and worrying more in the past year about racial discrimination against others (56% vs. 38%, p<0.001) and themselves (46% vs. 32%, p=0.019). In regression models, each additional domain an individual experienced discrimination conferred a 17% increased odds of plac-comps (aOR 1.17, 95% CI 1.01-1.35).

Conclusion: Discrimination – common, pervasive across the lifespan, and affecting multiple different aspects of life – is associated with a 'dose-dependent' increase in placentally-mediated pregnancy complications.

Health system barriers and facilitators to accessing non-barrier contraceptives among women sex workers in Vancouver, Canada: Findings from a longitudinal cohort study (2014-2022) Emma Stirling-Cameron*, Andrea Krüsi, Kate Shannon, Esteban Valencia, Kaylee Ramage, Shira Goldenberg,

Background: Despite purportedly universal health coverage in Canada, sex workers (SWs) experience suboptimal access to sexual healthcare. Given limited data regarding health system factors influencing access to non-barrier contraception among SWs, we aimed to assess the separate association between health system factors (health insurance coverage, access to family physicians) and difficulty accessing non-barrier contraceptives (hormonal, long-acting, and emergency) in a prospective cohort of women SWs in Vancouver, Canada.

 Methods: Baseline and semi-annual questionnaire data were from an open community-based cohort of women SWs from 2014-08 to 2022-08. Analysis was restricted to people of reproductive age who had never experienced hysterectomy or tubal ligation. Bivariate and multivariable logistic regression with generalized estimating equations modelled the association between health system factors and experiencing difficulty accessing non-barrier contraceptives in the past 6 months. Multivariable models were adjusted for a-prior confounders.

Results: Among 496 SWs over 8-years, 29% reported difficulties accessing non-barrier contraceptives at least once, 60% lacked health coverage at least once, and 16% never saw a family physician. SWs who lacked health coverage faced higher odds of experiencing difficulties accessing non-barrier contraceptives (AOR:1.69, 95% CI:1.27-2.25). Participants who saw a family physician faced reduced odds (AOR:0.81, 95% CI:0.58-1.14) of experiencing difficulties accessing non-barrier contraceptives.

Conclusion: SWs face gaps in access to non-barrier contraceptives, which was enhanced among those without access to health coverage and primary care. While the government of British Columbia has recently committed to providing non-barrier contraceptives for free, recipients must have provincial health insurance to access this benefit. Policy reform is needed to ensure all contraceptives are accessible for all, regardless of insurance status.

Associations of Neighborhood Vulnerability with Menopause Symptoms and Timing of Onset at Midlife in Project Viva

Izzuddin Aris*, Sheryl Rifas-Shiman, Wei Perng, Melissa Capotosto, Marie-France Hivert, Jorge Chavarro, Emily Oken,

Background: Neighborhood context is increasingly recognized as a key social determinant of women's health. The extent to which neighborhood stressors contribute to menopausal symptoms and timing of onset, however, remains understudied.

Objective: Examine the associations of neighborhood vulnerability during pregnancy through 12y follow-up with menopausal symptoms and timing of onset.

Methods: We geocoded residential addresses from 691 women at enrollment (mean 33.7y), 7, and 12y follow-up visits in Project Viva, and linked each location to census tract-level Social Vulnerability Index (SVI). We grouped SVI into quintiles comprising very low (<20th percentile), low (20th–<40th), moderate (40th–<60th), high (60th–<80th), or very high (≥80th) scores, based on nationwide distributions. Women reported total menopausal symptoms and age at natural menopause at ~18y post-enrollment. Linear and Cox proportional hazards regression evaluated associations of SVI with total symptoms score and timing of onset of natural menopause respectively, adjusting for age at enrollment, prepregnancy body mass index, race and ethnicity, education, household income, and prenatal smoking.

Results: In this study, 35%, 44%, and 48% of women resided in neighborhoods with very low SVI at enrollment, 7y, and 12y follow-up, respectively. SVI was not associated with total menopausal symptoms score. However, residence in neighborhoods with very high (vs. very low) SVI at 7y (adjusted hazard ratio 2.67; 95% CI 1.36–5.25) and 12y follow-up (adjusted hazard ratio 3.07; 95% CI 1.54–6.12), but not at enrollment, were associated with earlier onset of menopause.

Conclusion: Women who resided in neighborhoods with very high social vulnerability across the reproductive years, compared with very low vulnerability, reached menopause earlier. Future research should clarify whether initiatives that alter specific components of neighborhood environment would be beneficial in preventing earlier menopause onset.

Measuring county-level structural racism and its association with racial-ethnic disparities in pregnancy-related mortality ratios Chloe Barrera*, David Goodman, Sarah Blake, Lauren Christiansen-Lindquist, Alex Peahl, Michael Kramer,

Background Racial-ethnic disparities in US pregnancy-related mortality are significant. Structural racism is a recognized fundamental cause of health disparities, yet the relationship between measures of structural racism and pregnancy-related mortality remains understudied.

Methods Pregnancy Mortality Surveillance System data were linked with publicly available indicator data. We constructed county-level indicators as proxy measures of structural racism, including indicators of residential segregation and racial inequity ratios (eg, ratio of Black-to-White poverty rates) across six domains: 1) Segregation; 2) Incarceration; 3) Health; 4) Economic Status; 5) Employment; 6) Education. Indicators were averaged within each domain to develop domain-specific indices and a multidimensional structural racism index was calculated by averaging the domain-specific indices. We used multivariable Poisson generalized estimating equations to examine associations between measures of structural racism and Black/White pregnancy-related mortality.

Results Among the Black population, only the residential segregation index was positively associated with pregnancy-related mortality (Rate Ratio (RR) 1.12, 95% CI: 1.07, 1.18). Among the White population, all domain-specific indices except the residential segregation index were negatively associated with pregnancy-related mortality. Our multidimensional structural racism index was not associated with Black pregnancy-related mortality (RR 1.07, 95% CI: 0.95, 1.21) but was negatively associated with White pregnancy-related mortality (RR 0.75, 95% CI: 0.65, 0.88).

Conclusion Associations between measures of structural racism and pregnancy-related mortality were largely null for Black and negative for White pregnancy-related mortality. More research is needed to understand the complex relationship between structural racism and racial inequities in pregnancy-related mortality.

Association between density of food retailers and fitness centers and gestational diabetes mellitus in Eastern Massachusetts stefania papatheodorou*, Matthew Shupler, Jochem Klompmaker, Michael Leung, Joshua Petimar, Jean-Philippe Drouin-Chartier, Peter James, Anna Modest, Michele Hacker,

Background: Few studies have investigated the association between the food and physical activity environment with the risk of gestational diabetes mellitus (GDM) with conflicting results.

Methods: Medical records from 68,779 pregnant individuals living in Eastern Massachusetts from 2000-2016 were linked by residential address to the density of supermarkets, fast-food restaurants, full-service restaurants, convenience stores, and fitness centers at 500-, 1000- and 1500-meter (m) buffers. Two indices ('healthy food index'; 'restaurant ratio') assessed the relative availability of healthy versus unhealthy food retailers. Multivariable logistic regression quantified the association between exposure variables and GDM odds, adjusting for individual and area-level characteristics. Effect modification by socioeconomic status (SES) was assessed using the Area Development Index (ADI).

Findings: In the fully adjusted model, pregnant individuals living in areas with the highest density of fast-food restaurants had higher odds of GDM compared to individuals living in areas with the lowest density (500 m (odds ratio (OR):1.17 95%CI:[1.04,1.34]), 1000 m (1.36 95%CI:[1.16,1.59]), and 1500 m (1.15 95%CI:[0.97,1.36]). While other exposure variables were not associated with GDM odds, there was significant effect modification by ADI. Among participants living in the lowest SES (highest ADI) neighborhoods, those living in the highest supermarket density tertile had significantly lower odds of GDM at all buffers (500 m; 1000 m; 1500 m. The association between fast-food restaurant density with GDM odds was greater in lower SES areas.

Interpretation: A greater number of fast-food establishments, particularly in low SES neighborhoods, and a lower density of supermarkets in high SES areas were associated with higher GDM risk in Eastern Massachusetts.

Trends and racial/ethnic inequities in Maternal Cardiovascular Health in California Elleni Hailu*, Suzan Carmichael, Jonathan Snowden, Audrey Lyndon, Mahasin Mujahid,

Background: To address the maternal health crisis in the United States, it is important to closely examine the epidemiologic trends of maternal cardiovascular health (CVH), a leading determinant of adverse pregnancy-related outcomes.

Methods: We used state-wide birth hospitalization records from California (1997-2019; N=10,953,764) to examine the prevalence, trends, and racial/ethnic disparities of hypertensive disorders of pregnancy (HDP; chronic hypertension (HTN), gestational HTN, preeclampsia, eclampsia), and pre-pregnancy and gestational HTN separately. We also examined ideal CVH before and during pregnancy using the subset of the data with information available on clinical CVH indicators (2007-2019; N= 6,122,590) constructed based on smoking, HTN, diabetes, and Body Mass Index (kg/m2). We utilized a series of log-binomial and modified Poisson regression models (with robust standard errors) adjusting for year, maternal age, education, insurance, and parity to determine our estimates.

Results: The prevalence of outcomes increased over time for all racial/ethnic groups. Compared to Non-Hispanic White (White) individuals, Non-Hispanic Black (Black) birthing people had a higher risk of HDP (Risk Ratio (RR)=1.57; 95% Confidence Interval (CI): 1.55, 1.58), and both pre-pregnancy (RR=2.38; 95% CI: 2.34, 2.42) and gestational (RR=1.46; 95% CI: 2.34, 2.42) HTN. American Indian/Alaska Native individuals were less likely to have ideal CVH both before (RR=0.69; 95% CI: 0.68, 0.70) and during pregnancy (RR=0.64; 95% CI: 0.63, 0.65) compared to White birthing people. Racial/ethnic disparities for all outcomes widened over time, except for pre-pregnancy HTN, in which disparities comparing Black and American Indian/Alaska Native birthing people with White individuals slightly decreased during the study period.

Conclusion: Our findings confirm persistent racial/ethnic disparities in maternal CVH, highlighting the need to investigate the structural drivers of these inequities.

A series of emulated target trials to estimate the safety of antihypertensives for the management of non-severe gestational hypertension among pregnant individuals in Botswana Julia DiTosto*, Rebecca Zash, Denise Jacobson, Modiegi Diseko, Gloria Mayondi, Judith Mabuta, Mompati Mmalane, Joseph Makhema, Shahin Lockman, Roger Shapiro, Ellen Caniglia,

Antihypertensive therapy is critical for management of non-severe gestational hypertension (HTN), yet potential fetal consequences are unclear. Standard analyses may be subject to immortal time and selection bias. Conducting a series of emulated target trials (ETT) can avoid these biases by aligning start of follow-up with therapy initiation.

The Tsepamo Study has evaluated birth outcomes at government delivery sites in Botswana since 2014. We investigated antihypertensive therapy initiation ≥24 weeks gestation for management of non-severe gestational HTN on stillbirth and small-for-gestational-age (SGA) by conducting 16 sequential ETT of therapy initiation versus no initiation during each week from 24-39 weeks' gestation. For each ETT, pregnant individuals with no history of HTN were eligible if they had not previously initiated therapy and had ≥1 elevated non-severe blood pressure reading (140-159 mm Hg systolic or 90-109 mm Hg diastolic) within 1 week of each ETT start. Log-binomial models were used to calculate RR and 95% CI. Results were pooled across all trials with bootstrapping to obtain CIs. Sensitivity analyses applied more stringent eligibility criteria (i.e., excluding preeclampsia and requiring >1 elevated blood pressure at baseline).

Of 28,608 individuals, 9,524 (33.3%) initiated antihypertensives between 24-39 weeks' gestation. Comparing initiation to no initiation, the pooled RR was 1.18 (1.07-1.40) for stillbirth and 1.15 (1.08-1.27) for SGA. RRs varied by week of ETT start and were sensitive to definition of eligibility criteria. For stillbirth, the pooled RR was 1.07 (0.87, 1.23) when excluding preeclampsia and 0.90 (0.34, 1.32) when requiring >1 elevated blood pressure at baseline.

Our results suggest initiation of antihypertensive therapy for non-severe gestational HTN may increase risk of stillbirth and SGA. Results were sensitive to eligibility criteria definitions, suggesting potential for unmeasured confounding by HTN severity.

Low-dose aspirin prophylaxis for preeclampsia and the risk of postpartum cardiovascular outcomes: a propensity score analysis Ema Mujic*, Sojourna Ferguson, Christina D. Yarrington, Nyia Noel, Samantha E. Parker,

Background: The U.S Preventative Service Task Force recommends initiating low-dose aspirin (LDA) before 16 weeks of pregnancy to prevent developing preeclampsia among people with certain risk factors. While there are robust data supporting the effectiveness of LDA for the prevention of preeclampsia, limited data exist regarding its impact on postpartum outcomes.

Methods: We abstracted electronic medical record data on pregnant people who had a live birth from 2018-2019 and met criteria for LDA prophylaxis (n=1,862) at single safety-net hospital. We created propensity scores using major and moderate risk factors and prenatal care site and used 1:1 matching to identify unexposed (LDA-) matches for the 376 patients that received a prescription for LDA at ≤ 16 weeks of gestation (LDA+). Postpartum outcomes included anti-hypertensive use, postpartum hypertension and readmission. We calculated risk ratios (RR) and 95% confidence intervals (CI) for LDA and postpartum outcomes using log-binomial models. We also assessed the joint effect of LDA and preeclampsia on postpartum outcomes by calculating RRs for combinations of LDA and preeclampsia using those without either as the reference.

Results: After propensity score matching, our sample included 318 LDA+ and 318 LDA- patients with a similar distribution of preeclampsia risk factors. LDA+ was not associated with the postpartum outcomes examined in the overall cohort. However, in the presence of preeclampsia, LDA- patients had the highest risk of postpartum outcomes (e.g. hypertension; RR: 9.09; CI: 6.05, 13.65), while LDA+ patients saw an attenuation in risk (e.g. hypertension; RR: 6.77; CI:4.27, 10.74). (Figure)

Conclusion: Our findings suggest that LDA prescription does not decrease the risk of postpartum cardiovascular-related postpartum outcomes in diverse population of those at risk of preeclampsia. However, among those affected by preeclampsia, antepartum exposure to LDA may attenuate the risk of these outcomes.

Pregnancy outcomes

Racial/Ethnic Differences in the Risk of Preeclampsia/Eclampsia across Body Mass Index Categories Rana Chehab*, Anna Barcellos, Amanda Ngo, Mara Greenberg, Emily Wang, Mahasin Mujahid, Liwei Chen, Assiamira Ferrara, Yeyi Zhu,

Preeclampsia/eclampsia (PE/E) is a leading cause of maternal morbidity and mortality, and racial/ethnic disparities in PE/E are pervasive. Obesity is a major risk factor of PE/E, but it is unknown if obesity contributes to the risk of PE/E differently by race/ethnicity. To address this gap, we examined racial/ethnic differences in PE/E risk across body mass index (BMI) categories.

In a population-based cohort study of 386,596 pregnancies in Northern California in 2011-2020, the risk of PE/E (ascertained by ICD-9/10 codes and validated by chart review) across racial/ethnic-specific pre-pregnancy BMI categories was assessed using Poisson regression models adjusted for sociodemographic and clinical factors.

The age-adjusted PE/E prevalence was highest in Black (6.2% [95% CI, 5.9%-6.6%]), followed by Hispanic (5.3% [5.2%-5.4%]), Asian/Pacific Islander (4.2% [4.0%-4.3%]), and White (4.1% [4.0%-4.2%]) individuals. PE/E prevalence increased with increasing BMI categories (P-for-trend <.001) and differed by race/ethnicity (P-for-interaction <.001). Black individuals consistently had the highest PE/E prevalence across all BMI categories, and they reached higher PE/E prevalence at lower BMI categories compared to White individuals. For example, Black individuals with normal weight had a higher PE/E prevalence than White individuals with obesity class I (5.6% [5.1%-6.1%] versus 5.2% [4.9%-5.6%], respectively). The association of obesity with PE/E risk was strongest in Asian/Pacific Islander individuals (adjusted relative risk comparing obesity class II-III to normal weight, 2.70 [95% Cl, 2.43-3.00]) and weakest in Black individuals (1.45 [1.26-1.68]).

Black individuals had the highest PE/E prevalence and the weakest association of obesity with PE/E risk, suggesting limited applicability of obesity for PE/E risk stratification. Future efforts are needed to better understand the factors contributing to the racial/ethnic disparities in PE/E to inform tailored and equitable screening and prevention.

COVID-19 hospitalizations and hospitalization outcomes among children with immunocompromising conditions, MarketScan Commercial Database, 2020-2022 Regina Simeone*, Emilia Komans, Angela Campbell,

People who are immunocompromised have increased risk for infections compared with those who are not. Our objectives were to assess the association between presence of immunocompromising conditions (IC) in children and COVID-19 hospitalization, and whether hospitalization outcomes occurred more frequently in children with IC compared to those without. Using the MarketScan® Commercial Databases from January 1, 2020–December 31, 2022, eligible children were 0–17 years, continuously enrolled in participating insurance plans for ≥2 years, with ≥1 outpatient encounter. We identified children with IC as having ≥1 IC ICD-10-CM code(s) during a hospitalization, or ≥2 outpatient encounters with IC ICD-10-CM codes. Age, sex, and geographic region of residence were included in all models. We used Poisson regression with robust standard errors, additionally adjusted for non-COVID-19 hospitalizations to estimate the risk ratio (RR) and 95% confidence interval (CI) for any COVID-19 hospitalization. For COVID-19 hospitalization outcomes, we additionally adjusted for year and non-COVID-19 hospitalizations before first COVID-19 hospitalization. A negative binomial distribution was used for hospital length of stay. We included 3,116,239 children; 90,043 (2.9%) had IC and 78,855 (2.5%) had ≥1 hospitalization. Among 3,193 COVID-19 hospitalizations, 1,000 (31.3%) had an IC diagnosis. Compared to those without, children with IC were 5.8 times as likely to have a COVID-19 hospitalization (CI: 5.2, 6.4); among children with ≥1 hospitalization, those with IC were 1.3 times as likely to have a hospitalization with COVID-19 (CI: 1.2, 1.4). Among children with a COVID-19 hospitalization, those with IC had a similar risk of admission to the intensive care unit (RR=1.2, CI: 1.1, 1.4) and readmission within 30 days of COVID-19 hospitalization (RR=1.2, CI: 1.0, 1.5). Future work should assess drivers of COVID-19 hospitalization, specific IC, and hospitalization outcomes among children with IC.

Importance of infant follow-up data for the surveillance of possible birth defects Samantha Distler*, Suzanne Newton, Kate Woodworth, Alison Fountain, Van Tong,

Background: The Surveillance for Emerging Threats to Pregnant People and Infants Network (SET-NET) collects birth and follow-up data on pregnant people and their infants to understand prenatal exposure to COVID-19, HCV, or syphilis. Accurately and efficiently capturing possible birth defects helps address emerging public health threats. Here, we assess how follow-up data affect the completeness of birth defect information reported.

Methods: SET-NET captures birth defects from medical record abstraction and linkages to birth certificate and birth defect registries at birth and follow-up. Follow-up data are collected at multiple time points between two and 24 months of age. Data are then categorized with machine learning[1]. Eleven jurisdictions performed medical record abstraction on all infants, and 18 jurisdictions abstracted data on random samples. Results reflect unweighted counts and weighted prevalence.

Results: As of September 2023, 29 jurisdictions reported 1881 possible birth defects from 1000 liveborn infants across all SET-NET exposures. 1117 (59%) defects were reported at birth. 764 additional defects were reported at follow-up. The most common defects reported only at follow-up were atrial septal defects, microcephaly, macrocephaly, sternocleidomastoid muscle deformities, and craniosynostosis. The weighted prevalence of birth defects was 1.9% (95% CI: 1.2, 2.5) for defects reported only at birth and 4.6% (95% CI: 3.6, 5.5) for defects reported at birth or follow-up.

Conclusions: The weighted prevalence of possible birth defects more than doubled when follow-up data were included. The defects reported only at follow-up were largely consistent with the literature on malformations detected later in the first year of life[2]. Capturing birth defects reported both at birth and follow-up is crucial to improve the completeness of surveillance data.

[1]Newton SM, et al. (2023) Birth Defects Research, 116 e2267

[2]Thomas EG, et al. (2018) Birth Defects Research, 110 142-147

Unintentional Drowning Incidents Involving Children with Autism Spectrum Disorder Treated in US Emergency Departments, 2016-2019 Kristal Xie*, Stanford Chihuri, Ashley Blanchard, Carolyn DiGuiseppi, Caleb Ing, Guohua Li,

Background: Children with autism spectrum disorder (ASD) are at heightened risk of injury mortality, including unintentional drowning. The study aimed to explore the epidemiological patterns of unintentional drowning incidents involving children with ASD treated in US emergency departments (EDs).

Methods: Data for this study came from the Nationwide Emergency Department Sample (NEDS). Children aged 1-19 years diagnosed with ASD and treated in EDs from 2016 to 2019 were identified using ICD-10-CM code F84.0 from the NEDS. Unintentional drowning cases were identified using the CDC ICD-10 injury diagnosis matrix codes W65–W74. Weighted multivariable logistic regression models were used to estimate adjusted odds ratio (aOR) and 95% confidence interval (CI) of drowning-related ED visits associated with ASD.

Results: The weighted annual frequency of unintentional drowning incidents involving children with ASD treated in US EDs increased from 62 in 2016 to 91 in 2019. The hospital admission rate after an ED visit for unintentional drowning was significantly higher among children with ASD (35.14%; 95% CI 33.98, 36.30) than among children without ASD (22.02%; 95% CI 21.10, 22.94). Compared to children without ASD, unintentional drownings in children with ASD were more likely to have occurred in swimming pools (45.64% vs. 34.39%, $p < 0.05$), natural waters (14.30% vs. 12.95%, $p < 0.05$), and bathtubs (5.40% vs. 3.86%, $p < 0.05$). ED visits for children with ASD had an increased odds (aOR = 2.91; 95% CI 2.86, 2.96) of being due to unintentional drowning relative to ED visits for children without ASD.

Conclusion: There has been a marked increase in unintentional drowning incidents involving children with ASD treated in US EDs. ED-treated unintentional drowning incidents involving children with ASD are more likely to occur in swimming pools and require hospital admission than incidents involving children without ASD.

Tracking the Anatomy of a Disparity: Four Unique Typologies of Changing NHB-NHW Disparities in Preterm Birth Rates Across U.S. Counties Allison Stolte*, Joan Casey, Alison Gemmill, Hedwig Lee, Brenda Bustos, Ralph Catalano, Tim Bruckner,

Non-Hispanic Black – Non-Hispanic White (NHB-NHW) disparities in preterm birth (PTB; gestational age <37 weeks) are persistent in the US. Studies and programs addressing such disparities often target changes in NHB-NHW rate ratios or absolute differences. Whereas these measures offer important benchmarks for examining shifts in the relative burden of PTB, they mask absolute changes in subgroup rates. NHB-NHW disparities can decrease even as group-specific rates increase, such that decreasing disparities may not indicate improved population health. In this paper, we dissect the anatomy of a disparity—separately considering changes over time to NHB and NHW PTB—to develop a typological framework for assessing disparity trends. We then classify US counties into four typologies based on changes to their NHB-NHW absolute differences between two periods: 1995-1999 and 2015-2019. Institutional Progress counties, located around metropolitan areas (and especially in Maryland and California), experienced improvements in NHB and NHW PTB and in NHB-NHW disparities. These counties had the lowest NHB and NHW PTB rates in 2015-2019, serving as success stories for addressing disparities while improving population health. Politics of Despair counties, the largest group, experienced reductions in NHB-NHW disparities driven by faster increases in NHW PTB rates. This typology closely aligns with documented trends of increasing mortality rates unique to NHW adults primarily in the US South and rural areas. In Racism as a Fundamental Cause counties, improvements in PTB rates concentrated among NHW births. This process increased NHB-NHW disparities. These counties compose the smallest group and have relatively high 2015-2019 rates of NHB PTB. Finally, Institutional Harm counties experienced increases in NHB and NHW rates and in NHB-NHW disparities. These counties serve as 'cautionary tales' in which widespread harm concentrated among socially disadvantaged (here, NHB) groups. The four typologies uncover the many ways disparities change and can be used to study 'exemplary' counties, understand causes for these changes, and devise strategies for future improvements.

Child health and development

Prenatal exposure to race-based stressors and cardiovascular health: The Bogalusa Heart Study Emily Harville*, Maya David, Patrizia Santos, Lydia Bazzano, Maria Santos

Prenatal stress has been associated with cardiovascular health in offspring, and race-based stress may be particularly damaging. Bogalusa, Louisiana was a hotspot of the Civil Rights Movement and reactionary violence in the 1960s, while the Bogalusa Heart Study, a seminal study in childhood cardiovascular health, began in 1973. We aimed to examine whether cardiometabolic risk levels differed in children who were in utero during peak times of violence. We categorized time as "Bloody Bogalusa" (June-July 1965), early tensions (May 1964-May 1965), later tensions (August 1965-August 1966), and prior to (January 1960 to April 1964), and after this period (August 1966-December 1969). Mean levels of each cardiometabolic marker were examined by time period, stratified by race, with control for age, sex, and secular trend. Birthweight and gestational age were also examined. The study population was one-third Black (n=1277, 33.8%) and two-thirds white (n=2498, 66.2%). Mean age at study visit was 8.6 years. Sixty-two were born during the Bloody Bogalusa period, 437 in the period directly before, and 359 in the period directly after. The outcomes that most closely conformed to the hypothesis were glucose and gestational age: glucose levels were highest among Black children born during the Bloody Bogalusa period (beta=64.12 compared to the earliest period, p<0.01), and gestational age was lower for Black participants born during this time (beta=-1.29 weeks, p=0.05), while no difference was seen for white participants (p for interaction < 0.01 for both). However, for glucose, this is based on a very small number of births. In utero exposure was not associated with other outcomes. Effects of these prenatal exposures were insufficiently large to be clearly demonstrated in a sample of this size. Future studies will need to examine more detailed social and biological measures to identify which aspects of these events were relevant to health.

Using spatial Bayesian models to estimate associations between structural racism and severe maternal morbidity disparities in Georgia Jasmin Eatman*, Katherine Campbell, Kait Stanhope, Sheree Boulet,

The maternal health crisis is especially profound in the state of Georgia, where 35% of births are to Black-identifying people, and rates of severe maternal morbidity (SMM) exceed national averages. Our goal was to estimate associations between contemporary and historic indicators of structural racial discrimination (SRD) and Black-white county-level SMM disparities.

We used Georgia linked live birth/fetal death certificate and hospital discharge data for deliveries to Black and white birthing people for 2013-2020. Instances of SMM during hospitalization occurring intrapartum, delivery, or up to 42 days postpartum were included as an outcome event. Structural racism was defined at the county-level using multiple domains: residential processes, political representation, criminal justice, and historic oppression. We estimated the association of the change in SMM rate difference between Black and White birthing people with measures of SRD using Bayesian spatial models.

The sample included 709,335 deliveries to Black and White individuals and prevalence of SMM was higher among births to Black individuals (31.7 per 1,000) compared to White (18.0 per 1,000) with mean rate difference of 13.7 per 1,000 deliveries. Results of the SRD-SMM regression showed differences solely among residential processes measures comparing spatial polarization of income and the combination of race and income distributions. The estimated change in SMM rate difference between Black and white birthing people increased by 4.5 per 1,000 deliveries in the lowest income counties compared to the highest (B: 4.5, 95% CI: 1.1, 8.0) and increased by 3.8 per 1,000 for concentrated racial/economic disadvantage (B: 3.8, 95% CI: 0.2, 7.4).

Ecologic processes did not fully capture the relationship between SRD and SMM, highlighting the need for further research to elucidate the drivers of disparities in adverse maternal health outcomes.

Neighborhood Deprivation and Severe Maternal Morbidity: An Analysis Across Multiple Geographic Levels in California Sai Ramya Maddali*, Xing Gao, Mahader Tamane, Elleni Hailu, Suzan Carmichael, Mahasin Mujahid,

Neighborhood environments may be important drivers of racial disparities in severe maternal morbidity (SMM). Understanding the impact of neighborhood contexts on SMM requires an investigation of the relevant spatial scales for capturing area-level health effects. This study examined the associations between neighborhood deprivation and SMM across multiple geographic levels in California (i.e., county, census tract, and zip code). This study leveraged statewide data on all hospital births at ≥20 weeks of gestation (2011–2018, N = 3,761,681). SMM was defined as having at least 1 of 21 diagnoses and procedures (eg, blood transfusion or hysterectomy) outlined by the Centers for Disease Control and Prevention. The neighborhood deprivation index (NDI), a summary measure of 8 census indicators (e.g., poverty, unemployment, etc.), was calculated at the county (n = 58), census tract (n = 8057), and zip code levels (n = 1644). Mixed-effects logistic regression models accounting for area-level clustering were used to compare odds of SMM across neighborhood deprivation index quartiles (Q1[least deprived] to Q4[most deprived]), adjusting for sociodemographic and pregnancy-related factors and comorbidities. The prevalence of SMM was 1.6%. In fully adjusted models across all geographic units, the odds of SMM increased as NDI increased. The odds of SMM comparing Q4 vs. Q1 were 1.11 (95% CI 1.07, 1.14) at the census tract, 1.10 (95% C.I. 1.05, 1.15) zip code, and 1.05 (95% CI 0.10,1.13) county levels, respectively. NDI measured at the census tract and zip code levels was more associated with SMM risk compared to NDI measured at the county level. Results demonstrate how measures of neighborhood disinvestment may operate differently across geographic units, underscoring the importance of ensuring theoretical and operational relevancy when considering spatial levels of analysis.

Heat Exposure During Susceptible Windows of Spermatogenesis and Sperm Epigenetic Age

Carrie Nobles*, Timothy Canty, Pauline Mendola, Lindsey Russo, Kaniz Rabeya, Karen Schliep, May Shaaban, Akanksha Singh, Allison Ring, Rachael Hemmert, Neil Perkins, Matthew Peterson, Erica Johnstone, James VanDerslice, Richard Pilsner,

Introduction: Spermatogenesis is uniquely susceptible to redox stress, with age-related disruption of the blood-testes barrier associated with changes in sperm DNA methylation linked to reduced fecundity and pregnancy complications. Heat stress may cause similar disruptions, presenting a route through which high temperatures may impair men's reproductive health.

Methods: We evaluated exposure to high ambient temperatures and sperm epigenetic age in the Folic Acid and Zinc Supplementation Trial (2013-2018). Sperm epigenetic age, the acceleration or deceleration of age-related changes in sperm DNA methylation, was calculated in 1220 men enrolled near Salt Lake City, Utah. Utilizing local hourly temperature data, hours per day exceeding the 98th, 95th, 90th, and 75th percentile thresholds for dry bulb temperature (ambient air) and wet bulb temperature (relative temperature with 100% humidity) were calculated across spermatogenesis and susceptible windows of mitosis, meiosis I+II, spermiogenesis, and spermiation. Generalized linear models adjusted for season, fine particulate matter, and participant characteristics.

Results: During spermatogenesis, an additional 2 hours/day exposure to wet bulb temperatures ≥90th (16.1°C), ≥95th (17.2°C), and ≥98th (17.8°C) percentile thresholds was associated with 0.11 (95% CI 0.04-0.17), 0.18 (95% CI 0.08-0.28) and 0.33 (95% CI 0.12-0.53) years accelerated sperm epigenetic age, respectively. Associations were strongest during the windows of meiosis I+II and spermiogenesis (e.g. 0.08 [95% CI 0.02-0.14] and 0.08 [95% CI 0.03-0.14] years, respectively, for ≥95th percentile). Associations for dry bulb temperature were similar, although moderately attenuated.

Conclusions: Associations of high wet bulb temperatures, capturing impaired efficiency of sweating for cooling body temperature, and accelerated sperm epigenetic age adds evidence that heat-related disruption of spermatogenesis may adversely impact men's reproductive health.

Omics

Metabolic mechanisms underlying the association between the profertility diet and in vitro fertilization outcomes Robert Hood*, Donghai Liang, Yilin Wang, Youran Tan, Irene Souter, Dean Jones, Russ Hauser, Jorge Chavarro, Audrey Gaskins,

The pro-fertility diet is a dietary pattern composed of nutrients and foods most consistently associated with in vitro fertilization (IVF) success in women. We examined the potential biological mechanisms underlying the association between adherence to a pro-fertility diet and IVF outcomes using high-resolution metabolomics. Among 120 women undergoing an autologous oocyte IVF cycle (2007-2015), we collected a serum sample during ovarian stimulation and a follicular fluid sample during oocyte retrieval. Women completed a food frequency questionnaire upon enrollment to examine adherence to the pro-fertility diet pattern. Serum and follicular fluid samples were analyzed using liquid chromatography with high-resolution mass spectrometry. We identified metabolic features and biological pathways associated with the pro-fertility diet and two IVF outcomes (clinical pregnancy and live birth) via a meet-in-the-middle approach. In the follicular fluid, vitamin D3 metabolism was associated with adherence to the pro-fertility diet pattern and live birth. Additionally, vitamin D3 metabolism, vitamin B6 metabolism, and bile acid biosynthesis, were associated with both adherence to the pro-fertility diet pattern and clinical pregnancy. In the serum, only tryptophan metabolism was associated with adherence to the pro-fertility diet pattern and live birth. We confirmed the chemical identity of one metabolite with Level-1 evidence, 4-pyridoxate, which was higher in the serum and follicular fluid among women with stronger adherence to the pro-fertility diet pattern and among women with a live birth. The beneficial association between adherence to the pro-fertility diet and IVF outcomes may be mediated through vitamins D3 and B6 metabolism, and bile acid biosynthesis in the follicular fluid and tryptophan metabolism in the serum. These results provide insight in the important biological pathways underlying a dietary pattern providing optimal fertility benefits to women undergoing IVF.

Exposure to air pollution during pregnancy and gestational weight gain Meghan Angley*, Yijia Zhang, Uma Reddy, Ka Kahe,

Objective: High gestational weight gain (GWG) is associated with adverse maternal and fetal outcomes. Recent studies have identified exposure to air pollution as a risk factor for overweight and obesity in the general population. Few studies have examined the association between different types of air pollution during pregnancy and GWG.

Methods: We used data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-To-Be (nuMoM2b). nuMOM2b is multi-center study of women with singleton pregnancies enrolled during their first trimester. Average mean daily levels of PM2.5, PM10, O3 and NO2 during pregnancy were assigned to participants by linking participant addresses to air pollution monitoring data. GWG was determined by subtracting pre-pregnancy weight from last weight before delivery. Z-scores for GWG by pre-pregnancy BMI category were calculated to account for length of pregnancy. From these z-scores, GWG was categorized as low-moderate ($\leq$ 1 SD) and high (>1 SD). We adjusted for maternal age, race, insurance, education, poverty, season of conception and smoking and diet quality in the three months prior to pregnancy.

Results: We excluded participants whose pregnancies did not end in live birth and those with missing air pollution data. Of the 7,596 women included in the analysis, 14.5% had high GWG. After adjustment for confounders, PM2.5 (OR: 1.30 [95% CI: 1.04, 1.63], per 5 µg/m3 increase) was associated with high GWG, but not PM10 (OR: 0.84 [95% CI: 0.70, 1.01], per 10 µg/m3 increase), O3 (OR: 0.94 [95% CI: 0.74, 1.20], per 10 ppb increase) or NO2 (OR: 0.87 [95% CI: 0.70, 1.08], per 10 ppb increase).

Conclusions: Exposure to PM2.5 during pregnancy may be associated with high GWG. Future research includes exploring if the association may be due to increased inflammation or reduced physical activity.

Big Data/Machine Learning/AI

Who are we learning about when we use app data to study reproductive health? Jenna Nobles*, Hailey Ballard, Hailey Ballard

Data from menstrual- and pregnancy-tracking "apps" provide a new window into difficult- to-study dimensions of reproductive health, including menstrual irregularity, early pregnancy loss, and postpartum depression. App data are poised to significantly advance research on patterns, causes, and consequences of common reproductive health issues. A key challenge for health researchers is the potential sample selection of app users. App users are people who have smartphones and choose to track their health. We collected detailed data from a nationally-representative survey panel (n=2,644) in early 2023 on the use of menstrual and pregnancy apps, as well as a battery of questions about health and sociodemographic characteristics. We document significant variation in whether and why people use menstrual and fertility tracking apps by race, region, and most importantly, health. Using menstrual tracking app data, we show how this can distort estimates of health disparities. We then demonstrate an approach to address this issue by combining app data with complementary survey data.

Tampon use as a source of endocrine disrupting chemical exposure: Results from NHANES 2001-2004 Kristen Upson*, Mandy Hall, Jenni Shearston, Kathrin Schilling, Beizhan Yan, Khue Nguyen, Nancy Reame, Nicole Talge, Elizabeth Cordill, Marianthi-Anna Kioumourtzoglou,

Tampons are used by 50-86% of US menstruators and absorb menstrual fluid in the vagina. As the vaginal mucosa is permeable and highly vascularized, we hypothesize that tampons are a source of endocrine disrupting chemical (EDC) exposure. Tampons may become contaminated with EDCs during manufacture; antimicrobial and lubricant agents are also added. EDCs previously detected in tampons include phthalates, phenols, and perfluoroalkyl substances (PFAS). To investigate our hypothesis, we conducted a cross-sectional analysis using National Health and Nutrition Examination Survey (NHANES) data, years 2001-2004. The study population comprised menstruators ages 20-49 whose last menstrual period started within 30 days of NHANES interview and sample collection, with data on 8 urinary phthalate metabolites (MnBP, MiBP, MEP, MBzP, MEHP, MEHHP, MEOHP, MCPP; 2001-2004 cycles, unweighted n=427) 3 urinary phenols, (Bisphenol A (BPA), benzylphenone-3 (BP-3) and triclosan; 2003-2004 cycle, unweighted n=226) and 4 serum PFAS (PFOA, PFOS, PFHxS, PFNA; 2003-2004 cycle, unweighted n=172). We conducted multivariable linear regression to estimate the percent difference in EDC levels and 95% CIs with tampon use, adjusting for age, education, and smoking; for PFAS, we additionally adjusted for oral contraceptive use and nulliparity. Urinary concentrations were creatinine-corrected. Tampon use in the past 30 days was common (62%). We observed that tampon use was associated with 61% higher triclosan levels (95%CI: 18%, 117%), 43% higher PFOA levels (95%CI: 17%, 73%), 33% higher PFNA levels (95%CI: 6%, 68%), 22% higher PFOS levels (95%CI: -3%, 54%), 20% higher PFHxS levels (95%CI: -6%, 54%), and 19% higher MEHP levels (95%CI: -4%, 48%). No associations were observed for the remaining EDCs. Our results suggest increased exposure to select phenols, phthalates, and PFAS with tampon use. This is concerning given the adverse health associated with these EDCs and the frequency of tampon use in the US.

Post Dobbs: Distance to abortion facilities and depressive symptoms among racially/ethnically minoritized women of reproductive age Abhery Das*, Allison Stolte, Samantha Gailey,

On June 24, 2022, the US Supreme Court's decision on Dobbs v. Jackson Women's Health transformed the landscape of abortion access in the US by granting states the power to ban abortion. In the following months, several states implemented restrictive abortion laws that limited women's fertility decisions and hindered their access to comprehensive reproductive care. The symbolic dis/empowerment framework suggests that these new sociopolitical contexts may disempower women in ways that harm their psychological well-being. Indeed, one study reports greater mental distress among women of reproductive age following the Dobbs decision. The psychological burdens of Dobbs, however, likely manifest heterogeneously. Previous studies find that racially/ethnically minoritized women experienced disproportionate harms from pre-Dobbs restrictive reproductive health laws. More recently, many abortion-related lawsuits have targeted racially/ethnically minoritized women, which may heighten feelings of disempowerment among these groups. We test whether state-level disempowerment related to women's reproductive health, proxied as distance to abortion facilities, coincide with greater depressive symptoms among racially/ethnically minoritized women of reproductive age after the Dobbs decision. As our exposure, we utilize quartiles of within-state average driving distance (miles) to abortion facilities, captured at the county-level. For our outcome, we use the Patient Health Questionnaire-2, a clinically valid measure of depressive symptoms among 49,361 racial/ethnic minoritized women of reproductive age (18-49). We use biweekly surveys (repeat cross-section) from August 2020 – July 2023 from the nationally representative Census Household Pulse Survey. We find that women of color the furthest away from abortion facilities (quartile 4; >103 miles) show slightly greater depressive symptoms (Coeff: 0.13; SE: 0.04; p=0.003) than women of color closer to abortion facilities (quartile 1; <28 miles) after the Dobbs decision. Increased distance to abortion facilities may reflect feelings of restricted bodily autonomy and overall disempowerment that hinder the mental health of women of color at reproductive age.

Prenatal antiretroviral therapy initiation and early learning and development outcomes among HIV-exposed, uninfected children 4-6 years of age in Tanzania Nandita Perumal*, Arvin Saleh, Alfa Muhihi, Dana McCoy, Jonathan Seiden, Mohamed Bakari, Veneranda Mumburi, Nzovu Ulenga, Christopher Sudfeld, Karim Manji,

Background: Children who are exposed to human immunodeficiency virus (HIV) but are uninfected (HEU) are at a greater risk of suboptimal neurodevelopmental outcomes later in life, which may in part be due to exposure to combination antiretroviral therapy (cART) in-utero.

Objectives: We estimated the effect of timing of prenatal ART initiation on early learning and developmental outcomes among HEU children in Dar es Salaam Tanzania.

Methods: Data from an observational cohort study of children between 3-6.5 years of age born to HIV-infected pregnant women who were previously enrolled in a prenatal maternal vitamin D supplementation randomized placebo-controlled trial in Dar es Salaam, Tanzania, were used. Pregnant women in the parent trial were either previously on, or initiated, cART at trial enrolment between 12-27 weeks of gestational age. We used a rigorous and culturally adaptable tool – International Development and Early Learning Assessment (IDELA) – to assess early learning and development outcomes in children, including their early literacy, numeracy, motor, social-emotional, and executive functioning skills. Marginal structural models with stabilized inverse probability weights were used to estimate the mean difference in the standardized residual scores of early learning and developmental outcomes by timing of cART initiation. Maternal sociodemographic factors, HIV disease stage at enrolment, immune status, child age, sex, and trial regimen were accounted for in the models.

Results: Among 667 caregiver-child dyads who completed follow-up, 322 (48%) were on cART preconceptionally and 345 (52%) initiated cART during pregnancy, with 240/345 (70%) starting cART at <20 weeks of gestational age. Initiating cART preconceptionally compared to during pregnancy was not associated with overall or domain-specific early learning and developmental outcomes. However, among children born to women who initiated cART during pregnancy, starting cART at <20 weeks compared to ≥20 weeks of gestation was associated with lower overall early learning and development score (Mean difference [MD]: -0.255 SD; 95% CI: -0.509, -0.001) and executive function score (MD: -0.290SD; 95% CI: -0.541, -0.038).

Conclusion: Initiating cART earlier compared to later in pregnancy, but not preconceptionally, was associated with lower overall and executive functioning skills among HEU children in this study.

Vanishing twins likely contribute to the disparity in birthweight between Non-Hispanic Black and Non-Hispanic White periviable infants Allison Stolte*, Ralph Catalano, Joan Casey, Alison Gemmill, Brenda Bustos, Tim Bruckner, Tim Bruckner

Periviable births (<26 weeks gestation), which account for >40% of all infant deaths, are an important source of Non-Hispanic Black / Non-Hispanic White (NHB-NHW) infant mortality disparities in the United States. NHB-NHW disparities in infant mortality rates are highest in the periviable period, when NHB population-weighted rates of infant mortality exceed 2.5 times NHW rates. The relatively small mean birthweight among NHB (v. NHW) periviable births likely contributes to these mortality differences. Here, we consider a possible mechanism contributing to this periviable birthweight disparity: the vanishing twin syndrome. "Vanishing twin" is a phenomenon in which one twin fetus dies in utero. Exposures to environmental stressors that disproportionately harm NHB birthing persons and that slow in-utero growth can increase the likelihood of such fetal loss, particularly among male twins. The surviving fetus often exhibits a lower birthweight compared to "true" singletons of the same gestational age. Following this logic, we test the hypothesis that excess fetal loss among NHB male twins increases the NHB-NHW disparity in periviable singleton birthweights. We use a novel approach to estimate vanishing twins as a function of the NHB twin sex ratio, with the expectation that male pairs are more sensitive to environmental stressors than female pairs. Using 1995-2018 US Vital Statistics Natality File and Box-Jenkins time-series methods, we examine if lower than expected sex ratios among NH Black periviable twins—a proxy for vanishing twins—predict higher NHB-NHW disparities in periviable singleton birthweights (in grams) across monthly conception cohorts. We find that NHB-NHW disparities in periviable birthweights decline in cohorts with more than expected NHB male twin births (Coeff: -23.90; SE: 11.96, p<.05). Results suggest that vanishing twins—for Black males in particular—can affect the NHB-NHW disparity in singleton periviable birthweights by up to 18%.

Mental health

Association of Women with PCOS to a higher prevalence of having biological children with ASD-ADHD
Chinthana Thangavel*, pallavi dubey, Sireesha Reddy, Alok Dwivedi, Maria Villanos,

Introduction
Background: Autism spectrum disorder (ASD) is a serious neurodevelopmental disorder among children. Attention-deficit/hyperactivity disorder (ADHD) is a prevalent comorbid condition with ASD yielding substantial lifelong impacts. Metabolic conditions during pregnancy may be risk factors for ASD-ADHD in offspring. However, it is unclear if maternal polycystic ovary syndrome (PCOS)can be a risk factor for ASD-ADHD in their offspring.

Methods
Hypothesis: We hypothesized that maternal PCOS is a major risk factor for ASD or ADHD in children. Methods: We designed a case-control study in the Hispanic population and recruited women accompanying their children with or without a diagnosis of ASD and ADHD from the behavioral pediatrics clinics. We evaluated the conditions of mothers using a PCOS survey questionnaire. We evaluated risk factors, demographics, comorbidities, and pregnancy complications. Multiple logistic regression analyses will be conducted to determine associations between a mother's characteristics with offspring PCOS compared to controls.

Results
Results: 157 subjects were eligible and consented to PCOS screening. 88 mothers had children with ASD-ADHD while 69 were controls. The mothers in the ASD-ADHD group had a significantly higher prevalence of diagnosed PCOS compared to controls (p=0.023). The odds of ASD-ADHD were 6.35 (AOR=6.35, 1.23, 32.74, p=0.027) times in PCOS mothers compared to controls after adjusting for known confounders. The ASD-ADHD group mothers also had a higher prevalence of hirsutism and menstrual dysfunction.

Conclusion/Implications
Conclusion: Maternal PCOS is independently associated with substantially increased risks in offspring for comorbid ASD-ADHD.

Social Determinants of Health Mediate Racial and Ethnicity Disparities in Preeclampsia: Insights from the All of Us Program Olivia Kapera*, Baojiang Chen, Jaime Almandoz, Courtney Byrd-Williams, Sarah Messiah,

Introduction: Preeclampsia is one of the leading causes of maternal and perinatal morbidity and mortality. However, the relationship between preeclampsia and various social determinants of health (SDOH) is not well understood.

Methods. All of Us cross-sectional research program data of 2,287 pregnant individuals (18-44 years old) was analyzed. SNOMED codes confirmed preeclampsia cases (yes/no). Race and ethnicity were self-reported (Asian, non-Hispanic Black (NHB), Hispanic, and non-Hispanic White (NHW)). SDOH factors, including maternal education, insurance coverage, neighborhood cohesion and environment, food and housing insecurity, perceived discrimination and stress, and discrimination in medical settings, were obtained via standardized surveys. Multivariable mediation analyses, using multiple additive regression trees (MART), assessed whether SDOH factors meditate racial and ethnic disparities in preeclampsia.

Results: Of 2,287 individuals (mean age 37.6 [SD 5] years, 67% NHW, 21% Hispanic, 8% NHB, 3% Asian), 5% (n=108) had preeclampsia. Racial disparities (NHB vs NHW) in preeclampsia were partially explained by insurance coverage (Relative Effect 0.8), marital status (16.1), and healthcare access (5.1) (p<.001 for all). Perceived discrimination (-36.2), perceived stress (-6.0), age (-7.3), and education (-2.0) magnified this disparity (p<.001 for all). Ethnic group preeclampsia disparities (Hispanic vs NHW) were partially explained by perceived stress (7.2), marital status (15.8), and income (56.9) (p<.001 for all). Neighborhood cohesion (-10.4), discrimination in medical settings (-20.0), age (-48.2), and education (-25.0) magnified this disparity (p<.001 for all).

Conclusion: Findings reveal concerning trends, suggesting discrimination and stress disproportionately impact NHB with preeclampsia while neighborhood environmental factors impact Hispanics. These findings underscore the need for culturally competent targets in addressing preeclampsia disparities.

Maternal psychosocial stress in pregnancy and children's blood pressure trajectories from infancy to adolescence: Findings from Project Viva Farah Qureshi*, Kelsey Williams, Kelsey Williams

BACKGROUND: Psychosocial stress is associated with poor cardiovascular health across the lifespan, including during pregnancy, when the health impact of stress has the potential to extend intergenerationally. To date, few longitudinal studies have evaluated prenatal stress in relation to children's cardiovascular health. The goal of this study is to examine associations with children's blood pressure trajectories from infancy through mid-adolescence.

METHODS: Our sample included 1,780 mother-child dyads from Project Viva, a longitudinal pre-birth cohort based in Massachusetts that enrolled participants from 1999-2002. Psychosocial stress was assessed using validated, maternal-reported measures of depression, anxiety, and experiences of racial discrimination collected in mid-pregnancy (28 weeks gestation). Five assessments of children's systolic blood pressure (SBP) were collected in clinical exams during infancy (6m), early childhood (3y), mid-childhood (7y), early adolescence (12y), and mid-adolescence (17y). Associations were evaluated with SBP levels in each developmental period and with changes in SBP levels over time using mixed effects linear spline models adjusting for key confounders. Sex differences were also investigated using interaction terms and stratification.

RESULTS: There were no apparent associations between prenatal psychosocial stress and children's blood pressure levels across development. Despite apparent differences in blood pressure patterns between boys and girls, associations did not vary by sex.

DISCUSSION: Although psychosocial stress is a critical risk factor for cardiovascular disease, we did not find evidence that in utero exposure to maternal stress can have intergenerational impacts on children's blood pressure patterns over time. Our findings provide preliminary support for growing concerns about the assumed primacy of maternal exposures during pregnancy in psychosocial research on the developmental origins of disease.

Epidemiology of Macrocephaly in the Texas Birth Defects Registry, 1999-2019 Rachel Allred*, Dayana Betancourt, Lisa Marengo, Jacquelyn Aguilar-Martinez, Rebecca Howell, Ashley Dixon, Hye Na Jeon, Caitlyn Yantz, Fernando Arena, Joanne Nguyen, Margaret Drummond-Borg, Charles Shumate,

Authors: Allred RP, Betancourt D, Marengo L, Aguilar-Martínez J, Howell R, Dixon A, Jeon H, Yantz C, Arena F, Nguyen J, Drummond-Borg M, Shumate C

Background: Macrocephaly is defined as an occipitofrontal head circumference exceeding two standard deviations above same age and sex norms. Macrocephaly can present as isolated or non-isolated, varying in phenotype depending on if there is an underlying syndrome. The purpose of the present study was to describe the prevalence of macrocephaly in the Texas Birth Defects Registry (TBDR) between 1999-2019 by select infant and maternal characteristics.

Methods: All cases with a modified British Pediatric Association code of 742.400 in the TBDR between 1999-2019 were identified. All pregnancy outcomes, and definite and possible/probable diagnoses were included. Prevalence rates per 10,000 live births and 95% confidence intervals (CIs) were calculated by infant sex and maternal characteristics (age, education, race/ethnicity, diabetes history, urban/rural residence, and body mass index). In sensitivity analyses, prevalence calculations were repeated for: 1) definite, isolated cases excluding "benign" or "familial"; 2) definite, non-isolated cases; 3) definite, non-isolated cases excluding chromosomal and syndromic cases; and 4) definite, proportionate (at birth) cases.

Results: Overall, between 1999 and 2019, 14,637 cases of macrocephaly were identified, resulting in a prevalence rate of 18.16/10,000 live births (95% CI: 17.87-18.45). Most cases were live born (99%) and had a definite diagnosis (87%). More than half were classified as non-isolated (57%). Prevalence was significantly higher among males, and among cases whose mothers were older, Non-Hispanic White, had greater than high school education, resided in an urban area, had a history of diabetes, and were obese. Prevalence rate patterns did not change across sensitivity analyses.

Conclusions: To our knowledge, we are the first to describe the epidemiology of macrocephaly in a birth defects registry. The clinical significance of isolated macrocephaly is not well understood and warrants further investigation.

Racial and Ethnic Disparities in Under-5 Mortality among Children with Birth Defects in North Carolina Kristin Bergman*, Helen Atkinson, Nina Forestieri,

Birth defects are a leading cause of early childhood death. While several studies have examined racial/ethnic disparities in infant and childhood mortality attributable to birth defects, fewer have linked birth defect registry data with mortality data to assess disparities in mortality rates beyond infancy.

This analysis describes differences in under-5 mortality by maternal race/ethnicity among a retrospective cohort of 56,313 children liveborn 2003-2016 with one or more birth defects. North Carolina Birth Defects Monitoring Program records and birth certificate data were linked to 2003-2021 state death certificates to capture deaths within five years of birth. Mortality rates were calculated for the overall sample and by birth defect. Rate ratios (RR) adjusted for region of residence, maternal education, maternal age, and case classification (isolated, multiple, or chromosomal/syndromic) were computed to compare differences in mortality by maternal race/ethnicity (non-Hispanic [NH] White [n=32,553], NH Black [n=13,252], Hispanic [n=8,097], NH Non-White/Non-Black [n=2,411]).

Overall mortality rates (per 1,000 live births) were highest for NH Black children (92.4), followed by NH Non-White/Non-Black (77.1), Hispanic (76.3) and NH White (56.0). Compared to NH White children, all other racial/ethnic groups had higher mortality for several defects, including Trisomy 21 and cleft lip with cleft palate (CLP). The largest adjusted RRs were among NH Black (RR 2.98, 95% confidence interval [CI] 1.80-4.94), NH Non-White/Non-Black (RR 2.68, 95% CI 1.29-5.58), and Hispanic children (RR 2.29, 95% CI 1.29-4.09) with CLP.

Our analysis of a large cohort of children with birth defects revealed significant disparities in under-5 mortality, most evident among NH non-White populations. Analysis of linked birth and death records after the first year provides an opportunity to monitor survival among children with birth defects beyond infancy and address disparities at the population level.

Racial and Ethnic Inequities in Care Management for Birth Person-Infant Dyads Impacted by Neonatal Abstinence Syndrome in Massachusetts Alyssa Pochkar*, Mahsa Yazdy, Susan Manning, Eirini Nestoridi,

Background: Neonatal abstinence syndrome (NAS) in newborns results from in utero substance exposure that leads to withdrawal. We aimed to identify racial and ethnic inequities in care management of birth person-infant dyads impacted by NAS in Massachusetts (MA).

Methods: MA Department of Public Health (MDPH) collects data for NAS surveillance from birth certificates and medical records. NAS surveillance data for birth person-infant dyads delivering in MA during 4/1/2020-12/31/2021 were analyzed to estimate the prevalence of care management measures such as receipt of medication-assisted treatment (MAT) and Plans of Safe Care (POSC), infant discharge disposition, and documented referral to the Early Intervention (EI) program in the medical record by race and ethnicity. MDPH began collecting data on receipt of MAT and referral to EI in April 2021.

Results: Of the 1,388 infants diagnosed with NAS in MA, 81.2% were delivered to Non-Hispanic (NH) White, 7.5% to Hispanic, and 5.0% to NH Black birthing people. NH Black birthing people were less likely to receive a POSC (14.5%) than NH White birthing people (29.6%). Additionally, infants born to NH Black and Hispanic people were less likely to be discharged home to one or both parents (59.5% and 55.8%, respectively) compared to infants born to NH White people (69.8%). Among dyads with data on MAT and referral to EI program (535 dyads), 54.8% of NH Black and 61.0% of Hispanic birthing people received MAT, compared to 64.9% of NH White people; 48.8% of infants born to Hispanic people were referred to EI, compared to 61.1% of infants born to NH White people.

Conclusions: We identified racial and ethnic inequities in care management for families affected by NAS in MA. These results will be shared with MA's Perinatal Neonatal Quality Improvement Network to inform policies related to care of birth person-infant dyads affected by NAS and MDPH programs that serve these families.

Neonatal mortality prediction using the five-minute Apgar score among infants with birth defects Katherine Ludorf*, Renata Benjamin, Lisa Marengo, Mark Canfield, Tina Findley, Anthony Johnson, KuoJen Tsao, AJ Agopian,

Background: The Apgar score, a brief tool assessing the health of newborns in the delivery room, is predictive of neonatal mortality in the general population. However, its predictive performance in neonates with birth defects remains unexplored, despite its routine clinical use among this population. This study aimed to assess the Apgar score's ability to predict neonatal mortality in neonates with a spectrum of major birth defects.

Methods: We obtained statewide data on neonates with birth defects born between 1999 and 2017 from the Texas Birth Defect Registry (TBDR). Logistic regression was used to predict neonatal mortality (death within the first 28 days of life) based on the 5-minute Apgar score (<7 vs. ≥ 7), across a spectrum of 26 birth defect categories. Receiver operating characteristic (ROC) curves and area under the curve (AUC) values were calculated to evaluate discrimination capacity. Analyses were repeated among the subset of neonates with isolated birth defects, and we also repeated analyses, stratified by preterm term status.

Results: The 5-minute Apgar score yielded a relatively high predictive ability for neonatal mortality, with AUC values of 0.66-0.87 across various defect categories. The highest AUC values were observed for reduction defects of lower limbs (AUC 0.87) and spina bifida without anencephaly (AUC 0.83). Predictive capacity remained similar upon restriction to neonates with isolated defects (AUC 0.62-0.83), and upon restriction to preterm neonates (AUC 0.66-0.85) and term neonates (AUC 0.68-0.85).

Conclusions: The 5-minute Apgar score appears to be a valuable tool for predicting neonatal mortality in neonates with birth defects. These findings underscore the continued utility of the Apgar score as a rapid clinical assessment tool, even in complex cases with birth defects. Ongoing research may further refine the application of the Apgar score in this vulnerable population, benefiting both clinical practice and population health research.

Application of a Maternal Comorbidity Index to Predict Childhood Cancer Risk: A Population-Based Case-Control Study in Denmark (1977-2013) Tobiloba Adanma Adenekan*, Julia Heck, Cheng Yin, Johnni Hansen, Julia Heck

Background

A mother's health conditions before and during pregnancy could have important consequences for her child's health, including cancer development, as was observed in some prior studies.

Objectives

This study aimed to identify the impact of varying maternal comorbidities on the development of childhood cancers. This study applied an Obstetric Comorbidity Index (OCI) (Bateman, 2013) to examine maternal comorbid conditions in childhood cancer risk.

Methods

We conducted a population-based case-control study using the Danish National Patient Registry to obtain maternal health conditions and the Cancer Registry for child outcomes, at two time periods: cases (n=2578) and controls (64450) with ICD-10 diagnoses from 1994-2013, and the second population included cases (n=8339) and controls (n=208475) with ICD-8 and 10 diagnoses from 1977-2013. We estimated the risk of childhood cancer using conditional logistic regression.

Results

Multiple gestation pregnancy (OR=1.17, 95% CI 1.05, 1.30), maternal pre-existing diabetes (OR=1.68, 95% CI 1.14, 2.48), congenital heart disease (OR=2.62, 95% CI 1.13, 6.09) and previous cesarean delivery (OR=1.35, 95% CI 1.03, 1.75) showed an increased risk of childhood cancers (all types combined). In the 1977-2013 population, there was an increased risk of acute lymphocytic leukemia (ALL; OR=1.08, 95% CI 1.04, 1.13) and rhabdomyosarcoma (OR=1.13, 95% CI 1.01, 1.27) for each unit of increase on the OCI. Examining mothers that had a score of at least one in the OCI, there was a higher risk of ALL (OR=1.43, 95% CI 1.26, 1.62), non-Hodgkin lymphoma (OR=1.50, 95% CI 1.17, 1.91), Burkitt lymphoma (OR=1.71, 95% CI 1.12, 2.61), and rhabdomyosarcoma (OR=1.58, 95% CI 1.10, 2.26).

Conclusion

The results of the study show varying effects of exposure to one or more maternal comorbidities on individual pediatric cancer types, and an overall increased risk of several cancers in children with mothers who have 1 or more comorbidities.

Cumulative Incidence of Medical Complexity through Early Childhood and Associations with Birth Outcomes in a U.S. Military Birth Cohort Jackielyn Lanning*, Clinton Hall, Celeste Romano, Anna Bukowinski, Gia Gumbs, Jordan Taylor, Sarah Craig, Monica Lutgendorf, A. James O'Malley, Elizabeth Perkins, David David C. Goodman, Ava Marie Conlin, JoAnna Leyenaar,

Background: Children with medical complexity (CMC) have one or more chronic medical conditions that impact daily living. While CMC represent a small proportion of the pediatric population, they experience a disproportionate fraction of medical care and costs. This study estimated the cumulative incidence of CMC by age 60 months in a cohort of live births among United States military families and measured associations between CMC and birth outcomes.

Methods: Department of Defense Birth and Infant Health Research program data captured births among military families, 2005-2015. Healthcare claims through 60 months of age identified CMC using two validated algorithms: the Pediatric Medical Complexity Algorithm and the Complex Chronic Condition Classification System. Birth characteristics were compared by CMC status. Accounting for death as a competing event and loss to follow-up, the cumulative incidence of CMC by age 60 months was estimated and Fine-Gray regression models calculated adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for associations of CMC with birth outcomes.

Results: Overall, 980,246 live births were identified and the estimated cumulative incidence of CMC by age 60 months (n=104,077) was 11.3% (95% CI=11.3-11.4). CMC were more likely to be delivered by cesarean section (36.9 vs 27.4%) and have intensive neonatal care (23.0 vs 3.6%) than children without medical complexity. Hazard of CMC was highest for children born with vs without congenital anomalies (aHR=26.4; 95% CI=25.6-27.2), very preterm (<32 weeks' gestation) vs term (aHR=2.5; 95% CI=2.4-2.5), and very low birthweight (<1500 grams) vs normal birthweight (aHR=14.4; 95% CI=13.9-14.8).

Conclusions: Approximately 1 in 10 military children developed medical complexity by age 5; understanding the burden of CMC in this population can guide future research and planning of services. Adverse birth outcomes were highly associated with risk of medical complexity through early childhood.

Preterm birth and mortality from early childhood to young adulthood Asma Ahmed*, Sonia Grandi, Eleanor Pullenayegum, Sarah McDonald, Jason Pole, Shahirose Premji, Marc Beltempo, Fabiana Bacchini, Prakesh Shah, Petros Pechlivanoglou,

Background: Preterm birth (PTB) is a leading cause of neonatal mortality. However, evidence on mortality beyond the neonatal period is limited, especially in North America. We aimed to examine the effect of PTB on mortality from 1 to 36 years of age.

Methods: Using administrative data from Statistics Canada, we created a population-based cohort of children born in Canada in 1983-1996 (5 million births) and followed until 2019 (age 23-36 years) to ascertain deaths. We estimated risk differences (RD) and ratios (RR) for all-cause mortality using log-binomial regressions, and hazard ratios (HR) for cause-specific mortality using Cox proportional hazards models (censoring individuals who died from other causes) within prespecified age intervals. We accounted for observed confounding using coarsened exact matching on baseline characteristics (e.g., birth year, parental demographics).

Results: During the follow-up period, 72,662 individuals died (5,517 [1.7%] preterm and 49,034 [1.1%] term). PTB was associated with an increased risk of death in all age intervals, with the strongest association seen in early childhood (1-5 years) (RD 0.3%, 95% CI 0.3-0.4%; RR 2.8, 95% CI 2.6-3.0) and the weakest association in the 18-28 age group (RD 0.1%, 95% CI 0.0-0.1%; RR 1.1, 95% CI 1.1-1.2). For cause-specific mortality, PTB was associated with a higher risk of neurological and respiratory disease mortality across all age groups (HR 2.6 (2.2-3.0) and 2.2 (1.7-2.9) respectively, in the 18-36 age group). We also found increased risks of mortality due to cardiovascular, gastrointestinal, and endocrine-related causes and infections. Associations by gestational age (GA) categories showed higher risks with lower GA.

Conclusion: Individuals born preterm are at an increased risk of death from early childhood to their second and third decades of life, with higher risks as GA decreased. These findings suggest the need to consider long-lasting effects of PTB and may inform preventive strategies.

The association between cord blood mitochondrial DNA measures and childhood autistic traits: a prospective birth cohort study Xueqi Qu*, Heather Volk, Xiaobin Wang,

Background: Previous studies have reported on the association between mitochondrial DNA (mtDNA) measures and autism spectrum disorder (ASD). Few studies have examined mtDNA measures on quantitative autistic traits.

Methods: We evaluated the association between mtDNA measures (mtDNA content and heteroplasmic mutations) in cord blood and childhood autistic traits measured by the Social Communication Questionnaire (SCQ) and Social Responsiveness Scales (SRS) in about 400 children of the prospective Boston Birth Cohort (~65% Black, ~25% Latinx). MtDNA measures were assessed by the STAMP multiplex sequencing method. Multivariable linear regression was used for SCQ and SRS scores as continuous outcomes, adjusting for child sex, age, and mtDNA macro-haplogroups; and logistic regression was applied for dichotomous measures (cut-off value at 15 for SCQ and at 75 for SRS) adjusting for the same set of covariates.

Results: Children with heteroplasmic sites at oxidative phosphorylation (OXPHOS) or transfer ribonucleic acid (tRNA) genes had higher mean SCQ scores (Beta = 1.26, 95% Confidence Interval (CI): 0.22, 2.29) and a higher likelihood of having an SCQ score >= 15 (Odds Ratio (OR) = 2.38, 95% CI:1.00, 5.66). Although the effect of mtDNA heteroplasmy on total SRS raw score was not statistically significant, having heteroplasmic sites at OXPHOS or tRNA genes was associated with an increased likelihood of having SRS T score >=75 (OR=3.90, 95%CI: 1.37, 11.09). There was no association of mtDNA content nor total heteroplasmy with autistic traits.

Conclusion: In this prospective birth cohort, we found that mtDNA heteroplasmic mutation at functional genes contributed to higher scores of autistic traits or higher odds of SCQ or SRS exceeding clinical threshold. More research is needed to further replicate our findings and explore the utility of these mtDNA biomarkers for predicting future risk of ASD or serving as therapeutic targets.

Voice, Swallowing, Speech, and Language Problems in the United States Pediatric Population: The 2022 National Health Interview Survey (NHIS) Howard J. Hoffman*, Chuan-Ming Li, May S, Chiu, Stephen M. Tasko, Mabel L. Rice,

Communication is essential to early child development, yet many speech and language disorders go untreated. Increasing the proportion of children who receive treatment is a US public health priority included in Healthy People 2030. A Voice, Speech and Language (VSL) Supplement was included in the 2022 National Health Interview Survey (NHIS), the principal source of information on the health of the US civilian, noninstitutionalized population. A nationally representative sample (n= 6,125), representing 60.7 million children aged 3-17 years, is analyzed. Parents reported on their children's communication disorders (CD) of voice, swallowing, speech, or language, including the duration, severity, changes in past year, and healthcare visits for evaluation/treatment. An estimated five million children had CD lasting one week or longer during the last 12 months, a prevalence of 8.3% (12.6%, 6.6%, 5.9% by age groups, 3-7, 8-12, and 13-17 years). Males had a higher CD prevalence, 9.5% [95% confidence interval (CI): 8.4%-10.8%], compared to females, 7.1% [95% CI: 6.1%-8.2%]. Speech disorder prevalence was 5.9%, language, 3.6%, voice, 1.6%, and swallowing, 0.8%. CD prevalence increased significantly with decreasing parental education and household income. Health conditions associated with CD were poorer general health, early developmental delay, learning disability, sensory impairment (vision, hearing, and motor), anxiety or depression, and asthma. The proportion receiving healthcare last year was 49.1% for moderate and 74.3% for worse problems. Diagnosis with COVID-19 was not associated with increased CD, but likely led to fewer healthcare visits during the pandemic. Healthcare providers included speech-language pathologists, early intervention specialists, and occupational/physical therapists. VSL problems can be more severe when accompanied by other disorders, however, many manifest as idiopathic. When left untreated, VSL problems may have serious lifelong consequences.

Child health and development

Longitudinal twin growth trajectories, are twins destined to be smaller or do they catch up? Jessica Gleason*, Rajeshwari Sundaram, Kathryn Wagner, Katherine Grantz,

Background: Twins are smaller than singletons at birth. Mounting evidence suggests that intrauterine growth in twins is adaptively different from that of singletons to maximize survival in an intrauterine setting of shared resources. At question is whether twins catch up in growth to that of singletons and at what age. Few studies have evaluated twin growth longitudinally, and none have evaluated twin growth trajectories relative to singletons from birth through adulthood.

Methods: Using data from the National Longitudinal Survey of Youth – 1979 and Child and Young Adult, we compared growth trajectories of twins (n=254) and singletons (n=11,291) from birth through age 20 years. Height and weight were collected every two years from birth through the latest age at interview in 2020. We calculated and compared predicted means for each year of age using linear mixed effects models with quadratic and cubic terms for child age in months, cubic splines for age, and a random intercept and slope, including a nested intercept by family to account for clustering between twins and other siblings. Models were adjusted for child sex and birth year.

Results: Twins were smaller in height, weight, and BMI at birth, appearing to "catch up" at various ages. Differences in height ranged from 3.1 cm (95% CI 2.2, 4.0) at birth to 0.86 cm (0.1, 1.7) at age 8, with the difference becoming 0 by age 12 (β=0.03, -0.98, 1.04). For weight, twins remained from 1.1 kg (0.2, 1.9) smaller at age 5 to 2.0 kg (0.2, 3.9) smaller at age 13, with a 0.6kg (-2.7, 3.8) difference persisting to age 20. Twin BMI remained smaller through age 16 (β=0.8, 0.1, 1.5), with a small difference remaining at age 20 (β=0.3, -0.8, 1.4).

Conclusions: Although twins caught up to singletons in height by age 12, they remained slightly smaller in weight and subsequent BMI through adolescence. Persistent differences in weight may reflect differential accumulation of fat tissue, which may begin early in utero.

Community perceptions of childhood and prenatal lead exposure among historically marginalized and environmentally overburdened neighborhoods in Allegheny County, Pennsylvania Elora Kalix*, Elizabeth Swart, Michelle Naccarati-Chapkis, Barbara Fuhrman, Elizabeth Miller, Catherine Haggerty,

Background: Exposure to lead, a non-biodegradable, industrial heavy metal and systemic toxicant, during childhood or pregnancy can have numerous adverse effects on development. Though the passage of many policies in the US have significantly reduced or eliminated lead use, lead remains a ubiquitous environmental pollutant, especially in Allegheny County, PA, where early childhood blood lead level testing is mandated.

Methods: A mixed-methods survey designed to identify environmental factors and biological pathways that influence child and family health and promote thriving among historically marginalized and environmentally overburdened neighborhoods in Allegheny County is ongoing as part of The Pittsburgh Study, a community-partnered, longitudinal research initiative. Demographic characteristics and questions regarding lead exposure, water quality, and air quality were explored for this analysis. To date, 72 surveys have been administered to adults at health fairs, community events, and school events by community health workers.

Results: Respondents who have completed the survey are primarily female (80%), parents to children under age 18 and/or currently pregnant (71%), and unmarried (53%). Two-thirds of respondents reported household income below the regional median. Most (77%) respondents endorsed lead exposure concern, with 23% reporting extreme concern. Many participants reported low or no access to lead-free water (25%), clean outdoor air (36%), or not living near an industrial site (30%). Of respondents with children under age 5, 44% reported that their child's blood lead level had never been tested.

Conclusion: We identified suboptimal rates of blood lead level testing despite high lead exposure concern. Geospatial analyses are planned to guide screening and intervention initiatives to address inequities in lead exposure and testing across racial, ethnic, and socioeconomic lines within a public health precision framework.

Child health and development

Population-based recruitment of autism spectrum disorder risk groups in the newborn period: Feasibility and impacts of the COVID-19 pandemic Melanie Adkins*, Nicole Talge, Nicole Talge

Autism spectrum disorder (ASD) prevalence is 2-3%, and prospective studies of its antecedents rely upon sampling at-risk subgroups. However, data to guide the planning of such investigations are sparse and unlikely to span the pre-and post-pandemic years. We used findings from a study of full-term newborns with siblings who do (HR: higher risk) or do not (LR: lower risk) have an older sibling with ASD to inform this gap.

We recruited newborns from two hospitals that are responsible for >99% of mid-Michigan births (2017-2023). Prior to discharge, birth records staff approached parents with a survey to gauge study interest and screen for inclusion (age >18 years with parity > 2; singleton, full-term birth; HR or LR group membership). We then contacted parents of HR infants post-discharge to schedule in-person visits. For each HR infant who participated, parents of one LR infant matched for gestational age and sex was invited to enroll. Study visits took place at an outpatient clinic when infants were 4 weeks old.

We approached 93% of parents with newborns about the study (n=11,243), and 53% completed the screening survey; 64% of these parents had eligible infants, with 2% and 98% qualifying for the HR and LR groups, respectively. A smaller proportion of eligible HR infants enrolled compared to eligible LR infants (HR: 0.3, 95%CI 0.2, 0.4, LR: 0.6, 95%CI 0.4, 0.7). Survey completion and eligibility rates did not differ between the pre-(2017-2020) and post-pandemic periods (2021-2023). However, enrollment rates dropped from 35% to 14% for HR infants (%diff: 21%, 95%CI 2%, 40%) and from 68% to 30% for LR infants (%diff: 38%, 95%CI 4%, 73%) across these time periods. The enrollment drops did not differ between groups.

Our findings point to participation barriers in clinical research with newborns, particularly in the post-pandemic period and for families who have a child with ASD. This has important logistical and conceptual implications for future studies.

Longitudinal associations between caregiver emotional support and children's externalizing behaviors during the COVID-19 pandemic Farah Qureshi*, Alysse Kowalski, Nan Dou, Yan Wang, Maureen Black, Erin Hager,

Background: Social support is a key psychosocial resource related to better mental health. Among parents, it is possible that benefits extend intergenerationally to children, especially during times of heightened stress. This study aimed to evaluate longitudinal associations between caregiver-reported emotional support at the start of the COVID-19 pandemic and children's externalizing behavior over time.

Methods: Participants were 292 child-caregiver dyads (mean child age=3.7y). Caregivers reported emotional support in 2020 at the start of the pandemic (baseline [T0]), and their children's externalizing behaviors in follow-up assessments completed in 2021 (T1) and 2022-2023 (T2). Linear mixed models tested associations between caregiver emotional support and changes in children's externalizing behaviors, adjusting for relevant confounders, including caregiver depressive symptoms at baseline.

Results: Compared to the pre-pandemic period, children exhibited higher levels of externalizing behaviors at T1, which then declined from T1 to T2 (β=-0.34; 95% CI=-0.69, 0.01). Adjusting for sociodemographic factors, caregiver emotional support was associated with fewer child externalizing behaviors at T1 (β=-0.26; 95% CI=-0.46, -0.07), but no differences were found in the rate of decline observed from T1 to T2 ($p \geq 0.05$). After further adjusting for caregiver depression symptoms at baseline, associations at T1 were no longer apparent (β=-0.09; 95% CI=-0.25, 0.10).

Conclusion: The protective relationship observed between caregiver emotional support and children's mental health was strongly confounded by caregiver depressive symptoms, suggesting that efforts to enhance emotional support may not translate to better outcomes for children in the absence of mental health treatment for caregivers. Since prior work finds robust relationships between instrumental (i.e., financial) support and better parent and child mental health, it may be a preferred target for future intervention.

Changes in pregnancy-associated mortality during the COVID-19 pandemic: disparities by rurality Claire Margerison*, Xueshi Wang, Alison Gemmill, Sidra Goldman-Mellor,

Pregnancy-associated deaths (PAD; deaths during pregnancy or first year postpartum) due to obstetric causes, drug-related causes, and homicide all increased in the US during the COVID-19 pandemic, while pregnancy-associated suicide declined. We know little about whether these changes were uniform across rurality/urbanicity. We used US vital statistics mortality data from 2018-2021 to identify PAD among females aged 15-44. We calculated PAD ratios (deaths per 100,000 live births) by year, cause, and rurality (urban, suburban, rural) and 95% confidence intervals (CIs). We calculated the percent change in PAD ratios from pre-pandemic (2018 and 2019) to pandemic (2020 and 2021) by rurality. Prior to the pandemic, rural counties had the highest obstetric PAD ratio at 36.4 (95%CI: 32.2, 40.9), compared to 25.2 (23.0, 27.6) in urban and 24.5 (22.8, 26.3) in suburban areas. Suburban areas had the largest increase in obstetric PAD during the pandemic (70.6% increase vs. 49.6% and 48.1% for urban and rural areas, respectively). The pre-pandemic PAD ratio due to drugs was highest in suburban (9.3, 95% CI: 8.2, 10.4) and rural (8.8, 95% CI: 6.8, 11.1) compared to urban (5.1, 95% CI: 4.2, 6.3) counties. Drug-related deaths increased 115.9% in rural counties during the pandemic compared to 76.5% and 53.8% in urban and suburban counties, respectively. Pre-pandemic, the PAD ratio for homicide was 3.2 (2.4, 4.1) in urban counties, 3.4 (2.8, 4.1) in suburban counties, and 4.5 (3.1, 6.3) in rural counties. Urban counties experienced the largest increase (93.8%) in pregnancy-associated homicide, followed by suburban (47.1%) and rural (17.8%) counties. Only rural counties experienced an increase in suicide (25.7%) during the pandemic. Rural areas experienced a disproportionate increase in PAD due to drug-related causes and suicide during the pandemic, while suburban areas experienced the largest increase in obstetric deaths and urban areas experienced the largest increase in homicide.

COVID-19 Infection and Hypertensive Disorders of Pregnancy, 2020-2022 Angela Malek*, Chun-Che Wen, Kalyan Chundru, Julio Mateus, Hermes Florez, Brian Neelon, Jeffrey Korte, Dulaney Wilson, John Pearce, Sarah Simpson, Kelly Hunt,

Introduction: COVID-19 infection increases the risk of pregnancy complications; however, its association with hypertensive disorders of pregnancy (HDP) and its subtypes, preeclampsia and eclampsia (PE and E), remains unclear. We aimed to investigate the association between COVID-19 infection pre- and during pregnancy with these hypertensive conditions in South Carolina (SC).

Methods: We evaluated SC livebirth data (2020-2022) from 145,033 deliveries among pregnant people aged 12-52 years: 80,927 non-Hispanic White (NHW); 43,797 non-Hispanic Black (NHB); 13,150 Hispanic; and 7,157 of other race/ethnic groups. Linked birth certificate and hospitalization/emergency department (ED) visit data was used to define HDP, and hospitalization/ED visit data defined HDP subtypes (PE and E). Logistic regression models with matched pairs and covariate adjustment were conducted.

Results: The overall rate of HDP was 18.5% (22.7% in those with COVID-19 pre-pregnancy, 20.3% with 1st/2nd trimester infection, 19.6% with 3rd trimester infection, and 18.0% without COVID-19). On the other hand, 9.2% experienced PE or E (11.5% with COVID-19 pre-pregnancy, 10.7% with 1st/2nd trimester infection, 10.0% with 3rd trimester infection, and 8.8% without COVID-19). The odds of HDP increased by 9% (95% CI: 1.02-1.16) in those with COVID-19 pre-pregnancy compared to those without COVID-19, after adjusting for demographic, lifestyle and clinical factors (Table). Similarly, PE and E increased in those who had COVID-19 pre-pregnancy (OR=1.12, 95% CI: 1.03-1.21). COVID-19 infection during pregnancy was not associated with HDP or PE/E.

Discussion: Our data demonstrated pre-pregnancy COVID-19 infection is a significant independent risk factor of hypertensive disease during pregnancy even after accounting for the contribution of traditional risk factors, highlighting the importance of preventive measures including vaccination for people of reproductive age.

Table. Adjusted Odds of Hypertensive Disorders of Pregnancy (HDP) and Preeclampsia and Eclampsia in South Carolina among Pregnant People with and without COVID-19 Infection a

Predictor

HDP

Preeclampsia and Eclampsia

OR (95% CI)

OR (95% CI)

COVID-19

No history of COVID-19
referent
referent

Prior to pregnancy
1.09 (1.02-1.16)
1.12 (1.03-1.21)

First and/or second trimester
0.96 (0.90-1.03)
1.06 (0.97-1.15)

Third trimester
0.94 (0.87-1.02)
1.02 (0.91-1.13)

Age
1.01 (1.01-1.02)
1.02 (1.01-1.03)

Education level

< High school
1.07 (0.98-1.18)
1.21 (1.07-1.36)

High school graduate
1.01 (0.94-1.08)
1.08 (0.98-1.18)

Some college
1.07 (1.00-1.14)
1.11 (1.02-1.22)

≥College graduate
referent
referent

Rural residence (vs. urban)
0.91 (0.87-0.96)
0.95 (0.89-1.01)

WIC participation during pregnancy
0.96 (0.91-1.02)
0.94 (0.88-1.01)

Calendar time
1.00 (0.99-1.01)
0.99 (0.98-1.00)

Race/ethnic group

Non-Hispanic White
referent
referent

Non-Hispanic Black
0.98 (0.93-1.04)
1.09 (1.02-1.18)

Hispanic
0.75 (0.68-0.83)
0.82 (0.71-0.95)

Other
0.85 (0.74-0.96)
0.94 (0.78-1.11)

Medicaid
1.01 (0.95-1.08)
1.17 (1.08-1.27)

Tobacco use during or pre-pregnancy
1.06 (0.97-1.16)
1.04 (0.92-1.17)

Firstborn
1.79 (1.69-1.89)
2.00 (1.86-2.15)

Previous preterm delivery
1.52 (1.39-1.67)
1.69 (1.51-1.89)

Pre-pregnancy hypertension
2.59 (2.43-2.75)
3.74 (3.48-4.02)

Pre-pregnancy diabetes
1.38 (1.23-1.55)
1.73 (1.51-1.97)

Pre-pregnancy BMI

Underweight
1.38 (1.23-1.55)
0.91 (0.71-1.14)

Normal
referent
referent

Overweight
1.51 (1.41-1.61)
1.41 (1.29-1.55)

Obese
2.17 (2.05-2.31)
1.73 (1.60-1.88)

BMI, body mass index; COVID-19, coronavirus disease 2019; OR, odds ratio; WIC, Women, Infants, and Children.

a Matched Analysis (1:1 matching): The exposure group (COVID-19 never/prior to pregnancy/first or second trimester/third trimester) was aligned with the control group based on both (1) exact match for delivery quarter time, race/ethnic group, Medicaid, and (2) the nearest neighbor method for maternal age, with an age difference between the two groups ranging from −3 to 4.

Modification of the relationship between prenatal COVID-19 vaccination and ankyloglossia by insurance type Annette Regan*, Stacey Rowe, Sheena Sullivan, Flor Munoz, Jennifer Griffith, Matthew Coates, Onyebuchi Arah,

Background: Ankyloglossia (or tongue-tie) is a congenital condition that can challenge breastfeeding, speech development, and oral hygiene. Previous cohort studies have reported an increased risk of ankyloglossia following maternal COVID-19 vaccination. We hypothesized that this association is non-causal and was driven by improved access to healthcare among vaccinated individuals.

Methods: We evaluated the association between COVID-19 vaccination and ankyloglossia by insurance type (public vs. private), as a proxy for healthcare access among pregnant people in the US. We identified a privately insured pregnancy cohort using the Merative® MarketScan Commercial Database (n=372,813) and a publicly insured pregnancy cohort using the Multi-State Medicaid Database (n=358,719). Ankyloglossia diagnoses were identified using ICD-10-CM codes. COVID-19 vaccinations were identified from outpatient and inpatient drug records. We estimated maternal age-adjusted prevalence of ankyloglossia by insurance type and compared ankyloglossia prevalence by COVID-19 vaccination during pregnancy using robust Poisson regressions.

Results: Age-adjusted prevalence of ankyloglossia was 2.0% (95% CI 1.9, 2.1%) in the publicly insured cohort and 3.6% (95% CI 3.6%, 3.7%) in the privately insured cohort. After adjustment for confounders, COVID-19 vaccination during pregnancy was associated with ankyloglossia in the privately insured cohort (aPR 1.18; 95% CI 1.12, 1.23) but not in the publicly insured cohort (PR 0.94; 95% CI 0.82, 1.07). Insurance type (Medicaid vs. private) was identified as an effect modifier (P<0.001).

Discussion: Our preliminary analyses indicated higher rates of ankyloglossia diagnoses among privately insured individuals compared to Medicaid enrollees, and the association with COVID-19 vaccination varied by insurance type. These results could imply that previously reported associations were influenced by residual or uncontrolled confounding.

Environment/climate change

A non-persistent endocrine disrupting chemical mixture is associated with increased odds of persistent nausea during pregnancy Brad Ryva*, Blair Wylie, Antonia Calafat, Susan Schantz, Rita Strakovsky,

Background: Pregnant women are exposed to many endocrine disrupting chemicals (EDCs) from consumer products. Pregnancy-related nausea is common, can persist past the first trimester, and has unclear, possibly hormonal etiology. Thus, we evaluated associations of an EDC biomarker mixture with nausea persistence.

Methods: Illinois women (n=433) reported nausea since conception or last study visit (yes/no) at median 13, 17, 23, 28, 34 weeks gestation and at delivery. We categorized women as never having nausea, or as having typical (ends by 17 weeks gestation), persistent (ends after 17 weeks gestation), or intermittent nausea. Women provided five urine samples across pregnancy, which we pooled and analyzed for 16 phthalate, three paraben, and six phenol biomarkers. We used quantile-based g computation to assess associations of an EDC mixture with nausea persistence overall and considered differences by fetal sex.

Results: Most women were of high socioeconomic status and had typical nausea (42%), followed by persistent nausea (25%) and irregular nausea (24%); 9% of women never developed nausea. Each 10% increase in the EDC mixture was associated with 27% higher odds of persistent nausea (95% Confidence Interval (CI): 0.97, 1.66), driven by di(isononyl) cyclohexane-1,2-dicarboxylate (ΣDiNCH), di-2-ethylhexyl phthalate (ΣDEHP), and ethylparaben. In women carrying males, each 10% increase in the EDC mixture was associated with 66% higher odds of persistent nausea (95% CI: 1.06, 2.61), driven by ethylparaben, ΣDiNCH, and di-isononyl phthalate (ΣDiNP). The EDC mixture was not associated with nausea persistence in women carrying females (Odds ratio (OR):1.08; 95% CI: 0.74, 1.58). We did not identify associations of the EDC mixture with never developing nausea or with having intermittent nausea.

Conclusion: Future studies should explore hormonal pathways responsible for these findings and investigate if decreasing EDC exposure can reduce nausea persistence in pregnancy.

M-O-M-S™ on the Bayou: An Intervention for Post-disaster Mental Health in Pregnancy in Rural Louisiana – Caregiver and Childbearing Women's Perspectives Emily Harville*, Bianka Northland, Michelle Patterson, Karen Weis, Mary Schultheis, Gloria Giarratano, Anna Larussa

Childbearing women living in rural underserved communities hit by disaster are challenged to find mental health support. The purpose of this project was to develop guidelines for implementing the prenatal emotional support intervention, Mentors Offering Maternal Support™ (M-O-M-STM) post-disaster. A formative community needs assessment was conducted with stakeholders hit by Hurricane Ida, including women (n= 19) who were pregnant/postpartum at the time of the storm or during the following year, and caregivers (n=20) including obstetricians/midwives/pediatrician, nurses, mental health counselors, and community health workers. Interviews were conducted and transcribed, with thematic data analysis used to guide adaption of the intervention. Maternal health caregivers described vulnerabilities and mental health needs of women caused by health disparities and changes in lives resulting from disaster, through the themes, Caring for women vulnerable even before disaster, disaster affects everyone's mental health, Modifying care/need to be proactive, and Absolute need for the M-O-Ms. Women's perspectives of their emotional needs emerged in themes, surviving disruptions in motherhood and Emotional help needed! Women recommended suggestions for intervention delivery in the theme, Barriers to the M-O-M-S™ intervention, which included logistical issues like time and transportation. Community stakeholders welcomed a mental health support intervention for rural pregnant women and provided recommendations for local recruitment, provision of sessions, and overcoming barriers. Sessions were adapted to include childbearing disaster preparation. This study provided the groundwork for initial implementation and evaluation of a project aimed to improve post-disaster maternal mental health.

Environment/climate change

Extreme heat stress, emergency department visits and unplanned hospital admissions in children and adolescents Wen-Qiang He*, Gavin Pereira, Nan Hu, Raghu Lingam, Lindsay Hunt, Ollie Jay, Natasha Nassar,

Background

Extreme heat exposures are increasing with climate change. The health effects of heat exposure are well studied in adults, but the risks to children are less studied. This study aims to ascertain whether heat exposure is associated with an increase in the risk of emergency department (ED) visits, and all-cause and cause-specific hospital admissions among children and adolescents.

Method

The study included all emergency department (ED) visits and unplanned hospital admission in New South Wales from July 2001 to December 2019. Daily maximum heat stress (based on Universal Thermal Climate Index, UTCI) was estimated in the Statistical Area level 2 (SA2) of the children's residential address. We used distributed-lag nonlinear models with a quasi-Poisson distribution to estimate the association of heatwave (defined as >=2 consecutive days with daily maximum UTCI>=95th percentile in each SA2) with the relative risk (RR) of ED visits and hospital admissions, adjusting for temporal trends.

Result

A total of 8,240,170 ED visits and 1,427,736 unplanned hospital admissions were recorded among children and adolescents aged <=18 years in this study. The average number of ED visits and hospital admissions due to heat-related illness almost doubled during the heatwave days compared to non-heatwave days. Compared to non-heatwave days, heatwave days were associated with the increased risk of ED visits and hospital admissions due to infectious diseases and infectious enteritis by 5%-17% and heat-related illness by 80%-94%. Such findings were consistent for most of the subgroup analyses, and children at younger age (<1 year) and those from the most disadvantaged areas were more vulnerable to heatwave days for heat-related illness.

Conclusion

This study provides evidence for the potential harmful impact of heat stress in children from high income country. The particular vulnerable groups of heat stress might facilitate the future targeted mitigation strategy of extreme heat events.

Extreme temperatures and pregnancy loss in California Sandie Ha*, Sneha Ghimire, Valerie Martinez, Adeyemi Adebiyi, John Abatzoglou, Sneha Ghimire

Background: Climate change will increase the frequency, intensity, and duration of heat events, which may negatively impact pregnancy. We investigated the association between heat events and pregnancy loss.

Methods: This time-stratified case-crossover study included 17,516 emergency department (ED) visits with spontaneous pregnancy loss (miscarriage, stillbirth, or fetal death) as the primary diagnosis code during the warm season (Apr-Oct, 2011-2020) in California. Pregnancy losses were identified using the International Classification of Disease codes versions 9 and 10. Participants' residential zip codes were spatiotemporally linked to high-resolution daily weather and air pollution data estimated by previously validated models. Heat day was defined as a day with temperature >98th or >95th percentile of each zip code, and heat wave was defined as at least 2, 3, or 4 consecutive heat days. Conditional logistic regression models calculated the odds ratio (OR) and 95% confidence intervals (CI) by comparing heat day and heat wave exposures on the day of loss (lag 0) and each of the previous seven days (lags 1 – 6) with control periods selected using the time-stratified method. Models were adjusted for humidity, fine particles, and ozone.

Results: Heat day (>98th percentile) was associated with an elevated risk of loss 4-5 days post-exposure [ORlag4: 1.15 (1.05-1.28); ORlag5: 1.14 (1.03-1.26)]. Heatwave (≥2 days with temperature >95th percentile) was associated with an increased risk 3-4 days of post-exposure [ORlag3: 1.08 (1.00-1.18); ORlag4: 1.11(1.02-1.21)]. Associations were stronger when heatwave was defined using longer duration and on days with concurrent wildfire smoke. For example, heat day (>98th percentile) on wildfire smoke and non-smoke days was associated with 31% and 14% increased risk 4 days post-exposure, respectively.

Conclusions: Exposure to unusually hot days and heat waves may increase the risk of pregnancy loss, especially during a wildfire.

Ambient temperature during susceptible windows of spermatogenesis and impact on hCG+ pregnancy in an infertility treatment population Lindsey M. Russo*, J. Richard Pilsner, Timothy P. Canty, Pauline Mendola, Kaniz Rabeya, Karen C. Schliep, May Shaaban, Akanksha Singh, Allison Ring, Rachael Hemmert, Neil J. Perkins, James A. VanDerslice, C. Matthew Peterson, Erica Johnstone, Carrie J. Nobles,

Background: Male preconception exposure to temperature remains a critically under-addressed area of family planning. Animal studies have found spermatogenesis susceptible to heat stress; therefore, we examined ambient temperature and hCG+ pregnancy in the Folic Acid and Zinc Supplementation Trial (2013-2018) among couples seeking infertility treatment in Salt Lake City.

Methods: In the FAZST Trial (n=2,015 men), we evaluated four susceptible windows of ambient air pollution exposure during spermatogenesis (mitosis, meiosis I-II, spermiogenesis, spermiation) for semen samples provided during couple-level intrauterine insemination (IUI, n=505 couples and 1,223 cycles) or in vitro fertilization (IVF, n=221 couples and 280 cycles) treatment cycles over nine months of follow-up. Daily ambient temperature was abstracted from weather monitoring stations for Salt Lake City and averaged across each susceptibility window. Treatment-cycle probability of pregnancy was assessed for IUI and IVF cycles separately using generalized linear mixed models adjusted for fine particulate matter, ozone, age, and income, as well as interaction with warm (Apr – Sept) versus cold season (Oct – Mar).

Results: Overall, there were 133 (10.9%) IUI and 171 IVF hCG+ pregnancies (61.1%). For a 2° C increase in average ambient temperature in the warm season, we observed no clear association in models adjusted for age, income, and fine particulate matter [e.g., RR: 1.01, 95% CI: 0.95, 1.07 during meiosis]. Upon addition of ozone, a seasonal confounder, we observed a higher likelihood of IUI pregnancy during mitosis and meiosis [e.g., RR: 1.13, 95% CI: 1.03, 1.23 for meiosis]. We observed minimal impacts among IVF participants. No associations were observed during the cold season.

Conclusion: Overall, we observed few associations, but found an unexpected association when adjusting for ozone, which may suggest potential mediation or other complexity.

A prospective study of objective preconception sleep health and fecundability Chad M. Coleman*, Amelia K. Wesselink, Traci N. Bethea, Andrea S. Kuriyama, Tanran R. Wang, Margaret Seo, Jacob Pothen, Joe Kossowsky, Suzanne M. Bertisch, Lauren A. Wise,

Introduction: Fragmented sleep may inhibit routine hormonal fluctuations, which can impact ovulation and pregnancy initiation. There is epidemiologic evidence of an association between sleep and fertility; however, most studies have relied on self-reported sleep assessments, which may introduce bias.

Methods: We estimated prospectively the association between objective sleep health and fecundability, the per-cycle probability of conception, among 432 female-identified participants at risk of pregnancy in Pregnancy Study Online, a web-based preconception cohort study (2021-2023). Participants wore a study-issued Fitbit for 24 hours/day for up to two months during preconception to measure sleep characteristics, including duration (hours/day), efficiency (total sleep time divided by total time in bed), and wake after sleep onset (WASO; minutes awake after initial sleep onset). We averaged sleep measures across the first seven days of participation. Participants reported pregnancy status on bimonthly follow-up questionnaires. We used proportional probabilities regression models to estimate fecundability ratios (FRs) and 95% CIs, adjusting for socio-demographic, behavioral, and reproductive factors.

Results: Using life-table methods, 75% of participants conceived during 12 months of follow-up. The medians (interquartile ranges) for sleep duration, efficiency, and WASO were 7.2 (6.7-7.7 hours/day), 88.4% (87.1%-89.7%), and 56 (48-66 minutes), respectively. Compared with ≥7 hours/day (clinically recommended duration), FR (95% CI) for <7 hours/day was 1.08 (0.83, 1.42). The lowest quartile of sleep efficiency (≤87.0% vs. >89.0%) and highest quartile of WASO (>66.3 vs. ≤48.8 minutes) were associated with reduced fecundability (FR for sleep efficiency 0.82, 95% CI 0.55, 1.21; FR for WASO 0.73, 95% CI 0.50, 1.07). Results were consistent when exposures were modeled as continuous.

Conclusions: Reduced sleep efficiency and increased WASO may be risk factors for delayed conception.

Association between infertility causes and live birth outcomes post Preimplantation Genetic Testing for Aneuploidy (PGT-A) and Monogenic Disorders (PGT-M)

Chidinma Oli*, Amadou Barrow, Kelly Gurka,

Background: Assisted Reproductive Technologies (ARTs) play a crucial role in addressing infertility. The success of ARTs in achieving live births are impacted by chromosomal and genetic abnormalities. Preimplantation Genetic Testing for Aneuploidy (PGT-A) and Monogenic Disorders (PGT-M) aims to enhance live birth likelihood by identifying embryos without defects. However, it remains unclear how specific infertility causes influence the success of PGT.

Methods: We used the 2017-2018 United Kingdom Human Fertilisation and Embryology Authority (UK HFEA) data, a major global database for fertility treatments. We used multivariable logistic regression models to estimate the adjusted odds ratios (aORs) and 95% CI for the association between infertility causes and live birth occurrence post PGT-A and PGT-M adjusting for age, ethnicity, and type of ART treatment.

Results: Male factor (35.2%) and unexplained infertility (35%) were predominant causes of infertility. We found significant associations between infertility causes and live birth outcomes post PGT-A treatment (X2 = 18.04, P = 0.0010) and PGT-M treatment (X2 = 12.64, P = 0.0013). Compared to male factor infertility, women with unexplained infertility had increased odds of live birth post-PGT-A (aOR 1.20; 95% CI, 1.10–1.30). Conversely, women with infertility due to ovulatory disorder presented lower odds of live births post PGT-A (aOR 0.83; 95% CI, 0.69–0.99) and post PGT-M treatment (aOR 0.43; 95% CI, 0.23-0.80). Endometrial Infertility showed a non-significant trend towards increased odds of live birth post PGT-A (aOR 1.08; 95% CI, 0.89–1.30) and PGT-M (aOR 1.20; 95% CI, 0.94–4.18). Tubal disease infertility had comparable odds of live birth post PGT-A (aOR 1.05; 95% CI, 0.87–1.26) and PGT-M (aOR 0.94; 95% CI, 0.53–1.68).

Conclusions: Live birth occurrences post PGT varied with infertility causes, emphasizing the importance of personalized treatment plans in Assisted Reproductive Technologies to optimize outcomes.

Physical Activity and Risk of Spontaneous Abortion in a Danish Preconception Cohort Marie Dahl Jørgensen*, Ellen M. Mikkelsen, Mette Aadahl, Søren Brage, Jakob Tarp, Elizabeth E. Hatch, Kenneth J. Rothman, Lauren A. Wise, Anne Sofie Dam Laursen,

Background: About 15-30% of all pregnancies end with spontaneous abortion (SAB), making it one of the most common pregnancy complications. The evidence on the extent to which physical activity (PA) influences risk of SAB is inconsistent.

We evaluated the association between hypothetical replacement of pre-pregnancy sedentary time with different intensities of PA and the risk of SAB using data from a Danish preconception cohort.

Methods: We included 4,724 participants who conceived after entry in the SnartForældre.dk cohort from 2011 to 2023. Participants reported their PA levels via the International Physical Activity Questionnaire at baseline and on bimonthly follow-up questionnaires during preconception. We used data from the most recently completed questionnaire prior to conception. Pregnancy outcomes were identified via follow-up questionnaires, the Danish National Patient Registry, and the Medical Birth Registry.

We used Cox proportional hazards regression models to calculate hazard ratios (HR) and 95% confidence intervals (CI) with gestational weeks as the time scale. We used isotemporal substitution models to examine the effect of replacing durations of sedentary time with walking, moderate PA, and vigorous PA.

Results: The overall risk of SAB was 18% and median gestational age at loss was 7 weeks. The HRs for substitution of 30 minutes of sedentary time/day with 30 minutes of walking, moderate PA, or vigorous PA were 1.01 (95% CI 0.99-1.03), 0.98 (95% CI 0.89-1.09), and 0.91 (95% CI 0.79-1.04), respectively. Among participants with ≥7 hours of sedentary time/weekday, the association for replacement of sedentary time with vigorous PA was stronger (HR 0.80, 95% CI 0.64-1.00).

Conclusion: Replacing 30 minutes of sedentary time/day with walking or moderate PA had little association with risk of SAB. However, replacing sedentary time with vigorous PA was associated with a slightly lower risk of SAB, mainly among participants with ≥7 hours of daily sedentary time.

Proximity to traffic and infant mortality Valerie Martinez*, Sneha Ghimire, Sandie Ha,

Background: Infant mortality (IM) affects ~3.9 per 1,000 live births in California. Studies suggest a link between living near major air pollution sources such as roads, truck routes, or highways and health risks, but the impacts on IM remain unclear. We investigated the association between residential proximity to major roads, truck routes, and freeways in Fresno, California, a city marked with significant air pollution.

Methods: In this retrospective cohort study, we identified 103,566 singleton pregnancies from Fresno City, California, USA (2009-2019). Maternal addresses were geospatially linked to the nearest major road, truck route, and freeway identified by data from the California Department of Transportation. Proximity to sources was measured using Euclidean distance and categorized with different cut points including 500 ft and 1000 ft. IM was defined as any death of a livebirth before the first year. Logistic regression models estimated the odds ratio (OR) and 95% confidence intervals (CI) for the associations between proximity and IM while adjusting for education, race/ethnicity, neighborhood household income, and age.

Results: Mothers within 1000 ft of a highway had a 1.26-fold increase in odds of having a baby with IM compared to those further away (aOR: 1.26 95% CI: 1.03-1.54). Stratified analysis showed that associations between residence within 1000 ft of a freeway and IM were more prominent among mothers who had at least a high school education or made less than $31,730. We found no race or age-specific differences due to the small sample size. There was no statistically significant association between proximity to major roads or truck routes and IM.

Conclusion: Living near highways may increase IM risks, especially for mothers with lower education or income. While awaiting more studies, efforts to reduce environmental hazards among those living close to pollution sources are crucial, especially in socioeconomically vulnerable populations.

Is there non-participation bias in the Arkansas Center of the BD-STEPS Stillbirth Study, 2015-2021 Kari Weber*, Suman Maity, Wendy Nembhard,

Background: We compared the characteristics of women who had a stillbirth (fetal deaths ≥ 20 weeks gestation) and participated in the Arkansas site of the Birth Defects Study to Evaluate Pregnancy exposures (BD-STEPS) to those who did not participate.

Methods: The Arkansas Reproductive Health Monitoring System (ARHMS) actively monitors the state's birth outcomes, including stillbirths. ARHMS identifies stillbirths through hospital records and vital statistics and cases are reviewed by maternal-fetal medicine physicians with near complete ascertainment. Starting in 2014, all who experienced a stillbirth without a birth defect were invited to participate in BD-STEPS. We compared cases who did and did not participate from 2014-2021 using available demographic data for 2 phases of BD-STEPS (Phase 1: 2014-2018, Phase 2: 2018-2021), and the time lag between delivery and invitation for enrollment in the study. We used t-tests with standard deviation (SD) and Pearson's Chi-square to compare groups and multivariable logistic regression to estimate the odds of not participating, adjusting for other variables.

Results: Of 1,299 stillbirths, 1,094 (84%) chose not to participate. More non-participants were from Phase 1 (n=759, 87%) than Phase 2 (n= 335, 79%). There were more Hispanic and non-Hispanic (NH) white participants compared to NH Black cases. Participants and non-participants were similar in age, but participants had a mean time lag of 9 months (SD=3) compared to 16 months (SD=13) for non-participants. No participants had a time-lag ≥ 18-month while about 27% of non-participants did. Restricted to those with a time lag ≤ 12 months, adjusted analyses showed no significant differences between groups except that NH Black cases were more likely to be non-participants.

Conclusions: Based on limited available data, NH Black cases may be slightly underrepresented in our study. Decreasing the time lags between delivery and recruitment may help improve participation.

Preconception and first trimester markers associated with spontaneous abortion Elora Kalix*, Kalpana Betha, Catherine Haggerty, Brandie Taylor,

Background: Placental dysfunction can cause adverse pregnancy outcomes, including spontaneous abortion (SAB), preeclampsia, and preterm birth, all of which are common and global health concerns. However, it is unclear if preconception and first trimester markers of placental dysfunction and immunity are associated with SAB.

Methods: We conducted a nested case-control pilot study of preconception and first trimester plasma markers of angiogenesis (EGFL7, PIGF, sFLT1, PP13), danger associated molecular patterns (DAMPs; HSP 60 and 70, HMGB1), and oxidative stress (MDA, GSH) among 50 randomly selected women who experienced SAB and 100 randomly selected women who had a live birth from the Longitudinal Indian Family Health study. Markers were log-transformed (base 10), and means were compared between cases and controls at each timepoint. Multivariable logistic regression models assessed associations between each biomarker and SAB, adjusting for age, BMI, and gravidity.

Results: Preconception sFLT1 was significantly lower among cases compared to controls (<0.0001). First trimester sFLT1 (<0.0001), MDA (0.001), HSP60 (0.05), and PP13 (<0.0001) were significantly lower, and EGFL7 (0.05) and PlGF (0.02) were significantly higher among cases as compared to controls. After adjustment, preconception sFLT1 and first trimester sFLT1, MDA, HSP60, PP13, EGFL7, and PlGF were significantly associated with SAB.

Conclusions: Dysregulation of preconception and first trimester markers involved in placental angiogenesis were associated with SAB. First trimester oxidative stress markers and DAMPs were also associated with SAB. Further large-scale preconception studies are needed to determine if these markers can be used as early indicators of future impaired placentation and subsequent SAB.

Sexual orientation disparities in adverse pregnancy outcomes Payal Chakraborty*, Ellis Schroeder, Colleen A. Reynolds, Sarah McKetta, Juno Obedin-Maliver, S. Bryn Austin, Bethany Everett, Sebastien Haneuse, Brittany M. Charlton,

Background: Sexual minority (SM) individuals have health profiles—e.g., health behaviors; limited resources due to structural, interpersonal, and individual stigma—that may place them at higher risk for adverse pregnancy outcomes (APOs), yet little research has examined sexual orientation disparities in APOs.

Methods: We used pregnancy data from the Nurses' Health Study 3, an ongoing cohort of nurses and nursing students in the US/Canada. Pregnancies occurred from 1978–2023. We analyzed 6 self-reported APOs: preterm birth (PTB), low birthweight (LBW), and macrosomia (MAC) among live births (N=25,877) and gestational hypertension (gHTN), gestational diabetes (GDM), and preeclampsia (PRE-E) among pregnancies ≥20 weeks (N=26,176). We examined disparities among 5 sexual orientation groups: completely heterosexual (reference), heterosexual with same-sex experience; mostly heterosexual; bisexual; and lesbian. We used log-binomial models to estimate risk ratios (RRs) fit via weighted generalized estimating equations to account for multiple pregnancies per person and informative cluster sizes.

Results: Compared to pregnancies to completely heterosexual participants, those of SM groups combined had higher risks of GDM (RR[95%CI]: 1.15[1.00–1.34]), gHTN (1.33[1.18–1.50]), and PRE-E (1.23[1.07–1.42]); no significant differences were observed for PTB, LBW, and MAC. Pregnancies to heterosexual participants with same-sex experience and mostly heterosexual participants had a higher risk of gHTN (1.34[1.08–1.66]; 1.30[1.12–1.51]), respectively) and PRE-E (1.40[1.09–1.79]; 1.20[1.00–1.44]) and lesbian participants had a higher risk of gHTN (1.68[1.11–2.52]). Bisexual and lesbian participants had RRs with high magnitudes for most APOs.

Conclusions: SM individuals experience disparities in many APOs, and disparities differ by SM subgroup. Elucidating the pathways to reduce disparities (e.g., structural barriers, health care needs) is critical for achieving reproductive health equity.

Association of "double-positive" prenatal screening results for trisomies 21 and 18 with preterm birth and other perinatal outcomes: a population-based study in Ontario, Canada.

Kara Bellai-Dussault*, Shelley Dougan, Deshayne Fell, Tianhua Huang, Julian Little, Carolina Lavin-Venegas, Lynn Meng, Nan Okun, Mark Walker, Christine Armour, Beth Potter,

BACKGROUND

Multiple marker screening is offered to pregnant individuals in many jurisdictions to screen for trisomies 21 and 18. A "double-positive" screen result(positive for both trisomies 21 and 18, but both diagnoses are ruled out based on confirmatory testing) occurs rarely but poses a challenge for patient counselling due to limited evidence about expected outcomes. This study aimed to investigate the association of double-positive prenatal screening results with preterm birth and other perinatal outcomes.

METHODS

We conducted a population-based retrospective cohort study using province-wide registry data in Ontario, Canada. From pregnancies receiving screening with an estimated date of delivery from September 1, 2016, to March 31, 2021, we identified those with double-positive screening results where trisomies 21 and 18 were ruled out and compared them to pregnancies with screen negative results. The primary outcome was preterm birth. Secondary outcomes included a composite pregnancy outcome (pregnancy loss, stillbirth, or termination), other chromosomal abnormalities, admission to neonatal intensive care, cesarean delivery, small for gestational age, and preeclampsia. We used modified Poisson regression models adjusted for maternal factors and type of conception, with multiple imputation to address missing data for covariates.

RESULTS

Among 458 240 screened pregnancies, 863 (0.2%) had a double-positive result, and trisomies 21 and 18 were ruled out in 374 based on confirmatory testing. The risk of preterm birth was higher in pregnancies with a double-positive result compared to pregnancies with screen negative results: adjusted risk ratio 2.6 (95%CI 2.0-3.6). The risk also increased for all secondary outcomes studied except for preeclampsia.

CONCLUSION

Although rare, double-positive multiple marker screening results where trisomies 21 and 18 have been ruled out were associated with increased risk of preterm birth and other adverse perinatal outcomes.

Global health

Association between 1-Hour Glucose Challenge Test Values and Maternal Depression Risk in a Prospective Cohort from Dhulikhel, Nepal

Heather Seid*, Abha Shrestha, Archana Shrestha, Kalpana Chaudhary, Kelly Martin, Laura Byham-Gray, Shristi Rawal, Shristi Rawal

The link between hyperglycemia in pregnancy, particularly below the threshold for gestational diabetes and depression remains unclear, especially in low-income countries like Nepal. We investigated the association between self-reported maternal depression and glucose levels post 1-hour 50g glucose challenge test (GCT) in a peri-urban cohort of 244 singleton pregnant women recruited from a university hospital in Dhulikhel, Nepal. Participants (age 26.0±4.2 years) underwent a GCT between 24-29 weeks of gestation. Maternal depression scores were assessed with Patient Health Questionnaire-9 (PHQ9; scores 0-27) in the 1st trimester, and with Center for Epidemiological Studies Depression tool (CES-D; scores 0-60) in the 3rd trimester and 6 weeks postpartum. Linear and logistic regression models estimated the associations between maternal depression risk scores and GCT values (continuous and dichotomized to < 140 vs. ≥ 140mg/dL) at each visit. The mean GCT value in our sample was 115.9±25.6 mg/dL;16% had elevated GCT (≥140 mg/dL). Depression risk scores in the 1st, 3rd trimester, and at 6 weeks postpartum were 2.1±1.9, 6.1±1.2, and 6.0±0.7, respectively, with 5.3% at-risk for depression in the 1st trimester (PHQ-9 ≥ 5), but none at other timepoints (CES-D ≥16). GCT values were weakly correlated with CES-D scores in the 3rd trimester (r=-0.21; p=0.08) but was not correlated with depression scores in the other 2 timepoints. After adjusting for apriori covariates including pre-pregnancy BMI, 3rd trimester CES-D scores was significantly and negatively associated with GCT value [B (95% CI)=-5.4 (-9.9, -1.0). Consistently, odds of elevated GCT decreased with higher depression scores [OR (95% CI)=0.12 (0.02, 0.8)]. Contrary to our hypotheses, lower depression scores in the 3rd trimester were found to be significantly correlated with higher GCT values in our Nepalese cohort. Larger studies are needed to validate these findings and explore underlying physiological mechanisms.

Choice of hemoglobin elevation adjustment method on changes of estimations of the burden of anemia Corey Teply*, Will Gardner, Taylor Noyes, Ni Gusti Ayu Nanditha, Dong Keun Rhee, Nandita Perumal, Heather Taylor, Heidi Tandiono, Nicholas Kassebaum,

Background

Anemia is characterized by lower hemoglobin (Hb) concentrations, leading to a reduced oxygen supply to tissues, increasing the risk of adverse health outcomes. To properly assess anemia severity, Hb concentrations need to be adjusted for elevation given the body produces more Hb in response to the lower oxygen availability at higher elevations. This analysis compares estimations of the overall burden of anemia using different adjustment methods: (1) the World Health Organization (WHO) adjustment equation and (2) an equation proposed by Biomarkers Reflecting Inflammation and Nutritional Determinants of Anemia (BRINDA), whose equation reevaluates the relationship between Hb and elevation using a non-log-linear relationship.

Methods

Individual-level Hb concentrations (g/L) were extracted from population-representative household surveys from 84 countries. Unadjusted, WHO-adjusted, and BRINDA-adjusted Hb were categorized into WHO anemia definitions and survey data were collapsed to calculate severity-specific anemia prevalence. Each of the three parallel datasets were then modeled using spatiotemporal Gaussian process regression followed by ensemble distribution modeling.

Results

Our results indicate the total prevalence of anemia is higher when adjusted using the BRINDA method compared to the WHO method for elevations under 2,700 meters (m). Specifically, for preschool aged children, there are increases in total anemia prevalence of 10.0% (7.1%-12.9%), 15.5% (12.1%-18.6%), and 15.7% (12.4%-18.7%) between elevations of 400-800 m, 800-1,200 m, and 1,200-1,600 m, respectively. These trends were observed across all other demographics within this analysis.

Conclusion

Owing to its functional form assuming a log-linear relationship between elevation and Hb-adjustment, WHO-based elevation adjustment methods lead to much lower anemia prevalence when compared to BRINDA adjustment methods, which do not have the same assumption and are a better fit to empirical data.

Oral contraceptive pill use and blood lead concentrations in U.S. premenopausal individuals: Results from NHANES 2003-2012 Arianna Foster*, Mandy Hall, Nicole Talge, Dorothy Pathak, Renee Heffron, Robert Wright, Julio Landero, Michael Yin, Flavia Matovu, Quaker Harmon, Kenneth Mugwanya, Andrew Mujugira, Chenxi Li, Kristen Upson, Kristen Upson

Oral contraceptives (OCs) are used by 151 million people worldwide for pregnancy prevention and management of menstrual disorders. Most OCs contain estrogen, which can have a bone-sparing effect by suppressing osteoclast activity. We hypothesized that lower bone turnover with current OC use decreases mobilization of toxic metal lead (Pb) stored in bone to blood. To investigate whether current OC use is associated with lower blood Pb concentrations, we conducted a cross-sectional analysis using data from the National Health and Nutrition Examination Survey (NHANES) for years 2003-2012. The study population comprised premenopausal, non-pregnant individuals ages 20-44 years with an intact uterus, at least one ovary, and not currently using injectable contraception, who had data available on current OC use and blood Pb concentrations (unweighted n=2,884). We used multivariable linear regression to estimate the percent difference in blood Pb concentrations and 95% CI between current OC users and non-users (defined as those not currently using OCs); we adjusted for potential confounding factors and accounted for the complex survey sampling design. The geometric mean blood Pb concentrations in current OC users and non-users were 0.71 µg/dl (95%CI: 0.67, 0.75) and 0.84 µg/dl (95%CI: 0.82, 0.87), respectively. After adjustment, current OC users had 11% lower blood Pb levels (95%CI: -16%, -5%) than non-users. The association persisted in analyses (i) limited to never-smokers (unweighted n=1,784) to address potential residual confounding from smoking, a substantial source of blood Pb (-10%, 95%CI: -17%, -3%), and (ii) additionally adjusting for anemia status; Pb resides in red blood cells and OCs users tend to have less menstrual blood loss (-10%, 95%CI: -16%, -5%). As no safe level of blood Pb exists, and Pb can adversely affect all organ systems, even in adulthood, further research is warranted to replicate our findings of lower blood Pb concentrations with current OC use.

Long-Acting Reversible Contraception Failure Among Active Duty Service Members, 2017-2018 Clinton Hall*, Clinton Hall, Monica Burrell, Zeina Khodr, Celeste Romano, Gia Gumbs, Ava Marie Conlin, Kelly Elmore,

Background: Long-acting reversible contraception (LARC) use is higher among United States military service members compared with civilians, but characteristics of LARC failures in this population are not well understood. Sequelae of unintended pregnancies during military experiences, such as deployment, operations at sea, or assignment to remote areas underscore the need to investigate LARC failures.

Methods: In this descriptive, case-only study, service members with a subdermal implant or intrauterine device (IUD) insertion occurring 2017-2018 were identified using medical encounter data from the Military Health System Data Repository; patients with suspected LARC failure were flagged from records indicating pregnancy within 12 months following LARC insertion and no prior record of LARC removal or reinsertion. Suspected failure cases were validated using electronic health records. Bivariate analyses compared demographic, military, and clinical characteristics of confirmed failures by LARC type.

Results: Overall, 466 active duty service members with a suspected LARC failure were eligible for validation; 76 (16.3%) were confirmed as true cases, of which 36 (47.4%) received an implant and 40 (52.6%) an IUD. Most implant failures (58.8%) occurred among those placed during the luteal phase of the menstrual cycle, while most IUD failures (62.5%) occurred among those placed during the follicular phase. Mean time to failure for implants was 1.6 (standard deviation [SD] 1.8) months compared with 7.1 (SD 3.2) months for IUDs. Overall, 19 (52.8%) implant failures and 24 (60.0%) IUD failures resulted in a live birth.

Discussion: Providers opting to place subdermal implants later in the menstrual cycle should consider individualized patient counseling to reduce the likelihood of unintended pregnancy. Both providers and patients benefit from evidence-informed care; variation in knowledge of LARC practice guidelines may impact contraceptive failure and reproductive autonomy.

Severe Maternal Morbidity Among Adolescents Aged 10-19: A U.S. Multi-State Analysis

Marina Carvalho Magalhães*, Jonathan Snowden, Elliot Main, Jennifer Soh, Peiyi Kan, Ciaran Phibbs, Suzan Carmichael,

OBJECTIVE: To examine the overall and indicator-level incidence of severe maternal morbidity among adolescents (individuals <20 years old) and compare risks among adolescents to older age groups.

METHODS: This was a population-based study of California, Oregon, Michigan, and South Carolina births to individuals aged 10-55 years. We included prenatal, postpartum (42 days), and birth hospitalization discharge records linked to infant live birth and fetal death certificates from 2008-2020**.** Our primary outcome was severe maternal morbidity (SMM), defined using the Centers for Disease Control and Prevention index.

RESULTS: This study included 555,054 adolescents among 8,001,678 individuals aged 10-55. There were 23.6 cases of SMM per 1,000 adolescent births; incidence was highest among girls aged 10-14 (35.3). Compared to individuals aged 25-29, adolescents experienced higher rates of blood transfusion (13.6 vs 9.7) and eclampsia (2.0 vs 1.0). Crude relative risks (RR) for SMM were 1.27 (95% CI 1.24-1.30), 1.34 (95% CI 1.30-1.39) and 1.94 (95% CI 1.70-2.22) in ages 18-19, 15-17 and 10-14, respectively. Adjustments for payer, state, race-ethnicity, parity, and anemia explained excess risk among ages 15-19, but not the youngest adolescents (10-14) (RR 1.33, 95% CI 1.16-1.53); adjustment for pre-pregnancy comorbidities did not attenuate these risks. Patterns of SMM risk were similar when excluding blood transfusions. Risks were also elevated among the oldest age groups.

CONCLUSION: Adolescents are at increased risk for SMM which is largely explained by social disadvantage, parity, and anemia, but not pre-pregnancy comorbidities. Considering the co-occurring rise in maternal deaths and legislative restrictions on reproductive autonomy, and vulnerabilities among adolescents, these findings highlight the need for resources dedicated to preventing SMM in adolescents and should be considered during care for adolescents and public health planning.

Health equity

The Southern Center for Maternal Health Equity: Objectives and Design Emily Harville*, Maeve Wallace, Lizheng Shi, Carmen Green, Jeffrey Shaffer, Susan Perez, Kiara Cruz, Alessandra Bazzano, Zainab Jah, Rachel Reed, Melissa Evans, Abigail Gamble, Sherri Longo, Joseph Biggio, Lizheng Shi

Nowhere are racial inequities and poor maternal health in starker relief than in Louisiana and Mississippi, which consistently rank last in the U.S. on several indicators of reproductive health. The Southern Center for Maternal Health Equity is an academic, community, and clinical partnership between Tulane University, Reproductive Health Impact, and Ochsner Health. The Center's overarching goal is to address the root causes of maternal morbidity and mortality (bias, lack of access to care, health, and social policy), with a focus on Black women in the Gulf South. The Center's three research projects will test interpersonal, health system, and policy interventions creating a multilevel approach to advance maternal health and evaluate these strategies from cross-cutting perspectives, including cost-effectiveness, quality of care, and health equity. A cluster randomized trial will test a multifaceted behavior change intervention to reduce biased treatment in maternity care settings (Research Project 1). Research Project 2 will adapt and evaluate an enhanced remote monitoring package in maternity health deserts. Research Project 3 is a natural experiment to quantify the effects of Medicaid postpartum coverage extension and legislative mandates on maternal health outcomes. The Center's Training Core will provide training opportunities for early career scholars to strengthen and diversify future leaders in maternal health equity research, while the Community Partners Core will incorporate community priorities and expertise in all areas of the project and ensure results and benefits return directly to impacted communities. Through these transdisciplinary research and training initiatives, our mission is to contribute to efforts to make the Gulf South a place where all pregnant people and their families can thrive.

Infectious disease

Tdap and RSV Vaccine Recommendations and Practices for Pregnant Patients by Health Care Providers — Fall DocStyles Survey, United States, 2023

Ayeesha Sayyad*, Regina Simeone, Beatriz Salvesen von Essen, Jessica Meeker, Sascha Ellington, Rebecca Hall, Carrie Shapiro-Mendoza, Romeo Galang, Grayson Waits, Katherine Fleming-Dutra,

Respiratory syncytial virus (RSV) and Tdap (Tetanus toxoid, reduced diphtheria toxoid, and acellular pertussis) vaccination during pregnancy were recommended by the Centers for Disease Control and Prevention in 2023 and 2011, respectively, to reduce the risk of severe illness in infants. We used data from the 2023 DocStyles survey to describe provider practices for recommending and offering these vaccines to pregnant patients.

The Fall 2023 DocStyles survey, administered October 6 – 25, 2023, was a web-based nonprobability panel survey of U.S. Health Care Providers (HCPs). Our analysis included 1,371 respondents who reported caring for pregnant patients and were asked whether they recommended and offered Tdap and RSV vaccines to their pregnant patients. Adjusted prevalence ratios (aPR) and 95% confidence intervals (CI) estimated associations between provider type and affirmative responses to each question. Prevalence ratios were adjusted for provider age, gender, and years practicing medicine.

Providers had a median age of 47 years and 54.0% were male. Most respondents were Family Practitioners or Internists (65.6%), while 17.8% were Obstetrician-Gynecologists, and 16.6% were Nurse practitioners or Physician Assistants. Eighty percent of providers recommended the Tdap vaccine to their pregnant patients, and 73.7% offered the vaccination onsite. In contrast, 42.2% of providers offered the RSV vaccine to their pregnant patients, and only 23.1% offered onsite vaccination. Obstetrician-Gynecologists were more likely than Family Practitioners and Internists to recommend Tdap (aPR: 3.65, 95% CI: 2.09-6.35) and RSV (aPR: 3.24, 95% CI: 2.38-4.40) vaccines to pregnant people.

Public health messaging reinforcing recommended vaccinations during pregnancy is important for both HCPs and patients. HCPs caring for pregnant people play an important role in vaccine confidence and uptake, especially for newly approved vaccines, such as RSV.

The association between pediatric vaccine hesitancy and non-completion of the combined 7-vaccine series among US military families, 2010–2017 Monica Burrell*, Celeste Romano, Anna Bukowinski, Clinton Hall, Gia Gumbs, Ava Marie Conlin, Nanda Ramchandar,

Introduction: Recent work reported gaps in completion of the pediatric combined 7-vaccine series among US military families. To determine the role of vaccine hesitancy as a contributing factor to undervaccination, we examined the prevalence of vaccine-limiting patterns and measured the association between these patterns and vaccine non-completion.

Methods: Department of Defense Birth and Infant Health Research program data were used to identify children born at military facilities, 2010–2017. Immunizations were identified through age 2 years using vaccine administered and Current Procedural Terminology codes from military facility immunization records and outpatient health care records, respectively. Consistent vaccine limiters received <3 antigens at each vaccine visit (ie, all limited visits). Episodic vaccine limiters had ≥1 limited vaccine visit and only 3 visits with ≥3 antigens. Non-limiters had no limited visits or ≥4 visits with ≥3 antigens. Modified Poisson regression models estimated associations between vaccine-limiting patterns and non-completion of the combined 7-vaccine series by age 2 years.

Results: Overall, 248,135 children were identified for analysis. The prevalence of consistent vaccine-limiting was 0.3% (n=840); episodic vaccine-limiting was 17.0% (n=42,128). Each group was disproportionately represented among the population non-complete for the 7-vaccine series (1.3% and 34.3%, respectively). Consistent vaccine limiters had 6.0 (95% confidence interval [CI]: 5.7-6.1) times the risk and episodic vaccine limiters had 3.2 (95% CI: 3.1-3.2) times the risk of non-completion compared with non-limiters.

Conclusions: Although few US military parents consistently limited pediatric vaccinations, episodic vaccine-limiting throughout the first 2 years of life was common, and both vaccine-limiting patterns were associated with higher risk for vaccine series non-completion. Findings suggest greater attention to vaccine hesitancy is needed in this population.

Mental health

Associations between Maternal Nativity and Prenatal Depression by Racial and Ethnic Subgroups Kendria Kelly-Taylor*, Sara Aghaee, Joshua Nugent, Ayesha Sujan, Nina Oberman, Ai Kubo, Elaine Kurtovich, Charles Quesenberry Jr, Kathryn Ridout, Lyndsay Avalos,

US born persons present more adverse perinatal outcomes compared to non-US born, yet less is known how maternal nativity (US born vs. non-US born) is associated with prenatal depression among racial and ethnic subgroups (e.g., Mexican, Hmong). This study examined differences in prenatal depression (PND) diagnosis and severity by maternal nativity among a large cohort of pregnant persons universally screened for depression. A retrospective cohort study of pregnant persons receiving prenatal care at Kaiser Permanente Northern California from 2013 to 2019 (n=258,452) was conducted. Twenty racial and ethnic groups, and nativity were obtained from birth records, and depression diagnosis, severity (measured using Patient Health Questionairre-9 [PHQ-9]), and covariates (maternal age, parity, delivery year, education, and neighborhood deprivation) were captured via electronic health records. We calculated age-adjusted prevalence rates (PR) and used modified Poisson regression models to estimate adjusted relative risks (aRR). Among race/ethnic subgroups, non-US born persons had lower prevalence of PND compared to US born persons (PRrange:3.9-20.3%; PRrange:4.8-25.4%, respectively). Adjusted models documented equivalent or lower risk among non-US born persons. In contrast, the prevalence of severe depression (PHQ-9 score 15+) varied. Non-US born persons (vs. US born) had higher rates among Chinese (3.2% vs. 1.9%) and Hmong (4.6% vs. 3.2%) persons, yet lower rates among Black (3.9% vs. 8.1%) and Puerto Rican (1.9% vs. 6.8%) persons, for example. Adjusted models for severe depression showed non-US born Japanese, Chinese, and Vietnamese persons had higher risks compared to US born (aRR:3.45, 95%CI:1.16-10.27; aRR:2.31, 95%CI:1.71-3.14; aRR:1.90, 95%CI:1.24-2.90, respectively). Future research should continue to explore the relationship between nativity, prenatal depression and severity among racial and ethnic groups and investigate mechanisms for these associations.

Mental health

Trends and racial disparities in perinatal mental illness diagnosis Mahader Tamene*, Sai Ramya Maddali, Juan Cabrera, Marina Magalhães, Suzan Carmichael, Mahasin Mujahid,

Perinatal mental illness, including perinatal mood and anxiety disorders (PMAD) and serious mental illness (SMI), poses a critical public health concern, impacting up to 25% of birthing individuals. Untreated, these disorders have short and long-term consequences for birthing persons and their offspring. Findings on U.S. racial disparities in perinatal mental illness are mixed, and little is known about whether these disparities are changing over time. To address these gaps, we evaluated trends and racial/ethnic disparities in the prevalence of perinatal mental disorders (PMAD, SMI). We used a population-based cohort of all hospital births in California delivered ≥ 20 weeks gestation from 1997 – 2018 (N=10,853,422). We computed prevalence in perinatal mental disorders by race and ethnicity and examined racial and ethnic disparities in outcomes and trends using logistic regression. Perinatal mental disorder diagnoses occurred in 18.9 per 1,000 births, with PMAD occurring more frequently than SMI (16.6 and 5.0 per 1,000 births, respectively). The prevalence of perinatal mental illness diagnoses increased across all racial and ethnic groups over time, with Hispanic birthing persons experiencing the largest fold increase. While there was no clear evidence of racial disparities in PMAD, there were indications of such disparities in SM. Compared to non-Hispanic white birthing persons, Black birthing persons experience slightly elevated odds of SMI diagnosis (OR: 1.09, 95% CI: 1.06, 1.12). This relative disparity was less conclusive over time, with OR of SMI diagnoses increasing from 1997-2001 and 2008-2014 but decreasing from 2001-2008 and 2014-2016. These findings may be capturing ascertainment bias, differential access to adequate mental health care, racial bias in diagnosis, and stigma. Future research should investigate the social and structural drivers of racialized differences in perinatal mental illness diagnoses.

Mental health

A multi-cohort analysis of interacting prenatal and genomic risks in the development of childhood ADHD Laurie Haig*, Dogukan Koc, Kathleen Oros Klein, Francois Freddy-Ateba, Eszter Szekely, Celia Greenwood, Ashley Wazana, Jonathan Evans, Anqi Qiu, Alex Neumann,

Background: Attention deficit hyperactivity disorder (ADHD) is highly prevalent in children and has a multifactorial etiology. Both genetic and environmental factors, such as prenatal stress, contribute to disease susceptibility in a sex-specific manner. What is less well understood is the complex interplay of these factors in the pathophysiology of ADHD.

Objectives: To examine how the effect of maternal prenatal stress on developing ADHD at 4-7 years of age is moderated by child sex and polygenic risk for ADHD.

Methods: Data included 4 longitudinal cohorts from the DREAM BIG consortium (ALSPAC: N=14,009; GUSTO: N=1,176; MAVAN: N=590; Generation-R: N= 9778). Polygenic risk (PGS) for ADHD was computed using the latest genome-wide association study results. Prenatal maternal stress was assessed through a combination of two latent factors, capturing maternal affective symptoms (M) and prenatal sociodemographic adversity (A). Repeated assessments of ADHD symptoms between ages 4-7 years were combined into a composite. Cohort-specific analyses included linear regression and latent interaction analysis. Main and interaction effects were meta-analyzed using inverse variance weighting.

Results: Meta-analytic results from 3 cohorts provided evidence for the importance of both M and child sex on the development of ADHD symptoms (95%CI: 0.00637, 0.00684; 95%CI: -0.107, -0.0194), as well as moderation by sex, with a stronger influence of M in males compared to females (M*sex: 95%CI: -0.02181, -0.00147). Analyses in Gen-R are part of an ongoing collaboration, with results expected in early spring.

Conclusion: Preliminary results suggest an association between prenatal maternal affective symptoms and the development of ADHD, which is slightly stronger in males. No significant PGS-by-prenatal stress interaction effects were found. Overall, this work leverages harmonized constructs from 4 international studies to highlight the importance of prenatal factors in the development of ADHD.

The association between migraine and postpartum depression in Nurses' Health Study 3: a prospective cohort study Holly Crowe*, Kathryn Rexrode, Hadine Joffe, Brittany Charlton, Janet Rich-Edwards,

Migraine and mood disorders are frequently comorbid, but rarely studied longitudinally. Individuals with pre-pregnancy migraine may be more hormonally sensitive than non-migraineurs and therefore at greater risk of postpartum depression (PPD). We examined the association between physician-diagnosed migraine and PPD among participants in the Nurses' Health Study 3 (NHS3) (n=7,618 pregnancies among 5,387 individuals) between 2010 and 2023. At enrollment, NHS3 participants report if they have ever been diagnosed with migraine by a health care provider. Participants who report a pregnancy on a biannual questionnaire receive a postpartum questionnaire at ~5 weeks postpartum. Participants provide data on each reported pregnancy during their NHS3 participation. We ascertained PPD using the Edinburgh Postnatal Depression Scale (EPDS), a validated self-report screening tool. In separate models we defined the outcome as an EPDS score of ≥11 to maximize sensitivity and an EPDS score of ≥13 to maximize specificity. We further examined self-reported physician-diagnosis of postpartum depression. We used log-binomial regression, accounting for non-independence of repeated pregnancies within individuals, to examine the association between migraine and postpartum depression, adjusting for age and race. Overall, 26% of participants reported a history of migraine, and 8-18% reported PPD (EPSD cutoff of 11 and 13, respectively). Only 4% of participants reported a physician diagnosis of PPD. We found no appreciable association between pre-pregnancy migraine and PPD using EPDS cutoff of 11 (RR=1.02, 95% CI: 0.89-1.16) or 13 (RR=0.90, 95% CI: 0.74-1.08). Our findings indicate that migraineurs may be slightly less likely to receive a diagnosis of PPD (RR= 0.79, 95% CI: 0.61-1.02). While symptom levels and antidepressant use before, after, and during pregnancy were similar among migraineurs and non-migraineurs, migraineurs were slightly less likely to report a PPD diagnosis.

Who do we leave out when we exclude discordant birth certificate records? Ruby Barnard-Mayers*, Martha Werler,

Background: Many studies on maternal and child health use birth certificate data. However, this data is not always consistent, and individuals with discrepancies are often excluded from analyses, as their information can't be assumed to be reliable.

Objective: The purpose of this study is to understand who we exclude when we exclude discrepant records from birth certificate data.

Methods: Birth certificate data from the Pregnancy and Early Life Longitudinal (PELL) data system, which links birth certificate and hospital discharge records in Massachusetts from 2011 to 2018. For 4 conditions (pregnancy risk factor, delivery procedure, test or screening procedure, and labor and delivery complication) the birth certificate has a check box to indicate 'No." After each, the birth certificate has a list of specific conditions for checking off when present (

Results: Of the 552,806 births, 9,737 (1.8%) were discrepant. The most common discrepancy was for labor and delivery complications (67%), followed by tests and procedures (24%), parity (11%), pregnancy risk factors (6%), and finally delivery procedures (0.2%). Compared to birthing people with non-discrepant record, those with discrepant records were, on average, about one year older, were more likely to have private insurance (63.4% vs. 49.1%), were more likely to have a college degree (58.3% vs. 46.0%), were less likely to have a vaginal delivery (53.3% vs. 66.4%), and were less likely to have prenatal care (87.3% vs. 95.2%). Birthing people with discrepant records also appeared more likely to be non-Hispanic Black (18.4 vs. 9.9%) Distributions of BMI, parity, and country of birth were similar for the two groups.

Conclusion: Birthing people with discrepant birth certificate records differ from those without such discrepancies on socio-economic and reproductive indicators, raising the possibility of bias arising from their exclusion. Further research should focus on the potential impact excluding these people from analyses may have on results.

Evaluating a new approach to classify fetal growth restriction Thais Rangel Bousquet Carrilho*, Katherine Himes, Corinne Riddell, Lauren Skvarca, Jennifer Hutcheon,

Introduction: Fetal growth restriction is the leading cause of preventable stillbirth in the US and its consequences extend beyond the perinatal period. There is no gold standard definition of fetal growth restriction and available tools do a poor job in its classification. We aimed to evaluate the ability of a new approach for classifying fetal growth restriction that combines information on multiple indicators of pathologically-restricted growth at birth in identifying stillbirths due to uteroplacental insufficiency.

Methods: We used data from the Stillbirth Collaborative Research Network, a US population-based stillbirth case-control study (2006-2008). We used latent profile analysis to classify births as growth-restricted vs. non-growth-restricted using as covariates: birthweight z-score, ponderal index, hypertensive disorders of pregnancy, autoimmune diseases, and placental maternal and fetal vascular malperfusion lesions. Risk ratios (RRs) for stillbirth due to uteroplacental insufficiency in growth-restricted vs. non-growth-restricted births were calculated. We compared our findings with the classification of small-for-gestational-age birth (SGA, < 10th percentile).

Results: Our cohort included 1100 live births and 64 stillbirths with uteroplacental insufficiency as possible/probable cause of death. Births classified as growth-restricted by our model were 5.6-fold [95% CI: 3.5 to 8.6] more likely to end in stillbirth due to placental insufficiency vs. those classified as non-growth-restricted. The RR for stillbirth due to uteroplacental insufficiency in SGA births vs. non-SGA births was 4.2 [95% CI: 2.5 to 6.9].

Conclusion: A classification of fetal growth restriction based on latent profile analysis captured a higher percentage of stillbirths due to uteroplacental insufficiency than the conventional classification of SGA birth. The next step in this investigation program includes refining the model to improve its ability to identify growth-restricted births.

Does timing of fruit and vegetable introduction during infancy influence diet quality in middle childhood? Priscilla Clayton*, Diane Putnick, Ian Trees, Jordan Tyris, Tzu-Chun Lin, Edwina Yeung,

Early infant feeding practices not only impact short- and long-term health but also influence the formation of food preferences in childhood. However, how the timing of introduction to fruits and vegetables shape overall diet quality is not known.

Parents from the Upstate KIDS cohort reported whether they introduced fruits and vegetables to their infants at 4, 8, and 12 months of age. At 7 years of age, parents completed a 27-item food-frequency questionnaire used to determine diet quality based on the Youth Healthy Eating Index (YHEI) score. All singletons and one randomly selected multiple from each family with information were included (n=1288). Generalized linear models were used to examine the associations between timing of introduction of fruits and vegetables and diet quality in childhood, adjusting for mother's age, race/ethnicity, education, insurance status, pre-pregnancy BMI, child's gestational age, Women, Infants, and Children (WIC) participation, and breastfeeding duration.

Approximately 31% of infants were introduced to fruits and vegetables by 4 months. Infants introduced between 5-8 months had a higher mean [SD] YHEI score of 54.4 [11.3] compared to those introduced earlier (52.7 [10.79]) and later (50.5 [10.9]) (p=0.003). Compared to those introducing fruits and vegetables by 4 months of age, introducing fruits and vegetables between 5-8 months of age was associated with higher dietary quality (B: 1.68; 95% CI: 0.31, 3.04) at 7 years of age but not introducing between 9-12 months (B: -2.23; -5.21, 0.75). After adjusting for covariates, introducing between 5-8 months (B: -0.20 CI: -1.58, 1.76) and between 9-12 months (B: -2.30; -5.26, 0.66) was not associated with YHEI relative to 4-months.

Earlier or later introduction to fruits and vegetables than at the recommended 6 months was not associated with diet quality in school-aged children, although further investigation of other complementary foods is needed.

Changes in gestational diabetes subtypes and health services use following a screening policy change in British Columbia, Canada: An interrupted time series analysis Elizabeth Nethery*, Jennifer Hutcheon, Julie Lee, Patricia Janssen, Laura Schummers,

Background: In October 2010, provincial guidelines for gestational diabetes mellitus (GDM) were changed to use lower glucose levels for diagnosis, increasing the incidence of GDM. Whether the additional diagnoses were less severe ("diet-controlled") or more severe ("medication-dependent"), and impacts on specialists' services are not known. We examined the effect of a guideline change on GDM subtypes and endocrinologist visits.

Methods: We used a population-based linked cohort of all singleton pregnancies >28 weeks gestational age (2008-2019). We identified cases based on international classification of diseases coding on the delivery record and medication-dependent patients based on outpatient prescription records for glucose control medications during pregnancy. Endocrinology visits were identified via clinician billings to the provincial health system. We used an interrupted time series design using linear regression to estimate changes in subtypes (medication-dependent and diet-controlled) and endocrinology visits (any v. no visits) following the guideline change. We estimated risk ratios comparing the observed incidence of each GDM type with the expected incidence of each type in the post-policy period, controlling for underlying time trends.

Results: Among 472,595 singleton pregnancies, the incidence of diet-controlled GDM increased from 6.2% pre-2010 to 8.9% in the 2011-2019 period and endocrinology visits (any v. no visits) increased from 5.2% to 9.2%. From our interrupted time series models, we found an increase in diet-controlled GDM (level change: RR 1.33 [95% CI: 1.26, 1.41]) and in specialist visits (level change: RR [1.14 95% CI: 1.07, 1.21]). We found no change in the level or trend for medication-dependent GDM (level change: RR 0.94 [95% CI: 0.84 to 1.05]).

Conclusion: A guideline change resulted in a 33% increase in less severe diet-controlled GDM, a 14% increase in specialist visits, but had no impact on incidence of more severe, medication-dependent GDM.

Geographic access to primary care and racial and ethnic disparities in chronic conditions among US births, 2016-2020 Sheree Boulet*, Lauren Costley, Kaitlyn Stanhope,

Unequal access to preventive health care before and between pregnancies contributes to disparities in health status and increased risk for adverse perinatal outcomes. Few studies have examined primary care access as a potential driver of racial and ethnic disparities in chronic disease prevalence among US birthing people. We linked US natality data for 2016-2020 with HRSA's Area Health Resource Files and used Bayesian conditional autoregressive models to estimate county-level associations between geographic access to primary care (lagged by 1-year prior to birth) and rates of chronic conditions (obesity, hypertension, and diabetes) among 1,395 contiguous US counties with ≥50 births to Black and white people. Geographic primary care access was defined as designation as a primary care Health Provider Shortage Area (pcHPSA) and the number of primary care physicians per 100,000 population, categorized into tertiles. We assessed racialized disparities in chronic disease prevalence by modeling the difference in rate differences for non-Hispanic Black versus non-Hispanic white births, controlling for percent of families below the federal poverty level, unemployment rate, rurality, and the age and race structure of women of reproductive age (15-44 years). Overall, living in an pcHSPA or the lowest tertile of primary care provider density was associated with increased prevalence of obesity and hypertension. However, the Black-white disparity was generally consistent across pcHPSA designation and tertiles of primary care provider density. For example, the Black-white risk difference for obesity was 12.1 per 100 births (95% CI: 11.3-12.9) for pcHPSAs and 9.75 per 100 births (95% CI: 9.3-10.2) for non-pcHPSAs, while the adjusted β (standard deviation) for the difference in risk differences was .009 (.005). Geographic access to a primary care did not attenuate racial disparities in prevalence of chronic conditions among US birthing people.

Obstetric health

Obstetric Care Facility Closures and Healthcare Provider Experiences — Fall DocStyles Survey, United States, 2023 Jessica Meeker*, Jerome Leonard, Carrie Shapiro-Mendoza, Elizabeth Clark, Rebecca Hall, Romeo Galang,

Obstetric care facility closures (closures) in the US have exacerbated concerns about disparities in access to quality obstetric care, which is critical as maternal morbidity and mortality rates continue to rise. The purpose of this study is to report healthcare provider closures-related experiences. DocStyles, a web-based panel survey of a convenience sample of US primary healthcare providers US, was conducted October 6–25, 2023. Providers caring for pregnant women were asked about closures experiences, including those impeding transfer of high-risk patients to appropriate care, the importance and frequency of patient counseling on facility closures, and priority counseling-related topics. We calculated experience frequencies using R version 4.0.3. The sample of 1,371 respondents included family practitioners (35%), internists (30%), obstetrician-gynecologists (18%), and nurse practitioners/physician assistants (17%). Among respondents, 53% reported closures as a problem in connecting high-risk patients to a birth facility prepared to meet their health needs; 66% of rural and 52% of urban providers expressed this concern. A third of respondents (35%), reported if the birth facility where their patients typically deliver was closed or inaccessible, they would not have an alternative, or wouldn't have an alternative with the same level of care. Although 83% of providers reported the importance of talking with pregnant or postpartum patients about where to get emergency obstetric care in the case of closures, 54% had counseled zero, or very few of their patients. Among urban providers, 18% counseled all or almost all their patients, compared to 9% of rural providers. When asked which counseling topics should be included, providers reported knowing symptoms requiring emergency obstetric care (72%) and not waiting to seek care (66%) with the highest frequency. Provider experiences may inform efforts to ensure patients receive timely, quality obstetric care.

Postpartum Hemorrhage Trajectories in the United States Military Health System, 2013–2021 Sandra Maduforo*, Celeste Romano, Clinton Hall, Gia Gumbs, Ava Marie Conlin,

Background: A 2014 Military Health System (MHS) review identified higher rates of postpartum hemorrhage (PPH) at military vs civilian hospitals; by 2015, rates were reportedly similar. This work aimed to investigate trends in PPH in the MHS through 2021 and assess differences between military hospitals with distinct trajectories.

Methods: The Department of Defense Birth and Infant Health Research program was used to identify live born deliveries among US military families, 2013–2021. PPH was ascertained via diagnosis codes from delivery through 12 weeks postpartum. Annual rates of PPH were calculated by hospital type (military vs civilian) and for each military hospital. Military hospitals were then grouped by PPH rate trajectory: sustained high/increasing relative to other military hospitals (i.e., high), sustained low/decreasing (i.e., low), or variable. Risk factors were compared by trajectory.

Results: Among 643,065 identified deliveries, 45.5% occurred at a military hospital and 54.5% at a civilian hospital. Overall PPH rates at military hospitals declined from 2013-2015, falling below rates at civilian hospitals, but increased in subsequent years, exceeding pre-2015 rates at civilian and military hospitals. Compared to military hospitals with low (n=11) and variable (n=6) rate trajectories, those with high rate trajectories (n=14) had higher annual delivery counts (1206 high; 819 low; 958 variable), and deliveries were more likely to have several risk factors for PPH (e.g., preterm: 7.4% high; 4.8% low; 4.9% variable), but less likely to have others (e.g., anemia: 15.7% high; 18.9% low; 16.0% variable).

Conclusions: Despite an apparent decline in PPH at military hospitals from 2013-2015, rates rose from 2016–2021, with varying trajectories and associations with well-known risk factors. Findings suggest differences in measurement of PPH and warrant further assessment.

Severe maternal morbidity among US- and foreign-born Black women residing in California, 1997-2019

Safyer McKenzie-Sampson*, Chen Ma, Suzan Carmichael,

In the United States (US), Black women have the highest risk of severe maternal morbidity (SMM), compared to women of all other race/ethnicities. Past research has identified important nativity-based disparities in the risk of adverse perinatal outcomes among Black women, with foreign-born Black women having a significantly lower risk of preterm birth and low birthweight compared to US-born Black women. However, it remains unclear whether similar nativity disparities exist in the context of SMM. This study compares trends and odds of SMM among US- and foreign-born Black women in California.

Data for live births and fetal deaths to Black women living in California between 1997-2019 (n=636,364) who had linked vital record and hospital discharge data were used to compute the probability of SMM over time by maternal nativity, and to fit logistic regression models adjusted for related clinical and socio-demographic factors. We computed odds ratios (OR) and 95% confidence intervals (CI) comparing odds of SMM among foreign-born Black women of Caribbean and African descent to all US-born Black women.

While the probability of SMM increased steeply for all women during the study period, the trend was steepest for African-born women. African-born women also had the highest proportion of SMM (2.6%), compared to US-born (1.9%) and Caribbean-born (1.8%) women. Compared to US-born women, the adjusted odds of SMM was significantly higher for African-born women, OR 1.15 (95% CI 1.05, 1.25) and appeared lower among Caribbean-born women, OR 0.85 (95% CI 0.68, 1.07).

In this study of SMM among Black women in California, the odds of SMM were significantly higher among African-born Black women, compared to US-born Black women. Our work contrasts with previous nativity studies of adverse maternal and infant outcomes. Future studies should disaggregate SMM data among Black women as it may mask important nativity disparities.

Obstetric health

Use of telehealth did not mitigate persistent disparities in prenatal care access among American Indian women in North Dakota. Tara Stiller*, Anna Charlotta Kihlstrom, Nishat Sultana, Grace Njau, Matthew Schmidt, Anastasia Stepanov, Andrew Williams,

Background: In North Dakota (ND), there is a persistent disparity in prenatal care access among American Indian (AI) women compared to other racial groups. During the COVID pandemic, the expansion of telehealth emerged as a potential solution to disparate access to healthcare. This investigation examines the potential for telehealth to mitigate persistent racial disparities in prenatal care in ND.

Methods: Data were drawn from the 2020-2021 ND Pregnancy Risk Assessment Monitoring System (n=585; weighted n=10189). Late prenatal care was for those with prenatal care initiation >13 weeks gestation. Maternal race/ethnicity was self-reported. Use of telehealth for prenatal visits was self-reported and categorized as 'any telehealth use' vs. 'no telehealth use.' Those not using telehealth reported eight barriers (e.g., lack of internet, no telehealth appointments). Logistic regression estimated odds ratios and 95% confidence internals for late prenatal care among AI/AN and other race/ethnicity women compared to White women. Models included maternal sociodemographic, medical, and behavioral factors. Chi-square was used to examine the prevalence of prenatal care barriers by race/ethnicity.

Results: Compared to White women, AI women were twice as likely to receive late prenatal care (OR:2.40 95%CI:1.08,5.35). When telehealth was included in the model, the AI-White disparity was reduced by 2% (OR:2.35, 95%CI:1.05,5.26). Compared to White and Other race/ethnicity women, a higher prevalence of AI women reported lack of access to telehealth appointments(p<.01), computers(p<.01), phones(p<.01), and physical space(p<.01) as barriers to using telehealth.

Discussion. Despite telehealth emerging as a potential solution to disparate prenatal care access, the use of telehealth did not mitigate the persistent disparity in ND. In addition to community and healthcare infrastructure investment, culturally safe initiatives are needed to improve access to prenatal care for AI women in ND.

Fetal body composition in twins and singletons – are twins programmed to be smaller?

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Background: Twins and singletons have different fetal growth trajectories, with twin growth significantly slowing beginning in the third trimester of gestation relative to singletons. These differences may represent normal physiological adaptation in otherwise uncomplicated twin pregnancies. However, there is a lack of information about the sequential progression of fetal soft tissue development in both singleton and twin pregnancies.

Methods: In the NICHD Fetal 3D Study, serial abdominal and thigh measurements were obtained using three-dimensional ultrasonography in dichorionic twins (n=306) and singletons (n=2,525). Using linear mixed effects models, we compared marginal means at each week of gestation (15-36) for the following fetal soft tissue parameters: abdominal area, maximum subcutaneous tissue thickness (MSCTT), fractional thigh volume (TVol), fractional fat thigh volume (FFTVol), fractional lean thigh volume (FLTVol) and a FFTVol/TVol ratio, adjusting for relevant covariates.

Results: Twin abdominal measures were slightly larger than singletons from 17-26 weeks for area (2.1-41.3 mm2) and 18-24 weeks for MSCTT (0.04-0.07 mm) and becoming smaller thereafter (area=24.1-303.1 mm2; MSCTT=0.04-0.35 mm). Beginning at 15 weeks, thigh volumes were smaller for twins (diffTVol= -0.09 cm3, 95% CI: -0.13, -0.05; and diffFFTVol= -0.07 cm3, CI: -0.12, -0.02) relative to singletons, persisting through 36 weeks (diffTVol= -6.77 cm3, CI: -10.0, -3.52 and diffFFTVol= -4.98cm3, CI: -7.93, -1.71). FLTVol was also smaller for twins in all weeks of gestation. For the FFTVol to TVol ratio, twins still had a 1.3-3.2% smaller fat percentage for all weeks of gestation compared to singletons.

Conclusions: Despite third trimester twin growth deceleration, our discovery that twin thigh volumes consistently remain smaller from 15 weeks of gestation implies that twin growth adaptation may be predetermined in early pregnancy at a time when there is less competition for in-utero resources.

Obstetric health

Peripartum cardiomyopathy from 1980-2022, disparity trends in incidence, severity, and duration Sunny (Pei Yi) Lin*, Ke Pan, Christian Hernandez, Jennifer Faith, Maegan Dirac,

Introduction

The frequency of peripartum cardiomyopathy (PPCM) has previously been reported to vary across countries and ethnic groups, but many countries lack primary data on this disease. We aim to produce comparable estimates of the incidence, severity, and duration of PPCM for 204 countries between 1980-2022.

Methods

Data were extracted from peer-reviewed studies identified in a systematic review and primary clinical administrative dataset. We estimated the age-location-specific incidence of PPCM using DisMod-MR, a Bayesian meta-regression tool that borrows information from countries in the same region and a suite of predictive covariates to produce estimates where data are lacking. We also synthesized data on the duration and severity distribution of PPCM cases in the studies identified.

Results

We included 298 unique peer-reviewed sources and incorporated claims or inpatient data from six countries. The incidence rate of PPCM appears to have remained stable since 1990, but a tenfold variation was observed across countries. Incidence reporting was concentrated in North America, China, and South Asia while sparse in other countries and regions. High incidence was observed in many countries in South Asia and Latin America, but high-incidence countries were also scattered across other regions of the world. Age groups on the extreme ends of the reproductive age span displayed higher incidences, while ages 20-30 experienced the lowest rates of PPCM. Globally, the duration of PPCM ranged from 28 to 751 days. The severity of PPCM was commonly classified using the New York Heart Association (NYHA) functional classes; only 10% of cases were in class one, the majority (68%) of newly diagnosed cases being in classes three and four.

Conclusion

Our findings underscore the global variation in PPCM incidence rates. However, temporal trends and geographic patterns could be obscured by variations in case definitions. Our next steps include standardization of data collected using different case definitions and re-fitting the model to produce more like-versus-like comparisons.

The role of social support in prenatal care uptake for women with unwanted pregnancies
Adaeze Anamege*, Chidinma Oli, Sonila Dubare, Kelly Gurka,

Introduction: Prenatal care (PNC) uptake is significantly influenced by wantedness of a pregnancy. Social support is known to enhance PNC uptake, but it is unclear if this applies to women with unwanted pregnancies. This study explored the impact of social support on PNC uptake in such cases.

Methods: This retrospective study utilized data from the Centers for Disease Control and Prevention's 2017-2019 National Survey of Family Growth. Data were analyzed for 2,580 US women aged 15-50. Social support was gauged through emotional (partner availability) and instrumental support (public assistance). Bivariate analysis explored associations between sociodemographic variables, social support, and PNC uptake. Multivariable logistic regression assessed the association between social support and PNC uptake. All analyses were conducted in the SAS 9.4 statistical software.

Results: Women who initiated PNC were older on average (p = 0.0365), mostly married (p = 0.0033), wanted the pregnancy (p = 0.0461), and had emotional support (p = 0.0012). Among all women, there was a marginally significant difference in PNC uptake among those who had emotional support (Adjusted Odds Ratio [AOR] = 0.60; 95% Confidence Interval [CI] = 0.37-0.99) and those who received some public assistance (AOR = 0.54; 95% CI = 0.30-0.97). There were no significant differences in PNC uptake among women with unwanted pregnancies who received emotional (AOR = 0.73; 95% CI = 0.32-1.68) and instrumental support (AOR = 0.67; 95% CI = 0.25-1.85).

Conclusion: Women with unwanted pregnancies are less likely to initiate and keep attending PNC even with social support. Exploring additional support avenues, like peer support groups, could be beneficial. Connecting these women with others who faced similar situations, attended PNC, and experienced positive outcomes may encourage them to prioritize PNC visits, ultimately improving maternal and child health outcomes.

Receipt of Tdap or influenza vaccine during pregnancy and odds of clinical chorioamnionitis: a validated case-control study Clinton Hall*, Sandra Maduforo, Celeste Romano, Anna Bukowinski, Sandra Michelle Magallon, Gia Gumbs, Ava Marie Conlin,

Background: Receipt of the tetanus, diphtheria, and acellular pertussis (Tdap) or influenza vaccine during pregnancy has been positively associated with chorioamnionitis in recent studies using administrative medical data. However, the accuracy of diagnosis codes for chorioamnionitis is variable, especially for clinical chorioamnionitis (i.e., excluding subclinical, histologic disease) which may be more relevant to vaccine safety.
Methods: Live deliveries at two United States military hospitals, 2013-2018, were initially screened for chorioamnionitis using diagnosis codes. All screen positive deliveries and a random sample of screen negative deliveries were selected for chart review and validation. Study cases (clinical chorioamnionitis) were defined by the presence of fever and additional clinical symptoms during the delivery hospitalization; controls were defined by the absence of these criteria. Weighted multivariable logistic regression models estimated adjusted odds ratios (aORs) and 95% confidence intervals (CIs) for validated cases with receipt of Tdap and/or influenza vaccine during pregnancy.
Results: Overall, 1,868 deliveries were selected for validation and 1,650 (n=305 clinical cases, n=1,345 controls) were included in analyses. At delivery, mean age was 24.9 years for cases and 25.8 years for controls; 88.5% of cases and 64.9% of controls were nulliparous. Tdap vaccine was recorded in 84.3% of cases and 81.6% of controls (aOR 0.89, 95% CI 0.66-1.20) and influenza vaccine was recorded in 61.6% of cases and 63.0% of controls (aOR 0.90, 95% CI 0.68-1.18). Sensitivity analyses that considered timing of vaccine receipt and receipt of only one or both vaccines yielded similar null estimates.
Discussion: This study leveraged electronic health records to validate cases and controls and collect information on important clinical covariates; neither Tdap nor influenza vaccine receipt during pregnancy were associated with increased odds of clinical chorioamnionitis.

Primary adherence to antihypertensive medications during pregnancy Ugochinyere Vivian Ukah*, Gabriela Vazquez Benitez, Christina Ackerman-Banks, Julia F Simard, Kirsten R Ehresmann, Corinne M. Brown-Robinson, Elizabeth Grossman, Kristin Palmsten,

Introduction: Treatment of hypertensive disorders of pregnancy (HDP) is crucial to prevent further maternal morbidity such as stroke but little is known about adherence to treatment during pregnancy. We examined primary adherence to antihypertensive medications among patients with HDP.

Method: We used electronic health records (EHR) of prenatal care patients aged 16-49 years from a health care system located in Minnesota and Wisconsin who delivered between 2009-2021, had HDP (chronic/gestational hypertension, preeclampsia, HELLP syndrome, and eclampsia) and had continuous medical and pharmacy insurance coverage throughout pregnancy. We identified outpatient prescriptions for antihypertensives considered safe during pregnancy (i.e., calcium blockers, beta blockers, centrally acting drugs) from EHR and fills using pharmacy claim data. We calculated primary adherence during pregnancy, defined as filling the first outpatient prescription within 7 days. We examined the relation between patient characteristics and primary adherence, using log-binomial regression models to calculate the risk ratios (RR) and 95% confidence intervals (CIs).

Results: The cohort included 4,647 patients with HDP, of which 526 (11.3%) had an outpatient antihypertensive prescription during pregnancy. Labetalol (53%), nifedipine (21%), and methyldopa (11%) were the most prescribed medications. In total, 382 (72.6%) patients had primary adherence. Patients aged 35-39 years were less likely to have primary adherence, compared with those aged 30-34 years (RR 0.85, 95% CI 0.74-0.97), while patients with a Black versus White healthcare provider at their first prenatal visit were more likely to have primary adherence (RR 1.22, 95% CI 1.03-1.46).

Conclusion: While many patients with HDP in this study population demonstrated primary adherence with antihypertensive treatment during pregnancy, there is still need for improvement in adherence according to patient characteristics.

Z-drug use in the first trimester and risk of congenital malformations Kelly Fung*, Loreen Straub, Brian Bateman, Ayesha Sujan, Gregory Brill, Sonia Hernandez-Diaz, Krista Huybrechts,

Background: Sleep disorders are common in pregnancy and treated by non-benzodiazepine sedative hypnotics (also known as "Z-drugs"). However, there is limited evidence on the fetal safety of Z-drugs.

Objective: To evaluate the risk of congenital malformations after first-trimester exposure to Z-drugs.

Methods: This U.S.-based cohort study utilized data of pregnancies linked to live-born infants from public (2000-2018) and commercial (2003-2020) insurance databases. We defined major congenital malformations using validated algorithms and compared the risks of any malformation and organ-specific malformations in pregnancies with ≥1 dispensing of Z-drugs in the first trimester to those unexposed. Propensity score fine stratification was used to control for potential confounders, including demographics, comorbidities, healthcare utilization, and concomitant medication use. Fixed-effects meta-analysis was conducted to pool relative risks (RR) and 95% confidence intervals (CI).

Results: 11,651 of 2,506,106 publicly insured pregnancies and 10,925 of 1,784,143 commercially insured pregnancies had first-trimester Z-drug exposure. The absolute risk of any congenital malformation was 4.0% for exposed and 3.3% for unexposed pregnancies in the publicly insured cohort; the risks were 4.2% and 3.8% respectively in the commercially insured cohort. After adjustment for confounders, there was no evidence of elevated risk of any major malformation among exposed infants (pooled RR=1.01, 95% CI: 0.95-1.08). Exposure to Z-drugs did not appear to increase the risk of organ-specific malformations except for neural tube defects (pooled RR=1.74, 95% CI: 1.02-2.96). Results were consistent in sensitivity analyses, including those focused on filling ≥2 prescriptions.

Conclusion: Our findings suggest that Z-drug exposure in the first trimester does not elevate the risk of congenital malformations overall. Additional evidence is needed to confirm the signal observed for neural tube defects.

The Influence of Reproductive Access Restrictions on Out-of-State Abortion Care in Colorado, an Interrupted Time Series Analysis 2018-2023 Kelly DeBie*, Molly Gutilla, Kayleigh P. Keller, Jennifer L. Peel, Andreas M. Neophytou,

Title: The Influence of Reproductive Access Restrictions on Out-of-State Abortion Care in Colorado, an Interrupted Time Series Analysis 2018-2023

Background: Abortion access in the United States has been shaped historically by Roe v. Wade, a case which created a Constitutional right to abortion. States seeking to challenge Roe passed laws more restrictive than Roe would permit. Texas' SB8 was passed in 2021 and forbids abortion after detection of cardiac electrical activity around six weeks. Roe was overturned in 2022 removing the right to abortion and leaving reproductive care access decisions to states.

Methods: Utilizing data from January 2018 to August 2023 on induced termination of pregnancies from the Colorado Department of Public Health and Environment, an interrupted time series analysis using Quasi-Poisson regression was used to assess the association between changes in law and monthly counts of patients from Texas traveling to Colorado for abortion services. The Texas SB8 enactment date was selected for the interruption point of the analysis.

Results: Texas residents were over 5 times more likely to travel to Colorado for abortion procedures after the enactment of SB8. Rate Ratio: 5.44, (95 % confidence interval: 1.81, 16.32).

Discussion: State restrictions on access to abortion may require patients to travel to other states for healthcare. for abortion services. Changes observed here pre-date the repeal of Roe due to prior enacted state law.

Conclusion: This study contributes evidence of changes in out-of-state patients seeking abortion in Colorado though these results may not be generalizable to other states. Here we can only account for those holding the privilege of having the ability and resources to travel to other states for these procedures, which may represent only a fraction of the total who would otherwise desire in-state services.

Polygenic effect of gestational duration reducing maternal variants on birth weight in an ancestrally diverse cohort Tesfa Dejenie Habtewold*, Prabhavi Wijesiriwardhana, Richard J. Biedrzycki, Fasil Tekola-Ayele,

Introduction: The maternal genome influences gestational duration and birth weight. However, whether genetic variants that control gestational duration influence birth weight is unclear. This study aimed to investigate the impact of gestational duration-reducing variants on birth weight in 2,056 ancestrally diverse pregnant women from the NICHD Fetal Growth Studies – Singletons cohort.

Methods: Genetic risk score (GRS) was calculated using 20 maternal variants associated with gestational duration irrespective of their effect through fetal genome (GRSFMOM) and a subset of 14 variants with maternal-only effect (GRSMOM) based on the latest genome-wide association study in Europeans. The association between GRSs and birth weight (in grams, g) was tested using linear regression analyses adjusted for fetal sex, gestational age, maternal sociodemographic factors, and the top five genomic principal components. Sensitivity analysis was performed in women with spontaneous onset of labor.

Results: The third and fourth GRSFMOM quartiles were significantly associated with 66.1 g (95% CI=-122.6, -9.7, p=0.022) and 82.6 g (95% CI=-132.8, -32.4, p=0.001) lower birth weight compared to the first quartile, respectively. The association was attenuated among women with spontaneous onset of labor. The second and fourth GRSMOM quartiles were significantly associated with 88.3 g (95% CI=-138.1, -38.4, p=0.001) and 72.5 g (95% CI=-123.0, -21.9, p=0.005) lower birth weight, respectively. Among women with spontaneous onset of labor, the second GRSMOM quartile was significantly associated with a 115.7 g (95% CI=-177.3, -54.0, p < 0.001) lower birth weight.

Conclusions: Among ancestrally diverse pregnant women, the polygenic effect of European-derived maternal genetic variants that shorten gestational duration also lowered birth weight. The findings do not support the hypothesis that fetuses with a maternal genetic predisposition to shorter gestation grow faster.

A Counterfactual Analysis of Impact of Cesarean Birth in a First Birth on Severe Maternal Morbidity in the Subsequent Birth Shalmali Bane*, Suzan Carmichael, Julia Simard, Michelle Odden, Peiyi Kan, Jonathan Snowden, Elliott Main,

Severe maternal morbidity (SMM) is a sentinel outcome comprised of unexpected adverse outcomes (e.g., aneurysm) with significant short- and long-term consequences to maternal health. It is known that cesarean birth affects maternal outcomes in subsequent pregnancies, but specific effect estimates related to subsequent SMM are lacking. We sought to quantify the effect of cesarean birth reduction among nulliparous, term, singleton, vertex (NTSV) births (i.e., the most preventable cesarean births) on SMM in the second birth.

We examined birth certificates linked with maternal hospitalization data (2007-19) from California for NTSV births linked with second births (N = 779,382). The exposure was cesarean delivery in first birth and the outcome was SMM in the second birth. We used adjusted Poisson regression models to calculate risk ratios and population attributable fraction of SMM in the second birth and conducted a counterfactual impact analysis to estimate how lowering NTSV cesarean births could reduce SMM risk in second births (such that individuals with the lowest probability of cesarean delivery instead gave birth vaginally).

The adjusted risk ratio for SMM in the second birth given a prior cesarean birth was 1.68 (95% CI 1.50-1.89); 15.5% (95% CI 15.4%-15.5%) of this SMM may be attributable to prior cesarean birth. In a counterfactual analysis where 12% of the California population least likely to get a cesarean birth instead delivered vaginally, we observed 175 fewer SMM events in a population of individuals with a low-risk first birth and a subsequent birth.

Lowering primary cesarean birth among a NTSV population is one mechanism to decrease downstream SMM events in subsequent births and overall. Additionally, our findings reflect the importance of considering the cumulative accrual of risks across the reproductive life-course.

Associations of early-to-mid-pregnancy per- and polyfluoroalkyl substances with maternal gestational weight gain Maria Cinzori*, Diana Pacyga, Libeth Rosas, Sabrina Smith, June-Soo Park, Joseph Gardiner, Joseph Braun, Susan Schantz, Rita Strakovsky,

Background: Per- and polyfluoroalkyl substances (PFAS) are metabolic disruptors, but their impact on gestational weight gain (GWG) is unknown. Thus, we evaluated overall and pre-pregnancy body mass index (ppBMI)-specific associations of PFAS with GWG.

Methods: Pregnant Illinois women (n=486) reported weights pre-pregnancy and at their last obstetric appointment before delivery, which we used to calculate gestational age- and ppBMI-specific GWG z-scores (GWGz) using an international reference. We quantified serum perfluorononanoic acid (PFNA), perfluorooctane sulfonic acid (PFOS), perfluorooctanoic acid (PFOA), perfluorohexane sulfonic acid (PFHxS) and perfluorodecanoic acid (PFDeA) levels. We calculated ppBMI and categorized women as having under/normal weight (BMI<25 kg/m2), overweight (BMI 25–29.9 kg/m2), or obesity (BMI≥30 kg/m2). Using linear regression adjusting for potential confounders (e.g. age, race, employment, income, parity, smoking, alcohol use, stress), we evaluated associations of ln-transformed maternal PFAS levels with GWGz. We also explored differences by ppBMI using a multiplicative interaction term.

Results: In a sample of healthy women with low PFAS levels, the median (25th, 75th percentiles) GWGz was 0.4 (-0.3, 1.1). Overall, only PFNA and PFOS were associated with lower GWGz, but associations differed by ppBMI. In under/normal weight women, each 10% increase in PFNA (β: -0.8, 95% confidence interval (CI): -1.4, -0.2), PFOA (β: -0.3, 95%CI: -0.6, 0.0), PFOS (β: -0.3, 95%CI: -0.5, -0.1), and PFHxS (β: -0.2, 95%CI: -0.5, 0.0) was associated with lower GWGz. However, in women with obesity, each 10% increase in PFNA (β: 1.0, 95%CI: -0.1, 2.0), PFOA (β: 0.5, 95%CI: -0.1, 1.0), and PFDeA (β: 3.2, 95%CI: 0.4, 5.9) was associated with higher GWGz. We observed no associations in women with overweight.

Conclusions: Associations of PFAS with GWG may differ by ppBMI. Studies could consider implications of these findings for maternal and fetal health.

Ranking of Severe Maternal Morbidity Indicators by Delivery Mode Lindsay Womack*, Romeo Galang, Lindsay Admon, Elizabeth Clark, Alexander Ewing, Glen Satten, Jean Ko, Cynthia Ferre, Charlan Kroelinger,

Background: Maternal complications, including severe maternal morbidity (SMM), are higher in cesarean deliveries than vaginal deliveries. We determined which SMM indicators identify the most in-hospital mortality during delivery hospitalization by delivery mode.

Methods: Data were obtained from the 1993–2015 Healthcare Cost and Utilization Project's National Inpatient Sample, an all-payer database of hospital discharge records. Twenty-two SMM indicators were identified using ICD-9-CM diagnosis and procedure codes. Separate analyses were conducted for cesarean and vaginal deliveries. We calculated SMM indicator-specific prevalences, in-hospital mortality rates, and population attributable fractions (PAF) of mortality, and the indicators were then ranked by their PAF of in-hospital mortality.

Results: We identified 87,864,173 delivery hospitalizations (27.9% cesarean and 72.1% vaginal deliveries). There were 6,686 records with a discharge disposition of "died." Of these deaths, 71.2% occurred in cesarean deliveries. Most deaths had an SMM indicator (94.2% cesarean and 73.5% vaginal deliveries). Among cesarean deliveries, the top 5 ranked indicators were: cardiac arrest/ventricular fibrillation, conversion of cardiac rhythm, ventilation, temporary tracheostomy, and amniotic fluid embolism. Among vaginal deliveries, the top 5 ranked indicators were: conversion of cardiac rhythm, cardiac arrest/ventricular fibrillation, ventilation, temporary tracheostomy, and amniotic fluid embolism. The top 3 ranked indicators identified 73.8% of in-hospital mortality among cesarean deliveries and 57.7% of in-hospital mortality among vaginal deliveries.

Conclusions: The top 5 ranked indicators were similar by delivery mode. However, there were differences by delivery mode in the performance of SMM indicators in identifying in-hospital deaths. More work is needed to identify other factors associated with the 26.5% of in-hospitals deaths without any SMM indicator among vaginal deliveries.

The Association Between Hemoglobinopathy Carrier States and Anemia During Pregnancy

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Hemoglobinopathy carrier states, the presence of one abnormal copy of a hemoglobin variant, have largely unknown clinical manifestations during pregnancy despite their widespread regional frequency in sub-Saharan Africa due to their protection against severe malaria. We included 895 mother-infant dyads from MiPPAD, a randomized control trial in Benin that followed pregnant women less than 28 weeks' gestation through delivery, who received hemoglobin electrophoresis and had data collected on hemoglobin levels during antenatal visits and upon arrival for delivery. We investigated the extent to which trait status, including sickle cell trait and hemoglobin C trait, is associated with anemia over the course of pregnancy and at delivery and whether intrapartum malaria, as measured by placental parasitemia, mediates the association of carrier states with anemia at delivery (using gestational age-specific thresholds to account for physiologic hemodilution during pregnancy). We found that sickle cell trait, but not hemoglobin C trait, was associated with higher rates of anemia at delivery (OR = 1.59, 95%CI: 1.05, 2.40, p = 0.03). This relationship was exclusive to delivery and was not observed across the course of pregnancy (OR=1.05, 95%CI:0.80, 1,39, p = 0.70). Placental parasitemia did not substantially mediate the association between sickle cell trait and anemia at delivery: The odds of anemia amongst pregnant women with placental parasitemia did not differ by sickle cell trait status (OR = 1.00, 95%CI:0.99,1.01, p= 0.88). Likewise the odds of anemia through placental parasitemia among hemoglobin C trait carriers was not significant (OR = 1.08, 95%CI: 084, 1.40, p = 0.55). However, placental parasitemia was strongly associated with hemoglobin C trait (OR = 1.53, 95%CI: 1.09, 2.15, p = 0.01). Our findings demonstrate the distinct relationships that carrier traits have with anemia and malaria, two important predictors of maternal and neonatal outcomes, and suggest that sickle cell trait, but not hemoglobin C trait, is an important risk factor for maternal anemia with the highest risk period observed at delivery.

Exploring what drives the association between maternal depression prior to pregnancy and preterm birth Caitlin Meyer Krause*, Keegan Krause, Rebecca Campbell,

Background: Preterm birth (PTB, birth at <37 weeks' gestation) is persistently high in US pregnancies, particularly among some minoritized populations, and causes infant mortality, morbidity, and long-term disability. Maternal prenatal depression increases the risk of PTB; whether pre-pregnancy depression influences PTB is unknown.

Objective: To examine the associations between maternal pre-pregnancy depression and PTB.

Methods: This study used 2016-2021 Region V (Illinois, Indiana, Michigan, Minnesota, Wisconsin) Pregnancy Risk Assessment Monitoring System data to assess PTB by pre-pregnancy depression status (n=24,048). Binary depression status was self-reported for the period three months before pregnancy. Prevalence ratios were estimated using survey-adjusted Poisson regression models adjusted for race/ethnicity, age, education, marital status, pregnancy intention, and parity. Effect modification by maternal race/ethnicity and by self-reported prenatal depression status was explored.

Results: PTB occurred in 8.7% of births; 15.4% reported pre-pregnancy depression; two-thirds of those with pre-pregnancy depression also reported prenatal depression. Compared to mothers with no pre-pregnancy depression, those with pre-pregnancy depression had 1.30 times the prevalence (95% CI: 1.15, 1.47) of PTB, adjusting for covariates, however, in stratified models the positive association persisted only in women who also reported prenatal depression. In models stratified by race/ethnicity, increased PTB risk with pre-pregnancy depression was apparent only for NH White mothers.

Discussion: Mothers reporting depression pre-pregnancy had a higher prevalence of PTB, but associations were observed only for those with depression that persisted during pregnancy and only among NH White mothers. Prospective studies using validated depression scales are needed to improve understanding of the contribution of maternal depression longitudinally to PTB risk and opportunities for intervention.

Trends in risk of pregnancy loss among US women by urban-rural residence, 2000-2018: a new tool for small domain estimation Sarah Forrest*, Lauren Rossen, Katherine Ahrens,

Approximately 20% of pregnancies end in spontaneous loss, an outcome associated with adverse physical and psychological consequences. A previous study described increasing trends in the risk of self-reported pregnancy loss from 1990 to 2011, but it is unclear if those trends have continued or if they vary by factors such as urban-rural residence. Sample sizes of rural populations are typically small, limiting the availability of stable estimates for this population.

Data from the National Survey of Family Growth (2006–2019) were used to estimate rates of self-reported pregnancy loss (miscarriage, stillbirth, ectopic pregnancy) among US women (15–44 years) who reported at least one pregnancy conceived during 2000–2018 that did not result in induced termination (n = 17,314 women; n = 35,988 pregnancies). Trends in self-reported pregnancy loss were estimated by age group and urban-rural residence. A new small domain estimation tool, the Enhanced Modified Kalman Filter, was used to smooth estimates over groups and time. We compared relative 95% confidence interval (95% CI) widths ([upper bound-lower bound]/estimate) of model-based estimates to direct estimates.

Relative 95% CIs for model-based estimates were 35% and 53% smaller for urban and rural groups, respectively, than for direct estimates. The risk of self-reported pregnancy loss increased by a relative 3% annually for both urban and rural women 15-44 years (rate ratios [RRs]: 1.03, 95% CIs: 1.01, 1.04) from 2000-2018. The risk of loss increased among urban women aged 20-24 (RR: 1.01, 95% CI: 1.00, 1.01), 25-29 (RR: 1.01, 95% CI: 1.01, 1.02), and 30-34 (RR: 1.04, 95% CI: 1.03, 1.05) and among rural women aged 30-34 (RR: 1.02, 95% CI: 1.01, 1.03).

From 2000 to 2018, risk of self-reported pregnancy loss increased by a relative 1-4% annually among several age and urban-rural groups. A new small domain estimation tool provided substantial improvements in estimate precision relative to direct estimates.

Prenatal Oxidative Stress and Fetal Growth: Findings from a Pregnancy Cohort in New York City Carol Duh-Leong*, Akhgar Ghassabian, Whitney Cowell, Mengling Liu, Sarvenaz Shahin, Kurunthachalam Kannan, Kristyn Pierce, Yelena Afanasyeva, Leonardo Trasande,

Background: Adequate fetal growth relies on placental nutrient exchange, a process sensitive to environmental and social risk factors that increase inflammatory oxidative stress. Little is known about the timing of prenatal oxidative stress levels relative to fetal growth, which could increase our understanding of fetal growth periods more vulnerable to environmental exposures.

Methods: Within the New York University Children's Health and Environment Study prospective pregnancy cohort, we assessed associations between oxidative stress biomarkers (OSBs) and fetal growth (N=976). We obtained estimated fetal weight (EFW) based on clinical ultrasounds with the HadlockIII formula and predicted EFW at 20, 30, and 36 weeks using a linear mixed-effects model assuming nonlinear effects of gestation age. We measured lipid (8-iso-prostaglandin F2α, "8-iso-PGF2α"; Malondialdehyde, "MDA"), protein (o,o′−dityrosine, "diY"), and DNA (8−hydroxy−2′−deoxyguanosine, "8−OHdG") OSBs in urine at early (~11 weeks), mid (~20 weeks), and late (~30 weeks) pregnancy, adjusting for urinary dilution. We performed linear regression to examine OSBs in relation to EFW at the subsequent time point, adjusting for fetal sex, pregnant person's age, pre-pregnancy body mass index, race, ethnicity, education, income, marital status, employment, insurance, tobacco/alcohol use.

Results: We found that higher OSB levels at 20 weeks were associated with smaller EFW at 30 weeks (8-iso-PGF2α: -5.8 [95% Confidence Interval (CI): -9.5, -2.1]; MDA: -12.3 [95% CI: -20.9, -3.7]; diY: -9.8 [95% CI: -18.3, -1.3]; 8−OHdG: -15.3 [95% CI: -23.9, -6.7]); and at 36 weeks for 8-iso-PGF2α: -10.3 [95% CI: -17.5, -3.1]. We did not detect associations between OSBs at 11 and 30 weeks and subsequent EFW.

Conclusion: In our sample, higher OSB levels were associated with decreases in EFW when measured approximately 10 weeks apart in mid-pregnancy, contributing to our understanding of oxidative stress during periods of fetal growth.

Coffee Consumption and Risk of Spontaneous Abortion in a Preconception Cohort Study

Martha Koenig*, Martha Koenig, Amelia Wesselink, David Savitz, Kenneth Rothman, Lauren Wise, Elizabeth Hatch,

Background: Coffee consumption during pregnancy has long been studied as a potential risk factor for spontaneous abortion (SAB, pregnancy loss at <20 weeks gestation). Nausea and vomiting in early pregnancy (NVP) may lead people to reduce coffee intake. Additionally, NVP is associated with a reduced risk of SAB. Previous research has underscored the role of reverse causation when measuring this association, as non-viable pregnancies may allow continuing coffee consumption, causing upward bias.

Methods: We analyzed data from Pregnancy Study Online (PRESTO), an online preconception cohort study, to examine associations between coffee intake and risk of SAB. We collected information on coffee consumption and NVP on the early pregnancy questionnaire (EPQ). We identified incident SABs on the late follow-up questionnaire. We fit multivariable-adjusted Cox models with weeks of gestation as the time scale to estimate hazard ratios (HRs) for the effect of coffee intake on SAB and 95% CIs. In our main analyses, we restricted our sample to those who completed the EPQ at ≥6 weeks gestation, the typical time of NVP onset, and ≤10 weeks gestation.

Results: The HR for ≥1 cups/day (vs. none) was 1.26 (CI: 0.92, 1.73). Among those with NVP, coffee intake was positively associated with SAB (HR for ≥1 cups/day [vs. none] 1.41 (CI: 0.95, 2.07)); for those without NVP, coffee intake was not associated with SAB (HR=0.97 (CI: 0.56, 1.68)). When results were stratified by gestational week at time of EPQ completion, HRs for ≥1 cups/day (vs. none) were 1.16 (CI: 0.86, 1.56), 0.96 (CI: 0.55, 1.67), 1.43 (CI: 0.79, 2.58), 1.03 (CI: 0.46, 2.28), 1.71 (CI: 0.74, 3.97) and 1.34 (CI: 0.53, 3.38) for <6, 6, 7, 8, 9 and ≥10 gestational weeks, respectively.

Conclusion: Among those with NVP symptoms, ≥ 1 cup of coffee per day was associated with a slightly elevated risk of SAB. Sustained coffee consumption beyond 7 weeks gestation may be influential to understanding associations.

Maternal inflammation/oxidative stress markers during pregnancy and placental epigenetic age acceleration Prabhavi Wijesiriwardhana*, Tesfa Dejenie Habtewold, Richard J. Biedrzycki, Katherine L. Grantz, Cuilin Zhang, Jagteshwar Grewal, Fasil Tekola-Ayele,

Maternal inflammation/oxidative stress markers during pregnancy and placental epigenetic age acceleration

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Background: Altered placental aging is associated with pregnancy and neonatal complications, but early pregnancy markers of altered placental aging are scarce. This study aimed to i) determine the associations of trajectories and cumulative levels of maternal plasma markers of inflammation (C-reactive protein: CRP), DNA damage (8-hydroxydeoxyguanosine: 8-OHdG), and antioxidant defense (total antioxidant capacity: TAC) with placental epigenetic age acceleration (PAA); and ii) assess whether these associations vary by fetal sex.

Methods: Plasma CRP, 8-OHdG and TAC levels were measured in blood samples collected during pregnancy at 10-14, 15-26, 23-31, and 33-39 gestational weeks as part of the NICHD Fetal Growth Studies (n=300). Biomarker trajectory was determined by group-based trajectory modeling, and cumulative exposure across gestation was estimated by area under the curve (AUC). PAA was estimated by two epigenetic clocks that use 62 and 396 methylation sites (PAA62 and PAA396). The associations of biomarker trajectory groups (vs. low trajectory) and biomarker cumulative exposure tertile (vs. lowest tertile) with PAA62 and PAA396 were tested using linear regression adjusted for maternal age, education, insurance, parity, employment, and race.

Results: CRP high trajectory was significantly associated with 0.52 weeks lower PAA62 (95% CI=-1.03, -0.01). TAC second tertile exposure level was significantly associated with 0.52 weeks higher PAA62 (95% CI=0.09, 0.95), which strengthened among pregnancies with female fetuses (β=0.89, 95% CI=0.24, 1.54). 8-OHdG second and third tertile exposure levels were significantly associated with 0.51 weeks (95% CI=-0.89,-0.12) and 0.44 weeks (95% CI=-0.85,-0.03) lower PAA396, respectively among pregnancies with female fetuses.

Conclusion: Placental aging is decelerated in pregnancies with markers of increased inflammation and DNA damage and accelerated with increased antioxidant defense.

Maternal pre-pregnancy BMI and obstructed labor: a Burden of Proof study Ke Pan*, Maxwell Dodge, Nicholas Kassebaum, Aleksandr Aravkin, Nora Gilbertson, Reed J. Sorensen, Peng Zheng, Maegan Ashworth Dirac,

Background: Obstructed labor is a cause of maternal and perinatal morbidity and mortality. Maternal BMI may impact one or more of the determinants of obstructed labor. In this study, we aim to evaluate the relationship between pre-pregnancy BMI and obstructed labor.

Methods: We conducted a systematic review across six databases from 1980 to March 27, 2023. We applied a Bayesian, regularized, trimmed meta-regression approach, which incorporates between-study heterogeneity into uncertainty estimates and allows for non-linear dose-response relationships. We tested for potential systematic biases related to study attributes, including representativeness, exposure and outcome measurement, confounding control, and selection bias. The burden of proof risk function was used to identify the minimal excess risk level consistent with the data.

Results: We screened 2148 abstracts and included 42 studies. An elevated BMI was associated with a higher risk of obstructed labor, both in the unadjusted model and the model with bias covariates indicating which studies did not represent the general pregnant population, relied on self-reported BMI, employed non-standard definitions of obstructed labor, or failed to adjust for maternal race/ethnicity. Compared to the BMI of 18.5 kg/m2, the relative risk of obstructed labor at BMI of 25 kg/m2 and 30 kg/m2 were 1.4 (95% Confidence Interval (CI): 1.1-1.7) and 1.5 (95% CI: 1.2-1.9), respectively; these CIs incorporate between-study heterogeneity.

Conclusions: Even accounting for uncertainty due to between-study heterogeneity, we detected an increased risk of obstructed labor with increasing BMI and moderate evidence that this is a casual relationship. As global obesity rises, maternity service providers will face an increasing need to manage obstructed labor, unless pre-pregnancy obesity strategies are successfully implemented.

Association of prenatal antiseizure medication exposure with risk of individual neurodevelopmental disorders in children Loreen Straub*, Sonia Hernandez-Diaz, Brian Bateman, Yanmin Zhu, Helen Mogun, Krista Huybrechts,

Background: Prenatal valproate exposure is linked to neurodevelopmental disorders (NDDs), but evidence for other anti-seizure medications (ASMs) is scarce. We aimed to study the association between prenatal exposure to individual ASMs and a spectrum of NDDs in children.

Methods: Using two US-nationwide cohorts of women with epilepsy linked to their children, pregnancies with ≥1 ASM dispensing from gestational week 19 to delivery (synaptogenesis period) were compared to ASM-unexposed pregnancies. Individual ASMs considered included carbamazepine, lacosamide, lamotrigine, levetiracetam, oxcarbazepine, phenobarbital, phenytoin, topiramate, valproate, and zonisamide. NDDs included autism, attention-deficit/hyperactivity disorder (ADHD), learning disorder, speech/language disorder, coordination disorder, intellectual disability (ID), and behavioral disorder. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards models with propensity score overlap weighting for confounding control.

Results: The cohorts included 8,887 unexposed pregnancies. Exposed counts ranged from 219 (lacosamide) to 5,261 (levetiracetam). After adjustment, phenobarbital, valproate and zonisamide showed associations with multiple NDDs (HR range: 1.52 to 4.50). Risk increases were further observed for ID after lamotrigine (HR: 2.39; 95% CI: 1.20-4.73) and oxcarbazepine exposure (3.30; 1.29-8.41), and potentially for ID after topiramate (1.84; 0.75-4.51) and ADHD after lacosamide exposure (2.66; 0.77-9.21). No associations were seen for other ASMs and NDDs. Results were robust to sensitivity analyses.

Conclusions: Our findings strengthen the evidence of adverse effects of valproate and raise concern regarding risk increases for phenobarbital and zonisamide. Additional signals for some ASMs in the context of multiple testing and rare outcomes (resulting in imprecise estimates) require confirmation in follow-up studies as evidence continues to accumulate.

Impact of COVID-19 Infection on Severe Maternal Morbidity during the COVID-19 Pandemic in South Carolina: A Matched Analysis (2020-2022). Kalyan Chundru*, Jeffrey Korte, Chun-Che Chun-Che, Brian Neelon, Dulaney Wilson, Julio Mateus, John Pearce, Mallory Alkis, Sarah Simpson, Erin Alsbrook, Hermes Florez, Kelly Hunt, Angela Malek,

Introduction: Severe Maternal Morbidity (SMM), which is potentially fatal and more prevalent than maternal mortality, offers insights into the quality of maternal care. In light of healthcare infrastructural changes during the COVID-19 pandemic and the steady increase in SMM in the United States, our study assessed pre-pregnancy and trimester-specific impact of COVID-19 infections on SMM in South Carolina (SC).

Methods: We utilized 2020-2022 SC vital records linked to hospitalization/emergency department and death records. SMM was defined as one or more of 21 indicators identified by the Centers for Disease Control and Prevention (CDC), using the 10th Revision of the International Classification of Diseases (ICD) diagnosis and procedure codes. Health department data was available for COVID-19 infections. Pregnancies were matched on race/ethnicity, delivery quarter time, Medicaid eligibility, and maternal age and analyzed using logistic regression.

Results: Of 145,033 singleton deliveries to women aged 12-52 years, 6.9% had a COVID-19 infection pre-pregnancy, 6% in the 1st and/or 2nd trimester, 3.6% in the 3rd trimester, and 2.4% had SMM events during the study period. COVID-19 infection during the 1st and/or 2nd trimester [odds ratio (OR)=1.38, 95% CI: 1.19-1.60)] and 3rd trimester (OR=1.85, 95% CI 1.57-2.18) increased the odds of SMM (including blood transfusion events) compared to pregnancies without COVID-19 infection after adjusting for demographic, lifestyle and clinical risk factors. Further, the adjusted odds for all trimesters were even higher for SMM events excluding blood transfusion. However, SMM with or without transfusion events showed no association with COVID-19 infection pre-pregnancy (Table).

Conclusion: SMM was highest for pregnant people with COVID-19 infection during the 3rd trimester followed by infection during the 1st/2nd trimester, emphasizing the importance of preventative measures like vaccination during pregnancy to curb SMM rise in SC.

Table: Logistic regression models [OR (95% CI)] of severe maternal morbidity (SMM) with and without blood transfusion for pregnant people by COVID-19 infection status in South Carolina, 2020-2022.

Predictors
SMM *with blood transfusion*
SMM *without blood transfusion*

COVID-19 infection

   No history of COVID-19
Reference
Reference

Prior to pregnancy
1.09 (0.93, 1.28)
1.03 (0.85, 1.14)

First and/or second trimester
1.38 (1.19, 1.60)
1.54 (1.29, 1.83)

Third trimester
1.85 (1.57, 2.18)
2.22 (1.83, 2.68)

Maternal age at delivery
1.04 (1.02, 1.05)
1.04 (1.03, 1.05)

Education level

< High school
1.64 (1.33, 2.02)
1.72 (1.35, 2.19)

High school graduate
1.33 (1.13, 1.57)
1.30 (1.07, 1.58)

Some college
1.27 (1.07, 1.49)
1.24 (1.02, 1.50)

≥College graduate
Reference
Reference

Rural residence (vs. urban)
1.01 (0.90, 1.14)
0.99 (0.86, 1.14)

WIC participation during pregnancy
0.99 (0.87, 1.13)
1.00 (0.87, 1.17)

Delivery quarter time
0.96 (0.94, 0.99)
0.97 (0.94, 1.00)

Race/ethnicity

Non-Hispanic White

Reference
Reference

   Non-Hispanic Black
1.30 (1.14, 1.48)
1.38 (1.18, 1.61)

   Hispanic
0.93 (0.72, 1.18)
0.90 (0.66, 1.21)

   Other
1.31 (0.98, 1.73)
1.07 (0.72, 1.53)

Medicaid
1.38 (1.18, 1.61)
1.33 (1.11, 1.59)

Tobacco use during or pre-pregnancy
0.99 (0.80, 1.21)
1.00 (0.86, 1.14)

Firstborn
1.38 (1.2, 1.58)
1.37 (1.16, 1.60)

Previous preterm delivery
1.51 (1.25, 1.82)
1.60 (1.29, 1.98)

Pre-pregnancy hypertension
2.25 (1.96, 2.57)
2.57 (2.20, 3.00)

Pre-pregnancy diabetes
1.60 (1.27, 1.99)
1.89 (1.48, 2.39)

Pre-pregnancy BMI (kg/m2)

   Underweight (14.0<BMI<18.4)
1.15 (0.79, 1.62)
1.53 (1.01, 2.23)

   Normal (18.5≤BMI<24.9)
Reference
Reference

   Overweight (25.0≤BMI<29.9)
0.98 (0.83, 1.15)

1.03 (0.84, 1.26)

   Obese (BMI≥30)
1.09 (0.94, 1.25)
1.20 (1.01, 1.44)

BMI, body mass index; COVID-19, coronavirus disease 2019; OR, odds ratio; CI, confidence interval; WIC, Women, Infants, and Children.

The Supplemental Nutrition Program for Women, Infants, and Children and Birth Outcomes among Hispanic Mothers in California: A sibling control design Brenda Bustos*, Abhery Das, Allison Stolte, Samantha Gailey, Tim Bruckner,

Prior research finds that participation in the Supplemental Nutrition Program for Women, Infants, and Children (WIC) during pregnancy reduces risks of preterm birth and low birthweight. Many birthing persons who receive WIC benefits, however, also participate in Medicaid, the largest safety net program in the US. To the best of our knowledge, no prior research disaggregates the birth outcome benefits of WIC and Medicaid. Here, we use a unique, sibling-linked dataset of California births to estimate birth outcomes as they relate to receipt of WIC alone as opposed to receipt of both WIC and Medicaid in California (Medi-Cal). We focus on births to Hispanic mothers, who represent the largest fraction of births in California, as well as the highest proportion of WIC recipients in the state. We use program receipt (No WIC or Medi-Cal; WIC alone; Medi-Cal alone; WIC and Medi-Cal) as our independent variable and preterm birth (<37 weeks) and low birthweight (<2500 grams) as our outcomes of interest. We restrict our analytic sample to births to Hispanic mothers with at least two live singleton births in California between 2007 and 2015 (n = 942,274). Our sibling-control results show that Births to Hispanic mothers exhibit lower odds of low birthweight (OR: 0.82, 95% CI: 0.77, 0.87) and preterm birth (OR: 0.87, 95% CI: 0.84, 0.91) when mothers receive WIC benefits during pregnancy compared to when the mothers do not receive WIC benefits. While births associated with receipt of both WIC and Medi-Cal also exhibit lower odds of preterm birth (OR: 0.86, 95% CI: 0.79, 0.92), the protective findings do not extend to low birthweight. Future research should examine the extent to which participation in multiple means-tested programs, across various social systems, reduce racial/ethnic disparities in adverse birth outcomes.

Association between birthweight and cognitive function in middle-aged adults: the Bogalusa Heart Study
Eunsun Gill*, Ileana De Anda-Duran, Soo Jung Kang, David J. Libon, Wei Chen, Lydia A. Bazzano, Camilo Fernandez Alonso, Emily W. Harville,

Introduction: Although the relationship between low birthweight and impaired cognitive function (CF) before midlife has been demonstrated, the relationship between birthweight and cognition after midlife and potential racial disparities remain inconclusive. This study examined the association between birthweight and midlife CF stratified by race.

Methods: 1,032 subjects from the Bogalusa Heart Study (67% White, 33% Black, mean age 48.1 ± 5.3 years) were studied. Cognitive measures included episodic memory, executive abilities, attention/processing speed, language, and global CF. Each domain was standardized by gender and age, and averaged. The global CF was computed by averaging all cognitive domains. The standardized scores on the word and reading subtests in the Wide Range Achievement Test-III and the vocabulary subtest in the Wechsler Adult Intelligence Scale-III were used as an indicator of achieved education. Multiple linear regression was used to estimate the association between birthweight (per 100 grams) and CF, adjusting for age, gender, personal achieved education, parental education, and maternal hypertension and diabetes, with multiple imputation used to address missing covariates.

Results: For Whites and Blacks, each 100 gram increase in birthweight was associated with an increase of 0.006 and 0.007 standardized units in the global CF (SE: 0.003; p=0.027, SE: 0.003; p=0.036). In Whites, higher birthweight was associated with better executive abilities (beta (SE): 0.014 (0.006); p=0.015), but not in Blacks (beta (SE): 0.007 (0.007); p=0.319). Birthweight was associated with attention/processing speed in Blacks (beta (SE): 0.018 (0.008); p=0.021), but not in Whites (beta (SE): 0.004 (0.004); p=0.317).

Conclusions: By midlife, higher birthweight appears to reduce vulnerability with respect to selected executive abilities compared to other cognitive domains. Moreover, the impact of birthweight on selected cognitive abilities in midlife may vary by race.

Air pollution and preterm births in Fresno, California Valerie Martinez*, Sneha Ghimire, Sandie Ha,

Background: Preterm birth (PTB) impacts 9% of pregnancies in California (CA). Research suggests that air pollution and road proximity affect adverse pregnancy outcomes but their impacts on PTB are unclear. We investigated PTB risks in relation to acute air pollution exposure and residential proximity to major streets, truck routes, and freeways.

Methods: We identified 103,566 singleton pregnancies in Fresno, CA, a highly polluted city (2009-2019). We obtained daily ozone (O3) and particulate matter < 2.5 microns (PM2.5) levels from the San Joaquin Valley Air Pollution Control District, and road features from the CA Department of Transportation, then linked them to maternal address at delivery. First, a time-stratified case-crossover analysis (of 9,087 PTB cases <37 weeks gestation) compared exposure during case periods, defined as the day of delivery (lag0) and the prior week (lags 1-7), with that of control periods during which the event did not happen. Control periods were selected using the time-stratified approach. Conditional logistic regression models estimated odds ratio (OR) and 95% confidence intervals (CI) for each 5 ug/m3 increase in pollutants. Second, a cohort analysis using logistic regression models was conducted to estimate the associations between proximity to the nearest major street, truck route, or freeway and PTB, while adjusting for confounders.

Results: In warm season (May-Oct), O3 exposure was associated with 3-4% increased odds of PTB within one week (ORlag0 1.03, 95% CI 1.02,1.04; ORlag7 1.04, 95% CI 1.02, 1.05). Stronger PM2.5 associations were observed in American Indian/Alaskan Native, those who lived in a high-income census tract or had at least a high school education. No significant associations were observed for proximity to major streets, truck routes, or freeways.

Conclusion: Air pollution may contribute to PTB risks, emphasizing the urgent need for interventions to reduce air pollution, especially in underserved populations.

A series of emulated target trials to estimate the safety of antihypertensives for the management of non-severe gestational hypertension among pregnant individuals in Botswana Julia DiTosto*, Rebecca Zash, Denise Jacobson, Modiegi Diseko, Gloria Mayondi, Judith Mabuta, Mompati Mmalane, Joseph Makhema, Shahin Lockman, Roger Shapiro, Ellen Caniglia,

Antihypertensive therapy is critical for management of non-severe gestational hypertension (HTN), yet potential fetal consequences are unclear. Standard analyses may be subject to immortal time and selection bias. Conducting a series of emulated target trials (ETT) can avoid these biases by aligning start of follow-up with therapy initiation.

The Tsepamo Study has evaluated birth outcomes at government delivery sites in Botswana since 2014. We investigated antihypertensive therapy initiation ≥24 weeks gestation for management of non-severe gestational HTN on stillbirth and small-for-gestational-age (SGA) by conducting 16 sequential ETT of therapy initiation versus no initiation during each week from 24-39 weeks' gestation. For each ETT, pregnant individuals with no history of HTN were eligible if they had not previously initiated therapy and had ≥1 elevated non-severe blood pressure reading (140-159 mm Hg systolic or 90-109 mm Hg diastolic) within 1 week of each ETT start. Log-binomial models were used to calculate RR and 95% CI. Results were pooled across all trials with bootstrapping to obtain CIs. Sensitivity analyses applied more stringent eligibility criteria (i.e., excluding preeclampsia and requiring >1 elevated blood pressure at baseline).

Of 28,608 individuals, 9,524 (33.3%) initiated antihypertensives between 24-39 weeks' gestation. Comparing initiation to no initiation, the pooled RR was 1.18 (1.07-1.40) for stillbirth and 1.15 (1.08-1.27) for SGA. RRs varied by week of ETT start and were sensitive to definition of eligibility criteria. For stillbirth, the pooled RR was 1.07 (0.87, 1.23) when excluding preeclampsia and 0.90 (0.34, 1.32) when requiring >1 elevated blood pressure at baseline.

Our results suggest initiation of antihypertensive therapy for non-severe gestational HTN may increase risk of stillbirth and SGA. Results were sensitive to eligibility criteria definitions, suggesting potential for unmeasured confounding by HTN severity.

Sex specific association between placental inflammation and birth outcomes of a New York based cohort from 2010 to 2015 Norman Chamusah*, Dawn Misra, Carolyn Salafia,

Background: Most population-based perinatal studies have ignored the role of placenta. Furthermore, studies have rarely examined sex differences. **Objective:** To determine sex differences in placental pathology prevalence and whether sex moderates the relationship of placental inflammation to placental and fetal growth at delivery.

Methods: In a New York City hospital with mandated placental examination of an ethnically, and social diverse population, 2235 term singleton livebirths born from January 2010 to March 2015 had pathology data extracted at birth. Placental inflammation included acute and chronic inflammation diagnoses. Maternal and fetal acute inflammation (MAIR, FAIR) was scored in extraplacental membranes, chorionic plate (maternal) and umbilical cord and chorionic plate vessel (fetal). Chronic placental inflammation (CPI) was scored as "confined to basal plate and maternal-placental interface", and "villous infiltrates/chronic villitis". Placental efficiency outcomes included Beta (ratio of Ln placental weight (PW) to Ln birth weight (BW), and OER (ratio of the observed BW to BW predicted by regressing against placental size and shape measures). Appropriate statistical testing considered $p < 0.05$ significant.

Results: Prevalence of maternal chronic inflammation (CPI-Mat) were higher in males (13.3%) compared to females (9.0%). Similarly, both MAIR and FAIR varied by infant sex with prevalence of pathologies significantly higher in males. Additionally, chronic villitis was strongly associated with placenta and fetal growth measure, Beta ($p=0.002$) in females. While both MAIR and FAIR were strongly associated with Beta as with $p= 0.03$ and $p= 0.005$, respectively. However, CPI-Mat was not as strongly associated with Beta ($p=0.1$).

Conclusion: Sex-specific findings guide us to understanding fetal programming mechanisms associated with placental inflammation exposure. Results suggest male and female fetuses may have different responses to intrauterine stressors.

Vaginal bleeding during pregnancy and risk of cardiovascular diseases death: a register-based study in a national cohort of Norwegian mothers Abdu Kedir Seid*,

Vaginal bleeding during pregnancy and risk of cardiovascular diseases death: a register-based study in a national cohort of Norwegian mothers

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Introduction: Previous research reported that vaginal bleeding (VB) during early pregnancy is linked to a heightened risk of adverse pregnancy outcomes. However, the current evidence remains mixed and inconclusive. While increasing research in this area, there is limited knowledge of the association between VB and death due to cardiovascular diseases (CVD).

Aims: In this study, we investigated the association between early VB and CVD death among Norwegian mothers while adjusting for great obstetrical syndromes (GOS) (i.e., preeclampsia, preterm, and offspring for gestational age) and other potential confounders.

Methods: The study population was a national cohort of 1.5 million mothers with births registered in the Medical Birth Registry of Norway during the period 1967-2020. By measuring VB and GOS throughout the entire reproductive history, we followed mothers from the date of first childbirth to CVD death or December 31st, 2020, whichever occurred first. The association between VB and CVD death was estimated using the Cox proportional hazards model. Additional analysis was made using Poison regression on the link between VB and GOS indicators.

Results: Of 1,147,180 mothers meeting inclusion criteria, 5% reported VB in either the first, second, or third trimester during their lifetime pregnancy. Incidence of increasing pregnancy complications was observed among mothers exposed to VB compared to mothers not exposed to VB. However, we could not find any association between VB and CVD death.

Conclusions: Women experiencing VB in any trimester face an elevated risk of pregnancy-related complications, although there is no observed increase in the risk of CVD death throughout their lifetime pregnancy.

Neighborhood opportunity and residential instability: Associations with psychopathology symptoms in middle childhood Diane Putnick*, Jordan Tyris, Jordan McAdam, Akhgar Ghassabian, Pauline Mendola, Rajeshwari Sundaram, Edwina Yeung,

Children's neighborhoods have the potential to shape their health and development through opportunities available to the child. However, families with young children often move and most neighborhood research does not account for mobility. This study's primary goal was to disentangle the effects of neighborhood quality with those of residential instability on children's mental health in middle childhood.

1,946 children from the prospective Upstate KIDS birth cohort provided data. Home addresses at birth were geocoded and linked to the Child Opportunity Index (COI), a 29-indicator measure of neighborhood quality. Residential instability (moves) and social mobility (change in COI quintile) were tracked from birth to age 10. Children's attention-deficit/hyperactivity disorder (ADHD), problematic behavioral, and internalizing symptoms were measured via 3 parent-completed questionnaires at ages 7, 8, and 10. Structural equation models were fit using robust maximum likelihood estimation, and reports across ages were combined for ADHD, behavioral, and internalizing symptoms. Models were adjusted for maternal age, education, non-Hispanic White race/ethnicity, infertility treatment, private insurance, nulliparity, child sex, gestational age, and plurality.

Neighborhood opportunity at birth and social mobility were not associated with child psychopathology symptoms at age 7-10 years. Residential instability (M=2.22, SD=1.60, range=1-11) was associated with psychopathology symptoms. Each move between birth and age 10 was associated with .15 standard deviation (SD) higher ADHD (95% confidence interval [CI]=.08-.22) and problematic behavioral symptoms (95%CI=.07-.22) and .12 SD higher internalizing symptoms (95%CI=.04-.20).

Findings suggest that moving frequently may come at a cost to child mental health regardless of neighborhood opportunity. This cohort was of largely non-Hispanic white, higher socioeconomic status participants and findings require replication in other cohorts.

Relationships between the length of exposure to state-level eviction moratoria and perinatal outcomes among Medicaid and uninsured birthing people 2020-2021 Kaitlyn Stanhope*, Michael Kramer, Sara Markowitz,

Introduction: Limited data exists on how housing policies may impact outcomes for birthing people. In March and April 2020, 43 states implemented eviction moratoria. Our goal was to estimate associations between the length of exposure to moratoria and perinatal outcomes among Medicaid/uninsured people conceiving in March-May 2020 and giving birth to a live born infant.

Methods: We used data from United States natality files, 2020-2021. We defined the exposure as the number of months for which the individual was exposed to a state-level eviction moratoria, categorized as 0 (referent, no state-level moratoria), 1, 2, 3, 4, 5 or more. We estimated adjusted risk ratios and 95% confidence intervals using log binomial regression with generalized estimated equations for each outcome separately [preterm birth (PTB, < 37 weeks gestation according to combined estimate), very preterm birth (VPTB, < 32 weeks gestation), low birthweight (LBW, < 2500 grams), and very low birthweight (VLBW, < 1500 grams)]. We included individual (age, parity, race, ethnicity, likely single parenthood), county (rurality), and state-level covariates (unemployment, poverty, median household income, governor's party affiliation, Medicaid expansion, COVID-19 death rate through July 2020) as potential confounders. Results: We included 376,622 births. All complications were more common in states without moratoria. In adjusted models, having a moratorium in place for 4-5 months was associated with reduced risk of PTB (RR: 0.93, 95% CI: 0.86-1.02), VPTB (RR: 0.88, 95% CI: 0.79-0.98), LBW (RR: 0.93, 95% CI: 0.87-1.00), and VLBW (RR: 0.90, 95% CI: 0.79-1.01). There was no evidence of interaction on the additive scale.

Conclusions: People birthing in states with longer moratoria in place during the pandemic had improved birth outcomes, independent of the economic and political climate of the state.

Association of Discrimination in Medical Settings and Preeclampsia among Pregnant Women in All of Us Study Olivia Kapera*, Baojiang Chen, Jaime Almandoz, Courtney Byrd-Williams, Sarah Messiah,

Introduction. Factors contributing to maternal mortality in the U.S. are complex and are only partially understood. While studies have highlighted the impacts of racism and discrimination on well-being and health, to date, no studies have examined how the role of discrimination in maternal mortality varies by race and ethnicity. To address these gaps, we analyzed the association of discrimination and preeclampsia among a racially and ethnically diverse national sample of pregnant women participating in the All of Us study.

Methods. This cross-sectional study analysis of the All of Us research program data included 2,303 pregnant women ages 18-to-44 years. Discrimination was measured by proxy using a 7-item survey to assess courtesy, respect, service quality, being treated as competent, acting afraid, being treated as inferior, and being listened to during a healthcare visit. Adjusted logistic regression models generated odd ratios (aOR) of preeclampsia by discrimination in medical settings controlling for race/ethnicity, body mass index (BMI), gestational hypertension, gestational diabetes, and urinary tract infection.

Results. Mean sample age was 36.7 years (SD 5.01). The sample was 67% (n=1466) non-Hispanic White, 52% (n=1191) college graduate or higher, 42% (n=963) with annual income >$75K, and 58% (n=1336) married. Non-Hispanic Black (NHB) women were ~1.8 to 2.1 times more likely to develop preeclampsia if they experienced discrimination in medical settings compared to those who did not report these experiences controlling for other variables (p-value <0.05 for all items).

Conclusion. The study found NHB women are significantly more likely to develop preeclampsia if they experience discrimination in medical settings. These results underscore the need for a comprehensive strategy to address these inequities, encompassing reforms in the healthcare system and broader societal shifts to challenge discrimination and enhance health outcomes for all women.

Association between religious service attendance and perinatal outcomes: a secondary analysis of the Future Families & Child Wellbeing Study Stacie Shropshire*, Andrew Williams,

Background. Spirituality and religiosity are important social determinants of health with increasing research findings suggesting that religious involvement may be associated with improved health outcomes. However, few studies have examined maternal religiosity as a protective factor for perinatal outcomes. We explored the association between frequency of maternal religious attendance and risk of various perinatal outcomes.

Methods. Data were drawn from first and second waves from the Future Families & Child Wellbeing Study (n=2,320). Religious attendance (none/hardly ever/several times a year/several times a month/once a week or more) was a self-reported response to the question "About how often do you attend religious services?" Perinatal outcomes of initiation of prenatal care, breastfeeding initiation, pre-term birth, postpartum depression (PPD), pregnancy loss, low birthweight, maternal postpartum length of hospital stay, and hypertensive disorders of pregnancy, were drawn from survey responses and medical records. Logistic regression estimated odds ratios (OR) and 95% confidence intervals (CI) for the association between maternal religious attendance frequency and perinatal outcomes, overall and by race. Models were adjusted for sampling weights, religious preference, socioeconomic and behavioral factors.

Results. Compared to those who reported no religious attendance, women who attended services once a week or more (OR:3.89;95%CI:1.07,14.10) or several times a month (OR:6.98;95%CI:1.15,42.37) had higher odds of not experiencing pregnancy loss. Religious attendance did not predict any other perinatal outcome.

Discussion. Results suggest that maternal religious attendance frequency may be a protective factor for pregnancy loss, and this is unique among perinatal outcomes examined in this study. Further research is needed to understand the association between maternal religious attendance and mechanisms for perinatal outcomes.

Retention in Buprenorphine versus Methadone Treatment for Opioid Use Disorder in Pregnancy and Postpartum Chih-Wan Grace Lin*, Brian Bateman, Loreen Straub, Seanna Vine, Ayesha Sujan, Elizabeth Suarez, Sonia Hernandez-Diaz, Krista Huybrechts,

Retention in medicated treatment for opioid use disorder (MOUD) is crucial for maternal and neonatal safety in pregnant patients with OUD. While several clinical trials demonstrate higher treatment retention for methadone compared with buprenorphine outside of pregnancy, evidence during pregnancy is more limited.

We conducted a cohort study to assess retention in MOUD during pregnancy and through 1-year postpartum. Using nationwide Medicaid data from 2003 to 2018, we included pregnant women who initiated methadone or buprenorphine for OUD during the first trimester. Treatment discontinuation was assigned 60 days after the last treatment record. Time from initiation to discontinuation was assessed, and hazard ratios (HR) were estimated using Cox proportional hazards regression with propensity score overlap weights for confounding control. As a sensitivity analysis, we estimated the proportion of months covered (PMC) as months with evidence of treatment divided by total months in the study period. Odds ratios (OR) for PMC<80% were estimated using logistic regression.

We identified 701 and 1695 pregnancies initiating methadone and buprenorphine, respectively. Buprenorphine initiators were more likely to discontinue treatment during pregnancy (33% for buprenorphine vs. 25% for methadone; weighted HR 1.37, 95%CI 1.13-1.67) and through 1-year postpartum (59% vs. 48%; 1.36, 1.18-1.56) compared to methadone initiators. Similarly, buprenorphine initiators were more likely to have a PMC<80% than methadone initiators (weighted OR 1.42, 1.13-1.77 during pregnancy; 1.57, 1.28-1.91 through 1-year postpartum).

Pregnant women initiating buprenorphine during early pregnancy are more likely to discontinue treatment than those initiating methadone. Our findings highlight the importance of identifying and addressing barriers to treatment retention among pregnant women with OUD.

Substance Use

Prevalence and characteristics of prenatal cannabis use in Michigan: Results from a statewide population-based pregnancy cohort Ban Al-Sahab*, Omayma Alshaarawy, Kipling Bohnert, Hongxiang Qiu, Audriyana Jaber, Jean Kerver, Nigel Paneth,

Background: Prenatal cannabis use is a growing public health concern in the United States with potential significant health implications for both the mother and developing child. **Objective:** To assess the prevalence and associated characteristics of prenatal cannabis use in Michigan. **Methods:** Data are from a prospective statewide pregnancy cohort (MARCH- Michigan Archive for Research in Child Health) that is part of NIH's Environmental influences on Child Health Outcomes (ECHO) program. Pregnant people were recruited at first prenatal visit from 20 clinics in 2017-2022 and represented a stratified random sample of births in Michigan. Cannabis use was measured through self-reports of ever-use collected twice during pregnancy by interviewer-administered phone surveys and ascertained by measuring THC metabolites in urine samples collected up to three times in pregnancy. **Results:** Of 1346 pregnant participants, 1280 (95.1%) had information on cannabis use either from self-reports (N=1100), urine toxicology (N=1215) or both (N=1035). The prevalence of cannabis use during pregnancy was 16.5% (N=181) based on self-reports only, 21.0% (N=255) from urinalysis only and 24.4% (N=312) from combining self-reports and urinalysis. Participants who tested positive on the urinalysis had THC-COOH adjusted for creatinine concentrations ranging from 15.01 to 4694.89 ng/ml with a median of 133.92 ng/ml. There were 70 participants who tested positive for urinary THC-COOH but did not report cannabis use. Multivariate analysis of sociodemographic factors, psychosocial wellbeing, and concurrent use of other substances revealed a significant association between low income, low educational attainment, depression, adverse childhood experiences and tobacco smoking and prenatal cannabis use. **Conclusion:** Almost one of four pregnant people use cannabis in Michigan. Interventions that aim to reduce prenatal cannabis use may be warranted, especially among socioeconomically disadvantaged populations.

Interpersonal violence during pregnancy partially mediates the association between Adverse Childhood Experiences and postpartum depression (ND PRAMS 2017-2021) Nishat Sultana*, Anna Charlotta Kihlstrom, Tara Stiller, Lexie Schmidt, Grace Njau, Matthew Schmidt, Anastasia Stepanov, RaeAnn Anderson, Amy Stiffarm, Andrew Williams,

Background. Adverse Childhood Experiences(ACEs) and Interpersonal Violence(IV) both, independently, increase risk of postpartum depression (PPD). ACEs also predict IPV. However, data examining the potential mediating effect of IV in the relationship between ACEs and PPD are lacking, especially among rural samples in the United States.

Research Questions. Does IPV during pregnancy mediate the association between ACEs and postpartum depression?

Methods. Data for 3,016(weighted n=43,535) postpartum people were drawn from the 2017-2021 ND Pregnancy Risk Assessment Monitoring System survey. Participants self-reported(yes/no) to 10 ACEs(high ACES ≥2). An "any interpersonal violence" variable was created if participants reported "yes" to experiencing violence from a husband/partner, ex-husband/partner, family member, or someone else before pregnancy. Postpartum depression symptoms(yes/no) were determined based on the Patient Health Questionnaire-2. SAS PROC CAUSALMED was used to estimate the total effect, direct effect, and indirect effect for the potential mediation of IPV in the association between ACEs and PPD. This procedure estimated odds ratios and 95% confidence intervals for all models, adjusted for maternal demographic and health factors and weighted for complex survey design.

Results. The total effect of ACEs on PPD was associated with a 95% increased risk of PPD (OR:2.02 95%CI:1.89,2.14). There were indirect effects of ACEs on PPD via IV (OR:1.05, 95%CI:1.04,1.06), suggesting IV accounts for approximately 10% (95%CI:7.66,12.41) of the effect of ACEs on PPD.

Discussion. IPV accounts for a small percentage of the effect of ACEs on PPD. However, improving outcomes for postpartum people are key state and national public health goals, and any areas for improvement should be highlighted. Given the importance of PPD for postpartum people and their families, these data warrant consideration among public health and healthcare professionals.

Investigating the relationship between ambient temperature and reproductive hormonal changes among women attempting pregnancy Kaniz Rabeya*, Neil Perkins, Lindsey Russo, Pauline Mendola, Timothy Canty, Karen Schliep, Carrie Nobles,

Background: High ambient temperatures have been associated with adverse reproductive and pregnancy outcomes, however, the role of hormones has been understudied. We investigated the association between ambient temperature and reproductive hormones among women trying to get pregnant.

Method: A prospective time-to-pregnancy study (EAGeR trial, 2006-2012) enrolled 1228 women from Buffalo, Scranton, Denver, and Salt Lake City. Daily temperature was collected from weather monitoring stations and averaged across an early-to-mid follicular phase window (1-10 days after menses) and ovulation window (11-16 days). Daily diaries and fertility monitors tracked timing of menstrual cycles and ovulation. Estrone-3-glucuronide, estradiol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), progesterone, and pregnanediol glucuronide were measured in urine at ovulation and in the luteal phase (8 days after ovulation) in the first menstrual cycle. Generalized linear models estimated the association between temperature and hormones by warm (Apr. 1-Sept. 30) vs. cold (Oct. 1-Mar. 31) seasons adjusting for fine particulate matter and ozone.

Result: During the warm season, women exposed to 1°C higher ambient temperature in the early-to-mid follicular phase and ovulation windows had -0.03 (95% CI, -0.14, 0.08) ng/mL lower FSH and -0.12 (95% CI, -0.23, -0.01) ng/mL lower LH, respectively, at ovulation. Conversely, a 1°C increase of temperature in the cold season during the early-to-mid follicular phase and ovulation windows was associated with 0.15 (95% CI, 0.02, 0.28) ng/mL higher FSH and 0.12 (95% CI, 0.004, 0.24) ng/mL higher LH, respectively, at ovulation. Higher estradiol at ovulation was observed with higher temperatures in both seasons. Few associations were found during the luteal phase.

Conclusion: Both higher and lower temperatures were associated with lower FSH and LH at ovulation, suggesting hormones may be a sensitive pathway for impacts on reproductive health.

Associations between mycoestrogen exposure and sex steroid hormone concentrations in maternal serum and cord blood in the UPSIDE pregnancy cohort Carolyn Kinkade*, Lauren Aleksunes, Anita Brinker, Brian Buckley, Jessica Brunner, Christina Wang, Thomas O'Connor, Zorimar Rivera-Nunez, Emily Barrett,

Zearalenone (ZEN) is a fungal-derived toxin found in global food supplies including cereal grains and processed foods, impacting populations worldwide through diet. Because the chemical structure of ZEN and metabolites closely resembles 17β-estradiol (E2), they interact with estrogen receptors α/β earning their designation as 'mycoestrogens'. In animal models, gestational exposure to mycoestrogens disrupts estrogen activity and impairs fetal growth. Here, our objective was to evaluate relationships between mycoestrogen exposure and sex steroid hormone concentrations in maternal circulation and cord blood for the first time in humans. In each trimester, pregnant participants in the UPSIDE study (n=297) provided urine for mycoestrogen analysis and serum for hormone analysis. At birth, placental mycoestrogens and cord steroids were measured. We fitted longitudinal models examining log-transformed mycoestrogen concentrations in relation to log-transformed hormones, adjusting for covariates. Secondarily, multivariable linear models examined associations at each time point (1st, 2nd, 3rd trimesters, delivery). We additionally considered effect modification by fetal sex. ZEN and its metabolite, α-zearalenol (α-ZOL), were detected in >93% and >75% of urine samples; >80% of placentas had detectable mycoestrogens. Longitudinal models from the full cohort exhibited few significant associations. In sex-stratified analyses, in pregnancies with male fetuses, estrone (E1) and free testosterone (fT) were inversely associated with ZEN (E1 %Δ: -6.68 95%CI: -12.34, -0.65; fT %Δ: -3.22 95%CI: -5.68, -0.70); while α-ZOL was positively associated with E2 (%Δ: 5.61 95%CI: 1.54, 9.85) in pregnancies with female fetuses. In analysis with cord hormones, urinary mycoestrogens were inversely associated with androstenedione (%Δ: -9.15 95%CI: -14.64, -3.30) in both sexes, and placental mycoestrogens were positively associated with cord fT (%Δ: 37.13, 95%CI: 4.86, 79.34) amongst male offspring. Findings support the hypothesis that mycoestrogens act as endocrine disruptors in humans, as in animal models and livestock. Additional work is needed to understand impacts on maternal and child health.

Patterns in provider behavior around postpartum contraception among groups historically targeted for fertility control Natasha Sokol*, Anna Alikhani, Janet Johnson, Alison Weber, Leigh Senderowicz,

Background: Informed access to postpartum contraception is crucial to reproductive choice. Many people want postpartum contraception, but those who do not often encounter provider pressure to adopt/refusal to remove certain methods, or are instructed (often against evidence) on birth spacing. The US and field of obstetrics have a long history of controlling fertility of marginalized groups. We tested whether these groups were more likely to experience provider behaviors aimed at increasing contraceptive uptake versus informed contraceptive choice.
Methods: We analyzed the 2018-2021 Pregnancy Risk Assessment Surveys. Outcome measures were divided in two types of provider intervention: for increased contraceptive uptake (LARC insertion, instruction on birth spacing, or inquiry about postpartum contraceptive plans) and for increased informed choice (counseling on postpartum contraceptive methods). Weighted logistic regression models estimated the influence of patient sociodemographic characteristics on each outcome. Analyses were stratified by postpartum/prenatal visit attendance if applicable.
Results: Compared to non-Hispanic white respondents, non-Hispanic Black, American Indian/Alaska Native and mixed race respondents, and all Hispanic respondents had increased odds of reporting provider behaviors aimed at increasing contraceptive uptake (ORs: 1.19-6.99, and decreased odds of reporting provider behaviors aimed at increasing informed choice (ORs: 0.66-0.89). Patterns held for those with low income (ORs: 1.18-2.19 vs. 0.80), and who took the survey in a language other than English (ORs: 1.26-1.42 vs. 0.70). Trends persisted in models controlling for breastfeeding, prenatal care adequacy and whether the pregnancy was desired.
Conclusion: Groups historically targeted for fertility control were more likely to experience provider interactions aimed at increasing postpartum contraceptive uptake, and less likely to have informative interactions for reproductive choice.

Women's health

Association between 25-Hydxrovyvitamin D and Menstrual Cycle Length: A Cross-Sectional Study Anita Subramanian*, Lauren A. Wise, Tanran R. Wang, Martha R. Koenig, Andrea S. Kuriyama, Elizabeth E. Hatch, Anne Marie Z. Jukic,

Vitamin D may affect menstrual cycle length. However, limited work has been done in this area. We examined the association between 25-hydroxyvitamin D [25(OH)D] and menstrual cycle length. Cross-sectional analysis of baseline data from a web-based preconception cohort of female US residents aged 21-45, who had been trying to conceive for ≤3 cycles without the use of fertility treatment. At baseline, participants reported their typical menstrual cycle length when not using hormones. Final sample included those with non-missing menstrual cycle length and 25(OH)D measured at baseline (N=339). Concentrations of 25(OH)D were measured in serum samples from clinic visits (N=201) and blood spots collected via mail (N=131). We categorized cycle length in days into short (<26), normal (26-<35), and long (≥ 35) cycles. We examined the shape of the association between 25(OH)D and cycle length with restricted cubic splines. Based on this evidence, we modeled 25(OH)D both continuously and in categories (<30, ≥ 30). We used logistic regression to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of short or long cycles. Models were adjusted for age, race/ethnicity, BMI, education, exercise, alcohol intake, last method of birth control, prenatal vitamin use, and blood sample type. Median 25(OH)D was 32 ng/ml (IQR: 25-37 ng/ml); 44% had 25(OH)D levels <30 ng/ml and 56% had levels ≥30 ng/ml; 9% had short and 8% had long cycles. In fully adjusted models, a 10-ng/ml increase in 25(OH)D levels was associated with lower odds of short (OR=0.95, CI: 0.63-1.42) and long cycles (OR=0.72, CI: 0.43-1.22). Analysis of categorical 25(OH)D (<30 vs. ≥ 30) did not suggest associations but were limited by small numbers at the extremes of both cycle length and 25(OH)D. Higher levels of 25(OH)D were associated with lower odds of short and long cycles, albeit associations were imprecise. Sample collection is ongoing to support warranted future research.

Can we use classification and regression trees to compare cesarean delivery rates across populations? Ruby Barnard-Mayers*, Martha Werler,

Background: When researchers estimate the effect of delivery method on birth outcomes, cesarean deliveries (CDs) are often compared to a reference group of vaginal delivery. However, this reference group does not always satisfy the assumptions necessary to use vaginal delivery as a counterfactual to CD (e.g. cesarean sections due to breech births or twin gestation). The Robson Classification (or 10-group classification) is one of the most common systems used for the purpose of comparing cesarean section rates across populations (based on pregnancy characteristics) and is recommended by the WHO. However, there has not been much testing of the Robson Classification System for the purposes of epidemiologic analyses.

Objective: The purpose of this analysis is to test machine learning techniques by conducting classification and regression tree analysis (CART) and random forests to compare to the Robson classification system.

Method: Data for this analysis comes from the Pregnancy and Early Life Longitudinal (PELL) data system, comprising all birth certificate records in Massachusetts from 2011 to 2018. We used classification and regression trees (CART) and random forests to create groupings of individuals, using the same set of variables as used in the Robson classification system. We used the mean Gini decrease to calculate variable importance.

Results: Eight leaves (final groups) resulted from the CART analysis, two fewer than the Robson classification system. Trial of labor was the most important variable and preterm delivery was the least important. In the Robson classification system, the first branch for classification is plurality. Rates of CD varied across groups for each system. The highest contributor to CD rates were births with no trial of labor for the CART analysis and multiparous births to people with a prior CD for the Robson System.

Conclusion: The CART created different groups than the Robson system. These groupings may be better for causal analysis of CD.

Comorbidities and healthcare utilization among young adults with congenital heart defects by Down syndrome status – Congenital Heart Survey to Recognize Outcomes, Needs, and wellbeinG (CH STRONG), 2016-2019 Vanessa Villamil*, Karrie Downing, Jennifer Andrews, Matthew Oster, Maureen Galindo, Jenil Patel, Wendy Nembhard, Scott Klewer, Sherry Farr,

Background: About 50% of live births with Down syndrome (DS) have congenital heart defects (CHD). Yet little is known about the health and healthcare needs of adults with DS and CHD. Our aim was to examine comorbidities and healthcare utilization of adults with DS and CHD.

Methods: From 2016-2019, the Congenital Heart Survey to Recognize Outcomes, Needs, and well-beinG (CH STRONG) surveyed adults with CHD, ages 19-38 years, or a proxy (e.g. parent), identified from active birth defects registries in Arkansas, Arizona, and Atlanta. Multivariable Poisson regression generated adjusted prevalence ratios (aPR) and 95% confidence intervals for associations between DS and comorbidities and healthcare utilization, adjusting for covariates; prevalence estimates for these associations were standardized to the 9,312 CH STRONG eligible individuals by site, sex, race/ethnicity, birth year, and CHD severity.

Results: Among 1,500 respondents, 9.1% had DS. Compared to adults with CHD without DS, adults with CHD and DS were more likely to be male (55.5% vs 45.0%), <25 years old (51.8% vs 42.7%), non-Hispanic white (72.3% vs 69.3%), and have public insurance (77.4% vs 22.8%) (all $p<0.05$), but less likely to report cardiac comorbidities (5.5% vs 14.2%; aPR=0.27 [0.12-0.58]), emergency room (ER) visits (19.3% vs 32.5%, aPR=0.57 [0.40-0.83]), hospitalizations (6.2% vs 13.2%; aPR=0.56 [0.32-0.99]), cardiac-related hospitalizations (0.7% vs 5.3%; aPR=0.16 [0.04-0.67]), and delays in care due to cost (1.2% vs 19.6%; aPR=0.14 [0.04-0.43]) in the last year. Adults with CHD and DS compared to those without DS had no detectable differences in severe CHD (38.7% vs 33.8%; $p=0.25$) or receiving cardiology care in the last 2 years (52.6% vs 44.7%; aPR=1.05 [0.82-1.36]).

Conclusions: Adults with DS and CHD may have better access to care, resulting in fewer cardiac comorbidities and use of ER and inpatient care. However, all adults with CHDs may benefit from improvements in receipt of cardiology care.

The association between prenatal cannabis use and congenital birth defects in offspring: A Systematic review and meta-analysis Abay Tadesse*, Berihun Dachew, Kim Betts, Getinet Ayano, Rosa Alati,

Abstract

Background:

A body of research has examined the association between prenatal cannabis use and congenital birth defects in offspring; however, these studies have not been synthesised. We performed a comprehensive synthesis of existing research to test whether there is an association between prenatal cannabis use and congenital birth defects in exposed offspring.

Objective: The aim of this study was to conduct a comprehensive systematic review and meta-analysis of existing evidence to synthesise the association between prenatal cannabis use and congenital birth defects in exposed offspring.

Methods:

In line with the preregistered protocol (PROSPERO: CRD42022368623), we systematically searched PubMed/Medline, CINHAL, EMBASE, Web of Science, ProQuest, Psych-Info, and Google Scholar for published articles until 4 April 2023. The methodological quality of the included studies was appraised by the Newcastle-Ottawa Quality Assessment Scale (NOS). A meta-analysis was carried out to report the pooled effect estimates from the included studies. We further performed subgroup, leave-one-out sensitivity, and meta-regression analyses, which increased the robustness of our findings.

Results:

Thirty observational studies (i.e., fifteen case-control and fifteen cohort studies) with 229,930 cases of birth defects and 26,826,741 controls (healthy babies) were included in the final analysis. We found that offspring exposed to maternal prenatal cannabis were at greater risk of any birth defects (irrespective of specific body system) [RR = 1.56: 95 % CI 1.28 – 1.92, I2 =98.4%, p = 0.00], defects of the gastrointestinal [RR = 1.69: 95 % CI 1.37 – 2.09], cardiovascular/heart [RR = 1.47: 95 % CI 1.09 – 1.97], central nervous systems [RR = 1.43: 95 % CI 1.09 – 1.89], and facial/oral cleft [RR = 1.13: 95 % CI 1.08 – 1.18].

Thirty observational studies (i.e., fifteen case-control and fifteen cohort studies) with 229,930 cases of birth defects and 26,826,741 controls (healthy babies) were included in the final analysis. We found that offspring exposed to maternal prenatal cannabis were at greater risk of any birth defects (irrespective of specific body system) [RR = 1.56: 95 % CI 1.28 – 1.92, I2 =98.4%, p = 0.00], defects of the gastrointestinal [RR =1.69: 95 % CI 1.37 – 2.09], cardiovascular/heart [RR =1.47: 95 % CI 1.09 – 1.97], central nervous systems [RR =1.43: 95 % CI 1.09 – 1.89], and facial/oral clefts [RR =1.13: 95 % CI 1.08 – 1.18]. The robustness of our results was confirmed through subgroup, sensitivity, and meta-regression analyses.

Conclusion:

The findings from the current study suggest that maternal prenatal cannabis exposure is associated with a higher risk of birth defects in offspring. The findings highlight the importance of promotive and preventive strategies to reduce cannabis use during pregnancy that contribute to minimising the risk of birth defects in offspring.

Associations between diphenhydramine and specific birth defects stratified by imputed indication, National Birth Defects Prevention Study and Birth Defects Study to Evaluate Pregnancy exposureS Meredith Howley*, Eva Williford, Sarah Fisher, Martha Werler, Julie Petersen, Suzanne Gilboa, Craig Hansen, Elizabeth Ailes, Mollie Wood, Mairlyn Browne, Eva Williford

Diphenhydramine is used for various indications, including nausea and vomiting in pregnancy, allergy relief, and as a sleep aid. While diphenhydramine has been associated with increased risk for a small number of specific birth defects, findings from National Birth Defects Prevention Study (NBDPS; 1997–2011) were largely null. Yet, confounding by indication may persist as NBDPS did not collect indication. Data from Birth Defects Study to Evaluate Pregnancy exposureS (BD-STEPS; 2014–2019), a study conducted subsequent to NBDPS in a subset of sites, included questions on indication. Thus, we sought to use BD-STEPS data to impute missing indication in NBDPS data and generate estimates of the association between diphenhydramine and 12 birth defects in the combined data stratified by indication.

Cases included infants, stillbirths, or terminations with a birth defect. Controls included live born infants without a birth defect. Mothers of cases and controls reported early pregnancy medication use and BD-STEPS participants reported indication. We used a sequential regression multivariate imputation approach and created 50 datasets imputing missing values, including indication. We used Firth's logistic regression with propensity scores to calculate adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for the association between diphenhydramine and each birth defect stratified by indication. We pooled ORs across the 50 imputed datasets using Rubin's rules.

In NBDPS and BD-STEPS, 461 cases (2–3% of each birth defect) and 341 controls (2%) reported early pregnancy diphenhydramine use; 66% were missing indication, which were all NBDPS participants. The pooled ORs for the 12 defects across the three indications ranged from 0.6 to 2.0; all CIs included the null. Our findings confirm previous NBDPS null findings and suggest that confounding by indication is likely not a large source of bias in studies of early pregnancy diphenhydramine use and the 12 birth defects analyzed.

Birth defects

Why has gastroschisis been increasing over time and why is it more common in infants of young mothers? Rashida S. Smith-Webb*, Gary M. Shaw, Peter H. Langlois, Cynthia A. Moore, Martha M. Werler,

Background: Gastroschisis, a severe abdominal wall defect, is more prevalent in infants of young mothers and has been increasing over the past decades. Various factors have been associated with an increased risk for gastroschisis independent of maternal age. However, studies have not systematically explored whether these factors can explain the time trend or age association. We examined whether factors previously associated with gastroschisis in the National Birth Defects Prevention Study (NBDPS) can explain the increasing prevalence over time and the inverse association with maternal age.

Methods: We used data from the NBDPS for gastroschisis cases and controls with delivery dates from 1997-2011. We calculated crude ORs for the time trend (birth years 2005-2011 vs. 1997-2004) and maternal age (<25 vs. 25+ years). We then evaluated the potential confounding effects of 18 factors separately (exposures: alcohol, cigarettes, illicit drugs, oral contraceptives, cold/flu+ fever, genitourinary infection, polycyclic aromatic hydrocarbons (PAHs), diet quality, BMI; reproductive: parity, interpregnancy interval; social: race, acculturation, income). We considered an exposure a confounder if the crude OR (cOR) for the time trend or maternal age changed by at least 10% in logistic regression models.

Results: The cOR for the time trend was 1.28; 95% CI: 1.14, 1.44, and was attenuated by at least 10% after adjustment for exposure to PAHs (any occupational OR = 1.12; 0.96, 1.30; cumulative across all jobs OR = 1.11; 0.96, 1.30). The cOR for young maternal age was 7.76 (6.71, 8.97). The maternal age OR was attenuated after adjusting for paternal age by 30% (OR = 5.43; 4.55, 6.48) and parity by 15% (OR = 6.62; 5.71, 7.68). Adjustment for other factors did not materially change the cORs for either the time trend or maternal age.

Conclusion: None of the parental exposures examined substantially accounted for the increasing time trend or the higher prevalence among younger mothers.

Birth defects

Profile of individuals with IQ scores in the National Spina Bifida Patient Registry (NSBPR)
Sophia Drewry*, Heidi Castillo, Amy Heffelfinger, Jonathan Castillo, Jennifer Queally, William Walker, Kurt Freeman, Richard Adams, Pamela Murphy, Catharine Riley,

Individuals with spina bifida (SB) often have neurocognitive impairments. The range of cognitive impairment is variable among the entire SB population and can be influenced by SB lesion, hydrocephalus, shunt placement, and repair procedures. The purpose of this study is to describe the demographic and clinical characteristics of individuals who have IQ data reported within the NSBPR sample and gain insights into the distribution of IQ scores.

We conducted a preliminary descriptive analysis on 1,308 NSBPR participants aged 4-22 years across six different clinics from November 2019 – December 2022 comparing demographic, educational, and clinical characteristics of those with a reported IQ test (n=436, 33%) to those without (n=872, 67%). We used multinomial logistic regression models to compare participants with and without a reported IQ score, adjusting for race, insurance, SB type, and clinic type. We report the distribution of reported IQ scores among NSBPR participants and the relationship between IQ scores and specific variables, based on ANOVA tests.

Higher level of lesion, private insurance type and history of academic accommodations were associated with having an IQ test reported. Participants with partial or full-time academic accommodation were more likely to have an IQ test reported ($p<0.05$). Among those with a reported IQ test, the average IQ score was 81.3 (SD: 16.9). Those with higher level of lesion and partial or full-time academic accommodations had a lower average IQ score ($p<0.001$ for both).

These results may indicate that those with more severe presentation are more likely to have an IQ test submitted in the NSBPR subset. Individuals with higher levels of lesions, private insurance and who have reported academic accommodations more often have their IQ test results reported in the NSBPR. Continued research into these factors might improve understanding of barriers to receiving neuropsychological evaluations for individuals with SB.

Trends in Corticosteroid Use Among Males with Duchenne Muscular Dystrophy (DMD) During 2000-2015: Data from the MD STARnet Shiny Thomas*, Tahereh Neyaz, Kristin M. Conway, Paul A. Romitti, Aida S. Soim, Carla D. Zingariello, Joshua R. Mann,

Objective: To describe corticosteroid use among males with Duchenne muscular dystrophy (DMD) during 2000-2015 using data from the US population-based Muscular Dystrophy Surveillance, Tracking and Research Network (MD STARnet).

Methods: We included 373 oldest affected males with definite/probable DMD born and followed during 1/1/2000-12/31/2015 in six US sites. Kaplan-Meier (K-M) curve estimation was used to describe median ages (95% confidence intervals [95%CIs]) at first offer and use. Cox proportional hazards modeling was used to estimate adjusted hazard ratios (aHRs) and 95%CIs for offering and use of corticosteroids from birth cohort (2000-2004/2005-2009/2010-2015), race/ethnicity (non-Hispanic white [NH-W]/NH black [NH-B]/Hispanic/Other) and known DMD family history (yes/no); MD STARnet site was entered as a random effect.

Results: Most males were NH-W (68.1%), born before 2010 (89.3%), and had no known DMD family history (73.2%). Corticosteroids were offered to 75.6% of all males and 68.9% initiated use. Deflazacort was available to 31.5% of users, mostly NH-W males (86.4%). Corticosteroids were stopped by 20.6%, mostly due to behavior problems or weight gain. K-M estimation showed median ages of 6.8 years (95%CI=6.3,7.2) at first offer and 7.2 years (95%CI=6.8,7.6) at first use (n=41 missing age). Lower hazards were found for NH-B versus NH-W (offered: aHR=0.5, 95%CI=0.3,0.9; used: aHR=0.6, 95%CI=0.3,1.0) and known family history versus no known history (offered: aHR=0.8, 95%CI=0.6,1.0; used: aHR=0.6, 95%CI=0.4,0.9). Higher hazards were observed among males born 2010-2015 versus 2000-2004 (offered: aHR=2.8, 95%CI=1.4,5.4; used: aHR=1.8, 95%CI=0.4,0.90.7,4.7).

Discussion: The offering and use of corticosteroids differed by sociodemographic and family characteristics. Access to deflazacort, which may have less severe side effects than prednisone, differed by race/ethnicity. Potential disparities in access to alternative steroids should be further explored.

Child health and development

Twin-singleton infant growth differences exist independent of gestational age at birth Anna Booman*, Alex Foster, Miguel Marino, Teresa Schmidt, Jonathan M. Snowden, Janne Boone-Heinonen,

Background: Infant weight trajectory is routinely screened in clinical settings, with infants compared to a normative reference and interventions recommended. A common reference uses data from a population of singletons. Twins typically have lighter birth weight than singletons, in part due to earlier gestational age at birth (GA), so comparing them to this external reference may result in recommendations to increase feedings, with unknown appropriateness. Here, we compare growth trajectories of twins versus singletons, independent of GA, to inform twin-specific recommendations.

Methods: We used data from the PROMISE study, an electronic health record-based study derived from a network of community-based health care organizations. We included infants with a recorded GA and at least two weight measures before two years of age. We matched each of 320 twin males and 332 twin females to ten singletons on sex and GA (totaling 3,200 singleton males and 3,320 singleton females). Growth trajectories were fit using the Jenss mixed-effects model: parameters reflect (a) starting weight, (c) rate of growth in early infancy, (d) decreasing rate of growth in mid-infancy, and (b) rate of growth in late infancy.

Results: Twin males had the fastest weight gain in early infancy (c=1.70, 95% confidence interval [CI] 1.65, 1.75), catching up to and surpassing singleton males (c=1.59, 95% CI 1.58, 1.61) in weight by 8.5 months of life. Twin females had a similar rate of growth as singleton females throughout follow-up (e.g., c=1.52 for both), but given their lighter starting weight, caught up to, but did not surpass, singleton females by two years.

Discussion: Differences in growth between twins and singletons exist independent of GA and differ by infant sex. There may be unique factors related to twin gestation that affect infant growth beyond GA. Further research is needed to identify optimal growth and construct weight references for twins.

Parental opinions toward a hypothetical newborn screen for autism spectrum disorder

Sravya Emmadi*, Paige Cubberly-Decker, Melanie Adkins, Nicole Talge,

Early identification of ASD risk using biomarkers is an active area of research. However, parents are rarely consulted about this research agenda and its potential impact. Our pilot study examined parental opinions toward hypothetical applications of newborn screening (NBS) to ASD to address this gap. We also examined whether parental understanding of screening principles (e.g., probabilistic identification) impacted these opinions.

Our sample included parents interested in a separate study of newborns who completed an online survey (n=135, 69% response rate). We assessed opinions toward hypothetical applications of NBS to ASD by asking whether perceived benefits outweighed drawbacks or vice versa. Parents also read a short passage about screening programs and reported whether screening results indicate a condition is "definitely present" or "definitely not present;" endorsement of either statement was considered inaccurate. We used logistic regression to examine whether response accuracy (referent: yes) was associated with parent opinions (referent: benefits>drawbacks). We also adjusted for parity (60% multiparous), maternal education (36% < college), and whether a child household member was born preterm, has ASD, or is enrolled in early intervention (33%).

Approximately 80% of parents reported that benefits outweighed drawbacks when considering a hypothetical NBS application to ASD, and 54% inaccurately reported that screening will indicate whether a condition is definitely present or not present. Inaccurate responses were not associated with NBS opinions (OR=0.9, 95%CI 0.3, 2.6). This finding was unaffected after adjustment.

Our pilot suggests many parents support identification of ASD risk as early as the newborn period, but appreciation for the probabilistic nature of screening test performance is unrelated to variability in these opinions. Future research is needed for replication and to include all stakeholders, including autistic individuals themselves.

Higher birth weight is associated with stronger early-life visual cortex connectivity in female infants/toddlers Diana Pacyga*, Jake E. Thistle, Emily J. Werder, Jessie P. Buckley, Weiyan Yin, Zhengwang Wu, Gang Li, Tengfei Li, Li Wang, Joe Piven, John Gilmore, Weili Lin, Stephanie M. Engel, Kyle Burger,

Background/aim: Birth weight (BW) for gestational age is a critical indicator of fetal growth in the in utero environment. Poor fetal growth is a known risk factor for adverse behavioral/cognitive outcomes. Further, adult obesity is associated with aberrant function in the visual cortex. However, few studies have evaluated the relation between BW for gestational age and early-life functional brain network dynamics.

Methods: The Baby Connectome Project used resting-state functional magnetic resonance imaging to assess connectivity within seven canonical brain networks: dorsal attention, salience, limbic, frontoparietal, default mode, visual, and sensorimotor. For 90 infants/toddlers under the age of three (contributing 427 observations), we abstracted BW (kg) and gestational age at birth (weeks) from medical records and calculated sex- and gestational age-specific BW z-scores (BWz) using a U.S. reference chart. Using multiple linear mixed models, we evaluated associations of BWz as continuous measures and in tertiles with each network accounting for age at scan (linear and quadratic), sex, maternal age, and race/ethnicity. We stratified models to explore sex differences.

Results: Most infants/toddlers (66% female) were born to non-Hispanic White (71%) and college-educated (72%) mothers and had median (25th, 75th percentile) BWz of 0.3 (-0.6, 1.0). Overall, BWz was consistently associated with the visual network only among females. For example, each interquartile range increase in continuous BWz was weakly associated with increased visual connectivity (β: 0.02; 95% CI: 0.00, 0.04) in females, but not males (β: -0.01; 95% CI: -0.05, 0.03), and the association in females was strongest in BWz tertile 3 compared to 1 (β: 0.03; 95% CI: -0.01, 0.06), but not observed in males (β: 0.00; 95% CI: -0.07, 0.06).

Conclusion: Dovetailing research in adults, BWz may be associated with increased visual network connectivity in females in early-life.

Association between prenatal and childhood exposure to particulate matter and asthmatic symptoms in the children of the Cyprus MEDEA Cohort Stefania Papatheodorou*, Nicole Alkhouri, Veronica Wang, Panayiotis Yiallouros, Panayiotis Kouis, Pinelopi Anagnostopoulou, Petros Koutrakis,

Background: Asthma is highly prevalent among children, especially in the eastern Mediterranean region, where desert dust storms heighten susceptibility to exacerbation of respiratory asthmatic symptoms.

Aims: To examine the association between prenatal and childhood exposure to PM2.5 and PM10 and the development of ever and 12-month asthma or asthmatic symptoms before clinical exam and interview within the Mitigating the Health Effects of Desert Dust Storms Using Exposure-Reduction Approaches (MEDEA) cohort in Cyprus.

Methods: The study included 3,773 MEDEA cohort children (7-13 years old) from Nicosia and Limassol. Prenatal and 12 months before the clinical exam and interview PM exposure was calculated for each participant. Logistic regression was used to evaluate the association between prenatal exposure and ever outcomes, as well as 12-month exposure and 12-month outcomes. The models were adjusted for demographics, clinical characteristics, family history, season and long-term trends, and climatic factors. We examined effect measure modification (EMM) by age, sex, and BMI.

Results: For each 1 µg/m3 increase in PM10 levels during the prenatal period, the odds of ever having wheezing increased by 3% (95% Confidence Intervals [CI]: 2% to 4%), and ever doctor-diagnosed asthma increased by 4% (95% CI: 2% to 6%). We did not find any association between 12-month PM exposure and asthma or asthmatic symptoms a year before the interview. There was an indication for EMM by sex, where male participants had higher odds (1.08, 95% CI 5% to 10%) of ever asthma than females (0.97, 95% CI 0.95-1.03). There was no indication for EMM by age or BMI,

Conclusion: Our study shows that prenatal exposure to particulate matter increases the odds of having respiratory symptoms and asthma in children born in Nicosia and Limassol. Continued efforts are needed to identify the most vulnerable populations and develop strategies to reduce exposures and improve air quality.

Accuracy of cerebral palsy case definitions in administrative data Peter Socha*, Jennifer Hutcheon, Maryam Oskoui, Sam Harper,

Background: Many jurisdictions lack population-based cerebral palsy registries, leading researchers to classify cases using administrative data. We aimed to estimate the accuracy of common case definitions. Previous validation studies used registry diagnoses as the gold-standard, yet some cases may not be captured within registries. We therefore assessed the potential effect of registry sensitivity on estimates of case definition accuracy.

Methods: We used a cohort derived from a linkage of a population-based cerebral palsy registry of children born from 1999 through 2002 in six health regions in Quebec, Canada, and population-based physician-billing and hospitalization records through 2015. The cohort included all cases in the registry (n=302), all individuals with an Intenational Classification of Diseases code for cerebral palsy in their administrative data (n=346), and a sample of non-cases without a cerebral palsy code matched on age, sex, and region (n=6040). We calculated the sensitivity and specificity of six case definitions, assuming the registry was missing: no cases, 20% of cases, or 10% of cases with and 30% of cases without a positive case definition.

Results: If no cases were missing from the registry, the most sensitive definition was any code for cerebral palsy (sensitivity 65%, 95% CI 60-70%; specificity 99.92%, 95% CI 99.91-99.94%) and the most specific definition was a hospitalization code or two billing codes at least 14 days apart, before age 5 (sensitivity 47%, 95% CI 41-52%; specificity 99.97%, 95% CI 99.97-99.98%). The relative accuracy remained the same if the registry sensitivity was imperfect, but the estimated specificities were higher. The estimated sensitivities were only affected (lowered) if the registry sensitivity was higher among individuals with a positive case definition.

Conclusions: Case definitions for cerebral palsy had varying levels of sensitivity and specificity, which were meaningfully affected by registry specificity.

Associations of breast bud diameter with estradiol concentrations during minipuberty in infant girls Mandy Goldberg*, Shanshan Zhao, Andrea Kelly, Virginia A. Stallings, David M. Umbach, Walter J. Rogan, Natalie D. Shaw, Dale P. Sandler,

Background: Estradiol (E2) stimulates breast tissue development during critical periods in early life, including in utero and during puberty. Yet it remains unclear whether E2 produced during minipuberty, the postnatal activation of the hypothalamic-pituitary-gonadal axis, contributes to breast development in infant girls.

Methods: We used data from 136 girls from a prospective cohort study enrolled during 2010-2013 from the Philadelphia area to examine longitudinal associations of E2 during minipuberty with breast bud diameter in late infancy. We measured E2 in serum samples at study visits every 2-4 weeks from 2-32 weeks of age. We assessed breast bud diameter via ultrasound at the neonatal and 32-week visits. We applied multiple imputation for E2 concentrations below the limit of detection (2.99 pg/mL, 35% of samples). We log2-transformed both E2 and breast bud diameter for analysis. We examined the correlation (r) of breast bud diameter at the neonatal and 32-week visits. We then estimated the percent change ([2β-1] x 100%) in breast bud diameter at the 32-week visit per doubling in subject-specific geometric mean E2 from 2-32 weeks using linear regression with adjustment for neonatal breast bud diameter, feeding method, and other infant characteristics.

Results: The median breast bud diameter was 12.4mm at the neonatal visit and 13.7mm at the 32-week visit; there was no correlation between the measures at these time points (r: -0.06). The geometric mean E2 concentration from 2-32 weeks of age was 5.1 pg/mL (95% confidence interval [CI]: 4.7-5.4). A doubling in mean E2 concentration across minipuberty was associated with a 28% larger breast bud diameter at the 32-week visit (95% CI 12-46%).

Conclusions: Our results suggest that breast bud growth continues after birth in infant girls and is stimulated by endogenous E2 production during minipuberty. More research is needed to investigate the relevance of minipuberty to later breast development and disease.

Child health and development

Associations Between Maternal Hypertensive Disorders of Pregnancy and Vascular Birthmark Development in Infants

Jessica Wong*, Yajnaseni Chakraborti, Ellen Caniglia, David Margolis, Enrique Schisterman, Sunni Mumford, Stefanie Hinkle,

Background: Investigating the developmental origins of vascular birthmarks, such as port-wine stains (PWS) and hemangiomas, in the context of hypertensive disorders of pregnancy (HDP), offers a unique lens to explore the relationship between maternal health and infant dermatological outcomes. While often considered cosmetic, these birthmarks can signify serious conditions like Sturge-Weber Syndrome in facial PWS cases or vision impairment from hemangiomas near the eyes. Recognizing the shared developmental pathways between hemangiomas and preeclampsia (PE), this study examined the association between HDP and vascular birthmarks.

Methods: The Collaborative Perinatal Project (1959-1966) was a prospective study at 12 US clinical centers. Contemporary clinical guidelines defined HDP as chronic hypertension (HT), gestational HT, PE/eclampsia, and superimposed PE. Vascular birthmarks were diagnosed in infants at one year by general practitioners. Adjusted log-binomial regression models with multiple imputations for missing data estimated the association between HDP and infantile birthmarks, adjusting for confounders.

Results: Of 55,676 maternal-infant pairs, 50,487 were normotensive, 2,087 had chronic HT, 943 had gestational HT, 519 had PE, and 1,011 had superimposed PE. At one year, 1.3% of infants had hemangiomas, and 0.5% had PWS. For PWS, the RRs (95% CI) were 1.12 (0.48-1.76) for chronic HT, 1.01 (0.22-1.8) for gestational HT, 1.34 (0.35-2.34) for PE, and 2.25 (1.56-2.94) for superimposed PE. For hemangiomas, the RRs were 1.38 (0.98-1.78) for chronic HT, 1.01 (0.52-1.51) for gestational HT, 1.75 (1.2-2.3) for PE, and 0.95 (0.31-1.58) for superimposed PE.

Conclusion: This study suggests that superimposed PE could be associated with an increased risk of developing PWS, while PE might be linked to an increased risk of hemangiomas. These observations highlight the need for further exploration into the role of HT in the development of vascular birthmarks in infants.

Change in postpartum visit and postpartum contraception rates pre-COVID-19 to post-lockdown in six FQHCs Rebecca Campbell*, Rachel Caskey, Emma Gray, Cristina Barkowski, Jena Wallander Gemkow, Kristin Rankin, Sadia Haider,

U.S. maternal mortality increased during the COVID-19 pandemic. Comprehensive postpartum care including contraception benefits maternal health outcomes. The COVID-19 pandemic may have disrupted postpartum healthcare access in underserved populations. We utilize electronic health record (EHR) data for prenatal patients (n=2,265) from 6 FQHCs across 3 states from one year pre-pandemic (1/1/19) through one year after the first stay-at-home orders ("lockdown") (3/31/21). We investigate changes in rates of postpartum visit (PPV) and postpartum contraception (PPC) receipt in the post-lockdown vs. pre-pandemic periods, and characteristics predictive of changes in PPV and PPC rates. EHR clinical visits and prescription records were used to classify if patients utilized PPV and most/moderately effective PPC within 60 days postpartum, analyzed separately and as a composite variable: PPV & PPC, PPV only, no PPV. Risk differences comparing post-lockdown to pre-COVID-19 pandemic were estimated with binomial and generalized logistic regression models adjusted for age, race/ethnicity, language, and site. Effect modification (EM) by sociodemographic and clinical covariates was examined. Total patient volume fell 21% in the post-lockdown vs. pre-COVID-19 period. PPVs decreased by 9.6 (95% CI: -13.6, -5.6) and PPC by 8.0 (-13.3, -2.8) percentage points. In adjusted models for the composite outcome, PPV & PPC decreased by 9.3 percentage points (-13.05, -5.44), while PPV only was stable [-0.37 (-4.31, 3.58)]. EM was observed by OB comorbidity only: PPV & PPC decreased 2x more among those with vs. without a comorbidity, and PPV only increased in those with a comorbidity vs. no change in those without. These findings suggest a substantial, sustained impact of the COVID-19 pandemic on postpartum care and contraception in FQHCs. Patient and provider experiences post-lockdown require further examination to inform strategies to improve care access and maternal health outcomes.

Everything feels just a little heavier, more wrought with implications, you know? – A mixed-methods study examining lifestyle behaviors, health, and well-being of pregnant and postpartum women during the early months of the COVID-19 pandemic Elizabeth Widen*, Sara Dube, Jennifer Gonzalez, Gracia Dala, Michelle Wright, Megan Gray, Linda Kahn, Deborah Jacobvitz,

The COVID-19 pandemic has had a major impact on mental health, health care, and lifestyle behaviors, including perceived health, diet, physical activity, and sleep. Yet the pandemic's impact on all of these domains jointly has not been examined during pregnancy and postpartum. This mixed methods study was conducted among a subset of participants (n=22) in a pregnancy cohort study in Austin, Texas, who were pregnant or had recently delivered when the outbreak occurred. Measures were from the early second trimester up to 6 months postpartum. Findings from questionnaires were complemented by qualitative interviews during Spring/Summer 2020 about participant experiences during the early pandemic. From our quantitative data (n=22), most participants reported that the pandemic generally had a negative impact on their lives (81%), that they shifted to eating more at home (71%), and that they were less physically active (62%). Five major themes emerged in our qualitative interviews (n=22): (1) adaptation to pandemic restrictions, (2) psychosocial experiences, such as feelings of anxiety, guilt sadness, isolation, and frustration; (3) health behavior changes, (4) healthcare experiences, and (5) where they obtained general and perinatal related pandemic information. Of those who completed both pregnancy and postpartum interviews (n=8), all reported anxiety during both periods; however, those who delivered in Spring 2020 experienced more anxiety surrounding delivery and less social support than those who delivered in Summer 2020, who reported less anxiety surrounding hospital birth and greater social support, particularly after delivery. Overall, our findings confirm prior evidence that the COVID-19 pandemic had a marked impact on stress, anxiety, and worries, as well as lifestyle behaviors among pregnant and postpartum people. Our work provides lessons for healthcare practitioners about support need for pregnant and postpartum persons amid societal disruption.

Environment/climate change

High Ambient Temperature in Pregnancy and Risk of Childhood Acute Lymphoblastic Leukemia Tormod Rogne*, Rong Wang, Pin Wang, Nicole Deziel, Catherine Metayer, Joseph Wiemels, Kai Chen, Joshua Warren, Xiaomei Ma,

Background: High ambient temperature is increasingly common due to climate change and is associated with risk of adverse pregnancy outcomes. Acute lymphoblastic leukemia (ALL) is the most common malignancy in children, the incidence is increasing, and in the United States it disproportionately affects Latino children. We aimed to investigate the potential association between high ambient temperature in pregnancy and risk of childhood ALL.

Methods: We used data from California birth records (1982-2015) and California Cancer Registry (1988-2015) to identify ALL cases diagnosed <14 years and 50 times as many controls matched by sex, race/ethnicity, and date of last menstrual period. Ambient temperatures were estimated on a 1-km grid. Association between ambient temperature and ALL was evaluated per gestational week, restricted to May-September, adjusting for confounders. Bayesian meta-regression was applied to identify critical exposure windows. For sensitivity analyses, we evaluated a 90-day pre-pregnancy period (assuming no direct effect before pregnancy) and constructed an alternatively matched dataset for exposure contrast by seasonality.

Findings: Our study included 6,258 ALL cases and 307,579 controls. The peak association between ambient temperature and risk of ALL was observed in gestational week 8, where a 5 °C increase was associated with an odds ratio of 1.09 (95% confidence interval 1.04-1.14) and 1.05 (95% confidence interval 1.00-1.11) among Latino and non-Latino White children, respectively. The sensitivity analyses supported this.

Interpretation: Our findings suggest an association between high ambient temperature in early pregnancy and risk of childhood ALL. Further replication and investigation of mechanistic pathways may inform mitigation strategies.

Effect of extreme heat exposure on the associations between weekly gestational exposure to fine particulate matter and preterm birth in a North Carolina birth cohort Alison K. Krajewski*, Breanna Alman, Ambarish Vaidyanathan, Thomas J. Luben, Kristen M. Rappazzo,

Preterm birth (PTB;<37 weeks completed gestation) is associated with exposure to fine particulate matter (PM2.5). Recent studies suggest that extreme heat events (EHE) may further impact this association. We estimated the associations between PM2.5 and PTB, with different metrics for EHE. We examined the associations between gestational exposure to PM2.5 and PTB in a North Carolina birth cohort (N=552,567) from 2011-2015. Daily (24-hour average) PM2.5 concentrations from US Environmental Protection Agency's Fused Community Multiscale Air Quality Modelling System (fCMAQ) model were linked to a residential address at delivery, then averaged across each week of pregnancy, trimester, and entire pregnancy. A census tract indicator of EHE (maximum daily heat index above the 95th percentile for two consecutive days) was linked for the same time period. Modified Poisson regressions with robust errors were used to estimate risk differences (RDs) in PM2.5 per 10,000 births, adjusted for gestational parent race/ethnicity, age at delivery, Medicaid status, and rural-urban commuting area. Additional models included a dichotomous indicator of EHE (0 events, 1 or more events) as a co-exposure or an interaction term. The median PM2.5 concentration during pregnancy was 9.55 μg/m3, and PTB prevalence was 7.3%. The median number of EHE during pregnancy was 5 (range: 0-31). Overall, there were negative associations between PM2.5 and PTB, without adjustment for EHE (RDs ranged from -17 to -4), with adjustment for EHE (RDs ranged from -19 to 30), and with interaction (RDs ranged from -16 to -2). The strongest associations with EHE were in the third trimester, without PM2.5 [RD -226 (95% CI: -240, -212)], with PM2.5 [RD -282 (-297, -267)], and with interaction [-1022 (-1138, -906)]. Overall, we observed negative associations with gestational exposure to PM2.5 and PTB, with no evidence of interaction with EHE.

Oxidative stress as a potential mechanism linking gestational phthalate exposure to cognitive development in infancy Stephanie Eick*, Kaegan Ortlund, Andrea Aguiar, Francheska Merced-Nieves, Megan Woodbury, Antonia Calafat, Ginger Milne, Susan Schantz,

Objective: Gestational exposure to phthalates, endocrine disrupting chemicals widely used in consumer products, has been associated with poor recognition memory in infancy. Oxidative stress may represent one pathway linking this association. Hence, we examined whether exposure to phthalates was associated with elevated oxidative stress during pregnancy, and whether oxidative stress mediates the relationship between phthalate exposure and recognition memory.

Material and Methods: Our analysis included a subset of mother-child pairs enrolled in the Illinois Kids Development Study (IKIDS; N=144). Concentrations of monoethyl phthalate (MEP), sum of di(2-ethylhexyl) phthalate metabolites (ΣDEHP), sum of di(isononyl) phthalate metabolites (ΣDINP), and sum of anti-androgenic phthalate metabolites (ΣAA) were quantified in 2nd trimester urine samples. Four oxidative stress biomarkers (8-isoprostane-PGF2α, 2,3-dinor-5,6-dihydro-8-iso-PGF2α, 2,3-dinor-8-iso-PGF2α, and prostaglandin-F2α) were measured in 2nd and 3rd trimester urine. Recognition memory was evaluated at 7.5 months, with looking times to familiar and novel stimuli recorded via infrared eye-tracking. Novelty preference (proportion of time looking at a novel stimulus when paired with a familiar one) was considered a measure of recognition memory. Linear mixed effect models were used to estimate associations between phthalate metabolites and oxidative stress biomarkers. Mediation was assessed using a regression-based approach that was used to estimate direct, indirect, and total effects.

Results: The average maternal age at delivery was 31 years and 53.5% of participants had a graduate degree. A natural log unit increase in ΣAA, ΣDINP, and ΣDEHP was associated with a statistically significant increase in 8-isoprostane-PGF2α, 2,3-dinor-5,6-dihydro-8-iso-PGF2α, and 2,3-dinor-8-iso-PGF2α. The association was greatest in magnitude for ΣAA and 2,3-dinor-5,6-dihydro-8-iso-PGF2α (b= 0.45, 95% confidence interval= 0.12, 0.77). The relationship between ΣAA, ΣDINP, ΣDEHP, and novelty preference was partially mediated by 8-isoprostane-PGF2α and 2,3-dinor-8-iso-PGF2α.

Conclusions: Gestational exposure to phthalates is positively associated with oxidative stress markers, highlighting one mechanistic pathway through which these chemicals may impair early cognitive development.

Environment/climate change

Association between fine particulate matter (PM2.5) and severity of acute respiratory infections among young US children in the major cities in the United States: a claims-based cohort study Damien Foo*, Annette Regan, Seulkee Heo, Eric Schneider, Joseph Canner, Yimeng Song, Michelle Bell,

Background: Acute respiratory infections (ARIs) are a leading cause of morbidity and mortality among young children. Air pollution may play a role in the exacerbation of ARIs via inflammation, immunosuppression, and oxidative stress, yet this effect has been infrequently evaluated among young children.

Objectives: To evaluate the impact of short-term exposure to fine particulate matter (PM2.5) to ARI severity among children aged <5 years.

Methods: We analyzed data from a claims-based cohort of US children aged <5 years enrolled in a private health insurance plan who were diagnosed with an ARI between January 2018 and March 2020. We use daily monitored PM2.5 concentrations at the metropolitan statistical area level to estimate the short-term weekly exposure to PM2.5. We evaluated the association between short-term exposure to PM2.5 and the risk of hospital admissions and readmissions with an ARI, intensive care unit (ICU) admission, mechanical ventilation, prescription claim for antiviral medication, and length of stay using generalized linear models adjusting for individual-, ecological-, and community-level covariates.

Results: Of the 598,164 unique ARI episodes, we observed 3,511 antiviral prescription claims, 5,081 hospital admissions, 1,486 ICU admissions, 129 mechanical ventilations, and 61 hospital readmissions. The risk of an antiviral prescription claim increased by 11% (95% confidence interval [CI]: 1.07,1.15) per interquartile range increase in exposure to PM2.5 (3.37 µg/m3); this association was consistent irrespective of age group or influenza vaccination status. We observed a 6% and 11% increased risk of ICU admission (95% CI: 1.01, 1.10) and mechanical ventilation (95% CI: 1.06, 1.18), respectively, among children not vaccinated against influenza and no increase among vaccinated children.

Discussion: Short-term exposure to PM2.5 may contribute to ARI severity among young children. Influenza vaccination may modify the risk of severe ARI-associated outcomes.

Environment/climate change

Current breastfeeding and blood lead concentrations in U.S. premenopausal individuals: Results from NHANES 2003-2012 Mandy S. Hall*, Arianna V.E. Foster, Nicole M. Talge, Renee Heffron, Robert O. Wright, Julio Landero, Michael Yin, Flavia Matovu, Quaker E. Harmon, Kenneth Mugwanya, Andrew Mujugira, Chenxi Li, Kristen Upson,

To meet infant nutritional needs, calcium is mobilized from maternal skeleton during lactation. We hypothesized that greater bone remodeling with breastfeeding also increases mobilization of toxic metal lead (Pb) stored in bone to blood. We conducted a cross-sectional analysis using National Health and Nutrition Examination Survey (NHANES) 2003-2012 data. The study population comprised premenopausal individuals ages 20-42 with an intact uterus, ≥1 ovary, and blood Pb data (unweighted n=4,209). Accounting for the complex survey sampling, we used multivariable linear regression to estimate the percent difference in blood Pb levels and 95%CI by current breastfeeding status; we adjusted for age, education, smoking, alcohol use, NHANES year, 25-hydroxyvitamin D, calcium intake, energy intake, current hormonal contraceptive use, and pregnancy status. Those currently breastfeeding had a higher geometric mean Pb concentration (0.88 µg/dl, 95%CI: 0.80, 0.97) compared to others (0.77 µg/dl, 95%CI: 0.75, 0.78). Current breastfeeding was associated with 20% higher blood Pb levels (95%CI: 9%, 33%). We explored the underlying mechanism using NHANES 1999-2002 data that had bone turnover marker data (bone alkaline phosphatase (BAP) and N-terminal telopeptides (NTX)). We observed 46% higher BAP (95%CI: 32, 61) and 50% higher NTX (95%CI: 17, 91) with current breastfeeding. Among those not currently breastfeeding, those with higher BAP levels (third vs. first tertile) had 19% higher blood Pb levels (95%CI: 6, 33); those with higher NTX levels (third vs. first tertile) had 13% higher blood Pb levels (95% CI:-2, 31). We yielded similar results among those who had given birth in the past year. These data suggest increased blood Pb levels with current breastfeeding from greater bone turnover and skeletal mobilization of Pb. Given the health benefits of breastfeeding, replication of our findings and investigation into factors that mitigate skeletal mobilization of Pb are warranted.

Evaluating adult knowledge of child environmental lead exposures 5-8 years after the Flint water crisis Diana Haggerty*, Nate Peterson, Nicole Jones, Mona Hanna-Attisha, Jenny LaChance, Nate Peterson

After the Flint water crisis (FWC), a lead-in-water emergency that impacted the city of Flint, Michigan, the ongoing problem of lead exposure in United States' children was thrust into the spotlight. Our objective was to describe socio-demographic characteristics associated with a reporting adult's knowledge of their child's environmental lead exposure (ELE) among children enrolled in the Flint Registry (FR).

Adult respondents for children enrolled in the FR were asked if their child lives in or visits a home built prior to 1978 with chipping or peeling paint, has a sibling or playmate who was treated for lead poisoning or had an elevated blood lead level, or lives near an industrial site. Responses (yes, no, and don't know) were dichotomized into has knowledge (yes/no) or does not (don't know). We stratified by residency in the city of Flint, type of adult respondent (biological, step, adoptive, or foster parent vs. other), adult educational attainment, and duration of Flint residency during the FWC.

Our analysis included 6121 children (mean age 10.6 years) and 78% lived in the city of Flint. Most adult respondents were a parent (93.5%). Most adults knew if their child lived in a home built prior to 1978 (74.9%), if the child had a sibling or friend with an elevated blood lead level/poisoning (78.6%), and if they lived near an industrial site (85.6%). Adults of children living in Flint had less knowledge of housing age (25.8%), other children's blood lead levels (21.2%), and industrial site exposure (14.1%) compared to those who lived outside of Flint (17.5%, 17.7%, 9.6%, respectively). Knowledge also differed across adult respondent type, educational attainment, and duration of residency in Flint during the water crisis.

Though many adults reported knowing their child's ELEs, the frequency of not knowing was high for a community that experienced a lead-in-water crisis, suggesting lead awareness and mitigation education remain important childhood interventions.

Environment/climate change

The association between in-utero exposure to organophosphate esters in early and mid-pregnancy with birthweight is modified by maternal gestational diabetes Alicia Peterson*, Jennifer Ames, Yeyi Zhu, Juanran Feng, Monique Hedderson, Lisa Croen, Assiamira Ferrara,

Objective: Organophosphate esters (OPEs) are recently introduced flame retardants and plasticizers. This study assessed the relations between in-utero OPE exposure and birthweight-for-gestational-age Z-scores (BWZ). Potential effect modification by gestational diabetes (GDM) was assessed due to variations in associations possibly due to influences on nutrient metabolization, inflammation, and placental function.

Material and Methods: Urine from early (13.4±2.3 weeks) and mid (19.7±2.5 weeks) pregnancy was analyzed for eight OPEs and corrected for urinary dilution within the PETALS follow-up study participating in the NIH Environmental influences on Child Health Outcomes (ECHO) program. Linear regression models adjusted for mother's age, pre-pregnancy BMI, education, race/ethnicity, and parity assessed the association between OPE exposure (natural log transformed) and sex-specific BWZ. Interaction terms with GDM were included in analyses and models were stratified.

Results: Mothers (N=541) were 30.1±5.1 years old, 44% Hispanic, 20% Asian and 26% White, and 7% were diagnosed with GDM during pregnancy. Infants were born on average full term (39±2 weeks) weighing 3377±515 grams. Five OPEs were detectable in at least 50% of samples (BCEtP, BCPP, BDCPP, DBuP and DPHP) and showed moderate to strong correlations across the two urine collections (R= 0.28 – 0.75). While overall OPE exposure was not associated with BWZ, an interaction with GDM was observed for BCPP at both timepoints (p value <0.05). Specifically, exposure to higher levels of BCPP suggested a decrease in BWZ in infants of mothers with GDM (Early pregnancy: β -0.47, 95% CI -0.96, 0.02; Mid: β -0.36, 95% CI -0.78, 0.05), but not in infants of mothers without GDM (Early: β 0.002, 95% CI -0.67, 0.07; Mid: β -0.01, 95% CI -0.08, 0.06).

Conclusions: While these findings warrant replication in larger samples, they suggest that GDM may heighten susceptibility to prenatal exposure to specific OPEs on fetal growth.

Association of social and partner support with fecundability Molly Hoffman*, Collette Ncube, Sharonda Lovett, Julia Bond, Renée Boynton-Jarrett, Lauren Wise,

Background: Social connection is a key determinant of health and a priority area for the U.S. Surgeon General.

Methods: We used data from Pregnancy Study Online, a North American preconception cohort study (N=6,866). Eligible female participants completed a supplemental questionnaire (SQ) on psychosocial factors at baseline. We assessed past-year social support with an adapted 8-item version of the Berkman-Syme Social Network Index (SNI) and fecundability (per-cycle probability of conception) from bimonthly follow-up questionnaires. Summed SNI scores were categorized as <5 (socially isolated) and ≥5 (socially integrated). We assessed past-year partner support using 2 questions: "To what extent could you count on your partner to provide you with emotional support?"; "To what extent did your partner show you love and affection?" (response options: never, rarely, some of the time, most of the time, all the time). We used proportional probabilities regression to estimate fecundability ratios (FR) and 95% CIs, adjusted for age and history of infertility or miscarriage and weighted by the inverse probability of SQ completion.

Results: Social integration was common (93%) and associated with fecundability (FR 1.52; CI 1.32-1.74). Most participants reported "all the time" to questions about partner emotional support (53%) or love and affection (61%). Relative to those with no partner emotional support, fecundability was higher for those with support rarely (1.45; CI 1.07-1.95), some of the time (1.27; CI 1.03-1.56), most of the time (1.50; CI 1.25-1.79), and all the time (1.57; CI 1.32-1.87). Relative to those with no partner love and affection, fecundability was higher for those with partner love and affection rarely (1.09; 95% CI 0.63-1.89), some of the time (1.23; CI 0.90-1.68), most of the time (1.42; CI 1.06-1.90), and all the time (1.50; CI 1.12-1.99).

Conclusions: Social integration and partner emotional support and affection may have positive effects on fecundability.

Vegetarian Diets and Fertility Outcomes among Male Partners of Couples Undergoing Infertility Treatment Quynh Long Khuong*, Ellen Caniglia, Stefanie Hinkle, Enrique Schisterman, Julia DiTosto, Chanele Lomax, Erica Johnstone, Pauline Mendola, Jim Hotaling, Ginny Ryan, James Mills, Matthew Peterson, Douglas Carrell, Bradley VanVoorhis, Sunni Mumford,

Introduction: Infertility is a major global health concern and male factors contribute to approximately half the cases. Despite increasing popularity of vegetarian diets in recent years, evidence of an effect on male fertility is inconsistent. This study was conducted to evaluate associations between vegetarian diets and semen quality and live birth.

Methods: We applied the target trial emulation approach using data from the Folic Acid and Zinc Supplementation Trial (FAZST) conducted among couples seeking infertility treatment. Males aged 18 years or older completed four visits: baseline, 2-, 4-, and 6-month of follow-up for semen quality measurement; female partners aged 18-45 years were followed up to 18 months for live birth. We used linear mixed-effects models to compare six semen quality parameters between vegetarians and non-vegetarians, including semen volume and sperm concentration, motility, morphology, total motile count, and DNA fragmentation index. Log-binomial models were utilized for live birth, adjusting for relevant confounders.

Results: Among 2204 male partners, 30 followed a vegetarian diet for a median (interquartile range) of 9.0 (2.4–31.3) years at baseline. Probabilities of live birth were similar between vegetarians and non-vegetarians (33.3% vs. 35.3%; RR (95% CI): 1.00 (0.74–1.35)). No substantial differences in semen quality parameters were observed between the two groups, with β coefficients (95% CI) of 0.66 (0.10–1.23), -1.44 (-28.5–25.6), -1.79 (-8.29–4.72), -0.83 (-2.17–0.51), 17.5 (-51.8–86.8), 4.78 (-3.37–12.9), for semen volume, sperm concentration, motility, morphology, total motile count, and DNA fragmentation index, respectively.

Conclusion: We found no association between vegetarian diets and semen quality and live birth among male partners of couples seeking infertility treatment. These findings should be interpreted as exploratory with further studies needed to confirm our findings.

Association between Climatic Factors and Pregnancy Loss Stefania Papatheodorou*, Aashna Shah, Veronica Wang, Marc Weisskopf, Petros Koutrakis, Souzana Achilleos,

Background: Ambient climatic factors have been linked to multiple adverse pregnancy outcomes. However, only a few studies examined exposure to climatic factors and the risk of pregnancy loss. This study aims to examine the effects of climatic factors on pregnancy loss in Nicosia, Cyprus, an area that is highly affected by climate change.

Methods: Birth registry data for Nicosia, Cyprus from 2014-2019, were linked with daily meteorological and traffic pollution data (minimum and maximum temperature, ˚C; relative humidity, %; and NO2). Additional climactic variables (mean weekly temperature, standard deviation of the mean weekly temperature, heat index) were computed. We used a novel variation of time-series design and distributed lag models to explore the association between climatic factors and weekly live-birth identified conceptions (LBIC), to indirectly estimate pregnancy losses.

Results: In Nicosia (26,530 live births), an association between exposure to higher temperature and pregnancy loss was found between weeks 0-9, with the strongest association in weeks 0-1 weeks. Specifically, per 5 ˚C increase in mean temperature in week 0-1 we observed a lower rate of LBIC (Rate Ratio [RR]= 0.96 (95% confidence interval [CI]: 0.94 –0.98); the results for all other temperature-related and climatic exposures were similar. Furthermore, we found that temperature variability may have an impact in the later weeks of pregnancy. There is an association for weeks 20-35, with the strongest estimate in week 26 (RR= 0.93 (95% CI: 0.86 –0.99 per 5˚C increase in the standard deviation of the mean temperature).

Conclusion: Using the weekly conceptions ending in a live birth, we analyzed the association between climatic factors and pregnancy loss. The results show that exposure to higher temperatures and humidity is associated with pregnancy loss very early in pregnancy while temperature variability may have an effect between weeks 20-35.

Temporal Trends in Stillbirth and its Recurrence Risk in Successive Pregnancy in a Large Integrated Healthcare System Nana Mensah*, Vicki Chiu, Darios Getahun,

Background: We sought to examine the recent trends in stillbirths and their recurrence in successive pregnancies based on first-pregnancy stillbirth status and examined whether the recurrence risk is modified by race/ethnicity.

Methods: We performed a retrospective cohort study using data on 249,048 deliveries, extracted from the Kaiser Permanente Southern California electronic health records between 01/01/1998 – 12/31/2020. First, we examined temporal trends by comparing the most recent (2020) vs earlier (1998) rates. Recurrence risks were estimated for women with data on first two successive pregnancies (n= 124,524). Adjusted odds ratios (aOR) were used to estimate the magnitude of recurrence.

Results: Stillbirth rates from 1998 to 2009 remained relatively stable. From 2010 to 2020, stillbirth rates rose from 0.55% to 1.02%, respectively, representing an 85% increase in rates.

The percentage of stillbirth occurrence in second pregnancy among women with and without prior stillbirth were 1.51% and 0.33% respectively. After adjusting for maternal age, race/ethnicity, education, prenatal care and interpregnancy intervals, women who had a stillbirth in the first pregnancy had a nearly 7-fold (aOR, 6.7; 95% confidence interval [CI], 3.2-13.9) increased risk of having another stillbirth in the second pregnancy. Hispanic (aOR, 17.1; 95% CI, 6.7-43.4) women had higher risks of stillbirth recurrence.

Conclusion: Stillbirth in the first pregnancy is associated with an increased risk of stillbirth in a subsequent pregnancy. Furthermore, we observed that there is heterogeneity by race/ethnicity. Identifying at-risk populations may have implications for patient counseling.

Acute impact of air pollution on infant mortality in the San Joaquin Valley, California: A time-stratified case-crossover study Sneha Ghimire*, Alec M. Chan-Golston, Asa Bradman, Valerie Martinez, Sandie Ha,

Background: Infant mortality occurs at 5.60 deaths per 1,000 live births in the US. Evidence suggests air pollution may contribute to this risk. The San Joaquin Valley (SJV) of California continues to struggle with high levels of ozone (O3) and particulate matter ≤2.5 microns (PM2.5), highlighting a critical need to explore the link between these pollutants and infant mortality in this underserved area.

Methods: In this case-crossover study, we examined 1097 infant deaths (deaths < 1 year) in SJV, California (2016-2019). Daily O3 and PM2.5 levels were obtained from the SJV Air Pollution Control District's Community Multi-Scale Air Quality models and spatiotemporally linked to the maternal zip code at delivery. Conditional logistic regression models compared exposures shortly before infant death (case period) with times when no such event occurred (control periods) for the same mothers, thereby accounting for time-invariant factors. Case periods were the event day (lag0) and the preceding 14 days (lag1-lag14), with control periods selected by a time-stratified approach. Odds ratios (OR) and 95% confidence intervals (CI) were calculated for each 10-unit increase in exposures while adjusting for temperature and humidity.

Results: In the warm season (May-Oct), O3 exposure was associated with higher odds of infant death within two weeks with ORs ranging from 9-11%. The strongest association was observed within the same day of exposure (aOR lag0 1.11, 95% CI: 1.05,1.17). O3 associations were more pronounced among mothers aged 18-35 years and in high-income census tracts, though both low and high-income areas were affected. We found no sex-specific differences and were unable to explore race-specific variation due to a small sample.

Conclusions: Ozone exposure may influence infant mortality risk. As climate change progresses, rising temperatures are expected to increase ozone pollution. Thus, efforts to reduce air pollution exposures for infants are prudent.

Inpatient Hospital Costs Associated with Stillbirth in the US, 2016-2019 Ruiqi Cen*, Anthony Goudie, Wendy Nembhard, Wendy Nembhard

Background: Stillbirths occur more frequently in the US than infant deaths, and have significant impact on families, society, and the healthcare system. Despite their public health significance, current knowledge about the costs of stillbirths in the US is limited.

Methods: We used 2016-2019 data from the National Inpatient Sample of Healthcare Cost and Utilization Project (HCUP) to identify inpatient discharges for stillbirth and livebirth deliveries using International Classification of Diseases (ICD)-10 diagnosis codes from each record years old. Charges, length of stay (LOS), demographic factors (e.g., race/ethnicity), and maternal conditions (e.g., sepsis) were obtained from HCUP. Maternal conditions were identified using ICD-10 diagnosis and procedure codes. Hospitalization costs were calculated using the discharge and cost-to-charge ratio. Descriptive analyses and Gamma regression models were used to estimate hospitalization costs and LOS.

Results: In 2019, there were 26,480 inpatient discharges related to stillbirth deliveries and 3,382,834 inpatient discharges associated with livebirth deliveries. Total hospitalization cost among inpatient discharges related to stillbirth was $166.6 million dollars but increased to about $200 million dollars including professional fees. Mean hospitalization costs for a stillbirth were higher than for a livebirth ($6,293 vs $5,673) and this pattern persisted across the study period. Among stillbirths, non-White race/ethnicity, higher household income, region, and the presence of medical conditions increased mean hospitalization costs.

Conclusions: About $200 million is spent annually in the US on stillbirth-related hospitalizations. Each stillbirth inpatient incurred $620 more in hospitalization costs compared to their livebirth counterparts. Maternal complications greatly increased hospitalization costs among stillbirth inpatients.

Sexual Orientation Disparities in Pregnancy Loss: A Meta-Analysis of Three Longitudinal Cohorts Colleen Reynolds*, Payal Chakraborty, Tabor Hoatson, Jarvis Chen, Lori Chibnik, Janet Rich-Edwards1, Brittany Charlton, Payal Chakraborty

Background: Emerging research suggests sexual minority women may be at an increased risk of pregnancy loss, but these studies have adjusted for potential mediators and have not included certain subgroups (i.e., "mostly heterosexual" women).

Methods: We used data from three longitudinal cohorts: the Nurses' Health Study 2 and 3 and Growing Up Today Study (N=235,150 pregnancies from 85,547 participants). In each cohort, participants reported lifetime pregnancies and whether each pregnancy ended in an induced abortion, loss (miscarriage <20 weeks, stillbirth ≥20 weeks), ectopic/tubal, or livebirth, as well as their sexual orientation. We used log-binomial generalized estimate equation models to compare the risk of pregnancy loss among pregnancies to completely heterosexual participants (reference) to those among heterosexual participants with same-sex attractions/partnerships, mostly heterosexual, bisexual, and lesbian participants. To address confounding, selection, and multiple pregnancies per participant, models were weighted by the product of inverse probability of treatment, inverse probability of censoring, and inverse cluster size weights. Cohort-specific results were combined using fixed-effects meta-analysis.

Results: Pregnancies among heterosexual participants with same-sex attractions/partnerships (RR:1.07; 95%CI:1.02–1.13) as well as those among mostly heterosexual (1.27; 1.20–1.35), bisexual (1.50; 1.29–1.75), and lesbian (1.70; 1.45-1.99) participants were more likely to end in a loss than those to completely heterosexuals. Notably, risk of stillbirth was elevated among pregnancies to lesbian (3.48; 2.05–5.90) participants compared to those among completely heterosexuals; stillbirth risk was not elevated among other sexual minority subgroups.

Conclusion: Future research must examine mechanisms of sexual orientation-related inequities in pregnancy loss (e.g., heterosexism, maternal age, use of medically assisted reproduction, preconception health).

Genetics

Use of U.S. Administrative Data in Muscular Dystrophy Research: A Scoping Review Anne Havlik*, Natalie Street, Seth Perlman, Jamie Zimmerman, Catharine Riley,

Muscular dystrophies (MD) are a group of hereditary muscle disorders that result in progressive muscle weakness, decreasing mobility, and declining quality of life over time. Administrative healthcare data are a valuable resource that can augment public health surveillance and research, especially when small sample sizes are a challenge. A systematic literature search of Medline, Embase, CINAHL, and Scopus was performed to learn how U.S. administrative data have been used to study MD and identify opportunities and gaps in the research. Key search terms used were related to MD, administrative healthcare data, and healthcare utilization, which retrieved 1,270 bibliographic records; 854 unique abstracts and 53 full-text articles were reviewed. A standardized abstraction form was completed by 2 independent reviewers. Fifty studies met eligibility criteria and were included in the review. Studies used different approaches to MD case ascertainment, resulting in methodological and data quality heterogeneity. Seventeen publications included only claims administrative data, 9 included only inpatient administrative data, no publications included only outpatient administrative data, and 24 publications included at least 2 of these administrative data sources and other sources. Fifteen publications focused on pediatric populations, defined as including individuals less than 21 years of age. Thirty-five publications included populations outside of pediatric ages. This is the first scoping review of MD research using administrative data. Gaps identified include addressing differences in ICD code usage for MD subtypes, characterizing MD in young adult and older populations, and utilizing standardized diagnostic criteria as well as multiple sources of ascertainment. Implications may include enhanced evidence-based decision-making for individuals living with MD, their healthcare providers, and public health programs.

Global health

Evaluation of the Maternal Death Surveillance and Response (MDSR) System in the Kigoma Region, Tanzania Sifang Kathy Zhao*, Carly Malburg, Carrie Shapiro-Mendoza, Florina Serbanescu,

Background: In 2020, about 287,000 women died worldwide during or after pregnancy and childbirth. Most of these deaths occurred in low-income countries and are preventable. To reduce maternal mortality, many countries use Maternal Death Surveillance and Response (MDSR). Since 2015, Tanzania has used MDSR for monitoring deaths, reviewing causes, and implementing interventions. Kigoma, a Tanzanian region with the greatest need for improved maternal services, has not evaluated their MDSR.

Methods: Leveraging an ongoing collaborative evaluation with the Tanzania Ministry of Health, we visited all 11 hospitals and 29 health centers that provided maternity care in Kigoma during May 2023. We interviewed facility staff using a standardized questionnaire to assess how the 2019 Tanzania MDSR Guidelines were being implemented. We compared facility activities to national guidelines and assessed the regional MDSR system using the US Centers for Disease Control and Prevention guidelines for evaluating surveillance systems, specifically the attributes of acceptability (actual engagement in MDSR activities) and timeliness (reviews conducted within 7 days of death required by the national guidelines).

Results: Considering acceptability, all hospitals (100%) and most health centers (93%) had an MDSR coordinator, a review committee, and a formal system for reviewing maternal deaths. Only 36% of hospitals and 28% of health centers documented and reviewed community-occurring deaths. Reviews within 7 days of death were held in 73% of hospitals and 66% of health centers. Others held reviews monthly (27% hospitals; 3% health centers) or quarterly (24% health centers).

Conclusion: In Kigoma, acceptability of MDSR is high in hospitals and health centers. However, about 1 in 4 committees did not hold reviews within 7 days and most committees did not review community deaths. Improving timeliness and community reporting processes may strengthen MDSR and help reduce preventable maternal deaths.

Global health

GESTATIONAL WEIGHT GAIN AND ADVERSE PREGNANCY OUTCOMES IN SOUTH ASIAN AND SUB-SAHARAN AFRICAN WOMEN

Yuri Sebastião*, Ramachandran Thiruvengadam, Rasheda Khanam, Usma Mehmood, Jesmin Pervin, Ayushi , Bapu Desiraju, Fatma Kabole, Salahuddin Ahmed, Shaki Aktar, Md Chowdhury, Md Qazi, Imran Nisar, Javairia Khalid, Margaret Kasaro, Bellington Vwalika, Waqasuddin Khan, U Nu, Monjur Rahman, Sayedur Rahman, Gary Shaw, David Stevenson, Huan Xu, Bihila Bakari, Nitya Wadhwa, Ge Zhang, Sunil Sazawal, Nima Aghaeepour, Anisur Rahman, Fyezah Jehan, Abdullah Baqui, Jeffrey Stringer, Shinjini Bhatnagar,

Introduction: Studies of gestational weight gain and adverse pregnancy outcomes seldom focus on low-to-middle-income countries (LMICs), despite their high burden of morbidity and mortality. We examined gestational weight gain patterns and adverse pregnancy outcomes in a consortium of pregnancy cohorts from LMICs.

Methods: We analyzed data from five observational pregnancy cohorts in Bangladesh (2 cohorts), India, Pakistan, and Zambia. The study population comprised 15,286 singleton pregnancies with two/more maternal antenatal weight measurements. We estimated reference values for total pregnancy weight gain using longitudinal, random-intercept models and calculated weight-gain-for-gestational-age Z-scores. We then estimated the associated risks of preterm birth, low birthweight, and small-for-gestational-age, stratified by maternal body mass index (BMI), using marginal generalized linear models and plotted the non-linear trends in the association.

Results: The median baseline maternal and gestational age were 24 years and 12.9 weeks, respectively, with 23% of participants having underweight BMI. The median total gestational weight gain was 6.8 kg. The risk of preterm birth (13% overall) increased with lower weight gain Z-scores among underweight and normal BMI participants only. The risk of low birthweight (25% overall) increased with lower weight gain Z-scores in all BMI strata except obese participants. The risk of small-for-gestational age (36% overall) increased with lower weight gain Z-scores in all BMI strata.

 Conclusion: Gestational weight gain was associated with preterm birth, low birthweight, and small-for-gestational-age. Early pregnancy BMI modified the association between weight gain and outcomes in the study setting.

Diabetes and uterine fibroid diagnosis in midlife: Study of Women's Health Across the Nation (SWAN) Susanna Mitro*, Catherine Lee, Lauren Wise, Elaine Waetjen, Eve Zaritsky, Siobán Harlow, Samar El Khoudary, Daniel Solomon, Rebecca Thurston, Nanette Santoro, Monique Hedderson,

Background: Fibroids are non-cancerous uterine tumors that have been linked to cardiovascular risk factors. We examined prospectively the associations of glucose, insulin, sex hormone binding globulin (SHBG, a marker of insulin resistance), and diabetes with incidence of fibroid diagnoses in midlife.

Methods: Participants in the Study of Women's Health Across the Nation (SWAN) cohort (n=2570) reported fibroid diagnoses at enrollment (1996-1997) and 13 follow-up visits (1996-2013). At baseline and follow-up visits, we measured glucose, insulin, and SHBG in fasting blood samples and calculated homeostatic model assessment for insulin resistance (HOMA-IR). Diabetes was defined using glucose levels, self-reported diabetes, or diabetes medication use. We used discrete-time survival models to estimate hazard ratios (HR) and 95% confidence intervals (CI) for associations of time-varying biomarkers and diabetes with incident fibroid diagnoses, adjusted for demographics and healthcare utilization. We also evaluated effect modification by menopause status (hormone therapy use, premenopausal, perimenopausal).

Results: At baseline, 2.7% of participants (n=70) were using diabetes medication (n=11 using metformin). Time-varying glucose, insulin, HOMA-IR, and SHBG were not associated with incident fibroid diagnosis. However, diabetes was associated with a 28% lower incidence of fibroid diagnosis (adjusted HR: 0.72, 95% CI: 0.44, 1.17), driven by participants using metformin (adjusted HR: 0.49, 95% CI: 0.21, 1.12), though precision was limited. After stratification by menopausal status, higher HOMA-IR and insulin were associated with greater incidence of fibroid diagnosis during premenopause but not perimenopause, while the inverse association between diabetes and fibroids was strongest during perimenopause.

Conclusion: The effect of diabetes and biomarkers on fibroids may vary by menopause status. Fibroid risk may increase with insulin resistance and decrease with diabetes treatment.

Endometriosis typology and hyperlipidemia: Findings from the ARCHES retrospective cohort study Karen Schliep*, Bin Yan, Leslie Farland, Anna Pollack, Jing Wang, Saskia Spiess, Jessica Page, Jennifer Majersik, Alison Seitz, Hediyah Baradaran, Maggie Fuzak, Rachel Myer, Michael Varner,

Prior research has suggested endometriosis increases risk of hyperlipidemia; however, associations between endometriosis subtypes and hyperlipidemia have not been well-described. Additionally, data on whether race/ethnicity modifies the association between endometriosis and subsequent hyperlipidemia is lacking. Using the Utah Population Database, we performed a 25-year retrospective study (1996–2020) of 474,955 premenopausal women (n=81,838 women with endometriosis matched 1:5 by birth year (± 3 years) and birth state (UT/not UT) to n=393,117 women without endometriosis). Endometriosis cases were identified via electronic health records and categorized as superficial endometriosis (SE), ovarian endometriomas (OE) and/or deep infiltrating endometriosis (DE), or other site (OS) endometriosis (including bladder, abdomen, and lung). We used Cox proportional hazard models to estimate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for hyperlipidemia (ICD 9: 272.4* and ICD 10: E78.4*) comparing women with each type of endometriosis to women without endometriosis. Overall, women with, compared to without, endometriosis had a 1.34 higher aHR (95% CI: 1.28, 1.40) of hyperlipidemia after adjusting for birth state, birth year, race/ethnicity, age at baseline, and baseline parity, BMI, infertility, and smoking status. Compared to no endometriosis, women with OS had the highest aHR (1.76 [95% CI: 1.59, 1.96]), followed by DE and/or OE (aHR:1.54, [95% CI: 1.40, 1.69]), and SE (aHR: 1.22 [95% CI: 1.15, 1.28]). While we observed no effect modification by ethnicity, non-white vs. white women with endometriosis had a modest elevated risk for hyperlipidemia (aHR: 1.51 [95% CI: 1.32, 1.73] vs. aHR: 1.38 [95% CI: 1.34, 1.42]). Our findings indicate that women with endometriosis, notably OE, DE, and OS, have increased hyperlipidemia risk. This population, including under-represented women (~20% non-white Hispanic), may benefit from counselling regarding hyperlipidemia risk and prevention.

Birth outcomes and pregnancy complications among US service members by disaggregated Asian, Native Hawaiian and Pacific Islander, and American Indian and Alaska Native race and ethnicity, 2010-2021 Celeste Romano*, Clinton Hall, Monica Burrell, Anna Bukowinski, Jackielyn Lanning, Sandra Maduforo, Sandra Michelle Magallon, Zeina Khodr, Gia Gumbs, Ava Marie Conlin,

Introduction: A dearth of health disparities research has disaggregated data for US service members identifying as Asian and Native Hawaiian and Pacific Islander (NHPI) or reported health outcomes for racial and ethnic subgroups. Group representation is also underestimated when restricting group counts to those identifying as single race and non-Hispanic, especially for American Indian and Alaska Native (AIAN) and NHPI populations. Disaggregated estimates of health outcomes are needed to illuminate the experiences of military members identifying as Multiracial and Native and to elucidate patterns indiscernible in aggregated data.

Methods: Live births among pregnant service members were captured in Department of Defense Birth and Infant Health Research program data, 2010–2021. Self-reported race and ethnicity were obtained from personnel records. The prevalence of select birth outcomes and pregnancy complications, identified from medical encounter data, were calculated by disaggregated race and ethnicity.

Results: Overall, 216,017 births were identified among pregnant US service members and an increasing proportion occurred among Asian and Multiracial service members. Adverse birth outcomes and pregnancy complications varied in prevalence across racial and ethnic groups, particularly across Asian subgroups: Asian Indian and Filipino service members had consistently higher rates of adverse outcomes compared with other Asian subgroups and the total Asian population (eg, cesarean birth: 37.3% Asian Indian, 33.2% Filipino, 28.6% Asian). Multiracial AIAN and NHPI service members had higher rates of select adverse outcomes than their single-race, non-Hispanic counterparts (eg, low birth weight: 4.4 vs 3.8% AIAN; 4.9 vs 4.1% NHPI).

Conclusions: Increased attention should be paid to the disaggregation of racial and ethnic health outcomes among service members, especially given recognized disparities among racial and ethnic subgroups and the Multiracial population.

Association between discrimination and spontaneous abortion in a preconception cohort

Sharonda M. Lovett*, Lauren A. Wise, Jasmine Abrams, Molly N. Hoffman, Chad M. Coleman, Ruth J. Geller, Renée Boynton-Jarrett, Collette N. Ncube,

Introduction: Discrimination may increase risk of spontaneous abortion (SAB, pregnancy loss <20 weeks' gestation) via pathways such as heightened stress, limited access to societal resources, and exposure to adverse environments.

Methods: We examined associations of discrimination with SAB incidence among 5,586 participants who conceived in Pregnancy Study Online, a preconception cohort study (2013-2023). Eligible participants were 21-45 years, assigned female sex at birth, and U.S. or Canadian residents. We collected data on pregnancies and SABs at baseline and follow-up. Starting in 2019, we invited participants to recall discriminatory experiences using Williams' Everyday Discrimination and Major Experiences of Discrimination scales. We used age and race/ethnicity-adjusted Cox models to estimate hazard ratios (HR) and 95% CIs with gestational weeks as the time scale. We also explored effect modification by race/ethnicity.

Results: Seventeen percent of participants reported very high scores of everyday discrimination and 47% reported ≥1 event of lifetime discrimination. Job discrimination was the most prevalent lifetime experience (34%) while the most prevalent everyday experiences included others perceiving the participant as not smart (64%) and being treated with disrespect (63%). Everyday discrimination was positively associated with SAB. Relative to no everyday discrimination, HRs for low, medium, high, and very high scores of everyday discrimination were 1.11 (CI 0.90-1.37), 0.93 (CI 0.76-1.15), 1.13 (CI 0.91-1.39), and 1.20 (CI 0.97-1.49), respectively. Lifetime discrimination was also associated with higher SAB incidence (1 event: HR=1.02, CI 0.86-1.20, ≥2 events: HR=1.24, CI 1.07-1.45 vs. none). HRs for everyday discrimination, but not lifetime discrimination, were similar across race/ethnicity strata.

Conclusions: This is the first study of discrimination and SAB. Our findings suggest everyday and lifetime discrimination are associated with SAB incidence.

State patterns in maternal deaths due to disparity, 2018-2021 Lauren Rossen*, Ashley Hirai, Sarah Forrest, Amy Branum,

Maternal mortality is a major public health concern in the US. Given small numbers of events (generally <1000/year nationally), it is difficult to assess variation in maternal mortality and related disparities by state, as rates for many subgroups are unreliable. Spatial models can be used to produce more stable estimates for small geographic areas. A recent paper used spatiotemporal models to estimate state-level patterns in maternal mortality by race/ethnicity, but the focus was on trends over time from 1999-2019 and many single-year estimates were still unreliable.

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 2018-2021, tabulated by state of residence and race/ethnicity (Hispanic, and the following non-Hispanic [NH] groups: American Indian or Alaska Native [AIAN], Asian, Black, Native Hawaiian or Other Pacific Islander [NHOPI], and White). Log-binomial hierarchical Bayesian models with spatial random effects were used to estimate the number of maternal deaths per 100,000 live births by race/ethnicity, borrowing strength across states and racial/ethnic groups to produce more stable estimates of maternal mortality rates (MMRs). Deaths due to disparity were defined as the number of maternal deaths that could be avoided if all groups had the same rate as non-Hispanic White in each state.

The states with the largest annual number of maternal deaths due to disparities overall and for non-Hispanic Black women were Florida (15), Texas (14), Georgia (14), and New York (13). States with the highest percentages of maternal deaths due to disparity for NH Black women were New York, New Jersey, Colorado, and Mississippi (~66-71%). For NH AIAN women, Washington, Colorado, and Minnesota had the highest percentages.

More granular estimates of maternal mortality disparities at the state level could inform efforts to prevent maternal deaths and reduce inequities.

Health equity

Short- and long-term worry about racial discrimination and the risk of chronic hypertension (CHTN) and hypertensive disorders of pregnancy (HDOP) Sarah Heerboth*, Ebony Carter, Nadia Charguia, Rebecca Fry, Tracy Manuck,

Intro: Racial discrimination is associated with adverse health outcomes among Black individuals in the US, but the mechanisms are poorly understood. We hypothesized that discrimination-related worry is associated with stress and resultant vascular reactivity, and thus sought to determine if worry about racial discrimination is associated with CHTN and/or HDOP.

Methods: Primary analysis of a prospective cohort. Participants identifying as Black, White, and/or Hispanic, with singleton, non-anomalous gestations were recruited <22 weeks, 2017-2022, and completed the Krieger Discrimination Scale. Primary outcomes = CHTN ± HDOP (gestational HTN, preeclampsia, eclampsia), considered together and separately. We evaluated long-term (as a child/teen, > age 18) and short-term (as an adult, past 12 months) worries about others in their racial or ethnic group and themselves experiencing racial discrimination for each outcome.

Results: 435 individuals (43% Black, 38% White, 19% Hispanic) were included; 84 (20%) had CHTN ± HDOP (64 had CHTN, 38 had HDOP, 18 had both). Surveys were completed at a mean 17.1 (IQR 16.0-19.7) weeks. Compared to those without CHTN ± HDOP, those with CHTN ± HDOP reported more long-term worry about racial discrimination against others (51% vs. 29%, p<0.001) and themselves (45% vs. 25%, p<0.001). A similar percentage of those with and without CHTN ± HDOP reported short-term worry about racial discrimination against others (50% vs. 39%, p=0.15) and themselves (40% vs. 33%, p=0.30). In separate regression models, any childhood worry (aOR 3.5, 95% CI 1.2-11), any worry about others (aOR 4.5, 95% CI 1.2-17), and any worry about self (aOR 3.2, 95% CI 1.0-10), but not any worry as an adult (aOR 1.5, 95% CI 0.5-4.4) were associated with CHTN ± HDOP. Results were similar considering CHTN and HDOP separately.

Conclusion: Pregnant adults who as children worried about others or themselves experiencing racial discrimination have an elevated risk of CHTN ± HDOP.

Chlamydia, Gonorrhea, and Syphilis Infections among Pregnant Persons with Substance Use Disorders Jessica Frankeberger*, Christina Chambers,

Introduction: Sexually transmitted infections (STIs) in pregnancy are associated with numerous adverse maternal and infant outcomes. Identifying and treating STIs among high-risk groups, such as those with substance use disorders (SUDs), is essential. This study aimed to examine factors associated with chlamydia, gonorrhea, and syphilis in pregnant persons with SUDs.

Methods: We used a retrospective cohort study of pregnant persons who delivered singleton infants in California (CA) from 2011-2021. Birth certificates were linked by the Study of Outcomes of Mothers & Infants to maternal hospital records. SUDs and STIs were identified by ICD-9 or 10 codes in pregnancy. Logistic regressions examined the association of STIs and sociodemographic, prenatal care, rural vs. urban residence, and pregnancy interval.

Results: Among those with an SUD (n=62,904), 3.0% had chlamydia, 0.8% gonorrhea, and 1.5% syphilis documented in pregnancy. Of those with an STI, 11% had more than one infection. Chlamydia was associated with younger age (adjusted odds ratio [AOR]=0.94, 95% confidence interval [CI]=0.93-0.95); having Medicaid (AOR=1.21, 95%CI=1.07-1.38); being Hispanic (AOR=1.36, 95%CI=1.21-1.52) or non-Hispanic (NH) Black (AOR=1.66, 95%CI=1.44-1.90) vs. NH White; not having a high school degree (AOR=1.47, 95%CI=1.19-1.83); and receiving inadequate prenatal care (AOR=1.45, 95%CI=1.31-1.60). Similar results were found for gonorrhea and syphilis with two exceptions: syphilis was associated with older age (AOR=1.04, 95%CI=1.03-1.05) and rural residence (AOR=1.37, 95%CI=1.37-1.80). For those with a prior birth, short pregnancy intervals were associated with lower odds of all STIs (AOR=0.56-0.81).

Conclusions: Among pregnant persons with SUDs, STIs are associated with socioeconomic factors, being a racial/ethnic minority, and poor prenatal care. There remains unmet need and improved prevention and screening are required to ensure maternal and infant health among an already high-risk population.

Parental support in adolescence: a potential moderator of the relationship between experienced racial discrimination and suicidality outcomes in adulthood Natalie Guerrero*, Fangqian Ouyang, Patrick Monahan, Steven Brown, Tamika Zapolski, Matthew Aalsma,

Background

Racial discrimination experiences have significant negative impacts on multiple mental health outcomes. Thus it is critical to understand supportive factors that may help mitigate its effects. Supportive family environments positively impact adolescent health, yet less is known about the impact of family support on adult health outcomes as a consequence of experiences of racial discrimination.

Purpose

The primary objective of this study was to evaluate parental support in adolescence as a potential moderator of the relationship between racial discrimination and mental health, specifically suicidality, in adulthood.

Methods

We used data from waves I (grades 7-12), IV (ages 24-32), and V (ages 32-42) from the National Longitudinal Study of Adolescent to Adult Health. The primary exposure was racial discrimination at waves IV and V, measured by surveys of race-based discrimination adapted from the Everyday Discrimination Scale. The primary outcome was suicidality at wave V measured by the question "During the past 12 months, have you ever seriously thought about committing suicide?" The potential moderator, parental support at wave I, was measured using 10 questions about relationships with respondents' mother and father figures. Logistic regression was used to model suicidality outcomes. We adjusted for race and ethnicity, sex assigned at birth, self-rated health, education, housing, and insurance status in a multivariate logistic regression model. We included an interaction term to determine whether the relationship was moderated by parental support.

Results

The sample was racially and ethnically diverse. Nearly 11% were Hispanic. Non-Hispanic groups included: 59% White, 22% African-American, 4% multi-racial, 2.8% Asian, 0.5% American-Indian, and 0.7% other. Nearly 33% of the sample (N=1825) experienced racial discrimination at Wave IV or V. Over 46% of American-Indian and 39% of multi-racial participants experienced racial discrimination, as well as nearly 39% of African-American and 34% of Hispanic participants. Over 5% of the sample reported suicidality at Wave V. Univariate logistic regression models showed that racial discrimination was associated with an increased likelihood of suicidality during adulthood (Odds Ratio = 3.03, 95% Confidence Interval = [2.35, 2.92]). Multivariate models showed similar findings. However, maternal, paternal, and overall parental support in adolescence did not moderate

this relationship.

Conclusions

In this study, parental support in adolescence did not moderate the relationship between racial discrimination and suicidality in adulthood. Parental support includes a variety of behaviors that may not have been fully captured in the measures used in this study. Potential moderating effects should be evaluated using alternative measures of parental support that may better capture these behaviors.

Mental health

Differences in Prenatal Depression by Maternal Race and Ethnicity: A Retrospective Cohort Study Kendria Kelly-Taylor*, Sara Aghaee, Joshua Nugent, Ayesha Sujan, Nina Oberman, Ai Kubo, Elaine Kurtovich, Charles Quesenberry Jr, Kathryn Ridout, Lyndsay Avalos,

Existing studies suggest that Black and Hispanic persons experience significantly higher rates of prenatal depression compared to White persons, yet little is known how these rates differ among subgroups of Hispanic (e.g., Mexican) and Asian (e.g., Korean) populations. The study examined racial and ethnic subgroup differences in prenatal depression (PND) diagnosis and severity among a large cohort of pregnant persons universally screened for depression. A retrospective cohort of pregnant persons receiving prenatal care at Kaiser Permanente Northern California from 2013 to 2019 (n=258,452) were analyzed. Twenty racial and ethnic groups were obtained from birth records, and depression diagnosis, severity (measured using the Patient Health Questionairre-9 [PHQ-9]), and covariates (maternal age, parity, education, neighborhood deprivation, delivery year) were captured via electronic health records. We calculated age-adjusted prevalence rates and used modified Poisson regression models to estimate adjusted relative risks (aRR). Puerto Rican persons had the highest prevalence of PND (25.3%), followed by Native American (23.5%) and Black (20.9%) persons, while Hmong persons had the lowest prevalence (4.3%). Severe depression (PHQ-9 15+) was highest among Black persons (7.5%) and lowest among Asian Indian (2.9%) persons. Puerto Rican, Black, and Native American persons had higher risks of PND compared to White persons in unadjusted models (RR:1.34, 95%CI: 1.22-1.48; RR:1.08, 95%CI: 1.04-1.11, RR:1.17, 95%CI: 0.98-1.40, respectively). In the adjusted models, the associations were attenuated (aRR:1.05, 95%CI: 1.03-1.07; aRR:1.00, 95%CI: 0.99-1.01; aRR:1.03, 95%CI: 1.00-1.06, respectively). Substantial variation in the prevalence and risk of depression diagnosis and severity were observed. The findings suggest differences in maternal characteristics and socioeconomic factors may partially explain racial and ethnic disparities in prenatal depression.

Mental health

DSM-5 Eating Disorders in a National Sample of Sexual and Gender Minority Adults: Examining the role of body size and Adverse Childhood Experiences Christine Ramsey*, Phillip Schnarrs, Armin Dorri, Joshua Rosenberger, Stephen Russell, Amy Stone, Marissa Burgermaster,

Objectives: To estimate the prevalence of DSM-5 eating disorders (EDs) in a national sample of sexual and gender minority (SGM) adults, and to examine associations between adverse childhood experiences (ACEs), overweight and obesity, and eating disorder symptom severity.

Methods: Participants were 3,281 SGM adults recruited using a national Qualtrics research panel. Prevalence of EDs were reported overall and stratified by body mass index (BMI). Associations between ACEs, BMI, and ED symptoms were examined in adjusted linear regression models.

Results: 26.7% of participants met criteria for an ED, including: anorexia nervosa: 1.2%, atypical anorexia nervosa: 7.0%, bulimia nervosa: 7.0%, and binge eating disorder: 11.5%. 65% of participants with an ED reported an overweight or obese BMI. In adjusted models, having an overweight ($\beta=0.60$, $p<0.001$) or obese ($\beta = 1.03$, $p<0.001$) BMI and having more ACEs ($\beta = 0.10$, $p<0.001$) were associated with greater eating disorder severity.

Conclusions: EDs are prevalent in SGM adults, particularly in those with larger body sizes and ACEs.

Policy Implications: These findings caution against providing general weight-loss advice to individuals with overweight and obesity without first assessing EDs and ACEs.

Association between HPA Axis Dysregulation and Postpartum Depression/Anxiety in Breastfeeding vs Bottle-feeding Parents Katharine Bruce*, Kathryn Wouk, Karen Grewen, Brenda Pearson, Alison Stuebe, Anna Bauer,

Objective: Hypothalamic-pituitary-adrenal (HPA) axis dysregulation has been implicated in pathogenesis of perinatal mood disorders. We hypothesized that 1) postpartum depression/anxiety symptoms would be associated with HPA axis dysregulation, indexed by loss of expected adrenocorticotropic (ACTH)-cortisol (CRT) coupling, and 2) this association would vary by method of infant feeding.

Methods: Participants intending to breastfeed were recruited in their 3rd trimester of pregnancy. During a lab visit at 2 months postpartum, depression and anxiety symptoms were assessed (Beck Depression Inventory score ≥14 and/or Speilberger State-Trait Anxiety Inventory score ≥40). Participants then breast or bottle-fed their infants as they would at home. After a 10-minute rest, participants completed the Trier Social Stress Test (TSST), a standardized stressor involving speech and math tasks. Blood ACTH and CRT were measured 10 minutes after feeding, during each task, and at 10, 20, and 30 minutes recovery. Multilevel models evaluated whether coupling of ACTH at time j with CRT at time j+1 differed between those with and without depression/anxiety symptoms, and whether differences varied by feeding method.

Results: Of 205 participants who completed the TSST, 44 had depression/anxiety symptoms at the 2-month visit. Depression/anxiety was associated with reduced ACTH-CRT coupling (adjusted beta: -0.03; p-value: 0.04). Among those who breastfed, those with depression/anxiety showed greater blunting of ACTH-CRT coupling than those without (adjusted beta: -0.04; p-value: 0.02), while those who bottle fed had similar coupling patterns regardless of depression/anxiety (adjusted beta: -0.01; p-value: 0.85).

Conclusion: HPA axis response was blunted in those with postpartum depression/anxiety symptoms, and blunting varied by feeding method. Findings support HPA axis dysregulation in perinatal mood disorders. Future research should explore how infant feeding method may modify this relationship.

Mental health

Maternal Postpartum Depressive Symptoms and Infant Meal Frequency from 6 to 12 Months of Age Xuanxuan Zhu*, Jihong Liu, Edward A. Frongillo, Anwar T. Merchant, Bo Cai, Sara Wilcox,

Background. Feeding in early life is crucial. Maternal postpartum depression (PPD), a major maternal morbidity that may be related to adverse feeding practices, its association with infant meal frequency has remained unclear in high-income countries such as the United States (US). This study aims to evaluate the longitudinal association between PPD and the frequency of infant meals from 6 to 12 months of age.

Methods. Data came from the Infant Feeding Practices Study II, which followed mother-infant dyads from the third trimester of pregnancy until the infant was 12 months old. PPD symptoms were measured by the Edinburgh Postpartum Depression Scale (score range: 0-30) at 2 months postpartum with a score of 13 or higher classified as having PPD. Typical daily meal frequency in the past 7 days was reported every 1-1.5 months from 6 to 12 months postpartum. Linear mixed models were used to examine the longitudinal association between PPD symptoms and infant meal frequency.

Results. Among 1,997 mother-infant dyads, 9.4% of the mothers had PPD. The mean infant meal frequency on a typical day from 6 to 12 months postpartum was 6.5 ($\pm$1.4) and 6.7 ($\pm$1.2) feedings among mothers without and with PPD symptoms, respectively. Having PPD symptoms was associated with higher infant meal frequency from 6 to 12 months postpartum, both before and after adjusting for covariates (Crude: β= 0.17, 95% CI: 0.01, 0.33, p-value = 0.04; Adjusted: β= 0.21, 95% CI: 0.06, 0.37, p-value = 0.01).

Conclusion. Mothers with PPD symptoms were more likely to feed infants at a higher frequency during 6-12 months postpartum. Further, it might provide evidence for the mechanism of how postpartum affects infant growth. Additional studies measuring infant feeding practices are needed in the future with more comprehensive and objective measures such as the food group and feeding amount.

Men's health

Women's pregnancy history and partners' cardiovascular mortality Liv Grimstvedt Kvalvik*, Rolv Skjærven, Gerhard Sulo, Aditi Singh, Quaker E. Harmon, Allen J. Wilcox,

Background: A woman's full pregnancy history is associated with her risk of dying from atherosclerotic cardiovascular disease (CVD). We assessed whether a woman's total pregnancy history is associated with her spouse's risk of dying from CVD.

Methods: In this population-based, prospective study we used data from Norwegian registries including The Medical Birth Registry of Norway, in the period 1967-2020. We identified 566 187 men born after 1944 and registered as partner to women with a pregnancy in 1967 or later, and surviving to age 40. The main outcome is premature CVD mortality (up to age 69) across their partners reproductive history by categories of combined parity (1, 2, 3, or 4 recorded pregnancies) and number of complicated pregnancies (preterm delivery <35 gestational weeks, preeclampsia, placental abruption, perinatal death (stillbirth or death within first 7 days) and term or near-term birth weight <2700grams). Men whose partners had three pregnancies and no complications had lowest CVD risk and served as the reference group. Estimates were adjusted for women's birth year.

Results: For fathers contributing with up to two pregnancies, the risk of premature CVD increased with increasing number of complicated pregnancies. For men contributing to 3-4 pregnancies, the shape of the association was less clear, peaking at two complications [HR=1.8; 95% confidence interval 1.2-2.8).

Conclusions: While the number of pregnancy complications seem to increase CVD mortality for women in a linear pattern, this seem not to be the case for their partners. Pregnancy history seems to be less useful in prediction of men's risk of dying from CVD. CVD risk factors are known to increase risk of pregnancy complications. However, the correlations between partners of diet, SES, and other CVD risk factors are apparently not strong enough to produce a strong pregnancy-related CVD risk in male partners.

Validity of endometriosis diagnosis and subtypes within the Utah Population Database: Findings from the ENDO study Karen Schliep*, Amber Kiser, Karen Eilbeck, Leslie Farland, Anna Pollack, Jenna Krall, Jennifer Majersik, Saskia Spiess, Rachael Hemmert, Rachel Myrer, Michael Varner, Joseph Stanford,

Routinely collected health records are an attractive data source for life course epidemiology projects, particularly data sources with long intervals between exposures and outcomes. However, validation of primary exposure and outcomes should be conducted to identify potential misclassification. We compared linked ICD-9 Utah Population Database (UPDB) endometriosis diagnoses and subtypes (test method) with "gold standard" research-based endometriosis diagnoses and subtypes (reference method) within the Endometriosis, Natural History, Diagnosis, and Outcomes (ENDO) Study. Previously, we reported high inter- and intra-surgeon agreement for endometriosis diagnosis in the ENDO study. ENDO participants ages 18–44 with no prior endometriosis diagnosis from Utah who underwent gynecologic laparoscopy or laparotomy, regardless of indication, were eligible (n=412). We compared the accuracy between ENDO research diagnoses and medical record diagnoses over the same time frame (2007–2009). There were 173 (42%) with an ENDO gold-standard diagnosis, while 179 (43%) had a UPDB medical record diagnosis. For endometriosis diagnosis, we found relatively high sensitivity and specificity (0.88 [95% CI: 0.83, 0.93] and 0.87 [95% CI: 0.82, 0.91], respectively) and substantial agreement (kappa [κ] = 0.74]). We found similar high sensitivity, specificity, and agreement for superficial endometriosis (n=143, 0.86, 0.83, κ=0.65) and ovarian endometriomas (n=38, 0.82, 0.92, κ=0.58). However, deep infiltrating endometriosis (n=58) had lower sensitivity (0.12 [95% CI: 0.05, 0.21]) and agreement (κ=0.17), with high specificity (0.99 [95% CI: 0.98, 1.00]). US cohorts (BWHS, GUTS, NHSII) have reported high accuracy between self-report and medical record diagnoses for endometriosis (>70%) but that deep endometriosis is often absent in the medical records. This study showed that similar high agreement can be found for endometriosis diagnoses in administrative healthcare records, including the UPDB.

Evaluating pregnancy and infant health outcomes on a geographically dispersed population with universal health insurance: The Department of Defense Birth and Infant Health Research program Anna Bukowinski*, Gia Gumbs, Monica Burrell, Clinton Hall, Zeina Khodr, Jackielyn Lanning, Sandra Maduforo, Sandra Michelle Magallon, Celeste Romano, Ava Marie Conlin,

In existence for over two decades, the Department of Defense Birth and Infant Health Research (BIHR) program leverages administrative medical data to evaluate pregnancy and infant health outcomes among live births to US military medical beneficiaries, a population with universal health insurance through TRICARE. Included infants are born to active duty, Reserve/Guard, or retiree military members (i.e., sponsors) or their dependent spouses in the US and abroad. Data are compiled from the Military Health System Data Repository (MDR), which houses inpatient and outpatient encounter data from military and civilian facilities, and Defense Manpower Data Center (DMDC), which contains TRICARE enrollment and eligibility data, as well as demographic and military/occupational data on the sponsor. Using established linking algorithms, MDR and DMDC data are used to create sponsor-birthing parent-infant linkages to define the BIHR infant cohort, routinely capturing parent/infant data from the year prior to pregnancy through the first year of life and beyond. Outcomes (e.g., major birth defects, gestational diabetes) are identified from diagnostic and procedure codes and are examined overall and/or for specific populations (e.g., in utero vaccine-exposed infants). More nuanced assessments are possible when the birthing parent is the sponsor, as data for military personnel are more extensive. Electronic health records are also available for care received at military facilities, providing opportunities for validation and additional data collection. The BIHR program currently includes data on over 2.8 million infants born in 1998-2021, with approximately 100,000 infants added annually. Approaches are continuously reevaluated and refined to keep pace with evolutions in medical codes and military electronic data, thus ensuring that the program data are a reliable tool for continually monitoring the health of military families.

Molecular

Sexual dimorphism in human placental cell type composition during pregnancy: an RNA sequencing deconvolution secondary analysis Kyle Campbell*, Tiffany Russell, Kelly Bakulski, Elana Elkin,

The placenta is a vital transient organ for fetal development. Cellular composition directly impacts placental function. However, little is known about the sexual dimorphism in the cellular composition of the human placenta throughout pregnancy. To elucidate differences in cell composition by sex, we estimated cell type proportions from existing bulk placenta RNA sequencing data through deconvolution. We analyzed 12 publicly available bulk human placental RNA sequencing datasets. To identify sex-specific gene expression differences and enriched biological pathways, we conducted differential gene expression (fold-change>2, false discovery padj<0.05) and biological process gene set enrichment analysis (padj<0.05). To estimate placental cell type proportions, we deconvoluted bulk tissue samples with our external single-cell gene expression placental reference dataset. To test for differences in cell composition by sex stratified by trimester, we performed beta regression. We analyzed 165 female and 189 male samples across 12,023 genes. There were 160 first trimester samples, 16 second trimester samples, and 178 third trimester samples. We observed 73 differentially expressed genes in the first trimester, 3 in the second trimester, and 5 in the third trimester. Extravillous trophoblasts, a key developmental placental cell type, were more abundant in second trimester female placentas than male placentas (20.9 vs. 11.9%, p-value = 0.024). Cell proliferation pathways such as the hallmark G2/M cell cycle checkpoint (padj<0.001) were upregulated, and oxidative phosphorylation (padj=0.001) downregulated among male placentae compared to females in the second trimester. We observed evidence of sexually dimorphic placental cell composition alongside increased proliferation and decreased aerobic respiration among males vs. females during mid-pregnancy. Our results may provide insight into the etiology of sex-specific patterns of fetal-maternal health outcomes.

Nutrition/obesity

The association between maternal lactogenic hormones and breastfeeding outcomes

Danielle O'Hare*, Regina Schlichting, Courtney Hanson, Sadia Saizy, Seth Sherman, Rajesh Kumar, Pauline Mendola, Akila Subramaniam, Andrew Williams,

Placental lactogenic hormones, prolactin and lactogen, promote maternal adaptations for breastfeeding. Due to alteration of maternal metabolic and immune response, asthma may alter placental hormone levels which may impair lactation. We examined the association between lactogenic hormones and breastfeeding outcomes in women with and without asthma in the B-Well-Mom study.

Serum drawn at 30 weeks(range 27-36 weeks) gestation was available for 206 women (157 with asthma and 49 without). Prolactin(ng/mL) and lactogen(ng/mL) concentrations were measured via enzyme-linked immunosorbent assay method in duplicate and averaged. Participants self-reported breastfeeding initiation and 2-month breastfeeding duration. Logistic regression models estimated odds ratios and 95% confidence intervals for the association between hormone levels and breastfeeding outcomes, overall and by asthma status. Asthma*hormone interaction terms were fit.

Overall, 83.5%(N=172) of women ever breastfed and a greater proportion of women with asthma(84.7%, n=133)) breastfed than women without asthma(79.6%, n=39)). Women with asthma had lower mean levels of lactogen(9.8ng/ml vs 11.33ng/ml) and prolactin(6.5ng/ml vs 7.1ng/ml) than women without asthma. Compared to low levels(quartile 1), high levels of lactogen(quartile 3) were associated with increased odds of 2-month breastfeeding duration(OR:3.76 95%CI: 1.05, 13.50), and the association differed by asthma status(women with asthma OR: 5.26 95%CI:1.13,24.52; women without asthma OR:4.44 95%CI:0.16,119.78; p-interaction=0.04). Lactogen was not associated with breastfeeding initiation. Prolactin was not associated with breastfeeding outcomes.

Overall, high levels of lactogen are associated with longer breastfeeding duration. The benefit of high lactogen may be greater for those with asthma, given the significant interaction term. These results suggest that lactogenic hormones differ in women with and without asthma and can affect breastfeeding duration.

Nutrition/obesity

Sitting through dinner in toddlers: an early indicator of diet quality? Edwina Yeung*, Diane Putnick, Akhgar Ghassabian,

Autistic-like traits even in a general population have been associated with diet quality. Less is known about autism-related meal behaviors and diet quality as early as toddlerhood after foods have been introduced.

Parents of the Upstate KIDS study reported frequency of their toddlers consuming specific food items and other eating behaviors at 30 and 36 months. A quality score was calculated based on the Youth Healthy Eating Index (HEI) and using items on frequencies of vegetables, fruits, dairy, meat, fish, legumes, soy, eggs, and sweetened beverages and on weekly frequencies of fast food, breakfast intake and multivitamin use. Six items from the validated Brief Autism Mealtime Behavior Inventory (BAMBI) were calculated into a composite score to measure autistic-like behaviors in the context of mealtimes (range 6-28). Generalized linear models were used to account for repeated responses among 3245 toddlers, adjusting for maternal sociodemographics and pre-pregnancy BMI, paternal education, daycare use, and frequency of eating organic foods.

Food intakes of the same children at both time points (n=1955) had intraclass correlation coefficients of 0.43-0.51, in range with reports in adults. Mean (SD) HEI was 44.4 (8.6) and mean BAMBI was 10.7 (2.5). Higher BAMBI was associated with lower diet quality (B=-0.58; 95%CI: -0.68, -0.48). Therefore, individual BAMBI items were evaluated. Positive behaviors of willingness to try new foods (B=1.50; 95%CI: 1.27-1.73), being flexible about mealtime routines (B=0.55; 0.30-0.80) and remaining seated at the table until a meal is finished (B=0.86; 0.65-1.06) were independently associated with better HEI. Negative behaviors of self-injury and refusing foods that require chewing were associated with lower diet quality, but not aggressive behaviors at mealtime. Adjustment for birth outcomes, child sex and plurality did not alter results.

In conclusion, autistic-related meal behaviors can serve as indicators of diet quality in toddlers.

Maternal magnesium intake and preterm birth among nulliparous women Yijia Zhang*, Meghan Angley, Cynthia Gyamfi-Bannerman, Mirella Mourad, Ka Kahe,

Background and Objectives Magnesium is vital for maintaining uterine relaxation and preventing premature contractions. Its link to preterm birth has been studied, yet the evidence is primarily from small-scale clinical trials and observational studies conducted several decades ago. We examined the association between magnesium intake and preterm birth in a large cohort of nulliparous women in the United States.

Methods This study used data from the Nulliparous Pregnancy Outcomes Study: Monitoring Mothers-To-Be (NuMoM2b). After excluding women with chronic hypertension, pre-gestational diabetes, and chronic kidney disease, and women without dietary magnesium data, a total of 7,513 participants were included in the final analysis. The Modified Block 2005 Food Frequency Questionnaire was used to assess the intake of magnesium and other dietary constituents in the three months prior to pregnancy. Preterm birth was defined as a live birth before 37 weeks of gestation. Spontaneous preterm birth was defined as being preterm birth without indicated preterm delivery for maternal or fetal conditions. Multivariable logistic regression was used to calculate odds ratios (ORs) and 95% confidence intervals (CIs) for the associations between magnesium intake (in quartiles) and the outcomes.

Results After adjustment for potential confounders including demographic, lifestyle, medical, and dietary factors, higher magnesium intake was associated with lower odds of preterm birth (n=399). The adjusted ORs and 95% CI across quartiles 1 to 4 were 1.00, 0.86 (0.63, 1.16), 0.77 (0.55, 1.08), and 0.64 (0.41, 0.97), ptrend = 0.04. The association was attenuated when spontaneous preterm birth (n=266) was the outcome. The adjusted ORs and 95% CI across quartiles 1 to 4 were 1.00, 0.94 (0.65, 1.37), 0.89 (0.59, 1.34), and 0.76 (0.46, 1.28), ptrend = 0.28.

Conclusion The findings suggest that higher pre-conception magnesium intake is associated with lower risk of preterm birth.

Maternal early pregnancy body mass index and risk of insomnia in the offspring Mia Zhu*, Sven Cnattingius, Louise O'Brien, Eduardo Villamor,

Objectives: To investigate the association between maternal early pregnancy body mass index (BMI) and risk of insomnia in the offspring.

Methods: We conducted a nationwide cohort study among 3,281,803 singleton live births in Sweden born 1983-2015. Using national registries with prospectively recorded information, we followed participants for an insomnia diagnosis from 2 to up to 35 years of age. We compared insomnia risks by maternal early pregnancy BMI categories using hazard ratios (HR) with 95% confidence intervals (CI) from adjusted Cox models. To assess if this association was explained by unmeasured factors shared within families, we conducted sibling-controlled analyses among 1,724,473 full siblings and studied the relation of maternal full sisters' BMI and insomnia risk in 1,185,998 offspring.

Results: There were 7,154 insomnia diagnoses over a median follow-up age of 17.9 years. Maternal early pregnancy BMI was positively associated with offspring insomnia risk; compared with women with normal BMI (18.5-24.9), adjusted HR (95% CI) of offspring insomnia for maternal BMI categories overweight (BMI 25.0-29.9), obesity class I (BMI 30.0-34.9), and obesity classes II or III (BMI ≥35.0) were, respectively, 1.22 (1.14, 1.30), 1.60 (1.45, 1.77), and 2.11 (1.83, 2.45). Corresponding adjusted HR (95% CI) in sibling comparisons were, respectively, 1.32 (1.05, 1.65), 1.48 (1.03, 2.14), and 1.56 (0.91, 2.65). Associations with full maternal sisters' BMI were attenuated, suggesting a weak role for unmeasured shared factors. Early pregnancy BMI was also associated with primary insomnia in a dose-response manner. Pregnancy, birth, and neonatal complications were associated with risk of insomnia in offspring but did not substantially mediate the association between maternal obesity and offspring insomnia.

Conclusions: Maternal overweight and obesity severity are associated with offspring insomnia risk in a dose-response manner. This association is not fully explained by shared familial factors.

Comparison of Tdap vaccination immunogenicity between pregnant and non-pregnant women in an active duty population Zeina Khodr*, Anna Bukowinski, Gia Gumbs, Francisco Mimica Porras, Clinton Hall, Gabriel Pineda, Abigail Mangilog, Piotr Wisniewski, Ava Marie Conlin,

Background: It is recommended for pregnant women to receive a tetanus, diphtheria, acellular pertussis (Tdap) vaccine at 27-36 weeks of pregnancy to provide passive immunity to infants through the first months of life. Still, there are conflicting findings for how pregnancy status at vaccination may modify a woman's long-term immune response. Here we assessed change in anti-pertussis toxin (Anti-PT) immunoglobulin G (IgG) serum levels following Tdap vaccination in pregnant and non-pregnant women.

Methods: This retrospective, cohort study included 240 active duty women of childbearing age who were pregnant at Tdap vaccination, and 1:1 matched with non-pregnant women on age, time between vaccine and serum collection, and receipt of other same day vaccines (2011-2016). Pregnancy status was determined through linkage with the Department of Defense (DoD) Birth and Infant Health Research program and serum samples (0-6 weeks before and 9-15 months after Tdap vaccine) were obtained from the DoD serum repository. Associations of pregnancy status at time of Tdap vaccine with change in anti-PT IgG levels, standardized by time between vaccine and sample collection, were estimated through multivariable log-normal regression models.

Results: Anti-PT IgG levels increased from geometric mean titers of 7.2 U/ml (95% confidence intervals [CI]: 6.6–7.9) prior to Tdap vaccination to 24.9 U/ml (95% CI: 23.1–26.8) following vaccination for both pregnant and non-pregnant women. Models adjusted for matching variables, race and ethnicity, and military rank did not yield significantly different results for change in anti-PT IgG levels by pregnancy status at vaccination (b=-.05, p=.6089).

Conclusions: Immunogenicity of Tdap vaccine does not appear to be modified by pregnancy status at time of vaccine. Women Tdap vaccinated in pregnancy have similar immune responses as those vaccinated outside of pregnancy, and likely will not need more boosters than already outlined in the current schedule.

Maternal predictors of inflammation and oxidative stress pathways during early pregnancy

Barrett Welch*, Paige Bommarito, David Cantonwine, Ginger Milne, Alison Motsinger-Reif, Matthew Edin, Darryl Zeldin, John Meeker, Thomas McElrath, Kelly Ferguson,

Background. Inflammation and oxidative stress are critical to pregnancy, but most evidence has focused on downstream, non-causal indicators. Oxylipins are lipid mediators of inflammation and oxidative stress that act through many biological pathways. Our aim was to characterize predictors of circulating oxylipin levels based on maternal characteristics.

Methods. Our study consisted of 901 pregnancies in the LIFECODES Fetal Growth Study. We measured oxylipins in early pregnancy plasma and urine samples. We evaluated oxylipins across maternal predictors, including characteristics of participants' pregnancy, socioeconomic determinants, and obstetric and medical history.

Results. Current pregnancy and sociodemographic characteristics were the most important predictors of circulating oxylipins. Plasma oxylipins were lower and urinary oxylipins higher for participants with a later gestational age at sampling (13-23 weeks), higher prepregnancy BMI (obesity class I, II, or III), Black or Hispanic race and ethnicity, and lower socioeconomic status (younger age, lower education, or uninsured). For example, compared to those with normal or underweight prepregnancy BMI, participants with class III prepregnancy obesity had 45-46% lower plasma epoxy-eicosatrienoic acids, the anti-inflammatory oxylipins produced from enzymes, and had 81% higher urinary 15-series F2-isoprostanes (IsoP), an indicator of oxidative stress produced from non-enzymatic oxidation. Similarly, in urine, Black participants had 92% higher prostaglandin E2 metabolite, a pro-inflammatory oxylipin, and 41% higher 5-series F2-IsoP, an oxidative stress indicator.

Conclusions. In this large pregnancy study, we found that circulating oxylipins were different for participants of lower socioeconomic status or systematically marginalized racial and ethnic groups. Our results provide new insight into links between maternal predictors and inflammation and oxidative stress.

Exposure to organophosphate esters and gestational weight gain: New insights from a large prospective cohort Barrett Welch*, Paige Bommarito, David Cantonwine, Maria Ospina, Antonia Calafat, John Meeker, Thomas McElrath, Kelly Ferguson,

Background. Organophosphate esters (OPEs) are flame retardants and plasticizers widely used in consumer products and suspected of disrupting metabolic health during pregnancy. The aim of this study was to determine the associations between maternal exposure to OPEs and gestational weight gain, an important risk factor for short- and long-term maternal and child health.

Methods. Within the LIFECODES Fetal Growth Study of 900 pregnant participants (2008-2018), we measured OPE biomarkers in 3 urine samples per participant and abstracted maternal weight measures (median = 15 per participant) from medical records. Weight gain z-scores at delivery and across pregnancy were calculated using reference values for gestational age and prepregnancy BMI. Associations between averaged OPE biomarkers and total weight gain at delivery were estimated using linear (z-score) and multinomial (high or low vs. adequate) regression models, and longitudinal weight gain (z-scores) using linear mixed-effects models.

Results. Most participants had total weight gain that was high (56%) or adequate (37%) based on clinical guidelines. The majority of OPE biomarkers were inversely associated with weight gain. A doubling in bis(1,3-dichloro-2-propyl) phosphate (BDCIPP) was associated with a mean difference (MD) in total weight gain z-scores of -0.11 (95% confidence interval [CI]: -.17, -.05), which was consistent with longitudinal weight gain z-scores (MD = -0.12, 95% CI: -0.19, -0.05). Conversely, a doubling in di-n-butyl phosphate (DNBP) was positively associated with total weight gain (MD = 0.24, 95% CI: 0.03, 0.50). Associations were consistent across clinical categories of total weight gain.

Conclusions. In a large prospective cohort, biomarkers of OPE exposure were associated with maternal weight gain, including reduced or increased gains. These findings suggest that OPE exposure in pregnancy may impact maternal metabolism.

Low-dose aspirin prophylaxis for preeclampsia and the risk of postpartum cardiovascular outcomes: a propensity score analysis Ema Mujic*, Sojourna Ferguson, Christina D. Yarrington, Nyia Noel, Samantha E. Parker,

Background: The U.S Preventative Service Task Force recommends initiating low-dose aspirin (LDA) before 16 weeks of pregnancy to prevent developing preeclampsia among people with certain risk factors. While there are robust data supporting the effectiveness of LDA for the prevention of preeclampsia, limited data exist regarding its impact on postpartum outcomes.

Methods: We abstracted electronic medical record data on pregnant people who had a live birth from 2018-2019 and met criteria for LDA prophylaxis (n=1,862) at single safety-net hospital. We created propensity scores using major and moderate risk factors and prenatal care site and used 1:1 matching to identify unexposed (LDA-) matches for the 376 patients that received a prescription for LDA at ≤ 16 weeks of gestation (LDA+). Postpartum outcomes included anti-hypertensive use, postpartum hypertension and readmission. We calculated risk ratios (RR) and 95% confidence intervals (CI) for LDA and postpartum outcomes using log-binomial models. We also assessed the joint effect of LDA and preeclampsia on postpartum outcomes by calculating RRs for combinations of LDA and preeclampsia using those without either as the reference.

Results: After propensity score matching, our sample included 318 LDA+ and 318 LDA- patients with a similar distribution of preeclampsia risk factors. LDA+ was not associated with the postpartum outcomes examined in the overall cohort. However, in the presence of preeclampsia, LDA- patients had the highest risk of postpartum outcomes (e.g. hypertension; RR: 9.09; CI: 6.05, 13.65), while LDA+ patients saw an attenuation in risk (e.g. hypertension; RR: 6.77; CI:4.27, 10.74). (Figure)

Conclusion: Our findings suggest that LDA prescription does not decrease the risk of postpartum cardiovascular-related postpartum outcomes in diverse population of those at risk of preeclampsia. However, among those affected by preeclampsia, antepartum exposure to LDA may attenuate the risk of these outcomes.

Patterns of postpartum acute care utilization in a health care system in the Southeastern United States, 2021-2023 Clara Busse*, Brian Pence, Catherine Vladutiu, Katherine Tumlinson, Christine Tucker, Alison Stuebe,

Postpartum acute care utilization (PACU), including visits to an emergency department, obstetric triage, or urgent care ("outpatient"), and hospital admission, is an indicator of postpartum health status. We estimated the incidence of PACU and examined PACU patterns by sociodemographic factors, birth characteristics, and medical indications. Using electronic health record data from a quaternary maternity hospital in the Southeastern United States, we constructed a retrospective cohort of people aged ≥18 years who delivered ≥1 liveborn infant >20 weeks of gestation from July 1, 2021 to December 31, 2022. PACU data throughout the health care system were collected through March 31, 2023. Time zero for PACU was defined as the day of discharge from the birth hospitalization, not birthdate, to avoid immortal time bias. We excluded those with a hospital stay >6 days (n=29) allowing us to estimate the 12-week incidence of PACU. In this cohort of 6,041 postpartum people, 11.1% (95% confidence interval [CI]: 10.3%, 11.9%) had ≥1 outpatient visit (range: 0-6) and 3.2% (95% CI: 2.7%, 3.6%) had ≥1 hospital admission (range: 0-4) within 12 weeks of discharge. In bivariate analyses, some groups had a disproportionately high 12-week incidence of PACU. These populations included people who were non-Hispanic Black, English speaking, unmarried, had a Cesarean birth, had an infant in the intensive care unit, or had diagnosis codes indicating a high comorbidity burden or a major mental health disorder. The median time to first PACU was 10 days after the birth hospitalization discharge date for outpatient visits and 6 days for hospital admissions. Perinatal complications (e.g., endometritis, disruption of obstetric wound) and perinatal hypertension were the two most frequent indications for first outpatient PACU and first hospital admission. These findings can inform efforts to direct health resources to improve postpartum care.

Maternal asthma status modifies the relation between placental size and infant size at birth Regina Schlichting*, Sadia Saizy, Danielle O'Hare, Courtney Hanson, Raj Kumar, Seth Sherman, Akila Subramaniam, Pauline Mendola, Andrew Williams,

Pregnancies complicated by maternal asthma are at higher risk for low birthweight. While placental size is positively associated with birthweight, less is known regarding the role of the placenta among pregnancies complicated by asthma. Using the asthma-enriched B-WELL-Mom cohort we examined the association between placental size and infant size to better understand the potential modifying role of maternal asthma.

292 women(220 with asthma; 72 without) had placental weight(g), length(cm), width(cm), and thickness(cm) measured by pathologists. Birthweight(BW; g), length(BL; cm), and head circumference(HC; cm) were measured within 24 hours postpartum. Linear regression models estimated the association(β) and 95% confidence intervals(CI) between placental size and infant size. For each of the infant measures (BW, BL, HC), we fit separate models for each placental measures as the predictor of interest (weight, length, width, thickness). Asthma*placenta interaction terms were fit. Models, overall and by asthma status, were adjusted for maternal demographic and health factors, and infant characteristics.

On average, infant measures were 3078g for BW, 49cm for BL, and 33cm for HC, and average placental measures were 459gm for weight, 18cm for length, 16cm for width, and 2cm for thickness. Overall, there were positive associations between placental size and infant size. By asthma status, women with asthma typically had a stronger association (6 of 6 models) between placental length and width with infant size. For example, placental length had a stronger association with birthweight among women with asthma (68.69g, 95%CI:44.96,92.41) than without (32.53g 95%CI:-15.10,80.17; p-interaction<.20). The association between placental weight and birth size did not differ by asthma status.

Placental size measures were positively associated with infant size. Further research is warranted to better understand physiologic aspects of potential modifying role of maternal asthma.

Trends and racial/ethnic inequities in Maternal Cardiovascular Health in California Elleni Hailu*, Suzan Carmichael, Jonathan Snowden, Audrey Lyndon, Mahasin Mujahid,

Background: To address the maternal health crisis in the United States, it is important to closely examine the epidemiologic trends of maternal cardiovascular health (CVH), a leading determinant of adverse pregnancy-related outcomes.

Methods: We used state-wide birth hospitalization records from California (1997-2019; N=10,953,764) to examine the prevalence, trends, and racial/ethnic disparities of hypertensive disorders of pregnancy (HDP; chronic hypertension (HTN), gestational HTN, preeclampsia, eclampsia), and pre-pregnancy and gestational HTN separately. We also examined ideal CVH before and during pregnancy using the subset of the data with information available on clinical CVH indicators (2007-2019; N= 6,122,590) constructed based on smoking, HTN, diabetes, and Body Mass Index (kg/m2). We utilized a series of log-binomial and modified Poisson regression models (with robust standard errors) adjusting for year, maternal age, education, insurance, and parity to determine our estimates.

Results: The prevalence of outcomes increased over time for all racial/ethnic groups. Compared to Non-Hispanic White (White) individuals, Non-Hispanic Black (Black) birthing people had a higher risk of HDP (Risk Ratio (RR)=1.57; 95% Confidence Interval (CI): 1.55, 1.58), and both pre-pregnancy (RR=2.38; 95% CI: 2.34, 2.42) and gestational (RR=1.46; 95% CI: 2.34, 2.42) HTN. American Indian/Alaska Native individuals were less likely to have ideal CVH both before (RR=0.69; 95% CI: 0.68, 0.70) and during pregnancy (RR=0.64; 95% CI: 0.63, 0.65) compared to White birthing people. Racial/ethnic disparities for all outcomes widened over time, except for pre-pregnancy HTN, in which disparities comparing Black and American Indian/Alaska Native birthing people with White individuals slightly decreased during the study period.

Conclusion: Our findings confirm persistent racial/ethnic disparities in maternal CVH, highlighting the need to investigate the structural drivers of these inequities.

Birth spacing recommendations: a one-size-fits-all approach may not be appropriate Julie Petersen*, Mahsa Yazdy, Anne Marie Darling, Martha Werler,

Background: Guidelines strongly advise people who recently gave birth to wait 6 months before attempting the next pregnancy and consider interpregnancy intervals (IPI) of ≥18 months as optimal. We sought to evaluate whether age modifies associations between IPI and preterm birth.

Methods: We utilized data from the National Birth Defects Prevention Study (United States, 1997–2011) restricted to multiparas controls with livebirths in the two most recent pregnancies. IPI between the prior birth and the study pregnancy was categorized as <6, 6–11, 12–17, 18–23 (reference), 24–59, or ≥60 months. The study pregnancy was considered preterm if delivered at <37 0/7 weeks' gestation. We stratified by age at the prior birth, categorized as <25 (n=2484), 25–29 (n=1626), or ≥30 (n=1209) years. We estimated risk ratios (RR) between IPI and preterm birth using Poisson regression, adjusting for measured potential confounders. We conducted a multiple quantitative bias analysis to adjust for exposure-outcome dependent misclassification and selection bias. We computed e-values for any lower bounds of the RR 95% confidence intervals (LBCI) that were >1.0 after multiple bias adjustment.

Results: Preterm birth risk was highest with <6 months IPI (covariate-adjusted RR point estimates ≥1.3 in all age groups; 25–29 years had the strongest association). Preterm birth risk was lowest with 6–17 months IPI among ≥30 years. Associations tended to move downward but these patterns remained after adjustment for multiple biases, with the greatest attenuation among 25–29 years, although the LBCI for <6 months IPI remained >1.0 (e-value=2.4).

Conclusions: People ≥30 years may benefit from shorter IPI than currently recommended, possibly to avoid increased risks associated with advanced age (e.g., reduced fecundability, chronic health conditions, pregnancy complications). Residual confounding is unlikely to explain the <6 months IPI-preterm birth association among people 25–29 years.

Obstetric health

Incidence rate of fasting and postload hyperglycemia after a history of gestational diabetes mellitus Na Zeng*, Jimmy Yang, Shi Wu Wen,

Introduction Women with gestational diabetes mellitus(GDM) have a significant higher risk of future diabetes compared to those without GDM. The incidence rate of the diabetes among those women has been underestimated given that majority stakeholders relying on the fasting glucose alone or glycated haemoglobin missed a large portion of cases with impaired glucose tolerance alone. Furthermore, since the risk of complications, such as cardiovascular events, are different between fasting hyperglycemia and post-load hyperglycemia, summarising the incidence rate of various types of hyperglycemia after pregnancy would bear public health significance. This review aims to fill this gap in the scientific literature.

Methods and analysis Comprehensive literature searches were performed in the following electronic databases: MEDLINE, EMBASE and CINAHL to retrieve relevant papers from inception to Jul 12, 2023. Meta analyses were conducted for the estimated incidence rate for overall diabetes or prediabetes, further being categorised by fasting hyperglycemia, post-load hyperglycemia, and both of them respectively, if the included studies were relatively homogeneous($I2>50\%$). Inverse-variance random-effects model was used along with the Freeman-Tukey double arcsine transformation for stabilising the variances. Subgroup analyses were implemented according to the diagnosis criteria of GDM, diabetes, race, age group, follow-up time to increase the robustness of this review.

Results A total of 18 studies were selected to include for data analysis with a total of 1,070,000 women diagnosed with GDM and with postpartum oral glucose tolerance test (OGTT) during postpartum. The incidence rate of diabetes or prediabetes after GDM was found to be 100 per 1000 person-years (95%CI, 100-300). Specifically, the incidence rate of fasting hyperglycemia, post-load hyperglycemia, both were the same: 100(95%CI, 0-400), 100(95%CI, 100-400), 100(95%CI,100-200) per 1000 person-years respectively. Further subgroup analysis would be reported during the conference presentation.

Conclusion The available literature supports the perspective that the incidence rate of diabetes has been underestimated in recent decades. Our review findings stressed the significance of application of OGTT for postpartum diabetes screening to capture those with impaired glucose intolerance. The finding is very important for health service planning and evaluation, policy development. Large-scale long-term prospective studies, using the national data are warranted to provide firm evidence over coming years.

Other

National Institutes of Health (NIH) Peer Review Process, Application Assignment, and Opportunities for Review at the Center for Scientific Review (CSR) CYNTHIA AGUMANU MCOLIVER*,

The National Institutes of Health (NIH) administers >$48B (FY22) of federal funding for extramural biomedical research, with over 83% of these funds awarded to 300,000 scientists and 2,500 institutions nationwide. Applications are received through Grants.gov and then distributed to the appropriate scientific review group (either study section or special emphasis panel) following standard review guidelines. The Reproductive, Perinatal, and Pediatric Health (RPPH) study section and several others focus on neonatal, perinatal and pediatric exposures and outcomes, and maternal, obstetric, and reproductive health.

Each year, the NIH Center for Scientific Review (CSR) is responsible for conducting the initial scientific peer review of over 75% of the nearly 90,000 grant applications submitted to the NIH each year. CSR's mission is to see that NIH grant applications receive fair, independent, expert, and timely scientific reviews – free from inappropriate influences – so NIH can fund the most promising research.

The scientific review officer (SRO) leads the study section and is the designated federal official for the peer review meeting. The SRO's responsibilities include recruiting and inviting experts for peer review, conducting reviewer training, and implementing NIH and CSR policies and best practices for peer review. Aside from SRO recruitment of reviewers, members of the scientific community also can self-nominate for consideration for service as ad hoc members of peer review panels. This may involve sending biosketches/CVs to the SRO, face-to-face communications at conferences, or telephone calls. NIH values and supports the participation of early career scientists in the review process and has established the Early Career Review Program, https://public.csr.nih.gov/ForReviewers/BecomeAReviewer/ECR.

To learn more about the CSR peer review process as an applicant or potential reviewer, visit www.csr.nih.gov.

Prevalence and treatment of chronic hypertension during pregnancy in a U.S. cohort, 2008-2021 Stephanie Leonard*, Sara Siadat, Elliott Main, Krista Huybrechts, Yasser El-Sayed, Mark Hlatky, Jheanelle Atkinson, Brian Bateman,

Background: Treatment of chronic hypertension during pregnancy has been shown to reduce the risk of adverse perinatal outcomes.

Objectives: In this study, our objectives were to examine the patterns of use of antihypertensive medications among pregnant individuals with chronic hypertension, and to assess the impact of the updated 2017 hypertension guidelines of the American College of Cardiology and American Heart Association (ACC/AHA) on the prevalence and treatment of chronic hypertension during pregnancy.

Methods: We analyzed the MerativeTM Marketscan® Research Database of commercial insurance claims in the United States from 2007 to 2021. We included individuals with continuous enrollment from three months prior to pregnancy through delivery. We identified chronic hypertension cases and assessed oral antihypertensive medication use during pregnancy. We performed interrupted time series analyses to assess whether the 2017 ACC/AHA hypertension guidelines increased the proportion of individuals diagnosed with chronic hypertension or treated with oral antihypertensive medications during pregnancy.

Results: The prevalence of chronic hypertension steadily increased from 1.8% to 3.7% among 1,899,561 pregnancies between 2008 and 2021. Medication use for chronic hypertension in pregnancy was relatively stable (58-60%) over the study period, and varied modestly among subpopulations with high-risk comorbidities (56-67%). The proportion of pregnant individuals with chronic hypertension treated with methyldopa or hydrochlorothiazide decreased over the study period (from 29% to 3% and from 11% to 5%, respectively), while the proportion treated with labetalol or nifedipine increased (from 19% to 42% and from 9% to 17%, respectively). The 2017 ACC/AHA hypertension guidelines did not have a significant effect on the prevalence or treatment of chronic hypertension during pregnancy.

Conclusions: The prevalence of chronic hypertension in pregnancy doubled between 2008 and 2021 in this nationwide cohort of individuals with commercial insurance. During the study period, labetalol replaced methyldopa as the most commonly used antihypertensive. However, only about 60% of patients with chronic hypertension in pregnancy were treated with antihypertensive medications.

Incidence of pregnancy among childbearing-age women with warfarin treatment Motohiko Adomi*, Krista Huybrechts, Sonia Hernandez-Diaz1, Priyanka Anand, Seanna Vine, Elyse DiCesare, Ariel Freedman, Yanmin Zhu, Yanmin Zhu

Due to potential teratogenicity, warfarin is contraindicated in pregnancy except in patients with mechanical heart valves. Currently, there are no Risk Evaluation and Mitigation Strategies from regulatory agencies to prevent pregnancy among childbearing-age women on warfarin treatment. Since 45% of pregnancies in the US are unplanned, warfarin-exposed pregnancies are likely to occur. We therefore aim to estimate the incidence of pregnancy among childbearing-age female warfarin users and to examine pregnancy outcomes among those who become pregnant.

Using nationwide MarketScan 2003-20 and Medicaid 2000-18 databases, we identified a cohort of 12- to 55-year-old women who initiated warfarin. We followed patients until warfarin discontinuation, pregnancy start date, end of enrollment or study period, whichever occurred first. We matched the two cohorts by age and estimated (1) the incidence of pregnancy with bootstrap confidence intervals (CI) among warfarin users stratified by indications, and (2) the proportion of non-live births out of all pregnancies.

We identified 467,034 and 697,551 warfarin treatment episodes in MarketScan and Medicaid, respectively (mean age: in MarketScan and 41.7 in Medicaid). The incidence of pregnancy among warfarin users was 8.8 (8.4-9.3) per 1,000 person-year in MarketScan, and 18.6 (95% CI, 18.1-19.2) in Medicaid, which decreased to 10.9 (10.4-11.4) after matching on age. The incidence was 12.1 in MarketScan and 17.8 in Medicaid among patients with venous thromboembolism (VTE), and 5.4 in MarketScan and 7.1 in Medicaid among patients with valve disorders. In both cohorts, about 45% of warfarin-exposed pregnancies ended with non-live births.

It is not uncommon for childbearing-age women to become pregnant on warfarin treatment, with a higher incidence among patients with VTE than patients with valve disorders. The risk of non-live birth was higher among warfarin-exposed pregnancies compared with the general population.

Antidepressant and Psychotherapy Initiation Among Patients with New Episodes of Depression During Pregnancy Kristin Palmsten*, Jingran Cao, Lyndsay Avalos, Yihe Daida, Gabriela Vazquez-Benitez, Sonya Negriff, Amy Loree, Rebecca Rossom, Heather Lipkind, Sherryl Goodman, Celeste Pappas, Yannica Martinez, Kirsten Ehresmann, Elisabeth Seburg, Jingran Cao

In the United States (US), fewer than half of pregnant persons with a new episode of depression initiate antidepressants or psychotherapy. We identified predictors of treatment initiation among patients with a new depression episode during pregnancy. Using electronic health data from 5 US healthcare systems, we identified pregnancies ending in livebirth or stillbirth from 2008-2021 among prenatal care patients with a new depression episode (i.e., a depression diagnosis during pregnancy with no diagnosis, antidepressants, or psychotherapy in the 6 months before pregnancy), and no antidepressant or psychotherapy initiation before their first depression diagnosis during pregnancy. Treatment initiation was defined as an antidepressant or psychotherapy visit within 90 days of first depression diagnosis. We used modified Poisson regression to assess associations between potential predictors and treatment initiation (any versus no) adjusting for site and year. There were 34,194 (5%) patients with a new depression episode during pregnancy. The mean age was 30 years, 14% had public insurance, 35% were non-Hispanic White; 8% initiated antidepressants only, 15% initiated psychotherapy only, 6% initiated both, and 72% did not initiate either treatment within 90 days of diagnosis. Patients were less likely to initiate treatment when their first depression diagnosis occurred in obstetric (prevalence ratio [PR]: 0.30, 95% confidence interval [CI]: 0.29-0.32) or primary care settings (PR: 0.60, CI: 0.56-0.63) versus behavioral health settings; when they had gestational diabetes (PR: 0.79, CI: 0.75-0.83), a history of depression (PR: 0.78, CI: 0.75-0.81), or used other psychotropic medications (PR: 0.83, CI: 0.79-0.87). Patients with ≥1 previous birth (PR: 1.18, CI: 1.13-1.22) or anxiety (PR: 1.25, CI: 1.21-1.29) were more likely to initiate treatment. These findings suggest opportunities for interventions to facilitate treatment for new episodes of depression during pregnancy.

Patterns of Aspirin Use for Preeclampsia Prevention in an Ethnically Diverse Population-Based Cohort of Women in Canada Sabrina Chiodo*, Joel G. Ray, Zhiyin Li, Longdi Fu, Hilary K. Brown, Eyal Cohen, Isabelle Malhamé, Farzin Khosrow-Khavar, Falan Bennett, Arjumand Siddiqi, Sonia M. Grandi,

Introduction: The risk of preeclampsia and preterm births is reduced by low-dose aspirin prophylaxis. Among women at moderate or high risk of preeclampsia, clinical guidelines recommend aspirin initiation at <16 weeks' gestation. Real-world data on aspirin use in pregnancy and characteristics of these women are lacking, as aspirin is available over-the-counter rather than by prescription. Even in countries with universal healthcare, such as Canada, aspirin is not universally covered. This study evaluated aspirin use during pregnancy among a cohort of ethnically diverse women.

Methods: The study included women (15-49 years) with a recorded livebirth/stillbirth in Ontario, Canada (2018-2022). Linked health administrative databases captured prophylactic aspirin use <20 weeks. Clinical and sociodemographic characteristics of aspirin users vs. non-users were compared at 20 weeks' gestation, using standardized differences (SD), with a SD >0.10 indicating an important difference between exposure groups.

Results: Among 600,543 pregnant women, 3817 (0.6%) used aspirin daily. The mean age of aspirin users was 31 (±5) years, 43% were nulliparous, and 24% immigrants, of whom >95% originated from a non-Western nation. Among women with pregestational hypertension, 8% were on aspirin, and among those with pregestational diabetes, 6% were on aspirin. Aspirin users were more likely than non-users to be obese (SD=0.41), have a history of preeclampsia (SD=0.64), or pregnancy complications (SD=0.45). In contrast, non-users were less likely to have adequate prenatal care (SD=0.19) and to be seen by an obstetrician (SD=0.11), compared to aspirin users.

Discussion & Future Directions: These initial findings suggest suboptimal use of aspirin in women for which use is indicated, which may be related to social disparities. Forthcoming analyses will examine the effect of aspirin use on other pregnancy complications and whether these associations vary by sociodemographic factors.

A Target Trial of Pre-conception Switch from a Legacy Medication to a New Medication – An Application to Antiretroviral Therapy and Birth Outcomes
Ellen Caniglia*, Rebecca Zash, Modiegi Diseko, Judith Mabuta, Mompati Mmalane, Shahin Lockman, Gloria Mayondi, Gaerolwe Masheto, Joseph Makhema, Roger Shapiro,

Background: In-utero exposure to certain medications have differential effects on adverse birth outcomes. The introduction of new medications with more favorable safety profiles offers an opportunity to reduce risk by switching from high- to lower-risk medications prior to pregnancy. We emulated a target trial of pre-conception switch from a legacy high-risk medication (nevirapine, NVP) to a new lower-risk medication (dolutegravir, DTG) among individuals with HIV on adverse birth outcomes.

Methods: The Tsepamo Study has performed birth outcomes surveillance at delivery sites in Botswana since 2014. Among individuals on legacy HIV medication (NVP) in 2016, when the programmatic switch to DTG as standard of care began, we compared those who switched to DTG and then became pregnant with those who did not switch prior to pregnancy. We estimated adjusted risk ratios (RRs) for stillbirth, neonatal death, preterm delivery, very preterm delivery, small-for-gestational-age (SGA), very SGA, and combined endpoints of any adverse or severe adverse outcome. We also evaluated low (<50kg) and high (80kg) early pregnancy weight and hypertension in pregnancy.

Results: Of 4,265 eligible individuals, 26% switched from NVP to DTG prior to pregnancy. Comparing switchers with non-switchers, RRs (95% CIs) were 0.82 (0.75, 0.89) for any adverse and 0.84 (0.71, 1.00) for any severe adverse outcome. These differences were driven by SGA and very SGA. Switchers were less likely to have low and more likely to have high early pregnancy weight. Sensitivity analyses indicated little evidence for time-trends in birth outcomes over the study period.

Conclusions: Switching from legacy to newer medications with more favorable safety profiles prior to conception can improve birth outcomes. Among individuals with HIV, switching from NVP to DTG prior to pregnancy may reduce the risk of low maternal weight in early pregnancy and fetal growth restriction.

Associations of glyphosate and aminomethylphosphonic acid (AMPA) with length of gestation and birth size Kelsi Morris*, Brad Ryva, Maria Cinzori, Khyatiben Pathak, Patrick Pirrotte, Brook Lovell, Susan Schantz, Rita Strakovsky,

Background: Pregnant women are exposed to the herbicide glyphosate and its major metabolite aminomethylphosphonic acid (AMPA), but their associations with birth outcomes are unclear. We evaluated associations of glyphosate and AMPA with birth outcomes and considered differences by fetal sex and pre-pregnancy BMI (ppBMI).

Methods: Illinois pregnant women (n=300) provided urine samples at median 13 weeks gestation for glyphosate and AMPA assessment. We calculated gestational age at birth using ultrasound-confirmed due date and birth date. We measured body length and head circumference within 24 hours of birth and calculated sex-specific birthweight (BW)-for-gestational-age z-scores (BWz). In primary analyses, we used multivariable linear regression to evaluate associations of specific gravity-adjusted glyphosate or AMPA with birth outcomes. We conducted secondary analyses stratified by fetal sex in which we added a multiplicative interaction term to consider differences by ppBMI.

Results: The median (25th, 75th percentile) birthweight was 3515.3 g (3231.9, 3838.5) and gestational age at birth was 39.4 weeks (38.6, 40.3). Glyphosate levels were lower than in other U.S. women. Overall, each 2-fold increase in glyphosate was associated with -21.4g lower BW (95% confidence interval (CI): -48.7, 5.9) and -0.05 lower BWz (95%CI: -0.11, 0.01). These associations were due to women carrying males (BW: β = -31.2, 95%CI: -63.1, 0.7; BWz: β = -0.06, 95%CI: -0.1, 0.0). Further, in women with overweight or obesity carrying males, each 2-fold increase in glyphosate was associated with -40.7g lower BW (95%CI: -80.8, -0.6) and -0.08 lower BWz (95%CI: -0.2, 0.00). Glyphosate was not associated with other birth outcomes. AMPA was not associated with any birth outcomes.

Conclusion: This pilot study points to differences in associations of glyphosate with fetal growth by fetal sex and maternal ppBMI. Future studies may need to consider underlying mechanisms and implications of our findings.

Maternal and Neonatal Outcomes in Term Births for Gestational Diabetes Mellitus Complicated Pregnancies in the Consortium on Safe Labor Katherine Grantz*, Jessica Gleason, Edwina Yeung, Fasil Tekola-Ayele, Diane Putnick, Yong Ma, Christina Scifres, Zhen Chen,

Recommendations for delivery timing of gestational diabetes mellitus (GDM) complicated pregnancies suggest individualized management yet evidence-based guidelines to guide decision making are lacking. Detailed data on adverse outcomes by delivery week are also limited.

Electronic medical record data (2002-2008, 12 U.S. sites) from 8,524 GDM pregnancies and 159,421 pregnancies without any diabetes delivered at 37 to 40 weeks were used. A fetus at risk model was performed using modified Poisson regression with generalized estimating equations to calculate the adjusted relative risk (RR) of a composite adverse outcome for week of delivery compared to ongoing pregnancies. Composite outcomes were i. delivery (i.e., infections, lacerations, thrombosis); ii. maternal (i.e., death, hypertensive disorders, hemorrhage); iii. primary neonatal (i.e., death, sepsis, seizures, injury); iv. secondary neonatal (i.e., shoulder dystocia, transient tachypnea, hypoglycemia); and v. neonatal respiratory support/morbidity.

GDM pregnancies accounted for 7.7%, 6.5%, 4.9% and 2.8% of births at 37, 38, 39 and 40 weeks, respectively. Compared to expectant management, risk of maternal composite was higher for delivery at 37 weeks, 20.5% vs 11.6%, RR 1.71 (95%CI 1.51-1.92) and 38 weeks, 14.9% vs 9.4%, RR 1.64 (95%CI 1.44-1.86). The difference was driven mostly by hypertensive disorders in pregnancy (and not death or hemorrhage which remained rare <2%.) Risk of primary neonatal composite was higher at 37 weeks, 2.7% vs 1.1%, RR 2.00 (95%CI 1.32-2.97). There were no differences in delivery composite, secondary neonatal composite or neonatal respiratory support/morbidity at any week.

For GDM complicated pregnancies, earlier delivery at 37 and 38 weeks was associated with higher risk of maternal morbidity due to hypertensive disorders, and serious neonatal morbidity only for delivery at 37 weeks. Prospective data is urgently needed to determine optimal delivery timing for GDM-complicated pregnancies.

Fetal body composition and organ growth patterns in pregnancies complicated by first-trimester vaginal bleeding: NICHD Fetal 3D Study Alexandra Jean-Louis*, Jessica Gleason, Kathryn Wagner, Zhen Chen, Dian He, Roger Newman, William Grobman, Robert Gore-Langton, Seth Sherman, Magdalena Sanz Cortes, Edward Chien, Luis Goncalves, Alaina Bever, Jagteshwar Grewal, Katherine Grantz,

Background: In the NICHD Fetal Growth Study, women who self-reported more than one day of vaginal bleeding in the first trimester had lower estimated fetal weight (EFW) by 2-dimensional ultrasound at 35 to 39 weeks, and lower birthweight compared to women without bleeding. We extended these findings to explore associations between bleeding and fetal body composition and organ volumes by 3-dimensional (3D) ultrasound.

Methods: The NICHD Fetal 3D Study (2009-2013) included singleton pregnancies at low risk for fetal growth abnormalities (n=2634). Fetal fat and lean measures of arm, abdomen, and thigh, and organ volumes, including cerebellum, lung, kidney, and liver volumes were measured up to five times between 15-40 weeks using 3D ultrasound. Women were grouped by cumulative days of first trimester bleeding: 0 (reference), 1, or >1 day. Linear mixed models, with quadratic and cubic terms for gestational age, including global tests for overall differences in trajectories and weekly pairwise comparisons, were fit to compare bleeding groups for each 3D volume, adjusted for maternal age, race/ethnicity, and pre-pregnancy BMI.

Results: Most women had no bleeding (n=2144, 81.4%), while 211 (8.0%) bled for 1 day and 279 (10.6%) bled for >1 day. Compared to those with no bleeding (Figure), fetuses of women with >1 day of bleeding had smaller abdominal area (-78.4 mm2 to -293.8 mm2) between 29-40 weeks, and smaller fractional thigh volume (-2.2 cm3 to -4.1 cm3) between 36-40 weeks. Fetuses of women with 1 day of bleeding also had smaller liver volume compared to no bleeding (-3.8 cm3 to -6.1 cm3) between 29-33 weeks, though results were attenuated when adjusting for EFW.

Conclusion: First-trimester bleeding was associated with smaller fetal abdominal area, thigh, and liver growth. Fetal 3D measures may provide additional insight into how early pregnancy bleeding may potentially impact fetal growth and subsequent postnatal health outcomes.

Increasing access to certified nurse-midwives prevents use of medical interventions during labor: an application of g-computation Elizabeth Simmons*, Mollie Wood, Anna Austin, Alyssa Mansfield, Karen Sheffield-Abdullah, Kavita Singh,

Introduction: Prenatal care (PNC) led by a certified nurse-midwife (CNM) may reduce medical interventions and complications during labor and delivery, compared to physician-led care. We estimate the prevalence of cesarean sections, epidurals and labor inductions if we intervened to increase the number of low-risk pregnant people enrolled in PNC with a CNM.

Methods: This study used data from the Pregnancy to Early Life Longitudinal data system, which links 2014-2019 birth certificate and hospital discharge data in Massachusetts. The study population comprised birthing people aged 18-55 with a low-risk pregnancy who initiated PNC with a physician or CNM prior to 13 weeks gestation and had a live birth. The exposure was provider of PNC (CNM vs. physician). The outcomes were cesarean sections, epidurals and labor inductions. We used g-computation to estimate the percent change in the prevalence of outcomes under hypothetical scenarios where 10%, 20% and 50% more people enrolled in PNC with a CNM. Estimates were adjusted for potential confounders (payer, maternal age, education and race-ethnicity) identified using directed acyclic graphs, and 95% confidence intervals (CI) were estimated using bootstrap resampling.

Results: The study population included 124,785 pregnant people. One in ten saw a CNM for PNC. Those who attended PNC with a CNM were slightly younger, had fewer years of education, were less likely to be non-Hispanic, white and more likely to be Medicaid enrollees. A 10% increase in the number who underwent PNC with a CNM would result in 1% (95% CI: 0.01, 0.01) fewer cesarean sections, 2% (95% CI: 0.02, 0.02) fewer epidurals and 2% (95% CI: 0.02, 0.02) fewer labor inductions. The effect estimates were stronger for a 20% and 50% increase.

Conclusions: PNC with a CNM is a clinically-appropriate intervention among those with low-risk pregnancies. A scale-up of the use of CNMs may contribute to a decrease in use of medical interventions during labor and deliver.

Prenatal care and pregnancy outcomes before and during the COVID-19 pandemic: An interrupted time series study Laila Aboulatta*, Kaarina Kowalec, Lisa Lix, Mina Tadrous, Qier Tan, Sherif Eltonsy,

Background

The COVID-19 pandemic had a profound impact on healthcare service, but there is limited population-based evidence on the impact of the pandemic on prenatal care and pregnancy outcomes. Our aim was to investigate the impact of the pandemic on prenatal care visits, mode of delivery, breast feeding initiation(BFI) and Neonatal ICU(NICU) admissions.

Methods

Using Manitoba, Canada administrative health databases, we conducted a retrospective population-based study of live birth pregnancies before(April2008-February2020) or during(March2020-March2022) pandemic; for the latter period, they were defined as partially(March-November2020) or fully(December2020-March2022)exposed. We estimated monthly rates of insufficient prenatal care(<5 visits), c-section, BFI, and NICU. Interrupted time series analyses using season-adjusted generalized linear models were conducted to test immediate and lagged pandemic effects.

Results

Amongst 221,255 pregnancies insufficient prenatal care(4.5% vs. 3.9%) and c-section (28.2% vs. 23%) was higher during than before pandemic. The pandemic was associated with an abrupt increase in insufficient care by 36%(p<0.001) followed by a decline(β=-0.007,p=0.125). An abrupt rise in c-section by 11.7%(p<0.001), and NICU by 17.3%(p=0.77) were observed followed by declines(c-section β=-0.001,p=0.9;NICU β=-0.001,p=0.8). The pandemic was associated with an abrupt decrease in BFI(p=0.002) followed by increase(β=-0.002,p=0.007). There were no differences in insufficient care, c-section, BFI, and NICU among partially exposed pregnancies between two time periods. Among fully exposed pregnancies, there was an increase in BFI and NICU admissions during pandemic.

Conclusions

Our findings suggest that the COVID-19 pandemic was associated with increased rates of insufficient prenatal care and c-sections. Over the 2-year pandemic period, we observed increased NICU admissions and BFI, particularly amongst pregnancies in which full term occurred during pandemic.

Breastfeeding initiation rates and determinants in women with and without epilepsy Laila Aboulatta*, Alexandra Eden, Sherif Eltonsy,

Background
Breastfeeding initiation (BFI) rates in women with epilepsy (WWE) remains low despite evidence supporting breastfeeding initiation irrespective of the disease status. This study aimed to examine the rates and determinants for BFI amongst WWE and women without epilepsy (WWoE) in Manitoba, Canada.
Methods
We conducted a retrospective cohort study using province-wide health databases on pregnant WWE and WWoE from 1995 to 2019. Annual BFI rates for WWE and WWoE were examined. Factors influencing BFI, including maternal and infant characteristics, were assessed. Multivariable logistic regression models were used to quantify relationships between determinants and BFI in both groups.
Results
During the study period, 1,331 pregnant WWE and 357,334 WWoE were examined. On average, among WWE, 70.9% initiated breastfeeding compared to 81.8% among WWoE. We observed a significant increase in yearly trends of BFI in both WWE ($\beta=0.45$, $p=0.008$) and WwoE ($\beta=0.23$, $p<0.001$). In WWE, BFI was associated with caesarean delivery (OR=0.72,95% CI: 0.53-0.97), chronic pain (OR=0.67,95% Cl: 0.46-0.97), lower income (OR=0.34,95% Cl: 0.26-0.44), and gestational age (OR= 1.09,95% CI:1.01-1.18). In WwoE, BFI was associated with chronic pain (OR=0.83,95% Cl: 0.80-0.86), lower income (OR=0.45, 95%CI:0.44-0.46), mood and anxiety disorder (OR=0.84,95% CI:0.81-0.86), and gestational age (OR=1.13,95% Cl:1.12-1.14). The use of any ASM (OR=0.66,95% Cl:0.51-0.85), new generation (OR=0.86,95% Cl: 0.62-1.20), polytherapy (OR=0.46,95% Cl: 0.31-0.69) and gabapentin (OR=0.49,95% Cl: 0.17-1.24) reduced the likelihood of BFI among WWE.
Conclusion
BFI was approximately 10% lower in WWE compared to WWoE. Determinants such as low income, ASM use, and comorbidities were significant contributors to a reduced BFI in both groups. Further research is needed to investigate breastfeeding continuation in WWE.

Associations Between Experiences of Discrimination, Socioeconomic and Racial Polarization, and Birth Outcomes in the Atlanta African American Maternal Child Cohort

Jasmin Eatman*, Kaegan Ortlund, Anne Dunlop, Dana Barr, Cherie Hill, Patricia Brennan, Peter Barry Ryan, Donghai Liang, Elizabeth Corwin, Kaitlin Taibl, Youran Tan, Stephanie Eick,

BACKGROUND AND AIM: To investigate associations between self-reported experiences of racism, measures of racialized economic segregation at the census tract level (a proxy for structural racism), and birth outcomes among pregnant African American people.

METHOD: Participants addresses were geocoded to calculate The Index of Concentration at the Extremes (ICE) score for the census tract of residence during pregnancy. Experiences of racial and gender discrimination were measured during pregnancy using self-reported, validated questionnaires. Linear regression was used to estimate associations between self-reported experiences of discrimination and ICE scores with gestational age (in weeks) at delivery and birthweight for gestational age z-scores.

RESULTS: Participants living in areas of higher racialized economic privilege (as defined by ICEincome and ICErace-income) reported more frequent experiences of discrimination. An increase in frequency of self-reported experiences of discrimination was associated with reduced gestational age at delivery (β= -0.08, 95% confidence interval [CI] = -0.13, -0.03) but not with birthweight for gestational age. ICE scores were not associated with either birth outcome.

CONCLUSIONS: In this metro Atlanta cohort, self-reported experiences of racial discrimination, but not objective measures of racialized economic segregation, were associated with reduced gestational age among African American pregnant people.

Pre-conception health and ambient air pollution associated with preterm birth and low-birth weight among US singletons. Yohane Vincent Abero Phiri*, Timothy Canty, Carrie Nobles, Allison Ring, Jing Nie, Pauline Mendola,

Background and Aim:

Addressing pre-conception risk factors for neonatal health outcomes poses a challenge, as nearly half of pregnancies in the U.S. are unintended. We examined pre-conception health factors and ambient air pollution in association with preterm and low birthweight among all singleton births in the U.S. in 2018.

Methods:

We examined 2018 U.S. birth certificate data (n=3,564,682 infants) linked with county-level estimates of particulate matter ≤2.5µm (PM2.5) using MISR, MODIS, and SeaWiFS instruments. Maternal pre-conception risk factors and PM2.5 were assessed in relation to singleton preterm birth and low birth weight using logistic regression with generalized estimating equations, adjusting for parental sociodemographics and infant sex.

Results:

Preterm and low birthweight rates were 10% and 6.5%, respectively. Pre-conception risks such as diabetes, hypertension, previous cesarean, preterm birth, infertility treatment, and body mass index increased the odds of preterm birth. Diabetes (adjusted odds ratio (aOR)=2.30, 95% CI [2.23-2.37]) and hypertension (aOR=2.05, 95% CI [2.00-2.09]) before conception more than doubled the risk, while prior preterm delivery (aOR=3.04, 95% CI [2.99-3.09]) tripled it. Risk for low birthweight also increased with prior preterm delivery, hypertension, and diabetes. However, maternal body mass index (BMI) (aOR=0.987, 95% CI [0.986-0.989]) and the number of previous cesarean births (aOR=0.930, 95% CI [0.920-0.940]) reduced odds of low birthweight. Additionally, exposure to PM2.5 before and within the month of birth, especially in the spring and summer, was associated with both preterm and low birthweight.

Conclusion:

Pre-conception risk factors and air pollution were associated with preterm and low birth weight among U.S. singletons. The magnitude of these associations suggests that pre-conception health merits more attention to prevent poor pregnancy outcomes.

Keywords: Pre-pregnancy health; air pollution; infant health; unintended conception

Exposure to racial discrimination is associated with preterm birth (PTB) <35 weeks' but is not mitigated by individual-level coping responses Sarah Heerboth*, Ebony Carter, Nadia Charguia, Rebecca Fry, Tracy Manuck,

Intro: Racial discrimination is consistently implicated in PTB related racial disparities. We sought to quantify which types of discrimination are most strongly associated with PTB and evaluate if an individual's response to discrimination may mitigate PTB risk.

Methods: Primary analysis of a prospective cohort enriched for those at high a priori risk of PTB. Participants identifying as Black, White, and/or Hispanic, with singleton, non-anomalous gestations were recruited <22 weeks, 2017-2022, and completed the Krieger Scale, which evaluates 9 domains (e.g., school, work) and 7 responses (e.g., working harder, praying) to discrimination. The primary outcome was PTB <35 weeks. Secondary outcomes included PTB <32 and <37 weeks and delivery gestational age.

Results: 435 individuals (43% Black, 38% White, 19% Hispanic) were included; 108 (25%) delivered <37, 58 (13%) <35, and 31 (7%) <32 weeks. Surveys were completed at a mean of 17.1 (IQR 16.0-19.7) weeks. Discrimination in ≥1 domain was more common among those with PTB <37 (48% vs. 35%, p=0.02) and <35 (56% vs. 36%, p=0.003) but not <32 weeks (50% vs. 38%, p=0.18). The 163 individuals reporting any discrimination delivered ~1 week earlier on average (36.9 vs. 37.7 weeks, p=0.019). Those with PTB <35 weeks reported more discrimination in job opportunities (21% vs. 10%, p=0.018), at work (26% vs. 16%, p=0.05), and in public (33% vs. 15%, p=0.001) vs. those delivering ≥ 35 weeks. In regression models, discrimination in ≥1 domain was associated with PTB <35 weeks (aOR 2.22, 95% CI 1.19-4.13). None of the evaluated coping responses were associated with lower odds of PTB or mitigated the adverse effects of discrimination on PTB <35 weeks in regression models.

Conclusion: Racial discrimination is associated with an increased risk of PTB <35 weeks; effects are not reduced by individual-level coping responses, providing further evidence that broader systematic change is needed to reduce the negative effects of discrimination.

Associations between the domains of maternal physical activity during pregnancy and neonatal anthropometry Kathryn Wagner*, Jessica Gleason, Zhen Chen, Stefanie Hinkle, Cuilin Zhang, William Grobman, Daniel Skupski, Roger Newman, Jagteshwar Grewal, Katherine Grantz,

Prior literature on the associations between pregnancy physical activity (PA) and neonatal outcomes has focused on the relationship between total or exercise PA and birthweight. However, the domains of PA may be important. Neonatal anthropometry, including fat measures, may provide greater insight beyond birthweight.

In the NICHD Fetal Growth Study – Singletons, neonatal anthropometry (birthweight (BW); birth length (BL); circumferences – head (HC), mid-upper arm (MUAC), abdominal (AC), and mid-upper thigh (MUTC); and skinfold thicknesses – subscapular (SSF), tricep (TSF), abdominal (ASF), and anterior thigh (ATSF)) were assessed via neonatal visit (mean=1.8 days) or medical record abstraction (n=1502). First trimester PA domains, including household, occupational, transportation, and exercise were categorized into tertiles. Generalized linear models evaluated the associations, adjusting for covariates including caloric intake.

Household PA in the 3rd tertile (>159 MET-min/wk) was associated with smaller AC (-0.34 cm; 95% CI: -0.67, -0.01), TSF (-0.29 mm; -0.52, -0.06), and ATSF (-0.36 mm; -0.67, -0.04), compared to the 1st tertile (<84 MET-min/wk). Occupational PA in the 2nd (56-104 MET-min/wk) but not 3rd tertile was associated with increases in BL (0.40 cm; 95% CI: 0.08, 0.71), BW (98.30 g; 37.18, 159.43), HC (0.35 cm; 0.15, 0.56), MUAC (0.20 cm; 0.03, 0.37), and AC (0.60 cm; 0.31, 0.90), compared to the 1st tertile. Occupational PA in the 3rd tertile was associated with larger SSF (0.19 mm; 95% CI: 0.01, 0.37), compared to the 1st tertile. In contrast, transportation PA in the 2nd tertile (20-36 MET-min/wk) was associated with smaller SSF (-0.18 mm; 95% CI: -0.35, -0.004), compared to the 1st tertile. There were no differences in neonatal anthropometry across exercise PA tertiles.

Neonatal anthropometry varied by first trimester household, occupational, and transportation PA domains, indicating the importance of assessing different activity exposures.

Third Trimester Continuous Glucose Profiles in Gestational Diabetes and Impaired Glucose Tolerance: Implications for Birthweight and Gestational Weight Gain Tenzin Sangmo*, Arsala Khan, Esra Mucahit, Vanessa Martinez, Dhairya Upadhyay, Souptik Barua, Shauna Williams, Todd Rosen, Shristi Rawal, Shristi Rawal

This study aimed to i) characterize 3rd trimester continuous glucose monitoring (CGM) profiles among pregnant women with gestational diabetes mellitus (GDM) and impaired glucose tolerance (IGT) and ii) examine their associations with gestational weight gain (GWG) and birth weight (BW). Nineteen pregnant women (14 GDM, 5 IGT) were enrolled between 24-32 gestational weeks (GW) and asked to wear a FreeStyle Libre CGM sensor for up to 52 days (14 days across 3 visits). GWG and BW were abstracted from medical records. On average, CGM measurements spanned 33.4 ± 12.3 days across pregnancy. Key CGM metrics including 24-hr, daytime, nighttime and fasting glucose were higher among women with GDM and IGT compared to published normative values in healthy singleton pregnancies, although differences were significant only for women with GDM (all p-values <0.05). Several of the CGM metrics were positively correlated with BW; in linear regression models, adjusted for age and pre-pregnancy BMI, significant associations were observed for mean glycemic variability [β= 81.7 (95% CI)= 37.9, 125] and mean 24-hour glucose [β=16.7 (95%CI)=3.65, 29] across all 3 visits, and mean 24-hr glucose [β=14.4 (95%CI)=3.09, 25.6] and mean daytime glucose [β=0.45 (95%CI)=0.01, 0.90] during visit 1 (mean GW=29.6 ± 3.89). With respect to GWG, there was a significant and positive correlation for mean 24-hr [β=0.49 (95%CI)= 0.02, 0.97] and mean daytime glucose [β=0.45 (95%CI)=0.01, 0.90] during visit 1. As expected, this study found that CGM metrics were higher among women with GDM compared to normal singleton pregnancies, several of which were positively associated with BW and GWG. Findings were more prominent for the early third trimester, which could be attributed to the waning sample sizes in the latter 2 visits in the 3rd trimester. Large scale studies are needed to validate these findings and establish the clinical utility of CGM metrics in predicting adverse perinatal outcomes.

Term Cesarean Section and future Preterm Birth: Findings from a Low-risk Population

Anders Einum*, Quaker Harmon, Roy Miodini Nilsen, Linn Marie Sørbye, Nils-Halvdan Morken,

Background

The association between Cesarean Section (CS) and a future spontaneous and iatrogenic preterm birth (PTB) has been inconsistent. Accurate knowledge of the risks associated with CS in a first pregnancy informs clinicians and patients for subsequent pregnancies, particularly in cases where the initial clinical indication is poor and the potential for prevention is greatest.

Methods

We investigated 298,901 singleton sibling pairs in the population-based Medical Birth Registry of Norway from 1999-2020. Women were analyzed in groups of emergency and planned CS with vaginal births as the reference category in a first pregnancy term birth. The main outcome was second pregnancy PTB stratified by labor onset (iatrogenic and spontaneous) and by placental complications in both pregnancies. We used multivariable regression models including maternal and sociodemographic factors to estimate adjusted relative risks (aRR) with 95% confidence intervals (CI).

Results

1 214 women (0.4%) had a CS term delivery in their first pregnancy followed by PTB in their second pregnancy. Compared to vaginal delivery, the risk of iatrogenic PTB was higher in women with prior emergency CS (aRR 1.64, 95% CI 1.48, 1.81) and planned CS (aRR 2.55, 95% CI 2.05, 3.17). Spontaneous PTB was not associated with prior delivery mode. Among those with placental complications in both pregnancies, the risk of future spontaneous and iatrogenic PTB was 2.5-fold and 11-fold respectively compared to those with no placental complications in either pregnancy. Stratification by placental complications did not alter the associations between delivery mode and PTB.

Conclusions

Compared to vaginal delivery, CS in a first pregnancy increases the risk of iatrogenic, but not spontaneous, PTB in a second pregnancy. Although strongly associated with PTB, placental disease had limited influence on the estimates. These findings indicate that complications related to CS cause future clinical intervention in the preterm period.

Maternal Exposure to Endocrine-Disrupting Chemicals and 1- and 2-Year Postpartum Blood Pressure and Arterial Stiffness: Insights from the NYU CHES Study Rui Ling*, Eunsil Seok, Mengling Liu, Shilpi S. Mehta-Lee, Yu Chen, Anais Hausvater, Elaine Urbina, Leonardo Trasande, Linda G. Kahn,

Background: Phthalates and bisphenol are ubiquitous endocrine-disrupting chemicals that have been associated with adverse cardiovascular outcomes across the life course and including hypertensive disorders of pregnancy.

Methods: Our analysis included 679 adult mothers from the New York University Children's Health and Environment Study, a perspective birth cohort. Concentrations of 8 bisphenols and 22 phthalate metabolites were quantified in spot urine samples collected during each trimester of pregnancy. Outcomes included brachial artery distensibility (BrachD) and pulse wave velocity (PWV), mean arterial pressure (MAP), systolic blood pressure, and diastolic blood pressure (DBP) assessed at year 1 (<24 months) and year 2 (24–35 months) postpartum. Simple and covariate-adjusted linear regression models were used to examine associations of groupings of bisphenols and phthalate metabolites, averaged across pregnancy and log2-transformed, with the five specified outcomes of interest.

Results: After adjusting for covariates, we observed that bisphenols were positively associated with BrachD (β = 0.14; 95% CI: 0.00, 0.27) in year 2 and negatively associated with PWV (β = -0.11; 95% CI: -0.24, 0.01) in year 1 and MAP (β = -0.84; 95% CI: -1.61, -0.06) in year 2. Also, di(2-ethylhexyl) phthalate metabolites were positively associated with BrachD (β = 0.14; 95% CI: 0, 0.28) in year 1, and low molecular weight phthalate metabolites were negatively associated with MAP (β = -0.71; 95% CI: -1.27, -0.15) and DBP (β = -0.59; 95% CI: -1.08, -0.10) in year 2.

Conclusions: Results suggest that bisphenols and phthalates may be associated with reduced arterial stiffness and blood pressure 1-2 years postpartum. While inconsistent with prior studies, our findings may reflect the estrogenic and anti-androgenic properties of these classes of chemicals, emphasizing the need to examine the biological mechanisms linking these chemicals with cardiovascular outcomes in the postpartum period.

Associations Between Prenatal Hemoglobin Concentration, Birth Weight, and Gestational Age at Birth: A Systematic Review and Meta-Analysis using Burden-of-Proof Analysis

Dong Keun Rhee*, Ni Gusti Ayu Nanditha, Corey Teply, Heather Taylor, Heidi Tandiono, Taylor Noyes, Eunice Chung, Ihunanaya Okorie, Nandita Perumal, Nicholas Kassebaum,

Background: Previous meta-analyses evaluating the relationship between anemia and adverse birth outcomes define anemia as hemoglobin (Hb) level below a single threshold value, but do not assess the dose-response relationships between maternal Hb level, birth weight (BW), and gestational age (GA) at birth.

Methods: We systematically searched seven databases for peer-reviewed literature published during 1980-2022 in any language for studies evaluating the relationship between Hb level or anemia during pregnancy and BW and GA at birth (PROSPERO #CRD42022368239). We followed Burden-of-Proof methodology and used its novel Bayesian meta-regression tool, which relaxes the conventional assumptions of log-linearity and incorporates between-study heterogeneity, to estimate the mean risk function of the associations between maternal Hb and each of BW and GA.

Results: Of the 16,011 studies retrieved, 190 from 57 countries were eligible for inclusion. The data primarily reflected categorical low birth weight (LBW; <2500 grams BW) and preterm birth (PTB; <37 weeks GA at birth). The risk of LBW and PTB approached the null as maternal Hb level increased to 120g/L in a dose-response fashion. Relative to Hb of 120g/L, on average, Hb levels between 100-110g/L, 70-100g/L, and <70g/L were associated with an increased risk of LBW (Relative risk [RR] 1.14 [95% Uncertainty interval [UI]: 1.07-1.22], 1.62 [1.27-2.06], and 3.30 [1.80-6.05], respectively) and PTB (RR 1.10 [95% UI: 1.03-1.17], 1.42 [1.12-1.80], and 2.00 [1.25-3.20], respectively). Accordingly, 2.4%, 7.6%, and 2.7% of global LBW cases in 2021 and 1.7%, 5.2%, and 1.2% of PTB cases may be attributable to lower maternal Hb levels of 100-110g/L, 70-100g/L, and <70g/L, respectively.

Conclusions: There are negative dose-response relationships between maternal Hb during pregnancy and the risks of LBW and PTB. Further research is needed to understand these associations by anemia etiology and trimester-specific Hb measurement.

Preterm Birth and Maternal Telomere Length in Black Women Robin Page*, Brandi Taylor, Gang Han, Gabe Neal, Oluwadamilola Olowomeye, Kate Wall, Weiyi Huang, Kelli Kochan,

Purpose: We examined the relationship between preterm birth (PTB) and maternal telomere length.

Background: The US has the highest rate of PTB among developed nations. PTB in the US accounts for nearly 70% of deaths in the first year of life. Little is known about maternal telomere length and its association with PTB.

Methods: We recruited 82 Black women from 2 prenatal clinics in Texas to participate in the study. Due to missing data, our final sample size was 60. Women were enrolled in the study during the 2nd or 3rd trimester of pregnancy, prior to 37 weeks. Whole blood samples were obtained at the time of enrollment and buffy coat was collected prior to storage in a -80 Celsius freezer. After DNA extraction, T/S ratios were calculated using a quantitative PCR method. Number of weeks gestation at delivery were determined by research staff accessing patient delivery reports in the electronic health record. Preterm birth was considered delivery prior to 37 weeks gestation.

Results (Preliminary): The women who had preterm birth had significantly lower telomere length than those who had full-term births. The p-value was significant (p=0.01) in a logistic regression (PTB as outcome) and in a two group comparison (telomere length as outcome). The Cohen's D is 0.863, which is substantial.

Further analyses will account for other factors including survey measures of perceived stress and discrimination. We will also conduct a cross-ethnic comparison with data collected from a prior pilot study with a sample of 100 Mexican-origin women in Texas.

Policy Implications: Policies to expand access to healthcare services during pregnancy to high-risk women exposed to stress, including social determinants of health, should be implemented to address maternal and newborn wellbeing.

Counseling Women of Reproductive Age about Emergency Preparedness, Changes in Provider Attitudes – Fall DocStyles Survey, United States, 2021-2023 Jerome Leonard*, Romeo Galang, Rebecca Hall, Carrie Shapiro-Mendoza, Jessica Meeker,

Natural disasters and severe weather emergencies are increasing in frequency and severity. Women of reproductive age – including pregnant, postpartum, and lactating populations – face unique challenges during disasters that may be mitigated by emergency preparedness. A survey of healthcare provider attitudes and practices related to counseling women of reproductive age on emergency preparedness was administered in 2021 and 2023. Our analysis assesses changes in reported provider attitudes and practices comparing 2021 to 2023. Data were collected through Porter Novelli DocStyles, a web-based opt-in panel survey of healthcare providers in the United States. We calculated frequencies and confidence intervals (CI) of provider responses using R 4.3.0, and differences were assessed based on CI review. There were 1,503 respondents in the 2023 sample, including family practitioners (35%), internists (31%), obstetrician/gynecologists (Ob/Gyns) (17%), physician assistants (8%), and nurse practitioners (8%). Compared to the 2021 sample (n=1,503), a higher percentage of providers in the 2023 sample report emergency preparedness plans as very important from 51% (95% CI: 48%, 53%) to 56% (95% CI: 53%, 58%), counseling patients on emergency preparedness as very important from 31% (95% CI: 29%, 33%) to 42% (95% CI: 40%, 45%) and having counseled patients on emergency preparedness plans from 30% (95% CI: 27%, 32%) to 37% (95% CI: (34%, 39%). Compared to the 2021 sample, 2023 providers overall reported feeling similar levels of confidence in counseling patients on emergency preparedness plans from 53% (95% CI: 51%, 56%) to 51% (95% CI: 49%, 54%). However, Ob/Gyns reported a decrease in confidence from 70% in 2021 (95% CI: 64%, 75%) to 52% in 2023 (95% CI: 46%, 59%). These findings underscore the need for healthcare provider resources to support emergency preparedness counseling for this population.

The Impact of Marriage on Breastfeeding Duration: Examining the Disproportionate Effect of COVID-19 Pandemic on Low-Income Communities Anna Charlotta Kihlstrom*, Tara Stiller, NIshat Sultana, Grace Njau, Matthew Schmidt, Anastasia Stepanov, Andrew Williams,

Background. Marriage promotes breastfeeding duration through economic and social supports. The COVID-19 pandemic disproportionately affected low-income communities and impacted women's employment and interpersonal dynamics. This study explored the association between marital status and breastfeeding duration and the potential modifying effect of income in the context of the COVID-19 pandemic.

Methods. Data were from the 2017-2021 North Dakota Pregnancy Risk Assessment Monitoring System(weighted n=41433). Breastfeeding duration was self-reported, and 2-, 4-, and 6-month duration variables were calculated. Marital status(married, unmarried) was drawn from linked birth certificates . Income(≤$48,000, >$48,000) was self-reported. Infant birth date was used to identify pre-COVID(2017-2019) and COVID(2020-2021) births. Logistic regression estimated odds ratios and 95% confidence intervals for the association between marital status and breastfeeding duration outcomes. Models were fit overall, by COVID era and by income. Lastly, income models were further stratified by COVID era. Models were adjusted for maternal health and sociodemographic factors.

Results. Overall, married women consistently had 2-fold higher odds of breastfeeding across all durations during both pre-COVID and COVID eras. Pre-COVID, marriage was associated with at least 2-fold higher odds for all breastfeeding durations in low-income women (2-month duration OR2.73,95%CI1.64,4.52) and less so for high-income women (2-month duration OR1.63,95%CI0.93,2.86). During COVID, being married was a stronger predictor of breastfeeding duration for high-income women (2-month duration OR2.70,95% CI1.32,5.53) than low-income women (2-month duration OR2.28,95% CI1.04,4.98).

Conclusion. Marriage promotes breastfeeding duration, yet the benefit of marriage was reduced for low-income women during the COVID-19 pandemic. Health-promoting supports for low-income families are needing during public health crises like a pandemic.

A longitudinal cohort study examining urban-rural residence and factors associated with maltreatment allegations Abigail Newby-Kew*, Jared Parrish, Jodi Lapidus, Suzanne Zane, Lynn Marshall, Suzanne Zane

Background: Knowledge about child maltreatment and the complex array of factors that contribute to its occurrence is based mainly on the experiences of urban populations. We aimed to identify population-specific factors in the pre-birth period that are associated with child protective services (CPS) allegations in urban and rural populations.

Participants and Setting: Data were from the Oregon Longitudinal Child Abuse and Neglect Linkage project, a population-representative data source linking Oregon Pregnancy Risk Assessment Monitoring System (PRAMS) data for children born 2009–2011 with 2009–2018 CPS data.

Methods: We examined association between pre-birth factors reported in PRAMS and time to first CPS allegation using Cox proportional hazards regression (HR) and built unique multivariable models for children born to respondents who resided in rural or urban areas at time of delivery. Maternal demographics, stressors, social supports, pregnancy intendedness, morbidity, and smoking were included in the final models.

Results: Children in rural areas (n=1076) were 1.18 times as likely to experience a maltreatment allegation before age seven years relative to urban areas (n=4106). (29.5% [weighted] vs. 24.7% [weighted] respectively). For both populations, there were several characteristics similar in the final model and the strongest associations with maltreatment allegations were an income ≤ 100% of the federal poverty level (urban HR=1.97, 95%CI 1.58, 2.45; rural HR=2.31, 95%CI 1.62, 3.31) and maternal smoking (urban HR=2.18, 95%CI 1.72, 2.76; rural HR=2.68, 95%CI 1.88, 3.81).

Conclusion: While rates of maltreatment allegations were higher in rural compared to urban areas in Oregon, pre-birth factors associated with maltreatment allegations were similar in both areas. Communities can implement evidenced based child maltreatment screening and prevention strategies focused on similar pre-birth factors for both urban and rural residents.

Substance Use

Trajectories of Prescription Opioids Exposure in Pregnancy and Risk of Adverse Birth Outcomes Yi Wang*, Deborah Ehrenthal, Liwei Zhang,

Background: The dynamic interplay of duration, timing, and type of exposure to prescription opioids throughout pregnancy, may influence birth outcomes yet remains unexplored.

Method: Using repeated measures latent class analysis, we identified prenatal prescription opioids exposure trajectories —including medication for opioid use disorder (MOUD) and other pain management prescriptions (non-MOUD)—among Wisconsin Medicaid-insured singleton live births (2011-2019). We estimated neonatal birth outcomes associated with these distinct exposure trajectories, including neonatal opioid withdrawal syndrome (NOWS), small for gestational age (SGA), preterm birth, birth weight, and gestational age using logistic regressions.

Results: Five trajectory classes were identified: 1) stable MOUD treatment, 2) less consistent MOUD treatment, 3) chronic non-MOUD use, 4) intermittent non-MOUD use, and 5) low level use of MOUD and non-MOUD. Absolute NOWS incidence per 1,000 infant was 667 for class 1 (aOR: 21.19, 95% CI 17.45, 25.72), 570 for class 2 (aOR 15.37, 95% CI 12.53, 18.84), 235 for class 3 (aOR 19.79, 95% CI 16.24, 24.11), 67 for class 4 (aOR 6.35, 95% CI 5.11, 7.90), and 12 for class 5 (aOR 1.73, 95% CI 1.48, 2.03). Additionally, classes 1-4 had elevated risk of SGA, preterm birth, lower birth weight, and shorter gestational age, with no significant differences noted among these classes. An in-depth look at infants born to mothers with opioid use disorder revealed that those in the stable MOUD treatment had higher NOWS risk but higher birth weights and longer gestational age compared to those with less consistent MOUD treatment.

Conclusion: Longitudinal trajectory models elucidated the heterogeneity of opioids exposure and were informative in assessing associated risk.

Urban-Rural Differences in Maternal Interpersonal Violence Screening Before and During the COVID-19 Pandemic in North Dakota Andrew Williams*, RaeAnn Anderson, Shawnda Schroeder, Grace Njau, Tara Stiller, Nishat Sultana, Anna Charlotta Kihlstrom, Alexandra Schmidt,

Interpersonal violence rose during the COVID pandemic. As violence is a driver of maternal mortality, prenatal and postpartum screening for abuse is key. To develop evidence-based practices to reduce violence-related maternal mortality, we first aim to identify population trends. We examined urban-rural differences in prenatal and postpartum screening for abuse, and the potential modifying role of the COVID pandemic.

Data were drawn from the 2017-2021 North Dakota(ND) Pregnancy Risk Assessment Monitoring System(weighted n=39744). Metropolitan Statistical Areas(MSA) counties were 'urban' and other counties were 'rural.' 'Pre-COVID' pregnancies ended prior to March 2020 and 'COVID' pregnancies ended during or after March 2020. Mothers self-reported(yes/no) if they were asked about emotional or physical abuse by a healthcare worker prenatally or postpartum. Logistic regression estimated odds ratios and 95% confidence intervals for the association between rurality and abuse screening, overall and by COVID era. Models were adjusted for maternal demographic and health factors.

For both prenatal and postpartum screening, 5% more rural women reported being screened for IPV than urban women(p<.05). Compared to pre-COVID, screening for abuse prenatally fell 3%(p=.11) and postpartum fell 6%(p<.05) during COVID. Regression results suggest there was no statistically significant difference in odds of abuse screening by rurality pre-COVID. However, during COVID, rural women had approximately 60% higher odds of being screened for abuse prenatally(OR:1.58,95%CI:0.94,2.66) and postpartum(OR:1.58,95%CI:1.04,2.41). Trend analyses suggest a greater decline in screening during COVID among urban than rural women(p<.01).

Prenatal and postpartum abuse screening declined during COVID in ND, yet the decline was greater among urban women than rural women. Screenings that declined during the COVID pandemic should be addressed with evidence-based solutions, tailored to populations affected.

Non-emergency department outpatient healthcare utilization in the first 24 months' postpartum by rurality and pregnancy complications: a prospective cohort study from Maine Sydney Bebus*, Kristin Palmsten, Heather Lipkind, Christina Ackerman-Banks, Katherine Ahrens,

Objective: To estimate the rate of non-emergency department (ED) outpatient healthcare use among postpartum people by rurality of residence and pregnancy complications.

Methods: We used Maine Health Data Organization's All Payer Claims Data for women who delivered during 2007-2019 (N=121,905). We estimated rates of non-ED outpatient healthcare utilization during the first 24 months' postpartum by level of rurality (urban, large rural, small rural and isolated rural) and by pregnancy complications (prenatal depression, hypertensive disorders of pregnancy and gestational diabetes). We used an existing definition of non-ED outpatient visits based on bill type, place of service, and procedure codes. To estimate rate ratios (RR), we used Poisson regression with an offset for population at risk, adjusting for potential confounders and restricting the analysis to persons with continuous health insurance for the first 24 months postpartum.

Results: We found that 96% of persons had evidence of at least one non-ED outpatient visit in the first 24 months' postpartum. The mean monthly rate per 100 deliveries of non-ED visits was 86.1 among persons with continuous health insurance for the first 24 months postpartum (n=70,431). Persons living in rural areas had lower monthly rates of non-ED visits than persons living in urban areas (adjusted RR ranged from 0.87 [95% CI: 1.05, 1.10] in isolated rural areas to 0.91 [95% CI: 1.05, 1.10] in large rural areas). Persons with prenatal depression (aRR=2.07; 95% CI: 2.04, 2.11), hypertensive disorders of pregnancy (aRR=1.07; 95% CI: 1.05, 1.10), and gestational diabetes (aRR=1.11; 95% CI: 1.08, 1.14) had higher non-ED outpatient utilization than those without these conditions.

Conclusion: New practices and policies may be needed to improve outpatient healthcare access and utilization in rural areas. Persons with pregnancy conditions are accessing outpatient healthcare at higher rates, which may reduce the need for acute healthcare use.

Women's health

Endometriosis subtypes and risk of type 2 diabetes: ARCHES (Advancing Research on Cardiovascular Health and Endometriosis Study) retrospective cohort study Maggie Fuzak*, Maggie Fuzak, Bin Yan, Karen Schliep, Leslie V Farland, Michael Varner, Jing Wang, Jenna Krall, Hediyeh Baradaran, Anna Pollack,

Endometriosis is a chronic inflammatory condition affecting 11% of American women, characterized by endometrial-like tissue growth outside of the uterus. Chronic inflammation is a key feature of type 2 diabetes (T2D) that can disrupt glucose uptake and sensitivity to insulin. Despite the shared inflammatory states, prior studies have found inconsistent relationships between endometriosis and T2D. A population-based cohort study was designed using the Utah Population Database (UPDB) with women from 1992-2020 (N=470,974). We matched women with endometriosis to those without (1:5) by birth year (± 3 years) and birthplace (Utah/not Utah). Controls had to have follow-up in Utah at least as long as date of index endometriosis for matching cases. Endometriosis cases were extracted from electronic health records and characterized by subtypes [superficial peritoneal (SE), deep infiltrating and/or ovarian (DE and/or OE), and other site (including scar, abdomen, lung, bladder) (OS)]. A retrospective analysis was conducted using multivariable Cox proportional hazard models with adjusted hazard ratios (aHR) and 95% confidence intervals (CIs) for T2D (ICD 9: 250.x0, ICD 10: 250.x2 E11) comparing women with (n=80,960) and without endometriosis (n=390,014) and by endometriosis subtypes (SE n=39,995, OS n=19,079, DE and/or OE n=21,906). Overall, women with endometriosis had a greater risk of T2D after adjusting for body mass index (BMI), infertility, smoking, ethnicity, and race (aHR=1.40[1.35;1.45]) compared to women without endometriosis. When investigating subtypes, there was an elevated risk of T2D for all subtypes: SE (aHR=1.47[1.40;1.53]), DE and/or OE (aHR=1.29[1.20;1.39]) and OS (aHR=1.34[1.24;1.45]). These results emphasize the importance of understanding the relationship between chronic inflammatory conditions like endometriosis and metabolic disorders like T2D.

Physical activity trajectories from prepregnancy, throughout pregnancy, and postpartum

Natalie Rosenquist*, Botao Zhou, Janne Boone-Heinonen, Kimberly Vesco, Deborah Young,

Background: Physical activity (PA) is essential for a healthy lifestyle and current recommendations encourage women to maintain PA habits from preconception throughout pregnancy and postpartum. Few studies have investigated changes in PA throughout these time periods in the same analysis.

Objective: The objective of this study was to describe the patterns of PA changes from prepregnancy to postpartum, including each trimester of pregnancy, using trajectory modeling.

Methods: PA (minutes/week) was repeatedly measured in woman's electronic medical records in an integrated healthcare system. We defined five time periods: prepregnancy (up to 2 years before pregnancy onset date [POD]), 1st trimester (from POD to 90 days after), 2nd trimester (91 days after POD to 180 days), 3rd trimester (181 days after POD to delivery), and postpartum (from 91 days after delivery to 1 year). We used the median PA in each period to model trajectories using PROC TRAJ in SAS, controlling for race/ethnicity and age.

Results: A total of 141,472 women were included. Three distinct PA trajectories were identified: high PA (4.8%), moderate PA (62.6%), and low PA (32.6%). The high PA trajectory exhibited an average of 290 PA minutes in prepregnancy, followed by decreasing PA throughout pregnancy reaching 200 minutes in the 3rd trimester, then rebound to 250 minutes in postpartum. The moderate PA trajectory decreased from prepregnancy (110 minutes) to 1st trimester (80 minutes) then remained relatively flat (between 80-90 minutes) through postpartum. The low PA trajectory also decreased from prepregnancy (30 minutes) to 1st trimester (15 minutes), then increased slightly to 20 minutes in the 3rd trimester and postpartum.

Conclusions: Women with higher activity levels tend to decrease PA during pregnancy, but rebound during postpartum, nearly reaching prepregnancy levels. Women with low-moderate activity levels tend to maintain these activity levels throughout pregnancy and postpartum.